Safe motherhood: Severe acute maternal morbidity in the Netherlands

The LEMMoN study

Joost Zwart

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Dus moeten we dansen en moeten we vrijen
Moeten we lachen en drinken vol vuur
God verbood wat we allemaal deden
Leef toch je leven als je allerlaatste uur

(Uit: Niemand weet hoe laat het is, Youp van 't Hek)

Aan: Maaike, Hidde, Tijl en …

Contents

Abbreviations

AFE	amniotic fluid embolism
ARDS	adult respiratory distress syndrome
BMI	body mass index
BTL	blood transfusion laboratory
CBS	[Centraal Bureau voor de Statistiek], Statistics Netherlands
CI	confidence interval
CS	caesarean section
CTG	cardiotocography
FFP	free frozen plasma
HELLP	haemolysis, elevated liver enzymes, low platelets syndrome
ICSI	intracytoplasmatic sperm injection
ICU	intensive care unit
IVF	in vitro fertilisation
LEMMoN	[Landelijke studie naar Etnische determinanten van Maternale Morbiditeit in Nederland], Nationwide study into ethnic determinants of severe maternal morbidity in the Netherlands
LVR	[Landelijke Verloskunde Registratie], Dutch perinatal database
MOH	major obstetric haemorrhage
NSCOG	[Nationaal Signaleringscentrum Obstetrie en Gynaecologie], National Signalling Centre for Obstetrics and Gynaecology
NVOG	[Nederlandse Vereniging voor Obstetrie en Gynaecologie], Dutch society of Obstetrics and Gynaecology
OR	odds ratio
PRN	[Perinatale Registratie Nederland], The Netherlands Perinatal Registry
RBC	red blood cells
RR	relative risk
SAMM	severe acute maternal morbidity
VBAC	vaginal birth after caesarean section
WHO	World Health Organization

CHAPTER 1

General Introduction

Pregnancy and delivery are major life events. In high income countries, they are generally referred to as joyful events, the start of a new life being central. That pregnancy and delivery can adversely affect the mother's health is generally not the first concern. Sometimes, however, pregnancy and childbirth are severely disturbed, posing the mother's life at danger.

Severe acute maternal morbidity (SAMM) becomes more and more accepted as an important indicator of reproductive health in high income countries, in addition to existing maternal mortality statistics.[1-23] Ever since 1880, maternal mortality is registered in the Netherlands by Statistics Netherlands (CBS). Since 1983, it is more accurately registered by the Maternal Mortality Committee of the Dutch Society of Obstetrics and Gynaecology, including individual assessment of substandard care in each case.[24] The World Health Organisation facilitates international comparison of national maternal mortality ratios to assess the quality of reproductive and public health care worldwide.[25] However, since maternal mortality in high income countries has become extremely low, there is a growing interest to also include SAMM in the quality assessment process. It takes years to collect sufficient data to draw valid conclusions about trends in maternal mortality. Moreover, maternal deaths are not representative of the major problems encountered in daily obstetric practice. For instance, major obstetric haemorrhage seldom leads to maternal death nowadays, whereas it is a major cause of SAMM.[26;27] And finally, although analysing cases of maternal death is of vital importance, further reduction of maternal mortality will not likely have large effects on the quality of obstetric care anymore. In contrast, much improvement of quality of care may be gained through reduction of SAMM. Still, considering the course from normal pregnancy to maternal death as a continuum as described by Mantel et al[2], maternal mortality could further decrease by also focussing on SAMM.

There is a paucity of epidemiologic data on pregnancy and childbirth in the Netherlands. Despite a properly functioning national statistics unit (CBS) and the existence of the Dutch Perinatal Registry ('Landelijke Verloskunde Registratie', LVR), vital obstetric statistics are lacking. For instance, we do not know the exact caesarean section rate, the rate of women with a caesarean section in their obstetric history and pregnant women's body mass index. Moreover, until now the incidence of severe obstetric conditions such as eclampsia, uterine rupture and major obstetric haemorrhage in the Netherlands was unknown. As epidemiologic data serve as an important tool for signalling trends in obstetric practice, opportunities to improve the quality of obstetric care are likely missed. In the United Kingdom, a government-funded national perinatal epidemiology unit (NPEU) exists in Oxford, employing nearly 50 persons. In Scandinavian countries, national perinatal databases are kept more accurately, including linkage to the newborns and to national statistics.
There has been a growing interest in evaluating health services in recent years, clinical audit being

a vital part of this process. The awareness that quality improvement should start with quality measurement is rising. An important factor that has speed up this awareness was the Peristat-I report, in which Dutch perinatal mortality was said to be among the highest in Europe due to variations in epidemiologic registration.[28] This has led to the development of a national perinatal audit system.[29] Furthermore, improvement of the Dutch Perinatal Database is foreseen with an upcoming new set of minimally required data for each delivery, and a set of parameters is developed by the Quality Committee of the Dutch Society of Obstetrics and Gynaecology to monitor quality of obstetric care. This brings about opportunities for the implementation of the results of the study described in this thesis.

Internationally, a similar pattern can be observed in other high income countries. The United Kingdom traditionally played a leading role in assessing quality of obstetric care including maternal mortality statistics and clinical audit. They are now again leading in the development of a surveillance system for trends in obstetric practice and management. The United Kingdom Obstetric Surveillance System (UKOSS), was established in 2005 by the National Perinatal Epidemiology Unit to describe the epidemiology of a variety of uncommon disorders of pregnancy.[30] Advanced plans exist for a comparable European network to monitor even rarer conditions, but funding is still a problem. In the 2000-2002 triennial report of the confidential enquiry into the causes of maternal deaths a separate chapter dedicated to SAMM was included for the first time, based on data from the Scottish Programme for Clinical Effectiveness in Reproductive Health (SPCERH).[26] Various other groups internationally have investigated the rate of SAMM as a complementary marker of standards of care, including Canada, Australia and the United States.[11;20;21] The World Health Organisation is currently in the process of integrating these efforts into internationally accepted criteria for SAMM.[8] However, accurately defining SAMM appears very difficult and is of vital importance to facilitate international comparison.

The incidence of SAMM currently seems to increase in high income countries. This can be explained by various factors, including the rise in maternal age at childbirth, the rise of multiple pregnancies following assisted reproduction, the rise of caesarean section rates and the rise of pregnant mothers with complex medical conditions like cardiac disease, who did not reach reproductive age or were denied to become pregnant in the past. However, close monitoring of the incidence of SAMM is a necessary first requirement to reveal these patterns of obstetric practice and management.

This thesis describes the various aspects of SAMM in the Netherlands. During a two-year period, all cases of SAMM were collected in a nationwide design. The study was called LEMMoN, a Dutch

acronym for Nationwide study into Ethnic determinants of Severe maternal morbidity in the Netherlands [Landelijke studie naar Etnische determinanten van Maternale Morbiditeit in Nederland]. It was initiated by the Maternal Mortality Committee of the Dutch Society of Obstetrics and Gynaecology to extend the assessment of cases of maternal mortality to also include SAMM. As ethnicity appears to be a significant risk factor for maternal mortality and seems to be a risk factor for SAMM, special attention was paid to the ethnic background of women. A qualitative study on the patient-related perspectives of the experienced SAMM among immigrant women was embedded in this study, but detailed results are outside the scope of this thesis.

Aim of the studies presented in this thesis
The studies address the following questions:

1. What is the **incidence and case fatality rate** of SAMM in the Netherlands, overall and for different subgroups?
2. What are the **determinants** of SAMM in the Netherlands, overall and for different subgroups?
3. Is the incidence of SAMM, overall and for different subgroups, elevated in **non-Western immigrants** in the Netherlands, and if so, what is the additional risk and its determinants for different ethnic minority women?
4. What is the level of **substandard care** in the reported cases of SAMM and is substandard care assessment through audit meetings instructive and feasible at a national, regional and local level?
5. Is **ongoing registration** of SAMM for the purpose of reproductive health care quality measurement necessary and feasible, and if so, how can it best be implemented?

Outline of the thesis

Chapter 2 highlights some methodological considerations involved in the design of the LEMMoN study. While general methods were described in the respective chapters, some important aspects deserved a more detailed description than was possible in the published manuscripts. Additional information regarding definitions, selection of inclusion criteria and selection of denominator data is included. Furthermore, the actual performance of the LEMMoN study and results of sub analyses that are specific to the Netherlands, are also described in more detail.

Chapter 3 describes the general results of the LEMMoN study. All cases of SAMM that occurred during the two-year period from August 2004 until August 2006 in the Netherlands are summarised,

along with incidence figures and case fatality rates overall and for different subgroups of severe maternal morbidity. Risk factors are assessed as compared to the general pregnant population in the Netherlands, and substandard care analysis is described for a subgroup of women.

Chapter 4 addresses the differences between non-Western immigrant women and Western women in experiencing severe acute maternal morbidity. Population based relative risks are shown for each type of morbidity and for each of the larger ethnic minority groups in the Netherlands. By comparing Western and non-Western women with SAMM in a multivariable model, explanatory factors for the difference in SAMM are identified. Additionally, to obtain qualitative data related to immigration and acculturalisation, a subgroup of women were interviewed.

Chapter 5 presents an analysis of all intensive care unit admissions during the study period in the Netherlands. Risk factors and case fatality rates are assessed, reasons for admission are summarised and women admitted to intensive care are compared to women with SAMM not requiring intensive care.

Chapter 6 presents an analysis of all uterine ruptures during the study period in the Netherlands. Incidence and risk factors are assessed in women with scar rupture and rupture of the unscarred uterus. Risk of use of uterotonic agents for trial of labour after caesarean section is assessed and discussed. A comparison is made with previous recent findings in the Netherlands.

Chapter 7 presents an analysis of all cases of eclampsia during the study period in the Netherlands. The elevated incidence as compared to other Western European countries is described, and the reasons for the large difference are discussed. Substandard care was assessed in a subset of women.

Chapter 8 presents an analysis of the severest cases of major obstetric haemorrhage in the Netherlands: those necessitating arterial embolisation and/or peripartum hysterectomy.

Chapter 9 presents all cases of severe maternal morbidity and maternal mortality in women who are Jehovah's witnesses.

Chapter 10 presents the results of our efforts to quantify underreporting to the LEMMoN study. As underreporting is inevitable in large observational multicentre studies like LEMMoN, we

searched for possibilities to quantify this. Underreporting appeared to be especially significant in case of major obstetric haemorrhage. For this reason, we conducted a national survey of cases of major obstetric haemorrhage through blood banks in the Netherlands.

Chapter 11 describes the introduction of audit of SAMM in the Netherlands.

Chapter 12 contains the general discussion. Results and conclusions are summarised.

Chapter 13 contains a list of recommendations.

Chapter 14 summarises the thesis. This chapter also includes a summary in Dutch.

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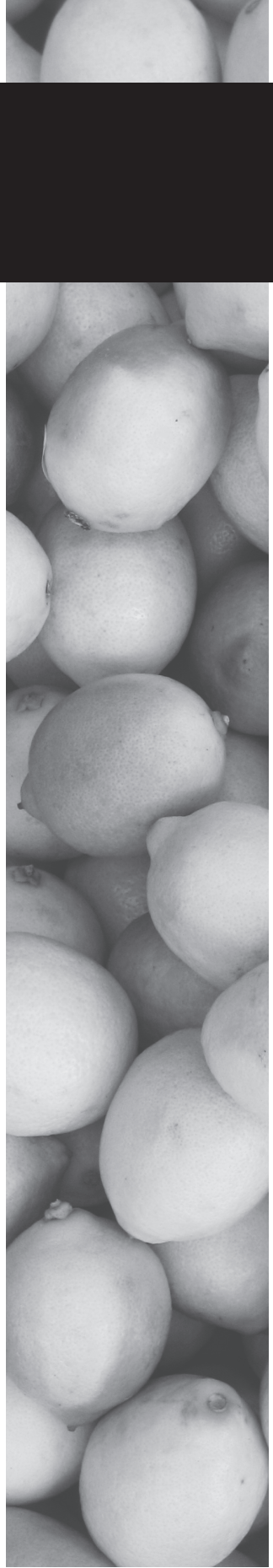
CHAPTER 2

Methodological aspects



Contents

2.1 Introduction

Much thinking and reading has preceded the start of the LEMMoN study. Some of the most important methodological considerations are described in the first part of this chapter. Complete description of the methods is in the respective chapters. The second part describes the actual running of the study in more detail than was possible in the published manuscripts. Special attention is paid to differences within the Netherlands.

Part 1 Methodological considerations

2.2 Considerations related to definition of severe maternal morbidity

Final inclusion criteria used in the LEMMoN study were defined after searching the literature using a pre-defined search strategy in PubMed (Figure 1).

Figure 1. Search strategy

("Morbidity"[MeSH] AND (maternal OR mother OR mothers) AND (pregnancy OR pregnant OR pregnancy complications) AND (severe OR severity) NOT (child OR infant)) OR ((maternal[title] OR mother[title] OR mothers[title]) AND morbidity[title]) OR (("intensive care"[Majr] OR "critical care"[Majr] OR (care[title] AND (intensive[title] OR critical[title]))) AND (pregnancy OR pregnant OR pregnancy complications OR maternal OR mother OR mothers) NOT (child OR infant)) OR ("Postpartum Hemorrhage"[MAJR] OR (Postpartum[title] AND (Haemorrhag*[title] OR bleeding[title] OR Hemorrhag*[title])) AND morbidity) OR ("Pregnancy Toxemias"[Majr] OR (severe[title] AND (pre-eclampsia[title] OR preeclampsia[title])) AND morbidity NOT (child OR infant)) OR (("uterine rupture"[Majr] OR "Uterine rupture"[Title Word]) AND morbidity)

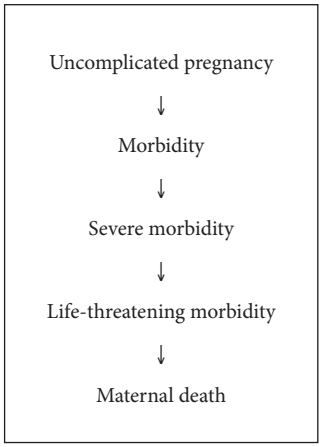
Maternal morbidity has been defined in 1989 by the World Health Organization as morbidity in a woman who has been pregnant (regardless of the site and duration of the pregnancy) from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes.[1] This definition does not take into account women who are still pregnant, and it fails to clearly define the postpartum interval. As most studies on maternal morbidity in high income countries include women up to six weeks postpartum, we included all severe acute maternal morbidity (SAMM) during pregnancy, childbirth or puerperium. Incidental and accidental cases were not excluded, but marked as such. Following the terminology used in maternal mortality

studies, this should actually be mentioned as 'Pregnancy-related morbidity' instead of 'Maternal morbidity'. Apparently, the WHO definition is not regularly used and needs to be adjusted to at least also include women who are still pregnant. This could be easily achieved by changing the first part of the definition into 'morbidity in a woman who *is or* has been pregnant…'.

The continuum of maternal morbidity

Maternal morbidity is thought to represent a continuum between two extremes: physiology and maternal mortality (Figure 2).[2]

Figure 2. Continuum of maternal morbidity



On this continuum, pregnancy can be complicated by morbidity, severe morbidity, life-threatening morbidity and maternal death. Life-threatening morbidity can result either in maternal death or in recovery or permanent disability. Life-threatening morbidity is also referred to as "near miss" maternal morbidity. This term is derived from sentinel event audit in the aviation industry. There is no universally accepted definition of a "near miss" because it is strongly influenced by local maternal health parameters. Mantel et al, who introduced the term, used the following striking definition: "a very ill woman who would have died had it not been that luck and good care were on her side".[2] It clearly expresses the factors that contribute to the difference between live and death, i.e. good care and luck. Strictly spoken, the term near-miss is incorrect: in the aviation industry, it refers to a near accident with no casualties or material damage involved. When used in the context of maternal health, there is already an 'accident' with a casualty, potentially suffering serious short and long term consequences. Therefore, we preferred to use the term severe acute maternal morbidity throughout this thesis.

Objective assessment of the severity of maternal morbidity remains difficult. When should one

consider it 'severe', and when is it a 'near miss'? A different way of selecting cases of SAMM is by using a predictive model or scoring system. Geller at al developed and tested such a system in the United States to select near-misses from a series of cases of maternal morbidity.[3;4] They used expert opinion as the gold standard and assessed the accuracy of different scoring systems in terms of sensitivity and specificity. A four-factor scoring system was recommended, including ICU admission, extended intubation, blood transfusion (>3 units) and surgical intervention. However, a two-factor scoring system with only ICU admission and transfusion (>3 units) yielded exactly the same results in their sample: 100% sensitivity and 78% specificity. The scoring systems largely used management based criteria.

Defining major obstetric haemorrhage

With respect to the definition of major obstetric haemorrhage (MOH), different options were considered: inclusion based on blood loss, transfusion need or drop of haemoglobin level. The latter was considered to be the most objective, but obviously depends on standardised assessment of pre- and post haemorrhage haemoglobin levels, which is difficult in all cases and not feasible at all in observational studies. Blood loss is known to be largely underestimated, especially in case of MOH.[5] Therefore, we considered inclusion based on transfusion need to be the best option. We thereby realised that this is a management based criterion and thus subject to local transfusion policy. Using a cut-off point of four units of packed cells, we expected not to miss cases of SAMM without including too many cases that eventually turned out to be less severe.

2.3 The reference population

Choosing the most appropriate reference population (denominator data) is crucial for calculating the most accurate incidence figures. As this study included all cases of SAMM during pregnancy, childbirth and puerperium, the ideal reference cohort would have been 'all pregnant women during the study period'. As these data were not available, we had to use alternative reference data. We could think of two possible sources for the denominator data, namely the Dutch perinatal database of the Netherlands Perinatal Registry and birth statistics from Statistics Netherlands.

Intuitively, using data from the Dutch Perinatal Database seemed to be the best choice. However, various problems were encountered, the most important being that the exact percentage of deliveries the database represents was unknown. Since deliveries under guidance of general practitioners are not included in this database, it is incomplete. This is thought to concern less than seven percent of all deliveries, but exact numbers of missing deliveries are unknown. The fact that nobody knows to what extent the Dutch Perinatal Database is incomplete, makes it less valuable as an epidemiologic tool. Furthermore, the Dutch Perinatal Database uses slightly different definitions than Statistics

Netherlands. Therefore demographic data from Statistics Netherlands could not merely be applied. For instance, there is a difference regarding the gestational age from which stillbirths are included and the assessment of ethnicity is different. Finally, there have been technical problems with uploading delivery data from a small number of hospitals for the year 2005, resulting in missing data.

Mainly due to the question of unknown representativity, we ultimately decided to use data from Statistics Netherlands as denominator data. These data were based on birth certificates for the exact study period, and we corrected them for multiple births and stillbirths of 24 weeks or over.

As complications of early pregnancy were included in the numerator but not in the denominator, the incidence we express is a ratio rather than a rate. It describes the number of cases of a specific obstetric condition in the Netherlands during the study period, divided by the number deliveries during that period.

Using the above mentioned method, we calculated the number of births this study represents as shown in Table 1. There were 371,021 deliveries in the Netherlands during the exact study period. Since the percentage of returned monthly communication cards was 96.7%, the study is thought to represent 358,874 deliveries.

Table 1. Denominator data

	2004 (last 5 months)	2005	2006 (first 7 months)	study period LEMMoN
Number of live births	81,030	187,910	106,717	375,657
Number of twins	5/12 * 3523	3027	7/12 * 3210	6367
Number of triple pregnancies	5/12 * 64	40	7/12 * 34	87
Number of stillborns ≥ 24w	5/12 * 1013	983	7/12 * 856	1904
Total number of deliveries	79,931	185,786	105,304	371,021

Source: Statistics Netherlands (CBS) 2007

Part 2 Actual performance and regional results of the LEMMoN study

2.4 Participation

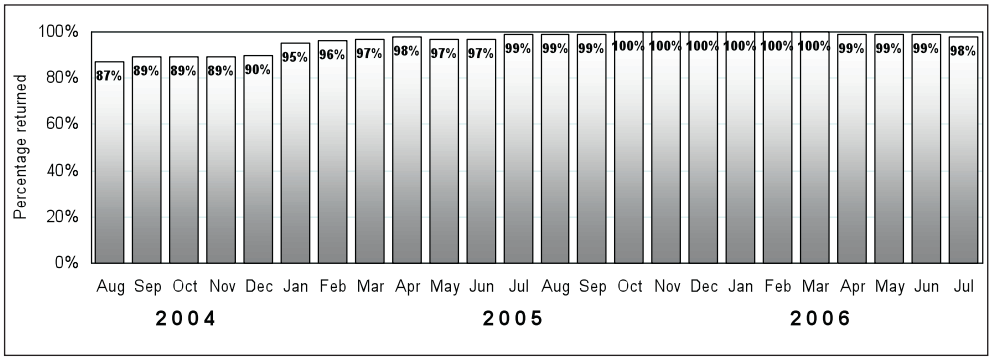
We succeeded to get participation in all 98 hospitals with a delivery ward in the LEMMoN study. Important features that brought about this universal participation included

- selection of the most dedicated clinicians to act as local coordinator of the study,
- clear and concise information delivery before initiation of the study,
- easy method of case ascertainment using the web-based system of the National Signalling Centre for Obstetrics and Gynaecology (NSCOG) provided by TNO Quality of Life, Leiden, the Netherlands,
- support with data collection on location if necessary,

- a two-monthly newsletter to keep attention to the study,
- LEMMoN cakes for the best including hospitals and
- continuous contacting of non-responders.

Response rates for every single month of the study are shown in Figure 3. Overall response rate was 96.7%. Human resources needed for data collection involved one full-time study coordinator, eight students who were part-time available for data collection and entry, an obstetrician to regularly remind non-reporting local coordinators to return their monthly response cards. We were able to run this study efficiently by making use of the National Signalling Centre for Obstetrics and Gynaecology (NSCOG), which delivered the experience and infrastructure for on-line reporting of cases of SAMM on a monthly basis. The use of this system has undoubtedly added to the high participation and response rates.

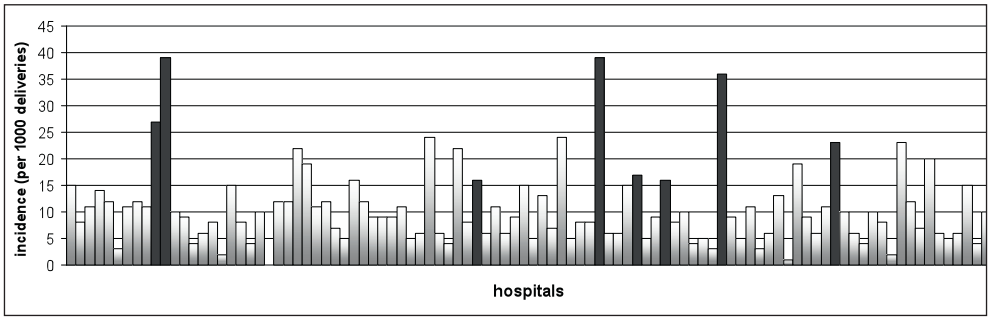
Figure 3. Monthly response rate



2.5 Incidence: local, regional and temporal differences

Incidence varied largely by hospital, as shown in Figure 4. Academic hospitals (dark bars) were likely to have a high-er incidence due to selection and referral pattern. For other hospitals, specific case mix of the hospital population may account for the differences found. Also, differences in local policy for transfusion and ICU admission likely influenced incidence, as well as eagerness to identify and report cases. After having addressed all these possible confounders, the incidence may reflect the quality of care in a specific hospital.

Figure 4. Variation of incidence by hospital*



***each bar represents a hospital in the Netherlands, dark bars represent academic teaching hospitals**

As shown in table 2, the incidence in academic hospitals was indeed about three times that of non-academic hospitals. Incidence was also higher in non-academic teaching hospitals as compared to non-teaching hospitals (relative risk 1.3; 95% confidence interval 1.1-1.5). Sub-analysis of incidence by delivery volume of hospital is shown in Table 3. A trend was observed towards increased incidence of SAMM in larger volume hospitals, also when excluding academic centres from analysis.

Table 2. Comparison of tertiary care centres: inclusion pattern, rate of SAMM and referral rate

	ICU	Uterine rupture	Eclampsia/ HELLP	MOH	Other	Reported cases (n)	Rate of SAMM	Referrals [n(%)]
AMC	29%	7%	11%	37%	**34%**	70	2.3	29 (41%)
VUMC	28%	8%	9%	48%	24%	126	**4.2**	33 (26%)
UMCG	31%	7%	**21%**	*29%*	26%	42	1.8	17 (40%)
LUMC	29%	6%	*4%*	50%	30%	105	4.0	37 (35%)
AZM	*15%*	7%	12%	51%	29%	41	1.7	6 (15%)
UMCN	41%	5%	8%	**79%**	10%	39	*1.5*	16 (41%)
Erasmus	34%	6%	*4%*	60%	19%	112	3.7	40 (36%)
UMCU	**49%**	6%	8%	62%	*4%*	84	2.1	34 (40%)

ICU=intensive care unit; MOH=major obstetric haemorrhage. Highest rates are in bold, lowest rates are in italic

A comparison was made of the inclusion pattern of SAMM between the eight academic centres in the Netherlands (Table 4). We noted large difference in the relative contributions of different subgroups to the overall SAMM incidence, except for uterine rupture. We also noted large differences in percentage of referrals from other hospitals among the SAMM cases, but these differences could not explain the differences in incidence.

Table 3. Incidence by type of hospital (2005)

Type of hospital	Number of deliveries	# LEMMoN	Incidence (/10,000)	RR (95% CI)
Non-academic teaching hospital (n=35)	54,742	595	**10.9**	1.3 (1.1-1.5)
Non-academic non-teaching hospital (n=55)	47,273	384	**8.1**	1.0
Academic centre (n=8)	11,805	327	**27.7**	3.4 (2.9-3.9)

RR=relative risk; CI=confidence interval

No marked seasonal variations were observed for SAMM overall and for different subgroups. Inclusion of cases by calendar month is shown in Figure 5. Overall incidence ranged from 77 to 133 cases per month. Trends in incidence during the study period were not noted for either of the subgroups of SAMM.

Table 4. Incidence by volume* (2005)

Volume (deliveries/year)	Number of deliveries	# LEMMoN	Incidence (/10,000)
<1000 (n=40)	29,035	233	**8.0**
1000-1500 (n=39)	42,384	402	**9.5**
>1500 (n=19)	32,077	344	**10.7**

***academic centres excluded**

We also performed a sub-analysis of SAMM by province in the Netherlands. The Netherlands is divided into 12 provinces. Although organisation and funding of health care is a nationwide issue, this analysis enabled us to study regional differences in SAMM. As shown in table 5 and figure 6, regional incidence of SAMM varied from 2.7 to 8.5 per 1000 deliveries. The incidence was clearly increased in the urbanised Western part of the country (the so-called 'Randstad') as compared to the more rural areas. To illustrate the influence of urbanisation on the incidence of SAMM, we calculated an urbanisation factor based on data from Statistics Netherlands.[6] After correction for this factor, differences in incidence appeared to have largely disappeared. This correlation could be caused by the higher rate of non-Western immigrant women and the higher rate of women with a low socio-economic position in the more urbanised parts of the country. These regional results illustrate the importance of case-mix analysis when comparing incidences between hospitals in the Netherlands.

Figure 5. Seasonal variation in number of inclusions

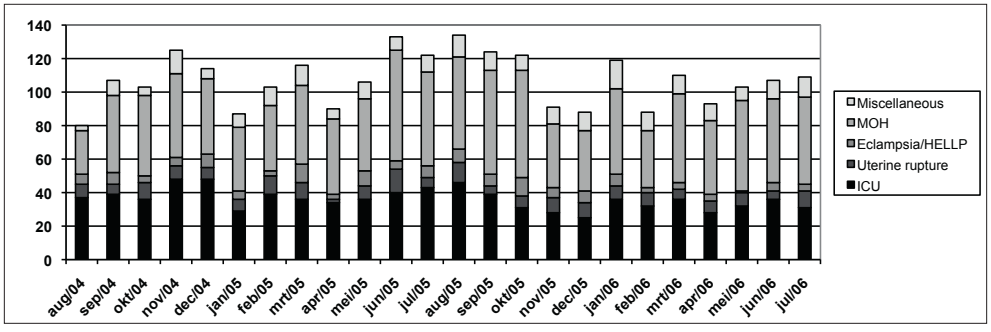


Figure 6. Distribution of severe acute maternal morbidity in the Netherlands

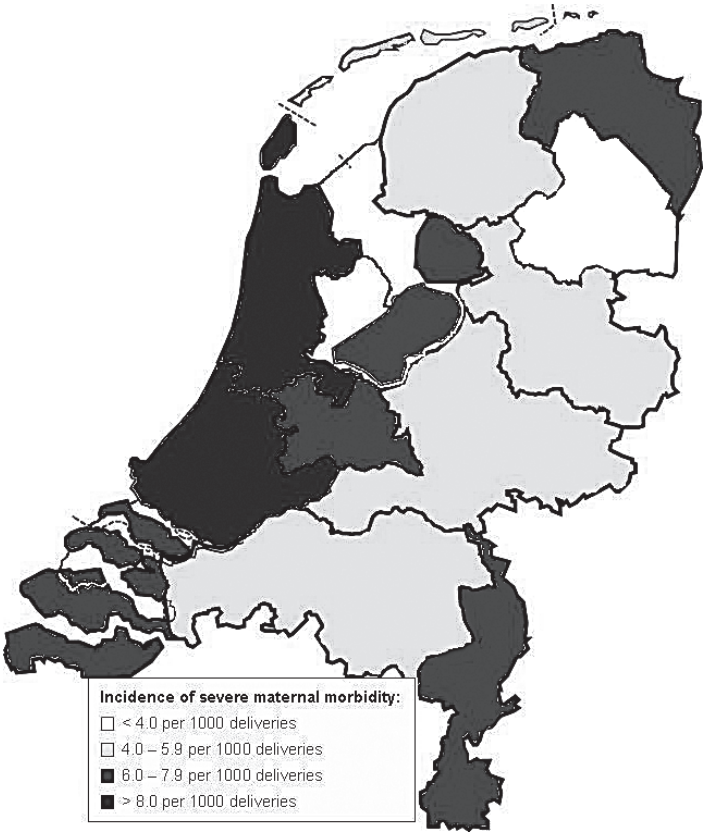


Table 5. Incidence of SAMM by province (arranged by urbanisation level)

	Reported cases	total births	Incidence SAMM	urbanisation factor*	Rate of non-Western women in LEMMoN
Zuid-Holland	697	81,750	**8.5**	0.76	54%
Noord-Holland	529	62,918	**8.4**	0.73	53%
Utrecht	210	30,968	**6.8**	0.65	30%
Flevoland	74	10,520	**7.0**	0.58	48%
Noord-Brabant	294	52,902	**5.6**	0.54	19%
Overijssel	138	27,789	**5.0**	0.51	10%
Gelderland	251	44,841	**5.6**	0.50	23%
Limburg	134	20,281	**6.6**	0.49	25%
Groningen	79	11,907	**6.6**	0.49	13%
Zeeland	52	7,843	**6.6**	0.40	20%
Friesland	67	14,743	**4.5**	0.40	12%
Drenthe	28	10,240	**2.7**	0.37	8%

Urbanisation factor calculated from data of Statistics Netherlands

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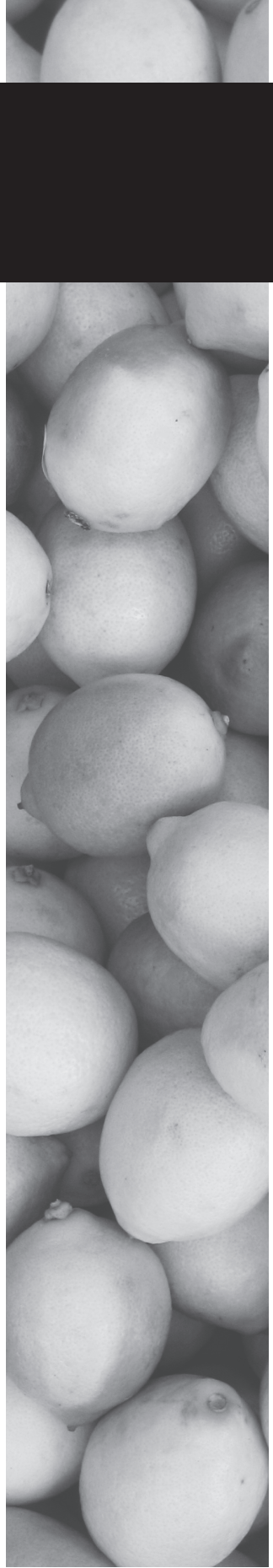
CHAPTER 3



Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population based study of 371 000 pregnancies

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Abstract

Objective: To assess incidence, case fatality rate, risk factors and substandard care in severe maternal morbidity in the Netherlands.

Design: Prospective population based cohort study.

Setting: All 98 Dutch maternity units in the Netherlands.

Methods: Cases of severe maternal morbidity were collected during a two-year period. All pregnant women in the Netherlands in the same period acted as reference cohort (n=371,021). As immigrant women are disproportionately represented in Dutch maternal mortality statistics, special attention was paid to the ethnic background. In a subset of 2.5% of cases substandard care was assessed through clinical audit.

Main outcome measures: Incidence, case fatality rates, possible risk factors, substandard care.

Results: Severe maternal morbidity was reported in 2552 cases, giving an overall incidence of 7.1 per 1000 deliveries. ICU admission was reported in 847 cases (incidence 2.4 per 1000), uterine rupture in 218 cases (incidence 6.1/10,000), eclampsia in 222 cases (incidence 6.2/10,000) and major obstetric haemorrhage in 1606 cases (incidence 4.5 per 1000). Non-Western immigrant women had a 1.3 fold increased risk of severe maternal morbidity (95% CI 1.2-1.5) when compared with Western women. Overall case fatality rate was 1 in 53. Substandard care was found in 39 of a subset of 63 women (62%) through clinical audit.

Conclusions: Severe maternal morbidity complicates at least 0.71% of all pregnancies in the Netherlands, immigrant women experiencing an increased risk. Since substandard care was found in the majority of assessed cases, reduction of severe maternal morbidity seems a mandatory challenge.

Introduction

Severe maternal morbidity gains interest as a new quality indicator of obstetric care.[1-4] The most important reason is the extremely low maternal mortality rate in Western countries, so that it takes years to collect the numbers needed to be able to draw valid conclusions from analysing cases of maternal mortality. Maternal deaths also tend to be more and more the result of rare complications, whereas regular life-threatening complications like major obstetric haemorrhage (MOH) are relatively underexposed as they less frequently lead to death nowadays.[2;3] The most important and difficult issue, however, is the definition of severe maternal morbidity. Different research groups have already addressed this issue and the World Health Organisation is in the process of integrating these efforts into internationally accepted criteria for severe maternal morbidity.[5-13] Recent studies demonstrate an increase in severe maternal morbidity in Western countries, possibly due to changes in management of obstetric complications and increasing age of pregnant women.[2;14;15]

A nationwide cohort study of severe maternal morbidity, called LEMMoN, was conducted in the Netherlands to assess incidence, case fatality rates, risk factors and substandard care overall and for different subgroups. As ethnicity appeared to be a significant risk factor for pregnancy related death[2;16;17] and seemed to be a risk factor for severe maternal morbidity, we are especially interested in the association of ethnicity with severe maternal morbidity.[18;19]

Methods

Women were included from 1st August 2004 until 1st August 2006. All 98 hospitals (100%) with a maternity unit in the Netherlands participated in the survey: 10 tertiary care centres, 33 non-university teaching hospitals and 55 other general hospitals. The annual number of deliveries per unit in 2005 ranged from 93 to 2655 (average: 1162). Women with high risk pregnancies and those with low risk pregnancies who develop complications deliver in hospital under the guidance of obstetricians (secondary or tertiary care, 59% of all births). Women with low risk pregnancies without complications, deliver under the guidance of midwives and family physicians (primary care), either at home (30% of all births) or in hospital under their responsibility (11% of all births).[20]

Final inclusion criteria were defined after searching the literature and after agreement with the national Maternal Mortality Committee of the Dutch Society of Obstetrics and Gynaecology. An expert panel of obstetricians advised about the design of the study. The main issues for setting our criteria were easy clinical applicability and univocality. Inclusion criteria are listed in Figure 1.

Figure 1. Inclusion criteria

Group 1: ICU admission
- Admission to intensive care unit or coronary care unit, other than for standard postoperative recovery

Group 2: Uterine rupture
- Clinical symptoms (pain, fetal distress, acute loss of contractions, haemorrhage) that led to an emergency caesarean section, at which the presumed diagnosis of uterine rupture was confirmed
- Peripartum hysterectomy or laparotomy for uterine rupture

Group 3: Eclampsia / HELLP syndrome
- Eclampsia
- HELLP-syndrome only when accompanied by liver haematoma or rupture

Group 4: Major Obstetric Haemorrhage
- Transfusion need of ≥ 4 units of packed cells
- Embolisation or hysterectomy for major obstetric haemorrhage

Group 5: Miscellaneous
- Other cases of severe maternal morbidity to the opinion of the treating obstetrician, not to be included in group 1-4

The last group was meant to include rare conditions of severe maternal morbidity (e.g. acute fatty liver of pregnancy), as well as severe manifestations of generally less severe conditions (e.g. severe early pre-eclampsia which did not require admission to ICU). Proven cases of pulmonary embolism could also be reported in this group. All cases during pregnancy, delivery and puerperium (limited to 6 weeks postpartum) were regarded as cases, including complications in early pregnancy. Cases were classified as 'early pregnancy' if one could not speak of a 'partus' and hence not of 'antepartum' or 'postpartum'. This by definition applies to cases in which pregnancy ends before 17 weeks of gestational age in the Netherlands, and it also applies to cases of second trimester instrumental abortion.

Ethnicity was defined by country of origin ('geographical ethnic origin'). We used the definitions of Statistics Netherlands, based on country of birth of the woman. When the woman was born in the Netherlands with at least one of her parents born abroad, she was considered to be from the same origin as her parent(s) from abroad. Women from other Western European countries and from North America, Japan and Indonesia were considered Western immigrants according to Statistics Netherlands because of their socio-economic and cultural position in the Netherlands. All other immigrant women were considered non-Western.

Maternal deaths were reported to the national Maternal Mortality Committee of the Dutch Society of Obstetrics and Gynaecology by the attending obstetrician as usual. These cases were added to our database. Women who had more than one condition were considered only once in the overall incidence figures, only the first group was counted. For example, a woman with MOH (group 4) who was admitted to the ICU (group 1) was only counted as an ICU admission. However, these cases were counted for

each condition in the sub analysis of the different groups.

In each hospital, a local coordinator reported all cases monthly using a standardised web based form. Absence of cases in a particular month was also communicated in order to control for underreporting. Cases were identified in the respective hospitals using multiple strategies, including maternity computer databases, labour ward diaries, staff reports, intensive care admission registers, blood transfusion registers, discharge data and personal communication. At the central office, cases were collected using the national electronic surveillance system of the Netherlands Surveillance Centre for Obstetrics and Gynaecology (NSCOG), a newly established non-profit organisation for scientific data collection, analogous to the NSCK for paediatrics (TNO Quality of Life, Leiden, the Netherlands).[21] Cases were initially notified by reporting initials and date of birth to LEMMoN, to minimise underreporting. Anonymised data were then obtained, consisting of a case record form with photocopies of relevant parts of the patient file. All cases were entered into an Access database by trained staff and each case was finally checked for correctness by the first author. We recorded maternal characteristics (age, Body Mass Index, parity, ethnicity, income, single household, language skills, smoking), all data on pregnancy and delivery, and data on the specific complication. A minimum of 87 items were entered into the database for each case, depending on the subgroup(s) of severe morbidity in which the case was included. We also recorded characteristics of each hospital (university or teaching hospital, annual number of deliveries). Socio-economic status was ascribed using the validated zip-code/socio-economic status indicator of Statistics Netherlands, based on home price and income, stratified into low, modest and high.[22]

Although 30% of women in the Netherlands deliver at home, all women with severe maternal morbidity as defined in our inclusion criteria will eventually have been referred to one of the maternity units. Therefore, this study represents all deliveries in the Netherlands during the study period. As a consequence, nationwide statistics could be used as reference values whenever appropriate. To control for underreporting, we crosschecked our data with different other databases: underreporting of uterine rupture and eclampsia was controlled for using the national perinatal database (LVR-2).[23] Underreporting of MOH was controlled for using data from a large representative sample of local blood transfusion laboratories in the Netherlands during a 20-month period. Cases that were found to be not reported to our study were only counted and were not added to the database.

Seven audit meetings were held throughout the country to assess substandard care in a selection of cases, using the audit criteria developed by the Dutch Maternal Mortality Committee.[24] Assessors were members of the LEMMoN expert panel as well as local staff. After individual assessment by each assessor, a plenary meeting was held to discuss all items found. At this meeting, complete patient files were present to optimize assessability. Substandard care was assumed if the majority of assessors judged this to be present.

For each group, incidence was calculated using the total number of births in the Netherlands during

the study period as the denominator. Denominator data for the number of deliveries in the Netherlands were obtained from Statistics Netherlands (CBS).[25] They were based on birth registries during the exact study period, corrected for multiple births and stillbirths of 24 weeks or over. Denominator data for the number of women from the different ethnic groups were obtained from Statistics Netherlands. For the four large immigrant groups and for non-Western immigrants overall, numbers of mothers of newborns were available. For the smaller subgroups, we had to rely on numbers of women of fertile age (15-40 years old) to calculate the denominator, thereby disregarding the difference in fertility rate among the different ethnic groups. Relative risks were calculated when reference data were available. National reference values for possible risk factors for severe maternal morbidity were obtained from Statistics Netherlands and from the LVR-2 database. Incidence figures in LVR-2 were multiplied by 59/100 to also represent all deliveries under primary care (41% in 2002).[23] Case fatality rates were calculated by dividing the number of deaths due to a specific condition by the number of severe maternal morbidities due to that condition. Possible risk factors were identified by calculating relative risks and 95% confidence intervals. Significance was assumed when the confidence interval did not cross one. Statistical analysis was performed using the SPSS statistical package 14.0 (SPSS Inc., Chicago, IL, USA).

Results

During the study period, there were 371,021 deliveries in the Netherlands. All 98 hospitals with an obstetric ward in the Netherlands agreed to participate. A maximum of 2352 (98*24) 'hospital-months' could be reported. Mainly due to later enrolment of some hospitals into the study, a total of 2275 'hospital months' were actually returned (97%). Regarding only those maternities occurring during the months each hospital actively participated in the study, the study represents 358,874 deliveries. A total of 2552 cases were reported during the study period. We received detailed data of 2513 of 2552 cases (98.5%). The overall incidence of severe maternal morbidity in The Netherlands was 7.1 per 1000 deliveries. Cases were divided over the five groups as indicated in Table 1.

Table 1. Numbers, incidence and case fatality rate per inclusion group.

	ICU admission	Uterine rupture	Eclampsia/ HELLP	MOH	Miscellaneous	Total
patients	847 (33.2%)	191 (7.5%)	135 (5.3%)	1146 (44.9%)	233 (9.1%)	2552 (100%)
complications*	847 (26.9%)	218 (6.9%)	239 (7.6%)	1606 (51.1%)	233 (7.4%)	3143 (100%)
data available	837 (98.8%)	218 (100%)	230 (96.2%)	1590 (99.0%)	228 (97.9%)	3102 (98.7%)
incidence (/1000 deliveries)	2.4	0.6	0.7	4.5	0.7	7.1
case fatality rate	1:29 (3.4%)	- (0%)	1:55 (1.8%)	1:201 (0.5%)	1:14 (7.3%)	1:53 (1.9%)

ICU=intensive care unit admission. MOH=Major obstetric haemorrhage. *one patient can have more than one complication.

Among the 2552 women included, 3143 complications were noted, 21.4% and 1.7% having two and three complications simultaneous, respectively. One woman had all four eligible complications. Two women were included twice during the study period in distinct pregnancies. Forty eight cases of pregnancy related death were reported to the Maternal Mortality Committee during the study period, giving an overall case fatality rate of 1 in 53 (1.9%). Incidence varied largely between hospitals in the Netherlands, ranging from 0 to 39.1 per 1000 deliveries. The mean hospital-incidence (regarding only the secondary and tertiary care deliveries in the respective hospitals) was 10.8 per 1000, 9.3 for non-university hospitals and 26.7 for university hospitals. In 2.8% of cases, the (first) complication occurred in early pregnancy, in 26.5% antepartum and in 70.7% postpartum. Characteristics of women included are shown in Table 2.

Table 2. Characteristics of women in the study.

	n	*%*
Age (mean 31·6)		
< 20 year	31	1.2%
20-35 year	1770	70.4%
35-40 year	590	23.5%
≥ 40 year	122	4.9%
Socio-economic status indicator		
low	701	31.6%
middle	994	44.9%
high	520	23.5%
unknown	298	
Smoking during pregnancy		
yes	175	12.0%
no	1290	88.0%
unknown	1048	
Body mass index (BMI)		
<18.5	48	2.8%
18.5-24.9	1018	60.2%
25.0-29.9 (overweight)	404	23.9%
30.0-34.9 (obese)	125	7.4%
≥ 35.0 (morbidly obese)	95	5.6%
unknown	823	
Geographical ethnic origin		
Netherlands	1864	74.4%
Morocco	116	4.6%
Turkey	87	3.5%
Surinam/Dutch Antilles	111	4.4%
sub-Saharan Africa	90	3.6%
other non-Western	146	5.8%
other Western	92	3.7%
unknown	7	

Possible risk factors for severe maternal morbidity are shown in Table 3. Overall, 21.1% of women were non-Western immigrants. The relative risk for non-Western women to experience severe maternal morbidity was 1.3 (95%-CI: 1.2-1.5) as compared to Western women. This elevated risk remained significant for each separate inclusion group (Table 4). Of the four largest immigrant groups in the Netherlands (Morocco, Turkey, Surinam and Netherlands Antilles), only Surinam women showed a significantly elevated risk as compared with native Dutch women (RR 1.4; 95% CI 1.1-1.7). Sub-Saharan African women had the highest risk (RR 3.5; 95% CI 2.8-4.3). Overall relative risks of women from the Middle East and South East Asia were 1.5 (95% CI 1.1-2.1) and 2.2 (95% CI 1.7-2.8).

Table 3. Risk factors for severe maternal morbidity.

risk factor	*LEMMoN*	*Netherlands*	*RR (95% CI)*
patient			
age ≥ 35	29.3%	24.7%†	1.2 (1.1-1.3)
age ≥ 40	4.8%	3.4%†	1.4 (1.2-1.7)
low income	31.6%	n/a	
single household	3.0%	n/a	
smoking during pregnancy	12.0%	n/a	
BMI ≥ 25 (overweight)	36.9%	31.7%†	1.3 (1.1-1.4)
BMI ≥ 30 (obese)	13.0%	9.1%†	1.5 (1.3-1.7)
non-Western immigrants	21.1%	16.8%†	1.3 (1.2-1.5)
chronic disease in general history	9.7%	n/a	
pregnancy			
initial antenatal care by obstetrician	35.8%	14.3%‡	3.3 (3.1-3.6)
prior caesarean section	19.3%	6.0%[26]	3.7 (3.4-4.1)
parity 0	49.9%	45.2%†	1.2 (1.1-1.3)
parity ≥3	5.1%	5.0%†	1.0 (0.9-1.2)
parity ≥6	0.4%	0.4%‡	1.2 (0.7-2.2)
multiple pregnancy	8.0%	1.7%†	4.9 (4.3-5.7)
artificial reproduction techniques: IVF/ICSI	4.7%	1.9%[27]	2.5 (2.1-3.0)
delivery			
home delivery	6.3%	31.6%†	0.1 (0.1-0.2)
induction of labour	26.5%	12.5%‡	3.1 (2.8-3.4)
caesarean section without labour	22.3%	5.9%‡	4.6 (4.2-5.0)
ventouse/forceps	12.7%	8.6%‡	1.6 (1.4-1.7)
caesarean section overall	43.6%	13.0%‡	5.2 (4.8-5.6)
breech presentation	7.9%	4.9%‡	1.7 (1.4-1.9)
preterm birth (<37w)	28.8%	5.8%‡	6.6 (6.0-7.2)
post term birth (≥42w)	5.3%	4.3%‡	1.3 (1.0-1.5)

n/a=data not available. *includes hypertension, diabetes, cardiac disease and coagulation disorders. National reference values from †Statistics Netherlands (exact study period) and ‡The Netherlands Perinatal Registry (LVR-2, 2005).

ICU admission

A total of 847 cases of ICU admission were reported, giving an incidence of 2.4 per 1000 deliveries. Of all cases of pregnancy related death, 29 were admitted to ICU before death, giving a case fatality rate of 1 in 29. The mean duration of ICU stay was 3.6 days (range 1-74). The main reasons for admission were MOH (47%), hypertensive disorders of pregnancy (33%), respiratory complications (8%) and cardiac complications (7%). Assisted ventilation, inotropic support and renal dialysis were necessary in 34.2, 8.6 and 1.9% of cases, respectively.

Table 4. Relative risk of severe maternal morbidity for non-Western immigrants

Geographical Ethnic Origin	non-Western immigrants	Western women	unknown	RR (95% CI)
ICU admission (n=837)	189	645	3	1.5 (1.2-1.7)
Uterine rupture (n=218)	48	170	0	1.4 (1.0-1.9)
Eclampsia/HELLP (n=230)	59	170	1	1.7 (1.3-2.3)
MOH (n=1590)	318	1268	4	1.3 (1.1-1.4)
Total (n=2513)	529	1977	7	1.3 (1.2-1.5)

ICU= Intensive Care Unit; MOH=Major Obstetric Haemorrhage.

Uterine rupture

A total of 218 cases of uterine rupture were reported, giving an incidence of 6.1 per 10,000 deliveries. No cases of pregnancy related death due to uterine rupture occurred. Admission to ICU occurred in 12% of cases and 21% experienced MOH. In 87% of cases, obstetric history revealed at least one caesarean section. Of the other 28 cases, 3 had a history of a known uterine scar due to myomectomy, tubectomy for isthmic pregnancy or dilatation and curettage. In 25 cases, there was no known uterine scar, 12 of whom did not have any possible known risk factor in general or obstetric history. In two cases, rupture occurred as a complication of second trimester dilatation and curettage for unwanted pregnancy. In six cases, uterine rupture complicated medically induced termination of pregnancy after 16 weeks of gestation.

Eclampsia and haemolysis, elevated liver enzymes, low platelets syndrome accompanied by liver haematoma or rupture

A total of 222 cases of eclampsia were reported, giving an incidence in the Netherlands of 6.2 per 10,000 deliveries. In addition, 19 cases of haemolysis, elevated liver enzymes, low platelets (HELLP) syndrome accompanied by liver haematoma (n=12) and/or liver rupture (n=7) were included. Two women had both eclampsia and HELLP syndrome accompanied by liver haematoma. There were four cases of pregnancy related death due to eclampsia/HELLP, case fatality rate being 1 in 55. Admission to ICU occurred in 42% of cases.

Table 5. Major Obstetric Haemorrhage, primary diagnoses

timing	*diagnosis*†	*n*	*(%)*
Early pregnancy	Ectopic pregnancy	29	(56.9%)
(n=51)	Spontaneous Abortion	10	(19.6%)
	Termination of pregnancy	10	(19.6%)
	Miscellaneous‡	2	(3.9%)
Antepartum	Placental abruption	61	(45.5%)
(n=135)*	Placenta praevia	54	(40.3%)
	Miscellaneous§	7	(5.2%)
	Unknown diagnosis	12	(9.0%)
Postpartum	Retained placenta or placental rests	703	(47.8%)
(n=1480)*	Uterine atony	567	(38.5%)
	Haemorrhage following CS	183	(12.4%)
	Perineal tears / episiotomy	148	(10.1%)
	Clotting disorders	116	(7.9%)
	Placenta accreta/increta/percreta	109	(7.4%)
	Rupture of cervix	58	(3.9%)
	Uterine rupture	44	(3.0%)
	Uterine inversion	13	(0.9%)
	Miscellaneous	65	(4.4%)
	Unknown diagnosis	10	(0.7%)

***In 76 cases both antepartum and postpartum diagnoses were coded; †Up to three diagnoses could be coded postpartum; ‡molar pregnancy and placenta percreta; §rupture of uterine/ovarian artery, rupture of ovarian cyst, placenta percreta, vasa praevia, retro placental haematoma, rupture of uterine vein.**

Major obstetric Haemorrhage

A total of 1606 cases were reported, giving an incidence of MOH in our study of 4.5 per 1.000 deliveries. There were eight cases of pregnancy related death due to MOH, case fatality rate being 1 in 201. Admission to ICU occurred in 27% of cases. Three percent of cases occurred in early pregnancy, 9% antepartum and 88% postpartum. Primary diagnoses are shown in Table 5. In 107 and 114 cases (6.7 and 7.2%), respectively hysterectomy and arterial embolisation were performed. In 14 cases (13%) hysterectomy was necessary after arterial embolisation failed to stop haemorrhage. Vice versa, in two cases embolisation was performed after hysterectomy. Intrauterine balloon catheters were used in 154 (9.7%) cases, (re)laparotomy was performed in 202 (12.5%) with B-lynch suture in 12 (0.7%) and ligation of arterial vessels in 21 (1.3%). The average amount of estimated blood loss was 3150cc (maximum 20,000cc). An average of 6.6 units of blood were transfused (range 0-50). Fresh frozen plasma and pooled thrombocyte suspension was given in 48.3% and 16.2% of cases, respectively. Recombinant factor seven (Novo-seven®) was administered in 64 cases (4.0%). In 178 cases (11.2%), MOH was accompanied by pre-eclampsia. Five cases of Jehovah's witnesses with MOH were included on the basis of hysterectomy or arterial embolisation

without transfusion (n=4), or final acceptance of blood products (n=1). Six others were reported because of ICU admission or as 'other severe maternal morbidity'.

Table 6. Cases reported as 'Other severe maternal morbidity' (n=233)

	n	(%)	examples
Obstetric	*100*	*(43%)*	
pre-eclampsia/HELLP	70	(30%)	early severe HELLP necessitating termination of pregnancy or with retinal detachment
Genital tract sepsis	8	(3%)	Group A streptococcal sepsis
AFLP	5	(2%)	
MOH in Jehovah's witnesses	3	(1%)	
Miscellaneous obstetric	14	(6%)	maternal hydrops syndrome, abdominal bleeding after laser therapy for TTTS
Non-obstetric	*128*	*(55%)*	
Cardio respiratory	20	(9%)	myocardial infarction after CS, cardiomyopathy, pleural empyema
Cerebral/neurological	19	(8%)	viral meningo-encephalitis, sagittal sinus thrombosis, cerebrovascular accident
Thrombo-embolism	30	(13%)	pulmonary embolism, portal vein thrombosis, vena cava thrombosis
Sepsis	4	(2%)	urosepsis, sepsis from cholangitis
Surgical	21	(9%)	splenectomy after trauma, colectomy due to Crohn's disease, appendectomy
Oncological	12	(5%)	Kaposi sarcoma with AIDS, vulvar cancer, acute lymphatic leukaemia
Anaesthetic complication	2	(1%)	acute life-threatening danger during intubation due to extreme obesity
Miscellaneous non-obstetric	20	(9%)	acute pancreatitis, sickle cell crises, severe immune thrombocytopenic purpura
Unknown	*5*	*(2%)*	

HELLP=haemolysis, elevated liver enzymes, low platelets syndrome; AFLP= acute fatty liver of pregnancy; MOH= major obstetric haemorrhage; TTTS= twin-to-twin-transfusion syndrome

Other severe maternal morbidity

A total of 233 cases were reported as other severe maternal morbidity (Table 6). Divided over all inclusion groups, 69 cases of thrombo-embolism were included: pulmonary embolism (n=44), amniotic fluid embolism (n=9), and thrombosis of pelvic, ovarian, mesenteric, portal vein, sagittal sinus, mesenteric vein, portal vein and vena cava (n=16). In addition to the 239 cases of eclampsia/severe HELLP included in group 3, 360 women with pre-eclampsia were included in the other groups. Thus, 23.9% of all cases had pre-eclampsia. Sepsis was reported in 84 cases (estimated incidence 2.3 per 10,000).

Underreporting

During the first five months of the study, we found only one case of uterine rupture and two cases of eclampsia that were not reported to LEMMoN, underreporting being estimated at 2 and 3%, respectively. Underreporting of MOH to the LEMMoN study appeared to be 35% (range 0-83%) in a large representative sample. Cases not reported to our survey appeared to be mainly the

relatively less severe cases of MOH, with 68% of unreported cases being transfused only 4 units of blood. Taking into account this degree of underreporting, the overall incidence of MOH in the Netherlands would be 5.8 per 1000 deliveries. Controlling for underreporting of ICU admission on a national level appeared unfeasible.

Table 7. Substandard care items and their contribution*

	n	%†
Patient	*55*	*6.6*
Delay in consulting doctor	30	3.6
Refusal of medical help or advise	15	1.8
Language barrier	10	1.2
GP/midwife	*164*	*19.9*
Inadequate antenatal care	44	5.3
Delay in recognition of symptoms/signs	58	7.0
Delay in referral to obstetrician	62	7.5
Obstetrician	*441*	*53.4*
Inadequate antenatal care	70	8.5
Delay in recognition of symptoms/signs	146	17.7
Delay in treatment after diagnosis	200	24.2
Delay in referral to tertiary care centre	25	3.0
Other consultant	*5*	*0.6*
Delay in consulting obstetrician	5	0.6
Health care system	*84*	*10.2*
Home birth influenced outcome	19	2.3
Birth in general hospital influenced outcome	40	4.8
Quality of transport influenced outcome	25	3.0

***after individual assessment of 59/63 cases by on average 14 assessors; †each item could maximally be scored 826 times (59 cases times 14 assessors)**

Audit

During seven audit sessions throughout the country, substandard care was judged to be present by the majority of assessors in 39 (62%) of 63 cases (Table 7).

Discussion

This study represents the first nationwide survey of severe maternal morbidity in the Netherlands and to date, by far the largest study in the literature. All aspects of severe maternal morbidity in the Netherlands have been mapped. The incidence in our study was 7.1 per 1000 deliveries, indicating that the average obstetric ward in the Netherlands encounters one case every month. We realize that incidence figures largely depend on the denominator chosen. We deliberately chose to express the incidence as the total pregnancy related risk of severe maternal morbidity per delivery. That means, we included complications of early pregnancy while we did only include deliveries from 24 weeks onward in the denominator. Therefore, the incidence is expressed as a ratio, not a rate. Leaving out all cases in early pregnancy and

before 24 weeks of gestation would have resulted in a slightly lower incidence of 6.8 per 1000.

There have been only two other large surveys addressing the overall incidence of severe maternal morbidity in Western countries.[7;9] Their reported incidences were 12.0/1000 in South-West England (n=48,865) and 3.8/1000 in Scotland (n=51,165). Our incidence is well within the range of the other two studies. However, the incidence figures are strikingly different, bearing in mind the relatively comparable health care systems and populations. These differences can be mainly explained by the differences in inclusion criteria. The inclusion criteria for MOH, which affect the overall incidence to a great extent as it concerns about half of all inclusions, was more liberal in the English study (blood loss of more than 1500cc) as compared to the Scottish (transfusion of five or more units of blood). Our definition of MOH was in between those two (transfusion of four or more units of blood), and so was our overall incidence. The large differences in reported incidences due to different inclusion criteria clearly reflect the need for internationally accepted definitions of severe maternal morbidity.

The high incidence of eclampsia in the Netherlands is worrying and should be subject of further research, especially seen in the light of the also high maternal mortality due to hypertensive disorders of pregnancy in the Netherlands.[3]

Case fatality rates for the different types of severe maternal morbidity ranged from 0% for uterine rupture to 3.4% for ICU admission, indicating the severity of cases included. Despite the difference in inclusion criteria, our overall case fatality rate is comparable to that in Scotland.[9]

Several risk factors were identified in this study. Due to the nationwide design of the study, we were able to reliably calculate relative risks based on available national reference data. However, for some of them it is important to realise that the condition could be the cause of severe maternal morbidity, but it could also represent the result of it. This is especially true for caesarean section and induction of labour, which were often performed because of the compromised maternal condition. Preterm birth is also closely related. With respect to artificial reproductive techniques, the trend towards single embryo transfer might well lead to reduction of severe maternal morbidity because women with multiple pregnancies were at higher risk.[28] We found Body Mass Index to be an important risk factor for severe maternal morbidity. Since the incidence of overweight and obesity is increasing rapidly in Western countries, we expect severe maternal morbidity to increase in the future. Home delivery appeared to be a strong protective factor for severe maternal morbidity in the Netherlands with a relative risk of 0.1 (95% CI 0.1-0.2). This again demonstrates the proper functioning of the Dutch risk selection system, in which low-risk pregnancies are cared for by midwives in private practices or family physicians outside the scope of the obstetrician.

As was already expected from maternal mortality statistics, non-Western ethnic background appeared to be an independent risk factor for experiencing severe maternal morbidity. Three of the four large immigrant groups in the Netherlands -Moroccan, Turkish, and Dutch Caribbean- however, were not

over-represented in our study. Surinam women were slightly over-represented, especially due to a high incidence of eclampsia. Members of the smaller ethnic minority groups were disproportionately more often represented in our study. Preliminary findings of the qualitative study which complemented the present registration study reveal several issues that may play an important role in their increased risk. Namely, women's relative short stay in the Netherlands, their lack of a social support network, their lack of knowledge of our health care system, communication problems with care providers, and health illiteracy. More qualitative in-depth research into the non-medical backgrounds of these women and the course of events preceding their complication is currently carried out and will shed light on patient-related backgrounds of the increased risk.

The main limitation of this study is that we did not record the individual characteristics of all maternities without severe maternal morbidity during the study period. Therefore, we could not adjust relative risks for confounding variables. Furthermore, despite our efforts, we cannot guarantee the completeness of data. Therefore, our reported incidence figures only represent a minimum level of severe maternal morbidity. Due to the nationwide nature of the study, we depended on the active participation of local coordinating obstetricians for completeness of data. We tried to meet this by keeping coordinators actively involved and providing help in collecting the data. Local coordinators not responding to our monthly request for cases where reminded repeatedly by e-mail and phone. And finally, we thoroughly controlled for underreporting. Underreporting of eclampsia and uterine rupture appeared to be very low during the first five months of the study, and we therefore decided not to control for it in the remainder of the study period. Underreporting of MOH was estimated at 35%, but appeared to be mainly due to relatively less severe complications requiring "only" four units of blood. We expect underreporting to be relatively low for the most severe conditions like acute fatty liver of pregnancy or amniotic fluid embolism, as these are very impressive clinical events that draw the attention of many clinicians involved and will not likely be missed.

The institution of Obstetric High Care (OHC) facilities in university hospitals posed a methodological challenge. Women, who would without any doubt have been treated at an ICU in a non-university hospital, were not admitted to ICU in university hospitals. Inclusion of all admissions to OHC facilities was not merely possible, as most of these admissions were for fetal rather than maternal indication. Coordinators in university hospitals were instructed to report OHC admissions for strict maternal indications as 'other severe maternal morbidity'. More than half of all inclusions in this group came from university hospitals.

The incidence of severe maternal morbidity in the different hospitals varied largely. Although this could be caused by differences in local case management, other possible explanations are bias due to the management based criteria, the degree of underreporting per hospital, and chance. Hospitals, of which we knew that the local coordinator was dedicated and the local system of recognition and reporting of

cases was supported by all clinicians, appeared to have higher incidence figures. Furthermore, incidence was by definition influenced by the management-based criteria 'admission to ICU' and 'MOH requiring four or more units of blood'. We noticed substantial variations in local policy for admission to ICU and transfusion of blood products.

The next step in the process of improving maternal care is to critically assess the course of events that led to the severe condition, as substandard care analysis serves as a basis to improve guidelines and clinical protocols. Substandard care was judged to be present in the majority of assessed cases, mainly at the level of the care providers, indicating that further analysis of cases and improvement of guidelines could reduce severe maternal morbidity.[24] Several local initiatives for auditing of severe maternal morbidity came to our knowledge since this study.

In order to confirm the apparent increase in severe maternal morbidity in Western countries, and to evaluate our own clinical practice in the Netherlands, we would need to establish an ongoing registration of severe maternal morbidity in the Netherlands. This should be incorporated in the Dutch Perinatal Database and be very comprehensive to assure cooperation of each maternity unit. Furthermore, the implementation of national registration of rare obstetric conditions, like UKOSS in the United Kingdom[30], would be valuable and the infrastructure is already in place in the Netherlands.[21]

This survey appears to be a valuable addition to the maternal mortality statistics which have already been registered for decades in the Netherlands. It gives a clear new insight in the problems encountered in obstetric practice nowadays and can serve as a reference work for severe maternal morbidity in the Netherlands and other Western countries. Improvement of the quality of obstetric care through auditing of cases of severe maternal morbidity seems a mandatory challenge.

Conclusion

Severe maternal morbidity complicates at least 0.71% of all pregnancies in the Netherlands, immigrant women experiencing an increased risk. Severe maternal morbidity should be considered internationally as a new indicator of the quality of obstetric care next to maternal mortality statistics. Since substandard care was found in the majority of assessed cases, reduction of severe maternal morbidity seems a mandatory challenge. Therefore, auditing of severe maternal morbidity at local or regional level should be encouraged in order to improve the quality of obstetric care and decrease the incidence of severe maternal morbidity and maternal mortality. Audit should be incorporated in our national public health policy as an instrument of quality control.

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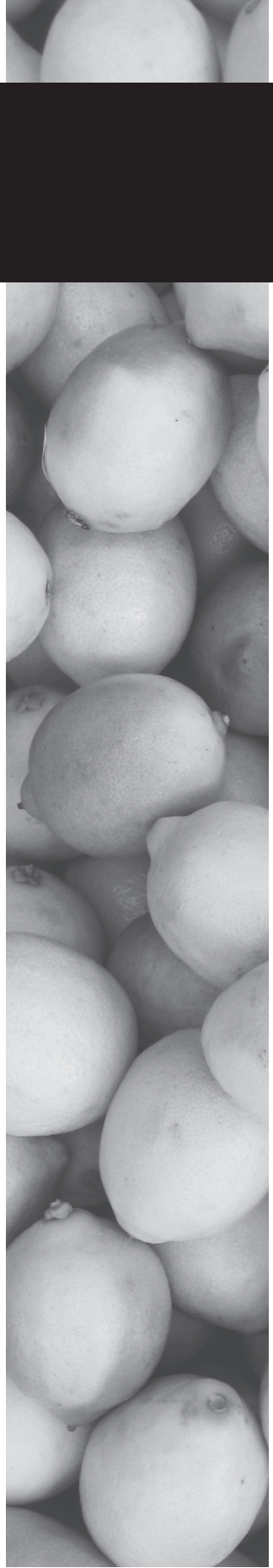
CHAPTER 4



Ethnic disparity in severe acute maternal morbidity: a nationwide cohort study in the Netherlands

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Abstract

Background: There are concerns about ethnic disparity in outcome of obstetric health care in high income countries. Our aim was to assess these differences in a large cohort of women having experienced severe acute maternal morbidity (SAMM) during pregnancy, delivery and puerperium.

Methods: All women experiencing SAMM were prospectively collected in a nationwide population-based design during a two-year period. Women delivering in the same period served as reference cohort. Population-based risks were calculated by ethnicity and by type of morbidity. Additionally, non-Western and Western women having experienced SAMM were compared in multivariable analysis.

Results: All 98 Dutch maternity units participated. A total of 2506 women with SAMM were included, 21.1% of whom were non-Western immigrants. Non-Western immigrants showed a 1.3-fold (95% CI 1.2-1.5) increased risk to develop SAMM. Great differences were observed among different ethnic minority groups, ranging from a non-increased risk for Moroccan and Turkish women to a 3.5-fold (95% CI 2.8-4.3) increased risk for sub-Saharan African women. Low socio-economic status, unemployment, single household, high parity and prior caesarean were independent explanatory factors for SAMM, although they did not fully explain the differences. Immigration-related characteristics differed by ethnic background.

Conclusions: Non-Western immigrants have an increased risk of developing SAMM as compared to Western women. Risks varied greatly by ethnic origin. Immigration-related characteristics might partly explain the increased risk. The results suggest that there are opportunities for quality improvement by targeting specific disadvantaged groups.

Introduction

Although high income countries have become multi-ethnic societies, still little attention is paid to explanations of ethnic disparities in outcome of obstetric health care. A three times elevated risk of maternal mortality has been reported for immigrants as compared to native women in the Netherlands.[1;2] This corresponds with findings from the United Kingdom, with black women even having a six-fold increased risk of maternal mortality compared to native women.[3] Maternal mortality, however, has become rare in high income countries and numbers are small, especially for the smaller ethnic minority groups. Little is known about the risk of severe acute maternal morbidity (SAMM) in immigrants as compared to native women. Therefore, we assessed data related to ethnicity in a large group of women with SAMM and related them to the cohort of all women giving birth in the Netherlands during the study period. Our aim was twofold: firstly, we wanted to assess the population-based incidence of SAMM in different ethnic groups in the Netherlands. Secondly, we wanted to assess adjusted risk factors for the differences between non-Western immigrants and Western women.

Methods

This study is part of a large nationwide cohort study of pregnant women to assess SAMM in the Netherlands, the LEMMoN study. Detailed methods of data collection were described previously.[4] The study enrolled cases of SAMM from 1st August 2004 until 1st August 2006 divided in five categories as shown in Figure 1. The study was centrally approved by the medical ethics committee of Leiden University Medical Centre.

Figure 1. Inclusion criteria for the LEMMoN study

Group 1: ICU admission
- Admission to intensive care unit or coronary care unit, other than for standard postoperative recovery

Group 2: Uterine rupture
- Clinical symptoms (pain, fetal distress, acute loss of contractions, haemorrhage) that led to an emergency caesarean section, at which the presumed diagnosis of uterine rupture was confirmed
- Peripartum hysterectomy or laparotomy for uterine rupture

Group 3: Eclampsia / HELLP syndrome
- Eclampsia
- HELLP-syndrome only when accompanied by liver haematoma or rupture

Group 4: Major Obstetric Haemorrhage
- Transfusion need of ≥ 4 units of packed cells
- Embolisation or hysterectomy for major obstetric haemorrhage

Group 5: Miscellaneous
- Other cases of severe maternal morbidity to the opinion of the treating obstetrician, not to be included in group 1-4

Study Population

All 98 hospitals with a maternity unit in the Netherlands participated in the survey: Eight tertiary care centres, 35 non-university teaching hospitals and 55 other general hospitals. In the Netherlands women with high risk pregnancies and women with low risk pregnancies who develop complications deliver in hospital under supervision of obstetricians (secondary or tertiary care, 59% of all births in the Netherlands). Women with uncomplicated low risk pregnancies deliver under supervision of midwives or family physicians (primary care), either at home (30% of all births) or in hospital (11% of all births).[5] In 2005, 10.3% of the total population and 16.8% of all delivering women were non-Western immigrants.[6] The four largest immigrant groups in the Netherlands originate from Turkey, Morocco and the former Dutch colonies of Surinam and the Dutch Caribbean. Turkish and Moroccan immigrants settled at first in the Netherlands as guest workers in the 1960s and 1970s, and ever since due to family reunion or marriage.

Definition of ethnicity

Ethnicity was defined by geographical ethnic origin. We used the definitions of Statistics Netherlands, based on country of birth of the woman.[6] Accordingly, women born in the Netherlands with at least one parent born abroad were considered to be from the same origin as their non-Dutch parent(s). Immigrants from other European countries, North America, Japan and Indonesia were considered Western immigrants because of their similar cultural and socio-economic background as compared to native Dutch women. Western immigrants and native Dutch women constitute the group of Western women. All other immigrants were considered non-Western and constitute the group of non-Western women.

Data collection

Included in the study were all women who experienced SAMM or death during pregnancy, childbirth or puerperium. Maternal socio-demographic characteristics (age, body mass index, geographical ethnic origin, socio-economic status, smoking, single household, unemployment, language skills, length of residence, immigration status), and obstetric characteristics were recorded for each case. We also recorded general history, categorised as hypertension, diabetes, cardicac disease, clotting disorders, thyroid disorders, epilepsy, pulmonary disorders, psychiatric disorders and miscellaneous. A woman was considered unemployed if her reported job was 'none', or if she had reported to be a mother, student or housewife. Overweight was defined as BMI $\geq$ 25.0, obesity as BMI $\geq$ 30.0. We used the six-digit postal code as a proxy for socio-economic status. For each postal code area, comprising of on average 25 persons, Statistics Netherlands has estimated a validated socio-economic status (SES) indicator by combining mean family income and house price.[7]

Statistical analysis

Denominator data were obtained from Statistics Netherlands.[6] They were based on birth registrations during the exact study period, corrected for multiple births and stillbirths after 24 weeks of gestation. To calculate population-based incidence by ethnicity, denominator data for the number of women from the different ethnic groups were also obtained from Statistics Netherlands. For the four largest immigrant groups and the aggregate group of other non-Western immigrants (consisting of women from sub-Sahara Africa, Middle East, Far East, Latin America and miscellaneous), numbers of mothers giving birth were used. For more specific sub-analysis of the smaller ethnic minority groups, we had to use numbers of women of fertile age (15-40 years) to calculate the denominator thereby neglecting differences in fertility rate. Population based relative risks (RR) with 95% confidence intervals (CI) were calculated for each immigrant group and type of SAMM, as compared to all Western women in the Netherlands.

To identify risk estimators for the differences in incidence of SAMM, odds ratios (OR) with 95%-CI were calculated for the whole group of non-Western immigrants having experienced SAMM as compared to Western women having experienced SAMM, with ethnicity defined dichotomous. Differences were assessed using the Chi square or Student T test whenever appropriate, considering p-values < 0.05 significant. Significant risk estimators in univariable analysis were entered into a multivariable regression model to calculate adjusted odds ratios for SAMM. Statistical analysis was performed using Statistical Package for the Social Sciences 14.0 (SPSS Inc., Chicago, IL, USA).

Results

Population-based incidences and relative risks

During the study period, there were 371,021 deliveries in the Netherlands. From all 2352 (98 hospitals, 24 months) monthly notification cards, 97% were returned. Therefore, the study represents 358,874 deliveries in the Netherlands. A total of 2552 cases of SAMM were reported. We received detailed data on 2513 cases (98.5%). Seven cases were excluded because of unknown ethnicity, leaving 2506 cases available for analysis; 529 non-Western immigrants (21.1%) and 1977 Western women. Geographical ethnic origin is shown in table 1. The overall incidence of SAMM was 7.1 per 1000 deliveries, 8.4 per 1000 among non-Western women and 6.3 per 1000 among Western women. The overall RR for non-Western immigrants to experience SAMM was 1.3 (95% CI 1.2-1.5). Large differences were observed among the different ethnic groups and the different categories of SAMM (Table 2). Especially sub-Saharan African women showed an increased RR irrespective of the morbidity category.

Table 1. Geographical ethnic origin (n=2513)

	n (%)	
Western Overall	1977	(78.7%)
The Netherlands	1864	(74.2%)
Western Europe	48	(1.9%)
Eastern Europe	27	(1.1%)
Miscellaneous Western	44	(1.8%)
non-Western Overall	529	(21.1%)
Morocco	116	(4.6%)
Turkey	87	(3.5%)
Surinam	82	(3.3%)
Dutch Caribbean	29	(1.2%)
Sub-Saharan Africa*	92	(3.7%)
Middle East*	34	(1.4%)
Far East*	53	(2.1%)
Latin America*	15	(0.6%)
Miscellaneous non-Western*	22	(0.9%)
Unknown	7	

*** referred to as 'other non-Western' in Figure 2**

The overall RR of SAMM in this subgroup was 3.5 (95% CI 2.8 to 4.3), ranging from 3.0 (95% CI 2.2-3.9) for major obstetric haemorrhage to 6.2 (95% CI 3.6-10.6) for eclampsia. Turkish and Moroccan women did not have elevated RRs for any of the morbidity categories. Surinamese women had elevated RRs for all categories of SAMM except for uterine rupture. Dutch Caribbean women only had an elevated RR for eclampsia.

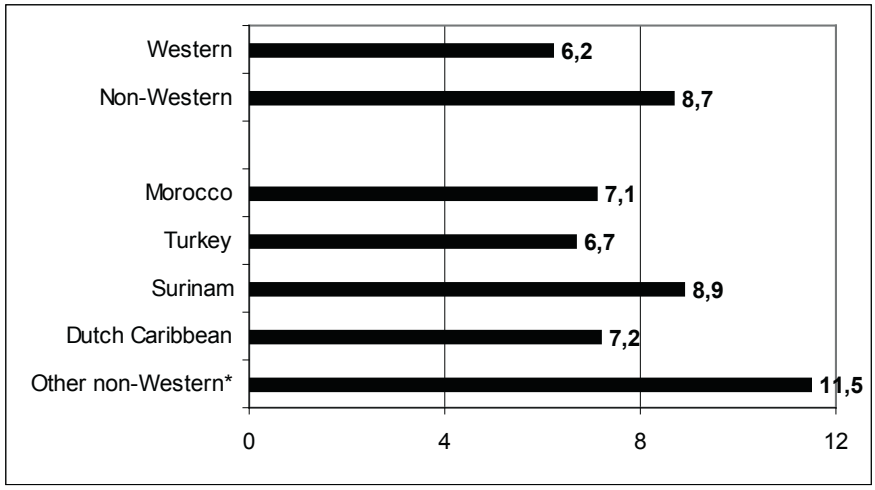
Table 2. Relative risks and 95% confidence intervals for severe acute maternal morbidity by ethnicity and by type of morbidity as compared to the Western women in the Netherlands

RR (95% CI)	n	ICU admission (n=837)	Uterine rupture (n=218)	Eclampsia (n=230)	MOH (n=1590)	Total† (n=2506)
Western	1977	1	1	1	1	1
Non-Western Overall	529	1.5 (1.2-1.7)*	1.4 (1.0-1.9)*	1.7 (1.3-2.3)*	1.3 (1.1-1.4)*	1.3 (1.2-1.5)*
Morocco	116	1.3 (0.9-1.7)	1.0 (0.5-2.0)	1.2 (0.7-2.3)	1.1 (0.8-1.4)	1.1 (0.9-1.4)
Turkey	87	1.0 (0.7-1.5)	1.4 (0.8-2.7)	1.1 (0.6-2.3)	1.0 (0.7-1.3)	1.1 (0.9-1.3)
Surinam	82	1.6 (1.1-2.2)*	1.2 (0.5-2.7)	2.4 (1.3-4.3)*	1.4 (1.0-1.8)*	1.4 (1.1-1.8)*
Dutch Caribbean	29	1.7 (1.0-2.9)	0.9 (0.2-3.7)	2.7 (1.2-6.2)*	0.9 (0.5-1.5)	1.1 (0.8-1.6)
sub-Saharan Africa	90	3.7 (2.6-5.3)*	3.9 (2.0-7.7)*	6.2 (3.6-10.6)*	3.0 (2.2-3.9)*	3.5 (2.8-4.3)*
Middle East	33	1.6 (0.9-2.9)	1.0 (0.3-4.2)	2.1 (0.8-5.6)	1.7 (1.1-2.5)*	1.5 (1.1-2.1)*
Far East	49	2.4 (1.5-3.8)*	1.9 (0.7-5.1)	1.4 (0.5-4.5)	2.4 (1.7-3.3)*	2.2 (1.7-2.8)*

ICU=Intensive Care Unit. MOH=Major Obstetric Haemorrhage. †=numbers do not add up to total as women could have more than one severe morbid condition; also includes cases included as 'Miscellaneous', *=significant.

Women from the Middle and Far East had an elevated RR overall but this reached only significance for major obstetric haemorrhage. RR for non-Western immigrant women overall was increased for all morbidity categories. Further analysis of the group of sub-Saharan African women revealed that risks were particularly elevated for women from Congo (RR 7.0, 95% CI 4.2-11.9), Ghana (RR 6.3, 95% CI 4.1-9.7) and Sudan (RR 5.9, 95% CI 2.8-12.3). Among Western immigrants, relative risks were comparable to or even lower than for native Dutch women. Population based incidence of SAMM by ethnicity is shown in figure 2. Since more specific data on ethnicity of mothers giving birth were not available for the smaller ethnic minority groups, we undertook a sub analysis using the number of women of fertile age as the denominator. This sub analysis revealed that incidence of SAMM was especially increased in women from sub-Sahara Africa with 150 cases per 100,000 women of fertile age as compared with 43 per 100,000 in Western women. For women from the Far East and Middle East, incidences were 93 and 65 per 100,000 women of fertile age, respectively.

Figure 2. Population-based incidence of severe maternal morbidity by ethnicity (per 1000 deliveries)



* **includes sub-Sahara Africa, Middle East, Far East, miscellaneous**

Risk estimators in non-Western immigrants vs. Western women with SAMM

We also compared non-Western and Western women who had experienced SAMM. Differences in characteristics between both groups are shown in table 3. Univariable analysis revealed that low SES, unemployment, single household, age under 20, age over 40, overweight, and diabetes were associated with SAMM in non-Western immigrants. Table 4 shows unadjusted and adjusted odds ratios for SAMM after adjustment for age, parity, SES, unemployment, single household, BMI, diabetes, prior caesarean delivery, antenatal care at booking by the obstetrician and late booking for antenatal care in a multi-

logistic regression model. Significant risk factors after adjustment were low SES (OR 5.0; 95% CI 2.9-8.4), unemployment (OR 4.0; 95% CI 2.6-6.2), single household (OR 2.7; 95% CI 1.2-6.4), overweight (OR 1.5; 95% CI 1.0-2.3), prior caesarean delivery (OR 1.9; 95% CI 1.2-3.2), antenatal care at booking by the obstetrician (OR 1.6; 95% CI 1.1-2.3), and parity ≥ 3 (OR 2.3; 95% CI 1.1-5.1). Entering age and body mass index as continuous variables did not change the estimates of interest essentially. Although ventouse delivery appeared to be a risk estimator in univariable analysis, it was not entered into the multivariable model because it was uncertain whether the ventouse constituted the risk factor or the consequence of severe morbidity itself.

Table 3. Characteristics of non-Western and Western women with severe acute maternal morbidity

	non-Western (n=529)		*Western (n=1977)*		*p-value*
Age in years (mean)	(31.4)		(32.2)		<0.001
< 20	16	3.0%	15	0.8%	<0.001
20-40	473	89.4%	1880	95.1%	<0.001
>40	40	7.6%	82	4.1%	0.001
Socio-economic status indicator					
Low	299	62.6%	401	23.1%	<0.001
Modal	130	27.2%	861	49.7%	<0.001
High	49	10.3%	471	27.2%	<0.001
Unknown	*51*		*244*		
Single household	43	8.1%	32	1.6%	<0.001
Unemployed	157	44.5%	148	11.4%	<0.001
Smoking during pregnancy	31	10.9%	145	12.3%	0.52
Body mass index in kg/m^2 (mean)	(25.8)		(24.4)		<0.001
<18.5	12	3.6%	36	2.7%	0.36
18.5 – 24.9	165	49.8%	851	63.4%	<0.001
25.0-29.9 (overweight)	93	28.1%	295	22.0%	<0.05
30.0-34.9 (obese)	34	10.3%	92	6.9%	<0.05
≥ 35.0 (morbidly obese)	27	8.2%	68	5.1%	<0.05
Unknown	*198*		*635*		
Chronic diseases					
any*	136	25.7%	485	24.5%	0.58
hypertension	24	4.5%	82	4.1%	0.69
Diabetes	13	2.5%	21	1.1%	<0.05
cardiac disease	17	3.2%	45	2.3%	0.22
clotting disorder	9	1.7%	53	2.7%	0.20

***groups mentioned beneath, thyroid disorders, epilepsy, pulmonary disorders, psychiatric disorders, miscellaneous**

Characteristics related to the immigration of the 529 non-Western women overall are shown in table 5. Thirty asylum seekers (6.5 %) or illegal women (2.4 %) were reported, mainly from sub-Sahara Africa. Of 91 of the women (43%), duration of stay in the Netherlands was five years or less. Language barriers were reported in 38% of all immigrants. Of 16 cases in which proper communication was deemed impossible, only in one case a professional interpreter was arranged. The most important possibly associated risk estimators for the differences in SAMM among the different ethnic groups are summarized in table 6. The rate of recent immigration was highest among women from sub-Sahara Africa, Middle East and Far East. Immigrants from Sub-Sahara Africa, Middle East, Far East and Turkey showed the highest rates of women with language barriers (65, 56, 49 and 49%, respectively). Nine of the 16 women in which proper communication was deemed impossible were Turkish or Moroccan immigrants.

Table 4. Unadjusted and adjusted odds ratios for severe acute maternal morbidity

Factor	*non-Western (n=529)*		*Western (n=1977)*		*univariable OR (95% CI)*	*multivariable OR (95% CI)***
Patient						
age < 20	16	3.0%	15	0.8%	4.1 (2.0-8.3)*	0.5 (0.2-2.0)
age ≥ 40	40	7.6%	82	4.1%	1.9 (1.3-2.8)*	1.0 (0.4-2.3)
low socio-economic status	299	62.6%	401	23.1%	5.5 (4.5-6.9)*	4.2 (2.9-6.0)*
single household	43	8.1%	32	1.6%	5.4 (3.4-8.6)*	2.9 (1.2-6.8)*
Unemployed	153	44.5%	156	11.4%	6.2 (4.8-8.2)*	4.1 (2.7-6.2)*
BMI ≥ 25 (overweight)	154	46.5%	455	33.9%	1.7 (1.3-2.2)*	1.5 (1.0-2.3)*
BMI ≥ 30 (obese)	61	18.4%	160	11.9%	1.7 (1.2-2.3)*	0.9 (0.5-1.5)
diabetes	13	2.5%	21	1.1%	2.3 (1.2-4.7)*	0.1 (0.0-2.5)
Pregnancy						
initial antenatal care by obstetrician	244	46.1%	697	35,3%	1.6 (1.3-1.9)*	1.6 (1.1-2.4)*
late booking (gestational age ≥20w)	39	9.3%	55	3.5%	2.8 (1.8-4.3)*	1.9 (0.8-4.3)
prior caesarean delivery	122	23.1%	357	18.1%	1.4 (1.1-1.7)*	1.9 (1.1-3.1)*
parity 0	217	41.0%	1031	52.3%	0.6 (0.5-0.8)*	1.3 (0.8-2.1)
parity ≥3	64	12.1%	63	3.2%	4.2 (2.9-6.0)*	2.3 (1.0-4.9)*
multiple pregnancy	34	6.4%	168	8.5%	0.7 (0.5-1.1)	
artificial reproduction techniques: IVF/ICSI	23	4.3%	97	4.9%	0.9 (0.5-1.4)	
Delivery						
home delivery	16	3.0%	149	7.5%	0.4 (0.2-0.6)*	
induction of labour	127	24.0%	532	26.9%	0.9 (0.7-1.1)	
Epidural						
caesarean delivery without labour	130	24.6%	411	20.8%	1.2 (1.0-1.6)	
caesarean delivery overall	243	45.9%	827	41.8%	1.2 (1.0-1.4)	
preterm birth (<37w)	159	32.1%	530	28.3%	1.2 (1.0-1.5)	
post term birth (≥42w)	34	6.9%	94	5.0%	1.4 (0.9-2.1)	

*** statistically significant; **Adjusted for age, parity, SES, single household, unemployment, BMI, diabetes antenatal care at booking by obstetrician, prior CS and late booking for antenatal care**

Table 5. Immigration characteristics of non-Western women (n=529)

	cases	*n (%)*
Immigration status		
Permanent	293	86.4%
Temporary	16	4.7%
asylum seeker	22	6.5%
Illegal	8	2.4%
unknown (n=190, 35.9%)		
Years since immigration		
≤1 year	30	14.2%
1-5 year	61	28.9%
5-10 year	46	21.8%
>10 year	*74*	35.1%
unknown (n=318, 60.1%)		
Language skills		
small language barrier	65	15.9%
considerable language barrier	73	17.9%
communication impossible	16	3.9%
no language barrier	254	62.3%
unknown (n=121, 22.9%)		
Interpreter used		
family member	68	17.1%
professional	9	2.3%
None	320	80.6%
unknown (n=132, 25.0%)		

Table 6. Demographic and immigration-related characteristics of women with SAMM by ethnic minority group*

	low SES	unemploy-ment	single household	≤5 years in NL	asylum seeker/ illegal	considerable language barrier
Morocco (n=116)	76	54	2	38	0	20
Turkey (n=87)	68	54	7	30	4	37
Surinam (n=82)	53	20	9	21	2	0
Dutch Caribbean (n=29)	68	37	31	38	0	4
Sub-Sahara Africa (n=92)	63	58	17	55	32	26
Middle East (n=34)	62	48	6	47	29	35
Far East (n=53)	37	43	0	59	6	31
Eastern Europe (n=27)	48	22	11	63	18	5

***numbers are percentages within each ethnic minority group**

Discussion

This study presents an overall picture of ethnic differences in SAMM in a nationwide design. Increased risk for non-Western women to experience SAMM was present among all categories of SAMM (intensive care unit admission, uterine rupture, eclampsia, major obstetric haemorrhage), although the relative risks were lower than previously reported for maternal mortality.[2;3;8] Ethnic differences were earlier reported for obstetric complications including pre-eclampsia,

low birth weight, perinatal death and SAMM.[9-14] In all these studies non-Western ethnic origin was found to be a risk factor. Very recently, a comparable national study was published on ethnic variation in SAMM in the United Kingdom.[14] Although this study only concerned some specific subgroups of SAMM and numbers in ethnic minority groups were small, the results are largely comparable. Like in the present study, black African (~sub-Saharan African) and black Caribbean (~Surinamese and Dutch Caribbean) women had the highest risks.

The increased incidence of SAMM among non-Western immigrants found in this study may be explained by genetic, socio-demographic and lifestyle related differences, but there are also several factors related to immigration that possibly influence the risk of SAMM. The role of these factors is difficult to quantify in comparative studies as indigenous women are not exposed to these risk factors. However, from the qualitative study that was conducted to complement the quantitative one presented in this article, it is clear that also patient-related and health care related factors play a role.[15] Immigration-related risk estimators mentioned in table 6 were confirmed in this study. Other related factors included: lack of health knowledge, asylum seeker or illegal status, weak social and economic position and as a consequence daily stress factors, factors related to (recent) immigration such as language barriers, small social (ethnic) network and inexperience with the system and policies of obstetric health care in the Netherlands.

Our study did not clearly confirm the recent finding that late booking for antenatal care is an important contributor to maternal morbidity among immigrants, although a trend was observed.[3;10]

It is striking that great differences in risks of SAMM existed between the distinct ethnic groups in the Netherlands. Turkish and Moroccan women showed relative and absolute risks comparable to Western women, while sub-Saharan African women showed a three to six-fold increased risk. Among the four largest immigrant populations with a relatively long history in the Netherlands, only Surinamese women were overall more susceptible to developing SAMM, mainly due to an elevated incidence of eclampsia. Dutch Caribbean women also had an elevated RR of eclampsia. This pattern could be caused by the relatively large proportion of women of black African descent among Surinamese and Dutch Caribbean women, since black African women were found to have an increased risk of experiencing pre-eclampsia by us and others.[11] Also, single household, which appeared to be an independent risk factor in this study, is more common among Dutch Caribbean women, leading to weak social networks and lack of social support.[12;16]

The currently most supported hypothesis is that ethnic disparity can be largely explained by the low SES of non-Western immigrants.[17] However, part of the disparity can not be explained using multivariable logistic regression models, as some important possible risk factors cannot be included in the model since they only apply to non-Western women. Like others, we also found

low SES to be an independent risk factor for SAMM in multivariable analysis. However, we found that this was not compatible with the most important observational finding that women from the large Turkish and Moroccan immigrant populations -residing in the Netherlands for more than 40 years- do not show elevated RR to experience SAMM despite their generally low SES. Therefore, the explanation for the differences in risk of experiencing SAMM should rather be sought in factors related to immigration. The strong social-ethnic networks and collectively shared experiences with the Dutch health care system of Turkish and Moroccan immigrant populations seem to prevent them from developing SAMM. Even though many Turkish and Moroccan women have recently come to the Netherlands because of family reunion or marriage, their risk was not increased despite frequently observed language barriers and acculturation problems.

Relative risks appeared to be especially increased in women from the smaller ethnic minority groups who recently arrived in the Netherlands. Short residence in the Netherlands possibly results in a weak social network and inadequate knowledge of the health care system, contributing to this increased risk. Other disadvantages related to recent arrival in the Netherlands are an illegal status, health insurance problems, communication barriers and inadequate health skills to participate in the interaction with health care providers.

The increased risk for non-Western immigrants was most definite in the category of eclampsia. This may not be surprising, as in hypertensive disorders, recognition and interpretation of often subtle signs and symptoms by obstetric health care providers plays an important role in the prevention of severe complications, and this can be hampered by communication barriers between patient and health care provider as was found in the qualitative analysis. We therefore recommend providing a leaflet to all pregnant women containing warning signs of pregnancy complications. This leaflet should be available in all appropriate languages.

This study has the following limitations. First, every definition of ethnicity is arbitrary. In our opinion the definition by geographical ethnic origin is the most objective, although it does not completely account for racial, cultural and socio-economic subgroup differences. Also, arbitrary choices have to be made with respect to geographical regions. Another limitation is that immigration characteristics were lacking in numerous cases. Cultural background is obviously not an item usually discussed by health care providers during antenatal or intrapartum care. Despite all our efforts data collection could be incomplete due to the large nationwide character of the study. However, especially for the severest complications, we are quite sure not to have missed a substantial amount of cases and inclusion bias towards Western or non-Western women is unlikely. For sub-analysis of the different small ethnic minority populations, we had to rely on numbers of women of fertile age as the denominator instead of mothers giving birth.

Although this may introduce some bias due to differences in fertility rates, the main analysis showed that the incidence of SAMM in the aggregate group of other non-Western immigrants was indeed almost twice as high compared with Western women.

Key-points

- Risk of severe maternal morbidity varies greatly by ethnicity, ranging from a non-increased risk for Moroccan and Turkish women to a 3.5-fold increased risk for sub-Saharan African women.
- More attention should be drawn to this subject in medical education and patient care.
- Although low SES is an important contributor in explaining health inequalities, it does not solely explain the increased risk of non-Western immigrants to experience SAMM.
- Immigration–related characteristics deserve more attention as explanation for inequality in health care outcome.
- The results suggest that there are opportunities for quality improvement by targeting health care reforms on specific disadvantaged groups.

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CHAPTER 5

Obstetric intensive care unit admission: a two-year nationwide population-based cohort study

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Abstract

Purpose: As part of a larger nationwide enquiry into severe maternal morbidity, our aim was to assess the incidence and possible risk factors of obstetric intensive care unit (ICU) admission in the Netherlands.

Methods: In a 2-year nationwide prospective population-based cohort study, all ICU admissions during pregnancy, delivery and puerperium (up to 42 days postpartum) were prospectively collected. Incidence, case fatality rate and possible risk factors were assessed, with special attention to the ethnic background of women.

Results: All 98 Dutch maternity units participated in the study. There were 847 obstetric ICU admissions in 358,874 deliveries, incidence being 2.4 per 1000 deliveries. Twenty-nine maternal deaths occurred, resulting in a case fatality rate of 1 in 29 (3.5%). Incidence of ICU admission varied largely across the country. Thirty-three percent of all cases of severe maternal morbidity were admitted to an intensive care unit. Most frequent reasons for ICU admission were major obstetric haemorrhage (48.6%), hypertensive disorders of pregnancy (29.3%) and sepsis (8.1%). Assisted ventilation was needed in 34.8%; inotropic support in 8.8%. In univariable analysis, non-Western immigrant women had a 1.4-fold (95% CI 1.2-1.7) increased risk of ICU admission as compared to Western women. Initial antenatal care by an obstetrician was associated with a higher risk and home delivery with a lower risk of ICU admission.

Conclusions: Population based incidence of obstetric ICU admission in the Netherlands was 2.4 per 1000 deliveries. Obstetric ICU admission accounts for only one third of all cases of severe maternal morbidity in the Netherlands.

Introduction

Pregnancy, delivery and puerperium can be complicated by severe maternal morbidity necessitating intensive care unit (ICU) admission. Management of the critically ill obstetric patient is very complex and requires cooperation of both obstetrician and intensivist/anaesthetist. One facility-based study has been performed in the Netherlands, which reported an incidence of 7.6 per 1000 deliveries.[1] However, this study was inevitably biased by the long (12-year) inclusion period, during which technological and therapeutic changes have occurred. Moreover, it was held in a tertiary care centre only.

The primary aim of this study was to assess incidence, case fatality rate and possible risk factors of obstetric intensive care unit admission on a population-based national level. As ethnicity appeared to be a significant risk factor for severe maternal morbidity and maternal death, we were especially interested in the association of ethnicity with obstetric ICU admission.[1-3]

Methods

This study was part of a broader nationwide enquiry into severe maternal morbidity in the Netherlands, called LEMMoN.[4] In this study, which enrolled cases from August 1st, 2004 until August 1st, 2006, all Dutch hospitals with an obstetric unit participated. This involves 10 tertiary care centres, 33 non-academic teaching hospitals and 55 general hospitals. There is no private obstetric care in the Netherlands. All hospitals with an obstetric unit are equipped with an ICU, subdivided into three levels. Level 1 ICUs are equipped for monitoring and treatment of patients with single organ dysfunction, if necessary with assisted ventilation. Patients with severe diseases can be monitored and treated at level 2 ICUs and level 3 ICUs are equipped for patients with very complicated diseases with multiple organ dysfunction, who need constant availability of an intensivist. According to the Netherlands Health Care Inspectorate, there are 49 level 1 units, 25 level 2 units and 24 level 3 units in the Netherlands.[5] In addition to a level 3 ICU, all tertiary care centres are also equipped with an obstetric high care unit, which has one-to-one nursery care and cardiac monitoring, but no assisted ventilation. There are no special obstetric ICUs in the Netherlands. Forty-one percent of all deliveries are considered low-risk pregnancies and take place under the responsibility of primary care providers, three quarters of which are home births. Any complication occurring in primary care will be referred to a hospital and thus be notified. ICU admission was defined as admission to an ICU or coronary care unit, but not to an obstetric high care unit. Short stay at an ICU only because of postoperative nursery, was not considered as an ICU admission.

Requests for notification of cases of obstetric ICU admission during pregnancy, delivery or puerperium were, along with other types of severe maternal morbidity, sent to all local coordinators

on a monthly basis. Cases were communicated to the National Surveillance Centre for Obstetrics and Gynaecology (NSCOG) in a web-based design. If no cases of obstetric ICU admission occurred, this was also reported. Reminders were sent to non-responders every month until they had returned the monthly notification card.

After notification, a completed case record form was sent to us, accompanied by anonymous photocopies of all relevant sections of the hospital case notes and correspondence. A detailed review of cases was completed by two of the authors (JZ and JD) and all cases were entered into an Access database. Cases of maternal mortality were reported to the national Maternal Mortality Committee of the Netherlands Society of Obstetrics and Gynaecology by the attending obstetrician as usual. These cases were eventually added to the database.

We recorded maternal characteristics (age, body mass index, parity, ethnicity, smoking), and all variables concerning pregnancy and delivery. We also recorded data specifically related to the ICU admission: admission and discharge date, diagnosis on admission, vital signs on admission, interventions and laboratory results. A total of 150 items were entered into the database for each case. Characteristics of each hospital were also recorded (university or teaching hospital, annual number of deliveries and level of ICU). Major obstetric haemorrhage (MOH) was defined as transfusion need of four or more units of packed cells or hysterectomy or embolization. When more than one diagnosis was provided, the case was classified according to the most serious condition.

Ethnicity was defined by country of origin ('geographical ethnic origin') and grouped according to the most common population groups in the Netherlands (Western, Moroccan, Surinam/Dutch Antilles, Turkish, sub-Saharan African and Central and Eastern Asian). Women born in the Netherlands with at least one parent born abroad were considered to be from the same origin as their non-Dutch parent(s). Women from other European countries, North America, Japan and Indonesia were considered Western immigrants according to Statistics Netherlands because of their cultural background and socio-economic position, which is comparable with Western women. All other immigrant women were considered non-Western.

Denominator data for the number of births in the Netherlands and national reference values for possible risk factors for obstetric ICU admission were obtained from Statistics Netherlands and The Netherlands Perinatal Registry (LVR-2).[6,7] The case fatality rate was calculated by dividing the number of deaths by the total number of ICU admissions. Relative risks and confidence intervals compared with the general pregnant population were calculated using univariable analysis. Odds ratios and confidence intervals compared with women with severe maternal morbidity not admitted to ICU were calculated using multivariable logistic regression analysis. Differences between groups were identified using the Chi square test, significance was defined as $p < 0.05$. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS 16.0). The study was centrally

approved by the medical ethics committee of Leiden University Medical Centre.

Results

Incidence

During the study period, 371,021 deliveries occurred in the Netherlands. From all 2352 (98 hospitals, 24 months) monthly notification cards, 97% were returned. Therefore, the study represents 358,874 deliveries in the Netherlands. A total of 2552 cases of severe maternal morbidity were reported to LEMMoN. Of those, 847 cases (33.2%) concerned ICU admissions. We received no detailed data in ten cases, leaving a total of 837 cases available for analysis. Characteristics of women are shown in Table 1. The population-based incidence of obstetric ICU admission was 2.4 per 1000 deliveries.

Table 1. Characteristics of women in the study

	n	%
Age (years, n=837)		
<20	13	1.6
20-34	579	69.2
35-39	201	24.0
≥40	44	5.3
Body Mass Index (kg/m^2, n=547)		
< 18.5	28	5.1
18.5 - 24.9	320	58.5
25 - 29.9 (overweight)	114	20.8
30 - 34.9 (obese)	45	8.2
≥ 35 (morbidly obese)	40	7.3
Chronic disease (n=837)[a]		
No disease	603	72.0
One or more diseases	234	28.0
Hypertension	47	5.6
Chronic Obstructive Pulmonary Disease	34	4.1
Cardiac disease	29	3.5
Thrombosis/clotting disorder	21	2.5
Diabetes	17	2.0
Other[b]	120	14.3

[a]Numbers do not add up to the total as women could suffer from more than one disease;
[b]Psychiatric disorders, migraine, autoimmune-, thyroid- and kidney diseases, epilepsy and malignancies

Incidence varied largely by hospital, ranging from 0 to 13.2 per 1000. The mean 'hospital-incidence', considering only births in that hospital under responsibility of the obstetrician and thus disregarding births under primary care, was 3.8 per 1000 overall; 8.7 for tertiary care centres and 3.4 for general hospitals ($p<0.05$). Regarding only non-academic hospitals, low-volume (<1000 deliveries) units had an incidence of 4.1 per 1000, intermediate-volume (1000-1500 deliveries) units 2.4 per 1000 and high-volume (>1500 deliveries) units 3.3 per 1000. The incidence of ICU admission was significantly increased

in low-volume hospitals as compared to other non-academic hospitals (p<0.05) and significantly lower in intermediate-volume hospitals as compared to other hospitals (p<0.001). In tertiary care centres, 20.2% of women were referred from other hospitals. In non-academic teaching hospitals 4.3% were referred from other hospitals. Differences by ICU-level are shown in Table 2.

Table 2. Characteristics of admission by intensive care unit level[a]

	Level 1		Level 2		Level 3		p-value
	n	%	n	%	n	%	
Number of women admitted to ICU[b]	266	35.6	230	35.1	341	29.7	0.01
Mean duration of ICU stay	1.9 days[c]		2.3 days[d]		3.2 days[e]		
Maternal mortality	4	1.5	10	4.3	15	4.4	0.11
Induction of labour	83	31.2	70	30.4	86	25.2	0.20
Inotropic support	10	3.8	18	7.8	46	13.5	<0.001
Assisted ventilation	32	12.0	87	37.8	172	50.4	<0.001
Diagnosis							
Major obstetric haemorrhage	110	41.4	120	52.2	151	44.3	0.05
Hypertensive disorders of pregnancy	111	41.7	46	20.0	67	19.6	<0.001
Cardiac disease	8	3.0	19	8.3	28	8.2	0.02
Sepsis	12	4.5	16	7.0	27	7.9	0.23
Pulmonary disease	6	2.3	12	5.2	25	7.3	0.02
Cerebral disease	2	0.8	3	1.3	14	4.1	0.01
Liver/pancreatic disease	4	1.5	2	0.9	8	2.3	0.39
Thrombo-embolism	2	0.8	4	1.7	7	2.1	0.42
Anaesthetic complication	3	1.1	4	1.7	5	1.5	0.85
Miscellaneous	8	3.0	4	1.7	9	2.6	0.65

[a]Intensive care unit levels are described in the methods section; [b]rates reflect percentage of all women with severe maternal morbidity; [c]data missing for 22 women; [d]data missing for 21 women; [e]data missing for 20 women.

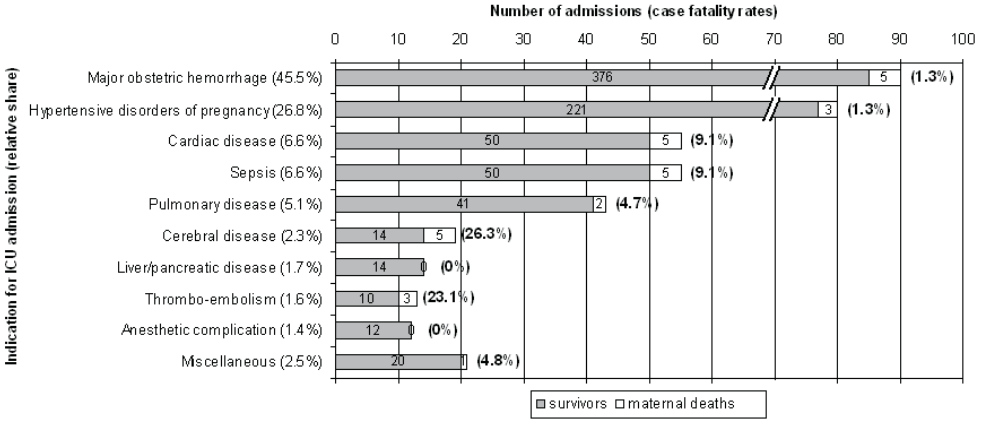
Rates of ICU admission for different subgroups of severe maternal morbidity were 12% for uterine rupture, 42% for eclampsia and 27% for major obstetric haemorrhage. Twenty-six women (3.1%) were admitted to ICU during early pregnancy, 191 (22.8%) antepartum and 620 (74.1%) postpartum. Mean duration of ICU stay was 2.9 days (range 1 to 71). Ninety-one women (10.9%) stayed in ICU for more than four days. Mean gestational age at admission was 36 weeks and 3 days. Of all women, 234 (28.0%) had at least one chronic disease (Table 1). Forty women (4.8%) had multiple chronic diseases.

Diagnoses at admission

Diagnoses at admission are shown in figure 1. Cerebral disease and thrombo-embolism had the highest case fatality rates with 26.3% and 23.1%, respectively. Regarding only antepartum diagnoses, 47.6% of

women were diagnosed with hypertensive disorders of pregnancy, 13.6% with MOH and 9.9% with sepsis. Women admitted postpartum were mainly diagnosed with MOH (55.2%) and hypertensive disorders of pregnancy (21.5%). Most frequent diagnoses during early pregnancy were MOH (50.0%) and sepsis (26.9%), mostly caused by ectopic pregnancy or abortion. Regarding differences between hospitals, MOH (39.9% vs. 47.4%) and hypertensive disorders of pregnancy (16.8% vs. 30.0%) were less diagnosed in tertiary care centres as compared with general hospitals. Rare life-threatening diseases like cardiac, liver/pancreatic, cerebral, septic and thrombo-embolic diseases were more frequently diagnosed in tertiary care centres (33.2% vs. 13.8%). Roughly the same results were found for high-volume hospitals in comparison with low-volume hospitals.

Figure 1. Indications for intensive care unit admission and their rate, absolute number and case fatality rate.



Interventions during ICU stay

Assisted ventilation was needed in 291 women (34.8%), inotropic support in 74 (8.8%) and renal dialysis in 16 (1.9%). Central venous and Swan Ganz catheter insertion were reported in 123 (14.7%) and 21 (2.5%) women, respectively. Packed cells were transfused in 505 women (60.3%, range 1-50). Fresh frozen plasma and pooled platelets were administered in 365 (43.6%) and 220 (26.3%) women, respectively. In 82 (9.8%) and 92 (11.0%) cases, arterial embolization and hysterectomy were performed because of MOH.

Possible risk factors of ICU admission

Non-Western women had a higher risk of being admitted to ICU than Western women. Especially women from sub-Sahara Africa and Eastern Asia experienced increased risks of ICU admission (Table 3). Other possible risk factors for ICU admission as compared with the general pregnant population and with women with severe maternal morbidity not admitted to ICU are shown in

table 4. A continuum of risk can be observed from lower risks in the general pregnant population to higher risks among women with severe maternal morbidity and highest risks among women with severe maternal morbidity admitted to ICU.

Table 3. Unadjusted relative risks of intensive care unit admission by ethnicity

	n	(%)	RR (95% CI)
Western	648	77.4	1
non-Western	186	22.2	1.4 (1.2-1.7)
Morocco	43	5.1	1.3 (0.9-1.7)
Turkey	26	3.1	1.0 (0.7-1.4)
Surinam	29	3.5	1.5 (1.1-2.2)
Dutch Antilles	14	1.7	1.7 (1.0-2.9)
sub-Saharan Africa	31	3.7	3.6 (2.5-5.1)
Central Asia	11	1.3	1.5 (0.8-2.7)
Eastern Asia	17	2.0	2.1 (1.3-3.4)
Unknown	3	0.4	

Maternal deaths

There were 29 maternal deaths during ICU stay, giving a case fatality rate of 1 in 29 (3.5%). Underlying causes of death and case fatality rates by diagnosis on admission are shown in figure 1. The most frequent mode of death was cerebral (cerebrovascular haemorrhage, encephalopathy, brain stem compression and thrombosis). Comparison of characteristics of deaths and survivors revealed no significant differences due to small numbers. Compared with women with severe maternal morbidity who were not admitted to ICU, women admitted to ICU had a significantly higher case fatality rate (3.4% vs. 1.1%, $p<0.001$).

Table 4. Risk indicators for obstetric ICU admission, as compared with non-ICU admission and as compared with the general pregnant population

	Obstetric ICU admission (n=837)	Severe maternal morbidity without ICU admission (n=1676)			Netherlands, general pregnant population (n=358,874)	
	(%)	(%)	unadjusted OR (95% CI)	adjusted* OR (95% CI)	(%)	unadjusted RR (95% CI)
Patient						
Age						
≥ 35 years	29.3	27.9	1.1 (0.9-1.3)		24.7	1.0 (0.8-1.1)
≥ 40 years	5.3	4.7	1.1 (0.8-1.7)		3.4	**1.6 (1.1-2.1)**
Body mass index (kg/m2)						
< 18,5 (underweight)	3.8	2.4	1.6 (0.9-2.9)		3.1	**1.7 (1.2-2.5)**
≥ 25 (overweight)	36.6	36.2	1.0 (0.8-1.3)		31.7	**2.0 (1.7-2.4)**
≥ 30 (obese)	15.6	12.0	**1.4 (1.0-1.8)**	1.3 (0.9-1.7)	9.8	**1.7 (1.4-2.2)**
Pregnancy						
Parity ≥ 3	6.7	4.2	**1.6 (1.1-2.3)**	1.6 (1.0-2.6)	5.0	**1.4 (1.0-1.8)**
Prior caesarean delivery	14.7	21.1	**0.7 (0.5-0.8)**	**0.5 (0.4-0.7)**	10.1	**1.5 (1.3-1.9)**
Artificial reproduction techniques: IVF/ICSI	5.6	4.4	1.3 (0.9-1.9)		1.9	**3.0 (2.2-4.0)**
Multiple pregnancy	8.4	7.9	1.1 (0.8-1.4)		1.7	**5.2 (4.1-6.6)**
Initial antenatal care by obstetrician	38.0	37.4	1.0 (0.9-1.2)		14.3	**3.7 (3.5-3.9)**
Delivery						
Home delivery	3.5	8.2	**0.4 (0.3-0.6)**	**0.4 (0.2-0.7)**	30.0	**0.1 (0.05-0.1)**
Induction of labour	28.6	25.1	**1.2 (1.0-1.4)**	**1.6 (1.2-2.0)**	12.5	**2.8 (2.4-3.3)**
Caesarean delivery overall	52.9	37.6	**1.9 (1.6-2.2)**	**1.5 (1.1-2.0)**	13.0	**7.7 (6.7-8.8)**
Prelabour caesarean delivery	31.2	16.9	**2.2 (1.8-2.7)**	**2.0 (1.5-2.8)**	5.9	**7.2 (6.3-8.4)**
Ventouse/forceps extraction	10.4	13.5	**0.7 (0.6-1.0)**	0.8 (0.5-1.1)	8.6	**1.3 (1.1-1.7)**

OR=odds ratio; CI=confidence interval; *all significant factors in univariable analysis were included in the multivariable logistic regression model. Significant values are in bold

Discussion

This report concerns by far the largest prospective cohort of obstetric ICU admissions in the literature. In the only other, comparably large study inclusion was performed retrospectively, with case ascertainment relying on ICD-9 codes.[8] The incidence of 2.4 per 1000 in the Netherlands is comparable with other high income countries considering the range of incidences of 2-4 per 1000 as mentioned by Zeeman.[9] However, the case fatality rate of 3.4% is well under the average of 6.8% in other studies.[9;10] The average duration of ICU stay was also lower than reported by others (3 vs. 5 days)[3;9;11-22] and women seemed to be older (mean age 32 vs. 29 years).[3;11;13-15;17-19;21-25] With respect to the moment of admission, our findings were comparable with other studies. In this study MOH was diagnosed almost twice as often

as on average in other studies (45.5% against 23.6%), although incidence varied largely from 5 to 53%.[3;9;11-27] On the other hand, respiratory disease and thrombo-embolism were diagnosed less than half as much in our study as compared with others (5.1% vs. 13.3% and 1.6% vs. 4.2%).[3;11-14;16-19;22-27] Only twenty women were admitted to ICU with peripartum cardiomyopathy (1 in 20,000 pregnancies). This is few in light of the reported incidence of 1 in 100 to 1 in 15,000 pregnancies.[28] Differences could be explained by the fact that most other studies were not population based, but mainly from level 3 ICUs. Tertiary care centres receive relatively more women with hypertensive disorders than women with MOH as this concerns an acute clinical problem that is mostly treated locally. The less frequent diagnosis of hypertensive disorders of pregnancy as compared to the other studies (26.8% vs. 36.3%) was surprising in the light of the elevated incidence of eclampsia recently found in the Netherlands.[29] This possibly reflects the underestimation of the risk of severe preeclamptic conditions in the Netherlands.[30] Over sixty percent received packed cells, which is more than others previously reported (47.3% in Canada and 32.0% in the United Kingdom).[12;20] As could be expected, we saw that tertiary care centres, high-level ICUs and high-volume hospitals treated more severely ill women with cardiac, liver/pancreatic, cerebral, thrombo-embolic and septic diseases as compared to general hospitals, level 1 ICUs and low-volume hospitals. Women who had their antenatal care with an obstetrician for any pre-existing medical or obstetric condition had an elevated risk of being admitted to ICU whereas women who delivered at home under supervision of the midwife had a decreased risk. These findings support the proper functioning of the system of selection between low- and high-risk pregnancies used in the Netherlands.

Another important finding in this study is the fact that only one third of all cases of severe maternal morbidity in the Netherlands were admitted to an ICU. The same was reported by Brace et al.[31] Therefore obstetric ICU admission alone is not a good surrogate for severe maternal morbidity. However, it seems appropriate to use ICU admission to describe maternal characteristics and associated factors, because we found no differences between women who were and were not admitted to ICU. Even so we can say that the most severe cases of severe maternal morbidity are generally included, as illustrated by the significantly higher case fatality rate and higher number of performed caesarean sections for maternal conditions of ICU women as compared to non-ICU women.

Since women with severe maternal morbidity had a baseline risk, odds ratios for ICU versus non-ICU women were not that high. Nevertheless, we found induction of labour and caesarean section to be adjusted risk factors. The protective effect of a previous caesarean section is probably caused by the fact that many of these women were included because of

uterine rupture, a condition that rarely necessitates maternal ICU admission.

With abortion being legal in the Netherlands, septic abortion proved to be rare. One death among four women with septic abortion was found during the study period as compared to 63 in a 10-year unicentre study from Argentina with a comparable case fatality rate.[32]

The main limitation of this study is that we were not able to correct population-based risk indicators for possible confounders as individual characteristics of the reference population were not available. Some relative risks are obviously confounded. The high relative risk among women who delivered by caesarean is probably confounded as caesarean delivery could be the consequence of the underlying disease for which the mother was admitted rather than the risk factor. This could also be true for induction of labour.

ICU admission is a management-based criterion and therefore by definition leads to inclusion bias. This is especially the case for tertiary care centres, where the threshold for ICU admission is high due to the presence of obstetric high care units. These women would probably have been admitted to ICU in other hospitals. Furthermore, we saw that the threshold for ICU admission was sometimes low in low-volume maternity units due to the fact that local protocols require intravenous therapy of pre-eclampsia to be monitored at an ICU due to logistic reasons. This probably also explains the relatively long duration of ICU stay in low-volume hospitals and the relatively high share of admissions for hypertensive disorders at level I ICUs.

Finally, results of the present study cannot be merely extrapolated to other countries. This was illustrated by Munnier et al, reporting marked differences in medical diseases, organ failure, and intensive care needs between a developed and a developing country.[33]

As shown, the management of critically ill women during pregnancy, delivery and puerperium is difficult and requires specific knowledge of the physiology and pathology of pregnancy. Therefore, both obstetrician and intensivist/anaesthetist should always be involved in the management of women admitted to ICU. As obstetric ICU admission is a rare event in Western countries, exposure of obstetricians and intensivists/anesthesists is low. This would plea for centralization of obstetric care, which is a very current issue in the Netherlands. Although underexposure to rare but life threatening complications might affect quality of care, this has to be balanced against the disadvantage of larger distances between obstetric services, which involves many more pregnant women.

Conclusions

ICU admission complicates 0.24% of pregnancies in the Netherlands. Although illnesses are generally very serious, case fatality rate is relatively low as compared to non-pregnant

patients admitted to ICU. Proper management of obstetric ICU admissions requires intensive cooperation of intensivist/anaesthetist and obstetrician. Since two thirds of all women with severe maternal morbidity in the Netherlands were not admitted to ICU, ICU admission is not a good parameter to assess the incidence of severe maternal morbidity in a specific population. It is, however, a good indicator of the most severe cases of maternal morbidity.

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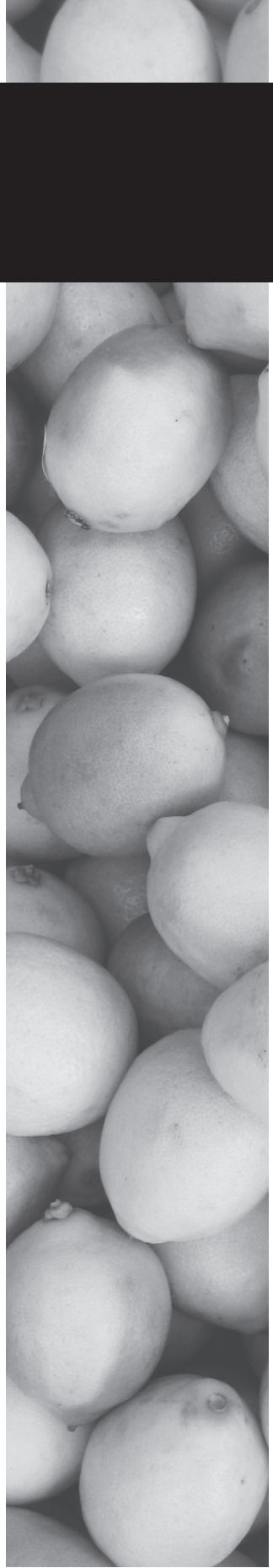
CHAPTER 6



Uterine rupture in the Netherlands: a nationwide population based cohort study

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Abstract

Objective: To assess incidence of uterine rupture in scarred and unscarred uteri and its maternal and fetal complications in a nationwide design.

Design: Population-based cohort study.

Setting: All 98 maternity units in the Netherlands.

Population: All women delivering in the Netherlands between August 2004 and August 2006 (n=371,021)

Methods: Cases of uterine rupture were prospectively collected using a web-based notification system. Data from all pregnant women in the Netherlands during the study period were obtained from Dutch population-based registers. Results were stratified by uterine scar.

Main outcome measures: Population-based incidences, severe maternal and neonatal morbidity and mortality, relative and absolute risk estimates.

Results: There were 210 cases of uterine rupture (5.9 per 10,000 pregnancies). Of these women, 183 (87.1%) had a uterine scar, incidences being 5.1 and 0.8 per 10,000 in women with and without uterine scar. No maternal deaths and 18 cases of perinatal death (8.7%) occurred. The overall absolute risk of uterine rupture was 1 in 1709. In univariable analysis, women with a prior caesarean, epidural anaesthesia, induction of labour (irrespective of agents used), pre or post term pregnancy, overweight, non-Western ethnic background and advanced age had an elevated risk of uterine rupture. The overall relative risk of induction of labour was 3.6 (95% confidence interval 2.7-4.8).

Conclusion: The population-based incidence of uterine rupture in the Netherlands is comparable with other Western countries. Although much attention is paid to scar rupture associated with uterotonic agents, 13% of ruptures occurred in unscarred uteri and 72% occurred during spontaneous labour.

Introduction

Uterine rupture is a rare complication of pregnancy potentially leading to severe maternal and foetal morbidity and mortality. Several risk factors have been identified, the most important being a uterine scar (mostly from previous caesarean) and the use of uterotonic agents for induction of labour.[1-5] The Netherlands has a caesarean delivery rate which is among the lowest in the world, although it is increasing. The same is true for countries worldwide, as a result of which the incidence of uterine rupture is likely to increase. The sheer quantity of recent reports on the safety of vaginal birth after caesarean (VBAC) demonstrates the increased awareness of this issue.

In a WHO systematic review of uterine rupture worldwide, the median incidence was 5.3 per 10,000 births.[6] If only population-based studies in high-income countries are taken into consideration, the mean incidence was around 3 per 10,000 deliveries. This figure, however, was based on only five of 83 included studies, the great majority being from low-income countries, facility-based, or only concerning women with a previous caesarean. A clear distinction is made between uterine scar rupture and rupture of an unscarred uterus. Scar rupture often presents less dramatic but the incidence is rising in Western countries. Rupture of the unscarred uterus is much more frequent in low-income countries due to obstructed labour and leads to more severe feto-maternal complications, being even an important cause of direct maternal death in these countries. It is, however, a rare event in Western countries with an estimated incidence of 0.6 per 10,000, based on only ten cases.[1] Our aim was to assess the population-based incidence of uterine rupture in the Netherlands, as well as the case fatality rate, the most specific symptoms and signs at diagnosis and possible risk factors.

Methods

This study was part of a larger nationwide enquiry into severe maternal morbidity in the Netherlands, called LEMMoN. Details on design of the LEMMoN study have been published elsewhere.[7] The study was centrally approved by the medical ethics committee of Leiden University Medical Centre. It enrolled cases from 1st August 2004 until 1st August 2006. In the Netherlands, there are 10 tertiary care centres, 33 non-academic teaching hospitals and 55 general hospitals. In 2005, the number of deliveries per hospital ranged from 93 to 2655 and 41% of deliveries were under guidance of a midwife or family physician, either at home (30%) or in the hospital (11%). Pregnancies in women with a uterine scar from a previous caesarean are considered high risk pregnancies. Although these women have to deliver in hospital under guidance of an obstetrician, they are allowed to have antenatal care with the midwife or family physician until 36 weeks of gestational age. The latest published caesarean delivery rate in the Netherlands is 14% in 2002.[8]

Uterine rupture was defined as the occurrence of clinical symptoms (abdominal pain, abnormal

fetal heart rate pattern, acute loss of contractions, vaginal blood loss) leading to an emergency caesarean delivery, at which the presumed diagnosis of uterine rupture was confirmed; or peripartum hysterectomy or laparotomy for uterine rupture after vaginal birth. Cases of scar dehiscence found during elective caesarean section without preceding clinical symptoms were not included. Women without a known uterine rupture or perforation were considered having an unscarred uterus, also after previous D&C or hysteroscopy, as these women will clinically be considered as having an unscarred uterus.

Requests for notifications of cases of uterine rupture were sent to all 98 local coordinators on a monthly basis. Cases were communicated to the National Surveillance Centre for Obstetrics and Gynaecology (NSCOG) in a web-based design. Absence of cases was also reported. Reminders were sent to non-responders every month until they had returned the monthly notification card.

After notification, a case record form was sent to us, accompanied by anonymous photocopies of all relevant parts of the hospital case notes and correspondence. A detailed review of cases was completed by one of the researchers (JJZ) and all cases were centrally entered into an Access database.

We recorded maternal characteristics (age, body mass index, parity, ethnicity, income, single household, language skills, smoking), obstetric history (including type of caesarean, type of incision and interpregnancy interval), all essential data on pregnancy and delivery, and neonatal outcome. We also recorded data on the specific complication, such as diagnosis-to-delivery interval, epidural analgesia, dilatation of the cervix at diagnosis, symptoms and signs at diagnosis, medicaments administered, and whether the foetus was (partially) extruded into the abdomen. A total of 108 items were entered into the database for each case. Characteristics of each hospital were also recorded (university or teaching hospital, annual number of deliveries).

Ethnicity was defined by country of origin ('geographical ethnic origin') and grouped according to the most common population groups in the Netherlands (Western Europe, Morocco, Surinam/Dutch Antilles, Turkey, Sub-Saharan Africa and Middle and Far East). We used the definitions of Statistics Netherlands.[9] Women born in the Netherlands with at least one parent born abroad were considered to be from the same origin as their parent(s) from abroad. Women from other Western European countries, and women from North America, Japan and Indonesia are considered Western immigrants according to Statistics Netherlands. All other immigrant women are considered non-Western. Major obstetric haemorrhage was defined as blood loss necessitating 4 or more units of red blood cells. Weekdays from 8am to 6pm were considered office hours (which equates to 30% of all hours during a week).

Denominator data for number of births in the Netherlands during the exact study period were obtained from Statistics Netherlands.[9] Births are registered based on birth certificates, which are mandatory by law beyond 24 weeks of gestational age in the Netherlands. Reference values for possible risk factors for uterine rupture were obtained from Statistics Netherlands (exact study period) and The Netherlands Perinatal Registry (LVR-2; 2005).[8] LVR-2 is the Dutch national perinatal database that covers nearly

100% of births under guidance of an obstetrician, in which parity, gestational age at delivery, mode of delivery, and place of antenatal care (midwife or obstetrician) are reliably registered. Each case is entered in the database by the attending clinician directly after birth. Data that were compared between cases and non-cases were collected using the same fact-sheet from LVR-2. Case fatality rate was calculated by dividing the number of deaths by the total number of cases.

To control for underreporting, we cross-matched our database with the LVR-2 database. During a five-month period, cases of uterine rupture reported to this database but not to us, were identified and local coordinators were sought to re-analyse these cases and report when appropriate.

Relative risks and confidence intervals were calculated in univariable analysis. Differences between groups were identified using Chi square or Student T tests. Significance was defined as $p < 0.05$. Statistical analysis was performed using the Statistical Package for the Social Sciences 14.0 (SPSS Inc., Chicago, IL, USA).

Results

During the study period, 371,021 deliveries occurred in the Netherlands. From all 2352 (98 hospitals, 24 months) monthly notification cards, 97% were returned. Therefore, the study represents 358,874 deliveries in the Netherlands.

Table 1. Maternal and neonatal morbidity due to uterine rupture by type of induction and mode of delivery

	MOH	hysterectomy	ICU admission	perinatal death*	asphyxia†	NICU admission‡
onset of delivery						
spontaneous (n=130)	19 (14.6%)	4 (3.1%)	11 (8.5%)	9 (6.9%)	21 (16.2%)	12 (9.4%)
induction cervical prostaglandins (n=28)	8 (28.6%)	5 (17.9%)	5 (17.9%)	3 (10.7%)	7 (25.0%)	2 (9.0%)
induction oxytocin (n=22)	6 (27.3)	2 (9.1%)	4 (18.2%)	2 (9.1%)	6 (27.3%)	2 (10.5%)
induction sulproston (n=4)	2 (50.0%)	1 (25.0%)	3 (75.0%)	0	0	0
induction mechanical dilatation (n=4)	0	0	0	0	0	0
caesarean without labour (n=20)	8 (40.0%)	5 (25.0%)	3 (15.0%)	4 (20%)	1 (5.0%)	8 (42.1)
mode of delivery						
spontaneous (n=12)	9 (75%)	4 (33.3%)	8 (66.7%)	0	0	0
ventouse (n=8)	4 (50%)	0	1 (12.5%)	1 (12.5%)	0	1 (12.5%)
caesarean (n=188)	30 (16.0%)	13 (6.9%)	17 (9.0%)	17 (9.0%)	35 (18.6%)	23 (12.9%)
overall (n=208§)	43 (20.7%)	17 (8.2%)	26 (12.5%)	18 (8.7%)	35 (16.8%)	24 (12.1%)

MOH=Major Obstetric Haemorrhage; (N)ICU=(Neonatal) Intensive Care Unit; *excluding death due to congenital malformations; †defined as pH directly postpartum < 7.00; ‡percentage among 198 neonates from 25 weeks of gestational age onwards; §excluding two cases of uterine rupture after instrumental abortion

A total of 218 cases of uterine rupture were reported, the incidence of uterine rupture being 5.9 per 10,000 deliveries. We received detailed information of all cases (100%). Eight cases were excluded because asymptomatic dehiscence of the uterine scar was found at elective caesarean, leaving 210 confirmed cases. No maternal deaths due to uterine rupture occurred during the study period. Other severe maternal and neonatal complications are listed in Table 1. Incidence varied largely by hospital, ranging from 0 to 45.2 per 10,000. The mean 'hospital-incidence', concerning only deliveries under secondary or tertiary care, was 9.3 per 10,000; 15.4 for tertiary care centres and 8.6 for general hospitals (p=0.03). Incidence figures did not differ by volume of maternity unit (data not shown). There was a trend towards more liberal use of prostaglandins for induction of labour in low-volume hospitals as compared to middle- and high-volume hospitals (24.4% vs. 13.0% of cases, p=0.29). Characteristics of women are shown in Table 2.

Table 2. Characteristics of women with uterine rupture.

	n	*%*
Age (mean 33.0)		
< 25 year	2	1.0%
25-35 year	134	63.8%
35-40 year	63	30.0%
≥ 40 year	11	5.2%
Socio-economic status		
low	54	28.4%
middle	75	39.5%
high	61	32.1%
unknown	*20*	
Smoking during pregnancy		
yes	18	15.0%
no	108	85.0%
unknown	*84*	
Body Mass Index (BMI)		
<18.5	3	2.1%
18.5-24.9	62	44.3%
25.0-29.9 (overweight)	47	33.6%
30.0-34.9 (obese)	16	11.4%
≥ 35.0 (morbidly obese)	12	8.6%
unknown	*70*	
Geographical ethnic origin		
Netherlands	158	75.2%
Morocco	9	4.3%
Turkey	10	4.8%
Surinam/Dutch Antilles	7	3.3%
sub-Saharan Africa	9	4.3%
other non-Western	13	6.2%
other Western	4	1.9%

Most ruptures occurred intrapartum (n=188; 89.5%). In 20 cases (9.5%) rupture occurred before the onset of labour, and in two cases (1.0%) as a complication of second trimester instrumental abortion. In 16 of the intrapartum cases (8.5%) rupture was only suspected after childbirth. Ten of these were spontaneous deliveries, five were ventouse deliveries and one rupture of the posterior uterine wall was diagnosed at re-laparotomy after caesarean delivery.

Clinical symptoms that led to the diagnosis of uterine rupture included abdominal pain (69%), abnormal fetal heart rate pattern (67%), vaginal bleeding (27%), hypertonia (20%) and acute absence of contractions (14%). Among 162 women with complete reporting of all five mentioned symptoms, 91 women (56%) presented with a combination of symptoms, the most frequently encountered combination being abdominal pain and abnormal fetal heart rate pattern (Table 3).

Of all 171 cases with emergency intrapartum caesarean, 31 ruptures (18.1%) occurred during the second stage of labour. In four women, dilatation at diagnosis was not mentioned, 15 women (8.8%) had no dilatation, and in the remaining 121 women, rupture occurred at 1 to 9 cm dilatation, with the highest incidence at 4 to 5 cm dilatation (n=41).

Table 3. Symptoms and signs at the moment of diagnosis

	presence of symptom	*combinations of two symptoms*			
		abnormal CTG	vaginal bleeding	hypertonia	acute absence contractions
abdominal pain	133/194 (68.6%)	90/189 (47.6%)	34/181 (18.8%)	34/181 (18.8%)	16/174 (19.2%)
abnormal CTG	134/201 (66.7%)		29/186 (15.6%)	31/185 (16.8%)	19/182 (10.4%)
vaginal bleeding	52/190 (27.4%)			12/179 (6.7%)	5/176 (2.8%)
hypertonia	38/188 (20.2%)				7/176 (4.0%)
acute absence of contractions	25/184 (13.6%)				

Possible risk factors are shown in Table 4. Of all women, 182 (86.7%) had at least one previous caesarean. Seven women (3.3%) were nulliparous, four of whom were primigravid. Non-Western immigrant women did have a significantly increased risk of experiencing uterine rupture as compared to Western women (relative risk [RR] 1.4; 95% confidence interval [CI] 1.0-1.9). Sub-Saharan African women had the highest risk (RR 3.9; 95% CI 2.0-7.7). Fifty-nine percent of uterine ruptures occurred outside office hours. Median interval between diagnosis and childbirth was 30 minutes (range 7-172) for ruptures occurring during office hours, and 40 minutes (range 9-240) outside office hours (p=0.09).

The two cases of uterine rupture during instrumental abortion were complications of second trimester termination of pregnancy at 21 and 22 weeks of gestation in unscarred uteri. Reasons for termination were unwanted pregnancy and bilateral facial cleft. Both women were referred from a

primary care abortion clinic. One of these women had a hysterectomy performed because of major obstetric haemorrhage. These two cases will further be disregarded as they concern complications of instrumental abortion and characteristics of delivery do not apply.

Table 4. Possible risk factors for uterine rupture

	LEMMoN	*Netherlands*	*RR (95% CI)*	*Absolute risk (overall 1 in 1709)*
Patient				
age ≥ 35	35.2%	24.7%*	1.7 (1.3-2.2)	1 in 1195
low income	28.4%	n/a		
single household	3.3%	n/a		
BMI ≥ 25 (overweight)	53.6%	31.7%*	2.5 (1.8-3.5)	1 in 1011
BMI ≥ 30 (obese)	20.0%	9.8%*	2.3 (1.5-3.5)	1 in 837
BMI ≥ 35 (morbidly obese)	8.6%	n/a		
non-Western immigrants	21.0%	16.8%*	1.4 (1.0-1.9)	1 in 1315
Pregnancy				
prior caesarean delivery	86.7%	10.1%[4]	65.1 (42.9-98.7)	1 in 198
short interpregnancy interval (≤ 12 months)	13.9%	n/a		
VBAC in obstetric history	10.5%	n/a		
nulliparity	3.8%	45.2%*	0.05 (0.02-0.10)	1 in 20,259
primiparity	78.1%	18.9%†	15.3 (11.1-21.3)	1 in 413
parity ≥3	5.8%	5.0%*	1.2 (0.6-2.1)	1 in 1493
multiple pregnancy	1.0%	1.7%*	0.5 (0.1-2.2)	1 in 3116
artificial reproduction techniques: IVF/ICSI	1.9%	1.9%[10]	1.0 (0.4-2.6)	1 in 1740
Delivery				
induction of labour	33.3%	12.3%†	3.6 (2.7-4.8)	1 in 629
induction of labour, prostaglandin	15.5%	n/a		
induction of labour, oxytocin	13.0%	n/a		
augmentation, oxytocin	24.2%	18.9%†	1.4 (1.0-1.9)	1 in 1336
epidural anaesthesia	40.1%	5.9%†	10.7 (8.1-14.1)	1 in 251
preterm birth (<37w)	13.0%	5.8%†	2.4 (1.6-3.7)	1 in 760
post term birth (≥42w)	9.2%	4.3%†	2.2 (1.4-3.6)	1 in 801

National reference values from *Statistics Netherlands (exact study period) and †The Netherlands Perinatal Registry (LVR-2; 2005); n/a: not available.

Scar rupture

Uterine rupture occurred in 183 women with a scarred uterus, population-based incidence being 5.1 per 10,000 deliveries. In two of these women, the localisation of rupture was not the uterine scar itself. All but one woman had a singleton pregnancy. Median gestational age was 40.2 weeks (range

17.2 to 42.7). One woman had a scar from previous myomectomy; the remaining 182 women had a scar from previous caesarean. All but six of these women (96.7%) had one previous caesarean, four had two and two had three previous caesareans. Previous caesarean was performed without labour in 72 women (39.6%) and during labour in 106 (58.2%). Three women had both types of caesarean in their obstetric history and in one the type of previous caesarean was unknown. In 18 women (9.9%) the previous caesarean was expedited before 36 weeks of gestation. In 53 women (29.1%) the previous caesarean was electively performed because of breech presentation. Incision had been low transverse in 177 cases, classical in one case, and in four cases, the type of incision was unknown.

Three women had a uterine rupture in their obstetric history. In the first one, caesarean delivery was planned because of a previous classical incision, but she experienced uterine rupture at 30 weeks. The second woman had a caesarean without labour performed at 35 weeks of gestation because of placenta praevia and thrombocytopenia. Peripartum hysterectomy was performed because of major obstetric haemorrhage due to uterine rupture and placenta praevia. The third woman experienced hypovolemic shock at 29 weeks of gestation. A fundal uterine rupture was found at emergency caesarean, along with three litres of intraabdominal blood and intrauterine fetal death. Peripartum hysterectomy was performed. In another woman, obstetric history revealed a scar dehiscence.

Table 5. Risk of uterotonic agents in trial of labour

onset of labour	*LEMMoN*		*Netherlands**		*RR (95% CI)*
spontaneous labour	77		2056		1.0
augmentation after spontaneous onset	43	35.8%	536	20.7%	2.1 (1.5-3.1)
induction of labour	47	37.9%	682	24.9%	1.8 (1.3-2.7)
oxytocin	20	20.6%	308	13.0%	1.7 (1.0-2.9)
prostaglandin	16	17.2%	203	9.0%	2.1 (1.2-3.7)
prostaglandin + oxytocin	6	7.2%	94	4.4%	1.7 (0.7-4.0)
mechanical dilation +/- oxytocin	5	6.1%	77	3.6%	1.7 (0.7-4.4)

***Reference values from a large representative sample from the Netherlands (n= 3274)[4]**

Trial of labour was attempted in 167 women (91.3%), four of whom had the previous caesarean performed before 34 weeks of gestation. The other 16 women (8.7%) had an emergency caesarean performed, most important indications being spontaneous onset of labour before planned elective caesarean, placenta praevia/percreta and suspicion of placental abruption. Relative risks of different uterotonic agents during trial of labour are shown in Table 5. In 22 of 183 cases (12.0%), prostaglandins were used for induction

of labour. Reasons for induction with prostaglandins included (nearly) post term pregnancy (n=10), intra uterine fetal death/multiple congenital abnormalities (n=5), elective (n=3), pregnancy induced hypertension (n=2), intra uterine growth restriction (n=1), and prelabour rupture of membranes (n=1). Prostaglandin analogues used included different variants of dinoproston (n=16), sulproston (n=2) and misoprostol (n=1). In three cases, two different prostaglandin analogues were administered successively. Individual assessment of regimens of administration in these 23 cases revealed no new insights. Dosages ranged from 0.5 to 2.0 mg with a minimal interval of four hours in between.

Mean interpregnancy interval, defined as the time between immediate previous caesarean and conception was 33 months (range 3-135). Only four women had an interpregnancy interval of less than six months. Twenty-two women (12.2%) had one to three VBACs in their history. Previous VBAC tended to be protective to the foetus, but the risk of severe maternal morbidity tended to be elevated (Table 6). Complete or partial extrusion of the foetus was reported in 21 and 29 cases (11.4 and 15.9%, respectively). In nine women (4.9%) uterine rupture was complicated by rupture of the bladder.

Table 6. Uterine rupture after previous vaginal birth after caesarean (VBAC)

severe morbidity/mortality	*VBAC n (%)*		*no VBAC n(%)*		*RR (95% CI)*
maternal					
ICU admission	4	18.2%	11	7.0%	2.6 (0.9-7.5)
major obstetric haemorrhage (≥4 units)	6	27.3%	20	12.7%	2.2 (1.0-4.8)
major obstetric haemorrhage (≥10 units)	2	9.1%	5	3.2%	2.9 (0.6-13.9)
hysterectomy	3	13.6%	7	4.4%	3.1 (0.9-11.0)
fetal					
perinatal death	1	4.5%	12	7.6%	0.6 (0.1-4.4)
asphyxia	3	13.6%	30	19.0%	0.7 (0.2-2.2)

ICU=intensive care unit

Rupture of the unscarred uterus

Besides the two ruptures complicating second trimester instrumental abortion, 25 women experienced rupture of an unscarred uterus, incidence being 0.7 per 10,000 deliveries. Median gestational age was 38.7 weeks (range 20.7-42.8). Factors possibly associated with the rupture were history of instrumental abortion or postpartum curettage (n=10), history of hysteroscopy (n=2), history of ectopic pregnancy (n=2), history of other pelvic surgery (n=1), endometriosis (n=2), uterine fibroids (n=1), and twin pregnancy (n=1). In 13 women (52%) we could not identify any risk factor. Severe maternal and neonatal morbidity and mortality were clearly more often observed among women with an unscarred uterine rupture as compared to uterine scar rupture (Table 7). In 11 women (44%) labour was induced, in all but one with prostaglandins. Four ruptures occurred before spontaneous onset of labour, three

were discovered postpartum. In 18 women (72%) rupture occurred outside office hours. Localisation of rupture included posterior wall (n=5), anterior wall (n=5), lateral (n=3), fundal (n=4), low uterine segment (n=2) and other (n=5). Cervix and bladder were involved in six and seven cases, respectively. Complete or partial extrusion of the foetus into the abdomen was reported in nine cases (36.0%). In one case, in which the woman presented with anhydramnios and diminished fetal movements at 32 weeks of gestation, uterine rupture was diagnosed antepartum by an intra abdominal leg on MRI.[11]

Table 7. Delivery and outcome in scar vs. non-scar uterine rupture

Item	*non-scar (n=25)*	*scar (n=183)*	*RR (95% CI)*
Delivery			
induction with prostaglandins	40.0%	12.1%	4.9 (1.7-11.2)
before 32 weeks of gestational age	24.0%	4.9%	6.1 (1.5-16.7)
prelabour emergency caesarean	16.0%	8.8%	2.0 (0.6-6.9)
Outcome			
ICU admission	36.0%	8.8%	5.5 (2.2-15.4)
≥ 4 units of blood transfused	56.0%	15.4%	6.8 (2.6-15.4)
≥ 10 units of blood transfused	16.0%	6.0%	3.7 (1.1-13.7)
hysterectomy	24.0%	6.0%	4.9 (1.7-15.8)
peripartum fetal death	24.0%	7.7%	3.8 (1.4-11.8)
asphyxia*	33.3%	31.4%	1.1 (0.2-6.3)
foetus completely extruded	28.0%	11.0%	3.0 (1.2-8.6)

*** percentages among 111 cases with a known umbilical cord pH directly after birth; ICU=intensive care unit**

Discussion

Thirteen percent of all uterine ruptures occurred in the unscarred uterus, the proportion being higher than reported before.[12] The overall incidence of uterine rupture of 5.9 per 10,000 is well within the range of incidences reported in Western countries.[6] The overall incidence reported in a WHO systemic review of uterine rupture was 5.3 per 10,000 for population-based studies, and 31 per 10,000 for facility-based studies.[6] Kwee et al. conducted a one-year prospective study of uterine rupture in the Netherlands, from which we could calculate a similar incidence of 5.8 per 10,000.[13] They, however, reported only three ruptures in unscarred uteri on a total of 98.

Although no cases of maternal death due to uterine rupture occurred in our study, each of the last four triennial reports of the Confidential Enquiry into Maternal and Child Health in the United Kingdom contained at least one case of maternal death due to uterine rupture, and the most recent report described two cases.[14]

This study includes the largest prospective report of uterine rupture in women without a

previous caesarean in a Western country. The only other study mentioned in the WHO systematic review reported a comparable incidence of 0.6 per 10,000 [6;15], attesting to the rarity of uterine rupture in the absence of a previous caesarean in Western countries. However, unlike previously reported,[16] we demonstrate that severe maternal and neonatal morbidity and mortality are clearly higher in these cases as compared to uterine scar rupture. Therefore, uterine rupture should always be suspected in case of clinical signs, particularly –but not exclusively– in the presence of risk factors such as previous caesarean section, primiparity, induction of labour, epidural anaesthesia, overweight or advanced age.

The majority of scar ruptures occur in the absence of macroscopic or clinical signs of blood loss. Contrarily, major haemorrhage, ICU admission and hysterectomy occur more frequent with rupture of the unscarred uterus. This is probably caused by a much lower index of suspicion in an unscarred uterus which may add to a delay in diagnosing uterine rupture. There may also be reduced blood loss in women with scar-rupture compared to unscarred uterine rupture. Major obstetric haemorrhage is also an important presenting symptom of uterine rupture diagnosed after childbirth, which represents 8.6% of all ruptures. Therefore, differential diagnosis of major obstetric haemorrhage after previous caesarean should always include uterine rupture.

Controversy remains regarding the additional risk of uterine surgical procedures in general history like D&C or myomectomy. Even though perforations are known to go unrecognized, evidence of a causal relationship remains only circumstantial.[17] However, we report 13 cases of uterine rupture in unscarred uteri in the absence of any known risk factor.

A major strength of this study is that we prospectively collected all cases of uterine rupture instead of relying on ICD-10 codes. Therefore, the definition of uterine rupture was uniform and could be explicitly confirmed. Other large studies had to rely on ICD-codes for case ascertainment[3;5], which have been shown to be only about 40% accurate.[18] Another key strength of the study is its nationwide and population based design, giving a precise and generalisable estimation of the incidence for a Western country. However, the nationwide design confers also the major limitation of the study, since specific reference values of the pregnant population, such as previous method of caesarean delivery or uterotonic agents used, are missing in the national registries. This was met by using reference data from a recent representative cohort of Dutch women attempting trial of labour collected by Kwee et al.[4] Unfortunately, we could not adjust relative risks for possible confounding variables, since only aggregated instead of individual data were available for the nationwide reference cohort of women without uterine rupture. Furthermore, data on previous scar closure was not available, but single layer closure is common practice in the Netherlands.

We found a 3.6-fold increased risk of uterine rupture after induction of labour as compared

to the general pregnant population, irrespective of agents used. Controversy remains with respect to earlier stated additional risk of induction of labour with prostaglandins. Several studies report that induction with prostaglandins confers the highest risk of uterine rupture (relative risk up to 15), but two large studies could not confirm this.[4;19;20] Case ascertainment was suboptimal using ICD-9 codes, and bias by indication may also have played a role. For the Dutch setting, Kwee et al. reported odds ratios among 3274 trials of labour of 2.2, 3.8 and 6.8 for augmentation, induction and induction with prostaglandins, respectively.[4] Using the same reference cohort, we could not confirm these high relative risks few years later although reported incidences of uterine rupture were similar. It is possible that the incidence has stabilised as a result of the rising prevalence of previous caesarean delivery on one hand, and the more restrictive use of uterotonic agents in women with a uterine scar on the other hand. When comparing our cohort of women experiencing uterine rupture during trial of labour to the cohort of Kwee et al. (2002-3), we observed significantly less induction of labour overall ($p=0.04$) and with prostaglandins ($p=0.005$).

Mechanical dilation of the cervix with Dilapam or balloon catheter seems to be a good alternative on theoretical grounds[21], although we also encountered one case of uterine rupture after induction by mechanical dilatation alone.

The majority of all uterine ruptures (80.5%) occurred during trial of labour. Assuming an estimated trial of labour percentage after caesarean in the Netherlands of 71.7%, and a percentage of women with a previous caesarean of 10.1% as reported by Kwee et al, 25,989 trials of labour were attempted in the Netherlands during the study period.[4] The risk of uterine rupture would then be 0.64%, which is considerably lower than reported by Kwee (1.47%; $p < 0.001$) and well within the range of reported incidences in large reviews and retrospective studies of 0.22-0.74%.[22]

A previous VBAC is generally considered to be a protective factor for the occurrence of uterine rupture and its complications during trial of labour. However, in our study this seems to only apply to the foetus, if at all. Risk of severe maternal morbidity seemed to be rather elevated after a previous VBAC. This is an important observation that needs to be addressed by future research.

With 29% of all previous caesareans being performed for breech presentation, we clearly show the negative side effects and long-term adverse consequences of routinely performing elective caesarean for breech delivery.[23-27]

Conclusion

While much attention has been paid to the risk of induction of labour, almost half of all scar ruptures occurred during spontaneous labour. Since the number of caesareans needed to prevent one uterine rupture is very high, the only means of reducing the incidence of uterine rupture is to minimise the number of inductions of labour and to closely monitor women with a uterine scar. Symptoms and signs of uterine rupture, in particular abnormal fetal heart rate pattern and abdominal pain, should be taken very seriously even in women with an unscarred uterus. Caesarean delivery should be promptly expedited in case of suspicion of uterine rupture. Between 2003 and 2006, the rate of uterine rupture associated with induction for trial of labour decreased significantly in the Netherlands. Ultimately, the best prevention is primary prevention, i.e. reducing the primary caesarean delivery rate. The obstetrician who decides to perform a caesarean has a joint responsibility for the late consequences of that decision, including uterine rupture.

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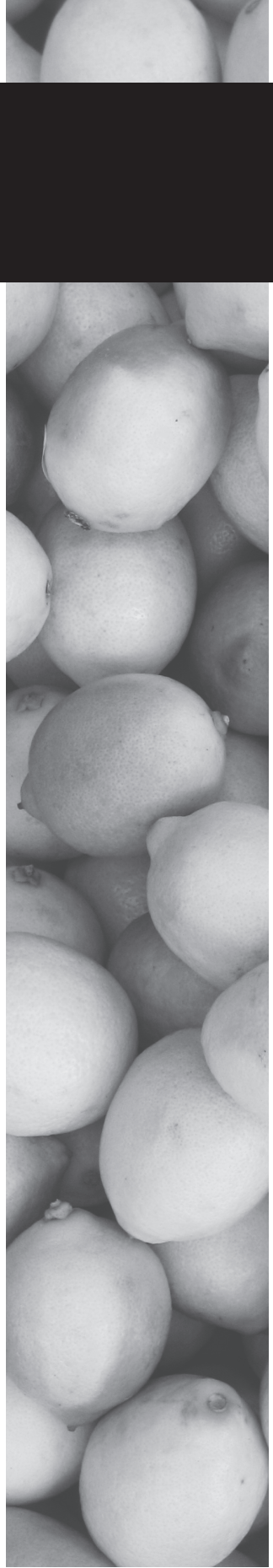
CHAPTER 7



Eclampsia in the Netherlands

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Abstract

Objective: The incidence of maternal mortality due to hypertensive disorders of pregnancy in the Netherlands is greater than in other Western countries. We aimed to confirm and explain this difference by assessing incidence, risk factors, and substandard care of eclampsia in the Netherlands.

Methods: In a nationwide population-based cohort study, all cases of eclampsia were prospectively collected during a 2-year period (2004 –2006). All pregnant women in the Netherlands in the same period acted as reference cohort (n=371,021). Substandard care was assessed in all cases. A selection of cases was extensively audited by an expert panel. Main outcome measures were incidence, case fatality rate, possible risk factors, and substandard care.

Results: All 98 Dutch maternity units participated (100%). There were 222 cases of eclampsia, for an incidence of 6.2 per 10,000 deliveries. Three maternal deaths occurred; the case fatality rate was 1 in 74. Risk factors in univariable analysis included multiple pregnancy, primiparity, young age, ethnicity, and overweight. Prophylactic magnesium sulphate was given in 10.4% of women, and antihypertensive medication was given in 39.6% of women with a blood pressure on admission at or above 170/110 mm Hg. Additionally, substandard care was judged to be present by an expert panel in 15 of 18 audited cases (83%).

Conclusion: The incidence of eclampsia in the Netherlands is markedly increased as compared with other Western European countries. Substandard care was identified in many cases, indicating the need for critical evaluation of the management of hypertensive disease in the Netherlands.

Introduction

Hypertensive disorders of pregnancy are one of the leading causes of maternal mortality and severe maternal morbidity worldwide. In the Netherlands, eclampsia/preeclampsia is the leading cause of maternal mortality, accounting for 60% of direct maternal deaths (Schutte JM, Steegers EA, Schuitemaker NW, Santema JG, de Boer K, Pel M, et al. Rise in maternal mortality in the Netherlands 1993–2005 [in press]).[1] The incidence of eclampsia has decreased dramatically over the past century in Western countries due to improved antenatal care and early management. Over the past decades, the incidence seemed to have stabilized, but since the publication of the Collaborative Eclampsia trial (1995)[2] and the Magpie trial (2002)[3], advocating the therapeutic and prophylactic use of magnesium sulphate, a further decline of incidence has been achieved in some countries.[4–6] Reported national incidences in Western European countries range from 2.4 per 10,000 deliveries in Finland to 5.7 per 10,000 deliveries in Sweden.[7;8]

Patient safety and adherence to national guidelines are key issues in the reduction of maternal and neonatal morbidity and mortality. In the presence of ample evidence for minimal standards provided by randomized trials, there is an unquestionable need for uniform application of standard approaches provided by guidelines. It is the aim of the Dutch Society of Obstetrics and Gynaecology to contribute to the development of evidence-based standardized approaches.

The primary aim of this study was to assess whether the incidence of eclampsia in the Netherlands is increased as compared with other European countries, as is the case for maternal death due to hypertensive disorders.[9] Secondly, we aimed to assess the management of eclampsia to explain the differences.

Materials and Methods

This study is part of a broader, nationwide enquiry into severe maternal morbidity in the Netherlands, called Nationwide Study Into Ethnic Determinants of Maternal Morbidity in the Netherlands (LEMMoN).[10] In this study, which enrolled cases from August 1, 2004, until August 1, 2006, all Dutch obstetric units participated. In the Netherlands, there are 10 tertiary care hospitals, 33 non-academic teaching hospitals, and 55 general hospitals with an obstetric ward. In 2005, the number of deliveries per hospital ranged from 93 to 2,655. Women with high-risk pregnancies and those with low-risk pregnancies who develop complications during pregnancy or child birth deliver in the hospital under the guidance of obstetricians (secondary or tertiary care, 59% of all births). Women with low-risk pregnancies without complications deliver under the guidance of midwives or family physicians (primary care), either at home (30% of all births) or in hospital under their responsibility (11% of all births). Most women with onset of preeclampsia before 32 weeks of gestational age are referred to a tertiary care centre. Any case

of eclampsia occurring outside of a hospital will be referred to a hospital and thus be notified. Eclampsia was defined as the occurrence of convulsions superimposed on preeclampsia and not attributable to other causes. Requests for notification of cases of eclampsia, along with other types of severe maternal morbidity, were sent to all local coordinators on a monthly basis. Cases were communicated to the National Surveillance Centre for Obstetrics and Gynaecology in a Web-based design by mentioning date of birth and initials of the woman. If no cases of eclampsia occurred, this was also reported. Reminders were sent to nonresponders every month until they had returned the monthly notification card. Local sources used by the local coordinators included daily staff meetings, labour ward delivery registers, intensive care admission registers, discharge registers, and personal communication.

After notification, a case record form was sent to us, accompanied by photocopies (made anonymous) of all relevant parts of the hospital case notes and correspondence. A detailed review of cases was completed by one of the researchers (J.J.Z.), and all cases were entered into an Access (Microsoft Corp., Redmond, WA) database. If information was deemed insufficient, additional data were requested. Cases of maternal mortality were reported to the national Maternal Mortality Committee of the Dutch Society for Obstetrics and Gynaecology by the attending obstetrician as usual. These cases were eventually added to the database.

We recorded maternal characteristics (age, body mass index, parity, and ethnicity), all variables concerning pregnancy and delivery, and neonatal outcome. We also recorded data on the specific complication, like seizure-to-delivery interval, number of seizures, symptoms and signs, blood pressures, laboratory values, and medicaments administered. A total of 130 items were entered into the database for each case. Characteristics of each hospital were also recorded (university or teaching hospital and annual number of deliveries).

Ethnicity was defined by country of origin ("geographical ethnic origin") and categorized according to the most common population groups in the Netherlands (Western, Moroccan, Surinam, Dutch Caribbean, Turkish, sub-Saharan African, Middle East, and Far East). We used the definitions of Statistics Netherlands, based on country of birth of the woman. Substandard care was defined as malcompliance with the recommendations in the guideline "Hypertensive Disorders in Pregnancy" of the Dutch Society of Obstetrics and Gynaecology[11] and was assessed in two different ways: first, substandard treatment of hypertension and prophylaxis of seizures according to the national guideline was assessed in all cases by the first author. Second, substandard care as judged by a national panel of experts analogously to the methodology of the ongoing analysis of maternal mortality in the Netherlands was assessed in a subgroup of 18 women. For this purpose, an audit meeting was organized. The panel, consisting of members of the Maternal Mortality Committee, members of the LEMMoN expert panel, members of the Managing Obstetric Emergencies and

Trauma course, and local staff of the 12 hospitals involved, assessed 12 cases of complicated eclampsia, selected by purposive sampling (cases with ICU admission, multiple seizures and availability of sufficient data). Substandard care was assessed using a standardized form with items related to patient, care providers and health care system, based on the national guideline.[11] A further six cases of eclampsia, which were assessed likewise during general audit meetings of the LEMMoN study, were added before analysis.

Main outcome measures of the study were incidence, case fatality rate, possible risk factors, and substandard care. Denominator data for the number of births in the Netherlands during the exact study period were obtained from Statistics Netherlands.[12] Births are registered based on birth certificates, which are required by law beyond 24 weeks of gestational age in the Netherlands. Reference values for possible risk factors for eclampsia were obtained from Statistics Netherlands (exact study period) and The Netherlands Perinatal Registry (LVR-2; 2005).[13] The Netherlands Perinatal Registry is the Dutch national perinatal database which covers nearly 100% of births under guidance of the obstetrician, in which parity, gestational age at delivery, mode of delivery, and place of antenatal care (midwife or obstetrician) are reliably registered. Each case is entered into the database by the attending clinician directly after birth. Data that were compared between cases and noncases was collected using the same fact-sheet from LVR-2.

Case fatality rate was calculated by dividing the number of deaths by the total number of cases.

To control for underreporting, we cross-matched our database with the Dutch perinatal database (LVR-2).[13] During a 5-month period, cases of eclampsia reported to this database but not to us were identified and local coordinators were asked to reanalyze these cases and report when appropriate.

Relative risks and confidence intervals were calculated in univariable analysis. Differences between groups were identified using χ^2, and significance was defined as $P<.05$. Statistical analysis was performed using Statistical Package for the Social Sciences 14.0 (SPSS Inc., Chicago, IL). The study was centrally reviewed by the institutional review board of Leiden University Medical Centre, and approval was obtained.

Results

All 98 obstetric units in the Netherlands participated in the study. During the study period, there were 371,021 deliveries in the Netherlands. From all 2,352 (98 hospitals, 24 months) monthly notification cards, 97% were returned, representing 358,874 deliveries.

Four of 226 reported cases of eclampsia were excluded because seizures were obviously caused by another illness, leaving 222 cases of eclampsia. For nine reported cases, we received no detailed data after notification, leaving a total of 213 cases available for analysis. Characteristics of women are shown in Table 1.

Table 1. Characteristics of study population.

	Eclampsia		*No eclampsia*	
	n	*(%)*	*n*	*(%)*
Age (mean 30.0 vs. 31.1)				
< 20 year	8	(3.8)	4645	(1.2)
20-35 year	160	(75.1)	279,026	(74.1)
35-40 year	39	(18.3)	79,756	(21.2)
≥ 40 year	6	(2.8)	13,056	(3.5)
Parity				
0	149	(70.0%)	169,971	(45.1%)
>0	64	(30.0%)	206,512	(54.9%)
Body Mass Index (BMI; kg/m^2)				
<18.5	5	(3.5)	n/a	(3.1)
18.5 - 24.9	84	(59.2)	n/a	(65.2)
25.0-29.9 (overweight)	33	(23.2)	n/a	(22.6)
≥ 30.0 (obese)	20	(14.1)	n/a	(9.1)
unknown	71			
Geographical ethnic origin				
Netherlands	147	(69.3)	280,752	(74.5)
Morocco/Turkey	16	(7.6)	29,368	(7.8)
Surinam/Dutch Antilles	15	(7.1)	13,211	(3.5)
other non-Western	25	(14.6)	20,552	(5.5)
other Western	9	(1.4)	32,812	(8.7)
unknown	1			

n/a: not available.

The incidence of eclampsia was 6.2 per 10,000 deliveries. There were three maternal deaths due to eclampsia, giving a case fatality rate of 1.4% (1 in 74). One woman died at home after repeated refusal of admission, two others died in the hospital after spontaneous term delivery. Other severe maternal and neonatal complications are listed in Table 2. Incidence varied largely by hospital, ranging from 0 to 30.9 per 10,000. The mean "hospital incidence" (only concerning cases under responsibility of the obstetrician) was 9.0 per 10,000 overall, 18.1 for tertiary care centres, and 8.5 for general hospitals. Incidence figures did not differ by volume of maternity unit (data not shown). First seizure occurred antepartum in 39.4%, intrapartum in 32.4%, and postpartum in 28.2% of cases. The median interval between first seizure and delivery was 8 hours for antepartum eclampsia (range 20 minutes to 11 days) and 1 hour for intrapartum eclampsia (range 0 minutes to 7 hours). For postpartum eclampsia, the median delivery-to-seizure interval was 5 hours (range 1 minute to 8 days). Fifty-one women (24.1%) had multiple seizures (range 2–5). The average duration of gestation was 37 weeks (range 22–42). Forty-one percent of the cases occurred preterm, 58% occurred at term (37– 42 weeks of gestation), and 1% post term. Preterm eclampsia occurred more often antepartum (odds ratio 9.9; 95% confidence interval 5.2–18.8), whereas at term eclampsia occurred more often intrapartum or postpartum.

Table 2. Major maternal and fetal complications

Complication*	number*	% of cases
Maternal		
Maternal death	3	1.4
ICU admission	89 (2)	41.8
HELLP	49 (1)	23.0
Referral to tertiary care centre	30	14.1
Major obstetric haemorrhage (≥10pc)	7	3.3
Cerebrovascular accident	7 (1)	3.3
Coma	5 (1)	2.3
(Suspicion of) placental abruption	5	2.3
Transient blindness	4	1.9
ARDS	3 (1)	1.4
Reversible Posterior Leuco-encephalopathy Syndrome	3	1.4
Pulmonary embolism	3	1.4
Two cases each of the following: disseminated intravascular coagulation (1), renal dialysis, sepsis, pneumonia	2	0.9
One case each of the following: cerebral oedema (1), hydrocephalus, Budd-Chiari syndrome, iatrogenic perforation of the stomach, conus-cauda syndrome due to intraspinal bleeding, myocardial ischemia, liver hematoma	1	0.5
Fetal (data available for 132 neonates)		
Intra uterine death	7 (1)	5.3
Neonatal death	4	3.0
pH < 7.00	10	9.1

*** between brackets are numbers occurring in cases of maternal death**

Multiple pregnancy, primiparity, young age, ethnicity, overweight, and complete antenatal care by the obstetrician were the most important factors associated with eclampsia (Table 3). In 18 women (8.5%) obstetric history revealed pregnancy-induced hypertension, preeclampsia or haemolysis, elevated liver enzymes, and low platelets syndrome. Thirteen women (6.1%) had pre-existent hypertension, six of whom were on antihypertensive medication before pregnancy.

Twenty percent of women had their first antenatal visit beyond 14 weeks of gestation, 7% beyond 20 weeks, and three women only booked at 32, 33, and 35 weeks of gestation. Two women had had no antenatal care at all at the moment of eclampsia. Booking was at least 1 month before the first seizure in all but four women.

In 38 cases (18%), the first seizure occurred at home, in six of them during or shortly after home delivery and in three others after discharge after hospital delivery. Twenty of these women had more than one seizure (54% of all out of hospital eclampsia cases). Of all 175 women experiencing eclampsia in the hospital, 111 (63.4%) were diagnosed as having preeclampsia on admission, and another 20 (11.4%) were admitted because of pregnancy-induced hypertension. Forty-four women (25.1%) were not known to be hypertensive and were admitted for other reasons, all but two intrapartum. The two women, who experienced antepartum eclampsia in the hospital, were admitted for regulation of diabetes and for observation of antepartum haemorrhage.

The mean systolic and diastolic blood pressure readings on admission were 157 mm Hg (range 105–230) and 98 mm Hg (range 57–137) among the 175 women with eclampsia in hospital and 169 mm Hg (range 80–240) and 109 mm Hg (range 60–164) among the women with eclampsia at home. On admission, 47.4% of cases had severe preeclampsia according to the criteria of the Dutch guideline.[11] Although prophylaxis of seizures is advised in these cases, only 15.4% received magnesium sulphate (Table 4). Premonitory signs and symptoms included headache (69%), upper abdominal pain (45%), nausea (49%), vomiting (28%), visual disturbances (41%), and hyperreflexia (55%). In 23 cases (10.8%), eclampsia occurred without any of these signs.

Table 3. Possible risk factors for eclampsia

risk factor	*Eclampsia*	*No eclampsia*	*RR (95% C.I.)*
Patient			
age < 20	3.8%	1.2%†	3.1 (1.5-6.3)
age < 25	17.8%	11.5%†	1.7 (1.2-2.4)
age ≥ 35	21.1%	24.7%†	0.8 (0.6-1.1)
BMI ≥ 25 (overweight)	37.3%	31.7%†	1.3 (0.9-1.8)
BMI ≥ 30 (obese)	14.1%	9.1%†	1.6 (1.0-2.6)
non-Western immigrant	26.4%	16.8%†	1.8 (1.3-2.4)
Surinam/Dutch Caribbean immigrant	9.6%	4.0%†	2.5 (1.3-4.9)
sub-Saharan African immigrant	6.8%	1.3%†	6.2 (3.6-10.6)
Pregnancy			
initial antenatal care by obstetrician	29.7%	14.3%‡	2.5 (1.9-3.4)
parity 0	70.0%	45.2%†	2.8 (2.1-3.8)
parity ≥3	2.4%	5.0%†	0.5 (0.2-1.1)
multiple pregnancy	9.9%	1.7%†	6.2 (4.0-9.7)
artificial reproduction techniques: IVF/ICSI	3.8%	1.9%[14]	2.0 (1.0-4.0)
Delivery (only for postpartum eclampsia, n=60)			
home delivery	8.3%	31.6%†	0.2 (0.1-0.5)
induction of labour	41.7%	12.5%‡	5.0 (3.0-8.4)
caesarean delivery without labour	18.7%	5.9%‡	3.7 (1.9-7.0)
ventouse/forceps	13.3%	8.6%‡	1.6 (0.8-3.4)
caesarean delivery overall	26.7%	14.0%	2.2 (1.3-4.0)
preterm birth (<37w)	31.7%	5.8%‡	7.5 (4.4-13.0)
post term birth (≥42w)	3.3%	4.3%‡	0.8 (0.2-3.1)

National reference values from †CBS (exact study period) and ‡LVR-2 (2005).

In 9.9% of all cases, eclampsia occurred despite prophylactic administration of magnesium sulphate. Magnesium sulphate was eventually administered in 96.2%. In 50.5% of these women diazepam was administered first. In the remaining cases, only diazepam was administered (n=3), treatment was only started after emergency caesarean delivery because of eclampsia (n=1),

treatment consisted of valproic acid (n=1), or maternal death occurred at home (n=1). Among the 51 women with multiple seizures, magnesium sulphate was initiated before the first seizure in four cases (7.8%), after the first seizure in 14 cases (31.1%), and only after the second or third seizure in 23 (51.1%) and four cases (8.9%), respectively. Three of the latter four concerned eclampsia at home, and successive seizures occurred in the ambulance or upon arrival at the hospital.

Antihypertensive treatment was initiated before the first seizure in 44 of 175 women (26.3%) with eclampsia in the hospital. On admission, 49 women (35.2%) had a systolic or diastolic blood pressure at or above the threshold of 170/110 mm Hg.11 In only 20 (40.8%) of these, antihypertensive drugs were initiated at that moment (Table 5). The most used intravenous agents were ketanserin (55.4%), labetalol (33.3%), and dihydralazine (8.3%).

Table 4. Warning signs and symptoms on admission in women and MgSO4 prophylaxis

Trigger	Specification	overall (n=175)	on MgSO4 [n=22 (12.6%)]	% of women with the feature*
Symptoms	severe headache/abdominal tenderness/ visual disturbances	61	14 (23.0%)	41.5%
Signs	severe hyperreflexia	23	8 (34.8%)	23.2%
lab values	liver enzymes >45; creatinin >100; thrombocytes <100	66	8 (12.1%)	51.2%
Proteinuria	stick + or >= 0.3 g/24h	102	13 (12.7%)	82.9%
Hypertension	diastolic BP >=110 or systolic BP >=170	49	10 (20.4%)	35.3%
severe PE†	BP >= 170/110 or BP >= 160/100 with serious symptoms/signs	65	10 (15.4%)	47.4%

BP, blood pressure; *cases where presence of the item is unknown were excluded; †according to the Dutch Guideline Hypertensive disease in pregnancy.

After cross-matching with the Dutch Perinatal Database, nine cases seemed not to have been reported to us. After a request for reanalysis of these cases to the local coordinators, six seemed to be incorrectly reported to the LVR as eclampsia. In one case, nobody responded to our request for reanalysis, and only two cases (3%) seemed to be truly underreported. These two cases were as yet reported. Because the underreporting seemed to be low, we decided not to repeat this analysis for the remainder of the study period.

During the plenary audit meetings, substandard care was judged to be present in 15 of 18 cases (83%; 95% confidence interval 59–96%) by the majority of assessors. In more than one half of these cases, substandard care was further classified as "major," indicating that different management might well have resulted in a different outcome. The majority of substandard care (87% of 312 items scored in total) was found at the level of the care providers, the main items being inadequate treatment of hypertension and inadequate seizure prophylaxis (33% and 38% of 225 eclampsia-related items scored, respectively).

Table 5. Blood pressure and antihypertensive treatment for eclampsia in the hospital (n=175)

Threshold	n	% of total*	antihypertensive treatment n(%) i.v.	Oral	none
BP on admission: diast>=110 or syst>=170	49	35.2	12 (24.5)	8 (16.3)	29 (59.2)
BP on admission: diast>=110	28	18.8	9 (32.1)	6 (21.4)	13 (46.4)
BP on admission: syst>=170	38	27.3	11 (28.9)	5 (13.2)	22 (57.9)
Severe pre-eclampsia on admission†	65	47.4	17 (25.8)	12 (18.2)	36 (54.5)
Highest recorded BP: diast>=110 or syst>=170	135	86.5	22 (16.3)	22 (16.3)	91 (67.4)

BP, blood pressure; *cases where blood pressure on admission is unknown were excluded; †according to the Dutch guideline 'Hypertensive Disease in Pregnancy'[11] (BP >= 170/110 or BP >= 160/100 with serious symptoms/signs)

Discussion

The incidence of 6.2 per 10,000 is clearly increased as compared with other neighbouring European countries (Table 6).

Table 6. Population-based incidence of eclampsia

Country	Period	n	Incidence (/10,000)
Europe			
Sweden[16]	1976-1980	74	2.9
Iceland[15]	1972-1991	40	4.6
Sweden[17]	1991-1992	80	3.3
UK[18]	1992	383	4.9
Finland[7]	1990-1994	77	2.4
Scandinavia[8]	1998-2000	210	5.0
Scotland[22]	2001-2002	25	4.9
Scotland[4]	2003-2005	55	3.5
UK[5]	2005-2006	214	2.7
Netherlands	**2004-2006**	**222**	**6.2**
Other			
USA[20]	1979-1986		5.6
USA* [21]	1988-1997	300	10.0
Canada[19]	1991-2001	973	3.8

*** representative sample instead of nationwide cohort**

Especially when compared with the more recently published studies in the United Kingdom and Scotland, our incidence seems to be twice as high. The results of our study are in line with earlier findings: maternal mortality due to hypertensive disorders in the Netherlands is three times as high as in the UK[6], and recent analysis revealed that substandard care was present in 26 of 27 cases.[1] Substandard treatment of hypertension was found in at least 60% of women and magnesium sulphate for seizure prophylaxis was administered in only 10% of cases, although we classified 47%

of cases as severe preeclampsia already on admission. The results of a clinical audit of a subset of 18 cases confirmed these findings. The nationwide design and support of this study, with 100% participation of Dutch maternity units, is its major strength. The major limitation of this study is that we did not collect individual data for the reference cohort of pregnant women in the Netherlands. Instead, we used nationwide incidence figures, which made it impossible to adjust relative risks for confounding variables in a multivariable model. Furthermore, despite multiple efforts, we cannot be sure that all cases have been reported to us. However, a cross-check for underreporting through the national perinatal database revealed minimal underreporting. Finally, we would have liked to have more cases assessed by the audit committee already, but unfortunately time and resources were limited. Substandard antihypertensive treatment and seizure prophylaxis, however, were assessed in all cases by the first author, and the audit process is continuing.

Our first concern is to check whether the reported cross-country difference is true or artificial, i.e., confounded by differences in study design or inclusion criteria. The Scottish ongoing surveillance system for eclampsia and other severe morbidities is very similar to our system and seems very reliable.[6,22] The two nationwide studies from the United Kingdom in 1992 and 2005 were both thoroughly expedited and had a very similar study design as ours.[5,18] Only the definition of eclampsia was stricter in the United Kingdom studies, thereby excluding 31 cases reported as eclampsia because abnormal laboratory values could not be confirmed. We doubt whether these cases should have been excluded, because eclampsia is primarily a clinical diagnosis, and abnormal laboratory values are not obligatory in our opinion. The incidence in the most recent study of Knight et al[5] would be only slightly higher (3.1/10,000) when cases were not excluded based on their definitions. Thus, our incidence of eclampsia seems to be truly increased. Although cross-country differences in population and prevalence of preeclampsia cannot be completely ruled out, it is unlikely that these differences play a significant role in explaining the difference.

Ethnic groups showing the highest incidence in our study are even more often represented in the United Kingdom, and overweight is also more prevalent.[6,23] Data on cross-country differences in prevalence of preeclampsia are not available. According to the Dutch guideline, treatment of hypertension is "strongly advised" with diastolic pressure of 110 mm Hg or more or systolic pressure of 170 mm Hg or more.[11] It is explicitly stated in the guideline that lower thresholds should apply in case of preeclampsia with signs and symptoms. In our study, many women were not treated according to this protocol when considering the highest systolic and diastolic blood pressures. Especially, systolic blood pressure too often did not trigger start of treatment, although it has been recognized that it is associated with the most serious maternal morbidity, especially cerebrovascular accidents.[24] Magnesium sulphate should not be regarded as an antihypertensive agent. Also regarding the decision to deliver preeclamptic women, Dutch obstetricians tend to be

too expectant. The median gestational age of all cases at the time of first seizure or delivery in our study was 38 weeks, with eclampsia even occurring post term in three cases. This is 3 weeks more than in the United Kingdom, where delivery after stabilization is explicitly recommended after 34 weeks.[5;25] With 50% of all women already being hospitalized because of preeclampsia, opportunities to prevent women from experiencing eclampsia were likely missed. Delivery should be pursued after 34 weeks in case of severe preeclampsia. A final aspect that could play a role in the increased incidence of eclampsia is the fact that proteinuria is not checked routinely during antenatal visits, causing delay in detection of preeclampsia. Also, pregnant women are often not informed about warning signs, which has led to significant patient delay in some instances. Routine checking of proteinuria in women with hypertension and a patient awareness leaflet could reduce these types of delay. Because there is clear evidence that magnesium sulphate is the
first-choice drug for treatment and prophylaxis of seizures, the use of diazepam should be strongly discouraged.[2] Incidence of hypertensive disorders in our study varied between women with different ethnic backgrounds, especially sub-Saharan African women seeming to have an increased risk (relative risk 6.2; 95% confidence interval 3.6 –10.6). This is in agreement with other reports.[6,22,26] The results are also consistent with the overall increased risk to immigrant
women of experiencing severe maternal morbidity in the Netherlands, but risks are more distinct for eclampsia than for other types of morbidity.[10] Despite several recent publications reporting declining incidences of eclampsia since the general introduction of magnesium sulphate for treatment and prophylaxis of seizures, we report a substantially higher incidence in the Netherlands as compared with other Western European countries.[4,5] Stricter adherence to the national guidelines is necessary to prevent eclampsia and other dramatic complications, including maternal death. The openness with which all participating obstetricians provided their data and participated in audits is encouraging, because these are important requirements for improvement in quality of care. The notion that training in obstetric emergency situations is important has become universal in the Netherlands, and the Managing Obstetric Emergencies and Trauma course is becoming an integral part of training of obstetricians and registrars. Ongoing local audit of cases of eclampsia will be implemented in the national quality assurance program to improve management and guidelines. Our study gives ample evidence that there is considerable room for improvement. Although we realize that there will always be unpreventable eclampsia, we feel that there is no reason for the Dutch incidence of eclampsia to be higher than in other Western European countries.

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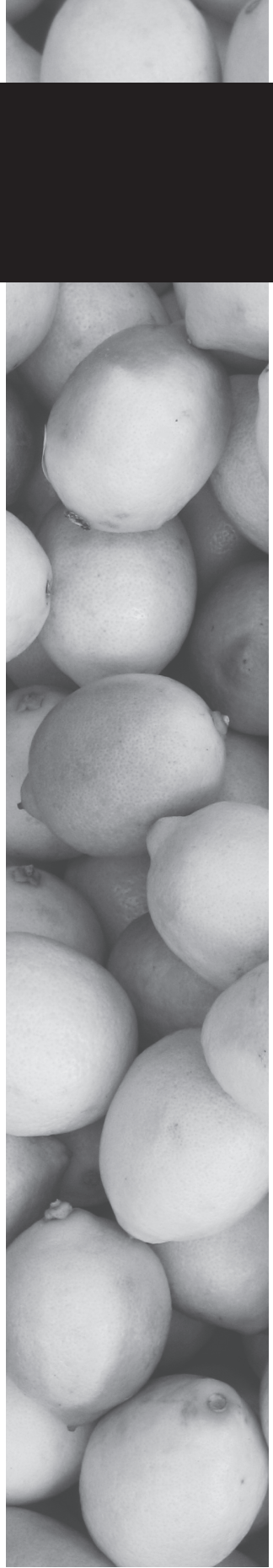
CHAPTER 8



Peripartum hysterectomy and arterial embolization for major obstetrical hemorrhage: a two-year nationwide cohort study in the Netherlands

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Abstract

Objective: To assess incidence, case fatality rates and risk factors of peripartum hysterectomy and arterial embolization for major obstetric haemorrhage.

Study design: Two-year prospective nationwide population-based cohort study. All pregnant women in the Netherlands during the same period acted as reference cohort (n=371,021)

Results: We included 205 women, overall incidence being 5.7 per 10,000 deliveries. Arterial embolization was performed in 114 women (incidence 3.2 per 10,000; case fatality rate 2.0%). Peripartum hysterectomy was performed in 108 women (incidence 3.0 per 10,000; case fatality rate 1.9%). Seventeen women had hysterectomy after embolization had failed to control haemorrhage. Caesarean delivery (RR 6.6; 95% CI 5.0-8.7) and multiple pregnancy (RR 6.6; 95% CI 4.2-10.4) were the most important risk factors in univariable analysis.

Conclusion: The rate of obstetric haemorrhage necessitating hysterectomy or arterial embolization in the Netherlands is 5.7 per 10,000 deliveries, with fertility being preserved in 46% of women by successful arterial embolization.

Introduction

Major obstetrical haemorrhage is the most frequent cause of severe acute maternal morbidity worldwide. Although maternal death due to haemorrhage is rare in Western countries, major obstetrical haemorrhage can lead to severe long-term sequelae and saving the mother's life sometimes demands the maximum of available resources. In the Netherlands, major obstetrical haemorrhage is responsible for 49% of obstetric admissions to intensive care units.[1] Recent studies demonstrate an increase of severe maternal morbidity related to major obstetrical haemorrhage in Western countries.[2-6] Possible explanations include the increasing age of women at birth, the increasing multiple pregnancy rate as a consequence of artificial reproductive techniques and the increasing caesarean delivery rate.

Since the maternal mortality ratio due to major obstetrical haemorrhage in Western countries is extremely low, and it therefore takes years to collect the numbers needed to be able to draw valid conclusions and learn lessons, severe maternal morbidity from obstetrical haemorrhage has gained interest as a new quality indicator of obstetric care.[2;7-9] An important indicator would be the number of peripartum hysterectomies or arterial embolisations for major obstetrical haemorrhage. Recently, the United Kingdom Obstetric Surveillance System (UKOSS) reported on the incidence of peripartum hysterectomy in the United Kingdom, which was 4.1 per 10,000 births.[10]

When facing major obstetrical haemorrhage that is intractable with conventional therapies, hysterectomy or embolization of the uterine and/or internal iliac arteries can be the last resort. Arterial embolization is increasingly the treatment of choice in these women in order to preserve fertility. A recent study concludes that fertility is not adversely affected by arterial embolization, and that women can conceive with normal pregnancy outcomes.[11] However, arterial embolization is not always appropriate, successful or available.

A nationwide cohort study of severe maternal morbidity, called LEMMoN, was conducted in the Netherlands to assess incidence, case fatality rates and risk factors for different types of morbidity, including major obstetrical hemorrhage.[12] Major obstetrical haemorrhage appeared to be the most frequent cause of severe maternal morbidity in the Netherlands, involving 51.1% of all women included. This article describes the most severe cases of major obstetrical haemorrhage from this study: women with peripartum hysterectomy or embolization. The main objectives of this study were firstly to describe the nationwide population-based incidence of arterial embolization and peripartum hysterectomy for obstetrical haemorrhage, and secondly to compare risk factors and outcomes of arterial embolization and peripartum hysterectomy for obstetrical haemorrhage.

Materials and Methods

Women were included from 1 August 2004 until 1 August 2006. All 98 hospitals (100%) with a

maternity unit in the Netherlands participated. Detailed methods were described previously.[12] In each hospital, a local coordinator reported all cases monthly using a standardized web-based form. Absence of cases in a particular month was also communicated to control for underreporting. Cases were identified in the respective hospitals using multiple strategies, including maternity computer databases, labour ward diaries, staff reports, intensive care admission registers, blood transfusion registers, discharge data and personal communication. All women with hysterectomy or arterial embolization due to obstetrical haemorrhage during pregnancy, delivery and puerperium (limited to six weeks postpartum) were included in the current study. Cases of first- or second-trimester instrumental abortion or termination of pregnancy up to 24 weeks were classified as 'early pregnancy'. Women who had hysterectomy after failed arterial embolization were analyzed in the hysterectomy group since hysterectomy was the ultimate treatment that stopped haemorrhage.

We recorded maternal characteristics (age, body mass index, ethnicity, single household and smoking), obstetric history, all data on pregnancy and delivery and specific data on major obstetrical haemorrhage (amount of blood loss, causes, surgical interventions, intensive care unit admission, blood products and medication administered, haemoglobin levels, clotting parameters). Body mass index was calculated using pre-pregnancy weight or weight measured during the first trimester. Cases with a missing value for a specific parameter were excluded when calculating the rate for that variable. We assessed the availability of arterial embolization in the Netherlands through a national survey.

Incidence was calculated using the total number of births in the Netherlands during the study period as the denominator. Denominator data for the number of deliveries in the Netherlands were obtained from Statistics Netherlands (CBS).[14] They were based on birth registries after correction for stillbirths of 24 weeks or over and multiple pregnancies. Relative risks (RR) with 95% confidence intervals (CI) and absolute risks were calculated if national reference data were available. National reference values for possible risk factors were obtained from Statistics Netherlands and the Netherlands Perinatal Registry.[15]

Case fatality rates were calculated by dividing the number of deaths after hysterectomy or arterial embolization by the number of cases of hysterectomy or arterial embolization. Cases in the arterial embolization and hysterectomy group were further analyzed by cause of haemorrhage. Although up to three causes could be reported, we classified women according to the most important cause of haemorrhage. We compared women in the current study to the total group of women having experienced major obstetrical haemorrhage in the Netherlands, defined as need for transfusion of four or more units of red blood cells.[12] Statistical analysis was performed using the SPSS statistical package 14.0 (SPSS Inc., Chicago, IL, USA). Approval of the Institutional Review Board was not necessary since all data were collected anonymously.

Results

During the study period, there were 371,021 deliveries in the Netherlands. All 98 hospitals with an obstetric ward in the Netherlands participated (100%). A maximum of 2352 (98 x 24) 'hospital-months' could be reported. Mainly due to later enrolment of some hospitals into the study, a total of 2275 'hospital-months' were actually returned (97%). Regarding only those maternities occurring during the months each hospital actively participated in the study, the study represented 358,874 deliveries.

Table 1. Possible risk factors for hysterectomy/arterial embolization for major obstetric emorrhage

	Hys/emb (n=205)	*Netherlands (n=358,874)*	*RR (95% CI)*	*Absolute risk (overall 1 in 1751)*
Patient				
age ≥ 35	43.4%	24.7%[a]	2.3 (1.8-3.1)	1 in 748
low income	26.7%	n/a		
Single household	3.4%	n/a		
BMI ≥ 25 (overweight)	28.2%	31.7%[a]	0.9 (0.6-1.2)	1 in 2060
BMI ≥ 30 (obese)	10.9%	9.8%[a]	1.1 (0.6-1.9)	1 in 1591
BMI ≥ 35 (morbidly obese)	4.7%	n/a		
non-Western immigrant	24.4%	16.8%[a]	1.6 (1.2-2.2)	1 in 1094
Pregnancy				
initial care by obstetrician	52.7%	14.3%[a]	6.7 (5.1-8.8)	1 in 262
prior caesarean delivery	26.8%	10.1%	3.3 (2.4-4.5)	1 in 529
placenta praevia	10.7%	n/a		
nulliparity	39.5%	45.2%[a]	0.8 (0.6-1.1)	1 in 2216
parity ≥3	7.3%	5.0%[a]	1.5 (0.9-2.5)	1 in 1167
multiple pregnancy	10.2%	1.7%[a]	6.6 (4.2-10.4)	1 in 265
artificial reproduction techniques: IVF/ICSI	9.5%	1.9%[17]	5.4 (3.2-9.0)	1 in 324
Delivery				
induction of labour	29.8%	12.3%[b]	3.1 (2.3-4.2)	1 in 568
caesarean delivery	49.8%	13.0%[a]	6.6 (5.0-8.7)	1 in 264
pre-labour caesarean delivery	23.9%	5.9%[a]	5.0 (3.6-6.9)	1 in 349
ventouse/forceps	11.7%	8.6%[a]	1.4 (0.9-2.2)	1 in 1242
home delivery	3.4%	31.6%[b]	0.1 (0.04-0.2)	1 in 218,826
breech delivery	9.3%	4.9%[a]	2.1 (1.3-3.4)	1 in 834
preterm birth (<37w)	17.8%	5.8%[b]	3.5 (2.5-5.1)	1 in 497
post term birth (≥42w)	4.5%	4.3%[b]	1.0 (0.6-2.1)	1 in 1683

National reference values from [a] Statistics Netherlands (exact study period) and [b]The Netherlands Perinatal Registry 2005; n/a: not available.

Hysterectomy or arterial embolization for major obstetrical haemorrhage was performed in 205 women (5.7 per 10,000 deliveries). This constituted 12.8% (205/1606) of all cases of major obstetrical haemorrhage reported to LEMMoN. Arterial embolization was performed in 114 women (incidence 3.2 per 10,000 deliveries), in 17 of whom hysterectomy was necessary as yet. Hysterectomy was performed in 108 women (incidence 3.0 per 10,000 deliveries). Four women died, two after embolization, one after hysterectomy and one after both procedures. Overall case fatality rate was 2.0% (4/205). In 95 women (46% of all cases) fertility could be preserved by the availability of arterial embolization.

Possible risk factors for arterial embolization or hysterectomy with reference to national data[14;15] are shown in table 1, including absolute risks. When comparing these therapies, women older than 35 years had a higher risk of hysterectomy than arterial embolization (RR 1.4, 95%CI 1.1-1.8), whereas nulliparae had a lower risk (RR 0.3, 95%CI 0.2-0.5).

Diagnosis

An overview of the causes of major obstetrical haemorrhage, in both the peripartum hysterectomy and the arterial embolization group, is shown in table 2. In 50% of women, more than one diagnosis was reported, most important combinations being uterine atony with disorders of placentation or placental remnants.

Table 2. Causes of major obstetric haemorrhage[a] (n=201[b])

Primary diagnosis	*hysterectomy (n=105) (%)*	*arterial embolization (n=96) (%)*
Disorders of placentation[c]	37 (35)	5 (5)
Uterine atony[d]	29 (28)	32 (33)
Uterine rupture	11(10)	0 (0)
Placental remnants[d]	10 (10)	30 (31)
Iatrogenic during surgery[e]	8 (8)	13 (14)
Genital tract laceration	4 (4)	11 (11)
Blood coagulation disorders	1(1)	0 (0)
Miscellaneous[f]	4 (4)	4 (4)
Placenta praevia as single diagnosis	1 (1)	1 (1)
Total placenta praevia	15 (14)	7 (7)

[a]only most important cause was considered; [b]for 4 women no diagnosis available; [c]includes morbidly adherent placenta (n=25), placenta praevia (n=2) and combination of both (n=12); [d]includes placenta praevia (n=1); [e]includes placenta praevia (n=2); [f]includes placenta praevia (n=2), placental abruption (n=2) and blood coagulation disorders (n=1)

The choice for arterial embolization or hysterectomy depended largely on the cause of major obstetrical haemorrhage. In case of uterine rupture or morbidly adherent placenta, 100 and 88% of women had a hysterectomy respectively. In contrast, in case of uterine atony and retained placenta/ placental remnants, only 45 and 25% had a hysterectomy.

Hysterectomy appeared to be strongly associated with placenta praevia and morbidly adherent placenta. Fifteen women (14%) had placenta praevia in the index pregnancy, thirteen of whom (87%) had a morbidly adherent placenta. Nine (60%) had a caesarean delivery in their obstetric history, as was the case for seven (54%) women with a morbidly adherent placenta.

Mode of delivery

In six women haemorrhage occurred in early pregnancy, resulting in embolization in one case after termination of pregnancy at 20 weeks of gestational age. In the remaining five cases, hysterectomy was performed after D&C (n=3), incomplete abortion (n=1) or placenta percreta (n=1). This last case consisted of a hysterectomy performed with the foetus still in utero at 16 weeks of gestational age because of placenta percreta growing into the bladder causing massive intra-abdominal haemorrhage.

In the remaining 199 cases, the overall caesarean delivery rate was 51% (64% and 38% respectively for hysterectomy and arterial embolization, RR 1.7 (95% CI 1.3-2.3).

RRs for hysterectomy or embolization related to mode of delivery are shown in table 1. RR of hysterectomy alone for major obstetrical haemorrhage after caesarean delivery was 3.6 (95% CI 2.5-5.2) as compared with women who had a vaginal delivery.

Other interventions

Different treatment strategies had been used before embolization or hysterectomy were eventually necessary (Table 3). Three women (1%) had no additional therapy at all, of which in one case caesarean hysterectomy was electively performed for placenta praevia. In the second case a woman had a placenta praevia percreta in the scar of a prior caesarean, which could not be removed. In the third case elective caesarean hysterectomy was performed in a woman with beta-thalassemia and placenta praevia. Four women were Jehovah's witnesses and did not receive any blood products at all, which in one case resulted in maternal death.

Figure 1.

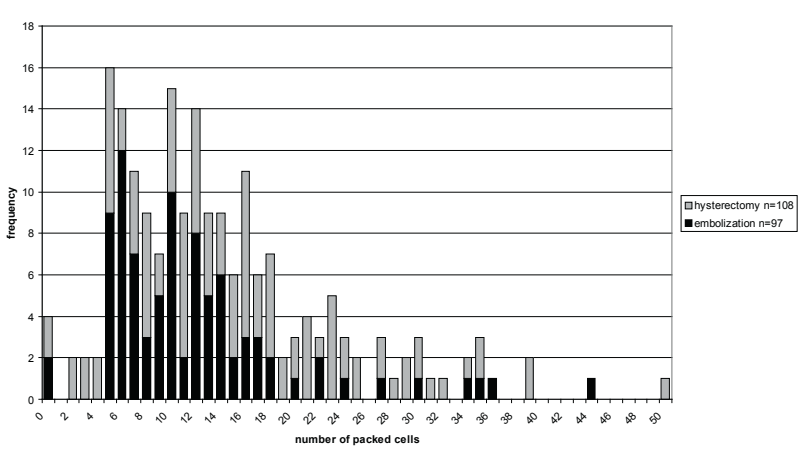

Table 3. Other interventions (n=205)

Therapy	*hysterectomy (n=108)* *n (%)*	*arterial embolization (n=97)* *n (%)*
Misoprostol	14 (13)	13 (13)
Syntocinon	87 (81)	87 (90)
Methergin	21 (19)	15 (15)
Sulproston	72 (67)	83 (86)
Plasma replacement therapy	86 (80)	75 (77)
Recombinant factor VIIa	19 (18)	14 (14)
Prothrombine complex	1 (1)	2 (2)
Fibrinogen	3 (3)	1 (1)
Red blood cells[a]	105(98)	89 (98)
Eight or more red blood cells[a]	86 (80)	59 (65)
Fresh frozen plasma[b]	90 (89)	86 (95)
Platelets[b]	61(62)	49 (53)
Manual placenta removal	17 (16)	16 (16)
Removal of placental remnants	30 (28)	44 (45)
Balloon therapy	23 (21)	29 (30)
Other surgical interventions[c]	11 (10)	6 (6)

[a] data missing for 7 women; [b] data missing for 13 women; [c] ligation of arteries, B-lynch suture, inspection

Blood transfusion requirements of both the arterial embolization and the hysterectomy group are shown in Figure 1. Women undergoing hysterectomy were transfused significantly more units of red blood cells (median 14) than women undergoing arterial embolization (median 10; p=0.002). Women in the hysterectomy group needed significantly more often massive transfusion, defined as eight or more units of red blood cells (RR 1.5; 95% CI 1.1-2.1) and were more often admitted to an intensive care unit (RR 1.6; 95% CI 1.1-2.4) as compared with women in the embolization group. Median hospitalization for hysterectomy was 10 days (range 2-65) versus 7 (range 1-38) for embolization.

Details of hysterectomy

An overview of different timing, procedures and complications of hysterectomy is shown in table 4. Sub analysis by primary cause of haemorrhage revealed no significant differences. Of 11 women with urinary tract lesions, eight had damage of the bladder and three of the ureter. Unilateral ovarian removal occurred in eight women (7%). Two women died after hysterectomy (2%). One woman had major obstetrical haemorrhage due to uterine atony after spontaneous vaginal delivery.

She died from cerebral damage caused by hemorrhagic shock. The other woman developed sepsis with intrauterine fetal death at 36 weeks of gestation. She developed postpartum haemorrhage and died from multi-organ failure.

Table 4. Procedure, timing and complications of hysterectomy (n=108)

Procedure	*n (%)*
Total hysterectomy	40 (37)
Supravaginal hysterectomy	52 (48)
Unknown	16 (15)
Timing	
Hysterectomy after vaginal delivery	41 (38)
Caesarean hysterectomy	29 (27)
Relaparotomy after caesarean	38 (35)
Complications	
Urinary tract lesions[a]	11 (10)
Removal of ovary	8 (7)
Infection[b]	8 (7)
Relaparotomy[c]	15 (14)
Sheehan syndrome	4 (4)
Paralytic ileus	3 (3)
DVT / Pulmonary embolism	3 (3)
Others	2 (2)
Maternal death	2 (2)

[a] including eight bladder lesions and three ureter lesions; [b] including two abscesses; [c] including one case of burst abdomen

Details of arterial embolization

Of all 98 obstetrically active hospitals in the Netherlands, 23% reported to have unrestricted availability of arterial embolization 24 hours a day and another 20% reported availability in consultation with the intervention radiologist. During office hours, percentages were 30 and 15, respectively. All tertiary care centres had 24-hour availability of an intervention radiology team.

Methodological details and complications of arterial embolization procedure are shown in table 5. Fifty-nine women (61%) received eight or more units of packed cells (median 10; range 0-44). Intensive care unit admission occurred in 67 women (69%). Of the twelve women developing symptoms and signs of infection after arterial embolization, nine (75%) had had caesarean delivery.

In 20 cases (18%), arterial embolization failed. In fifteen cases hysterectomy was necessary as yet to stop haemorrhage. In two cases uterine necrosis occurred resulting in hysterectomy, in one case intrauterine balloon tamponade stopped haemorrhage as yet, and two women died. In three cases the procedure could not be completed due to vasospasms (which terminated the bleeding).

One woman was embolised three times before hysterectomy was performed. During the first attempt both uterine arteries were embolised, followed by embolization and re-embolization of both internal iliac arteries. Failure rate varied by mode of delivery. Of 66 women with arterial embolization following vaginal delivery, 5 (8%) eventually underwent hysterectomy. Of 48 women with embolization after caesarean delivery, 12 (25%) eventually underwent hysterectomy (RR 1.9; 95% CI 1.3-2.8). Thirteen out of 20 women with failed embolization (65%) had one or more deliveries in obstetric history.

Table 5. Procedure and complications of embolisation (n=114)

Procedure	*n (%)*
Uterine artery *(42 bilateral, 3 left, 8 right)*	53 (46)
Internal iliac artery *(23 bilateral, 1 left)*	24 (21)
Combination of iliac and uterine artery	3 (3)
Hepatic artery	1 (1)
Unknown	33 (29)
Complication of Embolization	
Hysterectomy	17 (15)
Infection (9 after caesarean delivery)	9 (8)
ARDS	1 (1)
Laparotomy	3 (3)
Ischemic complaints	2 (2)
Maternal death	3 (3)

Comment

The LEMMoN study includes the first nationwide survey of major obstetrical haemorrhage in the Netherlands, comprising of 1606 cases (4.5 per 1000 deliveries).[9] In this article, the severest cases of major obstetrical haemorrhage, ultimately leading to arterial embolization or hysterectomy, have been mapped. The incidence in our study was 5.7 per 10,000 deliveries, 3.2 per 10,000 for arterial embolization and 3.0 per 10,000 for hysterectomy.

The European Perinatal Health Report (Peristat-II) recently reported nationwide incidence figures of peripartum hysterectomy varying between 2 and 10 per 10,000 deliveries.[19] Although the increasing attention to severe maternal morbidity is welcomed, the figures in this report should be interpreted cautiously as case ascertainment varied greatly between countries and detailed methods of data collection were not reported.

The incidence of hysterectomy for major obstetrical haemorrhage is increasing. A nationwide population-based Canadian study showed an increase of obstetrical haemorrhage necessitating hysterectomy from 2.6 per 10,000 deliveries in 1991-1993 to 4.6 per 10,000 in 1998-2000.[3] Further increase was suggested

recently by a regional population-based study from Canada, reporting an incidence of 8 per 10,000 deliveries in 1999-2006 [20] A nationwide cross-sectional study in the United States from 1998 to 2005 reported an increase as well.[6] Additionally, an Australian population-based study reported an overall increase of adverse outcomes in women with postpartum haemorrhage of 14.3% between 1999 and 2004.[5] Since hysterectomy is one of the severest complications of pregnancy, the necessity to examine differences and increase in incidence cannot be disregarded.

To our knowledge, this study includes the first report of nationwide incidence of arterial embolization in the literature. A factor that might bias the relatively low incidence of peripartum hysterectomy in the Netherlands is the relatively frequent use of arterial embolization, which prevented hysterectomy in half of all cases. We were not able to compare the availability of arterial embolization in the Netherlands with other countries, or with another period. In some countries, the existence of large, separate maternity hospitals hampers general availability of arterial embolization for major obstetrical haemorrhage. Although the low incidence of major obstetrical haemorrhage necessitating arterial embolization alone (about one case a year for an average Dutch obstetric unit) may not warrant the 24 hour availability of an interventional radiology team in every hospital, radiological intervention is also increasingly used in other non-obstetric acute situations and the trend towards centralization of obstetric care in the Netherlands will likely increase availability of arterial embolization over the next few years.

Several studies that aimed to identify risk factors for peripartum hysterectomy showed that caesarean delivery - in the current pregnancy and in the obstetric history - is an important risk factor. We confirmed this finding in this prospective population-based study, relative risk for hysterectomy or arterial embolization in women with a caesarean delivery being 6.6 for caesarean in the index pregnancy and 3.3 for previous caesarean. As the rates of caesarean delivery continue to rise rapidly worldwide, and peripartum hysterectomy most often is a remote complication of caesarean delivery, a further increase of the incidence of peripartum hysterectomy and arterial embolization can be expected. It is therefore of vital importance to identify causes of the increase in caesarean delivery rates. Reduction of these rates will likely prevent many cases of peripartum hysterectomy and arterial embolization.

Other possible risk factors for major obstetrical haemorrhage with subsequent hysterectomy or arterial embolization in this study included advanced maternal age, non-Western ethnic origin, multiple pregnancy, artificial reproduction techniques (resulting in many multiple pregnancies), breech delivery and preterm birth. The higher risk for hysterectomy with advanced maternal age could be explained by the fact that older women generally already have children, and clinicians will be more eager to preserve fertility in young and often nulliparous women. Body mass index appeared not to be a risk factor in this study.

During the study, only one woman who delivered at home required hysterectomy. This validates the proper functioning of selection of low-risk pregnancies in the Netherlands.

In the sub analysis of failed arterial embolization procedures, we found a 25% failure rate for arterial embolization following caesarean delivery. This implicates thorough consideration proceeding to embolization when facing major obstetrical haemorrhage after caesarean. Contrarily, the success rate of arterial embolization was significantly increased in nulliparous women, which has also been found in a trial of arterial embolization versus hysterectomy in the treatment of symptomatic uterine fibroids.[18] No explanation, however, was found for this phenomenon.

Apart from the failure rate and consequently loss of valuable time, there were few negative side-effects of arterial embolization. Indeed, the rate of intensive care unit admission in the arterial embolization group was significantly lower and women received significantly less blood products. These numbers may be biased by the fact that in critical situations the risk of a failing embolization will not be taken, and clinicians will proceed to immediate hysterectomy.

The main limitation of this study is that we did not record the individual characteristics of all maternities without hysterectomy or arterial embolization during the study period. Therefore, we could not adjust RRs for confounding variables. For some associated factors, it is important to realise that the condition could be the cause of severe maternal morbidity, but it could also represent the result of it. This bias by indication especially occurs in case of caesarean delivery, which was regularly performed because of (imminent) obstetrical haemorrhage. Likewise, preterm birth is also closely related. Due to the nationwide nature of the study, we depended on the active participation of local coordinating obstetricians for completeness of data. We tried to meet this by keeping coordinators actively involved and providing help in collecting data. Finally, we thoroughly controlled for underreporting. Underreporting of major obstetrical haemorrhage was estimated at 35% but appeared to be mainly due to relatively less severe complications requiring 'only' four units of red blood cells.[21] However, no underreporting of cases of hysterectomy or arterial embolization was found.

Fertility has been preserved in 95 women, almost half of all cases. Together with the lower rate of intensive care unit admissions, reduced need for blood products, shorter hospitalization and smaller invasiveness, arterial embolization seems to be an attractive alternative when facing severe, therapy resistant obstetrical haemorrhage. Ideally, these observational findings should be confirmed in a randomized trial but this will unlikely be designed due to ethical considerations. Only individual audit of cases could reveal important disadvantages of arterial embolization. Exact indications and contraindications for arterial embolization remain to be determined in future research. However, in face of the increasing number of caesareans worldwide, further distribution of knowledge and skills of embolization is necessary. Additionally, causes of this increase should be identified, in order to reduce the caesarean rate. This may lead to reduction of the incidence of major obstetrical haemorrhage, along with its morbidity and costs, and fertility can be spared substantially.

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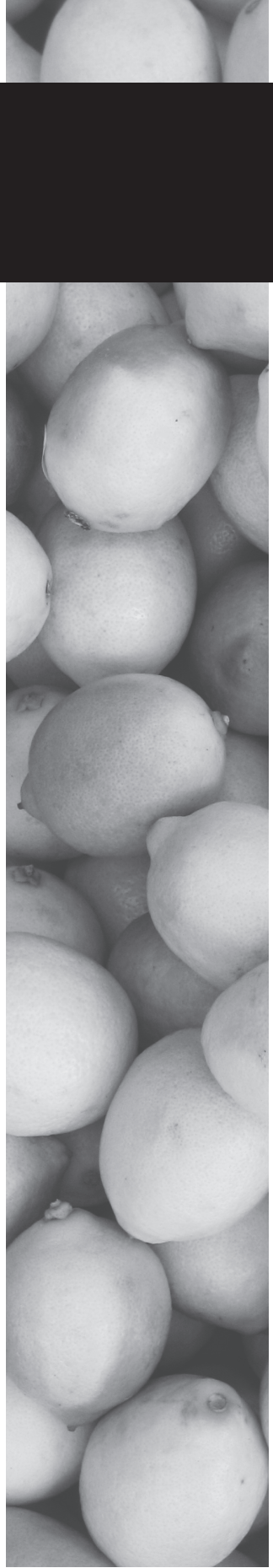
CHAPTER 9



Maternal mortality and severe maternal morbidity in Jehovah's witnesses in the Netherlands

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Abstract

Objective: To determine the risk of maternal mortality and serious maternal morbidity because of major obstetric haemorrhage in Jehovah's witnesses in the Netherlands.

Design: A retrospective study of case notes.

Setting: All tertiary care centres, general teaching hospitals and other general hospitals in the Netherlands.

Sample: All cases of maternal mortality in the Netherlands between 1983 and 2006 and all cases of serious maternal morbidity in the Netherlands between 2004 and 2006.

Methods: Study of case notes using two different nationwide enquiries over two different time periods.

Main outcome measures: Maternal mortality ratio (MMR) and risk of serious maternal mortality.

Results: The MMR for Jehovah's witnesses was 68 per 100,000 live births. We found a risk of 14 per 1000 for Jehovah's witnesses to experience serious maternal morbidity because of obstetric haemorrhage while the risk for the total pregnant population was 4.5 per 1000.

Conclusions: Women who are Jehovah's witnesses are at a six times increased risk for maternal death, at a 130 times increased risk for maternal death because of major obstetric haemorrhage and at a 3.1 times increased risk for serious maternal morbidity because of obstetric haemorrhage, compared to the general Dutch population.

Introduction

Jehovah's witnesses form a religious society with more than six million members worldwide, 29,500 of which live in the Netherlands. Based on biblical textures, Jehovah's witnesses refuse transfusion of blood or one of its primary components (red and white blood cells, platelets and plasma), even when red blood cell transfusion would be life saving.[1;2]

Major obstetric haemorrhage is the most frequent cause of serious maternal morbidity and is one of the most important causes of maternal mortality.[3;4] Refusal of blood in this medical emergency exposes women who are Jehovah's witnesses to an increased risk of maternal death.[5] We have undertaken a retrospective study of case notes to determine the maternal morbidity and mortality because of major obstetric haemorrhage in Jehovah's witnesses in the Netherlands.

Methods

A retrospective study of case notes of Jehovah's witnesses experiencing serious maternal morbidity and mortality was performed, using two different nationwide enquiries over two different time periods.

All deaths related to pregnancy in the Netherlands are reported to the Maternal Mortality Committee of the Dutch Society of Obstetrics and Gynaecology. Cases reported between 1983 and 2006 were included in a nationwide Confidential Enquiry into Maternal Deaths in the Netherlands. Maternal death was defined according to the World Health Organization's (WHO) International Classification of Diseases, tenth revision (ICD-10).[2;3]

Details about the patients (including religious affiliation) and the course of events that preceded the death of the women were present for all the cases that were included in this confidential inquiry and we selected all Jehovah's witnesses. If available, the original medical files were studied. Cases of serious maternal morbidity were selected from a nationwide enquiry into ethnic determinants of severe maternal morbidity (LEMMoN). All 98 maternity units in the Netherlands participated in this nationwide study. Cases of severe maternal morbidity were included during a 2-year period from 1 August 2004 until 1 August 2006 and classified in one or more of the following five categories: (1) Intensive Care Unit admission, (2) uterine rupture, (3) eclampsia or HELLP syndrome with liver haematoma or rupture, (4) obstetric haemorrhage requiring transfusion of 4 units of red blood cells or more and (5) other serious complications, not meeting the criteria of the other categories.[4] Detailed information and copies of relevant parts of the files were present for all cases that were included in the study. We selected and studied all cases of Jehovah's witnesses reported to this enquiry.

The incidence of maternal mortality and serious maternal morbidity in Jehovah's witnesses was compared with the total incidence of maternal mortality as reported to the Maternal Mortality Committee and with the total incidence of maternal morbidity as reported to the LEMMoN study. The total number of deliveries among Jehovah's witnesses was calculated using the annual national birth rate and the

total number of Jehovah's witnesses in the Netherlands in the years 1983 through 2006. These data are carefully registered by Statistics Netherlands (CBS) and the Watchtower Society respectively.[1;6]

Results

Mortality

In the period of 1 January 1983 to 1 January 2007, 538 cases of maternal mortality were reported to the Maternal Mortality Committee and included in the Confidential Enquiries into Maternal Deaths in the Netherlands. The number of direct maternal deaths (late maternal deaths included) was 385 and 30 of these direct maternal deaths were caused by obstetric haemorrhage.

Six cases of mortality in Jehovah's witnesses were identified. All were direct maternal deaths caused by major obstetric haemorrhage and the refusal of red blood cell transfusion was an important factor in the course of events leading to the death of these six women. Hypovolaemic shock causing cardiac failure or post-anoxic encephalopathy was the mode of death. The underlying causes of haemorrhage were: complication of caesarean section (n = 1),[7] uterine atony after manual removal and after spontaneous delivery of the placenta (n = 2). One woman was readmitted after 3 weeks because of severe haemorrhage because of retained placental fragments. Two women had HELLP syndrome. One of them developed disseminated intravascular coagulation (DIC) and postpartum haemorrhage. The other woman with HELLP syndrome also had sickle cell anaemia. She underwent a caesarean section. The procedure was uncomplicated and with limited blood loss, but she died on the ICU because of post-anoxic encephalopathy and cardiac failure (Table 1).

Hysterectomy was not performed in any of these women. The two women suffering from uterine atony were treated with uterine tamponade using an intrauterine balloon and in one of them, arterial embolisation was performed because of persistent bleeding (Table 1).

Between 1983 and 2006, the number of cases of direct and indirect maternal mortality in the Netherlands varied yearly between 10 and 31 cases. The total maternal mortality ratio (MMR) during the study period was 11.7 per 100,000 live births.[4,5] The MMR for direct maternal deaths was 8.4 and the MMR for maternal deaths caused by major obstetric haemorrhage was 0.67. When the six cases of maternal death in Jehovah's witnesses are subtracted, the MMR's are 11.4, 8.2 and 0.52 respectively.

The six selected cases were all direct maternal deaths because of obstetric haemorrhage. They represented 1.1% of total maternal deaths, 1.6% of total direct maternal deaths and 20% of direct maternal deaths caused by obstetric haemorrhage reported to the Maternal Mortality Committee between 1983 and 2006. The total number of deliveries in Jehovah's witnesses during these years was calculated to approximate 8850. This yields a MMR of 68 per 100,000 live births, which is six times higher than the MMR for the general Dutch population and 130 times higher than the MMR for maternal deaths because of major obstetric haemorrhage.

Table 1. Maternal mortality in Jehovah's witnesses.

Nr	Year , age and obstetric history	Course of events	Total blood loss and lowest Hb
1	1986 41y, G3P2	Delivery at term. VE because of prolonged second stage. Major haemorrhage. Readmission after 3 weeks because of persistent bleeding due to placental rest. Manual removal of placental rest. The next day hypovolemic shock due to haemorrhage caused myocardial infarction and death. Autopsy confirmed death due to haemorrhage. **Substandard care**: Not enough data available to identify substandard care	unknown
2	1986 21y, unknown parity OH: unknown	Admitted at 31 weeks because of eclampsia. Fetal death, spontaneous vaginal delivery. Haemorrhage, HELLP and DIC. Death 9 days post partum. **Substandard care:** Not enough data available to identify substandard care	unknown
3	1988 40y, G3P2	Emergency caesarean section at 40,6 weeks because of prolonged second stage and suspected CPD. Difficult extraction. Haemorrhage due to laceration of uterine incision and rupture of uterine vessels. Autopsy confirmed death due to hypovolemic shock. **Substandard care:** Complication of CS not identified as substandard care	4500 ml 1.8 g/dl
4	1995 22y, G4P0 OH: recurrent SA (3x)	Induction of labour at 40,6 weeks with syntocinon because of ruptured membranes for 24 hours. Epidural. Oxytocin because of prolonged first stage. VE because of fetal distress. Placenta spontaneous after oxytocin iv. Haemorrhage due to uterine atony and secondary coagulopathy. **Management:** oxytocin, methylergometrin, tamponade of uterus, sulproston iv and in utero. ICU admission. Volume replacement therapy. Death 3.5 hours post partum due to hypovolemic shock. **Substandard care:** No hysterectomy performed	Unknown 4.0 g/dl
5	1996 30y, G2P1 OH: PROM at 20 weeks, CS at 28 weeks.	Sickle cell anaemia. Admitted twice for sickle cell crisis. Threatening preterm labour at 29 weeks. Nifedipine as tocolytic. HELLP syndrome. At 30 weeks thrombocytopenia (49 x 10^9/L). CS because of maternal condition. ICU admission, death due to cardiac failure and postanoxic encephalopathy . **Substandard care:** CS performed on unstable patient	Unknown 5.9 g/dl (before CS)
6	2006 25y, G3P1 OH: CS, placenta praevia	Delivery at 40,4 weeks. VE because of prolonged second stage. Retained placenta with limited haemorrhage (300 ml). MRP. Haemorrhage due to uterine atony. **Management:** Oxytocin, misoprostol, sulproston, cyklokapron. Tamponade with uterine balloon. Embolisation of internal iliac arteries because of persistent bleeding. Recombinant factor VIII. Death on ICU due to cardiac failure. **Substandard care:** No hysterectomy performed	> 4000 ml 1.3 g/dl

VE = vacuum extraction, DIC = disseminated intravasal coagulation, CPD = cephalo-pelvic disproportion, SA = spontaneous abortion, PROM = premature rupture of membranes, CS = caesarean section, EPO = erythropoietin, IUFD = intrauterine fetal death, MRP = manual removal of the placenta,

Serious maternal morbidity

A total of 2552 cases were included in the nationwide enquiry into ethnic determinants of severe maternal morbidity. Among these, there were 1606 cases of major obstetric haemorrhage. From this study, we identified ten cases of serious maternal morbidity in Jehovah's witnesses (0.39% of included cases). The serious maternal morbidity in all ten cases were because of major obstetric haemorrhage (0.62% of cases of major obstetric haemorrhage) and refusal of red blood cell transfusion was an important causative or contributory factor in all of these.

The ten selected cases delivered in tertiary care centres (n = 4), general teaching hospitals (n = 3) and other general hospitals (n = 3). Home delivery under supervision of a midwife was planned in one woman (patient no. 15). She was transferred to hospital because of a prolonged first stage of labour and fever.

In seven women, haemorrhage occurred after vaginal delivery, one of which was a vacuum extraction and in the other three after caesarean section. The underlying causes of haemorrhage were: retained placenta (n = 2), uterine atony (n = 3), laceration of cervix and vagina (n = 2) and retained placental fragment with laceration of cervix (n = 1). The woman who underwent a vacuum extraction developed sepsis with coagulopathy and experienced haemorrhage without signs of uterine atony or laceration. One woman was readmitted 3 weeks after initial discharge from hospital because of severe haemorrhage of unidentified cause (Table 2).

Active management of the third stage of labour with oxytocin was carried out in all cases. Haemorrhage was treated with volume replacement, one or more uterotonic agents (oxytocin, sulproston, methylergometrin, misoprostol) and ferrous sulphate. In five women (patients no. 7, 8, 9, 10 and 16), this treatment was sufficient. Five patients (patients no. 11, 12, 13, 14 and 15) had haemoglobin concentrations of 3.7 g/dl or less. All five were admitted to the intensive care unit and received erythropoietin. One was treated with arterial embolisation and in two women, hysterectomy was performed. Two women (patients no. 11 and 13) were transferred to the Academic Medical Centre in Amsterdam because of the availability of hyperbaric oxygen therapy in this hospital, but in both cases, the treatment eventually was not necessary. One woman (patient no. 16) initially refused blood, but she decided to accept transfusion 1 day postpartum (Table 2).

In the years 2004 through 2006, the number of deliveries in the Netherlands was 358,874, corresponding with a birth rate of 11.9 per 1000 inhabitants.[4,6] A total of 1606 cases of serious morbidity caused by major obstetric haemorrhage were included in the LEMMoN study, yielding a risk of 4.5 per 1000 births.

During these years, a stable number of 29,500 active members were registered at the society of Jehovah's witnesses in the Netherlands.[1] Using national fertility statistics, it is estimated that, in the study period, there were 700 deliveries in women who are Jehovah's witnesses. This yields a 14 per 1000 risk for Jehovah's witnesses, 3.1 times higher than the risk for the total pregnant population.

Table 2. Severe maternal morbidity in Jehovah's witnesses.

Nr	Age, parity and obstetric history	Course of events	Total blood loss and lowest Hb
7	39y, G10P6 OH: IA, SA (2x) , preterm labour (4x)	Cerclage and progesterone because of recurrent SA and preterm labour. Spontaneous vaginal delivery at 41,4 weeks. Haemorrhage due to retained placental fragment and cervical laceration. **Management:** Oxytocin, sulproston. MRP. Suturing of cervix. Ferrous sulphate. **Substandard care:** Not identified	3800 ml 6.6 g/dl
8	40y, G18P7 OH : IUFD, recurrent SA (10 x), placental abruption, VE	Preterm labour at 35,5 weeks. Elective CS because difficult VE in obstetric history. Peroperative haemorrhage due to uterine atony. **Management:** Oxytocin, methylergometrin, sulproston, ferrous sulphate. **Substandard care:** Not identified	1500 ml 6.9 g/dl
9	27y, G2P1 OH: obstetric haemorrhage	Spontaneous vaginal delivery at 40,5 weeks. Retained placenta with moderate haemorrhage (700 ml). MRP. Haemorrhage due to uterine atony. **Management:** Oxytocin, sulproston, methylergometrin, ferrous saccharate. **Substandard care:** Not identified	3500 ml 6.0 g/dl
10	29y, G1P0	Spontaneous vaginal delivery at 39.5 weeks. Haemorrhage due to retained placenta. **Management:** Oxytocin. MRP. Ferrous saccharate. **Substandard care:** Not identified	2600 ml 3.9 g/dl
11	25y, G2P1	Induction with prostaglandins at 38,5 weeks because of pre-eclampsia. Haemorrhage due to laceration of cervix and vagina. **Management:** Suturing of cervix and vagina. Oxytocin, sulproston, tranexamic acid, recombinant factor VII. Embolisation uterine arteries after persistent bleeding. ICU admission, EPO, darbepoietin alpha, ferrous saccharate. MgSO4 because of convulsions of uncertain underlying cause. **Substandard care:** No hysterectomy performed	2800 ml 3.1 g/dl
12	28y, G1P0	Bells palsy at 38,5 weeks. Hypertension. Spontaneous labour at 40,2 weeks, oxytocin because of prolonged second stage. Haemorrhage due to laceration of cervix and vagina and secondary coagulopathy. **Management:** Suturing of cervix and vagina. ICU admission. Oxytocin, sulproston, cyklokapron, desmopressin, EPO, ferrous saccharate, coagulation factors [1]. **Substandard care:** Not identified	4000 ml 3.5 g/dl
13	25y, G2P1 OH: CS	Repeat elective CS at 40,4 week. Haemorrhage due to uterine atony. **Management:** Oxytocin, sulproston. Hysterectomy after persistence of bleeding. ICU admission. EPO, ferrous saccharate, dopamin, noradrenalin. **Substandard care:** Not identified	2000 ml 2.4 g/dl
14	39y, G3P1	Emergency CS at 40,5 weeks because of prolonged second stage. Haemorrhage 1000 ml. Management: Oxytocin, ferrous saccharate. After 15 days haemorrhage of unidentified cause and shock. **Management:** Misoprostol. Hysterectomy. ICU admission,. EPO, ferrous saccharate. **Substandard care:** :Not identified	unknown 2.6 g/dl

15	32y, G1P0	Spontaneous labour at 38,0 weeks. Intended home delivery. Transfer to hospital because of prolonged first stage and maternal fever (40.3°C). VE because of poor fetal condition on CTG. Sepsis with coagulopathy. Haemorrhage 1000 ml. **Management:** Oxytocin, sulproston, amoxicillin/clavunalate potassium. ICU admission. EPO. **Substandard care:** Planned home delivery. Hospital unprepared to refusal of transfusion. No non-transfusion declaration present.	1000 ml 3.7 g/dl
16	38y, G4P3 OH: preterm labour	Cer vical cer clage because of preterm labour in OH. Spontaneous labour at 39,1 weeks. Haemorrhage 1500 ml due to uterine atony. **Management:** Oxytocin, cyklokapron. ICU admission. Accepted blood transfusion one day post partum. **Substandard care**: Not identified	1500 ml 5.1 g/dl

IA = induced abortion, SA= spontaneous abortion, IUFD = intrauterine fetal death, CS = caesarean section, VE = vacuum extraction, EPO = erythropoietin, MRP = manual removal of the placenta. 1: recombinant factor VII, recombinant factor VIII, factor II / VII / IX / X

Substandard care

Substandard care in cases of maternal mortality and serious maternal morbidity is discussed and defined by the Maternal Mortality Committee. In our case series, substandard care was identified in five patients. In three patients (patients no. 4, 6 and 11), hysterectomy was not timely performed. One woman (patient no. 15) was planned to deliver at home. The hospital she was transferred to was not informed about her attitude towards blood transfusion and therefore not prepared for the situation. The required non-transfusion declaration was not present in her medical record. In patient no. 5, a CS was performed while she was haemodynamically unstable.

Discussion

We found that women who are Jehovah's witnesses are at a six times increased risk for maternal death, at a 130 times increased risk for maternal death because of major obstetric haemorrhage and at a 3.1 times increased risk for serious maternal morbidity because of obstetric haemorrhage, as compared to the general Dutch population.

To our knowledge, only three other studies studied the obstetric risks of women who are Jehovah's witnesses, including 332, 33 and 90 women. In the two largest studies, two cases and one of maternal death, respectively, were identified, resulting in a 44-fold and 65-fold increased risk of maternal death.[5;8] In our study, we used two large nationwide enquiries of maternal mortality and serious maternal morbidity. Therefore, a relatively large number of Jehovah's witnesses experiencing maternal morbidity or serious maternal morbidity could be selected. As the study was not performed in a prospective setting, we did not have exact data on the total number of deliveries in Jehovah's witnesses. We used demographic data to give a reliable estimation instead.

In the Nationwide Enquiry into ethnic determinants of severe maternal morbidity (LEMMoN), women were included in the category of major obstetric haemorrhage if the haemorrhage required

transfusion of 4 units of red blood cells or more. Consequently, Jehovah's witnesses could not be included in this category. Instead, they were included in the category for Intensive Care Unit admission or were reported in the last category, in which cases were reported if there were other serious complications that did not meet the criteria of the other categories.

It is important to realise that in case of acute haemorrhage, red blood cell transfusion is not always immediately required. Although guidelines suggest a transfusion threshold at a haemoglobin concentration of 7.0–8.0 g/dl, concentrations of 5.0 g/dl or more are usually well tolerated if isovolaemia is maintained. In a study on healthy individuals, Weiskopf et al. found that acute isovolumetric reduction of haemoglobin concentration to 5.0 g/dl does not appear to cause inadequate tissue oxygenation.[9]

There are limited data available on outcomes at concentrations below 5.0 g/dl. Two retrospective studies on patients who declined blood transfusion, mostly Jehovah's witnesses, found that morbidity and mortality rates were extremely high below this level,[10,11] but survival has been reported at Hb rates below 2.0 g/dl and even as low as 1.4 g/dl.[12;13]

Since the first introduction of the doctrine of blood by the society of Jehovah's witnesses, the policy has been changed several times, causing confusion in clinicians when they are confronted with these issues.[14;15] A clear statement about the acceptance of different blood components was published in the society's official magazine The Watchtower in 2004: 'Though all witnesses should refuse autologous or heterologous transfusions of blood or one of its major components, the society states that each member should decide for him or herself whether or not to accept treatment with other blood products like coagulation factors and erythropoietin'.[16;17] Sometimes, the use of a cell saver during surgery is accepted because continuity with the circulatory system is maintained. These individual choices can make a big difference in management options in cases of major obstetric haemorrhage. Therefore, the exact possibilities for each patient and the available alternatives to red blood cell transfusion should be discussed early in pregnancy.

Most hospitals are rarely confronted with the care for pregnant Jehovah's witnesses and even more scarcely with obstetric haemorrhage in these women. Therefore, centralisation of care for these patients is advisable and each hospital treating Jehovah's witnesses should have a protocol for the obstetric care and the management of obstetric haemorrhage of these patients.

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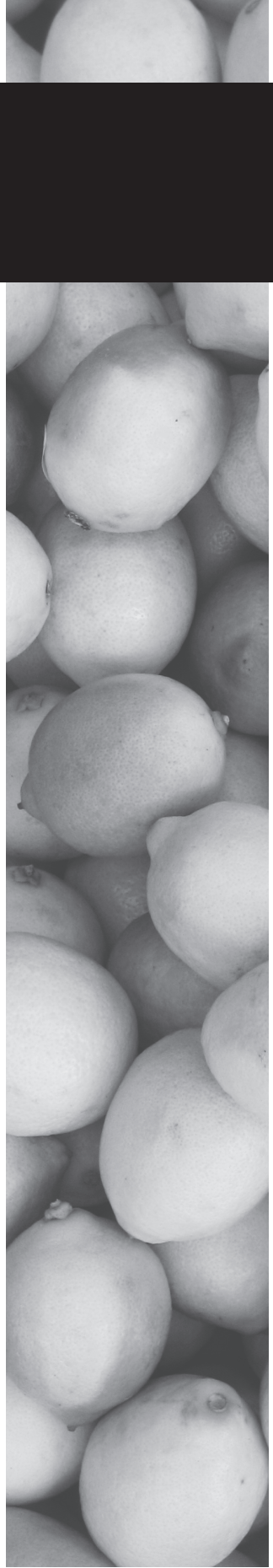
CHAPTER 10



Underreporting of major obstetric haemorrhage in the Netherlands

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Transfus Med 2009, in press

Abstract

Background: Major obstetric haemorrhage (MOH) is the main cause of severe maternal morbidity, incidence being estimated at 4.5 per 1000 deliveries. Cases are not routinely registered in the Netherlands.

Objectives: To quantify the degree of underreporting of MOH in a large nationwide survey of severe acute maternal morbidity in the Netherlands ('LEMMoN') and to estimate the true incidence of MOH in the Netherlands.

Methods: Retrospective cross match of the LEMMoN-database with the databases of local blood transfusion laboratories in 65 of 98 hospitals in the Netherlands during a 20-month period, using the capture-recapture method.

Results: From 16 of 65 centres, the reported transfusion data could not be confirmed by a local obstetrician for logistical reasons. These centres were excluded leaving 49 hospitals available for final analysis. In both databases together, 1018 unique cases of MOH were identified. Underreporting to LEMMoN was 35%. Hence, the true incidence of MOH in the Netherlands is at least 6.1 instead of 4.5 per 1000 deliveries.

Conclusion: The estimated underreporting of MOH of 35% is considerable. Underreporting is inherent to large observational multicentre studies and should be anticipated and quantified to facilitate fair comparison of epidemiologic data.

Introduction

Obstetric haemorrhage is a leading cause of maternal mortality and severe maternal morbidity worldwide, accounting for 25% of maternal deaths worldwide.[1;2] At least five percent of all deliveries are complicated by obstetric haemorrhage[3;4], with a need for blood transfusion in less than 1%.[5] A recent nationwide study into severe acute maternal morbidity in the Netherlands called LEMMoN revealed that 51% of all cases were due to MOH.[6] The incidence of MOH was estimated to be 4.5 per 1000 deliveries. Underreporting, however, is a universal problem of large observational multicentre studies. Even underreporting of a dramatic event was estimated at 26% in the Netherlands.[7] Underreporting of more regular complications is likely to be higher.

Availability of blood transfusion has largely contributed to the decline in maternal mortality in high income countries. Blood transfusion laboratories (BTLs) in the Netherlands are obliged by law to register the issuing of blood products. Also the return of non-administered blood products is generally registered properly. However, pre- transfusion registration does not usually include whether the transfused woman was pregnant. Therefore, assessment of the incidence of MOH using transfusion data is not that straightforward. The aim of the present study was to determine the degree of underreporting of MOH to the LEMMoN study, and thus provide a better estimation of the true incidence of MOH in the Netherlands.

Materials and Methods

Women with MOH were included in the LEMMoN study in the period between 1st August 2004 and 1st August 2006. All 98 hospitals in the Netherlands with a maternity unit (100%) participated in the survey. MOH was defined as the need for transfusion of four or more units of red blood cells (RBCs), or hysterectomy or arterial embolisation because of obstetric haemorrhage. All cases of MOH during pregnancy, delivery and puerperium (limited to 6 weeks postpartum) were enrolled, including haemorrhage in early pregnancy. Detailed methods were previously described.[6] In the Netherlands, obstetricians usually adhere to the so-called '4-5-6 rule' mentioned in the national guideline 'Blood Transfusion'.[8] This means practically that a healthy postpartum woman is not transfused until her Hb level drops below 4.0 mmol/l (6.4 g/dl) unless she has evident anaemic complaints.

In a regional pilot study, the feasibility of detecting cases of MOH using data from BTLs was assessed. It was concluded that recognition of pregnant women was not possible, and confirmation by checking with the local birth registers was obligatory to increase specificity. Underreporting of MOH was found to be 32% in this sample.

We asked all BTLs in the Netherlands to participate in this study. Participation of the BTLs was encouraged during a national meeting of the Society of Haematological Laboratories (VHL). Non-responders were repeatedly requested to provide data.

Participants were asked to provide an anonymous list of obstetric patients who received four or more units of RBCs during the study period. Obstetric patients could be identified in different ways depending on local registration habits. For instance, RBCs issued to the delivery ward or requested by obstetricians were considered. As most hospitals in the Netherlands have a combined obstetric/gynaecologic department, it was not possible to solely rely on registration of the department requesting the blood products. Also, blood products were regularly requested by the anaesthesiologist in the case of MOH, in which case the transfusion was not identified as being obstetric. Therefore, each list provided by a BTL was sent to the local LEMMoN-coordinating obstetrician of the hospital for confirmation using the local birth register. In this way we filtered the lists of BTLs for non-obstetric patients. Cases were matched by using date of birth of the mother and delivery date/transfusion date (plus or minus two days).

To assess the degree of underreporting of MOH to both sources (LEMMoN and BTLs), we applied the capture-recapture census method as described by Hook and Regal.[9;10] This statistical method was first used in biology in order to estimate population sizes and uses log-linear models to estimate the number of cases not identified by either of the sources. The most important assumptions for use of this epidemiologic tool were met in this study: (1) a closed population, (2) possibility of matching individuals from capture to recapture, (3) independency of capture in the first and second sample, and (4) homogeneous capture probabilities across all individuals in the population.

The LEMMoN study was centrally approved by the medical ethics committee of Leiden University Medical Centre. Separate approval for the underreporting study was not necessary due to its anonymous nature.

Results

Study sample

Sixty five of the 98 laboratories in the Netherlands eventually responded. Sixteen hospitals, of which the reported list could not be confirmed by a local obstetrician for logistical reasons, were excluded, leaving 49 hospitals available for final analysis. In total, 986 cases were reported by the 49 participating BTLs. The 49 hospitals appeared to be a representative sample of all hospitals in the Netherlands: the sample included three academic hospitals, 19 non-academic teaching hospitals and 27 other hospitals and centres were geographically equally distributed. Furthermore, the proportions of low, moderate and high volume hospitals were comparable to those of the Netherlands.

Underreporting

In 162 cases (16.4%), the woman appeared not to have delivered at or around the day of transfusion according to the local birth register, leaving 824 confirmed cases of MOH. During the same period,

727 cases of MOH were reported to LEMMoN by the 49 eligible hospitals. After cross matching, we identified 1018 unique cases of MOH from both databases during the study period (Table 1). The estimated number of women not identified through either of the sources, 'x' in table 1, was calculated to be 105. Thus the total number of women with MOH is estimated at 1123. Only 727 cases were reported to LEMMoN, underreporting being estimated at 35% (396/1123). The other way around, 27% (299/1123) of cases would have been missed by only relying on transfusion data from BTLs, after consecutive confirmation by birth registers. Using both sources together would have still yielded an underreporting of 9% (105/1123). The use of a cell saver for auto transfusion was reported to LEMMoN in only four cases. This item was not registered by BTLs.

Table 1. Cases of major obstetric haemorrhage identified through LEMMoN and through blood transfusion records

	Blood transfusion laboratories		
LEMMoN	*Reported*	*Not reported*	*Total*
Reported	533	194	727 (71.4%)
Not reported	291	*x*	291 (28.6%)
Total	824 (80.9%)	194 (19.1%)	1018 (100%)

LEMMoN= nationwide study into severe maternal morbidity in the Netherlands

Incidence of MOH

During the total LEMMoN study period, there were 1606 cases of MOH among 358,874 deliveries, with a rate of MOH of 4.5 per 1000 deliveries. Assuming that the degree of underreporting found in our study is nationally representative; the total number of cases of MOH in the Netherlands during this period is estimated to be 2173. The true incidence of MOH in the Netherlands is therefore estimated at 6.1 per 1000 (2173/358,874).

Sub analysis

When underreporting was categorised by the number of RBCs transfused, we saw a negative correlation between the severity of MOH and the rate of underreporting to LEMMoN (Table 2).

Table 2. Underreporting by severity of major obstetric haemorrhage

Number of RBCs	Reported to LEMMoN	Not reported to LEMMoN	Percentage of underreporting*
4	393 (54%)	209 (72%)	20.5%
5 to 8	225 (31%)	73 (25%)	7.3%
9 or more	109 (15%)	9 (3%)	0.9%
overall	727 (100%)	291 (100%)	28.6%

RBC=red blood cell; *percentage of all cases identified through both systems

Among the severest cases with more than eight units of RBCs transfused, only nine cases (3%) were not reported to LEMMoN. Most cases of underreporting to LEMMoN concerned women who received four units of RBCs. No cases of hysterectomy or arterial embolisation were missed. The degree of underreporting per hospital varied between 0 and 83%. Eleven hospitals (23%) had no underreporting at all. The level of underreporting was not related to the annual number of deliveries of a maternity unit. Among the three academic hospitals, underreporting was 13.0%, as compared to 29.5% in non-academic hospitals (Table 3).

Table 3. Underreporting by volume and type of maternity unit

	hospitals (n)	underreporting	p-value*
by volume (deliveries/year)			*0.016*
<1000	16	28.0%	
1000-1500	20	28.0%	
>1500	13	29.7%	
by type of hospital			*0.048*
academic	3	13.0%	
non-academic teaching	19	28.9%	
non-teaching	27	29.4%	

***T-test, one-sided**

Discussion

This study shows that the rate of underreporting of MOH in an observational multicentre study can be considerable. This will especially be the case in retrospective studies where case ascertainment relies on ICD 9/10 codes or discharge data that are not specifically registered for the purpose of research. In many of these studies, little or no attention is given to this problem. Thorough assessment of the rate of underreporting can give a more precise estimation of the true incidence. For MOH in the Netherlands, data collection through two distinct routes yielded a 29% increase in case ascertainment, and an underreporting of 35% could subsequently be calculated using the capture-recapture procedure. This epidemiologic tool is very useful in estimating the true incidence from multiple incomplete sources and is especially used for this purpose in low income countries. Mungra et al. found underreporting of maternal mortality in Surinam to be 65% using this method.[11] Underreporting of maternal mortality in the Netherlands between 1983 and 1992 was 26% without using the capture-recapture method, which is comparable to our findings.[7]

We found that underreporting was especially high among the least severe cases of MOH, necessitating 'only' four RBCs. It is reassuring that very little of the severest cases of MOH were missed by LEMMoN. This was also true for other items registered within the LEMMoN study, underreporting of eclampsia and uterine rupture being 2 and 3% respectively.[6] Underreporting

varied largely between hospitals. Seven of eight hospitals with an underreporting rate of more than 50% were small regional hospitals. The fact that these hospitals generally lack daily staff meetings could well play a role in the high underreporting rate. Eleven hospitals had no underreporting. Some of these hospitals had already included BTL data in their local strategy for ascertainment of cases of MOH, as now proves to be appropriate.

The registration of issue and administration of blood products is strictly regulated in the Netherlands. However, we also found 19% underreporting through the BTLs. We do not doubt that the issuing of all blood products is properly registered. This is however not the case for the demographic and medical data of the recipient. By linking the databases of the administration of blood products with that of the hospital patient administration system one may obtain information about (broad) patient categories that received defined blood products.[10-12] For this specific question we thought that it might be possible to identify all pregnant women that received blood transfusions. But apparently, not all pregnant women can be identified from the transfusion records. For instance, blood products requested by the anaesthesiologist could not be identified as administered to a pregnant or recently delivered woman. Since the pregnant status of a woman should be explicitly mentioned upon each request of blood products in order to know whether a cross-match has to be performed and whether (c, E and) Kell-compatible blood has to be transfused, it is disappointing that BTLs appear unable to identify all pregnant women from their databases. Another possible source of bias when using the BTL data is the under registration of units not transfused. This could have lead to an overestimation of the incidence of MOH. Although quantification was not possible, this bias will not likely have affected the final results to a great extend. Another disadvantage of this study is that women with obstetric haemorrhage remote from the date of delivery were possibly missed as they are not filed in the birth register around the transfusion date. This is especially true for haemorrhage complicating ectopic pregnancy as these women are not registered in the birth register and hence are difficult to identify. Although we encouraged local coordinators to also check for cases of ectopic pregnancy around the transfusion date, we are aware of the difficulty of identifying such cases retrospectively. The use of data only from BTLs to ascertain cases of MOH without confirmation of the local birth register appeared to be unfeasible, as 16% of cases identified by the BTLs were eventually found not to be related to pregnancy or delivery. These concerned mainly women after gynaecologic surgery.

Formulating a proper definition for MOH remains difficult. In the LEMMoN study, we choose to use management based criteria. The disadvantage of management based criteria is that management of cases differs between obstetricians, hospitals and countries, thereby introducing inclusion bias. Alternatively, we could have relied on estimated blood loss, but this is subjective and known to be largely underestimated.[13] The most objective alternative would have been to use

drop of haemoglobin level as criterion for the severity of obstetric haemorrhage. However, due to the observational nature of this study, standardised pre- and post- haemorrhage haemoglobin levels were not available. And even when they were, it would have been difficult to standardise the moments of haemoglobin assessment. Moreover, haemodilution of pregnancy would interfere with these values.

Due to differences in definition of MOH, comparison of incidences with other reported studies is difficult. Two other European studies with a comparable study design reported incidences of 6.7 and 3.8 per 1000 deliveries.[14;15] In both studies, underreporting was not assessed. The first study, from a large region in the UK, had a more liberal definition of MOH, which included women with an estimated blood loss of 1000ml. The second study, a nationwide survey from Scotland, included women with at least five units of RBCs. In a joint effort to compare incidences, we applied the Scottish criteria to the LEMMoN sample. The incidences of the two studies then appeared to be similar before correction of the incidence for underreporting. This could reflect that the true incidence in the Netherlands is higher as compared to Scotland, but it seems more likely that final case ascertainment in the Netherlands was better after assessing the rate of underreporting.

In conclusion, this study shows the crucial importance of the assessment of underreporting in large multicentre studies. Underreporting is high for relatively less severe morbidities and low for the most severe forms of maternal morbidity. We recommend using multiple sources to assess the incidence of MOH.

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CHAPTER 11

Introducing maternal morbidity audit in the Netherlands

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Abstract

Objective: To identify substandard care in selected cases from a nationwide prospective cohort study into severe acute maternal morbidity (SAMM) in the Netherlands called 'LEMMoN'.

Design: Prospective audit of selected cases of SAMM.

Setting: Nine audit meetings held throughout the Netherlands.

Population: All pregnant women in the Netherlands.

Methods: Before each meeting, SAMM details of selected cases were sent to all panel members for individual assessment by completing an audit form. During a subsequent plenary meeting, findings were discussed and substandard care factors as judged by the majority of assessors were scored.

Main outcome measures: Incidence of substandard care and recommendations for improving the quality of care.

Results: Substandard care was identified in 53 of 67 cases (79%). Specific recommendations were formulated concerning the procedure of audit and concerning local as well as national management guidelines.

Conclusion: Substandard care is present in four out of five cases of SAMM. Ongoing audit of cases is promoted both at national and local level.

Introduction

Maternal mortality has traditionally been used as an important indicator of health care, making comparison over time and between services possible. Detailed assessment of individual cases through audit by the Confidential Enquiry into Maternal Deaths in the United Kingdom has been acknowledged as a major contributor to the decline of maternal deaths in the UK over the past 50 years. Other countries have followed this example among which South Africa and the Netherlands. Nowadays, maternal mortality in high income countries is too rare to be used as a sensitive marker for the quality of services. Therefore, severe acute maternal morbidity (SAMM) has been introduced.[1-6] SAMM complicates at least 0.71% of all pregnancies in the Netherlands, and should be considered as a new indicator of the quality of obstetric care next to maternal mortality.[7] Auditing SAMM in order to identify substandard care has generally been accepted as complementary to maternal death reviews.[8] In this study we describe the introduction of SAMM audits in the Netherlands focusing on substandard care analysis.

Materials and Methods

This study was part of the nationwide prospective cohort study into SAMM in the Netherlands, called 'LEMMoN'. Cases were enrolled between August 1st 2004 and August 1st 2006. SAMM was classified according to disease-specific and management-based criteria and categorised into five groups (Figure 1). All 98 Dutch hospitals participated. Detailed methods are described previously.[7]

Figure 1. Inclusion criteria for SAMM

Group 1: ICU admission
- Admission to intensive care unit or coronary care unit, other than for standard postoperative recovery

Group 2: Uterine rupture
- Clinical symptoms (pain, fetal distress, acute loss of contractions, haemorrhage) that led to an emergency caesarean section, at which the presumed diagnosis of uterine rupture was confirmed
- Peripartum hysterectomy or laparotomy for uterine rupture

Group 3: Eclampsia / HELLP syndrome
- Eclampsia
- HELLP-syndrome only when accompanied by liver haematoma or rupture

Group 4: Major Obstetric Haemorrhage
- Transfusion need of ≥ 4 units of packed cells
- Embolisation or hysterectomy for major obstetric haemorrhage

Group 5: Miscellaneous
- Other cases of severe maternal morbidity to the opinion of the treating obstetrician, not to be included in group 1-4

From 2004 onwards, nine audits have been organised throughout the Netherlands and 71 SAMM cases (2.8% of all cases of SAMM) were assessed (Table 1). Audits included regionally or nationally selected SAMM cases. Some of them had specific topics: eclampsia, major obstetric haemorrhage (MOH) and selected SAMM after delivery under primary care (Table 1).

Table 1. Selected characteristics from seven SAMM audit meetings

Location	Date	Selection	SAMM (n)	Assessors (n)	Substandard care[2] (%)
The Hague	jun 2005	local (pilot: all cases)	14	17	86%
Groningen[1]	mar 2006	regional (severe cases)	12	23	75%
Leiderdorp[1]	sep 2006	regional (severe cases)	12	13	67%
Leeuwarden	sep 2006	local (MOH)	4	16	- [3]
Delft/Zwolle/ Amsterdam[1]	feb 2007	national (eclampsia)	12	8	92%
Utrecht[1]	oct 2008	national (primary care eclampsia)	8	18	63%
	nov 2008	national (primary care MOH)	9	24	89%

MOH=major obstetric haemorrhage; [1]Substandard care items available from five audits; [2]Substandard care by majority of the assessors after group discussion; [3]Recommendations in all four cases, but no consensus (%) on substandard care by majority of the assessors

The first pilot audit included all 23 SAMM cases in two hospitals during the first 10 months of the study, of which 14 were eventually selected for discussion during the panel meeting.[9] Since then, we applied initial selection and discussed all cases during the plenary meetings. During an in-depth MOH audit in Leeuwarden involving all local staff, recommendations were formulated in all four cases, but presence of substandard care by majority of the assessors was not formulated. For calculating the incidence of substandard care these cases were not included. During an in-depth eclampsia audit in Delft, nationally selected cases were discussed without the presence of medical staff (consultants, midwives or registrars) involved in the cases. It was noted that this left many questions unanswered and therefore, two additional audit meetings were held with involved staff present. These three audits are presented here as one. Concerning the MOH in primary care audit, cases were eligible when eight or more units of blood were transfused, and the woman was either admitted to intensive care or had undergone major surgery or arterial embolisation to stop the haemorrhage.

For each audit, panel members were selected from the LEMMoN advisory board and the national Maternal Mortality Committee, as well as local health care workers involved. Panel membership was variable but chosen in such a way that each audit included staff from university as well as non-university hospitals. Furthermore, members from different specialties (mainly obstetricians,

midwives, and internal medicine specialists) were selected with special attention to including members with experience in the audit process.

Each panel meeting considered four to fourteen cases. Anonymised notes from the LEMMoN database, selected by one member of the LEMMoN audit team (JZ), were sent to the panel members and included patient discharge letter, details from delivery, operation notes, laboratory results and a summary of file notes. Each panel member was requested to perform individual assessment of patient notes using a standardized audit form used by the Maternal Mortality Committee (Appendix B). Substandard care was identified at the level of the patient, the care provider or the organisation of health care (15 items). In case of eclampsia or MOH, additional substandard care items concerning management were scored. During the plenary meeting, SAMM cases were discussed and assessed for substandard care. If necessary the involved care provider was requested for additional information from the original patient file which was made available at the plenary meeting. Substandard care was firstly identified if care deviated from national guidelines. If national guidelines were not available, local protocols, best available evidence or expert consensus were used. Substandard care was assumed if the majority of assessors judged this to be the case.

Results

Of 358,874 births during the study period, 2552 SAMM cases were included in LEMMoN (7.1 per 1000 births). Of 67 SAMM cases discussed during the panel meetings, substandard care was judged to be present by the majority of assessors in 53 cases (79.1%). From five of the audits, including 53 cases (74.6%), more detailed scoring of substandard care items was available. From a total of 17,430 possible substandard care items (number of assessors X number of cases X 15 scoring items) 1223 (7.0%) were scored. Only 73 (6.0%) were identified at the level of the patient, 933 (76.3%) at the level of the care providers and 217 (17.7%) at the level of the organisation of health care (Table 2).

Pilot audit

During a pilot audit 23 SAMM cases were selected in two teaching hospitals in The Hague and these were assessed by 17 audit members.[9] Individual assessment of patient notes was judged to be possible in 16 cases (69.6%), with 18 cases classified as true SAMM (78.3%) and identification of substandard care during individual assessment in 10 cases (43.5%). Of five cases not classified as true SAMM, three where included due to MOH with transfusion of four units of red blood cells and two cases were admitted in ICU for observation because of pre-eclampsia and mild peripartum cardiomyopathy. Fourteen cases were subsequently selected by the panel members for plenary discussion with additional information from the original patient file. Of these, 12 cases

were classified as true SAMM (85.7%) and substandard care was judged to be present in 12 cases (85.7%). In one case, lack of information due to poor records was judged to be substandard. In addition to substandard care analysis, recommendations were made concerning future LEMMoN audits (Table 3).

Table 2. Substandard care items and their contribution during five SAMM audit meetings.

	n	%
Patient	**73**	**6.0**
Delay in consulting doctor	43	3.5
Refusal of medical help or advice	15	1.1
Language barrier	15	1.2
GP/Midwife	**367**	**30.0**
Inadequate antenatal care	92	7.5
Delay in recognition of symptoms / signs	113	9.2
Delay in referral to obstetrician	121	9.9
Inadequate risk selection*	41	3.4
Obstetrician	**559**	**45.7**
Inadequate antenatal care	88	7.2
Delay in recognition of symptoms / signs	181	14.8
Delay in treatment after diagnosis	255	20.9
Delay in referral to tertiary care centre	35	2.9
Other consultant	**7**	**0.6**
Delay in consulting obstetrician	7	0.6
Healthcare system	**217**	**17.7**
Home birth influenced outcome	103	8.4
Birth in general hospital influenced outcome	76	6.2
Quality of transport influenced outcome	38	3.1
Total	**1223**	**100.0**

*** only for primary care audits, percentage for total substandard care items**

Primary care audits

Of 358,874 births represented in the LEMMoN study, 145,703 (40,6%) were under the responsibility of primary care givers and 113,404 (31,6% of total) were home births.[7] Of 2552 SAMM cases, 227 (1.6 per 1000) were included after delivery under the responsibility of primary care provider, and 154 (1.4 per 1000) were included after home birth. During two audit sessions (one concerning MOH and one concerning eclampsia), 17 of these cases of SAMM after delivery under primary care (7.5%) were assessed.

From 1606 SAMM inclusions due to MOH, 140 (8.7%) were included after home delivery. Nine cases (6,4%) met the criteria and were assessed by 24 panel members. Substandard care was judged to be present by the majority of the assessors in eight cases (88.9%) and inadequate

risk selection was judged to be present by the majority of the assessors in four cases (44.4%). From a total of 4410 possible substandard care items (number of assessors X number of cases X 21 scoring items), 387 (8.8%) were recorded: 134 (34.6%) were at the level of the primary care provider and 72 (18.6%) concerned the management of MOH irrespective of the level of care. Specific recommendations were made concerning more stringent risk selection, delay in reaching the hospital and timing of referral (Table 3).

Table 3. Recommendations from selected SAMM audit meetings

Audit	Recommendation
General	- Additional information with patient records is often necessary for effective audit - Improve record keeping, especially concerning timing of interventions - Improve treatment guidelines concerning pre-eclampsia and MOH, for primary as well as secondary care
Eclampsia[10]	- Improve adequate treatment of hypertension - Improve adequate seizure prophylaxis
Primary care MOH	- Reduce the delay in reaching the hospital by timely referral (if placenta not delivered after 30 minutes) - Importance of IV access and initiation of resuscitation before transport to hospital - Discussion about the need and feasibility for misoprostol® at primary care level - Discussion concerning emergency transport and acceptance of home delivery in areas where referral to secondary care might result in delay - Need of delivery at ground floor due to regulations for emergency transport employees restricting them to carry patients downstairs - Repeated consultation from secondary care provider for suspected pre-eclampsia should lead to referral and continued secondary care, irrespective if patient classifies criteria
Primary care eclampsia	- Standard measuring of blood pressure is indicated two hours after delivery or before leaving the patient after home delivery

From 239 SAMM inclusions due to eclampsia or severe HELLP, all eight cases (3.3%) where delivery was under primary care were assessed by 18 panel members. Substandard care was judged to be present by the majority of the assessors in five cases (62.5%). Inadequate risk selection was identified by a minority of the assessors in four cases (ranging from 16.7% - 44.4% of assessors). From a total of 2940 possible substandard care items (number of assessors X number of cases X 21 scoring items), 221 (7.5%) were recorded: 69 (31.2%) were at the level of the primary care provider and 62 (28.1%) concerned the management of eclampsia irrespective of the level of care. Specific recommendations were made concerning the diagnosis and management of pre-eclampsia (Table 3).

Discussion

During nine audit meetings in the Netherlands, 67 SAMM cases were assessed and substandard care was identified in almost four out of five cases. Substandard care was judged to be present at the level of the patient and the level of the organisation of health care but mainly at the level of the care provider. For substandard care analysis, additional information from the original patient files was often required. However, even with the complete patient file available for assessment, substandard care analysis was not always possible. The lack of information as a result of inadequate record keeping can also be regarded substandard care. During the panel meetings, with availability of original patient file and discussion among panel members, the identification of substandard care increased. Although this pattern was consistent throughout all audits, the magnitude of the increase in substandard care identification during the pilot audit (from 43% after individual audit to 86% after group audit) has not been seen during successive audits (data not shown). This might reflect a learning curve for audit. The earlier reported lower incidence of substandard care in the LEMMoN study (61.9%) is due to the inclusion of individual audit results in that report compared with incidence after group audit here (79.1%).[7]

The incidence of SAMM due to eclampsia in the Netherlands is markedly increased compared with other Western countries.[10] Substandard care was identified in most cases of SAMM, mainly at the level of the care providers and often due to inadequate treatment of hypertension and inadequate seizure prophylaxis. As for maternal death due to hypertensive disease in pregnancy, in 26 (96%) out of 27 cases occurring in the Netherlands between 2000 and 2004, substandard care factors were present. [11] In 2005, the national guideline "Hypertensive disorders in pregnancy" of the Dutch Society of Obstetrics and Gynaecology has been adjusted and multiple papers and presentations have been given informing obstetricians concerning this issue.[12] However, the guideline and its implementation can still be improved.[11]

Half of all SAMM cases concern MOH.[7] Obstetric haemorrhage is the third direct cause of maternal death in the Netherlands with case fatality rate (CFR) of 1 in 201, compared with CFR of 1 in 53 for all SAMM cases. The relatively low CFR for MOH reflects the quality of blood supply in the Netherlands with patients having received up to 50 units of blood. Hence, half of the SAMM cases due to MOH (n=811) received more than four units of blood. From these figures it is clear that MOH is an important contributor to SAMM and not so much to maternal death. Where this might result in an attitude of acceptance towards morbidity, the risk of blood transfusion especially during the reproductive period should not be neglected. Audit revealed that there is ample room for improvement in the management of MOH. Skills trainings in obstetric emergencies like MOH should be implemented in any unit.[6;13] The Managing Obstetric Emergencies and Trauma course has been introduced in the Netherlands since 2003 and it is encouraged during these national

trainings to initiate regular local multidisciplinary skill trainings. A recent questionnaire indicated that at least 29% of Dutch obstetric units have regular skill trainings and 22% are in the process of organising these trainings [personal communication].

The lower risk for SAMM after delivery under the responsibility of the primary care giver (RR 0.1; 95% CI 0.1–0.2) seems to reflect the proper functioning Dutch system of risk selection.[7] However, also here substandard care was judged to be present in the majority of cases. Furthermore, inadequate risk selection in cases leading to severe MOH was present in almost half of cases. The definition retained placenta is used when the placenta has not been delivered within one hour after the birth of the baby.[14] In the Netherlands, women delivering under the responsibility of primary care givers are referred to secondary care in case of retained placenta and/or in case of severe bleeding (>1000 ml). For term pregnancy (which applies to all deliveries under primary care), however, the duration of the third stage of labour is under 15 minutes for 90% of deliveries.[15] Therefore, we recommend earlier referral to secondary care in case of retained placenta, especially due to delay in reaching secondary care as mentioned in table 3.

Concerning audit in general, although the effect of critical incident audit has not been proven in randomised controlled trials, it is clear that morbidity and mortality reviews do more good than harm.[16] Critical incident audit both monitors the quality of services and is a resource for professional learning.[13;17] The openness in provision of data and participation during these audits in the Netherlands is encouraging. Ongoing local audit of cases of eclampsia and MOH have already been implemented in the national quality assurance program to improve management and local guidelines. In addition to these national initiatives, auditing SAMM at local or regional level should be encouraged to improve the quality of obstetric care. In the Netherlands, however, obstetric audit is relatively new. After the results from Peristat in 2004, which indicated that Dutch perinatal mortality rates ranks unfavourably compared with other European countries, many measures have been taken in order to improve the quality of perinatal care. The most important are the initiation of the nationwide perinatal audit, better prenatal screening and the introduction of preconception care.[18] The national perinatal audit program includes training of audit members at regional and local level. In the near future, more health care workers will be familiar with obstetric audit and it is envisaged that the tradition of audit like in the United Kingdom, will eventually also be reached in Dutch obstetric health care.

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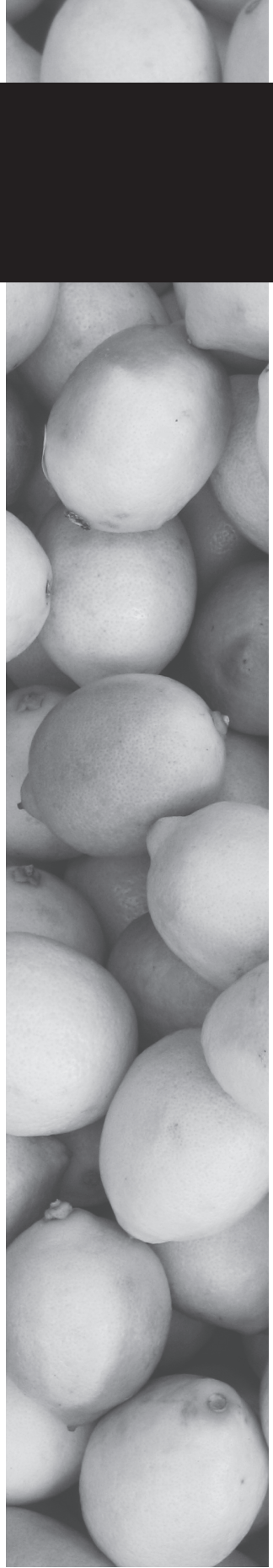
CHAPTER 12

General discussion



The LEMMoN study has provided an invaluable amount of obstetric epidemiologic data. The headlines are described in this thesis, and there are still many more publications to follow within the next years. Until now, data on the incidence of severe acute maternal morbidity (SAMM) in the Netherlands were scarcely available. Although the Netherlands has an excellent reputation regarding assessment of maternal mortality, the small numbers involved will not likely change clinical practice much on the short term. In order to improve care and make pregnancy even safer, there is a clear need in the Netherlands and other high income countries to extend routine data collection to also include the severest forms of SAMM.

International comparison

Data on SAMM in high income countries are increasingly published in the literature.[1-10] We recently published an overview of the various aspects of it.[11] Population-based studies till date are summarised in table 1.

Table 1. Severe acute maternal morbidity (SAMM) in high income countries, population-based studies*

Country	Year	Number of births	Rate of SAMM per 1000 births	CFR
Prospective studies, purposive case finding				
UK, South East Thames[3]	1997-1998	48,865	12.0	0.9
Scotland[1]	2001-2002	51,165	3.8	2.0
Ireland, Dublin[6]	2004-2005	49,829	3.1	1.3
The Netherlands	2004-2006	358,874	7.1	1.9
Retrospective studies, register-based				
Canada[7]	1991-2000	2,548,824	4.4	0.8
Finland[9]	2002	53,568	7.6	
USA[4]	1991-2003	50,600,000	5.1	2.0
Australia, New South Wales[2]	1999-2004	500,603	12.5	

*** nationwide unless otherwise stated**

Incidences range from 3.1 in Ireland to 12.5 in Australia, the differences largely depending on different inclusion criteria. All studies reported MOH to be the most important cause of SAMM. This subgroup also happens to be mostly prone to difference in inclusion criteria. In Scotland and Ireland, women were included only after transfusion of five units of red blood cells. In Australia and the UK, however, women with obstetric haemorrhage were included irrespective of their transfusion needs. In a one-to-one comparison of the raw data of the Scottish study and ours, we found that the difference in SAMM rate was fully explained by the different inclusion criteria

for MOH. Our inclusion criteria for MOH were in between the mentioned ones, and so was our incidence. A fair comparison of incidences in order to compare quality of care between countries is still hampered by differences in inclusion criteria of SAMM. The first step towards universal registration of SAMM as quality parameter of obstetric care is the introduction of internationally agreed criteria for SAMM. Currently, the World Health Organisation is in the process of formulating such criteria for international use.[12] In light of the large differences in obstetric practice between countries, organ system based criteria are recommendable to optimise comparison. However, case ascertainment based on such criteria is more difficult because standardised laboratory and vital parameters are required. This involves detailed documentation of cases, which is not always warranted outside the context of research purposes. For comparison between high income countries, with more comparable health care practices, it may be more efficient to use disease-specific and management based criteria as we did. This will certainly enhance participation rates at the cost, however, of completeness and data quality. As resources for epidemiologic data collection are scarce in the Netherlands, it is of vital importance to keep local time investment for data collection to a minimum. Time consuming procedures will inevitably lower participation rates. The final best way to collect data on SAMM remains to be determined.

Temporal trends in SAMM

There is alarming evidence that the incidence of SAMM is increasing. The retrospective register-based studies from Canada, Finland, the USA and Australia shed some light on this increase during the last two decades (Table 2).[2;4;7;9;10] In Canada, overall maternal morbidity seemed similar during 1991–1993 (4.40 per 1000 births) and 1998–2000 (4.25 per 1000 births).

Table 2. Temporal trends in severe acute maternal morbidity (SAMM) in high income countries*

Country	Period	Rate of SAMM per 1000 births	Increase
Canada[7]	1991-1993	4.6	0%
	1998-2000	4.6	
Finland[9]	1997	5.9	29%
	2002	7.6	
USA[4]	1991-1994	4.5	31%†
	1995-1998	4.7	
	1999-2003	5.9	
USA[10]	1998-1999	6.4	27%
	2004-2005	8.1	
Australia, New South Wales[2]	1999	11.5	21%
	2004	13.8	

***only retrospective, register-based studies available; †P for test of trend: 0.002**

However, a closer look at the numbers revealed that incidences of the severest forms of maternal morbidity had all increased. Higher rates of venous thrombo-embolism (RR 1.7; 95% CI 1.3–2.2), cerebrovascular disorders (RR 1.4; 95% CI 1.1-1.8), uterine rupture (RR 1.6; 95% CI 1.4–1.8), acute respiratory distress syndrome (RR 1.5; 95% CI 1.1–2.1), pulmonary oedema (RR 2.1; 95% CI 1.6–2.7), myocardial infarction (RR 3.7; 95% CI 1.2–11.4), haemorrhage requiring hysterectomy (RR 1.8; 95% CI 1.5–2.1) and assisted ventilation (RR 2.5; 95% CI 1.9–3.2) were observed. These higher rates were balanced by an apparent decrease of the rate of haemorrhage requiring transfusion, possibly reflecting a more restrictive use of blood products instead of a true decrease of the rate of haemorrhage. Adjustment for maternal age, multiple pregnancy and previous caesarean section did not change these overall results. Contrastingly, in Australia, a significant increase of overall SAMM was found to be fully explained by an increase in haemorrhage requiring transfusion. In Finland and the USA, rates increased by 27-31% during a 5-12 year period. In the Netherlands, a clear increase of the incidence of obstetric haemorrhage (>1000ml) from 5.0 to 7.5% during a 10-years period can be seen from the Dutch Perinatal Database statistics [personal communication]. One should be aware of the fact that all these studies used administrative data. Coding errors are known to occur to a certain degree in such studies, but in all studies an increasing trend is observed. Until date, prospectively collected data on temporal trends of SAMM are scarce. The only data we know of are from Scotland. In the 2006 annual report of the Scottish Confidential Audit of Severe Maternal Morbidity, a non-significant increase was reported from 5.4 per 1000 (95% CI 4.9-6.0) in 2003-2005 to 6.4 per 1000 (95% CI 5.8-7.1) in 2006.[13] The rate of major obstetric haemorrhage increased significantly from 3.7 per 1000 (3.4-4.0) to 5.0 per 1000 (4.4-5.6) during the same period as did the rate of acute respiratory distress syndrome. One of the American studies performed multivariable logistic regression and found out that the increase of incidence was mainly explained by the increase in caesarean delivery rate from 21.2% in 1998 to 31.1% in 2005.[10] The increase was not related to age or multiple births. The influence of ethnicity, body mass index, pre-existing maternal conditions and quality of care were not investigated. Future assessment of the incidence of SAMM in the Netherlands could confirm the increasing incidence in a prospective manner not relying on administrative data which are prone to coding errors. Furthermore, it would provide more insight into the reasons for the apparent increase.

High incidence of eclampsia

Rates of eclampsia have decreased in high income countries since the publication of the Collaborative Eclampsia trial (1995)[14] and the Magpie trial (2002)[15], advocating the therapeutic and prophylactic use of magnesium sulfate.[1;16] We found that the rate of eclampsia in the Netherlands appeared to be relatively high, even when compared to rates of the pre-magnesium sulphate era. When compared with the more recently published studies in the United Kingdom

and Scotland, our incidence seemed to be twice as high.

Substandard treatment of hypertension was found in at least 60% of eclamptic women and magnesium sulphate for seizure prophylaxis was administered in only 10% of these cases, although we classified 47% of cases as severe preeclampsia already on admission. Additionally, we found substandard care in 15 of 18 cases during extensive auditing. Evidence of substandard treatment of hypertensive disorders in pregnancy in the Netherlands is accumulating. It was highlighted already in 1998 based on the confidential enquiry into maternal deaths in the Netherlands.[17] More recently, maternal mortality due to hypertensive disorders in the Netherlands was reported to be three times as high as in the UK[18], with substandard care being present in 26 of 27 cases.[19] Gestational age at delivery in women with hypertensive disorders is three weeks higher in the Netherlands as compared with the UK, reflecting the too expectant management and underestimation of maternal risks by Dutch obstetric caregivers. Very recently, the Hypitat trial showed that induction of labour as compared to expectant management in women with mild hypertensive disorders at term yields better maternal outcome with a reduced caesarean section rate and comparable fetal outcome in the Dutch situation.[20]

Thanks to this accumulation of evidence, we have the impression that there is a growing awareness among Dutch obstetric caregivers, that has already lead to changing practice. The thresholds for treatment with anticonvulsive and antihypertensive medication have lowered and labour is induced earlier. The dogma that the foetus must reach term at any cost has been broken. Future assessment of the incidence of eclampsia is mandatory and will hopefully confirm the changes in management.

Intensive care unit admission

The rate of intensive care unit (ICU) admission in the Netherlands appeared to be 2.4 per 1000 deliveries. This is in the lower range of what is reported in the literature. Only few other studies reported population-based incidences of ICU admission, which are likely lower as compared to facility-based (often tertiary care) studies. This is also the case when comparing our results with an earlier study of ICU admissions in our own tertiary care centre, in which a three times higher incidence was reported.[21] Our finding that only a third of all cases of SAMM were admitted to ICU is consistent with that of the Scottish population-based study.[1] The important implication of this finding is that ICU admission rates cannot be used as a proxy of SAMM rates. It may, however, serve as a proxy for the most severe cases.

Moreover, ICU admission should not be merely used for (international) comparison of SAMM since it is a management based criterion subject to local, national and temporal differences in admission policy. This is illustrated already within the Netherlands by the great variation in ICU

admission rates by volume of hospital. Smaller hospitals showed a higher admission rate, but cases seemed less serious.

In light of the relatively high case fatality rate, proper management of obstetric ICU admissions requires intensive cooperation of intensivist/anaesthesist and obstetrician/perinatologist. Both their expertises are indispensable to deliver the high quality of care that is needed in these specific circumstances. Due to the rarity of obstetric ICU admission in high income countries, exposure of those clinicians to obstetric critical care is low. This would plea for centralisation of obstetric care, which is currently a hot issue in the Netherlands. Although underexposure to rare but life threatening complications might affect quality of care, this has to be balanced against the disadvantage of larger distances to obstetric services, which involves many more pregnant women. Timely referral of women with an (imminent) severe complication of pregnancy to a better equipped centre currently serves as the best compromise. Availability of an on-site intensive care unit, an on-site blood bank, an intervention radiologist, an on-site anaesthesiologist, obstetrician and neonatologist 24 hours a day, a cell-saver, and specific experience, as well as the distance to the nearest higher level of care, all have to be taken into consideration when deciding what is the safest location to treat the woman.

Major obstetric haemorrhage

MOH appeared to be by far the most important cause of SAMM. From the perspective of maternal deaths in the Netherlands, the large clinical impact of MOH was somewhat surprising since MOH is not a major cause of maternal mortality in the Netherlands anymore.[22] To illustrate the problem: the cases included in the LEMMoN study were transfused over 10,000 units of packed cells for an estimated 4.7 million litres of blood loss. Women received up to 50 units of packed cells. The general availability of safe blood products in the Netherlands has been one of the major reasons for the decline in maternal deaths in the past century. From our data, it is estimated that the maternal mortality ratio would have been seven times higher in the absence of blood transfusion, with much larger implications yet to be expected for the number of SAMM cases.[E. Briët, communication] Concerning the maternal mortality ratio, this would have left our country between some low or middle income countries like Iran, Northern Korea, Turkey, Argentina and Russia.

We found retained placenta/placental remnants to be the most important cause of MOH. This is in contrast with data presented in various obstetric text books, which report uterine atony to be the most important cause of obstetric haemorrhage. Although contradictory at first sight, this difference is well explained by the fact that uterine atony can be relatively easy managed with uterotonic agents and hence will not often reach the threshold for MOH. Vice versa, MOH mostly results from an identifiable cause. Local protocols should include a flow chart to identify and treat

this cause as quick as possible.

International comparison of rates of MOH is hampered by large differences in inclusion criteria as already discussed. Hysterectomy was one of the criteria used in the recently published Peristat-II report in a first attempt to quantify and compare SAMM in the 25 countries of the European Union and Norway.[21] Rates varied from 0.2 to 1.0 per 1000 deliveries, our hysterectomy rate of 0.3 per 1000 being among the lowest. Comparison is hampered by absence of data on arterial embolisation preventing hysterectomy and subsequent loss of fertility. In the Netherlands, both procedures are carried out with a similar frequency, with failure of embolisation occurring in about 15% of cases eventually resulting in hysterectomy. We are not aware of the availability of such data for other countries.

We also included ten Jehovah's witnesses in the LEMMoN study. Refusal of blood products implies a serious danger of life. Jehovah's witnesses obviously have an increased risk of experiencing maternal mortality and SAMM.[22] Using data of the LEMMoN study, this risk was estimated to be 1.4% which is three times higher than in the general pregnant population.[23] The fact that a home delivery was planned in one woman illustrates the underestimation of the risk by health care provider and patient.

Ethnicity

Increased risk for non-Western women to experience SAMM was present among all categories of SAMM, although relative risks were lower than previously reported for maternal mortality.[5;22] Great differences in risks of SAMM were found between the distinct ethnic groups in the Netherlands. Turkish and Moroccan women showed relative and absolute risks comparable to Western women, while sub-Saharan African women showed a three to six-fold increased risk among the different SAMM categories. Very recently, a comparable study was published on ethnic variation in SAMM in the United Kingdom.[26] Although this study only concerned some specific subgroups of SAMM, the results are largely comparable. Like in the present study, black African (~sub-Saharan African) and black Caribbean (~Surinamese and Dutch Caribbean) women had the highest risks.

The increased incidence of SAMM among non-Western immigrants found in this study may be explained by genetic, socio-demographic and lifestyle related differences, but there are also several factors related to immigration that possibly influence the risk of SAMM. The role of these factors is difficult to quantify in comparative studies as indigenous women are not exposed to these risk factors. Like other studies, we found low socio-economic status to be the most important independent risk factor for SAMM in multivariable analysis. However, Turkish and Moroccan immigrants in the Netherlands did not show increased risks of SAMM despite their relatively low SES. Therefore, the explanation for the differences in risk of experiencing SAMM should rather

be sought in factors related to immigration and integration. Data from the qualitative part of the LEMMoN study suggest that the strong social-ethnic networks and collectively shared experiences with the Dutch health care system of Turkish and Moroccan immigrant populations seem to prevent them from developing SAMM.[27] Even though many Turkish and Moroccan women have recently come to the Netherlands due to family reunion or marriage, their risk was not increased despite frequently observed language barriers and acculturation problems. Contrarily, relative risks were highest in women from the smaller ethnic minority groups (sub-Sahara Africa and Middle East) who more recently arrived in the Netherlands. This possibly results in a weak social network and inadequate knowledge of the health care system, contributing to the increased risk. Other disadvantages related to recent arrival in the Netherlands are an illegal status, health insurance problems, communication barriers and inadequate health skills to participate in the interaction with health care providers.[27]

Underreporting

In view of the significant underreporting of maternal deaths to the Maternal Mortality Committee, we spent much effort in assessing the degree of underreporting to LEMMoN.[28] Rates of underreporting found for the different categories of SAMM are shown in table 3. There was no source available for assessment of the underreporting of ICU admission. For uterine rupture and eclampsia, underreporting appeared to be very low as compared to the Dutch Perinatal Database (LVR-2).[29] For MOH, underreporting appeared to be 35% in a large national survey among blood transfusion laboratories. However, sub-analysis revealed that the majority of cases not reported to LEMMoN concerned relatively mild cases of MOH. Only three very severe cases (>10 units of red blood cells) were found to be not reported to LEMMoN, and no underreporting of hysterectomy or arterial embolisation was noted.

Table 3. Rates of underreporting to LEMMoN

SAMM category	Method and period of assessment	Rate
ICU admission	None available	-
Uterine rupture	Dutch perinatal database, Aug 04-Dec 04	2%
Eclampsia	Dutch perinatal database, Aug 04-Mrch 06	3%
Major obstetric haemorrhage	National sample of blood bank databases, Aug 04- Mrch 06	35%

The results of the survey suggest that data of local blood transfusion laboratories are helpful in identifying cases of SAMM, but identification of all cases through local transfusion databases is not feasible as the pregnant status of women is often unknown. It should not be too difficult to overcome this problem as this information is usually supplied upon each request of blood products by the

clinician. In some hospitals, the local coordinator already included data from the blood transfusion laboratory in his/her strategy for identification of cases, resulting in low rates of underreporting.

Mode of delivery

One of the most important explanations for the increasing incidence of SAMM in high income countries is the increasing caesarean section rate.[2;10] Table 4 summarises the relative risks of caesarean section, prelabour caesarean section and caesarean section in the obstetric history for different types of SAMM.

Table 4. Unadjusted risks of caesarean section (CS) for different types of SAMM

	CS overall	prelabour CS	previous CS
Severe acute maternal morbidity	5.2 (4.8-5.6)	4.6 (4.2-5.0)	3.7 (3.4-4.1)
ICU admission	7.7 (6.7-8.8)	7.2 (6.3-8.4)	1.5 (1.3-1.9)
Uterine rupture	n/a	n/a	65.1 (42.9-98.7)
Eclampsia	2.2 (1.3-4.0)	3.7 (1.9-7.0)	n/a
Major obstetric haemorrhage	3.1 (2.8-3.5)	3.0 (2.6-3.5)	2.9 (2.5-3.3)
Hysterectomy/arterial embolisation	6.6 (5.0-8.7)	5.0 (3.6-6.9)	3.3 (2.4-4.5)
Sepsis[30]	2.2 (1.3-4.0)	3.6 (1.9-6.9)	n/a

It is important to realise that caesarean section could be the cause of SAMM, but it could also represent the result of it, as it is often performed because of the compromised maternal condition resulting in inclusion into the LEMMoN study. Therefore, further analysis is currently performed to shed more light on the risk of SAMM directly attributable to the mode of delivery. This will reveal information that is crucial to the appropriate counselling of women in whom an (elective) caesarean section is planned. Keeping the caesarean rate as low as possible is one of the most important challenges of present-day obstetric care. Each obstetrician has to be aware of and take into account the possible long term consequences of the decision to perform caesarean section. The WHO recommendation that a population based caesarean rate between 5 and 15% is optimal, is not met anymore by most high income countries.[31] The relatively low caesarean rate in the Netherlands should be embraced as a great achievement which protects Dutch mothers and newborns against SAMM and mortality.

Audit

Audit of SAMM is highly instructive and feasible albeit time consuming. Preparation and organisation of regional or national audit meetings appeared to be laborious and time-consuming. The rate of substandard care found during SAMM audit meetings was 80% as compared to

25% reported in perinatal audit in the Netherlands.[32] This clearly highlights the urgent need for improvement of quality of obstetric care and this could be achieved through audit. We recommend routine audit of all cases of SAMM at the local level. This involves about one case per month for the average obstetric team, and could be implemented as a purposive annual audit meeting, as part of a meeting of the regional obstetric cooperative ['verloskundig samenwerkingsverband'], or as part of daily staff meetings whenever a case presents. The standard substandard care forms used in the LEMMoN study and derived from that used by the maternal mortality committee, could be used (Appendix B). With great interest, we await the first results of the Dutch Perinatal Audit, which will shortly have its kickoff. Results and experiences could be used for future implementation of more audit meetings at a regional or national level. To optimally disseminate the lessons learned from SAMM audit, it would be valuable to assemble an instructive training programme containing the most instructive cases of SAMM in the form of (anonymised) case vignettes.

Differences within the Netherlands

We noted marked differences in incidence of SAMM and other specific severe maternal conditions throughout the country. Although based on these findings, it would be interesting to be able to draw conclusions about quality of care delivered, there are multiple other explanations for the differences. The most important are the use of management based criteria subject to local differences in practice, differences in patient population and differences in case ascertainment. However, keeping these limitations in mind, we think it is possible to draw some conclusions from the numbers in individual situations. Moreover, the results should encourage obstetricians at the local level to audit their cases for better interpretation of the numbers, next to the important aspect of learning from adverse events. For better interpretation of differences in results found in the LEMMoN study, it would be very interesting to use the Dutch VOKS methodology to correct incidences for case mix.

Home delivery

From an international perspective, the Dutch obstetric care system is rather particular because of its two-tier system (primary vs. secondary/tertiary) and the high rate of home delivery (about 30% of all births). This particular character of Dutch obstetric health care obligates us to provide evidence that the system is equal to or even better than other international systems in use. For this reason, extensive sub-analysis of cases of SAMM that developed under primary care was initiated. The results of this sub-analysis are pending and are beyond the scope of this thesis. However, based on our own findings, we conclude that the Dutch system of selection of low-risk pregnancies is functioning properly. Due to careful risk selection during pregnancy and delivery, only 9.3% of

women included in LEMMoN (excluding early pregnancy) were under primary care at the moment SAMM arose, and only 6.3% delivered at home. The relative risk of SAMM in home delivery was 0.1 (95% CI 0.1-0.2), reflecting a ten-fold decreased risk as compared to women under care of the obstetrician for any medical reason. A similar pattern is observed when looking at the rate of women primarily under responsibility of an obstetrician. This rate was 35.8% among women included in LEMMoN, as compared to 14.3% in the general pregnant population.

Preliminary data suggest that there was no difference in SAMM rate between women with low-risk pregnancies delivering at home and women with low-risk pregnancies delivering in hospital to their own choice under responsibility of a primary care giver, suggesting that the delay in reaching the hospital does not essentially add to SAMM.[32] There are obviously some examples where this type of delay played a role in the developing of SAMM, but numbers appeared to be small. Women with an indication to deliver in hospital under responsibility of a primary care giver based on their general or obstetric history ('medium risk') indeed had an increased risk of developing SAMM, mainly due to MOH [Masterthesis JAJM Mesman, 2009, unpublished].

Despite the absence of a crucial role for the Dutch risk selection system in the rate of SAMM, we emphasize that a two-tier based system is prone to substandard care on theoretical grounds due to discontinuity of care. Each referral moment has an inherent risk of suboptimal transfer of information and it is therefore of crucial importance in the current Dutch system to warrant optimal cooperation between health care providers involved in the obstetric chain. Suboptimal cooperation between primary care givers and obstetricians will undoubtedly result in substandard care and hence increasing risk of SAMM. Finally, it is of crucial importance to strictly adhere to the risk selection protocols to warrant personalised optimal care for each pregnant woman. High-risk pregnancies are better cared for in secondary and tertiary care, low-risk pregnancies are better cared for in primary care.[33]

Definition of SAMM

Definitions constitute one of the biggest challenges of the international study of SAMM. There is, however, a clear need for internationally comparable data on SAMM in high income countries since maternal mortality has dropped to very low levels. Different research groups have already addressed this issue.[1;3;12;34-37] The quest was started by Mantel et al. in 1998 in South Africa, who first proposed to extend the 'learning-from-adverse-events-thought' to include SAMM.[36] He promoted the use of organ system based criteria instead of management based criteria, because the latter largely depend on local policies which may largely differ between (and within) countries. The major objection to organ system based criteria, however, is that they require more extensive documentation of cases, which is not routinely performed

outside the context of research. Moreover, conditions such as eclampsia are not straightforward to define in terms of confirmable organ dysfunction. This was illustrated by comparison of cases of eclampsia included in the Netherlands and the United Kingdom, revealing that 31 Dutch cases of eclampsia would not have been included in the UK study because abnormal laboratory values could not be confirmed (chapter 5).

Enquiries into maternal mortality have taught us that clear definitions are crucial for national and international comparison of data. Compared to maternal mortality, much more difficulty is encountered in defining SAMM. Even though maternal mortality itself is a straightforward definition –there is little discussion whether a woman is dead or not-, the exact classification of maternal death (direct, indirect, late, fortuitous) appears difficult. This applies even more to SAMM.

The inclusion criteria we adopted in the LEMMoN study were appropriate to identify SAMM in the Netherlands. Among 23 cases that were extensively audited by an expert panel, 71% of cases were classified as true severe maternal morbidity.[37] Depending on the severity of cases that needs to be identified, one could consider restricting MOH to only those women in need of five instead of four units of packed cells. This would halve the total number of cases included, thereby optimising specificity at the cost of sensitivity (i.e., identified cases are more severe, but some severe cases are likely to be missed). These considerations are well addressed by Geller et al, who aimed to define a conceptual framework of SAMM.[35;39]

The group of 'Other severe maternal morbidity' gives us a valuable insight into what type of different SAMM would have been missed. This group would not be suitable for use in international comparison because inclusion is largely subjective. Large differences in inclusion of cases into this group were already noted between the eight academic teaching hospitals in the Netherlands, rates ranging from 4 to 34% of all cases. These rates probably importantly depend on the ICU admission policy: the stricter the policy of ICU admission, the more cases of SAMM will be left to include as 'other severe maternal morbidity'. It would be interesting to further analyse cases included in the miscellaneous group to get more insight into what cases would have been missed in the absence of a miscellaneous group. By comparison of these cases to the gold standard of judgement by the clinician, the severity could be assessed. Subsequently, it would be interesting to know how many of these cases would have been missed in other studies on SAMM using other inclusion criteria. Initial rough analysis of the summary data of this group presented in chapter 3 reveals that many truly severe cases would have been missed. Of note, 35% of maternal deaths would have been missed without including a miscellaneous group.

Conclusion

The LEMMoN study has provided a valuable overview of SAMM in the Netherlands. Incidences of different types of maternal morbidity are now known and can serve as a reference for future assessment in the Netherlands and other countries. Trends in incidence should be monitored continuously, and further research is warranted to explain changing patterns and target interventions to reduce SAMM. Non-Western immigrants appeared to be at increased risk of developing SAMM, but risks were less pronounced than in maternal mortality. Especially sub-Saharan African woman appeared to be at risk. Audit of severe maternal morbidity is feasible and highly instructive. Continuous auditing of severe maternal morbidity is mandatory in view of the high rate of substandard care found during SAMM audit meetings: 80% of cases as compared to 25% for perinatal mortality. This indicates that women are paying a considerable price for the increased importance of the fetus as a patient.

Res Clin Obstet Gynaecol 2009;23:297-304.

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CHAPTER 13

Recommendations

1. Ongoing registration of SAMM for the purpose of quality assurance in reproductive health is mandatory to detect epidemiologic trends. The National Surveillance Centre of Obstetrics and Gynaecology (NSCOG) provides the infrastructure to collect data on SAMM and other rare conditions during pregnancy, like the United Kingdom Obstetric Surveillance System (UKOSS) does in the UK. Like in several other European countries, funding should be provided by the government (in the UK) or by professional societies (in Scandinavia).

2. We recommend routine local auditing of all cases of SAMM. Auditing of SAMM should be an item during the regular quality assurance visits taking place every five years in each obstetric ward in the Netherlands.

3. Routine national or regional audit of a selection of SAMM cases in addition to the ongoing maternal mortality audit could improve the quality of obstetric care in the Netherlands. This could be incorporated in the perinatal audit system which is established in the Netherlands at present.

4. Important risk factors like body mass index, ethnicity and previous caesarean section are not registered in The Dutch Perinatal Registry at present. Registration of these items is urgently needed. The registry should include all deliveries in the Netherlands, also those under guidance of general practitioners.

5. The inclusion criteria used in the LEMMoN study are appropriate for use in Western countries. For logistical reasons, we recommend elevating the threshold for major obstetric haemorrhage to five or more units of packed cells.

6. Internationally agreed criteria for SAMM should be developed by the World Health Organization for the purpose of quality assurance in reproductive health.

7. More aggressive antihypertensive treatment and insult prophylaxis is warranted in women with severe hypertensive disorders of pregnancy to reduce the increased incidence of eclampsia in the Netherlands. This reduction should be assessed by ongoing registration of SAMM cases (see 1.)

8. A multi-language patient leaflet should be developed with warning signs for complications of pregnancy and childbirth, especially pre-eclampsia.

9. Women considering an elective caesarean section should be counselled that the absolute risk of major obstetric haemorrhage necessitating arterial embolisation or peripartum hysterectomy is 1 in 250. Regarding long term consequences, uterine rupture in women with a previous caesarean section is 1 in 200, with perinatal mortality in 9% of cases.

10. The results of this thesis highlight the proper functioning of the Dutch obstetric system with selection of high-risk and low-risk pregnancies. The risk of SAMM during home delivery was 10-fold reduced as compared with hospital delivery.

11. Centralisation of obstetric care in large birth centres will yield more experience with the treatment of rare obstetric complications. We did not find any evidence, however, that the incidence of severe obstetric complications was reduced in larger birth centres as compared to smaller ones.

12. In case of fetal heart rate abnormalities or continuous abdominal pain during vaginal birth after caesarean (VBAC), uterine rupture should be strongly suspected and immediate caesarean should be expedited without further assessment with fetal blood sampling.

CHAPTER 14

Summary / Samenvatting

This thesis describes the results of the LEMMoN study, a two-year nationwide study into severe acute maternal morbidity (SAMM) in the Netherlands. The study ran from 1 August 2004 until 1 August 2006. All hospitals with an obstetric ward in the Netherlands participated in the study. For the first time, this study sheds light on the incidence, case fatality rate, risk factors and substandard care in SAMM in the Netherlands. As immigrant women are disproportionately represented in Dutch maternal mortality statistics, special attention was paid to the ethnic background.

In **Chapter 1**, the reasons that lead to the designing of the LEMMoN study are clarified. The international and national perspectives are discussed. SAMM gets more and more accepted as a new parameter of the quality of obstetric health care in Western countries, in addition to the maternal mortality statistics. While maternal mortality rates are very low in Western countries nowadays, several recent studies have reported an increase of the incidence of SAMM during the last decades in Western countries worldwide. Within the Netherlands, there is no system in place to register obstetric complications. Severe morbid conditions are currently not registered in the Dutch perinatal database LVR. The same goes for known risk factors of pregnancy complications like body mass index and caesarean section in obstetric history. **Chapter 2** highlights some methodological considerations involved in the design of the study. While general methods were described in the respective chapters, some important aspects deserved a more detailed description than was possible in the published manuscripts. Additional information regarding definitions, inclusion criteria and selection of denominator data is included. Furthermore, the actual running of the LEMMoN study and results of sub analyses that are specific to the Netherlands, are also described in more detail.

Chapter 3 presents the general results of the LEMMoN study. Ninety-seven percent of all monthly communication cards were actually returned, which made LEMMoN represent 358,874 deliveries in the Netherlands. SAMM was reported in 2552 cases, giving an overall incidence of 7.1 per 1000 deliveries. ICU admission was reported in 847 cases (incidence 2.4 per 1000), uterine rupture in 218 cases (incidence 6.1/10,000), eclampsia in 222 cases (incidence 6.2/10,000) and major obstetric haemorrhage in 1606 cases (incidence 4.5 per 1000). Overall case fatality rate was 1 in 53. Major obstetric haemorrhage accounted for half of all cases of SAMM.

Results related to ethnicity are described and discussed in **Chapter 4**. Non-Western immigrant women had a 1.3 fold increased risk of SAMM (95% confidence interval [CI] 1.2-1.5). Risks were increased among all different types of SAMM, with the largest differences noted in eclampsia. Great differences were observed among different ethnic minority groups, ranging from non-increased risk for Moroccan and Turkish women to a 3.5-fold increased risk for sub-Saharan African women (95% CI 2.8-4.3). Differences remained significant after correction for

low socio-economic status, unemployment, single household, high parity and prior caesarean in multivariable logistic regression analysis, suggesting that other factors are also involved. Additional explanatory variables found in the observational part of the study were lack of health knowledge and factors related to migration such as short residence in the Netherlands and lack of social networks. This suggests that there are opportunities for quality improvement by targeting specific disadvantaged groups.

Chapter 5-8 discuss the results of the different inclusion groups of LEMMoN.

Chapter 5 describes all intensive care unit (ICU) admissions in the Netherlands during the study period. A total of 837 cases were analysed, involving one third of all inclusions in LEMMoN. Incidence of ICU admission in the Netherlands was 2.4 per 1000 deliveries. Twenty-nine maternal deaths occurred, resulting in a case fatality rate of 1 in 29 (3.4%) as compared to 1 in 53 for SAMM in general. Most frequent reasons for ICU admission were major obstetric haemorrhage (48.6%), hypertensive disorders of pregnancy (29.3%) and sepsis (8.1%). Assisted ventilation was needed in 34.8%; inotropic support in 8.8%. Initial antenatal care by an obstetrician was associated with a higher risk and home delivery with a lower risk of ICU admission. It was concluded that using obstetric ICU admission as an indicator of quality of obstetric care reveals only one third of all cases of SAMM in the Netherlands.

Chapter 6 describes all cases of uterine rupture in the Netherlands during the study period. A total of 210 women were analysed, accounting for 6.9% of all complications in LEMMoN. Population-based incidence was 5.9 per 10,000 deliveries, which is comparable to other Western countries. Of these women, 183 (87.1%) had a uterine scar, incidences being 5.1 and 0.8 per 10,000 in women with and without uterine scar. No maternal deaths and 18 cases of perinatal death (8.7%) occurred. Most frequent symptoms in women with uterine rupture were abdominal pain and CTG abnormalities. Vaginal bleeding, hypertonia and acute absence of contractions were often not present. The overall absolute risk of uterine rupture was 1 in 1709, increasing to 1 in 198 in women with a prior caesarean section and 1 in 251 in women with epidural anaesthesia. In univariable analysis, women with a prior caesarean, epidural anaesthesia, induction of labour (irrespective of agents used), pre or post term pregnancy, overweight, non-Western ethnic background and advanced age had an elevated risk of uterine rupture. The overall relative risk of induction of labour was 3.6 (95% CI 2.7-4.8). The rate of induction of labour in the Netherlands had decreased as compared to 2002-2003. Although much attention is paid to scar rupture associated with uterotonic agents, 13% of ruptures occurred in unscarred uteri and 72% during spontaneous labour.

Chapter 7 describes all cases of eclampsia in the Netherlands during the study period. A total

of 222 women were analysed, accounting for 7.6% of all complications in LEMMoN. We found an incidence of 6.2 per 10,000 deliveries, which appeared to be twice as high as compared with recent data from other Western countries. Three maternal deaths occurred, case fatality rate being 1 in 74. Risk factors in univariable analysis included multiple pregnancy, primiparity, young age, ethnicity and overweight. Substandard care was identified in the majority of cases: prophylactic magnesium sulphate was only given in 10.4% of women and antihypertensive medication was given in 39.6% of women with a blood pressure on admission at or above 170/110 mmHg. Additionally, substandard care was judged to be present by an expert panel in 15 of 18 audited cases (83%). We concluded that these results, in combination with the high proportion of maternal mortality due to hypertensive disorders in the Netherlands, warranted critical evaluation of the management of hypertensive disease in the Netherlands.
Major obstetric haemorrhage (MOH) appeared to be the single largest cause of SAMM, involving 51.1% of all complications in LEMMoN. In total, 1606 cases were included. **Chapter 8** describes all cases of hysterectomy and arterial embolisation for MOH in the Netherlands during the study period. This group of 205 cases was thought to include the severest cases of MOH, representing 12.8% of all cases of MOH. The overall incidence was 0.57 per 1000 deliveries. Arterial embolisation was performed in 114 women (incidence 0.32 per 1000; case fatality rate 2.0%). Peripartum hysterectomy was performed in 108 women (incidence 0.30 per 1000; case fatality rate 1.9%). Seventeen women had hysterectomy as yet after failed arterial embolisation. Caesarean section (RR 6.6; 95% CI 5.0-8.7) and multiple pregnancy (RR 6.6; 95% CI 4.2-10.4) were the most important associated factors in univariable analysis. The rate of peripartum hysterectomy was in the lower range of incidences reported in the Peristat-II report, population-based incidences of arterial embolisation are not available from the literature. Fertility could be preserved in 46% of these women due to successful arterial embolization.
Finally, 233 cases were reported as 'other severe maternal morbidity', as assessed by the treating clinician. These cases are summarised in Chapter 3.

Jehovah's witnesses are known to have an increased risk of experiencing maternal mortality and SAMM due to major obstetric haemorrhage. This risk was quantified in **Chapter 9** using the LEMMoN database and data from the confidential enquiries into maternal deaths in the Netherlands from 1983-2006. We found a 1.4% risk for Jehovah's witnesses to experience SAMM due to major obstetric haemorrhage and a maternal mortality ratio of 68 per 100,000 live births. Women who are Jehovah's witnesses have a 3.1 times increased risk of SAMM due to major obstetric haemorrhage and a 100 times increased risk of maternal death due to major obstetric haemorrhage, as compared with the general pregnant population in the Netherlands.

We have spent much effort in assessing underreporting to the LEMMoN study. We could not find any way to assess underreporting of ICU admission on a national level. Underreporting of uterine rupture and eclampsia, as revealed by comparing with the LVR, appeared to be very low (2-3%). Underreporting of MOH appeared to be significant, and we therefore initiated a large nationwide survey by collecting data from blood transfusion laboratories throughout the Netherlands. Results are described in **Chapter 10**. We received blood transfusion data from 65 of 98 maternity wards in the Netherlands and compared them to the data from the LEMMoN study from the respective hospitals during the same 20-month period. Eighteen of 65 centres were excluded as their reported blood transfusion data could not be confirmed by a local obstetrician for logistical reasons, leaving data from 47 hospitals available for analysis. During the study period, 824 cases were identified by the blood transfusion laboratories and 727 cases by LEMMoN. In total 1018 unique cases were identified. After cross matching, an underreporting of 29% was found. Therefore, a more realistic estimation of the true incidence of MOH in the Netherlands would be 5.7 instead of 4.1 per 1000 deliveries. Underreporting appeared to be especially substantial among less severe cases of MOH. No cases of peripartum hysterectomy or arterial embolisation for MOH were missed. It is concluded that underreporting should be anticipated and quantified in all large multi-centre surveys for a more reliable estimation of the true incidence and to facilitate comparison of epidemiologic data.
Chapter 11 describes the introduction of audit of SAMM in the Netherlands. From 2005 onwards, seven SAMM audit meetings were organised throughout the Netherlands. A panel was formed, consisting of experts and local staff of the hospitals involved. Before each meeting, SAMM details of selected cases were sent to all panel members for individual assessment. During a plenary meeting, individual findings were discussed and substandard care factors as judged by the majority of assessors were scored. During the seven meetings, substandard care was identified in 53 of 67 cases (79%). Specific recommendations were formulated concerning local as well as national management guidelines. It appeared that data from the LEMMoN study reflected SAMM in the Netherlands and substandard care is present in four out of five cases. Ongoing audit of cases is promoted both at national/regional level and local level.

Chapter 12 contains the general discussion, with multiple aspects of SAMM being discussed consecutively.

Samenvatting

Dit proefschrift beschrijft de resultaten van de LEMMoN studie, een 2 jarige landelijke studie naar ernstige maternale morbiditeit ('Severe Acute Maternal Morbidity, SAMM) in Nederland. Alle ziekenhuizen met een afdeling verloskunde in Nederland participeerden in de studie, die liep van 1 augustus 2004 tot 1 augustus 2006. Voor het eerst is hiermee inzicht verkregen in de frequentie, mortaliteit en risicofactoren van ernstige maternale morbiditeit in Nederland, alsmede de factoren die wijzen op tekortschietende zorg (substandaard zorgfactoren) die daarbij een rol spelen. Wij waren speciaal geïnteresseerd in het verband tussen etniciteit en ernstige maternale morbiditeit, omdat etniciteit een significante risicofactor blijkt te zijn voor moedersterfte en ernstige maternale morbiditeit.

In **Hoofdstuk 1** wordt beschreven wat de aanleiding was voor het opzetten van de LEMMoN studie. Internationale en nationale perspectieven worden besproken. SAMM wordt in toenemende mate geaccepteerd als een nieuwe kwaliteitsparameter voor de kwaliteit van verloskundige zorg in westerse landen, in aanvulling op de maternale sterfte statistieken. Terwijl de maternale sterfte in westerse landen tegenwoordig zeer laag is, tonen verschillende studies wereldwijd dat er de laatste jaren sprake lijkt te zijn van een stijging van de incidentie van SAMM in westerse landen. In Nederland is momenteel geen registratiesysteem aanwezig voor obstetrische complicaties. Ook in de huidige Landelijke Verloskundige Registratie (LVR) worden ernstige maternale complicaties helaas niet geregistreerd, evenals bepaalde risicofactoren voor zwangerschapscomplicaties zoals body mass index en keizersnede in de voorgeschiedenis.

In **Hoofdstuk 2** worden enkele methodologische overwegingen besproken die een rol speelden bij het ontwerp van de studie. Hoewel de methodologie in het algemeen uitgebreid beschreven is in de respectievelijke hoofdstukken, waren er enkele aspecten die een meer gedetailleerde uiteenzetting verdienden dan mogelijk was in de gepubliceerde artikelen. Ook aanvullende informatie betreffende definities, inclusiecriteria en selectie van de referentiepopulatie is in dit hoofdstuk te vinden. Daarnaast wordt het daadwerkelijke beloop van de LEMMoN studie beschreven en worden enkele resultaten van subanalyses binnen Nederland besproken.

Hoofdstuk 3 beschrijft de resultaten van de LEMMoN studie in grote lijnen. Zevenennegentig procent van alle maandelijkse meldkaartjes werd daadwerkelijk geretourneerd, waardoor de LEMMoN studie 358.874 bevallingen in Nederland representeert. Er werden 2552 gevallen van SAMM gerapporteerd met een overall incidentie van 7,1 per 1000 bevallingen. Opname op de intensive care (IC) werd gerapporteerd in 847 gevallen (incidentie 2,4 per 1000), uterusruptuur in 218 gevallen (6,1/10.000), eclampsie in 222 gevallen (incidentie 6,2/10.000) en ernstige fluxus in 1606 gevallen (incidentie 4,5 per 1000). Overall case fatality rate was 1 op 53. De helft van alle gevallen betrof ernstige fluxus.

Resultaten met betrekking tot etniciteit staan beschreven in **Hoofdstuk 4**. Niet-westerse immigranten hadden een 1,3 keer zo hoog risico op SAMM (95% betrouwbaarheidsinterval 1,2-1,5). Het verhoogde risico gold voor alle vormen van SAMM, waarbij de grootste verschillen gezien werden bij vrouwen met eclampsie. Er werden grote verschillen gevonden voor verschillende etnische minderheden, variërend van een niet-verhoogd risico voor Marokkaanse en Turkse vrouwen tot een 3,5-voudig verhoogd risico voor vrouwen uit Afrika onder de Sahara. (95% betrouwbaarheidsinterval [BI]2,8-4,3). Verschillen bleven significant na correctie voor sociaaleconomische status, werkloosheid, alleenstaande moeder zijn, pariteit en keizersnede in de voorgeschiedenis in multivariate logistische regressie analyse. Dit suggereert dat er nog andere dan deze factoren een rol spelen. Met name moet men hierbij denken aan migratiegerelateerde factoren zoals korte verblijfsduur in Nederland, gebrek aan sociale netwerken en gebrek aan kennis van het Nederlandse gezondheidszorgsysteem. De uitkomsten suggereren dat er mogelijkheden lijken te zijn voor verbetering van de kwaliteit van zorg door interventies te richten op specifieke etnische minderheidsgroeperingen.

In de hoofdstukken 5-8 worden de resultaten beschreven van bestudering van de verschillende inclusiegroepen binnen de LEMMoN studie.
In **Hoofdstuk 5** worden alle IC opnames tijdens de zwangerschap en het kraambed in Nederland gedurende de studieperiode beschreven. In totaal werden 837 casus geanalyseerd, hetgeen een derde van het totaal aantal inclusies in de LEMMoN studie betrof. De incidentie van IC opname in Nederland was 2,4 per 1000 bevallingen. Er waren 29 gevallen van maternale sterfte, hetgeen een mortaliteit geeft van 1 op 29 (3,4%) vergeleken met 1 op 53 voor SAMM overall. De meest voorkomende redenen voor IC opname waren ernstige fluxus (48,6%), hypertensieve aandoeningen van de zwangerschap (29,3%) en sepsis (8,1%). Beademing was nodig in 34,8%, behandeling met inotropica in 8,8%. Vrouwen die al primair onder controle waren van de gynaecoloog, hadden een verhoogd risico op IC opname, en vrouwen die thuis waren bevallen een verlaagd risico. Geconcludeerd werd dat men door alleen naar IC opnames te kijken, twee derde van alle gevallen van ernstige maternale morbiditeit mist.
In **Hoofdstuk 6** worden alle gevallen van uterusruptuur in Nederland gedurende de studieperiode beschreven. In totaal werden 210 vrouwen geanalyseerd, 6,9% van alle inclusies in de LEMMoN studie. De populatie gebaseerde incidentie was 5,9 per 10.000 bevallingen, hetgeen vergelijkbaar was met andere westerse landen. In 183 gevallen (87,1%) was sprake van een litteken uterus. De incidentie van ruptuur met en zonder litteken was respectievelijk 5,1 en 0,8 per 10.000 bevallingen. Er waren geen gevallen van maternale sterfte en 18 gevallen van perinatale sterfte (8,7%). De meest voorkomende symptomen van uterusruptuur zijn continue buikpijn en

suboptimaal CTG. Vaginaal bloedverlies, hypertonie of atonie zijn vaak afwezig. Het overall absolute risico op uterusruptuur was 1 op 1709 bevallingen en steeg naar 1 op 198 in vrouwen met een litteken uterus en 1 op 251 in vrouwen die epidurale anesthesie hadden tijdens de partus. In univariate analyse bleek het risico op uterusruptuur tevens verhoogd na inleiding van de baring (op welke wijze dan ook), bij prematuriteit, serotiniteit, overgewicht, hogere maternale leeftijd en niet-westerse etniciteit. Het relatief risico van inleiding van de baring was 3,6 (95% betrouwbaarheidsinterval 2,7-4,8). In vergelijking met de studie van Kwee et al. in 2002-2003 was het percentage inleidingen bij vrouwen met een sectio litteken in Nederland gedaald. Hoewel in de literatuur veel aandacht wordt besteed aan de associatie van uterusruptuur met een sectio litteken en met het inleiden van de baring, vond 13% van de rupturen plaats bij vrouwen zonder uterus litteken en 72% tijdens spontane weeënactiviteit.

In **Hoofdstuk 7** worden alle gevallen van eclampsie in Nederland tijdens de studieperiode beschreven. In totaal werden 222 vrouwen geanalyseerd, 7,6% van alle inclusies in LEMMoN. We vonden een incidentie van 6,2 per 10.000 bevallingen, hetgeen twee keer zo hoog bleek te zijn als in andere westerse landen. Er waren drie gevallen van maternale sterfte (mortaliteit 1 op 74; 1,4%). Risicofactoren in univariate analyse waren meerlingzwangerschap, primipariteit, jonge maternale leeftijd, niet-westerse etniciteit en overgewicht. Substandaard zorg werd vastgesteld in de meerderheid van de casus: profylactisch magnesiumsulfaat was slechts in 10,4% van de gevallen gegeven en antihypertensiva in 39,6% van alle gevallen waarbij de bloeddruk bij opname al 170/110 of hoger was. Daarnaast werd bij 15 van 18 tijdens audit bijeenkomsten geanalyseerde casus (83%) geconcludeerd dat er sprake was van substandaard zorg. Wij concludeerden dat deze resultaten, in combinatie met het relatief hoge aandeel van hypertensieve aandoeningen in de moedersterfte, kritische evaluatie vereiste van het Nederlandse beleid bij hypertensieve aandoeningen in de zwangerschap.

Ernstige fluxus bleek de belangrijkste oorzaak te zijn van ernstige maternale morbiditeit in Nederland, verantwoordelijk voor 51,1% van alle complicaties in de LEMMoN studie. In totaal werden 1606 gevallen gemeld gedurende de studieperiode (incidentie 4,1 per 1000 bevallingen).

In **Hoofdstuk 8** worden alle gevallen van uterusextirpatie of embolisatie vanwege ernstige fluxus in Nederland gedurende de studieperiode beschreven. Deze serie van 205 patiënten representeert de ernstigste gevallen binnen de fluxus groep (12,8% van alle gevallen van ernstige fluxus). De overall incidentie van uterusextirpatie danwel embolisatie voor ernstige fluxus was 0,57 per 1000 bevallingen. Er werden 114 gevallen van embolisatie gemeld (incidentie 0,32 per 1000; mortaliteit 2,0%) en 108 gevallen van uterusextirpatie (incidentie 0,30 per 1000; mortaliteit 1,9%). Zeventien vrouwen ondergingen alsnog een uterusextirpatie na mislukte embolisatie. Keizersnede (RR 6,6; 95% BI 5,0-8,7) en meerlingzwangerschap (RR 6,6; 95% BI 4,2-10,4) waren

de belangrijkste risicofactoren in univariate analyse. De incidentie van uterusextirpatie voor ernstige fluxus in Nederland was in de lagere regionen vergeleken met de incidentie in andere landen, zoals gerapporteerd in het Peristat II rapport. Voor embolisatie zijn geen populatie incidenties bekend uit de literatuur. In 46% van de hier beschreven vrouwen kon de toekomstige fertiliteit worden gespaard door middel van succesvolle embolisatie.
Tenslotte werden 223 gevallen van 'overige maternale morbiditeit' (naar het oordeel van de behandelend arts) gerapporteerd. Een overzicht van deze casus wordt gegeven in Hoofdstuk 3.

Het is bekend dat Jehovah's getuigen een verhoogd risico hebben op ernstige maternale morbiditeit en maternale sterfte. Dit risico is gekwantificeerd in **Hoofdstuk 9** door gebruik te maken van de LEMMoN database en gegevens van de Commissie Maternale Sterfte over de jaren 1983-2006. Jehovah's getuigen hadden een absoluut risico van 1,4% op ernstige maternale morbiditeit door ernstige fluxus. De maternal mortality ratio was 68 per 100.000 levendgeborenen. Relatief hadden Jehovah's getuigen een 3,1-voudig verhoogd risico op ernstige maternale morbiditeit door ernstige fluxus en een 100-voudig verhoogd risico op maternale sterfte door ernstige fluxus, in vergelijking tot de algemene zwangere populatie in Nederland.

Onderdeel van de LEMMoN studie was een uitgebreide analyse van de onderrapportage van ernstige maternale morbiditeit. Er bleek geen mogelijkheid te zijn om onderrapportage van IC opnames landelijk vast te stellen. Onderrapportage van uterusruptuur en eclampsie, vastgesteld door vergelijking met gegevens van de LVR, bleek laag te zijn (2-3%). Onderrapportage van ernstige fluxus bleek significant te zijn en om die reden initieerden wij een grote landelijke survey waarin we transfusie data verzamelden van zo veel mogelijk bloedtransfusie laboratoria in Nederland. De resultaten van deze survey staan beschreven in **Hoofdstuk 10**. We ontvingen data van 65 van de 98 ziekenhuizen met een verloskunde afdeling in Nederland en vergeleken die met de data in de LEMMoN studie van dezelfde ziekenhuizen gedurende dezelfde studieperiode van 20 maanden. Achttien van de 65 ziekenhuizen werden geëxcludeerd omdat het niet lukte de gerapporteerde bloedtransfusiegegevens te laten verifiëren door een obstetricus om logistieke redenen. Data van de overige 47 ziekenhuizen waren beschikbaar voor analyse. Gedurende de studieperiode werden 824 casus geïdentificeerd door de bloedtransfusie laboratoria en 727 via de LEMMoN studie. In totaal werden 1018 unieke casus geïdentificeerd. Na cross-matching werd een onderrapportage van 29% gevonden. Dat betekent dat een meer realistische benadering van de werkelijke incidentie van ernstige fluxus in Nederland 5,7 per 1000 bevallingen is, in plaats van 4,1 per 1000. Onderrapportage bleek met name substantieel te zijn onder de minder ernstige gevallen van ernstige fluxus. Er waren geen gevallen van uterusextirpatie of embolisatie

in verband met fluxus gemist. Wij concludeerden dat rekening zou moeten worden gehouden met onderrapportage in alle grote multicentrische epidemiologische studies om tot een meer betrouwbare benadering van de werkelijke incidentie te komen en zodoende betere vergelijking van epidemiologische data mogelijk te maken.

Hoofdstuk 11 beschrijft de introductie van audit van ernstige maternale morbiditeit in Nederland. Sinds 2005 hebben wij zeven audit bijeenkomsten georganiseerd door het hele land. Een panel werd samengesteld, bestaande uit experts en stafleden en arts-assistenten van de betrokken ziekenhuizen. Voorafgaand aan iedere bijeenkomst werden gedetailleerde gegevens van geselecteerde casus verzonden naar alle panelleden voor individuele beoordeling. Tijdens een plenaire bijeenkomst werden vervolgens de bevindingen bediscussieerd en werden substandaard zorg factoren bepaald bij meerderheid van stemmen. Substandaard zorg werd gevonden in 53 van de 67 geanalyseerde casus (79%). Specifieke aanbevelingen werden geformuleerd voor implementatie in lokale en landelijke richtlijnen. Over het algemeen was men van mening dat de casus uit de LEMMoN studie ernstige maternale morbiditeit betroffen. Substandaard zorg bleek aanwezig in vier van de vijf casus. Voortgaande audit van gevallen van ernstige maternale morbiditeit wordt van harte aangemoedigd, zowel op landelijk/regionaal als op lokaal niveau.

Hoofdstuk 12 betreft de algemene discussie, waarin vele aspecten van ernstige maternale morbiditeit in Nederland de revue passeren.

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Publications

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van Dillen J, Mesman J, **Zwart JJ**, Bloemenkamp KWM, van Roosmalen J. Introducing maternal morbidity audit in the Netherlands. Submitted.

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●

Natuurlijk had de LEMMoN studie in de eerste maanden enige kinderziektes. Dat het hele project in onwaarschijnlijk korte tijd (3 maanden) van de grond is gekomen is mede te danken aan de voortvarendheid bij het Nationaal Signaleringscentrum van TNO. Rob, Ab en Annelies: zeer veel dank voor de vruchtbare samenwerking. Annelies, je was cruciaal en gezellig!

●

Waar zouden we zijn geweest zonder alle lokale coördinatoren! Zij hebben ieder op hun eigen manier belangeloos een geweldige bijdrage geleverd aan het welslagen van LEMMoN. De 100% deelname is uniek. Daar mogen we met zijn allen heel trots op zijn als Nederlandse gynaecologen, denk ik. Heel veel dank, LEMMoN is ook een beetje van jullie!

●

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●

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●

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●

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●

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●

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●

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●

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●

Allerliefste Maaike. Wat ben ik gelukkig met je, en wat ben ik trots dat je het hebt volgehouden! We hebben heel wat weekendjes en etentjes in te halen. Aan de slag!

Curriculum Vitae

Joost Zwart werd geboren op 19 oktober 1972 in Wageningen. Hij voltooide het VWO aan het Minkema college in Woerden. Van 1991 tot 1993 studeerde hij Medische Informatiekunde aan de Universiteit van Amsterdam. Daarna studeerde hij van 1994 tot 2001 Geneeskunde aan de Rijksuniversiteit Leiden. In 1999 liep hij stage in een moeder-kind ziekenhuis in Brazilië. Na het behalen van het artsexamen in 2001 werkte hij 2½ jaar als ANIOS Obstetrie & Gynaecologie, aanvankelijk in het Leyenburg ziekenhuis in Den Haag (hoofd Dr. P.A. de Jong) en later in het Groene Hart ziekenhuis in Gouda (hoofd Dr. J.C.M. van Huisseling). Van mei 2004 tot december 2007 werkte hij als AIOSKO in het Leids Universitair Medisch Centrum aan de LEMMoN studie, waarvan de resultaten in dit proefschrift beschreven zijn. In 2007 startte hij met zijn opleiding tot gynaecoloog in het Leidse opleidingscluster; de eerste anderhalf jaar in het Groene Hart ziekenhuis in Gouda (opleider Dr. J.C.M. van Huisseling), en momenteel in het Leids Universitair Medisch Centrum (opleiders Prof. Dr. G.G. Kenter en Prof. Dr. J.M.M. van Lith).

Hij woont in Leiden met Maaike Veenbergen en hun twee zoons Hidde (6) en Tijl (3).

Appendix A

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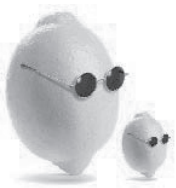
L ANDELIJKE studie naar
E TNISCHE determinanten van
M ATERNALE
Mo RBIDITEIT in
N EDERLAND



= *AUDIT FORMULIER* =

CASUS NR: ☐☐☐☐

1. Beoordelaar

1. Verloskundige ☐
2. Gynaecoloog 2e lijn ☐
3. Gynaecoloog 3e lijn ☐
4. AIOS Gynaecologie ☐
5. Overige ☐

Codering:
0 = nee
1 = ja
8 = niet te beoordelen
9 = niet van toepassing

2. Substandard Care

LET OP: ZIE CODERING VOORZIJDE!!!

A. Patiënt

- ❑ Patient delay op essentieel moment
- ❑ Weigert medisch advies of behandeling
- ❑ Taalbarrière? Bv: Geen adequate communicatie gewaarborgd

B. Huisarts **WEL / NIET (zeker) betrokken bij behandeling**

- ❑ Inadequate (antenatale) controles volgens richtlijn NVOG
- ❑ Ondanks klachten/symptomen belangrijk delay bij herkennen ziektebeeld
- ❑ Belangrijk delay bij doorverwijzing naar 2e lijn

C. Verloskundige **WEL / NIET (zeker) betrokken bij behandeling**

- ❑ Inadequate (antenatale) controles volgens richtlijn NVOG
- ❑ Ondanks klachten/symptomen belangrijk delay bij herkennen ziektebeeld
- ❑ Belangrijk delay bij doorverwijzing naar 2e lijn

D. Gynaecoloog **WEL / NIET (zeker) betrokken bij behandeling**

- ❑ Inadequate (antenatale) controles volgens richtlijn NVOG
- ❑ Ondanks klachten/symptomen belangrijk delay bij herkennen ziektebeeld
- ❑ Diagnose was gesteld, echter juiste therapie bleef te lang geheel of gedeeltelijk achterwege
- ❑ Inadequate doorverwijzing naar hoger echelon

E. Andere 2e lijns arts **WEL / NIET (zeker) betrokken bij behandeling**

- ❑ Belangrijk delay bij consulteren van een gynaecoloog

F. Organisatie gezondheidszorg

❑ Partus in thuissituatie had negatieve invloed op verloop

❑ Partus in 2e lijn had negatieve invloed op verloop

❑ Transportkwaliteit of –capaciteit had negatieve invloed op verloop

G. Bij Uterusruptuur

❑ Indicatie tot of wijze van inleiding was niet volgens richtlijn NVOG

H. Bij Eclampsie/HELLP

❑ Patiënte werd onvoldoende gestabiliseerd voor vervoer

❑ Patiënte werd onvoldoende gestabiliseerd voor partus/sectio

❑ Behandeling hypertensie was onvoldoende obv richtlijn NVOG

❑ Behandeling of preventie van convulsies was onvoldoende obv richtlijn NVOG

J. Bij Fluxus

❑ Patiënte werd onvoldoende gestabiliseerd voor vervoer

❑ Intraveneuze toegangsweg(en) te laat aangelegd

❑ Suboptimale behandeling van de fluxus obv richtlijn NVOG

❑ Bloedproducten niet voldoende of niet snel genoeg beschikbaar

Ruimte voor specificatie substandard care ongeacht oorzaak

3. Algemeen

Was het beoordelen van substandard care goed mogelijk met de beschikbare gegevens?

1. NEE ❑
2. JA ❑

Welke extra gegevens zijn noodzakelijk voor adequate beoordeling van substandard care?

Is er naar uw mening sprake van 'ernstige maternale morbiditeit'?

1. NEE ❑
2. JA ❑

Vindt u het zinvol dat deze casus plenair besproken wordt tijdens de Audit bijeenkomst?

1. NEE ❑
2. JA ❑