

# Maternal Mortality From Preeclampsia/Eclampsia

Labib Ghulmiyyah, MD,\* and Baha Sibai, MD<sup>†</sup>

Preeclampsia/eclampsia is one of the 3 leading causes of maternal morbidity and mortality worldwide. During the past 50 years, there has been a significant reduction in the rates of eclampsia, maternal mortality, and maternal morbidity in the developed countries. In contrast, the rates of eclampsia, maternal complications, and maternal mortality remain high in the developing countries. These differences are mainly due to universal access to prenatal care, access to timely care, and proper management of patients with preeclampsia–eclampsia in the developed countries. In contrast, most of maternal deaths and complications are due to lack of prenatal care, lack of access to hospital care, lack of resources, and inappropriate diagnosis and management of patients with preeclampsia–eclampsia in the developing countries. Preeclampsia/eclampsia is associated with substantial maternal complications, both acute and long-term. Clear protocols for early detection and management of hypertension in pregnancy at all levels of health care are required for better maternal as well as perinatal outcome. This is especially important in the developing countries.

Semin Perinatol 36:56-59 © 2012 Elsevier Inc. All rights reserved.

**KEYWORDS** preeclampsia, eclampsia, maternal death

Preeclampsia refers to a syndrome characterized by the new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman.<sup>1</sup> Eclampsia refers to the development of grand mal seizures in a woman with gestational hypertension or preeclampsia.<sup>2</sup> Preeclampsia is a frequent disorder, with a reported incidence of 2%–8% among pregnancies. Geographic, social, economic, and racial differences, however, are thought to be responsible for incidence rates up to 3 times higher in some populations.<sup>2</sup> Preeclampsia, more than being proteinuric gestational hypertension alone, is a state of exaggerated systemic inflammation and remains a leading direct cause of maternal morbidity and mortality worldwide. Preeclampsia/eclampsia probably accounts for more than 50,000 maternal deaths worldwide each year.<sup>3,4</sup>

Although the rate of severe preeclampsia–eclampsia and the number of maternal deaths from hypertension in pregnancy have fallen steadily over recent years in some developing countries, in places where maternal mortality is high, most of these deaths are still associated with preeclampsia

and eclampsia. Even in countries with low maternal mortality, a substantial proportion will be due to preeclampsia/eclampsia.<sup>5,6</sup> For example, in the United Kingdom, preeclampsia and eclampsia together account for 15% of direct maternal deaths and two-thirds are related to preeclampsia.<sup>7,8</sup> Preeclampsia/eclampsia remains one of the most common reasons for women who die during pregnancy worldwide, as 12% of all maternal deaths is caused by eclampsia.<sup>8</sup> Not surprisingly, the rate of preeclampsia and eclampsia is higher in the developing countries because of absent prenatal care and lack of access to proper hospital care.<sup>5</sup> For example, the highest rate for eclampsia was reported from Nigeria as 99/100 deliveries and the lowest in United Kingdom as 2.7/10,000 deliveries.<sup>9</sup>

Zhang et al<sup>10</sup> in their survey of approximately 300,000 deliveries reported that severe maternal morbidity was associated with hypertensive disorders of pregnancy in the United States. The data were obtained from the National Hospital Discharge Survey from 1988 to 1997. The overall incidence of hypertensive disorders in pregnancy was 5.9%. Eclampsia was reported at 1.0 per 1000 deliveries. The incidence of eclampsia, severe preeclampsia, and superimposed preeclampsia remained unchanged during the 10-year period.<sup>10</sup> Women with preeclampsia and eclampsia had a 3- to 25-fold increased risk of severe complications such as abruptio placentae, thrombocytopenia, disseminated intravascular coagulation, pulmonary edema, and aspiration pneumonia.

\*Department of Obstetrics and Gynecology, American University of Beirut Medical Center, Beirut, Lebanon.

<sup>†</sup>Department of Obstetrics and Gynecology, University of Cincinnati, Cincinnati, OH.

Address reprint requests to Baha Sibai, MD, Department of Obstetrics and Gynecology, University of Cincinnati, 51 Goodman Drive, Cincinnati, OH 45267-0550. E-mail: baha.sibai@uc.edu

**Table 1 Maternal Complications in Preeclampsia**

Acute
Eclampsia
Stroke
Abruptio placentae/disseminated intravascular coagulation
HELLP syndrome
Liver hemorrhage/rupture
Pulmonary edema/aspiration
Adult respiratory distress syndrome
Acute renal failure
Death
Long-term
Chronic hypertension
Diabetes mellitus
Chronic renal failure
Coronary artery disease
Neurologic deficit
Premature death

HELLP, hemolysis, elevated liver enzymes, low platelets.

African American women not only had higher incidence of hypertensive disorders in pregnancy, but also tended to have a greater risk for most severe complications.<sup>10</sup> These findings suggest that preeclampsia and eclampsia constitute a worldwide public health problem to be dealt with, especially in developing countries.<sup>5,6</sup>

## Acute and Long-term Maternal Complications of Preeclampsia

Preeclampsia is associated with substantial maternal complications, both acute and long-term (Table 1).<sup>11-21</sup> The deaths that occur secondary to preeclampsia mainly result from eclampsia, uncontrolled hypertension, or systemic inflammation. Most of these maternal deaths are caused by intracerebral hemorrhage.<sup>13,16</sup> Approximately 20% of women with preeclampsia develop hypertension or microalbuminuria within 7 years of a preeclamptic pregnancy, as compared with only 2% among women with uncomplicated pregnancies. In a recent meta-analysis, Bellamy et al<sup>20</sup> showed that after a pregnancy complicated by preeclampsia, women had an increased risk for hypertension (3.7; 95% CI, 2.70-5.05), ischemic heart disease (2.16; 95% CI, 1.86-2.52), stroke (1.81; 95% CI, 1.45-2.27), and venous thromboembolism (1.19; 95% CI, 1.37-2.33). The risk of death from cardiovascular and other causes is also increased in these women. Women with early-onset severe preeclampsia appear to be at highest risk. Therefore, preeclampsia raises a red flag concerning the risk of cardiovascular and neurologic disease in later life.<sup>20,21</sup>

## Maternal Mortality and Morbidities

Although the maternal mortality rate in the United States is approximately 7.5 per 100,000, most studies suggest that the

actual number of maternal deaths is larger because of the continuing problem of underreporting.<sup>12</sup> Maternal mortality has decreased over the past half of the 20th century, but preventable cases continue to occur. The majority of the approximately 600,000 annual maternal deaths take place in developing countries, whereas Western Europe and the United States probably have preventable cases.<sup>22-25</sup>

It is well known that preeclampsia and eclampsia carry a high risk for severe maternal morbidity. Compared with Caucasians, African American women have higher incidence of hypertensive disorders in pregnancy and suffer from more severe complications. The dangers of a high systolic blood pressure, especially in combination with a low platelet count, seem to be much underestimated in relation to intracerebral hemorrhage.<sup>26</sup> Especially, the combination of endothelial disease, thrombocytopenia, and sudden changes in blood pressure results in high risks for cerebral complications in women with preeclampsia.<sup>13,26</sup>

Compared with hospitalizations without any hypertensive disorders, the risk of severe obstetric complications was 3.3-34.8 times for hospitalizations with eclampsia/severe preeclampsia and 1.4-2.2 times for gestational hypertension. In the United States, the number of delivery hospitalizations with hypertensive disorders in pregnancy is increasing, and these hospitalizations are associated with a substantial burden of severe obstetric morbidity.<sup>27</sup>

In reviewing all maternal deaths in the United States, among almost 1.5 million deliveries within 124 Hospitals, Clark et al<sup>24</sup> reported 95 maternal deaths occurred in 1,461,270 pregnancies (6.5 per 100,000 pregnancies). Median maternal age of women who died was 29 years (range, 13-42). The leading causes of death were complications of preeclampsia, pulmonary thromboembolism, amniotic fluid embolism, obstetric hemorrhage, and cardiac disease.<sup>24</sup>

## Maternal Complications in Severe Preeclampsia and Hemolysis, Elevated Liver Enzymes, Low Platelets Syndrome

Severe preeclampsia is associated with increased risk of maternal mortality (0.2%) and increased rates of maternal morbidities (5%), such as convulsions, pulmonary edema, acute renal or liver failure, liver hemorrhage, disseminated intravascular coagulopathy, and stroke. These complications are usually seen in women who develop preeclampsia before 32 weeks' gestation and in those with preexisting medical conditions (Table 2).<sup>26-28</sup>

Hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome is associated with an increased risk of maternal death and increased rates of maternal morbidities, such as pulmonary edema, acute renal failure, disseminated intravascular coagulopathy, abruptio placentae, liver hemorrhage or failure, adult respiratory distress syndrome, sepsis, and stroke.<sup>29</sup> The rate of these complications will depend on the population studied, the laboratory criteria used to establish the diagnosis, and the presence of associated preexisting

**Table 2** Maternal Complications in Severe Preeclampsia and HELLP Syndrome

Complication	Severe Preeclampsia	HELLP Syndrome
Blood transfusion	3%	25%
Disseminated intravascular coagulopathy	0%	15%
Wound disruption	2%	14%
Renal failure	0%	3%
Pulmonary edema	3%	8%
Intracranial hemorrhage	0%	1.5%

medical conditions (chronic hypertension, lupus) or obstetric complications (abruptio placentae, peripartum hemorrhage, fetal demise, eclampsia). The development of HELLP syndrome in the postpartum period also increases the risk of renal failure and pulmonary edema (Table 2).<sup>28</sup> In addition, severe preeclampsia and HELLP syndrome are major causes of admission to the intensive care unit.<sup>29,30</sup>

## Eclampsia

Although eclampsia is associated with an increased risk of maternal death in developed countries (0%-1.8%),<sup>2,5,30-33</sup> the mortality rate is as high as 15% in developing countries (Table 3).<sup>2,14-16</sup> The high maternal mortality reported from the developing countries was noted primarily among patients who had multiple seizures outside the hospital and those without prenatal care.<sup>5,6,13,14</sup> In addition, this high mortality rate could be attributed to the lack of resources and intensive care facilities needed to manage maternal complications from eclampsia.<sup>5,6,13</sup> A recent review of all reported pregnancy-related deaths in the United States for the years 1979-1992 identified 4024 pregnancy-related deaths.<sup>12</sup> A total of 790 (19.6%) were considered to be due to preeclampsia-eclampsia; of these, 49% were considered to be related to eclampsia. The authors found that the risk of death from preeclampsia or eclampsia was higher for women aged >30 years and for those with no prenatal care, as well as for African American women. The greatest risk of death was found among women with pregnancies at or before 28 weeks of gestation.<sup>12</sup> Pregnancies complicated by eclampsia were also associated with increased rates of maternal morbidities, such as abruptio pla-

**Table 3** Maternal Complications in Eclampsia<sup>a</sup>

Complication	%
Death	0-15
Aspiration pneumonia	2-10
Pulmonary edema	3-12
Abruptio placentae	7-10
Disseminated coagulopathy	7-20
Acute renal failure	5-10
Cardiopulmonary arrest	2-10
Stroke	1-10

<sup>a</sup>Lower values are for developed countries and higher values for developing countries.

**Table 4** Factors Associated With High Rates of Eclampsia and Maternal Mortality and Morbidities in the Developing Countries as Compared With Developed Countries

Lack of and/or poor prenatal care
Delay in early diagnosis
Progression to severe eclampsia
Delay in treatment
Lack of access to hospital care
Lack of access to transportation to clinic
Lack of transport from clinic to hospital
Lack of transport from hospital to tertiary facility
Lack of well-trained staff and personal
Lack of proper resources
Medications
Equipment, laboratory
Intensive care unit

centae, disseminated intravascular coagulopathy, pulmonary edema, aspiration pneumonia, and cardiopulmonary arrest. Adult respiratory distress syndrome and intracerebral hemorrhage are rare complications among eclamptic series reported from the developed world.<sup>21</sup> It is important to note that maternal complications are significantly higher among women who develop antepartum eclampsia, particularly among those who develop eclampsia remote from term.

## Disparity in the Rate of Eclampsia and Maternal Complications From Preeclampsia-Eclampsia Between the Developing and Developed Countries

As previously discussed, there are substantial differences in the rates of eclampsia, maternal death, and maternal complications from hypertensive disorders of pregnancy among various countries.<sup>2,6,9</sup> Despite the availability of magnesium sulfate for the prophylaxis and treatment of eclamptic seizures, the rates of eclampsia and maternal complications remain very high. This is because magnesium sulfate will only prevent eclamptic seizures in women who are hospitalized with severe preeclampsia during labor and immediately postpartum. In the developing countries, most women will not be identified early, as most cases of eclampsia develop at home and/or during transport (Table 4). It is important to emphasize that these differences are mainly due to many of the factors listed in Table 4.

## Conclusions

Hypertensive disease in pregnancy complicated by preeclampsia/eclampsia requires proper antenatal care, early recognition and referral, adequate treatment, and timely delivery. The lack of protocols for disease management or failure to follow clinical protocols of care contributes toward avoidable medical factors. Clear protocols for management of

hypertension in pregnancy at all levels of health care are required for better maternal as well as perinatal outcome.

## References

- Sibai BM: Maternal and uteroplacental hemodynamics for the classification and prediction of preeclampsia. *Hypertension* 52:805, 2008
- Sibai BM: Diagnosis, prevention, and management of eclampsia. *Obstet Gynecol* 105:402-410, 2005
- Duley I: Maternal mortality associated with hypertensive disorders of pregnancy in Africa, Asia, Latin America and the Caribbean. *Br J Obstet Gynaecol* 99:547-553, 2005
- Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. *Lancet* 345:1455-1463, 1995
- Goldenberg RL, McClure EM, MacGuire ER, et al: Lessons for low-income regions following the reduction in hypertension-related maternal mortality in high-income countries. *Int J Gynecol Obstet* 113:91-95, 2011
- Danso KA, Opare-Addo HS: Challenges associated with hypertensive disease during pregnancy in low-income countries. *Int J Gynecol Obstet* 110:78-81, 2010
- Altman D, Carroli G, Duley L, et al: Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: A randomised placebo-controlled trial. *Lancet* 359:1877-1890, 2002
- Walker JJ: Pre-eclampsia. *Lancet* 356:1260-1265, 2000
- Knight M, UKOSS: Eclampsia in the United Kingdom 2005. *Br J Obstet Gynaecol* 114:1072-1078, 2007
- Zhang J, Meikle S, Trumble A: Severe maternal morbidity associated with hypertensive disorders in pregnancy in the United States. *Hypertens Pregnancy* 22:203-212, 2003
- Khan KS, Wojdyla D, Say L, et al: WHO analysis of causes of maternal death: A systematic review. *Lancet* 367:1066-1074, 2006
- MacKay AP, Berg CJ, Atrash HK: Pregnancy-related mortality from preeclampsia and eclampsia. *Obstet Gynecol* 97:533-538, 2001
- Moodley J: Maternal deaths associated with hypertensive disorders of pregnancy: A population-based study. *Hypertens Pregnancy* 23:247-256, 2004
- Dasari P, Habeebullah S: Maternal mortality due to hypertensive disorders of pregnancy in a tertiary care center in Southern India. *Int J Gynaecol Obstet* 110:271-273, 2010
- Onuh SO, Aisien AO: Maternal and fetal outcome in eclamptic patients in Benin City, Nigeria. *J Obstet Gynaecol* 24:765-768, 2004
- Urassa DP, Carlstedt A, Nyström L, et al: Eclampsia in Dar es Salaam, Tanzania—Incidence, outcome, and the role of antenatal care. *Acta Obstet Gynecol Scand* 85:571-578, 2006
- Ghazal-Aswad S, Badrinath P, Sidky I, et al: Confidential enquiries into maternal mortality in the United Arab Emirates: A feasibility study. *J Obstet Gynaecol Res* 37:209-214, 2011
- Sibai BM, Ramadan MK: Acute renal failure in pregnancies complicated by hemolysis, elevated liver enzymes, and low platelets. *Am J Obstet Gynecol* 168:1682-1690, 1993
- Almerie MQ, Matar H, Almerie Y: A 20-year (1989-2008) audit of maternal mortality in Damascus, Syria. *Int J Gynaecol Obstet* 112:70-71, 2011
- Bellamy L, Casas JP, Hingorani AD, et al: Pre-eclampsia and risk of cardiovascular disease and cancer in later life: Systematic review and meta-analysis. *BMJ* 335:974, 2007
- Yerdelen D, Karataş M: Neurological complications without eclampsia during pregnancy in Turkey. *J Obstet Gynaecol Res* 37:202-208, 2011
- Schutte J, Schuitemaker N, van Roosmalen J, et al: Substandard care in maternal mortality due to hypertensive disease in pregnancy in the Netherlands. *Br J Obstet Gynaecol* 115:732-736, 2008
- Karolinski A, Mazzoni A, Belizan JM, et al: Lost opportunities for effective management of obstetric conditions to reduce maternal mortality and severe maternal morbidity in Argentina and Uruguay. *Int J Gynecol Obstet* 110:175-180, 2010
- Clark SL, Belfort MA, Dildy GA, et al: Maternal death in the 21st century: Causes, prevention, and relationship to cesarean delivery. *Am J Obstet Gynecol* 199:36.e1-36.e5, 2008
- Allen VM, Campbell M, Carson G, et al; for the Canadian Maternal Morbidity Working Group: Maternal mortality and severe maternal morbidity surveillance in Canada. *J Obstet Gynaecol Can* 32:1140-1146, 2010
- Martin JN Jr, Thigpen BD, Moore RC, et al: Stroke and severe pre-eclampsia and eclampsia: A paradigm shift focusing on systolic blood pressure. *Obstet Gynecol* 105:246-254, 2005
- Kuklina EV, Ayala C, Callaghan WM: Hypertensive disorders and severe obstetric morbidity in the United States. *Obstet Gynecol* 113:1299-1306, 2009
- Sibai BM: Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. *Obstet Gynecol* 103:981-999, 2004
- Tuffnell DJ, Jankowicz D, Lindow SW, et al: Outcomes of severe pre-eclampsia/eclampsia in Yorkshire 1999/2003. *Br J Obstet Gynaecol* 112:875-880, 2005
- Zeeman GG, Wendel GD Jr, Cunningham FG: A blueprint for obstetric critical care. *Am J Obstet Gynecol* 188:532-536, 2003
- Zwart JJ, Richters JM, Öry F, et al: Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: A nationwide population-based study of 371,000 pregnancies. *Br J Obstet Gynaecol* 15:842-850, 2008
- Andersgaard AB, Herbst A, Johansen M, et al: Eclampsia in Scandinavia: Incidence, substandard care, and potentially preventable cases. *Acta Obstet Gynecol Scand* 85:929-936, 2006
- Zwart JJ, Richters A, Öry F, et al: Eclampsia in the Netherlands. *Obstet Gynecol* 112:820-831, 2008