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## Eclampsia: Still a Problem in Bangladesh

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### Abstract and Introduction

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#### Abstract

This descriptive study, conducted at Dhaka Medical College and Hospital, Bangladesh, includes 2956 consecutive eclamptic patients who were admitted between 1998 and 2000 and evaluates their outcomes after treatment with magnesium sulfate. Although magnesium sulfate controls convulsion efficiently, death from eclampsia remains high in our country. Thus, a second purpose of this study was to identify additional factors responsible for death from eclampsia. Among 32,999 obstetric patients admitted to the hospital during the years 1998 to 2000, 2956 were eclamptic, yielding an incidence of 9%. The antepartum/intrapartum and postpartum incidences of eclampsia were 80% and 20%, respectively. Among the patients with eclampsia, 79% had good prognosis without any added complication except convulsion, and 21% had other complications. For the period 1998 to 2000, the rate of maternal death from eclampsia was 8.6%, which was lower than that of the immediate past year (1997) for which the mortality was 16%. Changing the protocol from diazepam to magnesium sulfate for control of convulsion significantly reduced the incidence of death. But reduction of the risk of death was difficult when patients had developed complications. Most of the patients in the group who had complications died (98%); these complications developed as a result of a delayed decision for treatment. Therefore, efforts should be directed at developing awareness to receive treatment at an appropriate time to prevent the development of eclampsia and to reduce the mortality from eclampsia and its complications.

#### Introduction

Eclampsia is a potentially fatal disorder of pregnant women that has been prevalent since the time of Hippocrates; it remains an important cause of maternal mortality throughout the world, accounting for about 50,000 deaths worldwide.<sup>[1]</sup> In developed countries, eclampsia complicates about 1 in 2000 deliveries.<sup>[2]</sup> In developing countries, the prevalence of eclampsia varies widely, from 1 in 100 to 1 in 1700.<sup>[3-5]</sup> It is a common problem in developing countries because illiteracy, lack of health awareness and education, poverty, and superstitious beliefs prevent women from seeking medical advice during pregnancy.

The incidence of eclampsia is extraordinarily high in Bangladesh -- 7.9% (not including pre-eclampsia), according to the results of a house-to-house survey.<sup>[6]</sup> In this country, only 2.3% women end their pregnancy under medical supervision (whether it be abortion or delivery);<sup>[7]</sup> the rest have no access to obstetric care. As a result, most preeclampsia cases remains unrecognized until severe complications, such as eclampsia, occur. Because Dhaka Medical College and Hospital has a special eclampsia unit and is the largest tertiary referral government hospital in the country, the incidence of eclampsia is even higher in this hospital setting, at 9 %.

Eclampsia is the third major cause of maternal death in Bangladesh (16%),<sup>[8]</sup> preceded by hemorrhage and sepsis. In developed countries, deaths from hemorrhage and infection have almost disappeared and eclampsia has become the prime killer, indicating that death from eclampsia is particularly difficult to prevent.<sup>[9]</sup> Although eclampsia is the third major cause of maternal death in Bangladesh, it is the major cause in our hospitals. This is because postpartum hemorrhage and sepsis can be managed efficiently in the hospital (eg, reversing shock as a result of postpartum hemorrhage) if patients can get there; that is, deaths from these conditions usually occur outside the hospital setting. Patients with eclampsia, however, develop complications gradually; by the time they reach the hospital, complications have become so severe that they cannot be reversed easily.

Until recently, the treatment of eclampsia varied throughout the world. The basic principles of management are (1) control of convulsion, (2) control of severe hypertension, (3) initiation of steps to effect delivery, and (4) general nursing care. The use of anticonvulsant treatment varies in different parts of the world. A large multicenter study has shown that magnesium sulfate is the ideal anticonvulsant,<sup>[10]</sup> and it is superior to both phenytoin and diazepam in the management of eclampsia. Magnesium sulfate for this purpose was first suggested in 1906<sup>[11]</sup> and has been popular for more than 66 years in the United States. After a pilot study was conducted at Dhaka Medical College and Hospital between May 1995 and June 1996, magnesium sulfate was chosen to replace diazepam for use as an anticonvulsant and has been used in Bangladesh since 1998. In addition, the more current Magpie trial,<sup>[12]</sup> in which Bangladesh was one of the participating countries, showed that magnesium sulfate reduced the risk of developing eclampsia.

This report describes the current management protocol for eclampsia and outcome of this management in terms of maternal mortality and considers additional factors that are responsible for death due to eclampsia in Bangladesh.

## Materials and Methods

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This study was done in Dhaka Medical College and Hospital, which is an urban tertiary referral hospital and is the largest hospital in Bangladesh. It was approved by an institutional review board that consisted of the Head of the Department and other Professors of the Department of Obstetrics and Gynecology. This hospital deals mainly with referral patients. The number of annual obstetric admissions is 10,000 to 11,500, and the number of eclampsia cases is 800 to 1100 per year. The hospital has an eclampsia care unit, so patients from Dhaka city and nearby districts are referred here for better management. Of note is that most of the eclamptic patients are born in rural areas and belong to a lower social class. As a result, most have never received antenatal care.

For this descriptive study, data obtained from 2956 eclamptic patients who been admitted between the years 1998 and 2000 were reviewed. Eclampsia was documented by high blood pressure (up to 140/90 mm Hg; an indicator of hypertension), edema, proteinuria (defined as passes of albumin in urine documented by heat coagulation test), and convulsion associated with pregnancy after 20 weeks of gestation. On admission, a detailed history was taken from the patient or the patient's attendant, as appropriate. A thorough clinical examination was done, and a bedside test for albuminuria was performed.

Patients were classified into 2 groups. One group was classified as good-outcome group; these patients were eclamptic but had no complications of eclampsia or other medical or obstetric complications. The other group was the poor-outcome group, who had complications related to eclampsia or other obstetric complications not related to eclampsia (eg, obstructed labor, prolonged labor, postpartum hemorrhage). Complications were diagnosed mostly clinically as follows:

1. Renal failure was diagnosed by the absence of passage of urine, even with an injection bolus dose of furosemide and on the basis of abnormal results for renal function tests.
2. Hepatic failure was diagnosed by jaundice (yellow discoloration of conjunctiva, urine), increased serum bilirubin, and elevated levels of serum glutamic oxaloacetic transaminase (SGOT) (alanine aminotransferase) and serum glutamic pyruvic transaminase (SGPT) (aspartate aminotransferase).
3. Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome was diagnosed by elevated levels of SGOT, SGPT, bilirubin, lactate dehydrogenase (LDH); the presence of jaundice; and low platelet count.
4. Heart failure was diagnosed by bilateral crepts in lungs, respiratory distress, and engorged neck vein.
5. Cerebrovascular accident was diagnosed by coma (Glasgow coma scale < 8), paresis or paralysis, and lowered blood pressure.
6. Disseminated intravascular coagulation (DIC) was diagnosed by bleeding from prick point, bedside clotting test, estimation of the coagulation parameters bleeding time (BT), clotting time (CT), and, in a few cases, fibrinogen degradation products (FDP) and fibrinogen.
7. Pulmonary edema was diagnosed by bilateral coarse crepitation and frothy secretion from mouth.

8. Abruptio placenta was diagnosed by presence of antepartum or intrapartum hemorrhage and sonographically diagnosed localization of the placenta in the upper segment.

Obstructed labor and postpartum hemorrhage are not complications of eclampsia, but the risk for these complications is high. So when eclampsia was associated with these complications, the patient's condition was poor. All admitted patients were reviewed.

The management protocol of the unit included the following:

1. Control of convulsion
2. Control of blood pressure
3. Labor management
4. Management of complications

### **Control of Convulsion in Eclampsia**

Magnesium sulfate was the drug of choice for controlling convulsion. The dose schedule was 4 g magnesium sulfate in 12 mL distilled water administered intravenously (IV) slowly over 15 minutes, with 3 g in each buttock as a loading dose; then 2.5 g was administered to alternate buttocks every 4 hours for 24 hours after administration of the first dose. For recurrent convulsion, another 2.5 g IV is given slowly over 5 minutes. Patients were monitored every half hour for the first few hours, then hourly, by observing respiratory rate, knee jerk, and urine output. Other clinical parameters were also evaluated. Part of our research entailed administering only the loading dose to some patients to determine whether it was effective in controlling convulsion and which did not otherwise affect the patients' condition.

Patients with oliguria, anuria, respiratory depression, and absent knee jerk were treated with diazepam, as magnesium sulfate is contraindicated for these patients. Those patients who were very moribund and had no convulsion at or after admission did not require any anticonvulsant.

### **Control of Blood Pressure**

Blood pressure was controlled either by injection of hydralazine, 20 mg in 200 mL normal saline intravenously (IV) at 10 drops/minute and titrated according to response, or bolus 5 mg IV repeated if necessary using 2 to 5 mg at 15-minute intervals to keep the diastolic blood pressure between 90 and 100 mm Hg. This treatment was followed by oral nifedipine or methyldopa, atenolol singly or in combination with nifedipine, according to need.

### **Labor Management**

Labor was managed according to our standard labor management protocol. A prolonged first stage was curtailed by lower segment cesarean section (LSCS) (ie, performed for arrest of the active phase of labor), and the second stage was cut short by either ventouse or forceps. When patients were not in labor, it was induced by introduction of extra-amniotic Foley's catheter, prostaglandins, oxytocin, and artificial rupture of membranes, as appropriate. Again, the first stage was curtailed by LSCS and the second stage by forceps or ventouse.

Other indications for LSCS were cephalopelvic disproportion, malpresentation, history of previous cesarean section, fetal distress, intrauterine growth restriction (IUGR), uncontrolled fit, antepartum hemorrhage, and obstructed labor. In certain cases in which the fetus had not matured (as determined by history of last menstrual period, ultrasound, and clinical assessment) and the maternal condition was stable within 24 hours of observation (ie, blood pressure settled, convulsion controlled, all test results within normal or near normal, and patient had no complaints), steroids were administered to induce fetal lung maturity and pregnancy was continued until 36 weeks. Pregnancy was terminated either after completion of 36 weeks or any complications developed in the mother or fetus. Note that the cutoff of 36 weeks for delivery was decided on the basis of the finding that support survival rate is not satisfactory before 36 weeks; to terminate before 36 weeks was thus not reasonable. In addition, the number of neonatal intensive care beds is very limited in the hospital and few private beds are available, which are very expensive for poor patients.

### Treatment of Complications

Patients were jointly treated by an obstetrician and other physicians from the hospital faculty, such as a nephrologist, neurologist, cardiologist, or ophthalmologist. Complications were diagnosed by clinical examinations and on the basis of test results.

The cause of death was determined from the clinical diagnosis. Postmortem examination was not undertaken in any case. (Postmortems are done only in cases of accidental deaths.) A comparison was made between the outcomes of the patients with and without complications by performing a chi-square test. A *P* value of  $< .5$  was considered as significant.

### Results

During the study period from 1998 to 2000, a total of 32,999 obstetric patients were admitted to the obstetric unit at Dhaka Medical College and Hospital. There were 2956 cases of eclampsia, yielding an overall incidence of 9%. Antepartum/intrapartum eclampsia occurred in 77% of cases, and 20% were postpartum eclampsia ( Table 1 ). The incidence of eclampsia with different complications was 21%, which included renal failure, 20 (0.7%); hepatic failure, 15 (0.5%); heart failure, 15 (0.5%); cerebrovascular accident (CVA) and coma, 85 (2.9 %); pulmonary edema, 305 (10.3%); DIC, 30 (1.0%); HELLP syndrome (only clinically obvious cases confirmed by elevated SGOT, SGPT, LDH, and low platelet count), 55 (1.9%); and abruptio placenta, 50 (1.7%) ( Table 2 ). Other resulting obstetric complications that are not related to eclampsia were postpartum hemorrhage, 30 (1.%), and prolonged and obstructed labor, 20 (0.7%).

**Table 1. Patient Profile**

Patient Profile	Antepartum Eclampsia	Postpartum Eclampsia	Total (%)
No. of patients	2354	602	2956
Patients without complications (good-outcome group)	1937	394	2331 (78.85)
Patients with complications (poor-outcome group)	487	138	625 (21.14)
No. of deaths	200	55	255 (8.63)

**Table 2. Eclampsia With Different Associated Complications and Other Obstetric Complications**

Complications	Number	% of Total Eclampsia
<b>Complications of Eclampsia</b>		
Pulmonary edema	305	10.31
Renal failure	20	0.68
Hepatic failure	15	0.50
Heart failure	15	0.50
CVA/coma	85	2.88
Abruptio placenta	50	1.70
HELLP syndrome (clinically evident)	55	1.87

DIC	30	1.01
<b>Other Obstetric Complications</b>		
Postpartum hemorrhage	30	1.01
Obstructed labor	20	0.68
<b>Total</b>	<b>625</b>	<b>21.14</b>

*CVA = cerebrovascular accident; HELLP = hemolysis, elevated liver enzymes, and low platelet count*

We were not able to determine how many patients had severe or nonsevere preeclampsia before seizures occurred. Most of the seizures in postpartum patients occurred within 24 hours of delivery. Of the patients with complications, 366 patients received magnesium sulfate, 140 received diazepam, and 119 received nothing. Death among patients who were treated with diazepam was 70, no anticonvulsant, 80, and magnesium sulfate, 100. Five patients who did not have complications and received magnesium sulfate died.

The main cause of death was pulmonary edema (46.3%), which had been treated with injection frusemide (in patients with crepitations), oxygen inhalation, oropharyngeal suction, and fluid restriction. Pulmonary edema develops as a result of either heart failure or aspiration. Our cases were mostly due to aspiration associated with aspiration pneumonia. The patients who died had arrived at the hospital already with massive edema, with frothy secretions and gasping. Some of the patients died very soon after admission; nothing could be done. The next most significant causes of death were CVA and coma (23.5%) ( Table 3 ). Of the poor-outcome group (ie, the group with complications), 250 patients (98%) died. Mortality was significantly lower among patients who had no other complications except convulsion ( Table 4 ).

**Table 3. Causes of Death**

<b>Causes</b>	<b>Number</b>	<b>% of Total Deaths</b>
Renal failure	5	1.96
Hepatic failure	5	1.96
Heart failure	3	1.18
HELLP syndrome	15	5.88
Postpartum hemorrhage with irreversible shock	9	3.52
Abruptio placenta with shock	5	1.96
CVA/coma	60	23.52
Obstructed labor	5	1.96
Cardiac arrest during general anesthesia	15	5.88
Pulmonary edema	118	46.28
Respiratory arrest	3	1.18

Pulmonary embolism	6	2.36
Undetermined	6	2.36
<b>Total</b>	<b>255</b>	<b>100</b>

*CVA = cerebrovascular accident; HELLP = hemolysis, elevated liver enzymes, and low platelet count*

**Table 4. Outcome of the Patients in Terms of Mortality**

Outcome	Good outcome group	Poor outcome group	Total	P Value
Died	5 (1.96%)	250 (98.03%)	255	.001
Survived	2326	375	2701	

Df =1,  $\chi^2 = 989.81$

### Limitations of the Study

Of course, this is not a well-designed controlled study. It is the description of the management and outcome of cases during a period of 3 years. Almost all of the patients came to the hospital after the development of convulsion. As a result, we could not record the cases as antepartum or intrapartum when they came with established labor. Most of the persons accompanying the patients were not so aware to mention clearly when onset of convulsion and onset of labor occurred. Most of the patients had not had an antenatal checkup, so we could not identify the severity of disease before the development of convulsion.

For this report, we are concerned primarily with the fate of the mother in terms of mortality, so we do not mention here anything about outcomes for the babies. As the data of previous years were not recorded in the same manner in which we observed the cases of this series, we did not compare the outcome of diazepam and magnesium treatment. We only cited the death rate occurring in the diazepam era.

### Discussion

Eclampsia remains a major killer in Bangladesh. It is conventionally considered to be the end stage of preeclampsia. The etiology of preeclampsia is unknown, and the direct cause of eclamptic convulsions is also not known. Eclampsia is a multisystem disorder, which presents an interdisciplinary challenge to obstetricians and other physicians, who need to be familiar with pregnancy physiology and the current concepts in the pathogenesis and pathophysiology of severe preeclampsia and eclampsia. A team of obstetricians, other specialists such as cardiologists, nephrologists, and neurologists, an anesthetist, and nurses with interest and experience are needed in an intensive care unit to protect eclamptic mothers from death.

In the eclampsia care unit of Dhaka Medical College Hospital, there are 10 beds for eclamptic patients, which are almost always occupied. Moreover, in the winter and rainy seasons, when incidence is increased, the number of

patients exceeds the allocated beds<sup>[13]</sup>; 2 or 3 patients along with their babies need to be kept in a single bed. These very high-risk patients require intensive monitoring, thorough investigation, and prompt and rational treatment whenever necessary. But the lack of some investigative facilities and the patient overload sometimes hinder standard care. Patients having only minor systemic disturbances, and problems were easy to control with rapid recovery after delivery. Other patients who were desperately ill with renal failure, hepatic failure, cardiac failure, DIC, CVA, HELLP syndrome, and severe pulmonary edema were difficult to manage. Although prevention or stabilization of convulsions may be an important aim, it is clear that convulsions are not the only risk to the mother.

The Collaborative Eclampsia Trial<sup>[10]</sup> found the incidence of morbidity ranging from 12.4% to 25.3%, whereas Douglas and Redman<sup>[2]</sup> found that 35% of the women with eclampsia had at least 1 other complication. In our series, 21.1% of patients suffered serious morbidities other than convulsions. The various serious morbidity factors had a greater influence on mortality than convulsion itself.

Eclampsia is also an important cause of maternal death in many parts of Africa, Asia, the Caribbean, and Latin America.<sup>[1]</sup> Deaths associated with hypertensive disorders of pregnancy are the most difficult to prevent in developing as well as developed countries.<sup>[14,15]</sup> The burden of death from eclampsia is great. How could it be prevented? Leitch and colleagues<sup>[16]</sup> reported that after the inception of the National Health Service, which allowed free comprehensive antenatal care for all, a significant reduction in the incidence of eclampsia occurred in the United Kingdom, probably as a result of the early detection of preeclampsia and its management. The declining incidence of eclampsia is probably also due to improvement of general health and welfare, the ongoing development of antenatal care, reduction in parity, improvement in the treatment of hypertension, and earlier delivery.<sup>[16]</sup>

In our experience, the majority of cases of eclampsia occurred in patients who had no (78%) or irregular (20%) antenatal care, and the majority of eclamptic patients who died had arrived at the hospital at a later stage of the disease with grave complications. Table 4 shows that 98% of patients from the group who presented with complications other than convulsion died. After the introduction of magnesium sulfate to control convulsion, the development of subsequent complications decreased. As a result, the death rate between the years 1998 and 2000 was also lower compared with that in 1997, when diazepam was used for controlling convulsion. However, once a complication has already developed, magnesium sulfate cannot prevent the sequelae of complications.

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Hemorrhage and infection, which cause a vast number of deaths in developing countries, may be preventable by relatively simple procedures, without any need for high-technology hospital facilities. But unfortunately, our social, economic, and geographic barriers often make it difficult and impossible to provide the necessary basic medical care to prevent maternal deaths from hemorrhage and infection. For eclampsia, the provision of care is even more difficult.

Lack of education and poverty are the main obstacles to seeking treatment. The 3 principal reasons for delay in seeking treatment in Bangladesh are (1) the delay in making the decision to seek medical assistance, (2) difficulty getting transportation to reach the hospitals, and (3) difficulty obtaining appropriate treatment in the hospitals, which may lack sophisticated investigation, treatment facilities, and skilled medical personnel.

Development of health awareness and implementation of antenatal care for all pregnant women may reduce the incidence of eclampsia. The Magpie trial showed that preventive magnesium sulfate for all severe cases of preeclampsia can reduce the risk of development of eclampsia and maternal death by 58% and 45%, respectively.<sup>[12]</sup> So an effort must be made to prevent the development of eclampsia. Efforts must also be made to improve eclampsia management in an attempt to reduce death from eclampsia. In addition, a prime aim should be to establish an eclampsia survey registrar to accurately determine the incidence of eclampsia and the morbidity and mortality associated with it.<sup>[17]</sup> Recently, Shamsuddin and colleagues, from Bangabandhu Sheikh Mujib Medical University, conducted research in a community setting in Bangladesh whereby they administered magnesium sulfate in eclampsia as soon as they developed convulsion to prevent both morbidity and mortality from eclampsia. They showed that development of complications was 3% and 6.8% and death rate was 2.3% and 10.4% in the intervention and nonintervention group, respectively (unpublished data). This suggests that the high rate of mortality in our series is due to the delay in starting treatment.

It is time that doctors took a new look at this major obstetric problem. If all cases of eclampsia occurring in Bangladesh can be reviewed regularly to provide an analysis and overview of what is happening, it might lead to better prevention and management.

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