Critical Care Obstetrics
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EDITED BY

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Epidemiology of Critical Illness in Pregnancy

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Introduction

The successful epidemiologic evaluation of any particular disease or condition has several prerequisites. Two of the most important prerequisites are that the condition should be accurately defined and that there should be measurable outcomes of interest. Another requirement is that there must be some systematic way of data collection or surveillance that will allow the measurement of the outcomes of interest and associated risk factors. The epidemiologic evaluation of critical illness associated with pregnancy has met with mixed success on all of these counts.

Historically, surveillance of pregnancy-related critical illness has focused on the well-defined outcome of maternal mortality in order to identify illnesses or conditions that might have led to maternal death. Identification of various conditions associated with maternal mortality initially came from observations by astute clinicians. One of the best examples is the link described by Semmelweiss between hand-washing habits and puerperal fever. In most industrial and many developing countries, there are now population-based surveillance mechanisms in place to track maternal mortality. These often are mandated by law. In fact, the World Health Organization uses maternal mortality as one of the measures of the health of a population [1].

Fortunately, in most industrialized nations the maternal mortality rates have fallen to very low levels. Recent statistics for the United States suggest that overall maternal mortality was 11.5 maternal deaths per 100,000 live births during 1991–97 [2]. Despite this impressively low rate of maternal mortality, tracking maternal deaths may not be the best way to assess pregnancy-related critical illnesses since the majority of such illnesses do not result in maternal death. As stated by Harmer [3], “death represents the tip of the morbidity iceberg, the size of which is unknown.” Unlike mortality, which is an unequivocal endpoint, critical illness in pregnancy as a morbidity outcome is difficult to define and, therefore, difficult to measure and study precisely.

There are many common conditions in pregnancy such as the hypertensive diseases, intrapartum hemorrhage, diabetes, thyroid disease, asthma, seizure disorders, and infection that occur frequently and require special medical care, but do not actually become critical illnesses. Most women with these complications have relatively uneventful pregnancies that result in good outcomes for both mother and infant. Nevertheless, each of these conditions can be associated with significant complications that have the potential for serious morbidity, disability and mortality. The stage at which any condition becomes severe enough to be classified as a critical illness has not been clearly defined. However, it may be helpful to consider critical illness as impending, developing, or established significant organ dysfunction, which may lead to long-term morbidity or death. This allows some flexibility in the characterization of disease severity since it recognizes conditions that can deteriorate rather quickly in pregnancy.

Maternal mortality data collection is well established in many places, but specific surveillance systems that track severe complications of pregnancy not associated with maternal mortality are rare. It has been suggested that most women suffering a critical illness in pregnancy are likely to spend some time in an intensive care unit [3–5]. These cases have been described by some as “near-miss” mortality cases [6,7]. Therefore, examination of cases admitted to intensive care units can provide insight into the nature of pregnancy-related critical illnesses and can compliment maternal mortality surveillance. However, it should be noted that nearly two-thirds of maternal deaths might occur in women who never reach an intensive care unit [5].

The following sections review much of what is currently known about the epidemiology of critical illness in pregnancy. Some of the information is based on published studies; however, much of the data are derived from publicly available data that are collected as part of nationwide surveillance systems in the US.
Pregnancy-related hospitalizations

Pregnancy complications contribute significantly to maternal, fetal, and infant morbidity, as well as mortality [8]. Many women with complicating conditions are hospitalized without being delivered. Although maternal complications of pregnancy are the fifth leading cause of infant mortality in the US, little is known about the epidemiology of maternal complications associated with hospitalizations. Examination of complicating conditions associated with maternal hospitalizations can provide information on the types of conditions requiring hospitalized care. In the US during the years 1991–92, it was estimated that 18.0% of pregnancies were associated with non-delivery hospitalization with disproportionate rates between black (28.1%) and white (17.2%) women [9]. This 18.0% hospitalization rate comprised 12.3% for obstetric conditions (18.3% among black women and 11.9% among white women), 4.4% for pregnancy losses (8.1% among black women and 3.9% among white women), and 1.3% for non-obstetric (medical or surgical) conditions (1.5% among black women and 1.3% among white women). The likelihood of pregnancy-associated hospitalizations in the US declined between 1986–87 and 1991–92 [9,10].

More recent information about pregnancy-related hospitalization diagnoses can be found in the aggregated National Hospital Discharge Summary (NHDS) data for 1998–99. These data are assembled by the National Center for Health Statistics (NCHS) of the US Centers for Disease Control and Prevention. The NHDS data is a survey of medical records from short-stay, non-federal hospitals in the US, conducted annually since 1965. A detailed description of the survey and the database can be found elsewhere [11]. Briefly, for each hospital admission, the NHDS data include a primary and up to six secondary diagnoses, as well as up to four procedures performed for each hospitalization. These diagnoses and procedures are all coded based on the International Classification of Diseases, ninth revision, clinical modification. We examined the rates (per 100 hospitalizations) of hospitalizations by indications (discharge diagnoses) during 1998–99 in the US, separately for delivery (n = 7965173) and non-delivery (n = 960023) hospitalizations. We also examined the mean hospital lengths of stay (with 95% confidence intervals, CIs). Antepartum and postpartum hospitalizations were grouped as non-delivery hospitalizations.

During 1998–99, nearly 7.4% of all hospitalizations were for hypertensive diseases with delivery, and 6.6% were for hypertensive diseases not delivered (Table 1.1). Mean hospital length of stay (LOS) is an indirect measure of acuity for some illnesses. LOS was higher for delivery-related than for non-delivery-related hospitalizations for hypertensive diseases. Hemorrhage, as the underlying reason for hospitalization (either as primary or secondary diagnosis), occurred much more frequently for delivery- than non-delivery-related hospitalizations. Non-delivery hospitalizations for genitourinary infections occurred three times more frequently (10.45%) than for delivery-related hospitalizations (3.19%), although the average LOS was shorter for non-delivery hospitalizations.

Hospitalizations for preterm labor occurred twice as frequently for non-delivery hospitalizations (21.21%) than for delivery-related hospitalizations (10.28%). This is expected since many preterm labor patients are successfully treated and some of these hospitalizations are for “false labor.” Liver disorders were uncommonly associated with hospitalization. However, the mean hospital LOS for liver disorders that occurred with non-delivery hospitalizations was over 31 days, compared with a mean LOS of 3 days if the liver condition was delivery related. Coagulation-related defects required 14.9 days of hospitalization if not related to delivery compared with a mean LOS of 4.9 days if the condition was delivery related. Hospitalizations for embolism-related complications were infrequent, but generally required extended hospital stays.

The top 10 conditions associated with hospital admissions, separately for delivery- and non-delivery-related events, are presented in Figure 1.1. The chief cause for hospitalization (either delivery or non-delivery related) was preterm labor. The second most frequent condition was hypertensive disease (7.37% for delivery related and 6.61% for non-delivery related) followed by anemia (7.13% vs 5.05%). Hospitalizations for infection-related conditions occurred twice more frequently for non-delivery periods (11.65%) than during delivery (5.75%). In contrast, hospitalization for hemorrhage was more frequent during delivery (4.43%) than non-delivery (3.26%). These data provide important insights into the most common complications and conditions associated with pregnancy hospitalization. The LOS data also give some indication of resource allocation needs. While this is important in understanding the epidemiology of illness in pregnancy, it does not allow a detailed examination of illness severity.

Maternal mortality

The national health promotion and disease prevention objectives of the Healthy People 2010 indicators specify a goal of no more than 3.3 maternal deaths per 100 000 live births in the US [12]. The goal for maternal deaths among black women was set at no more than 5.0 per 100 000 live births. As of 1997 (the latest available statistics on maternal deaths in the US) this objective remains elusive. The pregnancy-related maternal mortality ratio (PRMR) per 100 000 live births for the US was 11.5 for 1991–97 [13], with the ratio over threefold greater among black compared with white women [14]. Several studies that have examined trends in maternal mortality statistics have concluded that a majority of pregnancy-related deaths (including those resulting from ectopic pregnancies, and some cases of infection and hemorrhage) are preventable [1,15,16]. However, maternal deaths due to other complications such as pregnancy-induced hypertension, placenta previa, retained placenta, and thromboembolism, are considered by some as difficult to prevent [17,18].
From the 1960s to the mid-1980s, the maternal mortality ratio in the US declined from approximately 27 per 100,000 live births to about 7 per 100,000 live births (Figure 1.2). Subsequently, the mortality ratio increased between 1987 (7.2 per 100,000 live births) and 1990 (10.0 per 100,000 live births). During the period 1991–97, the mortality ratio further increased to 11.5 per 100,000 live births—an overall relative increase of 60% between 1987 and 1997. The reasons for the recent increases are not clear. Several maternal risk factors have been examined in relation to maternal deaths. Women aged 35–39 years carry a 2.6-fold (95%
CI 2.2, 3.1) increased risk of maternal death and those over 40 years are at a 5.9-fold (95% CI 4.6, 7.7) increased risk. Black maternal race confers a relative risk of 3.7 (95% CI 3.3, 4.1) for maternal death compared with white women. Similarly, women without any prenatal care during pregnancy had an almost twofold increased risk of death relative to those who received prenatal care [19].

The chief cause for a pregnancy-related maternal death depends on whether the pregnancy results in a live born, stillbirth, ectopic pregnancy, abortion, or molar gestation (Table 1.2). For the period 1987–90, hemorrhage was recorded in 28.8% of all deaths, leading to an overall pregnancy-related mortality ratio (PRMR) for hemorrhage of 2.6 per 100000 live births, followed by embolism-related deaths (PRMR 1.8), and hypertensive diseases (PRMR 1.6). Among all live births, hypertensive diseases (23.8%) were the most frequent cause of death. Among stillbirths (27.2%) and ectopic (94.9%) pregnancies, the chief cause of death was hemorrhage, while infections (49.4%) were the leading cause of abortion-related maternal deaths.

Understanding the epidemiology of pregnancy-related deaths is essential in order to target specific interventions. Improved population-based surveillance through targeted reviews of all pregnancy-related deaths, as well as additional research to understand the causes of maternal deaths by indication will help in achieving the Healthy People 2010 goals.
Table 1.2 Pregnancy-related maternal deaths by underlying cause: USA, 1987–90. From Koonin et al. [53].

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>All outcomes</th>
<th>Outcome of pregnancy (% distribution)</th>
<th>PRMR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>Live birth</td>
<td>Stillbirth</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>28.8</td>
<td>21.1</td>
<td>27.2</td>
</tr>
<tr>
<td>Embolism</td>
<td>19.9</td>
<td>23.4</td>
<td>10.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>17.6</td>
<td>23.8</td>
<td>26.2</td>
</tr>
<tr>
<td>Infection</td>
<td>13.1</td>
<td>12.1</td>
<td>19.4</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>5.7</td>
<td>6.1</td>
<td>2.9</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>2.5</td>
<td>2.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Others/unknown</td>
<td>12.8</td>
<td>11.1</td>
<td>13.6</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

* Pregnancy-related mortality ratio per 100,000 live births.
† Includes both spontaneous and induced abortions.

Table 1.3 Perinatal mortality rates among singleton and multiple gestations by gestational age and high-risk conditions: USA, 1995–98.

<table>
<thead>
<tr>
<th>High-risk conditions</th>
<th>20–27 weeks</th>
<th>28–32 weeks</th>
<th>33–36 weeks</th>
<th>≥37 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PMR</td>
<td>Relative risk (95% CI)</td>
<td>PMR</td>
<td>Relative risk (95% CI)</td>
</tr>
<tr>
<td>Singleton</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of births</td>
<td>n = 103,755</td>
<td>n = 352,291</td>
<td>n = 1,072,784</td>
<td>n = 13,440,671</td>
</tr>
<tr>
<td>Hypertension</td>
<td>200.4</td>
<td>0.6 (0.5, 0.7)</td>
<td>53.1</td>
<td>0.6 (0.5, 0.6)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>308.9</td>
<td>1.1 (1.0, 1.2)</td>
<td>73.1</td>
<td>1.4 (1.3, 1.5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>287.0</td>
<td>1.0 (0.9, 1.1)</td>
<td>60.8</td>
<td>1.2 (1.1, 1.3)</td>
</tr>
<tr>
<td>SGA</td>
<td>467.4</td>
<td>2.3 (2.1, 2.5)</td>
<td>196.3</td>
<td>6.2 (6.0, 6.4)</td>
</tr>
<tr>
<td>No complications</td>
<td>297.6</td>
<td>1.0 (Referent)</td>
<td>38.8</td>
<td>1.0 (Referent)</td>
</tr>
<tr>
<td>Multiple</td>
<td>n = 23,055</td>
<td>n = 76,329</td>
<td>n = 147,627</td>
<td>n = 187,109</td>
</tr>
<tr>
<td>Hypertension</td>
<td>183.5</td>
<td>0.7 (0.6, 0.8)</td>
<td>21.4</td>
<td>0.5 (0.4, 0.6)</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>251.6</td>
<td>1.0 (0.9, 1.1)</td>
<td>36.6</td>
<td>1.1 (1.0, 1.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>214.9</td>
<td>0.8 (0.7, 1.1)</td>
<td>28.7</td>
<td>0.9 (0.7, 1.2)</td>
</tr>
<tr>
<td>SGA</td>
<td>394.5</td>
<td>2.0 (1.6, 2.4)</td>
<td>133.4</td>
<td>6.8 (6.3, 7.4)</td>
</tr>
<tr>
<td>No complications</td>
<td>251.1</td>
<td>1.0 (Referent)</td>
<td>23.4</td>
<td>1.0 (Referent)</td>
</tr>
</tbody>
</table>

CI, confidence interval; PMR, perinatal mortality rate per 1000 births; SGA, small for gestational age births.
Hypertension includes chronic hypertension, pregnancy-induced hypertension, and eclampsia.
Hemorrhage includes placental abruption, placenta previa, uterine bleeding of undermined etiology.
No complications include those that did not have any complications listed in the table.
Relative risk for each high-risk condition was adjusted for all other high-risk conditions shown in the table.

Perinatal mortality

Perinatal mortality, defined by the World Health Organization as fetal deaths plus deaths of live-born infants within the first 28 days, is an important indicator of population health. Examination of the maternal conditions related to perinatal mortality can provide further information on the association and impact of these conditions on pregnancy outcomes. Table 1.3 shows the results of our examination of perinatal mortality rates among singleton and multiple births (twins, triplets and quadruplets) by gestational age and high-risk conditions. The study population comprises all births in the US that occurred in 1995–98. Data were derived from the national linked birth/infant death files, assembled by the National Center for Health Statistics of the Centers for Disease Control and Prevention [20]. Gestational age
was predominantly based on the date of last menstrual period [21], and was grouped as 20–27, 28–32, 33–36, and ≥37 weeks. Perinatal mortality rates were assessed for hypertensive (chronic hypertension, pregnancy-induced hypertension, and eclampsia), hemorrhage (placental abruption, placenta previa, and uterine bleeding of undetermined etiology), diabetes (pre-existing and gestational diabetes), and small for gestational age (SGA) births (defined as birth weight below 10th centile for gestational age). We derived norms for the 10th centile birth weight for singleton and multiple births from the corresponding singleton and multiple births that occurred in 1995–98 in the US. Finally, relative risks (with 95% CIs) for perinatal death by each high-risk condition were derived from multivariable logistic regression models after adjusting for all other high-risk conditions.

Perinatal mortality rates progressively decline, among both singleton and multiple births, for each high-risk condition with increasing gestational age (Table 1.3). Among singleton and multiple gestations, with the exception of SGA births, mortality rates were generally higher for each high-risk condition, relative to the no complications group. Infants delivered small for their gestational age carried the highest risk of dying during the perinatal period compared with those born to mothers without complications. Among singleton births, the relative risks for perinatal death for SGA infants were 2.3, 6.2, 7.8, and 5.5 for those delivered at 20–27 weeks, 28–32 weeks, 33–36 weeks, and term, respectively. Among multiple births, these relative risks were similar at 2.0, 6.8, 7.5, and 8.6, respectively, for each of the four gestational age categories.

### Pregnancy-related intensive care unit admissions

Evaluation of obstetric admissions to intensive care units (ICUs) may be one of the best ways to approach surveillance of critical illnesses in pregnancy. Unfortunately, there are no publicly available population-based databases for obstetric admissions to ICU that provide sufficiently detailed information to allow in-depth study of these conditions. Therefore, it is reasonable to examine descriptive case series to provide information on these conditions. We reviewed 33 studies published between 1990 and 2006 involving 1955111 deliveries and found an overall obstetric-related admission rate to ICU of 0.07–0.89% (Table 1.4). Some of the variation in the rates may be explained by the nature of the populations studied. Hospitals that are tertiary referral centers for large catchment areas typically receive a more concentrated high-risk population. These facilities would be expected to have higher rates of obstetric admissions to an ICU. However, these studies provided sufficient data to allow the exclusion of patients transported from outside facilities. Community-oriented facilities are probably less likely to care for critically ill obstetric patients unless the illnesses develop so acutely that they would preclude transport to a higher-level facility. The largest study of pregnancy-related ICU admissions involved 37 maternity hospitals in Maryland and included hospitals at all care levels [22]. This study found a nearly 30% lower admission rate to ICUs for obstetric patients from community hospitals compared with major teaching hospitals. Another source of variation is the different criteria for admission to the ICU used at different institutions. Finally, there are major differences in the inclusion criteria used for these studies that further contributes to the variability in reported ICU utilization rates.

Reported maternal mortality for critically ill obstetric patients admitted to an ICU is approximately 8.4% (Table 1.4). This reflects the true seriousness of the illnesses of these women. The wide range of mortality from 0% to 33% is due to many factors. Most of the studies were small and just a few deaths may affect rates significantly. The populations studied also differ in underlying health status. Reports from less developed countries had much higher mortality rates. The time period of the study can have an impact. In general, earlier studies had higher maternal mortality rates. These earlier studies represent the early stages of development of care mechanisms for critically ill obstetric patients. They probably reflect part of the “learning curve” of critical care obstetrics, as well as differences in available technology [52]. Regardless, the mortality rate from these ICU admissions is several orders of magnitude higher than the general US population maternal mortality rate of 11.5 per 100,000 live births. Therefore, these cases are a good representation of an obstetric population with critical illnesses.

### Illnesses responsible for obstetric intensive care unit admissions

Examination of obstetric ICU admissions provides some insight into the nature of obstetric illnesses requiring critical care. Data were pooled from 26 published studies that provided sufficient details about the primary indication for the ICU admission (Table 1.5). It is no surprise that hypertensive diseases and obstetric hemorrhage were responsible for over 50% of the primary admitting diagnoses. Specific organ system dysfunction was responsible for the majority of the remaining admissions. Of those, pulmonary, cardiac, and infectious complications had the greatest frequency. From these reports, it is apparent that both obstetric and medical complications of pregnancy are responsible for the ICU admissions in similar proportions. There were 16 studies that provided information on 1980 patients as to whether the primary admitting diagnosis was related to an obstetric complication or a medical complication [4,22,23,25,26,36–38,40,42,43,46,49–51,54]. The pooled data indicate that approximately 69.3% (n = 1373) were classified as obstetric related and 30.7% (n = 607) were due to medical complications. These data clearly highlight the complex nature of obstetric critical care illnesses and provide support for a multidisciplinary approach to management since these patients are quite ill with a variety of diseases.
Table 1.4 Obstetric admission rates to an intensive care unit (ICU) and corresponding maternal mortality rates from 33 studies.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year(s)</th>
<th>Location</th>
<th>Inclusion criteria</th>
<th>Total deliveries</th>
<th>Obstetric ICU Admissions (rate)</th>
<th>Obstetric ICU deaths (rate)</th>
<th>Fetal/neonatal deaths per ICU admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mabie &amp; Sibai 1990 [22]</td>
<td>1986-89</td>
<td>US</td>
<td>–</td>
<td>22,651</td>
<td>200 (0.88%)</td>
<td>7 (3.5%)</td>
<td>–</td>
</tr>
<tr>
<td>Kilpatrick &amp; Matthay 1992 [23]</td>
<td>1985–90</td>
<td>US</td>
<td>Up to 6 weeks PP</td>
<td>8000*</td>
<td>32 (0.4%)</td>
<td>4 (12.0%)</td>
<td>6 (18.8%)</td>
</tr>
<tr>
<td>El-Soh &amp; Grant 1996 [25]</td>
<td>1989–95</td>
<td>US</td>
<td>Up to 10d PP</td>
<td>–</td>
<td>96 (–)</td>
<td>10/93 (10.8%)</td>
<td>10 (10.4%)</td>
</tr>
<tr>
<td>Monaco et al. 1993 [26]</td>
<td>1983–90</td>
<td>US</td>
<td>16 weeks to 2 weeks PP</td>
<td>15,323</td>
<td>38 (0.25%)</td>
<td>7 (18.4%)</td>
<td>4 (10.5%)</td>
</tr>
<tr>
<td>Panchal et al. 2000 [27]</td>
<td>1984–97</td>
<td>US</td>
<td>Delivering admission</td>
<td>822,591</td>
<td>1023 (0.12%)</td>
<td>34 (3.3%)</td>
<td>–</td>
</tr>
<tr>
<td>Afessa et al. 2001 [28]</td>
<td>1991–98</td>
<td>US</td>
<td>–</td>
<td>–</td>
<td>78 (–)</td>
<td>2 (2.7%)</td>
<td>13 (16.7%)</td>
</tr>
<tr>
<td>Gilbert et al. 2000 [29]</td>
<td>1991–98</td>
<td>US</td>
<td>Up to 6 weeks PP</td>
<td>49,349</td>
<td>233 (0.47%)</td>
<td>8 (3.4%)</td>
<td>–</td>
</tr>
<tr>
<td>Hogg et al. 2000 [30]</td>
<td>1989–97</td>
<td>US</td>
<td>15 weeks to 6 weeks PP</td>
<td>30,405</td>
<td>172 (0.57%)</td>
<td>23 (13.4%)</td>
<td>2 (1.2%)</td>
</tr>
<tr>
<td>Munnr et al. 2005 [31]</td>
<td>1992–2001</td>
<td>US</td>
<td>–</td>
<td>–</td>
<td>58,000</td>
<td>174 (0.3%)</td>
<td>4 (2.3%)</td>
</tr>
<tr>
<td>Mahutte et al. 1999 [4]</td>
<td>1991–97</td>
<td>Canada</td>
<td>14 weeks to 6 weeks PP</td>
<td>44,340</td>
<td>131 (0.30%)</td>
<td>3 (2.3%)</td>
<td>–</td>
</tr>
<tr>
<td>Baskett &amp; Sternadel 1998 [6]</td>
<td>1980–93</td>
<td>Canada</td>
<td>&gt;20 weeks and PP</td>
<td>76,119</td>
<td>55 (0.07%)</td>
<td>2 (3.6%)</td>
<td>–</td>
</tr>
<tr>
<td>Hazzelgrove et al. 2001 [5]</td>
<td>1994–96</td>
<td>England</td>
<td>Up to 6 weeks PP</td>
<td>122,850</td>
<td>210 (0.17%)</td>
<td>7 (3.3%)</td>
<td>40/200 (20.0%)</td>
</tr>
<tr>
<td>DeMello &amp; Restall 1990 [33]</td>
<td>1985–89</td>
<td>England</td>
<td>20–42 weeks</td>
<td>9,425</td>
<td>13 (0.14%)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Selo-Ojeme et al. 2005 [34]</td>
<td>1993–2003</td>
<td>England</td>
<td>14 weeks to 6 weeks PP</td>
<td>31,097</td>
<td>22 (0.11%)</td>
<td>1 (4.5%)</td>
<td>1 (4.5%)</td>
</tr>
<tr>
<td>Stephens 1991 [35]</td>
<td>1979–89</td>
<td>Australia</td>
<td>Up to 4 weeks PP</td>
<td>61,435</td>
<td>126 (0.21%)</td>
<td>1 (0.8%)</td>
<td>–</td>
</tr>
<tr>
<td>Tang et al. 1997 [36]</td>
<td>1988–95</td>
<td>China</td>
<td>Up to 6 weeks PP</td>
<td>39,350</td>
<td>49 (0.12%)</td>
<td>2 (4.1%)</td>
<td>4 (8.2%)</td>
</tr>
<tr>
<td>Ng et al. 1992 [37]</td>
<td>1985–90</td>
<td>China</td>
<td>Delivery related</td>
<td>16,264</td>
<td>37 (0.22%)</td>
<td>2 (5.4%)</td>
<td>–</td>
</tr>
<tr>
<td>Cheng &amp; Raman 2003 [38]</td>
<td>1994–1999</td>
<td>Singapore</td>
<td>Up to 1 week PP</td>
<td>13,438</td>
<td>39 (0.28%)</td>
<td>2 (5.1%)</td>
<td>–</td>
</tr>
<tr>
<td>Heinenon et al. 2002 [39]</td>
<td>1993–2000</td>
<td>Finland</td>
<td>18 weeks to 4 weeks PP</td>
<td>23,404</td>
<td>22 (0.14%)</td>
<td>1 (4.5%)</td>
<td>–</td>
</tr>
<tr>
<td>Keizer et al. 2006 [40]</td>
<td>1990–2001</td>
<td>Netherlands</td>
<td>Obstetrics admissions with illness</td>
<td>18,581</td>
<td>142 (0.76%)</td>
<td>7 (4.9%)</td>
<td>35 (24.6%)</td>
</tr>
<tr>
<td>Bouvier-Colle et al. 1996 [41]</td>
<td>1991</td>
<td>France</td>
<td>Up to 6 weeks PP</td>
<td>140,000*</td>
<td>435 (0.31%)</td>
<td>22 (5.1%)</td>
<td>58 (13.3%)</td>
</tr>
<tr>
<td>Koeberle et al. 2000 [42]</td>
<td>1986–96</td>
<td>France</td>
<td>Up to 6 weeks PP</td>
<td>27,059*</td>
<td>46 (0.17%)</td>
<td>2 (4.3%)</td>
<td>–</td>
</tr>
<tr>
<td>Munnr et al. 2005 [31]</td>
<td>1992–2001</td>
<td>India</td>
<td>–</td>
<td>157,694</td>
<td>754 (0.48%)</td>
<td>189 (25%)</td>
<td>368 (48.81%)</td>
</tr>
<tr>
<td>Ryan et al. 2000 [43]</td>
<td>1996–98</td>
<td>Ireland</td>
<td>–</td>
<td>26,164</td>
<td>17 (0.07%)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Cohen et al. 2000 [44]</td>
<td>1994–98</td>
<td>Israel</td>
<td>20 weeks to 2 weeks PP</td>
<td>19,474</td>
<td>46 (0.24%)</td>
<td>1 (2.3%)</td>
<td>10 (21.7%)</td>
</tr>
<tr>
<td>Lewinoohn et al. 1994 [45]</td>
<td>8 yrs</td>
<td>Israel</td>
<td>–</td>
<td>–</td>
<td>58 (–)</td>
<td>4 (6.9%)</td>
<td>–</td>
</tr>
<tr>
<td>Loverro et al. 2001 [46]</td>
<td>1987–1998</td>
<td>Italy</td>
<td>–</td>
<td>23,694</td>
<td>41 (0.17%)</td>
<td>2 (4.9%)</td>
<td>5 (12.2%)</td>
</tr>
<tr>
<td>Okafor &amp; Aniebue 2004 [47]</td>
<td>1997–2002</td>
<td>Nigeria</td>
<td>–</td>
<td>6,544</td>
<td>18 (0.28%)</td>
<td>6 (33%)</td>
<td>–</td>
</tr>
<tr>
<td>Demirkiran et al. 2003 [49]</td>
<td>1995–2000</td>
<td>Turkey</td>
<td>–</td>
<td>140,455*</td>
<td>125 (0.89%)</td>
<td>13 (9.6%)</td>
<td>–</td>
</tr>
<tr>
<td>Mirghani et al. 2004 [50]</td>
<td>1997–2002</td>
<td>UAE</td>
<td>–</td>
<td>23,383</td>
<td>60 (0.26%)</td>
<td>2 (3.3%)</td>
<td>–</td>
</tr>
<tr>
<td>Suleiman et al. 2006 [51]</td>
<td>1992–2004</td>
<td>Saudi Arabia</td>
<td>Up to 6 weeks PP</td>
<td>29,432</td>
<td>64 (0.22%)</td>
<td>6 (9.4%)</td>
<td>8/55 (14.5%)</td>
</tr>
<tr>
<td>Summary (pooled data)</td>
<td></td>
<td></td>
<td></td>
<td>1,955,111</td>
<td>4,389 (0.22%)</td>
<td>395/4,718 (8.4%)</td>
<td>640/2,499 (25.6%)</td>
</tr>
</tbody>
</table>

PP, postpartum; (–) indicates data not provided or unable to be calculated (these values excluded from summaries of columns).

* Estimate calculated based on data in paper.

Causes of mortality in obstetric intensive care unit admissions

When specific causes of mortality for the obstetric ICU admissions were reviewed, 26 studies gave sufficient data to assign a primary etiology for maternal death (Table 1.6). Of a total of 138 maternal deaths, over 57% were related to complications of hypertensive diseases, pulmonary illnesses, and cardiac diseases. Other deaths were commonly related to complications of hemorrhage, bleeding into the central nervous system, malignancy, and infection. More importantly, despite an identified primary
Chapter 1

Table 1.5 Complications primarily responsible for admission to the intensive care unit for obstetric patients: data summarized from 26 published studies [4–6,22–26,28,31,32,35–37,39,40,42–51].

<table>
<thead>
<tr>
<th>Category</th>
<th>Category examples</th>
<th>n</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive diseases</td>
<td>Eclampsia, pre-eclampsia, HELLP syndrome, hypertensive crisis</td>
<td>1176</td>
<td>37.4</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>Shock, abruptio placentae, postpartum hemorrhage, accreta, uterine rupture</td>
<td>647</td>
<td>20.6</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pulmonary edema, pneumonia, adult respiratory distress syndrome, asthma</td>
<td>287</td>
<td>9.1</td>
</tr>
<tr>
<td></td>
<td>- thromboembolic diseases, amniotic fluid embolus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>Valvular disease, arrhythmia, cardiomyopathy, infarction</td>
<td>187</td>
<td>5.9</td>
</tr>
<tr>
<td>Sepsis/infection</td>
<td>Chorioamnionitis, pyelonephritis, malaria, hepatitis, meningitis, miscellaneous</td>
<td>288</td>
<td>9.2</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Intracranial hemorrhage, seizure (non-eclamptic), arteriovenous malformation</td>
<td>92</td>
<td>2.9</td>
</tr>
<tr>
<td>Anesthesia complication</td>
<td>Allergic reaction, failed intubation, high spinal</td>
<td>47</td>
<td>1.5</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Pancreatitis, acute fatty liver of pregnancy, inflammatory bowel disease, gailbladder disease</td>
<td>64</td>
<td>2.0</td>
</tr>
<tr>
<td>Renal</td>
<td>Renal failure</td>
<td>30</td>
<td>1.0</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Thrombotic thrombocytopenic purpura, sickle cell disease, disseminated intravascular coagulation, aspiration</td>
<td>32</td>
<td>1.0</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Diabetic ketoacidosis, thyroid storm</td>
<td>52</td>
<td>1.7</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Various</td>
<td>17</td>
<td>0.5</td>
</tr>
<tr>
<td>Other</td>
<td>Insufficient information to assign to specific organ system but included anaphylaxis, trauma, drug and overdose/poisoning</td>
<td>227</td>
<td>7.2</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>3146</td>
<td>100%</td>
</tr>
</tbody>
</table>

etiology for the maternal deaths, nearly all cases were associated with multiorgan dysfunction, which again emphasizes the complex condition of these critically ill women.

As noted earlier, obstetric and medical complications of pregnancy are equally represented in all admissions to the ICU (Table 1.5). However, nearly 40% of all maternal deaths in the ICU were directly related to obstetric conditions (mainly hypertensive diseases, hemorrhage, amniotic fluid embolism and acute fatty liver of pregnancy) with the remaining deaths due to medical conditions (Table 1.6).

**Perinatal loss 101st obstetric intensive care unit admissions**

When considering the implications of critical illness for obstetric patients, the focus is usually on the mother. However, it is important to re-emphasize that many of these conditions also may have a significant impact on fetal and neonatal outcomes. There is surprisingly little detailed information available on these perinatal outcomes in pregnancies complicated by critical illnesses. However, there are data on perinatal outcomes based on specific disease conditions. Maternal high-risk conditions associated with perinatal mortality in the US are presented in Table 1.3. However, these data do not separate outcomes by severity of maternal illness. We were able to identify 18 studies that provided information on fetal or neonatal mortality rates for obstetric admissions to the ICU (Table 1.4). Fetal and/or neonatal deaths were identified in 640 of the pooled 2499 cases, resulting in an overall mortality rate of 25.6%. Reported rates ranged from 1.2–48.8%. If the large report from India is removed [31], there were 272 of these deaths among 1745 cases, with a mortality rate of 15.6%. These proportions may not reflect a true perinatal mortality rate since some of the losses may have occurred before 20 weeks gestation. In addition, the denominator includes a number of postpartum admissions for conditions not expected to impact fetal or neonatal mortality. Nevertheless, the high loss rate highlights the importance of considering the fetus when managing critical illnesses in pregnancy.

**Summary**

In summary, understanding the nature of critical illness in pregnancy is an important and evolving process. We have clearly grown beyond simple mortality reviews for assessment of pregnancy-related critical illness. However, our currently available tools and databases for examining these patients still need improvement. Reports of critically ill women admitted to the ICU have further refined our understanding of these diseases. However, targeted surveillance of obstetric ICU admissions is needed to identify variations in care and disease that may affect management. As our understanding of these conditions continues to mature, we will hopefully gain greater insight into the specific nature of these conditions that will lead to improved prevention strategies and better therapies for the diseases when they occur. In our view, these data will improve our ability to plan and allocate the necessary resources to adequately care for these often complex and severe illnesses.