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

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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

^aNumbers do not add up to the total as women could suffer from more than one disease;

^bPsychiatric 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

^aIntensive care unit levels are described in the methods section; ^brates reflect percentage of all women with severe maternal morbidity; ^cdata missing for 22 women; ^ddata missing for 21 women; ^edata missing for 20 women.

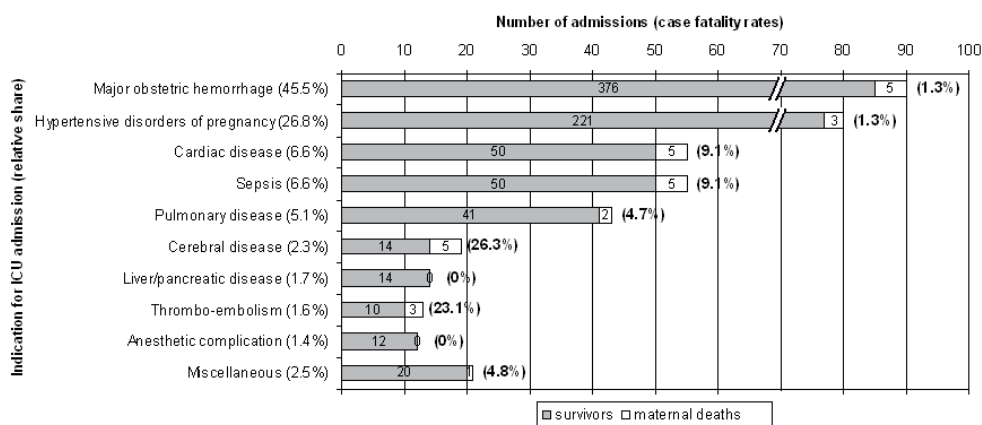
Rates of ICU admission for different subgroups of severe maternal morbidity were 12% for uterine rupture, 42% for eclampsia and 27% for major obstetric haemorrhage. Twenty-six women (3.1%) were admitted to ICU during early pregnancy, 191 (22.8%) antepartum and 620 (74.1%) postpartum. Mean duration of 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)
<i>Patient</i>						
<i>Age</i>						
≥ 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)
<i>Body mass index (kg/m2)</i>						
< 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)
<i>Pregnancy</i>						
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)
<i>Delivery</i>						
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/anesthesiologists 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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