Safe motherhood : severe maternal morbidity in the Netherlands. The LEMMoN study

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CHAPTER 10

Underreporting of major obstetric haemorrhage in the Netherlands

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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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