FACTORS THAT PREDICT VERY SEVERE MATERNAL MORBIDITY AMONG ECLAMPTIC MOTHERS MANAGED AT MUHIMBILI NATIONAL HOSPITAL.

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Muhimbili University of Health and Allied Sciences

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By

Mohammed Salmin Shagdara, MD

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Medicine in Obstetrics and Gynecology of the Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that he has read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences in Dar es Salaam, a dissertation entitled: **Factors That Predict Very Severe Maternal Morbidity Among Eclamptic Mothers Managed at Muhimbili National Hospital**, in fulfilment of the requirements for the degree of Master of Obstetrics and Gynaecology of the School of Medicine.

.....

Dr Projestine MUGANYIZI

(SUPERVISOR)

Date.....29/11/2010.....

DECLARATION AND COPYRIGHT

I, **Dr Mohammed Salmin SHAGDARA** declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature.....

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DEDICATION

This book is dedicated to my wife Salma and my daughters Rania, Manal and Nafisa.

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ABBREVIATIONS

ABD = Assisted breech delivery

ANC = Antenatal clinic

C I = Confidence interval

CFR = Case fatality rate

C/S = Caesarean section

EOC = Essential obstetric care

Hb = Haemoglobin

ICU = Intensive care unit

I/M = Intramuscular

I/V = Intravascular

IUFD = Intra Uterine Fetal Death

IUGR = Intra Uterine Growth Restriction

LCVE = Low cavity vacuum extraction

MgSO4 = Magnesium sulphate

MNH = Muhimbili National Hospital

NGT = Naso-gastric tube

OR = Odds ratio

SBF = Still birth fresh

SBM = Still birth macerated

SVD = Spontaneous vertex delivery

VSM = Very severe morbidity

WD = Ward

WHO = World Health Organization

ABSTRACT

Background: Eclampsia is a condition known to be associated with serious obstetric complications including severe maternal morbidity and mortality. Although eclampsia as an entity causes severe morbidity, from a practical point of view and literature, most eclamptic patients clinically recover within 72 hours of childbirth. A proportion of mothers, however, , develop very severe morbidity as indicated by the need for prolonged admission in ICU, and extra medical/ nursing care measures. This study focuses on predictors of very severe morbidity among eclamptic mothers.

Objectives: To identify factors that independently predict very severe maternal morbidity outcome among eclamptic patients admitted at Muhimbili National Hospital (MNH).

Materials and Methods: A retrospective, cross sectional-analytical study was conducted at MNH and eclamptic mothers with very severe morbidity (VSM) were identified. Using Multiple Logistic Regression, the odds of factors that predict VSM and their 95% Confidence Interval were calculated.

Results: A total of 366 eclamptic patients were studied. Out of these, 132 (36.1%) had VSM. From all the eclamptic mothers, 121 patients needed duration of stay in ICU of more than three days, 20 patients needed insertion of naso-gastric tube for feeding, 14 patients needed physiotherapy, and 49 patients needed resuscitation drugs. Factors that independently predicted VSM were, mode of delivery [OR 2.80, 95% C I (1.50 – 5.10)], time interval from admission to delivery [OR 2.25, 95% C I (1.23 – 4.10)], and number of fits [OR 1.81, 95% C I (1.04 – 3.14)].

Conclusions: These results underscore the importance of prompt, timely and less invasive delivery in prevention of VSM among eclampsia patients.

Recommendations: More efforts are needed to improve and strengthen the municipal hospitals to be able to provide standard care for eclamptic mothers in order to avoid VSM and death.

1.0 INTRODUCTION:

Background: Eclampsia is a potentially fatal disorder of pregnant women that remains an important cause of maternal morbidity and mortality throughout the world.[1] It is estimated that every year eclampsia is associated with about 50,000 maternal deaths worldwide, most of which occurs in developing countries.[1, 2] Approximately 63 000 women worldwide die of eclampsia and pre-eclampsia, and 99% of these deaths occur in low income countries. The reported maternal mortality rates from eclampsia range from 0% to 1.8% in some centres in high-income countries, to as high as 15% in Nigeria and Bangladesh.[3] Eclampsia is a presence of generalized tonic-clonic convulsions in a pregnant woman with pre-eclampsia after the 20th week of gestation and within 7 days of delivery.[4]

Local situation: In a study done in 1999 – 2000, it was observed that Dar es Salaam's hospital and population-based incidences of eclampsia were 200/10 000 and 67/10 000, respectively. The case-fatality rate for eclampsia was 5.0% for women who delivered at MNH and 16% for those referred to MNH after being delivered elsewhere. The screening coverage for signs of pre-eclampsia was more than 85%, except for proteinuria (33%). Fewer than 50% of the women who developed eclampsia had been referred from the ANC clinic and less than 10% were admitted to the antenatal ward at MNH before onset of eclamptic fits.[5]

Maternal mortality: The Tanzania Demographic Health Survey (TDHS 2004 - 05) reports that, the maternal mortality ratio estimates for Tanzania is 578 / 100,000 live births.[6]

The maternal mortality ratio between 1999 and 2005 for Muhimbili National Hospital was 512 per 100,000 live births. Of these, eclampsia claimed 23.5% becoming the leading cause of maternal death at Muhimbili National Hospital, followed by postpartum haemorrhage (23.3%) and anaemia in pregnancy (11.3%). Operative deliveries and abstract deliveries had high chance of maternal mortality.[7]

Eclampsia is found to be primarily a condition of young prim gravid women, and old women (>40 yrs), i.e. occurred in extreme of ages. Nulliparas were six to eight times more susceptible to pre-eclampsia/eclampsia than multiparae.[8]

The onset of eclamptic convulsions could be ante partum (38–53%), intra partum (18–36%), or postpartum (11–44%).[9] Also in the study done in Northern Nigeria, the pattern was ante partum (32.9%), intra partum (54.1%) and postpartum (13%). Out of 207 patients, 51.7% of the patients were delivered by caesarean section, where 10.6% of the 207 patients died.[2]

Maternal morbidity: More than fifty percent of severe morbidities associated with eclampsia in under-resourced countries were associated with cerebral haemorrhage, and therefore lowering of very high blood pressure is a key component in the management of hypertensive crisis of pregnancy. Cerebral complications, mainly cerebral haemorrhage, were the pathological cause of death in approximately 50% of cases and eclampsia was the commonest clinical condition leading to death from hypertensive disorders of pregnancy in South Africa between the years 2002 and 2004.[10, 11]

In one study done in Kampala in 2003, they saw that for each maternal mortality there were 10 to 15 maternal morbidities. Almost all referrals to Mulago Hospital had indicators of low status like poor ANC attendance, un-tackled risk factors at ANC, unplanned pregnancies, poor education, low income etc in addition to poor obstetric services, with lots of emergency transfers in labor. These contributed to the suffering of these women leading to their morbidities and mortalities.[12]

For 1991-2003, the severe maternal morbidity rate in the United States was 5.1 per 1000 deliveries. For every maternal death, approximately 50 women experienced severe morbidity. Most women who were classified as having severe morbidity, had blood transfusion, hysterectomy, or eclampsia. Severe morbidity was more common at the extremes of reproductive age and for black women, compared with white women.[13]

Admission to intensive care had been used as a surrogate marker for very severe maternal morbidity in some studies. An eclamptic seizure does not usually cause coma but is a significant morbidity which if untreated can have fatal consequences. Most previous studies on severe maternal morbidity had used eclampsia as a marker, and the risk of death from an eclamptic seizure was between 1.5 and 2.5%. After identifying avoidable factors in maternal care, maternal mortality in developed countries has declined considerably. With declining rates, maternal mortality can no longer act as a sole marker for quality of care for a pregnant woman.[14]

There are, however, a larger number of women that experience significant severe morbidity related to pregnancy and delivery. One author focused on this group and found

that the causes of very severe morbidity did not directly correlate with the causes of maternal deaths.[15]

Every pregnant woman- even if she is well-nourished and well- educated- can develop sudden life threatening complications that require high quality obstetric care. Attempt to predict these complications have not been successful, since most complications are unexpected and the majority of women with poor pregnancy outcomes do not fall into the high risk category. Other factors which contribute tremendously to maternal morbidities and mortalities from eclampsia are the three delays or barriers; to seek care, to access care and to receive appropriate care. The higher rate of morbidity in developing countries has been attributed to lack of antenatal care, delay in seeking treatment, delays in referrals, poor transport facilities, and delay in effecting treatment.[4, 16, 17]

Maternal morbidity includes a broad spectrum of severity and can include complications and conditions that are associated with any pregnancy outcome. Although there is no established way to identify what maternal conditions to consider as morbidity, extending maternal health surveillance to include the identification and review of pregnancy complications and the factors that are associated with them has the potential to improve maternal health by providing information to influence the delivery of health services and health policy. Identifying women who experienced severe maternal morbidity provides cases for review of care and offers the opportunity to better understand the continuum of severity and the factors that are associated with preventability.

Management: The basic principles of eclampsia management are; control of convulsion, control of severe hypertension, initiation of steps to effective delivery, and general quality nursing care. A large multicenter studies had shown that magnesium sulphate was the ideal anticonvulsant, a drug of choice, used to prevent or control convulsions, and it was superior to both phenytoin and diazepam (Duley L, Henderson-Smart D - 2003)[18, 19] and lytic cocktail (Duley L, Gulmezoglu AM - 2000)[20] in the management of eclampsia. Another multi-centres study, like The Magpie Trial Collaborative Group 2000, showed magnesium to be superior to both placebo and traditional anticonvulsant drugs for women with preeclampsia and eclampsia.[21, 22, 23]

Antihypertensive medications, like hydralazine, labetalol, nifedipine, and sodium nitroprusside, were administered as needed to control severe hypertension, and were so effective in maintaining diastolic blood pressures between 90 and 100 mmHg.[24, 25] Eclampsia was demonstrated to be insidious and sometime unpredictable, where 14% of eclamptic patients did not present with prodromal symptoms before.[26] Alexander et al, set criteria for severe gestational hypertension who received intravenous magnesium sulphate prophylaxis, and women with non severe hypertension did not. They showed that selective magnesium sulphate prophylaxis resulted in an increased overall incidence of eclampsia in non severe gestational hypertension.[27]

In one study, among the 110 patients with postpartum eclampsia, eclampsia developed in 62% > 48 hours after delivery (range 3-23 days). During the 20-year period of this study the frequencies of eclampsia at less than 32 weeks' gestation and of postpartum eclampsia were found not to vary between the first 10-year period and the more recent 10-year

period.[24] However, when eclampsia occurred before 34 wks of gestation, it became a major cause of maternal and neonatal morbidity and mortality. To neonates due to lung immaturity, while to eclamptic mothers due to risk or temptation of prolongation of pregnancy to attain foetal lung maturation.[28]

Prevention: Deaths and morbidities from preeclampsia and eclampsia are often preventable. Prenatal care, early detection, and careful monitoring and treatment during pregnancy are essential to prevent serious complications. It is important for clinicians to identify women with pre-existing hypertensive disorders, a prior history of hypertension, or a family history of hypertension, and to educate women about the early warning signs of preeclampsia. It was noted that very severe morbidity from preeclampsia or eclampsia increased with increasing maternal age. Women who had received no prenatal care had a higher risk of death from preeclampsia or eclampsia than women who had received any level of prenatal care.[29]

2.0 REVIEW OF LITERATURE:

Maternal mortality is frequently described as 'just the tip of the iceberg', implying that there is a vast base to the iceberg which remains largely not described. That vast base is the severe maternal morbidities. This is partly true as the literature is full with hospital-based studies, case studies and anecdotes describing acute and chronic morbidities associated with pregnancy and delivery. What does remain relatively unknown is the prevalence of morbidity in the population as a whole. The number of such studies is limited, mainly because they are difficult to design, implement and analyse. Severe maternal morbidity has many dimensions: aetiology, severity, duration and time of onset, accumulation and sequelae, each with different causes, consequences and implications for treatment.

Women who develop preeclampsia or eclampsia during pregnancy were at an increased risk of abruption placenta, acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulopathy and even maternal death. Renal or hepatic failure was also frequently listed as morbidities that led to death. Disseminated intravascular coagulation was a contributing condition in 15% of hypertension deaths. The risk of death from preeclampsia or eclampsia was higher for older women than for younger women. The largest percentage of preeclampsia and eclampsia deaths was attributed to cerebrovascular complications, primarily cerebrovascular haemorrhage.[29]

Pregnancies complicated by eclampsia was also associated with increased rates of clinically specific maternal morbidities, such as abruption placenta, disseminated intravascular coagulopathy (DIC), pulmonary oedema, acute renal failure, aspiration pneumonia, cardiopulmonary arrest, haemolysis, retinal detachments, elevated liver

enzymes, low platelets (HELLP) syndrome and liver hematoma. It is important to note that maternal complications were significantly higher among women who developed ante-partum eclampsia, particularly among those who developed eclampsia remote from term.[13]

Almost similar results were obtained for maternal morbidity and mortality in another study where eclampsia remained a significant complication of pregnancy that carried high maternal mortality and morbidity rates. Also ante-partum onset eclampsia carried greater risks, and onset at ≤ 32 weeks' gestation was particularly dangerous to patients.[20]

Eclampsia remains a challenge to even the most experienced Obstetricians, mainly because the exact aetiology is not known, but eclampsia is also a preventable condition if pre-eclampsia is detected early and treated promptly.[30]

The exact pathophysiologic condition of eclampsia is unknown. One of the main theories is that eclampsia is an expression of hypertensive encephalopathy, currently been named as posterior reversible encephalopathy syndrome (PRES). It is thought that, in the presence of endothelial dysfunction, an acute increase in blood pressure exceeds the upper limit of cerebral auto-regulation. Forced dilation of cerebral arteries is followed by blood-brain barrier disruption and the formation of vasogenic cerebral edema, due to local hyperperfusion. The syndrome of PRES is reversible clinically by the lowering of blood pressure and termination of the pregnancy. Nevertheless, it is hypothesized that, when vasogenic edema becomes severe enough, it can result in reduced tissue perfusion and cytotoxic edema because of irreversible ischemic changes that lead to brain white matter lesions.[31, 32]

Neurological manifestations and symptoms of eclampsia are varied. Besides seizures, other common symptoms include, headache, cortical blindness, blurring of vision, aphasia, psychosis, facial nerve palsy, cerebral hemorrhage, retinal blindness, retinal edema, cerebral edema, hemiparesis and other focal weakness.[33] Multiple studies have described various abnormalities noted on CNS imaging studies. Both CT and MRI scans have revealed numerous abnormalities such as cerebral edema, focal infarction, intracranial hemorrhage, and posterior leukoencephalopathy.[9] The above derangements relate to our outcomes of use of resuscitation drugs, longer duration of hospital stay, use of nasogastric tube for feeding and need for physiotherapy.

The known cure for this disease is prompt delivery, i.e. a firm decision to foetal/placenta deliverance within 12 hrs, maximum 24 hrs, must be reached. Expedient delivery after stabilization of mother's vitals, initiates the resolution of eclampsia, hence less morbidities.[24, 25]

One study showed that when admission – delivery interval was less than 12 hours irrespective of mode of delivery; recovery rate without the occurrence of serious maternal complication was 82.6% compared with 59.4% in the 12 – 48 hrs group and 39% in the more than 48 hrs group. Intra-category comparison on effect of mode of delivery on maternal morbidity did not reveal a significant correlation. Admission – delivery interval played an important role in determining severity of maternal morbidity in the immediate postpartum period. Termination within 12 hrs of admission helped prevent avoidable serious severe maternal morbidity in cases of severe pre-eclampsia and eclampsia. This was more so in the subset of women with HELLP syndrome where the complication rate

exceeded 80% with delay in termination. The mode of delivery had no impact on severity of maternal morbidity.[34]

The very severe morbidity from eclampsia varied with the number of seizures, the quality of treatment, and the speed with which treatment was made available. Eclampsia mandates immediate delivery within 24 hours as per WHO guidelines.[35]

Levels of maternal mortality and morbidity tell us about the risk attributable to pregnancy and childbirth as well as the performance of health systems in terms of access to health care and the quality of care provided. However, accurate assessment of these indicators has been problematic.[36]

The concept of very severe maternal morbidity is relatively new in maternal care, but is increasingly becoming important in areas with low maternal mortality ratios or where the geographic area is small. The use of data collected has been shown to be a mechanism for identifying health system failures or priorities in maternal health care more rapidly than maternal deaths. Its routine use as an indicator, however, is limited due to the lack of uniform criteria of identification of the cases at present.[37, 38.]

A study on early risk assessment of severe pre-eclampsia by using symptoms and laboratory tests to predict significant maternal morbidity was done in Mississippi. Severe pre-eclampsia or eclampsia with or without HELLP's syndrome were studied to develop parameters associated with low, moderate, and high risks for the subsequent development of significant maternal morbidity involving the hematologic and coagulation, cardiopulmonary, and hepato-renal systems. The presence of nausea and vomiting,

epigastric pain, or both and high levels of lactate dehydrogenase, aspartate aminotransferase, and uric acid concentrations, was predictive of high risk of morbidity.[39]

A study done in eleven regions of nine European countries, on incidence of three severe obstetric conditions: pre-eclampsia/eclampsia, postpartum haemorrhage and sepsis, had difficulties in applying the definition across the countries, even though the above three were the leading causes of very severe maternal morbidities, and ICU admissions. Mothers Mortality and Severe Morbidity (MOMS) was a European initiative aimed to overcome these problems by using common definitions and collecting population-based data. Yet the reported incidence varied significantly across the countries.[40]

Another study done in Sweden, to identify factors predicting for maternal or foetal complications, only the diastolic blood pressure and gestational age could predict severe maternal complications (i.e. any of the HELLP syndrome, placental abruption, oliguria, and eclampsia). Independent variables were blood pressure and biochemical variables as well as maternal age, weight, parity and gestational age at appearance of preeclampsia and delivery.[41]

One study identified correlates of a prolonged length of stay (PLOS) in women hospitalized for pre-eclampsia/eclampsia in Texas 2004 – 2005. PLOS was defined as a stay greater than 5 days. The crude incidence of PLOS was 17.5%. Advancing maternal age was positively associated with PLOS: for every 10-year increase in maternal age, there was a 20% increase in risk of prolonged lengthy hospital stay.[42]

The parity was investigated to demonstrate its effect on major maternal morbidity in the eclamptic mother with, or without HELLP Syndrome. The study revealed that eclampsia was significantly more common in nulliparas than in parous patients, but the later often demonstrated major maternal morbidity associated with eclampsia (50%) than did nulliparas. Unless parous patients with severe preeclampsia with or without HELLP syndrome developed eclampsia, their disease acuity did not differ significantly from their nullipara's counterparts.[43]

A study in South Africa showed that SAMM (severe acute maternal morbidity) was seven times greater than the mortality. Substandard care was similar in cases of SAMM and mortality and uncomplicated hypertensive patients. Audit of SAMM was informative, could be conducted more frequently, and in small sample population groups. It also allowed interviews of patients, hence problems of inefficient documentation was obviated.[44]

One study tried to determine the prevalence of severe acute maternal morbidity (SAMM) worldwide by reviewing 30 studies worldwide in the systematic review for W.H.O. Fourteen studies used defined SAMM condition while the remainder used a response to an event such as admission to intensive care unit as a proxy for SAMM. Criteria for identification of cases varied widely across studies. Prevalence's varied between 0.80% – 8.23% in studies that used disease-specific criteria, 0.38% – 1.09% in the group that used organ-system based criteria, and 0.01% – 2.99% in studies that used management-based criteria. It was not possible to pool data together to provide summary estimates or comparisons between different settings due to variations in case-identification

criteria. Authors saw the need to set and standardize uniform criteria to classify patients as SAMM.[45]

Most of the authors assessed very severe maternal morbidities by dealing with specific diagnosis (i.e. specific clinical conditions of morbidity) e.g. abruption placenta, DIC, pulmonary oedema, HELLP Syndrome, acute renal failure, aspiration pneumonia, CVA, or cardio-pulmonary arrest. However when we take eclampsia as an entity and study its very severe morbidity outcome indicators, we see lack of previous studies focusing on indicators of very severe maternal morbidity among eclamptic mothers.

Admission to ICU for eclamptic mothers were not described in details e.g. days or duration of stay, what was done to patients e.g. NGT insertion for feeding, resuscitation drugs used to save lives, or physiotherapy after resolution of the disease.

3.0 STATEMENT OF THE PROBLEM:

Eclampsia is a leading cause of maternal mortality at Muhimbili National Hospital, according to the study by Kazaura et.al, done between 1999 -2005. So even though eclampsia is common at Muhimbili National Hospital, there is no study done on the predictions of very severe maternal morbidity, and there is no documentation to determine factors that could independently predicts very severe maternal morbidity and its outcome among eclamptic patients managed at Muhimbili National Hospital. The higher the maternal mortality in eclamptic patients directly reflects the higher number of patients with very severe maternal morbidity.

4.0 RATIONALE OF THE STUDY:

Determinants like demographic factors of the patients, management of the disease, disease factors, with their *association* to very severe maternal morbidity like duration of stay in ICU, need for naso-gastric tube for feeding, need for resuscitation drugs, and need for physiotherapy need to be measured at Muhimbili National Hospital. Understanding of very severe morbidity and their prediction will help to put focus on prompt and appropriate interventions together with good quality nursing care.

5.0 RESEARCH QUESTION:

What factors predict very severe maternal morbidity to the patient after an eclamptic fit?

6.0 OBJECTIVES:

6.1 Broad objective;

- To study predictors of very severe maternal morbidity outcome among eclamptic mothers admitted at Muhimbili National Hospital.

6.2 Specific objectives; -

1. To determine the proportion of eclamptic mothers admitted at ICU who developed VSM
2. To determine the association of the specified demographic, management and disease risk factors with occurrence of VSM.
3. To study how the specified risk factors predicts very severe maternal morbidity among eclamptic mothers.

7.0 METHODOLOGY:

7.1 Study setting:

Muhimbili National Hospital is a consultant, tertiary - referral centre, receiving patients from all over the country, but mainly from three district municipal hospitals of Amana, Mwananyamala and Temeke. MNH with a daily deliverance of about 40 women per day, is situated in Dar es Salaam, the country's largest city which has a total population of 3.4 million with an annual growth rate of 4.3%, according to 2002 national population Census. Most of the services here are provided free of charge. The municipal hospitals cannot monitor eclamptic patients, or eclampsia complications, or anticipated premature deliverance due to ICU facilities inadequacy; hence all diagnosed cases of eclampsia, after initiation of MgSO4 are referred to Muhimbili National Hospital for further management. The MNH also serves as teaching hospital for the Muhimbili University of Health and Allied Sciences which is the public and largest medical university in Tanzania.

7.2 Study design:

A retrospective, cross sectional-analytical study design was taken. Case notes of all eclamptic patients who were admitted at MNH ICU ward from 1st of Jan 2008 to 31st of Dec 2008 was reviewed and information needed extracted.

7.3 Study population:

All admitted patients in Obstetric ICU at MNH, with a diagnosis of Eclampsia from 1st of Jan 2008 to 31st of Dec 2008. The target population in this study were all pregnant patients or those in puerperium period who developed fits in the wards, en route to hospital, at home but later brought to the hospital or cases that were referred from the peripheral clinics or hospitals.

7.4 Sampling procedure:

Number of patients who were admitted in obstetrics ICU, from 1st of Jan 2008 to 31st of Dec 2008 was all eligible for enrolment. This number was 628 according to database records. Admission electronic records and admission books were used to produce the list of patients and file numbers and other supplementary information about patients. All their files were retrieved, and studied. Files were tracked according to the checklist, which was frequently cross-checked against available files.

7.5 Inclusion criteria:

All admitted patients in Obstetrics ICU who were diagnosed to have eclampsia, were eligible for the study.

7.6 Exclusion criteria:

Patient admitted in Obstetrics ICU, who had no fits, or had eclampsia with any of the following diagnosis; epilepsy, meningitis, cerebral malaria, fainting attacks, hypoglycaemia, hyperglycaemia, chorea gravidarum, encephalitis, HIV encephalopathy.

7.7 Data collection procedure:

Medical records at Muhimbili National Hospital. Two trained research assistant were recruited to assist the principal investigator in the study. Research assistants were responsible for collecting and sorting out the files. Extraction of information from the files and filling up of the questionnaires was done by the Principal Investigator. The list of files was cross-checked frequently with the availability of files to be studied by the Principal Investigator, to improve the data collection.

7.8 Data analysis:

Each questionnaire was assigned with an identification number. Data entry was done through Statistical Package for the Social Sciences (SPSS) 16.0 for statistical analysis. Cross tabulation was done and comparisons were made using the *chi square test* for categorical variables i.e. age, parity, gestational age, mode of delivery, time interval from admission to delivery, occurrence of fits, number of fits and hospitals which referred patients to MNH. Multiple logistic regression analyses were conducted to calculate odds ratios and 95% confidence intervals that helped to estimate the effect of explanatory variables on very severe morbidity outcome. The level of significance was taken as P value < 0.05. All variables with significant p-values in the bivariate analysis were included in the multivariate analysis to assess how independently each variable predicted the very severe maternal morbidity.

7.9 Ethical issues:

Clearance was sought from the Ethical Committee/ Research and Publication Committee of the Muhimbili University of Health and Allied Sciences, and granted. Permission from the Director of Muhimbili National Hospital also requested and granted. Study began after the clearance being obtained. No names of the patients were recorded; instead code numbers were used to collect data.

Care of eclamptic mothers at MNH

Eclampsia patients who are admitted at MNH come with their antenatal cards and a referral note. They are initially registered in the hospital's electronic database which registers their demographic information, referral details and the admitting ward. The patients are then transferred to a special 10 bed Intensive Care Unit (ICU) where more details are extracted and entered in a ward's register book.

Maternal socio-demographic information is detailed in the antenatal card, referral note and patient's case note all of which are retained by the hospital after discharge.

Care in the ICU at MNH is offered by doctors and nurses who are trained in managing eclampsia according to the existing protocol. There is always a rotating specialist in charge of the ward who conducts at least two rounds daily. Any new patient is attended by a resident doctor and the specialist on duty within one hour. Drugs are administered by the nurses who also provide nursing care to the patients. The usual management protocol for eclamptic patients includes intravenous MgSO4 to prevent and control eclamptic fits. A loading dose of 4g is given slowly intravenously (over 5-10 minutes) followed by a maintenance dose of 1g hourly for 24 hours (counted from the last fit or delivery). Rapid control of blood pressure is achieved by a slow intravenous Hydrallazine (10 mg) repeated 20-30 minutes to control the diastolic blood pressure between 90-100 mmHg. Long term control of blood pressure is achieved with Methyl dopa. As part of routine care, delivery should be achieved within 12 hours after admission. Induction of labor if necessary is achieved by vaginal Misoprostol or Oxytocin. Any divergence from this protocol is individualized and discussed with a specialist.

Vital signs are checked and recorded on a special sheet half hourly. Number of fits, deep tendon reflexes, urinary protein levels, medication and hourly urine output are also documented. Labor progress and delivery details are recorded on the partogram. Mothers who have delivered and who show good progress in terms of control of fits, improved level of consciousness, improved vital signs including the blood pressure are usually transferred to postnatal ward after completion of a maintenance dose of MgSO4.

The decision to transfer a patient to an ordinary postnatal ward is reached based on the specialist's opinion during a ward round and after documentation in the case note. The usual duration of stay in ICU is 48-72 hours regardless of the mode of delivery.

8.0 CRITERIA FOR VERY SEVERE MATERNAL MORBIDITY:

Presence of any of these conditions defines a very severe maternal morbidity.

- Duration of stay in ICU; those patients who stayed in Obstetrics ICU for more than three days due to severity of the disease.

- Need for naso-gastric tube for feeding; those patients who needed this method of feeding because of subconscious levels which hindered their swallow reflex.

- Need for physiotherapy; those patients who needed physiotherapy after recovering from eclampsia so as to regain their lost normal muscles and/or joint functions i.e. patients with focal neurological deficits.

- Need for resuscitation drugs like lasix, adrenaline, mannitol, steroids, etc; those patients whom the resuscitation drugs were used to save their lives during the illness e.g. mannitol or steroids to reduce brain oedema. Steroids for foetal lung maturity were not taken as the criteria for resuscitation drug usage.

9.0 RESULTS:

A total of 628 mothers were admitted to obstetrics ICU, among them 366 had eclampsia. The age of eclamptic mothers ranged from 13 to 48 years, with a mean of 23.11 (standard deviation of 5.41). There were 18 maternal deaths among the 366 eclamptic patients giving a case fatality rate of 4.9%, while 132 patients (36.1%) met the criteria for very severe maternal morbidity. Patients who had longer duration of stay of more than 3 days in ICU were 121 (33.1%). Those who needed NGT for feeding were 20 pts (5.5%), needed physiotherapy were 14 pts (3.8%) and needed resuscitation drugs were 49 pts (13.4%). A total of 75 mothers had incomplete data especially with regards to gestation age and intrapartum events, thus were excluded in some of the calculations.

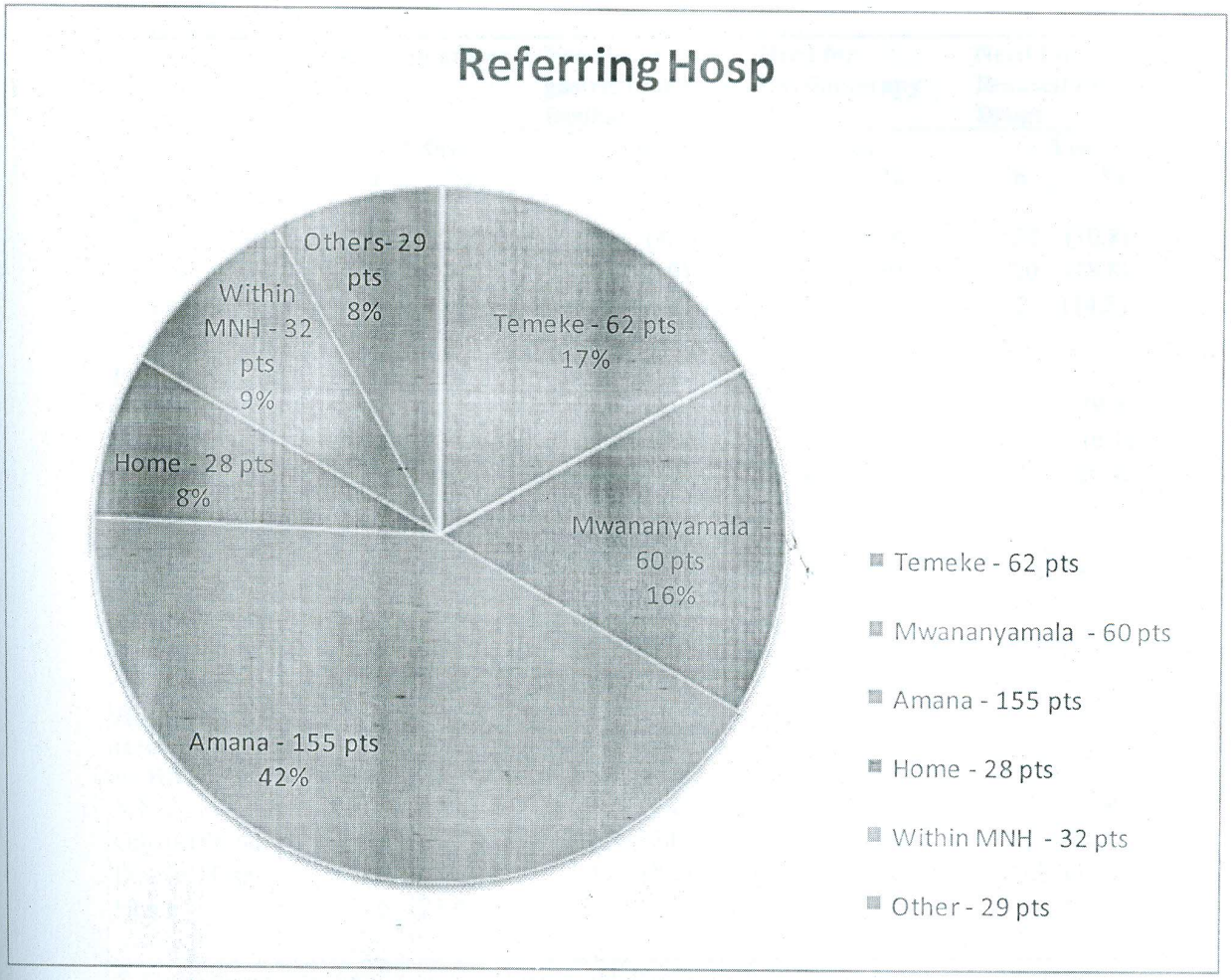
The baseline characteristics of eclamptic patients are summarized in Table 1. Mothers who were 24 years old or younger constituted the highest number of patients (69%), while primigravida accounted for more than 55%. Almost 60% were delivered vaginally, while 4 patients died before they were delivered.

Table 1: Baseline characteristics of eclamptic patients, admitted in Obstetrics ICU in 2008 at MNH.

Age	(n = 366)	
	n	%
≤ 24 years	251	68.6
25 - 34 years	101	27.6
≥35 years	14	3.8
Parity		
0	202	55.2
1 - 2	137	37.4
≥ 3	27	7.4
Gestational age*		
< 33 weeks	63	17.2
33 - 36 weeks	103	28.1
> 36 weeks	129	35.2
Mode of delivery†		
SVD	206	56.3
C/S	145	39.6
Others ††	11	3.0
Time interval from admission to delivery**		
≤ 12:00 hours	166	45.4
12:01 - 24:00 hours	82	22.4
≥ 24:01 hours	43	11.7
Occurrence of fit		
Ante partum	270	73.8
Intra partum	25	6.8
Post partum	71	19.4
Number of fits		
One	94	25.7
Two	123	33.6
Three or more	149	40.7

* Data of 71 patients were not available in the files; these were postpartum eclamptic pts.
** Data of 75 patients could not be retrieved; these 71 pts were postpartum eclamptic pts whose data were not recorded, and 4 patients died before delivery.
† Four patients died before they were delivered.
†† Others include LCVE, ABD and destructive delivery.

Figure 1: Distribution of referring hospitals of eclamptic patients to Muhimbili National Hospital in 2008



In figure 1 above, patients referred to Muhimbili National Hospital from district/ municipal hospitals were 277 patients (75.7%). Each individual contribution is shown in the fig above. Other referrals came from Mkuranga, Cardinal Rugambwa-Ukonga, Kigamboni Navy, Bagamoyo, Lugalo and private hospitals.

Table 2: Association between specified demographic and indicators of very severe morbidity

	Duration of stay in ICU		Need for naso-gastric tube for feeding		Need for Physiotherapy		Need for Resuscitation Drugs	
	> 3 days		Yes		Yes		Yes	
	n	%	n	%	n	%	n	%
Age								
≤ 24 years	81	(32.3)	12	(4.8)	12	(4.8)	27	(10.8)
25 - 34 years	34	(33.7)	7	(6.9)	7	(6.9)	20	(19.8)
≥ 35 years	6	(42.9)	1	(7.1)	1	(7.1)	2	(14.3)
Parity								
0	65	(32.2)	4	(2.0)	4	(2.0)	20	(9.9)
1 – 2	46	(33.6)	12	(8.8)	12	(8.8)	22	(16.1)
≥ 3	10	(37.0)	4	(14.8)	4	(14.8)	7	(25.9)
Gestational age*								
≤ 33 weeks	27	(42.9)	5	(7.9)	5	(7.9)	13	(20.6)
33 - 36 weeks	39	(37.9)	3	(2.9)	3	(2.9)	8	(7.8)
> 36 weeks	38	(29.5)	5	(3.9)	5	(3.9)	15	(11.6)
Hosp which referred patients to MNH								
MNH	5	(15.6)	2	(6.2)	2	(6.2)	3	(9.4)
Others (Private)	16	(55.2)	4	(13.8)	4	(13.8)	7	(24.1)
District Hosp	94	(33.9)	14	(5.1)	14	(5.1)	35	(12.6)
Home	6	(21.4)	0		0		4	(14.3)

* Gestational age details of 75 pts were not available, these were among the postpartum eclamptic pts and those 4 pts who died undelivered.

Table 3: Association between management of the disease, disease factors, and indicators of very severe maternal morbidity

	Duration of stay in ICU		Need for naso-gastric tube for feeding		Need for Physiotherapy		Need for Resuscitation Drugs	
	> 3 days		Yes		Yes		Yes	
	n	%	n	%	n	%	n	%
Mode of delivery†								
SVD	56	(27.2)	11	(5.3)	11	(5.3)	28	(13.6)
C/S	59	(40.7)	5	(3.4)	5	(3.4)	15	(10.3)
Others	6	(54.5)	2	(18.2)	2	(18.2)	2	(18.2)
Time interval from admission to delivery†								
≤ 12:00 hours	38	(22.9)	6	(3.6)	6	(3.6)	19	(11.4)
12:01 - 24:00 hours	34	(41.5)	4	(4.9)	4	(4.9)	9	(11.0)
≥ 24:01 hours	32	(74.4)	1	(2.3)	1	(2.3)	4	(9.3)
Occurrence of fit								
Ante partum	96	(35.6)	11	(4.1)	11	(4.1)	33	(12.2)
Intra partum	8	(32.0)	2	(8.0)	2	(8.0)	3	(12.0)
Post partum	17	(23.9)	7	(9.9)	7	(9.9)	13	(18.3)
Number of fits								
Two or less	63	(29.0)	5	(2.3)	5	(2.3)	16	(7.4)
Three or more	58	(38.9)	15	(10.1)	15	(10.1)	33	(22.1)

† Data on 75 pts could not be retrieved.

From table 2 A, the specified demographic was cross tabulated to the indicators of very severe maternal morbidity to see their association. Parity with the need for NGT (p = .002), and parity with the need for resuscitation drugs (p = .036) showed a level of significance. Also gestational age with the need for resuscitation drugs (p = .047) showed significant value. The other variables of specified demography to the indicators of very severe morbidity did not show a level of significance, hence no correlation seen between independent variables and VSM.

From table 2 B, the management of the disease and disease factors, were cross tabulated to the indicators of very severe maternal morbidity to see their association. Mode of delivery with longer stay at ICU (p = .010), time interval from admission to delivery with longer stay at ICU (p = .000) and number of fits with longer stay at ICU (p = .048) showed a level of significance. Also mode of delivery with the need for NGT (p = .000) and number of fits with the need for NGT (p = .001) showed statistical significant value. Also mode of delivery with the need for resuscitation drugs (p = .000) and number of fits with the need for resuscitation drugs (p = .000) showed level of significance. The association of the specified demographic, management of the disease and disease factors with the need for physiotherapy, none of the independent variables gave a value of significance after cross tabulation, hence no correlation seen with dependent variables (need for physiotherapy).

The multiple logistic regression analyses were performed to determine whether the specific maternal variables were significant predictors of very severe maternal morbidities. The specific maternal variables of interest were then combined to have one outcome variable (dependent) which is the measurement of very severe maternal morbidity.

Table 4: Multiple regression analysis to predict very severe maternal morbidity among eclamptic patients admitted at Obstetric ICU

Variable	Bivariate Analysis OR (95% CI)		Multivariate Analysis OR (95% CI)	
Mode of delivery				
SVD	1.00		1.00	
C/S	1.82	(1.16 – 2.85)	2.80	(1.50 – 5.10)
Instrumental Delivery	2.92	(0.85 – 10.05)	3.18	(0.82 – 12.35)
Time interval from admission to delivery				
≤ 12:00 hours	1.00		1.0	
12:01 - 24:00 hours	2.35	(1.32 – 4.17)	2.25	(1.23 – 4.10)
≥ 24:01 hours	10.40	(4.28 – 25.24)	11.10	(4.72 – 25.97)
Parity				
0	1.00		1.00	
1 - 2	1.14	(0.73 – 1.80)	1.99	(0.98 – 4.02)
≥ 3	0.54	(0.68 – 3.49)	1.25	(0.25 – 6.23)
Gestational age				
≤ 33 weeks	1.00		1.00	
33 - 36 weeks	0.55	(0.29 – 1.05)	0.65	(0.30 – 1.41)
> 36 weeks	0.41	(0.22 – 0.77)	0.61	(0.28 – 1.34)
Number of fits				
One	1.00		1.00	
Two	1.26	(0.70 – 2.28)	1.28	(0.62 – 3.14)
Three or more	2.08	(1.18 – 3.66)	1.49	(0.75 – 3.10)

10.0 DISCUSSION:

Eclampsia was found to be primarily a condition of young primigravida women, consistent with the current findings in our study that more than 68% of patients were less than 24 years old and more than 55% were primigravida. This was also found in most studies, e.g. in Nigeria 58.5% of eclamptic patients were less than 20 years and 78% were primigravida[2], in Malaysia 50% were less than 25 years old, and 62% were primigravida[26]. Similar results where 67% of patients were less than 25 years were previously reported at the same hospital[16]. One author point out that eclampsia was a disease of prim gravid women, and even calculated the ratio of nulliparas to multipara as 6 – 8 to 1.[8]

Our findings showed that eclampsia was common at or near to term, as greater percentage of eclampsia (35.2%) in this study had occurred after 36 weeks of gestation. This was also true to most of the studies conducted elsewhere, e.g. in Nigeria had as high as 62.5% [30] and at MNH majority of 46% of the patients were in 37 – 42 weeks category[16].

On the occurrence of fits, our study showed ante partum 73.8%, intra partum 6.8% and postpartum 19.4%. Almost similar results were obtained by different authors, where a range of ante partum 38 - 53%, intra partum 18 - 36% and postpartum 11 – 44% was obtained[9] and at MNH 47% were ante partum, 41% and 12% were intra partum and postpartum respectively.[16] A study in Northern Nigeria, ante partum was 32.9%, intra partum was 54.1% and postpartum was 13.0%[2]

In delivery interval from admission, 45.4% of patients were delivered in less than 12 hours category, while 22.4% in 12 – 24 hours category, conforms to WHO guidelines. There was no improvement in delivery interval, as the previous study at the same hospital

showed one third of admitted patients (33.3%) were not delivered within 24 hours[16], similarly in our study it was 32.2%. Delivery by vaginal was 56.3% while caesarean section was 39.6% which was higher compared to that of 25% in a study done at the same hospital in 2006.[16]

The source and pattern of admission has not changed, as municipal hospitals referred three quarters of all the eclamptic patients referred to MNH in this study, compared to the same figure of three quarters in earlier study[16].

A case fatality rate (CFR) of 4.9% in our study has not improved compared to that seen at similar hospital in a study done in 1999 to 2000 of 5.0% [5] and another done in 2006 of 7.7% [16]; however the UN guidelines on EOC, the CFR should be less than 1%.
In developed countries CFR is lower, but in some other developing countries is even higher, 9 – 32% e.g. a CFR of 22.33% reported in northern Nigeria[17].

Longer duration of stay in ICU of more than three days was seen more in older women compared to the younger women in this study (table 2). Almost 43% were in 35 years or more age group category. This correlates with other studies which demonstrated that very severe morbidity increased with increase in maternal age.[28] One author found that the risk of severe morbidity and mortality was higher for older women compared to younger women.[29] Another study by showed that advancing maternal age was positively associated with prolonged length of stay in ICU.[39]

Parous women had longer stay in ICU (37%) compared to nulliparas (table 2 A). This was also seen by another author, where eclampsia although occurred more in nulliparas, but more parous women had severe maternal morbidity compared to nulliparas.[40]

Eclampsia before 34 weeks of gestation, was a major cause of maternal morbidity.[28] Also eclampsia before 32 weeks was associated with severe forms of maternal morbidity.[36] In our study, we also found that eclampsia before 33 weeks carried almost 43% of those who stayed longer in ICU compared to other gestational age group categories. Another study in Sweden, found that Diastolic Blood Pressure and gestational age could predict maternal morbidity.[38]

Mode of delivery showed a statistical significant value in duration of stay in ICU, and even after controlling the confounders, it was highly significant, i.e. mode of delivery did contribute to lengthy stay in ICU. This did not correlate to one study, which showed that the mode of delivery had no impact on severity of maternal morbidity.[31]

Time interval from admission to delivery showed a statistical significant value, and even after regression analysis showed a highly significance value. The longer the time interval is, the more frequency of fits are, the longer duration of stay in ICU due to slow recovery is, and the more very severe morbidity.

Hospitals which referred patients to MNH did not give a significant p value, even when regression analysis was done, meaning that referring hospitals did not contribute to the longer stay of patients in ICU.

When analyzing association of the specified demographic, management and disease factors on the need for naso-gastric tube for feeding, parity, mode of delivery and number of fits showed that they contributed to the outcome of interest of very severe morbidity. Parous women contributed a major number of those who needed NGT, and so was those with more number of fits. After multiple regression analysis number of fits still showed to contribute to severe maternal morbidity, but parity lost its significance (table 3). One study had similar findings compared to our study, as pointed out that very severe morbidity varied with the number of seizures, the quality of treatment and speed of treatment available.[32]

In the association of the specified demographic, management and disease factors on the need for physiotherapy after resolution of eclampsia, none of the independent variables could show their contribution to very severe maternal morbidity. Due to small sample size, some of the indicators of VSM were not very prevalent, the adverse events were few leading to the wide 95% confidence intervals in some regression analyses.

Analysis of specified demographic, management and disease factor on the need for resuscitation drugs after eclamptic fit, parity, gestational age, mode of delivery and number of fits showed a relationship of these variables with the outcome of very severe maternal morbidity. Of the parous eclamptic patients majority of those who needed resuscitation drugs were multiparas. Eclampsia before 33 weeks and 22% of those who had multiple seizures needed resuscitation drugs mostly compared to their respective group's categories. This correlates to other studies.[28, 32, 38, 40]

Multiple logistic regression analyses were performed to determine whether specific maternal variables were significant predictors of very severe maternal morbidity; mode of delivery, time interval from admission to delivery and number of fits showed statistical significance. This proved that the variables contributed to the predicted outcome. Variables which did not show significance before regression analysis, but showed significance after the analysis showed that the variable contributed to the outcome, but was masked by other factors e.g. small sample size.

Hospital referring patients to MNH was not statistically significant in predicting very severe morbidity, irrespective of poor clinical presentation at admission. Three quarters of all eclamptic patients were coming from municipal hospital, indicating that majority of pts who had VSM were coming from those hospitals, yet we could not establish the contribution of referring hospitals to VSM. Large sample size study is needed to show its contribution to VSM. After bivariate analysis; gestational age, mode of delivery, time interval from admission to delivery and number of fits, showed statistical significant values, but on multivariate analysis gestational age lost its significant value after controlling the may be contributing factors to the outcome. Our study differed from one study, which showed that mode of delivery had no impact on severity of maternal morbidity.[31] In our study, it is three times more risky to have very severe maternal morbidity if delivery was operative or instrumental.

When deliverance was delayed by more than 24 hours, the risk of very severe maternal morbidity was eleven times more, while with more number of fits, the risk almost doubled.

12.0 CONCLUSION:

Eclampsia poses an important obstetric problem world-wide, particularly in developing countries. The unacceptable high case fatality rate in eclampsia is a satire upon the very concept of safe motherhood. The problem of averting this tragedy lies in the early detection and treatment at the first appropriate level.

These results underscore the importance of prompt, timely and as less invasive delivery as possible in prevention of VSM among eclampsia patients.

Mode of delivery, time interval from admission to delivery and number of fits can be used to predict the very severe maternal morbidity.

Ineffective pre-referral management of eclampsia and the failure to expedite delivery remain the key underlying factors. Future interventions should target community education and improvement of case management at all the referral facilities including MNH

13.0 RECOMMENDATION:

There is a need to improve documentation of relevant information regarding the disease. Most of the referred patient's files missed essential data, e.g. time of occurrence of first fit, time of initiation of MgSO4 before referral, in postpartum eclamptic patients.

There is a need to design the specific parameters to measure very severe maternal morbidities in eclamptic patients, as various studies used different criteria to study severe morbidities

Larger scale studies or multiple study centres comprising large sample sizes are needed to study very severe maternal morbidity, to improve the outcome result of interest.

More efforts are needed to improve and strengthen the municipal hospitals e.g. competent health care personnel, operating theatres, quality ICU, availability of essential drugs like anti hypertensive, MgSO4 and resuscitation drugs, as delays in intervention was associated directly with very severe maternal morbidity.

Prompt, timely and appropriate actions on eclampsia patients are needed, so as to avert the dangers of very severe morbidity to eclamptic mother.

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