

Perinatal outcome of severe obstetric complications: findings of a 10-year hospital-based surveillance study in Italy

This article was published in the following Dove Press journal:
International Journal of Women's Health

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Objective: To assess incidence and clinical patterns of severe maternal morbidities related to pregnancy. To determine associated feto-maternal outcomes and economic costs for the institution.

Methods: Observational study in a tertiary care Italian public hospital during a 10-year period. To identify severe obstetric complications, the following management-based criteria were adopted: need for intensive care unit admission, blood transfusion ≥ 5 units, emergency peripartum hysterectomy/laparotomy and arterial embolization. Impact of severe obstetric complications on facility resources was estimated considering length of hospital stay, need for additional surgery and transfusion.

Results: A total of 151 cases were identified, most frequent obstetric morbidities being major obstetric hemorrhage (50.3%) and hypertensive disorders (19.2%). Pre-term birth, caesarean section and sub-saharan African origin were factors significantly associated with severe morbidity. Maternal mortality and maternal mortality to morbidity ratios were 17 per 100,000 live births and 3:151, respectively. Stillbirth rate was 4.4%. Massive use of blood products and prolonged admissions concurred to increase hospital expenditures.

Conclusion: Institutional severe maternal morbidities may be effectively monitored by implementing a surveillance program and selecting a combination of management-based criteria which define the extremely morbid cases. Focusing on causes and risk factors associated with adverse obstetric situations has the potential to improve quality of care, prevent maternal life-threatening complications and perinatal mortality, reduce hospital expenditures.

Keywords: maternal near miss, organ dysfunction, severe obstetric morbidity, intensive care unit

Introduction

Maternal mortality rates have substantially declined in high-income countries where current estimates fall in the range of 10.4 to 13.7 per 100,000 live births.¹ Widespread institutional deliveries and access to effective interventions within the health facilities have been contributing factors to the radical change. In a low mortality setting, few pregnant women who develop a severe complication die, whereas a much larger proportion of them, although affected, escape death. The in-depth analysis of surviving patients has the advantage of better understanding how to promote safer obstetric care and prevent future complications and deaths.^{2,3}

Widely used as an indicator of quality of care, obstetric morbidity has lacked a common definition over a long period of time, especially so for the very severe cases, the near miss, considered a proxy for maternal mortality.⁴

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In 2011, the World Health Organization (WHO) has proposed the adoption of new restrictive criteria to define a maternal near miss among severe morbidities. Accordingly, a near miss should be identified with a life-threatening condition causing organ dysfunction, based on clinical, laboratory and management markers.^{5,6}

This study, conducted in a large academic hospital of northern Italy, assesses prevalence and causes of severe obstetric cases identified following the latest WHO criteria and evaluates the materno-neonatal outcome and the impact on hospital resources.

Materials and methods

Study type, setting and duration

This is an observational prospective study of severe maternal complications occurring from January 2007 to December 2016 at the University Hospital of Verona, a referral institution with a mean annual number of 1750 deliveries and an average C-section rate of 32.8%.

Study participants

The following intervention-based and organ dysfunction criteria were used to identify cases at any time during pregnancy and up to 6 weeks after delivery: admission to Intensive Care Unit (ICU), blood transfusion ≥ 5 units, emergency peripartum hysterectomy/laparotomy, interventional radiology. According to the WHO criteria, admission to ICU, laparotomy and interventional radiology are considered critical interventions for potentially life-threatening complications, while massive transfusion and hysterectomy are included among dysfunctional criteria, corresponding to a coagulation/hematological and uterine dysfunction, respectively, hence to a near-miss.⁵

Data collection

Medical records within the obstetric ward and ICU provided the data which were entered in an Access database: nationality, reproductive history, antenatal care, gestational age, mode of delivery, medical and surgical care given during hospital stay, perinatal outcome. Pregnant women transfused for chronic conditions such as hemoglobinopathies (sickle-cell anemia, beta-thalassemia) were excluded.

Immigrant women were divided into 5 sub-groups according to country of origin and regional aggregates: Sub-Saharan Africa, Arab States, Central and Eastern Europe and Commonwealth of Independent States (CIS),

South East Asia and the Pacific, Latin America and the Caribbean.⁷

Newborn acid-base analysis was performed in all deliveries by a qualified operator immediately after birth using a RAPID Point 405 Blood Gas analyzer (Siemens Healthcare Diagnostics) placed in the delivery room. Cutoff values for identifying fetal metabolic acidosis were pH below 7.05 and base deficit (BD) in excess of 12 mmol/L, in cord artery according to reference studies.⁸

The study respected ethical rules set by our local ethical committee.

Statistical analysis

Analysis was performed using the software Microsoft[®] Office Excel 2010 (Microsoft Corp.WA, USA). Crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, as estimators of the relative risk of near-miss. To account simultaneously for the effect of several potential confounding factors, multiple logistic regression was used, with maximum likelihood fitting, to obtain ORs and corresponding 95% CIs. Significance was assumed when the CI did not cross 1.

Results

In the 10-year study period, 151 cases were identified, giving a rate of 15.1 (range 5–17) per year and an incidence of 8.6 (range 4.5–11.9, median value 7.9) per 1000 deliveries over a total of 17,560 women who gave birth during the same interval. Selected intervention-based criteria are detailed in [Table 1](#): several cases fulfilled multiple criteria.

Most obstetric complications were treated in ICU (66.9%) or received a massive transfusion (40.4%); the combination of these two criteria identified 145/151 (96.0%) of our study cases. The two dysfunctional criteria, ie, massive transfusion and hysterectomy, identified 104/151 cases (68.9%), approximately half of them (56.7%) receiving treatment in ICU.

The most frequent obstetric morbidity was major hemorrhage, affecting 76 patients (50.3%): primary underlying causes were several utero-placental factors (70 cases) including fibroids and placenta accreta and praevia, uterine atony while 6 cases developed coagulopathy secondary to severe pre-eclampsia.

Among patients admitted in ICU, 42 (41.6%) were neither massively transfused nor hysterectomized or treated with arterial embolization. Most frequent complications justifying ICU admission were hypertensive disorders and

Table 1 Severe maternal morbidity (SMM) according to intervention-based criteria (N=151)

Criterion	N (%)	Incidence (per % deliveries)
ICU admission	101 (66.9)	5.8
Transfusion \geq 5 units of blood products	61 (40.4)	3.5
Emergency peripartum hysterectomy*/laparotomy	52 (34.4)	3.0
Arterial embolization	13 (8.6)	0.7

Note: *Hysterectomies: N=24 (1.4% deliveries).

hemorrhagic complications; sepsis and several other causes affecting the pulmonary, cardiovascular and renal function made intensive treatment necessary for 42.6% of the women (Table 2). Cases of pre-eclampsia requiring ICU admission represented 2.9% of total PIH patients admitted in the obstetric ward.

Mean age of severely affected patients (32.9 ± 6.0 years; range 19–48) did not differ from that of the total parturient population (31.7 ± 5.4 years; range 15–55).

We also compared the morbidity cases with the healthy control group for a number of selected variables (Table 3): factors significantly associated with severe obstetric morbidity were pre-term birth (OR 7.06, 95% CI 4.84–10.29), caesarean section (OR 4.97, 95% CI 3.18–7.76) and multiple pregnancies (OR 2.00, 95% CI 1.08–3.71). In view of the large immigrant population assisted in our obstetric ward, origin of the patient was also taken into consideration. Among the entire group of immigrants, sub-saharan African patients were at higher risk for a severe complication (OR 1.83, 95% CI 1.06–3.14). Three maternal deaths occurred during the study period giving a MM ratio of 17 per 100,000 live births.

Mean birthweight of newborns delivered by severely complicated parturients was $2238 \text{ g} \pm 1038$ (range 300–4300 g); moreover, all selected indicators of adverse impact on fetoneonatal well-being are detailed in Table 4 and differed significantly from the findings in the control population.

Indicators of costs for the health system were units of blood or plasma transfused, length of hospitalization, use of operating theater for minor interventions such as D&C

and for laparotomies/hysterectomies with the exclusion of C-section (Table 5).

Discussion

Reduction of maternal mortality in high resource countries has caused maternal-death confidential enquiries to become less informative, hence the growing importance of severe maternal morbidity as an alternative health indicator in the monitoring process of adverse events leading to mortality.

There is a general consensus that this complementary strategy is valuable in promoting obstetric care and implementing policy guidances targeted at reducing maternal deaths.^{5,6,9}

In spite of mortality reduction, maternal deaths still occur and accordingly we have to report a rate of 17 demises per 100,000 livebirths during our study period. Three patients were lost due to different specific causes, which included sepsis from an illegally induced abortion in early pregnancy, aortic dissection in 3rd trimester, amniotic fluid embolism during labor.

In recent years, studies on severe morbidity have provided a wide range of results depending on the setting and on the choice of the method of identification.

A European-based systematic review has identified severe morbidity adopting management-based criteria such as ICU admission or emergency hysterectomy, alone or in combination with specific disease and organ dysfunction criteria. Transfer rates to ICU ranged from 0.4 to 7.3 per 1000 deliveries whereas mixed criteria gave rates of 0.9–7.2 per 1000.¹⁰ Our findings seem to confirm

Table 2 Obstetric admissions to ICU (N=101)

Severe obstetric morbidity	N (%)	Primary underlying cause
Hypertensive disorders	29 (28.7)	Severe pre-eclampsia (82.7%), eclampsia (3.5%), HELLP syndrome (13.8%)
Severe hemorrhage	29 (28.7)	Placenta praevia or accreta (41.4%), uterine atony (41.4%), placental abruption (17.2%)
Septicemia	4 (4.0)	Illegally induced abortion
Other causes	39 (38.6)	H1N1 pneumonia, ab-ingestis pneumonia, coma, DVT, renal failure, drug toxicity, severe hypoxemia

Table 3 Risk factors for severe maternal morbidity (SMM): comparison between cases and the general parturient population

Variable	SMM N=151 N (%)	Other parturients N=17,409 N (%)	OR (95% CI) without adjustment	OR (95% CI) with adjustment
Maternal age (year) ≥ 40	19 (12.6)	1168 (6.7)	2.001* (1.23–3.25)	1.40 [§] (0.83–2.63)
Immigrant status	62 (41.1)	6267 (36.0)	0.81 (0.58–1.11)	–
East. Europe and Central Asia	22 (14.6)	2302 (13.2)	1.11 (0.71–1.76)	–
Arab States	7 (4.6)	1089 (6.3)	0.72 (0.34–1.56)	–
Sub-Saharan Africa	16 (10.6)	1061 (6.1)	1.826 (1.084–3.08)	1.83 ^{§*} (1.06–3.14)
S-East Asia and the Pacific	12 (7.9)	1390 (8.0)	0.99 (0.550–1.79)	–
Latin Am. and the Caribbean	5 (3.3)	424 (2.4)	1.37 (0.56–3.36)	–
Nulliparity	81 (53.6)	8381 (48.1)	1.342 (0.967–1.86)	1.34 [§] (0.95–1.90)
Gestational age at delivery				
≤ 37 weeks	102 (67.5)	2636 (15.1)	12.99* (9.10–18.55)	7.06 ^{§*} (4.84–10.29)
≤ 32 weeks	57 (37.7)	726 (4.2)	13.97* (9.97–19.58)	7.33 ^{§§*} (5.04–10.66)
Cesarean section	112 (74.2)	5645 (32.4)	8.335* (5.50–12.6)	4.97 ^{§*} (3.18–7.76)

Notes: * $p < 0.05$. [§]The model includes: age (≥ 40), immigrant status, nulliparity, gestational age ≤ 32 , cesarean section. ^{§§}The model includes: age (≥ 40), immigrant status, nulliparity, gestational age ≤ 37 , cesarean section.

the European estimates: prevalence of admissions in ICU in our study is 5.8 per 1000, and with regard to emergency hysterectomies the rate of 1.4 per 1000 is rather close to the 0.4–2.0% reported by the above-mentioned authors.¹⁰

With the aim of providing comparable results, our study has adopted the WHO approach: massive transfusion and peripartum hysterectomy have identified most life-threatening complications, which, by WHO definition, are considered near miss for maternal mortality.⁵ According to the two stricter criteria, 104 patients who had features of organ dysfunction gave a corresponding near miss rate of 5.9 per 1000 deliveries.

In addition, we extended our surveillance to patients requiring either admission to ICU or complementary critical interventions like peripartum laparotomy and interventional radiology since these criteria are appropriate to define a potentially life-threatening complication which may progress to an almost fatal condition.⁵

In our institution, care in ICU is reserved to severely affected cases and only in rare instances women are transferred for a short post-cesarean or post-delivery intensive monitoring. After excluding these latter cases, we identified a subgroup of patients who had not received a massive transfusion nor had been hysterectomized but whose conditions were severe enough to require intensive care, often

including intubation, ventilation and use of vasoactive drugs. This sub-group adds an additional 2.7 per 1000 to our near miss estimate and brings the overall incidence to 8.6 cases per 1000 deliveries.

If we focus only on patients with a viable gestational age and exclude morbid cases associated with ectopic pregnancy and septic abortions, the figure decreases to 7.8 per 1000 births.

This incidence falls within the range of 9.5–16.0 severe morbidities per 1000 births, provided by a European reference study and the finding of 3.6 per 1000 deliveries reported by O'Malley and co-workers in their study based on WHO selective criteria.^{11,12}

In view of these comparisons, we suggest that the approach to severe maternal morbidity should be based on multiple criteria and this idea should be shared with other authors.¹³

As researchers strive to provide uniform and comparable near miss rates, their effort is still hampered by several major drawbacks, mainly differences in setting, resources, design and identification criteria chosen for each single study.

Blood transfusion, a marker often used to assess the degree of severity of a maternal complication, is a good example of this inadequacy: in any severe hemorrhagic

Table 4 Impact on feto-neonatal well-being: comparison between newborns from severe maternal morbidity (SMM) cases and the control parturient population

Variable	SMM newborns ^a N=158 N (%)	Control newborns ^a N=18,100 N (%)	OR (95% CI)
Low birth weight (LBW)	84 (53.2)	2382 (13.2)	7.49 (5.46–10.26)*
Very low birth weight (VLBW)	40 (25.3)	729 (4.0)	8.07 (5.60–11.64)*
5 mins Apgar score ≤7	20 (12.7)	485 (2.7)	5.26 (3.26–8.48)*
Metabolic dysfunction ^b	5 (3.2)	97 (0.5)	6.06 (2.43–1.11)*
Admission in neonatal intensive care unit	69 (43.7)	1900 (10.5)	6.61 (4.80–9.08)*
Stillbirth	7 (4.4)	104 (0.6)	8.02 (3.67–17.53)*

Notes: ^aincludes all twins in both groups; ^bpH <7.05 and BD ≥12; *p<0.05.

Table 5 Impact on facility resources

Variable	N (%)
Units of emocomponents transfused	858
mean ± S.D. (range)	5.7±10.7 (0–101)
Hospital stay (dd)	1524
mean ± S.D. (range)	10.1±10.0 (2–105)
Major surgery	39/151 (25.8)
Minor surgery	17/151 (11.2)

event, the number of units transfused depends on the individual judgment in the specific setting. The cutoff value of 5 units identifies a peripartum hemorrhage of extreme gravity, turning transfusion in a life-saving measure.⁵ In a high resource setting, this is likely the case, but the higher transfusional level may be inappropriate in a low resource country, where blood products are by definition very scarce and rarely meet the needs.

Analysis of the clinical aspects of severe pregnancy complications shows a significant association of early gestational age and C-section with obstetric events that threaten the woman's life. Mode of delivery is definitely affected by primary obstetric complications and the surgical solution is often the best choice to preserve the maternal-fetal well-being. Our results also draw the attention on the higher risk of maternal complications among women over 40 years of age and immigrant women. As for the first aspect, having a first child later in life is becoming more common due to social changes and availability of ARTs. Accordingly, among European women, Italians have the highest mean age at first pregnancy (31.1%) and the highest rate (6.1%) of a first child after 40.¹⁴

With regard to the relevance of foreign patients, during the 10-year interval, prevalence of first-generation immigrant parturients in our institution steadily increased from 24.8% in 2006 to 44.2% in 2015. This study has identified a minority

group of sub-saharan African women significantly associated with severe morbidity, a finding that confirms previous observations sustaining the likelihood of an adverse perinatal outcome within the large multi-origin migrant population.^{15–17}

Severe obstetric morbidity has a significant impact on fetal outcome: this causal relationship is more obvious in those cases where stillbirth occurs, but it is also likely in newborns of higher gestational age showing signs of metabolic dysfunction. Previous studies have found a relevant difference in stillbirth rates among women with obstetric complications compared to women without complications.¹⁸ Among our patients, fetal demise occurred significantly more often than expected in an uncomplicated pregnant population, the result of intrapartum distress and severe prematurity.

Finally, the burden for the institution needs to be mentioned in view of the frequent use of large amounts of blood products and surgical resources for cases in need of major surgery, often a peripartum hysterectomy. Need for transfusion is by far increased when compared with the mean prevalence of 1.3 blood units per 100 deliveries observed during the total study period. Prolonged hospitalization also increases institutional expenditures associated with maternal complications, exceeding by far the duration of 4.0 days that represent the mean hospital stay of a patient admitted for any reason in the obstetric ward.

This study has some limitations that should be noted. First, it is based on the results of a single institution and therefore lacks the strength of a multicenter study. A second limitation relates to ICU admission, which despite representing a simple way to monitor severe complications occasionally may include cases that do not reach the near miss level. Finally, despite the fact that we monitored obstetric complications prospectively, cases were not subject to review through an auditing process and their avoidability therefore was not assessed.

Despite these limitations, our long-term surveillance provides epidemiological data on severe maternal

morbidity in a tertiary care facility of a high-income Italian region, in the absence of other published reports. To our knowledge, there is only one study covering a regional sample of ICU admissions and the choice of strict criteria for identification adopted in our study warrants a potential cross-country comparison.¹⁹

Conclusion

The most severe adverse events which complicate pregnancy provide a 10-year scenario of obstetric near miss. We envisage this study may encourage other national institutions to more effectively address this crucial health issue in a common effort to reduce acute and severe complications, avoid long-term disabilities, prevent maternal deaths.

Ethics approval and consent to participate

All human subjects provided written informed consent; all medical records were anonymized and maintained with confidentiality. The study was a clinical practice evaluation and in lieu of a formal ethics committee, the principles of Helsinki Declaration were followed. The registered number was not requested.

Data sharing statement

The data that support the findings of this study are available on request from the corresponding author [GZ].

Acknowledgment

The abstract of this paper was presented with interim findings at the 19th National Congress of the Italian Society of Perinatal Medicine (Società Italiana di Medicina Perinatale, SIMP) in Naples, January 19th–21st, 2017. The poster abstract was published in the *J Pediatr Neonat Individual Med*. 2017;6(1):e060125. doi:10.7363/060125.

Author contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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