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REVIEW ARTICLE

Epidemiology of obstetric critical illness

S. Einav,[a] M. Leone[b]
[a]*Intensive Care Unit, Shaare Zedek Medical Center and Hebrew University School of Medicine, Jerusalem, Israel*
[b]*Department of Anesthesiology and Intensive Care Medicine, Hôpital Nord, Assistance Publique Hôpitaux de Marseille, Aix Marseille University, Marseille, France*

ABSTRACT
Obstetric intensive care unit (ICU) admissions comprise only a small part of severe maternal morbidity. The incidence rate of both remains relatively unclear due to inconsistent definitions across publications, although this has begun to be addressed. There is a relative paucity of information regarding disease-specific survival following obstetric ICU admission, but outcomes are clearly related to the cause of admission and the quality of care. The ratio between maternal near-miss cases (many of whom are admitted to ICUs) and maternal death may provide insight into the preventability of death.
Hemorrhage and pre-eclampsia constitute the leading causes of ICU admission and have relatively low mortality rates, perhaps demonstrating the impact of informed care in managing obstetric critical illness. Obstetric sepsis, heart disease and anesthesia complications should be the focus of future research. The incidence of obstetric sepsis has been increasing in the last decade, with mortality rates remaining relatively high. The incidence of obstetric heart disease is increasing and maternal complications have been attributed to fractionated care of mothers within this category. Anesthesia complications remain a predominant cause of maternal death and likely intensive care admission.
Data are lacking regarding the relative proportion of cases per disease that remain treated outside the ICU; and the outcomes of various management strategies. The only study of the health status of survivors of obstetric ICU admission revealed that six months after hospital discharge, one in five women still had a poorer health-related quality of life than those of a reference age- and sex-matched cohort.

Keywords: Pregnancy complications; Pregnancy; Peripartum; Critical care; Critical illness; Epidemiology

Introduction

Maternal wellbeing hinges upon multiple causes, such as gross domestic product (Fig. 1) and the quality of the local healthcare system and its priorities.[1] Maternal death is often preceded by fractionated care and at times may be preventable.[2–7] However, like any other condition, medical disorders leading to maternal death should be addressed appropriately along the spectrum of care. While great advances have been made with regards to risk management, diagnosis, prevention and early treatment of pregnancy-associated diseases, much still remains to be learned about obstetric critical illness.

Several issues have hindered progress on this front. The medical community has only recently realized that, although global maternal mortality rates (MMR) are decreasing,[8] maternal morbidity is increasing in developed countries.[9] The MMRs of developed countries are low. Therefore, despite tertiary care, clinicians may tend to view maternal death as almost inevitable.[10] However, debriefings after maternal death repeatedly demonstrate that the quality of treatment is only as good as that of the lowest level of care provided by the multidisciplinary team, so there remains room for improvement.[11,12] For more than two decades, the intensive care unit (ICU) death rates observed in the obstetric population have been lower than those predicted by commonly used ICU scoring methods.[10,13–16] This has led to complacency rather than to the understanding that this population is highly responsive to therapy. Pregnant women are almost uniformly excluded from clinical trials. Causes for this exclusion include classification of pregnant women as a "vulnerable" population, concerns regarding the legal implications of potential harm to the fetus and skepticism regarding the willingness of pregnant women to participate in research. Pregnant women are also excluded from many observational trials, due to uncertainty regarding the impact of the physiology of pregnancy

Correspondence to: S. Einav, Surgical Intensive Care, Shaare Zedek Medical Centre affiliated with the Hebrew University, POB 3235, Jerusalem 91031, Israel.
E-mail address: einav_s@szmc.org.il

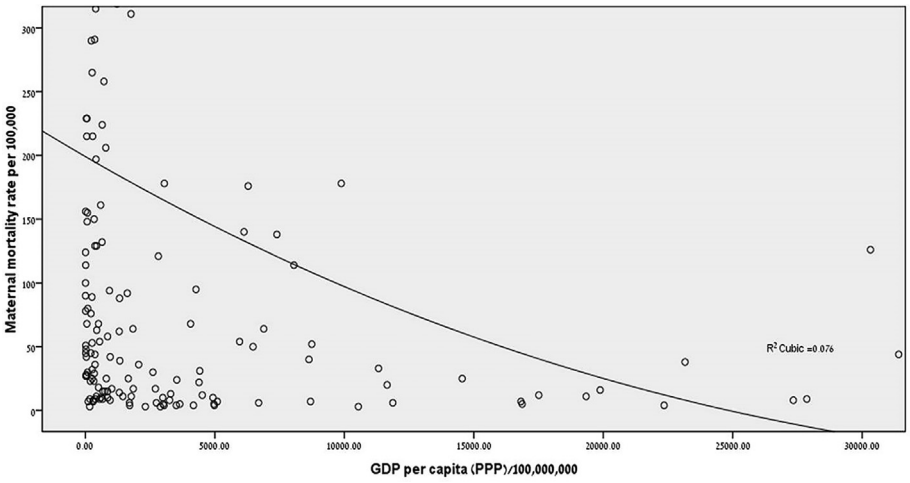

Fig. 1 National maternal mortality rates plotted as a function of national gross domestic product (purchasing power parity). All data were taken from the CIA fact book database (public domain). Values were cut off at MMRs >300 per 100 000 and GDP > $30 000 000 000 000 to enable visualization

on study results. Consequently, when a pregnant woman is critically-ill, there are few data to inform prescribing and even less to inform treatment. Finally, major questions remain regarding the actual definition of maternal or obstetric critical care.

Definition of obstetric or maternal critical care

Neither the term "maternal critical care" nor the term "obstetric critical care" encompasses the full range of intensive care delivered to women who are pregnant or peripartum. The term "maternal intensive care" suggests that the woman being treated must be a mother. This term implicitly excludes, for example, women admitted to intensive care following abortion. The Merriam-Webster dictionary defines the term "obstetric" as "of, relating to, or associated with childbirth". Hence the term "obstetric intensive care" suggests that the cause of ICU admission must be directly related to the pregnancy. In this review, as in many other papers, these terms are used interchangeably.

Obstetric critical care has been defined as "the specialized management of critically-ill obstetric patients via an interdisciplinary approach in which the optimization of the clinical variables of pregnant women should be approximated to the maternal-fetal unit needs as a whole".[17] The epidemiology of obstetric critical care is confounded by differences in definition of both "obstetric" and "critical care".[18]

The definition of "obstetric" is confounded by variability in the time-frame post delivery which is still considered associated with that pregnancy. The World Health Organization (WHO) defines maternal mortality as "the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes."[19] As a result, obstetric critical care admissions are often identified as women having an ICU admission during pregnancy or up to 42 days after termination of pregnancy for any cause.[20] However, severe pregnancy-related morbidity may occur several months after termination of pregnancy. For example, cardiomyopathy of pregnancy can manifest weeks to months after delivery and presentation may even be delayed for up to one year.[21] Data from 214 general ICUs across Great Britain showed that the ratio of women defined as critically-ill was one "currently pregnant" to five "recently pregnant".[11] The United Kingdom (UK) 2015 Confidential Enquiries report noted that nine in 100 000 women died within six weeks of delivery/the end of pregnancy, whereas 14 additional women in 100 000 died between six weeks and one year later.[22] No similar registry exists in the United States of America (USA). However, the USA Fourth Trimester project was recently established to improve maternal care in the vulnerable period after delivery.[23] Inclusion of cases admitted to the ICU up to one year after delivery may therefore significantly increase the number of obstetric ICU admissions.

The definition of "critical illness" is confounded by different means of identifying critically-ill pregnant or peripartum women, for example by admission to an ICU, by the occurrence of organ failure and/or by the requirement for a life-saving intervention. When ICU admission is the criterion used, critically-ill women observed/treated in high-risk obstetric units or labor wards are potentially overlooked.[11] A selective approach to obstetric ICU admission is often advocated, based on studies showing higher maternal survival rates following ICU admission for direct obstetric causes versus admission for indirect causes.[24] Although more data on maternal morbidity and mortal-

ity are required to determine the validity of this argument, observation outside of the ICU is becoming common practice in some developed countries.[25,26] Reports may also miss maternal admissions to specialized units (e.g. cardiac, neurological) as a result of heart disease and/or stroke.

When critically-ill obstetric cases are identified by the occurrence of one (or more) acute organ failure, this classification, which hinges on the number of failing organs required to fulfill the definition, may overlook cases such as those with massive hemorrhage without subsequent organ failure. One study of pregnancy-associated utilization of ICU services in Texas from 2002 to 2010 demonstrated that even though 26.5% of the women were graded as suffering from high severity of illness, organ dysfunction was rarely observed (6.2%).[27] Coding issues may further confound this definition, as they have with regards to maternal death.[28]

Finally, the incidence of obstetric critical care may be determined by the proportion of cases receiving acute life-saving interventions such as hysterectomy, mechanical ventilatory support, renal replacement therapy, extracorporeal mechanical oxygenation or liver support. Provision of any treatment modality depends on its availability. In some developing countries, antihypertensive medications are only sometimes available; ventilators, suction devices and even intensive care may be unavailable.[29] While such extreme shortages rarely occur in developed countries, the susceptibility of the pregnant population to H1N1 during the 2009 pandemic highlighted similar issues arising from the selective availability of extracorporeal membrane oxygenators. Moreover, even when the required means of support are available, the indications for many such interventions are not standardized.

Maternal critical illness and intensive care unit admission

Since the establishment of the first ICU in Copenhagen in 1953 by Bjorn Aage Ibsen, ICUs have been discrete geographic areas within the hospital where all cutting-edge resuscitative services are provided. Obstetric intensive care often does not follow this model, as depending on local culture and capabilities, critically-ill obstetric cases are often treated in various locations throughout the hospital. Therefore, few reports provide a truly encompassing view of obstetric critical illness.[11,17] Severe maternal morbidity occurs at higher rates than maternal ICU admission and has been estimated to have an incidence of 2% among obstetric admissions in the UK[11] and of 2.5% of hospital deliveries in the USA.[11,30] Older women bear the highest rates of severe, life-threatening morbidities.[31] In developing countries, epidemiological estimates of maternal critical illness throughout pregnancy suggest that up to 15% of women who deliver suffer from some form of critical illness.[32] This discrepancy stems from multiple causes, including the availability and accessibility of maternity healthcare services in the community, the quality of preventive care, the time to access hospital and/or critical care, the availability of resources and the availability of facilities capable of providing advanced interventions.

There is little information about the prevalence of obstetric admissions to ICUs. In 2010, Pollock et al. conducted a systematic review of the literature and estimated the incidence was 0.7 per 1000 births in developed countries and 13.5 per 1000 births in developing countries.[33] Since then, several large database reviews have shown a more than four-fold greater incidence in developed countries (Table 1), ranging between 2.4 and 4.4 per 1000 deliveries.[25,27,34,35] Although this incidence has yet to be validated by real-time data collection, it is often substantiated by smaller studies.[13,36,37]

Obstetric critical illness comprises a predominant cause of ICU admission among young women in developed countries. In the UK, 12.1% of the women aged 16–50 who were admitted to an adult general ICU were obstetric cases.[11] Many of these admissions do not necessarily occur in the peripartum period,[11] which is considered to be the time of greatest maternal risk during pregnancy. At the time of admission for delivery alone, the incidence of ICU admission ranges from 1 per 125 to 910.[10,11,34,36–41] This incidence is higher than the population-based incidence of severe sepsis and septic shock.[42]

Maternal near-miss

In 2008 it was proposed that "the ratio of maternal deaths to severe morbidity may reflect the standard of maternal care" and therefore that audits of severe

Table 1 Major population-based studies reporting obstetric intensive care unit admissions

Study	Country	Data collection period	Total ICU admissions	Maternal ICU admissions	Deliveries	Incidence ICU admissions per 1000 deliveries	Maternal deaths	Incidence maternal death per 1000 deliveries
Oud[27]	USA	2001–2010	–	158 410	3 635 581	43.6	414	0.11
Zwart[34]	Netherlands	2004–2006	–	847	358 874	2.4	29	0.08
Chantry[25]	France	2006–2009	–	11 824	3 262 526	3.6	154	0.05
Wanderer[35]	USA	1999–2008	–	2927	698 379	4.2	53	0.08

ICU: Intensive care unit.

maternal morbidity should complement maternal mortality reports.[43] However, a systematic review of 82 studies from 46 countries revealed that, at least up to 2011, the literature still varied significantly in the criteria used to identify maternal near-miss cases. As a result, the prevalence rates ranged from 0.6%–14.98% for cases identified using disease-specific criteria, from 0.04% – 4.54% for cases identified using treatment criteria, and from 0.14%–0.92% for cases identified by the occurrence of organ dysfunction. Regardless of these broad ranges, adjustment still revealed higher rates in developing countries and an 8% annual increase in the rate of near-miss identified by emergency hysterectomy, mainly due to trends occurring in North and Latin America.[32] Like the WHO data showing that the decrease in global maternal mortality has yet to meet the expected rate of improvement,[8] these findings suggest that there are still variables amenable to improvement in maternal care.

In 2009, the WHO working group on maternal mortality first defined maternal near-miss as "a woman who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy". In order to ensure that all cases are identified, the working group proposed registering cases that fulfilled any one of three criteria: the presence of a pre-specified disease (e.g. pre-eclampsia, infection) accompanied by a related complication (e.g. stroke, septic shock), the need for a specific intervention (e.g. blood transfusion, emergency hysterectomy), or the occurrence of a pre-defined organ system dysfunction.[44] Some centers in Latin America have already embraced these definitions, demonstrating a ratio of maternal near-miss to maternal death of 19 to 1.[45] Regardless of ICU admission, questions must be asked regarding prior quality of care in each case of obstetric critical illness, as many such cases comprise a "maternal near-miss".

To date, few countries routinely collect data regarding severe maternal morbidity or "maternal near-miss" and investigations of maternal death are seldom made public. Such data can improve the quality of obstetric care, as interventions should be determined by the local prevalence of maternal complications and targeted to local culture, context and capabilities.[46] One such example is the 2016 UK Confidential Enquiry report that highlighted the increasing compartmentalization and physical separation of services, which limits interdisciplinary communication and coordination when managing maternal heart disease in the UK.[47]

Causes of maternal ICU admission

Tuncalp et al.[32] studied 82 publications from 46 countries and concluded that while the reported prevalence of severe maternal mortality varied almost 25-fold based on disease-specific criteria (0.6–14.98%), and almost seven-fold for organ dysfunction-based criteria (0.14–0.92%), variation was much higher, almost 100-fold, for management-based criteria (0.04–4.54%). This discrepancy suggests that many of these women were not receiving intensive care despite the severity of their condition. This assumption is supported by UK Intensive Care National Audit and Research Centre data which showed that approximately 1 in 350 women were admitted to Level 2 and 3 ICUs while 1 in 50 women required "only" Level 1 intensive care and were therefore being treated in maternity units.[48] Case identification is often hampered by database limitations in identifying the presence of pregnancy coinciding with an indirect cause of ICU admission. At the same time, ICUs are not obligated to report the pregnancy status for women admitted for non-obstetrical causes. One study showed that states adopting a checkbox for pregnancy status in death certificates more than doubled their maternal mortality rates, while those that did not had only a modest increase. This difference was largely attributable to improved identification of pregnancy, particularly in women more than 40 years old.[49]

The incidence and mortality trends of maternal ICU admission and mortality differ by disease and by location.[50] For example, the rate of hypertensive diseases in pregnancy is generally stable and these have very low mortality rates. Minimizing the use of latex gloves has led to a decrease in the rate of anaphylaxis.[51] Maternal sepsis is increasing in the USA[52] and decreasing in the UK.[53] Mortality from maternal cardiac disease is stable, as is the rate of thrombo-embolism.[53] In the UK, an increase in maternal deaths from hemorrhage was observed. This heterogeneity suggests the presence of opportunities for improvement.

The causes of maternal ICU admission are classified as those related directly to pregnancy (i.e. obstetric hemorrhage, hypertensive diseases of pregnancy, puerperal sepsis, thrombo-embolic phenomena, acute fatty liver), those indirectly related to pregnancy (i.e. disease exacerbations due to pregnancy) and those seemingly coincidental to the pregnant state (e.g. trauma, non-puerperal sepsis). Epidemiological reports may include coincidental causes in the indirect category (e.g. the UK MBRRACE reports) or exclude them altogether (e.g. the WHO reports). The two main causes of obstetric ICU admission are hypertensive diseases and massive hemorrhage (Table 2). An informal search of the literature performed for the purpose of this review demonstrates that although these two causes together comprise about one-third of obstetric ICU admissions, reports published from different countries vary greatly in case mix (Table 3). The causes of these differences are likely multifactorial and include socio-economic factors[54,55], environmental causes,[56] the quality of care both pre-delivery (i.e. longitudinal follow-up of pregnant women) and at the time of crisis,[57,58] surgical practice (e.g. the rate of cesarean delivery)[59], racial disparities,[60–62] and probably local ICU admission practices as well.

Table 2 Causes of severe maternal morbidity resulting in intensive care unit admission in major population-based studies

Study	ICU admissions (n)	Hypertensive disease of pregnancy n (%)	Obstetric hemorrhage n (%)	Sepsis/ infection n (%)	Other direct obstetric complications n (%)	Non-direct obstetric complications n (%)	Anesthetic complications n (%)
Oud[27]	158 410	36 978 (23.3)	11 005 (6.9)	1746 (1.1)	3140 (2.0)	15 550 (9.8)	139 (0.1)
Zwart[34]	847	224 (26.8)	381 (45.5)	55 (6.6)	13 (1.6)	152 (18)	12 (1.4)
Chantry[25]	11 824	2636 (22.3)	4043 (34.2)	425 (3.6)	718 (6.1)	3845 (32.5)	66 (0.6)
Wanderer[35]	2927	875 (29.9)	551 (18.8)	207 (7.1)	472 (16.1)	1594 (54.5)	66 (0.4)

ICU: intensive care unit.

The proportion of ICU admissions due to maternal hypertension and hemorrhage seem similar in developing and developed countries (39.8% vs 32.5% for hypertension and 25.0% vs 21.5% for hemorrhage).[33] Many clinicians believe that other medical priorities supersede the need for professional intensive care management of critically-ill obstetric women.[25,26] For example, in cases with massive peripartum hemorrhage, facilitating rapid transfer to repeat surgical hemostasis may constitute an overarching consideration, leading to selection of treatment in a post-anesthesia care unit with proximity to an operating room, rather than in a less proximate ICU. Such practices probably lead to incomplete reporting of severe maternal hemorrhage.

Cardiac disease is becoming another leading cause of obstetric maternal ICU admission and it comprised almost one-fifth of admissions in one USA population-based study.[35] Early reports often omitted ICU admissions to cardiac ICUs, probably reflecting a lack of interdisciplinary communication. Such reports are no longer acceptable. The 2016 Confidential Enquiry report on maternal death emphasized the importance of interdisciplinary collaboration in the management of maternal heart disease[47] and this should be reflected in reporting, as well as in clinical practice.

The fourth most common causes of ICU admission are infections and sepsis.[35] The main causes of sepsis are urogenital infections.[63,64] Pollock et al. reported that approximately 5% of obstetric ICU admissions were due to sepsis.[33] As with other causes, the proportion of intensive care admissions due to maternal sepsis varies (Table 3), although some of the variation is attributable to inconsistent terminology. The first time a definition for maternal sepsis was proposed was 2017, in a consensus development meeting convened by the WHO and jhpiego (https://www.jhpiego.org). They defined maternal sepsis as follows: "A life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or in the post-partum period".[65] The postpartum or post-abortion period was determined to be within 42 days of termination of pregnancy. It was suggested that organ dysfunction should be determined by ICD-10 disease classification in both suspected and confirmed cases. Suspected cases are those women likely to have severe maternal infection who present with early signs and systemic effects (allowing timely initiation of treatment). This proposal has yet to be formally embraced by any professional medical society.

A UK report estimated the absolute risk of obstetric intensive care admission with severe sepsis as 41 per 100 000 pregnancies (95% CI 2.9 to 5.6).[63] This is quite high given that the overall population incidence of sepsis (usually in much older patients) ranges between 47 and 119 per 100 000.[66–69] In some places, almost one-quarter of all maternal near-miss cases and one-half of maternal deaths have been attributed to infection, and substandard care can be identified in over one-half of these cases with severe maternal outcomes.[70] It is generally accepted that the early diagnosis of sepsis promotes survival. However, the physiological criteria conventionally used to diagnose sepsis in the non-pregnant population (i.e. heart rate, respiratory rate) often overlap both in normal pregnant women and in those with sepsis/infection. Thus, several scoring systems have been studied for identifying sepsis in pregnant women[71] and some have undergone validation.[72] Their utility in this unique population is being researched, as are other factors related to maternal sepsis. For example, antibiotic prescription for pregnant or postpartum women with suspected infection has not necessarily been shown to prevent progression to severe sepsis.[73] It remains unclear whether prescription does not necessarily equate to treatment or whether other factors come into play. For example, pregnancy is associated with immunologic changes resulting in an increased susceptibility to infection, especially those due to intracellular bacteria,[74] and female hormones may modulate the host immune response to infection.[75] Pre-existing medical problems also predispose to sepsis during pregnancy.[76] Chronic liver disease and congestive heart failure are associated with particularly high rates of sepsis during pregnancy (adjusted odds ratio 41.4 and 20.5 respectively),[52] as is obesity.[77,78] Given all these factors, the main focus of current research should remain early identification of maternal sepsis.

Finally, anesthesia complications remain a leading cause of maternal mortality. In developing countries,

Table 3 Causes of severe maternal morbidity resulting in intensive care unit admission in smaller studies

Author (reference number)	ICU admissions (n)	Hypertensive disease of pregnancy n (%)	Obstetric hemorrhage n (%)	Sepsis/infection n (%)	Other direct obstetric complications n (%)	Non-direct obstetric complications n (%)	Anesthetic complications n (%)
Aldawood[16]	75	21 (28)	16 (21)	12 (16)	5 (0.67)	21 (28)	–
Igbaruma[109]	101	42 (41.6)	38 (37.6)	12 (11.9)	2 (2)	7 (6.9)	–
Sadler[110]	42	3 (7)	14 (33)	10 (24)	1 (2)	14 (34)	–
Yousuf[111]	150	80 (53.3)	28 (18.7)	18 (12)	10 (6.7)	14 (9.3)	–
Rios[41]	242	152 (62.8)	27 (11.1)	12 (5)	–	–	–
Seppanen[108]	291	166 (57)	74 (25.4)	3 (1)	24 (8.2)	24 (8.2)	–
Crozier[112]	60	9 (15)	20 (33.3)	6 (10)	3 (5)	22 (36.6)	–
Yuqi[113]	487	212 (58.7)	133 (36.8)	26 (20.6)	16 (4.4)	100 (20.5)	–
Ozcelik[114]	57	17 (29.7)	9 (15.8)	4 (7)	2 (3.5)	24 (42)	1 (1.8)
Farr[*115]	135	–	–	–	–	–	–
Dasgupta[116]	205	55 (26.8)	71 (34.6)	27 (10.8)	5 (2.4)	47 (30)	–
Rathod[117]	765	221 (28.9)	337 (44)	61 (8)	–	93 (12.2)	–
de Greve[118]	190	12 (6.3)	23 (12.1)	13 (96.8)	98 (51.6)	44 (23.2)	–
Ibrahim[119]	99	30 (30.3)	21 (21.2)	7 (7.1)	19 (19.2)	19 (19.2)	3 (3)
Ng[39]	67	17 (25)	39 (58)	1 (2)	–	9 (13.4)	1 (2)
Gombar[**120]	151	51 (33.8)	37 (24.5)	41 (27.1)	36 (23.9)	6 (4)	–

ICU: intensive care unit.

[*]Data taken from modern cohort only – data for indications for ICU admission was not split into historical vs modern cohorts; data not extracted.

[**]Some patients had more than one diagnosis.

2.8% of total maternal deaths, 3.5% of maternal deaths resulting from obstetric complications and 13.8% of deaths after cesarean section have been attributed to complications of anesthesia.[79,80] These include, for example, failed airway management, cardiovascular collapse following epidural top-ups and total spinal anesthesia.[81] Exposure to general rather than neuraxial anesthesia, and delivery of anesthesia by non-physicians rather than anesthesiologists, have both been associated with increased MMRs (more than three-fold and almost double, respectively).[79] This finding should not be dismissed as irrelevant to developed countries, despite the controversy it may cause.[82] In the USA, for example, many hospitals have relatively small obstetric caseload volumes, suffer a shortage of physicians with the relevant expertise and fulfill only minimum obstetric staffing requirements.[83] Maternal death appears to peak during nursing shift transitions and on weekends and holidays,[84] suggesting the importance of the immediate availability of professional obstetric care.

As maternal age[85,86] and comorbidities (e.g. heart disease,[87] obesity[88,89]) increase and assisted reproduction becomes widely available,[90,91] the rate of maternal critical illness is expected to rise. These changes are occurring in parallel to a decrease in fertility rates in developed countries. The UK-CAPS study attributed 24% of obstetric deaths to anesthetic complications.[81] As the number of deliveries drops, the medical expertise required to treat cases with greater complexity may be lost.[92] Of some concern is the inverse association existing between hospital obstetrical caseload and the rate of postpartum complications,[93] particularly with respect to the management of peripartum hemorrhage.[94]

Outcomes

When a pregnant woman is critically-ill, both the mother and fetus are at risk. Pregnancy and neonatal outcomes are beyond the scope of this review. However, these are related first and foremost to the cause of maternal ICU admission and to the maternal condition at the time of ICU admission. Hence, optimization of maternal care is a common goal. Only recently has interest been redirected from pregnancy outcomes to maternal outcomes,[9,95] so there are few data regarding obstetric intensive care.

As with other disease categories, the question of whether ICU admission improves maternal outcomes remains unclear. However, contrary to most other diseases, there are indirect data suggesting that obstetric ICU admission may be associated with a decreased prevalence of some of the more commonly observed obstetrical complications. Some UK data show a high prevalence of maternal critical illness due to hypertensive disease of pregnancy,[11,48] while the Confidential Enquiries report shows consistently low rates of maternal death from hypertensive disorders.[47] In France, the most frequent causes of ICU admission were also associated with the lowest ICU disease severity.[25] Such findings may indicate the success of ICU intervention for specific diseases, but instead can lead to questions regarding the need for intensive care for critically-ill obstetric women.[25]

Maternal mortality after intensve care unit and hospital admission

Population-based studies suggest that the incidence of maternal death following ICU admission ranges from 0.3% to 3.5% (Table 1).[25,27,34,35] In contrast, individual reports indicate an overall mortality ranging between 0% and 52% of admissions.[33] As expected, reports demonstrating lower case-fatality rates often originate from high-income countries (Table 4), but this finding is inconsistent. While some of these differences can be attributed to case mix, there seems to be leeway for improvement.

Two potential loci for improvement discussed earlier are the early identification of cases and the availability of multidisciplinary consultation to provide integrative intensive care regardless of patient location. An additional focus point for improvement may be the timing of ICU discharge and post-ICU care. Many obstetric deaths occur after discharge from the ICU or following ICU re-admission. The proportion of women who died in a subsequent ICU admission was almost double among obstetric cases compared to an age- and sex-matched non-pregnant cohort.[11] This finding requires further elucidation, as it raises questions about the quality of overall care throughout admission.

Obstetric mortality following intensve care unit admission for specific diseases

While the causes of maternal ICU admission and maternal death are generally similar, the incidences of these causes and their death rates do not necessarily correlate. Maternal survival following ICU admission is directly related to the cause of admission and the ICU case mix may differ. It is therefore best to refer to population-based studies of maternal mortality per disease (Table 2).

Pre-eclampsia is a common cause of maternal death in some developed countries[96] but less so in others.[47] Developed countries with similar rates of pre-eclampsia have been shown to differ significantly in the incidence of eclampsia and in the rate of related maternal death.[97] The reasons for these differences remain to be elucidated. Pregnancy-related stroke occurs in 30 per 100 000 pregnancies and only one-third of these (12.2 per 100 000) are hemorrhagic.[98] Acute renal failure occurs more frequently, in about 1% of women with pre-eclampsia.[99] Pre-eclampsia is a predominant cause of acute pulmonary edema in preg-

Table 4 Proportions and incidences of obstetric intensive care unit admissions and maternal case fatality rates in small studies

Author (reference number)	No. medical centers	Country	Data collection period	ICU admissions (n)	Maternal ICU admissions	Deliveries (n)	Incidence of ICU admissions per 1000 deliveries	Maternal deaths	Incidence maternal deaths per 1000 deliveries
Aldawood[16]	Single-center	Saudi Arabia	1999–2009	11 000	75	50 000	1.5	6	0.12
Igbaruma[109]	Single-center	Nigeria (Benin)	2009–2012	870	101	11 308	8.9	43	3.80
Sadler[110]	Single-center	New Zealand	2010–2011	–	42	15 000	2.8	0	0
Yousuf[111]	Single-centre	Pakistan	2011–2013	–	150	–	–	57	–
Rios[41]	Four centers	Argentina	2008–2010	6271	242	30 053	8.05	5	0.17
Seppanen[108]	Four centers	Finland	2007–2011	–	291	–	–	1	–
Crozier[112]	Single-center	Australia	2006–2008	–	60	8151	7.36	1	0.12
Yuqi[113]	Single-center	China	2009–2016	3867	487	30 438	16	9	0.3
Ozcelik[114]	Single-center	Turkey	2006–2014	–	57	27 143	2.1	6	0.22
Farr[115]	Single-center	Austria	2011–2014	–	135	9000	15	6	0.67
Dasgupta[116]	Single-center	India (Kolkata)	2011–2015	881	205	98 226	2.09	69	0.7
Rathod[117]	Single-center	India (Bangalore)	2010–2013	–	765	61 625	12.4	119	1.93
de Greve[118]	Single-center	Belgium	2000–2012	–	190	27 418	6.93	2	0.07
Ibrahim[119]	Single-center	Sudan	2012	–	99	5400	18.33	22	4.07
Ng[39]	Single-center	Hong Kong	2006–2010	31 993	67	20 130	3.33	2	0.1
Gombar[120]	Single-center	India (Chandigarh)	2007–2012	–	151	21 943	6.88	47	2.14

nancy[100] and maternal death in pre-eclampsia is associated with hypertensive crises and right heart failure.[101] Future studies should focus on the role of monitoring (e.g. cardiac and thoracic ultrasound)[102,103] in guiding fluid and drug administration in this population.

The incidence of massive postpartum hemorrhage in developed countries ranges from 23–91 per 100 000 deliveries,[104,105] the most common cause being uterine atony.[104,105] The case-fatality rate of women receiving massive transfusion peripartum is <1%.[104,105]

More than 75 000 maternal deaths per year have been attributed to puerperal sepsis, occurring mostly in developing countries.[106] In developed countries, puerperal sepsis is relatively rare. Population-based studies from the US and the UK suggest that sepsis in any form occurs in 29–47 per 100 000 pregnancies and that the incidence and severity of obstetric sepsis is increasing.[52,76] Interestingly, this increase has been shown to correlate with higher rates of organ failure and increased costs, despite lower ICU admission rates and no change in in-hospital mortality.[52] Death from sepsis occurs in 1.8–3 in 100 000 pregnancies.[52,63] Data from almost 200 ICUs across Great Britain suggested that pulmonary infections were the most common source of sepsis among women who died and that respiratory dysfunction was a risk factor for death.[63] However, this finding may have been biased by data collection during the H1N1 epidemic.

Although the survival rate after maternal cardiac arrest is extremely high (~60%), the mortality rates for specific causes of maternal critical illness differ significantly before and after cardiac arrest has occurred. This difference is most striking for hemorrhage (1.3% vs 45%) and hypertensive disorders (1.3% vs 25%). But even in diseases where the likelihood of maternal death in the ICU is much higher a priori, the likelihood of survival will decrease significantly after maternal arrest has occurred. The respective ICU death rates for thromboembolism, sepsis and cardiac disease are 23.1%, 9.1% and 9.1%, compared with 47.5%, 53.5% and 35% after maternal cardiac arrest associated with these diseases has already occurred. These data stress the importance of early detection of maternal critical illness to prevent terminal maternal deterioration.[34,107]

Maternal health-related quality of life following obstetric intensive care unit admission

Only one study has examined maternal health-related quality of life after hospital discharge in ICU survivors. Conducted in Finland, it compared data obtained from interviews with 114/291 women who had experienced an obstetric ICU admission with that from a reference age- and sex-matched cohort. Women admitted to the ICU had a lower overall health status post-discharge than reference cases. Although their health status mostly improved over six months, at the time of

follow-up almost one in five women (18.4%) still had a poorer health-related quality of life than those from the reference cohort. Multiparous women have lower scores than primiparous women.[108] While these results seem encouraging, it is important to remember that these are young women who should look forward to a full life.

Conclusions and suggestions for future improvements

Severe maternal morbidity is on the rise in developed countries, yet the decline in global maternal death rates and relatively low death rates associated with obstetric hemorrhage and hypertensive diseases of pregnancy in some developed countries (both of which have occurred in association with an increasing rate of ICU admission) highlight the potential preventability of obstetric critical illness. Declarations that critically-ill pregnant and peripartum women do not require admission to an ICU should therefore be viewed as no more than baseless opinions until such time as data is generated regarding disease-specific survival, with and without ICU admission, in this population. Ideally, these data should be collected in real time by an international registry of obstetric comorbidities and critical illness.

Intensive care admissions comprise only a small part of obstetric critical illness. Intensive care remains underutilized for obstetric critical illness even in developed countries. Misconceptions regarding the level of care provided to these women in countries from which many of the publications originate (e.g. the UK) may be a significant contributor to this issue. Many are unaware that in such places even the level of basic obstetric screening, monitoring and treatment is significantly higher than that existing elsewhere, not to mention the intermediate care maternity units that specialize in such care. The culture of discussion regarding the "redundancy" of maternal critical care should be substituted with a standardized yet detailed description of the level of expertise, training and monitoring provided in alternative settings that have achieved improved outcomes, as this would enable cross-country comparisons. An additional setback to the use of critical care services is the paucity of tools to identify critical illness in this population. Disseminating the use of appropriate scoring systems may improve this aspect of care.

Further contributing to the predicament of critically-ill pregnant and peripartum women is the issue of fractionated care, which leads to ICU admission of many of these complex cases after decompensation has occurred. In many places, the obstetrician treats only the pregnancy and the cardiologist treats only the heart. Efforts should be made to create specialized multidisciplinary maternal care pathways, particularly, yet not only, with regards to obstetric sepsis, heart disease and anesthesia. Referral of such cases to specialized centers (whether outpatient or in-hospital) at an early stage of pregnancy would allow tailoring of treatment to the individual case and enable creation of a multidisciplinary delivery plan, including, if required, planned ICU admission.

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