Maternal Mortality From Preeclampsia/Eclampsia

Labib Ghulmiyyah, MD,* and Baha Sibai, MD†

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.

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Preeclampsia refers to a syndrome characterized by the new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman.1 Eclampsia refers to the development of grand mal seizures in a woman with gestational hypertension or preeclampsia.2 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.2 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.3,4

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.3,6 For example, in the United Kingdom, preeclampsia and eclampsia together account for 15% of direct maternal deaths and two-thirds are related to preeclampsia.7,8 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.8 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.3 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.9

Zhang et al10 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.10 Women with preeclampsia and eclampsia had a 3- to 25-fold increased risk of severe complications such as abruptio placenta, thrombocytopenia, disseminated intravascular coagulation, pulmonary edema, and aspiration pneumonia.

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Table 1 Maternal Complications in Preeclampsia

<table>
<thead>
<tr>
<th>Acute</th>
<th>Long-term</th>
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<tbody>
<tr>
<td>Eclampsia</td>
<td>Chronic hypertension</td>
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<tr>
<td>Stroke</td>
<td>Diabetes mellitus</td>
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<tr>
<td>Abruptio placentae/disseminated intravascular coagulation</td>
<td>Chronic renal failure</td>
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<tr>
<td>HELLP syndrome</td>
<td>Coronary artery disease</td>
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<tr>
<td>Liver hemorrhage/rupture</td>
<td>Neurologic deficit</td>
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<tr>
<td>Pulmonary edema/aspiration</td>
<td>Premature death</td>
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<tr>
<td>Adult respiratory distress syndrome</td>
<td>HELLP, hemolysis, elevated liver enzymes, low platelets.</td>
</tr>
<tr>
<td>Acute renal failure</td>
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<tr>
<td>Death</td>
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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. These findings suggest that preeclampsia and eclampsia constitute a worldwide public health problem to be dealt with, especially in developing countries.

**Acute and Long-term Maternal Complications of Preeclampsia**

Preeclampsia is associated with substantial maternal complications, both acute and long-term (Table 1). 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. 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 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.

**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. 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.

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. Especially, the combination of endothelial disease, thrombocytopenia, and sudden changes in blood pressure results in high risks for cerebral complications in women with preeclampsia.

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.

In reviewing all maternal deaths in the United States, among almost 1.5 million deliveries within 124 Hospitals, Clark et al 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.

**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.

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. 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...
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). In addition, severe preeclampsia and HELLP syndrome are major causes of admission to the intensive care unit.

**Eclampsia**

Although eclampsia is associated with an increased risk of maternal death in developed countries (0%-1.8%), the mortality rate is as high as 15% in developing countries (Table 3). 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. 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. A recent review of all reported pregnancy-related deaths in the United States for the years 1979-1992 identified 4024 pregnancy-related deaths. 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. Pregnancies complicated by eclampsia were also associated with increased rates of maternal morbidities, such as abruptio placentae, disseminated intravascular coagulopathy, pulmonary edema, aspiration pneumonia, and cardiopulmonary arrest.

**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. 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.

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