OBSTETRIC OUTCOME OF ECLAMPTIC PATIENTS MANAGED WITH DIAZEPAM COMPARED WITH PATIENTS MANAGED WITH MAGNESIUM SULPHATE AT MUHIMBILI NATIONAL HOSPITAL

A retrospective cohort study

By

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A Dissertation submitted in partial fulfilment of the requirements for the degree of Master of Medicine (Obstetrics and Gynaecology) of the University of Dar Es Salaam.

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the University of Dar Es Salaam, a dissertation entitled *"Obstetric outcome of eclamptic patients managed with diazepam as compared with patients managed with magnesium sulphate at Muhimbili National Hospital,"* in partial fulfillment of the requirement for the Degree of Master of medicine (Obstetrics and Gynaecology).

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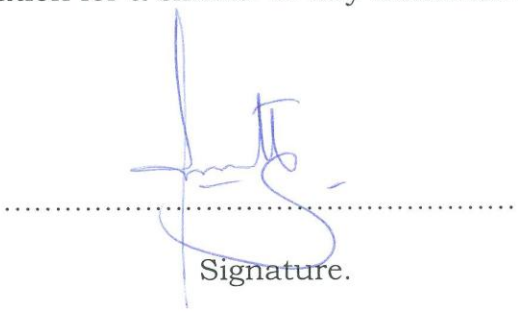
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DEDICATION

Dedicated to my mother, Petronila, for her unfailing support and whose dedication made all my studies possible; to my sons Francis and Paul, Anunciatha and my little daughter Faith Nyabagaya who knew my love even if not always present during this very tiring period.

ABSTRACT

Background: Eclamptic seizures in association with the syndrome of pre-eclampsia remain an important cause of maternal and perinatal deaths. Diazepam, from among other drugs, has remained the main drug in use for many years in the management of eclampsia at the MNH and in other medical facilities throughout Tanzania. Magnesium sulphate has been reintroduced more recently at the MNH. Systematic documentation on the obstetric outcome either of the use of diazepam or Mgso4 in the treatment of eclampsia has not been documented and was clearly needed.

Objectives: To compare Obstetric outcome of patients with eclampsia managed with diazepam and those managed after introducing magnesium sulphate. The obstetric outcome variables included; Recurrences of seizures, maternal deaths, fetal Apgar scores and duration of maternal stay under intensive care.

Design: Retrospective cohort study.

Setting: MNH, Dar Es Salaam, Tanzania.

Patients: To select patients for participation in the study the files of patients were reviewed. Out of a total of 945 pregnant women with eclampsia who were admitted at MNH during the two study periods, 630

met the criteria for inclusion in the study. 312 were on diazepam from January to October 2000 and 318 were on Mgso4 from January to October 2001.

Methodology: The author compared the observed obstetric variables in 318 patient files that were given MgSo4 with 312 who were given diazepam. The instructions for loading doses, 24 hours maintenance therapy and treatment of additional convulsions were according to the well-defined treatment protocols.

Results: Use of MgSo4 resulted into fewer recurrences of convulsions than diazepam (14.5% vs. 45.2%, $P < 0.01$). {The absolute risk reduction (ARR) of 30.7% converts to a number of eclamptic women who need to be treated with MgSo4 rather than diazepam to prevent 1 recurrent convulsion}. A trend toward lower maternal mortality was noted after introducing MgSo4 than when diazepam was used (3.1% vs. 5.1%, $P = 0.21$. There was a significant differences in the number of asphyxiated babies with Apgar scores < 7 at 5 minutes and had less serious infant morbidity and mortality i.e. (10.5% MgSo4 versus 29.6% diazepam), $p = 0.00$. Mothers stayed less time under intensive care facilities (65.2 %Mgso4 vs. 37.0 %diazepam), ***P = 0.00.***

Conclusions: MgSo4 was more effective than diazepam for reducing recurrent convulsions. The use of Mgso4 showed a trend towards reduced maternal mortality, less stay time under intensive care and better fetal outcome in terms of Apgar score at 5 minutes when it was used.

Recommendations: Since Mgso4 is more effective and cheaper than diazepam, should be adopted in places not in use in the management of eclamptic fits in Tanzania

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OPERATIONAL DEFINITIONS

1). **Eclampsia**: Is the occurrence of one or more generalized tonic clonic convulsion in association with the syndrome of pre-eclampsia or Pregnancy Induced Hypertension.

2). **Preeclampsia**: is an occurrence of hypertension (blood pressure of >130/90mmHg) in a pregnant woman with proteinuria ± edema after 20 weeks gestation in a previously normotensive woman.

3) **Maternal mortality**: A death in a woman while pregnant, or within 42 days after termination of pregnancy irrespective of duration, site of pregnancy from any cause related or aggravated by the pregnancy, or its management but not from incidental causes.

4) **Perinatal mortality**: the sum of stillbirths and deaths within seven days of life.

5) **Stillbirths**: Is when a fetus dies in utero having gestation age >28 weeks.

6). **Effectiveness**: Is the degree to which a system featuring has capabilities to meet the user's needs. (from standard dictionary 1990).

7). **Maternal mortality Ratio**: Is the number of maternal deaths per 100,000 live births.

8).**Eclamptic fit:** Is sterio-type-tonic-clonic movements that occur in a pregnant woman in association with a clinical syndrome of pre eclampsia.

ABBREVIATIONS

Mgso4: Magnesium Sulphate.

MUCHS: Muhimbili University college of Health Sciences.

MNH: Muhimbili National Hospital.

SVD: Spontaneous Vaginal Delivery

LCVE: Low Cavity Vacuum Extraction

C/S: Caesarean Section

SB: Stillbirth

SBM: stillbirth macerated

SBF: stillbirth fresh.

SBP: Systolic Blood Pressure.

DBP: Diastolic Blood Pressure.

ICU: Intensive Care Unit also referred to as eclampsia room.

1. INTRODUCTION AND LITERATURE REVIEW

The effectiveness of magnesium sulphate (MgSo4) in the control of eclamptic fits may not be obvious, unless there is systematic documentation of its effects on the obstetric outcome in eclampsia. If its effectiveness is clearly evident this is more likely to result in it being more widely used in Tanzania.

Diazepam has remained the drug of choice for the management of eclamptic fits in Tanzania. It is the drug recommended by the current Standard Treatment Guidelines (STG) and National Drug List for Tanzania (NEDLIT), second edition of 1997 [29]. It is therefore, included in the essential drug kit, not only for eclampsia but also for management of other types of convulsive disorders.

Magnesium sulphate is not a new drug at this hospital. It was the anticonvulsant used for eclampsia in the early 1970's and 80's. The reasons that it ceased to be used are not clear. Antidotal evidence indicates that, the main reason why it has not been used is its unavailability. It has not easy to identify other possible reasons to why it has not been used since its use in the 1970s and '80s in the management of eclampsia is not documented.

Eclampsia is a disorder of pregnancy characterized by occurrence of one or more convulsions in association with the syndrome of pre-eclampsia. Pre-eclampsia, is a multi-system disorder characterized by a rise in blood pressure, proteinuria and occasionally oedema[10]. It carries a serious risk of maternal and fetal morbidity and mortality. The negative impact of this on the limited resources of care and utilization of hospital beds is well documented. [4,17,18,20,22]

Eclampsia is known to be common in first pregnancy, which is also true for severe pre-eclampsia. In the UK, eclampsia occurs in approximately 20% of primigravidas and 10% in multigravidas.[25] Studies show that there is a J-shaped curve of the incidence of eclampsia with age, with a slight increase in very young primigravidas and a more marked increase in older primigravidas.[26] It commonly occur in the antepartum period and the minority of cases may initially manifest in the postpartum period [1,3,5]. In 1994 Douglas and Redman in UK found that 44 percent of seizures in eclampsia occurred postnatal, the remainder being antepartum (38%) and intrapartum (18%)[2].

The pathophysiology of eclampsia is thought to involve cerebral vasospasm leading to ischaemia, disruption of the blood brain barrier

and cerebral oedema. Neurological complications may include coma, focal motor deficits and cortical blindness. Cerebrovascular haemorrhage is a complicating factor in 1-2% [2] of patients.

It also causes multiple organ failure and a number of both metabolic and haematological derangements. These may include, pulmonary edema, disseminated intravascular coagulation (3%) and thrombocytopaenia.[6] Other complications like, haemolysis, elevated liver enzymes and low platelet count (HELLP syndrome) occur in (3%) renal failure (4%) and adult respiratory distress syndrome (3%).[2]

These complications are also responsible for bad obstetric outcome observed in patients with eclampsia apart from eclamptic fits alone.

Over half a million women die of pregnancy related causes annually and 99% of these deaths occur in the developing world. [11] Eclampsia alone accounts over 50,000 maternal deaths a year worldwide. [5]

In developed countries the incidence of eclampsia has declined from 74.1 per 10,000 to 7.2 per 10,000 deliveries in the last 60 years (1930's to 1980's). [4] The reasons for this decline are said to be a result of the prevention of pre eclampsia using the standardized drugs like Mgso4, in addition to universal better antenatal care services. Currently the incidence in UK is approximated to be 4.9 per 10,000 deliveries or less (i.e. one in every 2000 pregnancies), though

is still a factor in 10% of direct maternal deaths. The maternal case fatality rate was as low as 1.8% and about 35% of women had at least one major complication· [2,5]

In many developing countries eclampsia remains high, causing a significant maternal and fetal morbidity and mortality particularly when it occurs in the antepartum period. [7,8·] Tanzania is among developing countries in which maternal and perinatal mortality due to eclampsia is high[3]. The exact incidence of eclampsia in this country is largely unknown and the few available data are those from Muhimbili National Hospital. At this hospital, eclampsia accounts not only for the commonest single cause of maternal deaths, but also, the second highest cause associated factor in fetal loss.[12]

Kairuki in 1978 found an incidence of 3.1 per 1,000 deliveries. [13] Kaisi in the same year noted the overall perinatal mortality to be 42.3 per 1000 deliveries.[12]. Kapesa 1985 found an incidence of 4.8 per 1,000 deliveries.[14] All these figures are far old but higher than 1.04/ 1,000 deliveries found by Bansal et al at Pumwani maternity hospital in Nairobi Kenya in1978. [15]

Kiwale in 1999 revealed an incidence of **24.2** per 1,000 deliveries at MNH. This incidence is 6 to 8 times higher than reported before at this hospital. This figure is higher than **19** per 1,000 deliveries found by Breen in Zululand –South Africa in 1996.[17]. Kiwale also found that, 51% of fits occurred antepartum and 80.2% of those who had antepartum eclampsia presented before 37 weeks. Out of those, only 8.6% occurred before 28 weeks. [3] There was a corresponding maternal death of **22.2**%, with an overall case fatality rate of 5.6%. [3] In the year 2000 maternal deaths due to eclampsia accounted for about **25.9%,** as the number one cause of maternal mortality replacing hemorrhage and anemia[16]. All the recent information is from data available when diazepam was used and before magnesium sulphate was re-introduced at the hospital in December 2000.

Despite of vast literature and many theories that describe immune mal-adaptation, genetic predisposition, placental and vascular mediated factors, the aetiology of gestational hypertension remains largely uncertain [(19)]. These factors are less preventable and therefore, make a rational approach to prediction, prevention and management difficult.

Morbidity and mortality in eclampsia is related to numbers of convulsions. Greater the number of convulsions, the more the maternal cerebral anoxia, hematological and metabolic derangements.[17] The prevention of seizure activity in pre-eclampsia and recurrent seizures in eclamptic patients is an essential aspect of management.

The standard management of eclamptic fits is the use of anticonvulsant that prevent further seizures in order to reduce the risk of maternal and fetal morbidity and mortality. The choice of the agent had been a subject of discussion over many years. Drugs like Magnesium Sulphate, diazepam, phenytoin, lytic cocktail (promethazine, pethedine and chlorpromazine) and others have been used for similar purpose. Diazepam has been a drug most preferred in many places elsewhere, including this country.

Diazepam depresses the central nervous system (CNS) by binding to specific receptors in the CNS. This causes increase in the inhibitory effects of a neurotransmitter – Gamma Acetyl Butyric Acid (GABA).

It relaxes muscle by inhibiting spinal polysynaptic afferent pathways, where it acts as anticonvulsant by enhancing pre-synaptic inhibition.[33] Over-dosage of diazepam causes drowsiness, over-

sedation and ataxia. Confusion, reduced reflexes and coma may rarely occurs, because, diazepam has a wide safety margin. Minimal effects on respiration, pulse and blood pressure may occur under extreme over dosage that is usually done by mistake but not under the treatment protocols.

On the other hand, Mgso4 was widely recommended and accepted for use in the management of fits in eclampsia after the evidence from the Collaborative Eclampsia Trial of 1995. The management of eclamptic fits using Mgso4 provides more adequate control of fits than diazepam [5,17,35] and has been said to offer the best prognosis to both mother and fetus. [5,17]. It appears to act primarily by relieving cerebral vasospasm.[27]. It can reverse distal cerebral arterial vasoconstriction and prevent vascular endothelial damage, probably by release of prostacyclin, which results in the inhibition of platelet clumping. Eclampsia, as a multi-system disorder, is not yet known whether MgSo4 has beneficial effect on any other organs[5].

The first report for the use of Mgso4 dates back as to 1906 when it was used in German as intra-thecal injection in the treatment of tetanus. Its widespread use followed the initial reports of its intravenous administration in the management of convulsions in eclampsia by Zuspan and Prichart in the 1950's and 60's.[6]

Published studies from the USA describe its safe use and its effect in the control of fits in eclampsia, but its acceptance and use has been low in countries like UK and other Anglophone countries.

For example, in the Hutton's survey in 1992 revealed only 2% of UK consultants used Mgso4 as first line therapy in eclampsia, preferring diazepam and phenytoin. [18] In 1995 a large multi-center trial recruiting1680 women demonstrated a 52% lower risk of recurrent seizures (95% CI, 64 to 37% reduction) with Mgso4 than Diazepam (i.e. mgso4 13.2% versus 27,9% Diazepam) and 67 % lower than phenytoin sodium.[5] After the 1995 controlled eclampsia trial, many countries including the UK, started to accept the use of Mgso4.

A similar study in South Africa by Minyoglee et al (1996) showed that, the use of diazepam failed to prevent recurrence of fits in **58.8%** compared to **10%** for Mgso4. [(8)] He also found a significant maternal mortality in those patients with multiple fits, occurring in the presence of high diastolic blood pressure (mean DBP113 +/-15.6 mmHg). Majority of fits (90.1%) happened at home and in 70.3% of patients, fitted before 37 weeks (mean Gestational Age of 33.3 weeks). About 77.3% of fits occurred antepartum and 4.5% in postpartum period. There was perinatal mortality rate of **47.7%** with

maternal complications of varied severity [8]. Antepartum eclampsia was shown to cause more serious maternal and fetal consequences than intrapartum and less severe when develops postpartum. [1,8,23]. For example, in a retrospective analysis of 69 maternal deaths due to eclampsia done over 17 years by Sawhney H. et al found that, 28% died undelivered and 52.4% had recurrent convulsions more than 10 prior to admission and Maternal Mortality Rate was low as **4.1%** when Mgso4 was used [20]. (Sawhney H, Aggrwal N, *et al* 2000) · For this reason, safer and effective drug is required to prevent convulsions in order to get satisfactory obstetric outcome during antepartum period.

2.0.STATEMENT OF THE PROBLEM AND RATIONALE OF THE STUDY

Eclampsia is a serious condition and often life-threatening complication of pregnancy contributing to a high maternal and perinatal mortality at MNH. It constituted **4%** of all obstetric admissions and accounted for about **25.9%** of all direct maternal deaths at the hospital for the year 2000.

In 1999, Kiwale found the incidence of eclampsia of **24.2** per 1000 deliveries, which represented **22.2%** of all maternal deaths with an overall case fatality rate of **5.6%.** He reported a perinatal mortality rate of **356 per 1,000** live births.

This was three times higher than the estimated national level of **115 per 1,000** live births. It is estimated that about **10%** of maternal deaths are associated with eclampsia worldwide.

Diazepam was the drug mainly used for the management of eclamptic fits at the hospital. Ineffective control of recurrent fits using diazepam may be one reason to why there was unsatisfactory obstetric outcome reported in patients with eclampsia at MNH. Basing on literature from elsewhere, mgso4 is superior to diazepam in eclampsia and offers better obstetric outcome in patients with eclampsia.

The clinical experience of MgSO4 in the management of eclampsia at MNH and in Tanzania at large is insufficiently known. Therefore the use of Mgso4 at the hospital had to be systematically documented.

This retrospective cohort study was therefore designed to demonstrate if any; a change in the pattern of both maternal and fetal outcome, reduction in seizure recurrence and the duration of stay under intensive care before and after introducing Mgso4 at the hospital.

Secondly, it was important to evaluate if diazepam was inadequate for controlling eclamptic fits and whether the current use of Mgso4 at this hospital may be recommended for use as a drug of choice by other medical facilities or hospitals not using it in Tanzania.

2.1. RESEARCH QUESTION

Is there any change in maternal and fetal outcome before and after introducing Mgso4 in the control of eclamptic fits at MNH?

2.2. HYPOTHESIS

Null Hypothesis

There was no difference in obstetric outcome before and after introducing Mgso4 in the management of eclampsia at MNH.

Measures of Obstetrical Outcome

The observed measurable obstetrical outcome variables were:

1. Maternal deaths,

2.Recurrence of convulsions,

3.Duration of stay in the eclampsia room,

4.Foetal outcome in terms of Apgar score at 5 minutes.

3.0. STUDY OBJECTIVES

3.1. Broad objective

To compare Obstetric outcome of patients with eclampsia managed with diazepam with those managed after introducing magnesium sulphate at MNH.

3.2 Specific objectives

1. To compare seizure recurrence rate (over a 24 hours period) among eclamptic patients before and after introducing Magnesium sulphate at MNH.
2. To compare the maternal outcome in terms of maternal deaths among eclamptic patients before and after introducing Magnesium sulphate at MNH.
3. To compare the fetal outcome in terms of Apgar scores among eclamptic patients before and after introducing Magnesium sulphate at MNH.
4. To compare the duration of stay in the eclampsia-room among eclamptic patients managed with diazepam and those managed after introducing Magnesium sulphate at MNH.

4.0. METHODOLOGY

4.1.1.Study design

Retrospective Cohort study.

4.1.2.Duration of the study periods

This covered two periods of equal duration:

1. **January to October 2000** was referred to as diazepam group, the period when diazepam was used.
2. **January to October 2001** was referred to as Mgso4 group, after Mgso4 was introduced.

NOTE: Equal periods of the two consecutive years were considered in order to take care of any climatic and seasonal variations in relation to eclamptic fits.

4.1.3. Study area

Muhimbili National Hospital, Dar es Salaam, Tanzania.

MNH is the largest referral and consultant hospital in Dar es Salaam and Tanzania as a whole. The hospital has a neonatal and maternity block (NMB) that receives the referred obstetrics patients with high risk factors. A high-risk antenatal clinic is also conducted in the same building. It has seven wards, which include: Neonatal unit, Labour ward and other five antenatal or postnatal wards. One of the postnatal wards is reserved for women who deliver normally.

It is in this ward where an Intensive Care Unit is located to care for eclamptic and other obstetrical patients with serious conditions.

The room has 9 beds and is designed to have reduced noise and light stimuli. It has well-experienced nurse-midwives who care for eclamptic and other seriously sick patients.

The remaining four wards cater for all patients with antenatal and postnatal problems of less severity, including, the post-eclamptic patients, the referred and those within the center. At the hospital, eclampsia was managed in a similar manner as recommended by the center and as described in the management part of this study.

4.1.4. Study population

Data was collected from all files of:

1. Eclamptic patients admitted in eclampsia room that was treated with diazepam between January and October 2000 and,
2. Eclamptic patients who were admitted in eclampsia room that was treated with magnesium sulphate between Jan and October 2001.

4.1.5. Inclusion criteria for eclampsia

All files of pregnant women who were documented to have an eclamptic fit(s) with clinical findings of elevated blood pressure more than >130/90mmhg, significant proteinuria with or without edema.

4.1.6. Exclusion criteria

1.Patients who were diagnosed as epileptic with history and clinical findings suggesting the diagnosis of epilepsy or other disorders causing convulsions like cerebral malaria, meningitis or hypoglycemia.

2. Patients whose files were lost, having incomplete or missing information.

4.1.7. Sample size determination

This was determined according to the following formula:

$$n = \frac{\{z_{\alpha/2}\sqrt{2p(1-p)} + z_{\beta}\sqrt{[p_1(1-p_1)+p_2(1-p_2)]}\}^2}{(p_1-p_2)^2}$$

Where,

n =sample size

Z=point on standard normal distribution such that an area to the right of it is z_x. i. e. $\mathbf{Z\alpha/2=1.96}$ where α is set at 0.05

$\mathbf{p=(p_1+p_2)/2}$

$\mathbf{p_1}$ and $\mathbf{p_2}$ were the proportions of fit(s) recurrences reported for magnesium sulphate and diazepam respectively by the *Evidence from the Collaborative Eclampsia trial, 1995.*

α=Level of significance, β=Probability of failing to detect an existing difference, set at **0.01** and $\mathbf{1-\beta}$ is referred to as power of the study.

If, P_1= 13.2%

P_2= 27.9%

Note that Ratio of mothers given mgso4 to those who were given diazepam is 1:1

Power= 99%,

Therefore, n= 287 **per group.**

TOTAL n= 574.

NOTE: *This sample size was calculated for the purpose of getting the minimum number of patients' files required by the study for the purpose of making reliable statistical tests despite of the specified period.*

4.2. METHODS

4.2.1. Study instruments

Data was extracted from files recorded using a standardized pre designed and pre-tested instrument. Two nurse-midwives working in ICU and ward 35 were recruited and trained to assist in checking all files thoroughly for information and data recording.

Admission books were requested from the nurse in-charge of the eclampsia room. A list was made of all file registration number, delivery number and name of the patient. This list was made available to the record attendants in the obstetrics' medical records. Two record attendants were involved in the retrieval of these files.
For incomplete files, the missing information was retrieved from the daily nursing report book, delivery book, a computer database or ward's admission and discharge forms. If most of the relevant information in that file regarding a particular patient was not obtained, that file was excluded from the study at the initial stages of data collection. Any missing file among those required was regarded as a lost one.

Any patient's file that met the inclusion criteria, i.e. an eclamptic fit(s), elevated blood pressure or proteinuria and other documented

signs for the clinical diagnosis of eclampsia} was included in the study. The inclusion was irrespective of when or where the fits had occurred, singletone or multiple pregnancies, whether the baby has been delivered or not and whether anticonvulsant treatment had already been given or not. All files documented to have had fits due to other causes of convulsive disorders, (cerebral malaria; meningitis and hypoglycemia) were excluded from the study sample.

Study variables such as age of the patient (in years) gravidity, parity and gestational age (in weeks) were recorded. Gestational age at admission or delivery was calculated from the date of the recorded last menstrual period or by extrapolation from the booking date and roughly compared with the recorded fundal height. The date and time of admission, diagnosis, birth records, discharge or death, were recorded from the patients' partograph, antenatal card, ICU observation charts or from the daily nursing report book.

Blood pressure on admission, proteinuria and any documented complication related to eclampsia and mode of deliveries (SVD, LCVE Caesarean Section) were recorded. Maternal outcome were determined as alive or dead. Any patient documented to have died

before administration of either of the drugs, was excluded from the study. One patient was excluded on this basis.

Any fit(s) recorded after administration of the drugs and on maintenance dosages within 24 hours of admission were regarded as recurrence(s), but those noted to occur before the administration of the drugs were NOT regarded as recurrences in this study.

The fetal outcome in terms of Apgar score at 1 and 5 minutes were recorded in the two study groups. Sex and birth weights of babies were also recorded for the interest of fetal characteristics. Only the foetal outcome of the first twin was analyzed for convenience.

4.2.2. MANAGEMENT OF ECLAMPSIA

The management strategy followed the recommended guidelines for care of patients from the time of admission, progress in the ward and follow up. The author describes this in order to get an overview on how the patients were normally cared. The recorded variables were according to what is described here.

Patients are admitted either directly from home or as referred from the privately owned hospitals and from the three municipal hospitals namely, Temeke, Amana and Mwananyamala. From the reception nurse midwives send patients directly to the eclampsia room for

admission. The admitting nurse will take a short history about the fits from the escorting nurse or relatives. She performs a general examination of the patient, insert urethral catheter, take urine for protein estimation using albustics and finally record the findings on the Intensive Care Unit observation charts. Any further fits are recorded on these charts (by a + sign) for the rest of the stay. The nurses will immediately administer the required anticonvulsant and inform the resident on call to review her and take appropriate measures.

Normally one specialist is responsible for the daily supervision of this room (ICU) and would make 2-3 rounds everyday, during morning, afternoon and evening hours. One resident who is permanently assigned to work in this room under his direct supervision assists this specialist.

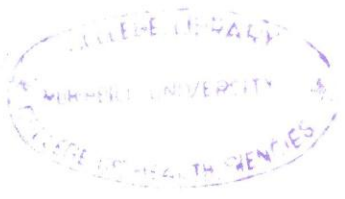
During the study periods there were about 5 Nurse officers and 7 Nurse-midwives, 12 Health attendants and 6 Ward attendants working in this special room under 3 duty shifts: morning afternoon and a night shifts. Out of the total 12 nurse-midwives only 9 participated fully in the daily management of patients and were distributed in the 3 shifts while the other 3 were involved in administrative duties. The room had 9 beds. It was assumed that, if

all beds could be occupied per unit time; this makes the nurse to patients' ratio of 1:3. There was no gross change of staff and this number was maintained almost throughout in the two periods of the study and there was no additional of new equipment.

Treatment protocols for eclampsia include, reduction of blood pressure, prevention of further seizures and provision of other supportive therapies. The airway is secured by left lateral positioning of the patient; suction of secretions and occasionally oxygen is administered.

Normally, prophylactic antibiotics (like IV Ampicillin and Metronidazole) are given to all eclamptic patients to prevent aspiration pneumonia and sepsis. Other types of antibiotics are added depending on the individual's severity of the clinical condition. Other management protocols and treatment measures are described below.

Once the patient recovers within or after 24 hours of treatment, she is transferred to the respective postnatal ward for continued treatment and care till discharge. After discharge or death, all files are normally sent to the obstetrics medical records for keeping.



For the purpose of this study, the follow-up of the recorded variables was up to discharge from hospital or death. For example, the time between admissions, transfer out; discharge or death was recorded to determine the mean- time-length of stay under intensive care.

TREATMENT OF SEIZURES

4.2.3. Mgso4 treatment protocol

According to the displayed protocol, magnesium sulphate is given intravenously. The intravenous route is preferred because intra-muscular injections are painful and according to literature it is complicated by local abscess formation in 0.5% of cases.

A loading dose of 4g Mgso4 in 20cc of Normal saline is given IV over 5-10 minutes. This is followed by a maintenance infusion of 4g in 500 mL of normal saline, which are administered 4 hourly (1g/h) and continued for at least 24 hours after the last seizure. Recurrent fits are treated by an extra bolus dose of 2g dissolved in 10 cc of normal saline given IV as described by the protocol.

This Protocol was well displayed on the board and guidelines were strictly adhered to. Treatment usually commenced immediately after the patient was admitted. A little practical delay of drug administration was observed when there was a shortage of stock on the shelf or when there was one nurse attending several patients simultaneously. The administration of Mgso4 was said to be simple.

Well-trained nurse-midwives working in eclampsia room could safely administer Mgso4 with no difficulties. The above Mgso4 protocol was the one introduced at the hospital in December 2000.

Magnesium sulphate toxicity causes loss of deep tendon reflexes, followed by respiratory depression and ultimately respiratory arrest. If deep tendon reflexes are absent, further doses of magnesium sulphate had to be withheld until reflexes return. Significant respiratory depression is treated with 1g IV calcium gluconate given over 10 minutes.

Magnesium sulphate is excreted through the kidney therefore; regular monitoring of serum levels had to be considered in women with oliguria (urine output < 100ml/4h). The therapeutic range is believed to be between 2 and 4mmol/l.

During the study period, there was no electronic monitor for oxygen saturation or facilities for estimation of serum levels of Mgso4. Therefore, doctors and nurses relied on clinical assessment of patellar reflexes and respiratory rates. The assessment of patellar reflexes was performed hourly in all patients but with less frequent in those with stable respiration and patellar reflex.

4.2.4.Diazepam treatment protocol

A-loading dose of 20mg IV Diazepam was given over 2 minutes followed by a maintenance repeat doses of either 10mg 4-6 hourly IV per 24 hours OR a maintenance dose of 40-60 mg of diazepam in 500mL of Normal Saline or 5% dextrose titrated at a rate of 20-30 drops per minute for repeated fit(s). A drip rate could be increased or decreased to achieve a required level of consciousness over 24 hours depending on the response.

Diazepam causes Drowsiness as one of its side effects. Some of these patients were reported to be drowsy or oversadated. The dosages were regulated to achieve a certain level of sedation but still arousable.

NOTE: The above diazepam protocols was the one being used at the hospital before December 2000 and was considered as standard regimen for the purpose of this study.

4.2.5.Treatment of hypertension, Fluid therapy, Investigation and Delivery

Hypertension

At this hospital, treatment of severe hypertension (blood pressure > 160/110mmHg) is usually done using IV Hydrallazine 10mg every 30 minutes until Diastolic Blood Pressure (DBP) < 110mmHg is achieved. Maintenance doses are achieved by oral tablets, hydrallazine 50mg 8hourly and/or methyldopa 250-500mg given 8

hourly, once the patient is able to take. The dosages are regulated depending on the response. Both of these drugs can precipitate fetal distress and therefore continuous fetal heart rate monitoring is necessary. These are clinically monitored using foetal stethoscope since there is no electronic foetal monitoring.

Fluid therapy

Close monitoring of fluid intake and urine output is mandatory. Preloading the circulation with 500 ml colloid prior to regional anaesthesia or vasodilatation with hydrallazine may reduce the risk of hypotension and fetal distress. There is a risk of volume expansion that can precipitate pulmonary edema and diuretic therapy is limited to women with eclampsia.

Fluid therapy is therefore, limited to maintenance crystalloid, 85ml/h with adequate urine output in proceeding hours, except for patient who are dehydrated with electrolyte imbalance. Normal saline is usually recommended.

Investigations

Frequent monitoring of haemoglobin, platelet count, transaminases, urea and creatinine together with oxygen saturation are necessary but some were not routinely done partly due to inadequate laboratory facilities. However, routine investigations may be of no importance. Cerebral imaging (MRI or CT) is not indicated in

uncomplicated eclampsia. However, imaging may be necessary to exclude cerebral haemorrhages and other serious abnormalities in women with focal neurological deficits or prolonged coma.

Lumbar puncture for CSF analysis and thick blood smear are occasionally taken to exclude bacterial meningitis and cerebral malaria respectively. Every patient who is admitted in this ward has a routine peripheral blood smear taken for malaria parasites and those found to have a positive smear gets anti malaria treatment.

Delivery

The definitive treatment of eclampsia is delivery. At this hospital labour is managed actively. It is inappropriate to deliver an unstable mother even if there is fetal distress. Once seizures are controlled, severe hypertension treated, and hypoxia corrected, delivery is expedited. Vaginal delivery is most preferred and Low Cavity Vacuum Extraction (LCVE) is usually performed to assist patient in second stage of labour. Caesarean section is likely to be required in primigravidas under other obstetric indications. After delivery, high dependency care is to be continued for a minimum of 24 hours.

4.2.6. PILOT STUDY

A mini survey was performed to test the data-collecting instrument and to determine whether files and information could be obtained. For the month of June 2000 alone 32 out 56 files (67%) were retrieved containing adequate data on the key variables. Some of the information missing from the two files was easily obtained from the daily nursing report book. The quality of data found from the daily nursing report book and that obtained from the files were the same.

4.3. DATA PROCESSING AND ANALYSIS

Data from the study variables were entered into EPI-Info (version 6) Software for processing and analysis. Comparison of percentages of observed variables between Mgso4 and diazepam groups were done using Chi-squared (χ^2) test.

4.3.1. LIMITATIONS

1. Number of fit (s) reported to have occurred at home may not be reliable. Some were reported as several fits, but for clinical purposes these were multiple fits and were recorded as two and above.
2. Other rare causes of convulsions (like encephalitis due to viral infections) could not be excluded as they lacked a diagnostic criterion for patients presenting with fits having normal blood pressures without proteinuria.

3. Missing files 185(19.6%), files lacking essential information 96(10%) and 34 (3.6%) files not meeting the diagnostic criteria for eclampsia had to be excluded. As a result it is possible that some important data was not available for the study.

4. Information in the files was not systematically recorded and as a result it was time consuming trying to find the essential information from the files.

5. The already existing key variables were measured at two time frames and it is likely to have some variables measured more vigilant with the introduction of a new drug than before so, affecting the consistent of the measuring criteria.

This study based on the already existing variables that the author had no control with. So, its outcome may not be judged as conclusive but gives the basic and important maternal-foetal outcome in eclampsia using Mgso4 as opposed to diazepam.

4.3.2. Potential sources of bias

The following were likely to affect some of the outcome variables in the study.

1. Some referred patients who were documented to have been given Mgso4 might have received doses of diazepam before admission and hence seizure recurrence prevented.

2. Inter-observer reliability was not determined. The variation in data recording between assistants assigned for data collection was neither tested nor accounted for (e.g. some fits may have been recorded as recurrences before the drug was administered).

3. There may have been a bias in selection. Some of the files were not retrieved from the medical records. Selection tended to base more on retrievable files so, representing a systematic bias.

NOTE: Training of assistants, close supervision, daily checking and editing of the collected data still ensured the consistency of the information.

4.3.3. ETHICAL CLEARANCE

The study proposal was presented to consultant obstetricians in the department and clearance was requested from MUCHS publications and ethical clearance committee. The study dealt with past records and no consent was required. There was no physical involvement of patients and therefore, there was no major ethical issues in this study.

The drug cost: Magnesium sulphate versus diazepam

Diazepam

In this cohort study, 312 women (Jan-Oct 2000) received diazepam and 318 women (Jan-Oct 2001) were given Mgso4.

The total minimum dose for diazepam (20mg stat then 10mg 4hourly per 24 hours) equals 80mg per 24 hours. i.e. 8 ampoules of 10mg each, costing 80/= per ampoule as per MSD prices. The total cost for 312 patients x 8 ampoules x 80/= equals Tshs=199,680/=. (199.60 US Dollars)

Magnesium sulphate

The minimum dose for Mgso4 was 4gms stat, followed by 4gms, 4 hourly per 24 hours, making a total of 7 doses, which equals 28gms per patient per 24 hours. The total amount of (318 x28gms) approximately 9000gms Mgso4 was used.

NOTE

Mgso4 crystals was sold at Techno vet (T) Ltd at Tshs 6,000/= per 4kgs. The 4kgs of mgso4 crystals were dissolved in 20 Liters of sterile water to make a 20 % Mgso4 solution.

This was then packed in a 250 ML bottle and sterilized at 120 Degrees Centigrade at 2 pressure bars for 15 to 20 minutes. Once well prepared it had a shelf life estimation of two years.

This amount was enough for 142 patients. There were no handling difficulties reported. For the 318 patients who received Mgso4 needed less than 12 kg of Mgso4 crystals, costing less than Tshs 18,000.

The cost of bottles, preparation and other production costs were estimated not to exceed Tshs 50,000/=, making a total of 68,000/= equivalent to 68 US Dollars. So, the use of Mgso4 was cheap and cost effective than Diazepam.

5.RESULTS

During the two study periods (i.e. January – October 2000 and January – October 2001), **945** (3.3%) out of **28,445** admissions were cases of eclampsia admitted at the hospital. There were **15,454** deliveries from January to October 2000 and **12,991** deliveries for January – October 2001. This makes a total of **28,445** deliveries at the hospital for the two periods. In the year 2000, there were **77** maternal deaths. Out of these, **19** (25%) were due to eclampsia.

In the year 2001, **59** maternal deaths occurred, **14** (24.5%) of which were due to eclampsia.

Data was collected from **630** patient files to compare the study variables before and after introducing Mgso4. There were 96 patient files with incomplete information and 185 were completely missing. These were excluded at initial stages of data collection together with 34 files, which did not meet the diagnostic criteria for eclampsia.

Out of 630 patient files studied a total of 26 maternal deaths were identified, 16 deaths occurred in the period when diazepam was used and 10 deaths occurred after Mgso4 was in use.

In the comparison of the two study periods the group variables were well balanced. The demographic distribution of age, gestational age

and gravidity along the comparison groups are summarized in table 1, 2 & 3below.

TABLE 1.Distribution of maternal age by anticonvulsant regimen used (n =630)

Age group	Anticonvulsant regimen: Diazepam No	Diazepam %	Mgso4 No	Mgso4 %	Total
15-19	136	(43.6%)	135	(42.5%)	271(43.0%)
20-24	102	(32.7%)	105	(33.0%)	207(32.9%)
25-29	49	(15.7%)	50	(15.7%)	99(15.7%)
30-34	15	(4.8%)	23	(7.2%)	38 (6.0%)
35-40	10	(3.2%)	5	(1.6%)	15 (2.4%)
Total	312	(49.5%)	318	(50.5%)	630(100%)

P-Value=0.50

- **Age:** Maternal age ranged from15-40 years with a mean age of **21.6 ± 5.1**(SD) for diazepam group and **21.5± 4.8**(SD) for Mgso4 group. The overall mean age was **21.6 ± 4.9**SD. Thus maternal age was similar in the two-anticonvulsant regimens (***P-Value=0.50***)
- The young primigravida aged below 20 years constituted **43.0**% of the study population.
- Majority (478/630 = 75.9%) of pregnant women who had eclampsia were aged below 25 years.

Table 2. Gestational age by anticonvulsant protocol used

Gest. Age	Diazepam	Mgso4	
	No %	No %	Total %
20-34	81(26.0%)	85 (26.7%)	166(26.3%)
35-37	94(30.1%)	93 (29.2%)	187(29.7%)
38-42	137(43.9%)	140 (44.0%)	277(44.0%)
Total	312(49.5%)	318 (50.5%)	630 (100%)

P-value = 0.96

Gestation age

- The overall mean gestational age at deliveries was **36.0 ±3.94 (SD).**

- As seen in table 2 above, there was no significant difference in gestational age between the two groups (***P- Value = 0.96***), indicating that gestation age distribution was well balanced between the two-anticonvulsant regimens.

Table 3. Distribution of gravidity by the type of anticonvulsant protocol used (n=630)

Gravidity	Diazepam No %	Mgso4 No %	Total %
Gravida 1	222 (71.2%)	239 (75.2%)	461 (73.2%)
Gravida 2-8	90 (28.8%)	79 (24.8%)	169 (26.8%)
Total	312 (49.5%)	318 (50.5%)	630 (100%)

P-value=0.26

Gravidity:

- Primigravidas formed the largest percentage accounting for (**73.2%)** in both groups**;**
- The rest (26.8%) were in the second pregnancy and above and 21 (3%) patients had twin deliveries.
- The difference observed in gravidity between the two periods of treatment was not statistically significant ***(P-value = 0.26)***.

MATERNAL OUTCOME

Table. 4. Observed maternal outcome before and after introducing Mgso4 protocols (n= 630)

Maternal Outcome	Anticonvulsant used					
	Diazepam		Mgso4			
	No	%	No	%	Total	%
Alive	296	(94.9%)	308	(96.9%)	604	(95.9%)
Died	16	(5.1%)	10	(3.1%)	26	(4.1%)
Total	312	(49.5%)	318	(50.5%)	630	(100%)

P-Value=0.21

- This table shows a slightly higher proportion of deaths due to eclampsia observed in the group treated with diazepam 16 (**5.1%).** between Jan. to October 2000.
- Comparatively, a lower proportion of deaths 10(**3.1%)** due to eclampsia was observed in a group of women after introducing Mgso4 (Jan-Oct 2001).

- However the difference (of **2%)** was not statistically significant ***(P – value = 0.21).***
- The overall case fatality rate was **4.1%**.
- The documented maternal complications varied in severity and observed to occur in only 3.8 % of patients studied. Some of the serious maternal complications were aspiration pneumonia, pulmonary oedema, cardiac arrest and or acute respiratory failure. Cortical blindness was reported in one patient.

Table 5. Overall distribution of maternal outcome by age

Maternal outcome

Age group	Alive		Died		
	No	%	No	%	Total %
15-19	262	(96.7%)	9	(3.3%)	271(43.0%)
20-24	198	(95.7%)	9	(4.3%)	207(32.9%)
25-29	95	(96.0%)	4	(4.0%)	99(15.7%)
30-34	36	(94.7%)	2	(5.3%)	38 (6.0%)
35-40	13	(86.7%)	2	(13.3%)	15 (2.4%)
Total	604	(95.9%)	26	(4.1%)	630 (100%)

P-value =0.43

- Although more deaths were observed at young age below 25 years, **(69.2%)** maternal outcome was found to be independent of mother's age ***(P-value =0.43).***

TABLE 6. Age-specific maternal mortality by treatment used

Age group	Diazepam		Mgso4		P - Value
	No	%	No	%	
15-19	4/136	(3.0%)	5/135	(3.7%)	0.72
20-34	10/166	(6.0%)	5/178	(2.8%)	0.14
35-40	2/ 10	(20.0%)	0/5	(0.0%)	0.46
Total	16/312	(5.1%)	10/318	(3.1%)	0.21

- Age-specific maternal mortality was compared in relation to anticonvulsants used in the two treatment periods, and there was no significant statistical difference even when maternal age was taken into account:

  (***P- values were 0.72, 0.14 and 0.46***).

- However, maternal mortality difference was more pronounced in the age group of 20-34 years (6.0% with diazepam as compared to 2.8% with Mgso4).

RECURRENCE OF SEIZURES

Table 7. Recurrence of seizures as observed before and after introducing Mgso4 (n=628)

Seizure Recurrence	Anticonvulsant protocol used Diazepam		Mgso4			
	No	%	No	%	Total	%
0-Rec	170(54.8%)		272(85.5%)		442(**70.4%**)	
1-9-Rec	140(***45.2%***)		46 (***14.5%***)		188(**29.6%**)	
Total	310(49.4%)		318 (50.6%)		628(100%)	

P-value < 0.01

- Recurrence of convulsions was one of the important primary outcome variables. Recurrence of fits was not observed in about **70.4%** of the patients studied.
- Recurrence of fits in two patients (0.3%)in the diazepam group was not documented.
- Recurrence of fits ranged from 1-9 and overall occurred in 188/628 **(29.6%)** of patients in both groups.
- In this comparison, 140/310 (**45.2**%) patients receiving diazepam protocol had at least one or more recurring fit(s).
- As compared from when Mgso4 was introduced, only [46/318 (**14.5%**] had similar fit recurrences.

- The difference was 30.7%. This means that, **30.7 %** fewer women using Mgso4 than diazepam protocol had further fits.
- This difference in recurrence of seizures between the two study groups was highly significant from the statistical point of view (***P-value < 0.01)***.

FOETAL OUTCOME.

Table 8. Distribution of foetal outcome in term of Apgar score at 5 minutes before and after introducing Mgso4.

	Anticonvulsant		
	Diazepam	Mgso4	
APGAR-5	No %	No %	Total %
Score-0	87 (28.1%)	55 (17.3%)	142 (**22.6**%)
1-3	12 (3.9%)	13 (4.1%)	25 (4.0%)
4-6	93 (30.0%)	68 (21.4%)	161(25.6%)
7-10	118 (38.1%)	182 (57.2%)	300 (47.8%)
Total	310 (49.4%)	318 (50.6%)	628 (100%)

P-value < 0.01

- A total of 628 foetuses were analysed. Two pregnant women died with undelivered foetuses.
- Out of those 21 (0.3%) were first twin babies from eclamptic mothers with twin pregnancies. There were no triplets.
- A total of 142 (**22.6%**)foetuses were SB's with Apgar score 0.

- Foetuses with Apgar score 1-3 had severe birth asphyxia; Apgar score 4-6, moderate birth asphyxia while Apgar score of 7 to 10 at 5minutes were referred to as normal babies.
- An overall total asphyxiated babies' were186 (**29.6%**) with Apgar score less than 7 at 5 minutes.
- There were more asphyxiated babies when diazepam was used [105/310 (**33.9%**)] than when Mgso4 [81/318 (**25.5%**)] was introduced by a difference of **8.4%**.
- A better Apgar scores at 5 minutes were observed in foetuses that their mothers received Mgso4 (**57.2%**) as compared to **38.1%** of patients on diazepam. The difference was as big as **19.1%.**
- About 13 (**2.1%**) deliveries were abortions with gestation age less than 28 weeks.
- For women compared among the treatment groups before delivery were 500 (79.4%)
- The differences observed were highly statistically significant with ***P-value < 0.01***.

THE DURATION OF STAY

Table 9. The duration of stay in eclampsia room before and after Mgso4 (n =607)

Duration in ICU (in hrs)	**Anticonvulsant used** Diazepam		Mgso4		
	No	%	No	%	Total No %
6-24	39 (13.1%		84 (27.1%)		123 (20.3%)
25-36	71 (23.9%)		118 (38.1%)		189(31.1%)
37-456	187 (63.0%)		108 (34.8%)		295(48.6%)
Total	297 (48.9%)		310 (51.1%)		607(100%)

P-value < 0.01

- Total of 607(96.3%) were successfully transferred to postnatal wards after intensive care and 23 patients died in ICU before transfer. The remaining 3 died in their respective wards after being transferred. One of these had underlying immunodeficiency and died suddenly while the other two remained sick and died within two weeks of stay without recurring fits. No one died among those transferred early than 24 hours.
- Overall 295(**48.6%)** stayed more than 36 hours.
- One patient stayed a maximum of 456 hours, (19 days).

- Under normal circumstances an eclamptic patient had to stay in ICU for a minimum of 24 hours after the last fit.
- In this comparison, few patients 110/297 **(37%)** stayed up to 36 hours or less in the Diazepam group as compared to 202 **(65.2%)** more patients in the same duration after Mgso4 was introduced.
- The difference of **28.2%** in this comparison was highly statistically significant ***P-value < 0.01.***

OUTCOME MEASURES

The prespecified primary measurable outcome variables were maternal deaths, recurrence of convulsion, and foetal Apgar score at 5 minutes and the duration of stay in the eclampsia room.

The secondary outcome variable were the potentially life threatening events associated with eclampsia like, pulmonary edema, aspiration pneumonia renal or liver failure and disseminated intravascular coagulation as measures of morbidity. These outcome variables were as determined by the attending doctors and nurses. The causes of maternal deaths were validated by the author through review of the case notes and clinical summary made by the attending doctors.

5.2.DISCUSSION

The term Eclampsia is derived from the Greek words meaning "like flash of lightning". It has been known since Hippocrates' time as a convulsive disease occurring in pregnant women and a significant maternal disease manifested by functional derangement of multiple organs, subsequently causing death. Pre-eclampsia which may precede eclampsia, is a condition characterized by rise in blood pressure, proteinuria and edema. Other symptoms include severe headache, epigastric pain blurred vision and palpitations. (1,4).

In this study, all 630 patients whose files studied had at least one or more eclamptic fit(s). The occurrence of an eclamptic fit, elevation of blood pressure and proteinuria documented in patients' file were the selection criteria. The aim of the study was to compare an obstetrical outcome of eclamptic patients before and after introducing Mgso4. The comparison based on existing variables extracted from patient files before and after Mgso4 was introduced in December 2000. The key principle was that, we had high maternal morbidity and mortality rates with poor perinatal outcome among patients with eclampsia before introducing Mgso4 at the hospital[3].

Both Diazepam and MgSO4 have been widely used in different parts of the world for many years. Fifty years of experience with MgSO4 in the USA has shown, it is effective and safe. Foetal-maternal outcome is reported to be better with MgSO4 than diazepam.[3, 5,35]. This also has been found by this study. MgSO4 carry risk of Central Nervous System depression, respiratory embarrassment resulting in anoxia and cardiac arrest[35]. These side effects are said to be rare, although they could be potential and direct cause of maternal deaths if they are undetected. There was no patient documented to have side effects due to Mgso4. However, one patient developed cardiac arrest in the course of treatment with Mgso4 under the same protocol. It is not possible to suggest that, the patient died due to these side effects since there were no any other documented signs of toxicity.

The clinical observation in terms of better obstetrical outcome using Mgso4 as opposed to diazepam in eclampsia at Muhimbili National Hospital is hereby documented by this study.

Maternal age ranged from 15-40 years with a mean age of 21.6±4.9 SD. Majority of eclamptic mothers (**75.9**%) aged below 25 years and **73.2%** of them were primigravidas. The young primigravidas aged below 20 years constituted 43% of the study population. However the

occurrence of eclampsia among the study population was tapering down with increasing age. The distribution of age, gestational age and parity found in this study follows similar demographic patterns observed in other studies.[3,8,36]. However, patients aged less than 25 years accounted for the majority of the eclamptic patients; reasons for this may partly be explained by immune maladaptation of teenagers and young mothers to the stresses of pregnancy[3].

Blood pressure recorded on admission is one of the important diagnostic requirements in eclampsia. The overall systolic blood pressure at admission varied between 90 and 247mmHg and DBP ranged from 56 to 214 mmHg respectively. There was a mean systolic blood pressure of **159.3± 21.5 (SD)** mmHg and diastolic blood pressure of **99.3 ±15.6** (SD) mmHg. The same distribution was rather similar in the comparison groups. Proteinuria was found in 590 **(93.7%)** of patients, the rest **6.3 %** had no proteinuria. This is far less than 29% documented by Sibai *et. Al* [24,35]. These suggest that, eclamptic fit may occur without proteinuria.

In this study, 370(**61.0%)** presented with eclamptic fits during the antepartum period **18.4**% intrapartum and the rest 130(**20.6%)** were postpartum. This indicates that almost **80%** of the fits occurred before delivery. These are slightly higher than (**77.3%)** occurring

before delivery and 4.5% postpartum respectively as found by Minyoglee, in South Africa 1996. Many studies have documented antepartum eclampsia to cause more serious maternal and foetal obstetrical outcome than intrapartum and less severe when developed postpartum[1, 8,23].

Maternal Outcome

Maternal death was one of the most important outcomes of eclampsia. While there are many deaths due to eclampsia at our setting, maternal deaths due to eclampsia in USA[35] and UK [2] are reported to be very rare. In this study, there were a total of 26 maternal deaths due to eclampsia with an overall case fatality rate of **4.1%.** This was similar to 4.1% found by Sawhney H et al in the year 2000 but lower than 6.5% found by Kiwale 1999[3], and 14.4% by Adetoro in Nigeria 1989 [36].

The difference in the risk of death was difficult to demonstrate, since it was very small. Of the 26 patients who died, 16 (**5.1**%) occurred when diazepam was used and 10 (**3.1**%) after Mgso4 was introduced. The difference in mortality reduction was by **2%.** This difference was not statistically significant. ***P = 0.21***. The trend towards reduction of maternal mortality in favor of Mgso4 was substantial enough to have clinical significance [5,8].

The immediate causes of maternal deaths were occasionally difficult to ascertain since causes may be multifactorial. Eclampsia alone was a pre requisite apart from the well-known complications. Of the 26 patients 6(23.1%) died of aspiration pneumonia, (2 out of 6 were in Mgso4 group) 12 patients (46.2%) died of eclampsia, mentioned as a direct cause. Patients who died of cardiac arrest were 2(7.6%) and 3 (11.5%) died of pulmonary edema. The rest died of other complications like pulmonary embolism 1 (3.8%) and acute respiratory failure 1 (3.8%).

However, the immediate cause of death could have resulted from unidentified pathologies like; cerebral hemorrhages, hypoxic encephalopathy, thromboembolism, hepatic rupture and anaesthetic related accidents. Maternal complications varied in severity and occurred in only 12 (**3.8%**) patients' files studied. This was lower than 35% found by Douglas et al in UK 1994, where modern diagnostic facilities are available[2]. Most of these were respiratory complications observed when diazepam was the drug in use, probably because of the sedative effects of diazepam.

Fits recurrence

Recurrence of convulsions was the second primary outcome variable. In this comparison140/320 (**45.0%**) of patients on diazepam had recurrent fits at least one or more episodes. Only 46/318 (**14.5%**) patients on Mgso4 had similar recurrent fit(s). There was an absolute reduction of fit recurrence by **30.5%.** This means that 30.5 per 100 fewer women given Mgso4 had further fits. This difference was strongly statistically significant, ***P-value < 0.01.*** Other investigators [5,8,22] also observed similar findings.

The difference of 30.5% was relatively less than 48.8% in a study done in south Africa [8], (10% for MgSO4 Versus 58.8% for Diazepam), but relatively more than 14.7% found by the Collaborative Eclampsia Trial 1995(13.2% for Mgso4 versus 27.9% for diazepam) [5].

Despite the inevitable reduction in power of subgroup analysis, the results were consistent irrespective whether the comparison was before or after delivery or whether anticonvulsant was previously given or not.

A significant number of patients fitted in the category of relatively low blood pressure, not exceeding or even less than 130/90mmHg. This suggests a poor correlation between occurrence of seizures and severity of Hypertension. This is partly explained by the fact that

seizures may be attributed to platelets thrombi and hypoxia due to localized vasoconstriction and/or foci haemorrhage in the cerebral cortex[35] apart from unidentified rare causes of convulsions that lacked a diagnostic exclusion.

Better maternal and foetal outcome observed with Mgso4 lies on this fact of preventing recurrence of seizures. The mechanism of action of Mgso4 is by dilating the cerebral blood vessels, therefore, relieving the vasoconstriction. It acts peripherally by lowering the amount of acetylcholine released at the Neuro-Muscular-Junction.

It can cause transient mild hypotension during IV loading, transient mild decrease in uterine activity in active labour and tocolytic effect in premature labour[35]. The tocolytic effect of mgso4 might have partly overcome by active management of labour using oxytocin.

Foetal Outcome

There were 142/628(**22.6%**) stillbirths (SB's) making a perinatal mortality rate of **226 per 1000** live births. This figure was less than 356 per 1000 live births found by Kiwale in 1999[3] at the hospital. However, this figure should not be taken as a true representative of perinatal mortality as seen at the hospital simply because deaths that occurred in the neonatal unit within the first seven days of life

could not be traced due to limitations of time. In addition a different filing and recording system is used.

The perinatal mortality of 226 per 1000 live births was still high in this special group of patients than the estimated national level of **115 per 1,000** live births. However, both figures are higher than 10 per 1,000 in Europe and 85 per 1,000 in India[32].

The total number of asphyxiated babies were186 (**29.6%).**

Majorities of the sufferers 161/486 (**33 %**) were born from mothers who had their first fit(s) before delivery. Better foetal Apgar score 7+ was observed in patients in the Mgso4 group (**57.2%)** as compared (**38.1%**) in the diazepam group. The difference of **19.1%** was highly statistically significant with a ***P-value< 0.01.***

The perinatal mortality and birth asphyxia in diazepam group were still higher when they were corrected for Gestation Age and birth weight. The majority weighed less than 2.500kg. In both groups, high perinatal mortality was partly explained by prematurity [2,8] with Gestation age of 36 weeks and below which agreed with other studies.[3] The perinatal mortality of 22.6% deliveries was lower than 49-58% reported by the 1995 eclampsia trial[5]. However, babies of women who were given Mgso4 with gestational age below 37 weeks

had better outcome than in the diazepam group. The Foetal side effects of diazepam that include, respiratory depression, hypotonia, poor feeding and thermoregulatory problems[34] can partly explain this.

The greatest risk for fetus is when eclamptic fits are multiple with long periods of maternal anoxia in the antepartum and intrapartum period. Here the foetal life is further compromised due to placental insufficiency that has already occurred. Other risks were related to pre-term delivery and Intra Uterine Growth Retardation (IUGR), while stillbirths were explained by intrauterine birth asphyxia and deaths due to Respiratory Distress Syndrome (RDS) [35].

Duration of stay in Intensive Care Unit

This study has revealed patients treated after introducing MgSO4 to have a shorter stay in eclampsia room than when diazepam was used and therefore, has reduced a greater impact on the resources of care and utilization of hospital beds. Only 110 **(37%)** of patients stayed a maximum of 36 hours in the Diazepam group as compared to 202 **(65.2%)** in the Mgso4 group, with a difference of **28.2%.**

A shorter duration of stay under intensive care favoured Mgso4. This has greatly minimized the load of care within the context of scarce resources of care available. The difference observed in the comparison was highly statistically significant with; ***p- value < 0.01***.

5.2. CONCLUSION

With the introduction of Mgso4, patients with eclampsia have been shown to have better obstetric outcome than when diazepam was in use. It has shown a significant reduction of re-occurring fits, a clinically significant trend in reduced maternal morbidity and mortality, improved fetal outcome and less hours and even days that have been spent under intensive care.

Adequate control of eclamptic fits remains the most important factor in reducing maternal morbidity/mortality and perinatal deaths resulting from eclampsia. Fits were better controlled with Mgso4 than diazepam. The study has evaluated this in clinical context and has shown the failure of the existing diazepam choices in the management of eclampsia in Tanzania.

Since Mgso4 exerts its therapeutic effects on the cerebral complications of eclampsia, it is therefore important to look forward to see how it can be used in severe pre-eclampsia !

5.3. RECOMMENDATION

Increasing evidence on the effectiveness of MgSO4 in the management of eclampsia is now available. In addition, clinical-based- practices and protocols have been developed to guide clinical decision. It is therefore recommended that:

- In a poor country like Tanzania with scarce public health resources and inadequate antenatal care Mgso4 should be adopted in other medical facilities or hospitals where currently not using it in Tanzania. The main reasons being that it is safe and cheap. The adoption may start with referral centers, regional and finally to district hospitals. This goes with a full range of services and equipment supplies required for eclampsia care.
- The ministry of health should include Mgso4 in its Standard Treatment Guidelines (STG) and National Drug List for Tanzania (NEDLIT) for management of eclampsia.

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