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FACULTE DE MEDECINE ET DES SCIENCES BIOMEDICALES

REPUBLIC OF CAMEROON
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UNIVERSITY OF YAOUNDE I
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FACULTY OF MEDICINES AND BIOMEDICAL SCIENCES

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

EVALUATION OF THE EFFICACY AND TOXICITY OF MAGNESIUM SULFATE IN THE MANAGEMENT OF SEVERE PREECLAMPSIA AND ECLAMPSIA IN TWO TERTIARY HOSPITALS IN YAOUNDE

By

OBASE MUSONO RALPH, MD
Matricle: 20S1973

Dissertation submitted in partial fulfillment of the requirements for the award of a specialization diploma (DES) in Obstetrics and Gynecology

SUPERVISOR
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Academic year 2023 – 2024

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DEDICATION

This piece of work is dedicated to my parents, Pa OBASE Elias MUSIMA (of blessed memory), and Ma. OBASE Christine IKOMBE

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Sincere gratitude to my supervisor Prof MBU Robinson ENOW, and co-supervisor Dr EBONG Cliford EBONTANE without whose academic endorsement this project wouldn't have been successful. Their relentless availability at each stage in the progress of this work, ensured that it was conducted within the appropriate scientific framework.

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Special gratitude to my Mom, OBASE Christine, and all my siblings, especially OBASE Fruition and OBASE David; your words of encouragement and prayers sustained me. My friend, NGUESSI Jacques provided financial and moral supports.

Ultimately, I thank God Almighty; to Him be all the glory.

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182	BOOM II YAP	L	Medical microbiology
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187	VOUNDI VOUNDI Esther	L	Medical virology
188	ANGANDJI TIPANE Prisca epse ELLA	AL	Clinical Biology/Hematology
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236	MENGONG epse MONEBOULOU Hortense	L	Pediatric dentistry
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240	GAMGNE GUIADEM Catherine M	AL	Dental surgery
241	KWEDI Karl Guy Grégoire	AL	Oral surgery
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251	MPONDO MPONDO Emmanuel	P	Pharmacy
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253	ANGO Yves Patrick	AL	Chemistry of natural substances
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259	ABA'A Marthe Dereine	AL	Drug Analysis
260	FOUMANE MANIEPI NGOUOPIHO Jacqueline Saurelle	AL	Pharmacology
261	MINYEM NGOMBI Aude Périne epse AFUH	AL	Pharmaceutical Regulation

Key

P= Professor

AP = Associate Professor

SL = Senior Lecturer

L = Lecturer

AL = Assistant Lecturer

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LIST OF ABBREVIATIONS

Acronym	Meaning
ACOG	American College of Obstetricians and Gynecologists
ANC	Antenatal Conssultation
APA	Antiphospholipid Antibody
APE	Acute Pulmonary Edema
BMI	Body Mass Index
CVA	Cerebrovascular Accident
DBP	Diastolic Blood Pressure
HELLP	Hemolysis, Elevated Liver enzymes, Low platelet
ICU	Intensive Care Unit
IUFD	Intrauterine Fetal Demise
IUGR	Intrauterine Growth Restriction
IM	Intramuscular
IUFD	Intrauterine Fetal Death
IUGR	Intrauterine Growth Restriction
IV	Intravenous
MFMU	Maternal-Fetal Medicine Units
$MgSO_4$	Magnesium Sulfate
MMR	Maternal Mortality Ratio
SPE	Severe preeclampsia
PlGF	Placental Growth Factor
SBP	Systolic Blood Pressure
VEGF	Vasculare Endothelial Growth Factor
WHO	World Health Organization
YCH	Yaounde Central Hospital
YGOPH	Yaounde Gyneco-Obstetrics and Paediatrics Hospital

ABSTRACT

Background: Magnesium sulfate ($MgSO_4$) is the anticonvulsant of choice for the prevention and control of eclamptic seizures, however, there are variations in dosages and concerns about its toxicity.

Objective: This study sought to evaluate the efficacy of suboptimal dose and standard dose regimens of $MgSO_4$ in the management of severe preeclampsia and eclampsia, and its adverse effects.

Methods: We conducted a prospective hospital-based analytic study in two tertiary hospitals in Yaoundé including 123 women with severe preeclampsia and eclampsia, recruited through nonprobability consecutive and exhaustive sampling. The subjects were divided into two therapeutic groups: those who received incomplete doses of $MgSO_4$ for various reasons (group A, n = 41), and those who received the standard doses (group B, n = 82).

Results: The mean age of the participants was 30.5 ± 7.3 years, and the mean gestational age at diagnosis was 35.6 ± 4.1 weeks. The rate of control of convulsions with $MgSO_4$ was 92.7% in group A and 95.1% in group B (OR: 1.5; 95% CI: 0.3 – 7.2; P = 0.58). The case fatality rate was higher in group A (14.6%, OR: 0.2; 95% CI: 0.1 – 0.9; P = 0.03), while prevalence of maternal complications (46.3%; OR: 3.1, 95% CI: 1.3 – 7.2; P = 0.01), fetal complications (59.8%, OR: 2.5, 95 CI: 1.2 – 5.6; P = 0.02), caesarean delivery rate (66.7%; OR: 2.6, 95% CI: 1.2 – 5.5; P = 0.02), and perinatal deaths (32%; OR: 1.3, 95% CI: 0.6 – 3.1; P = 0.49) were higher in group B. Multiple logistic regression show that standard $MgSO_4$ dose regimen was associated with decreased maternal mortality, decreased rate of admission into the ICU, and higher 5^{th} minute APGAR scores. The prevalence of adverse effects was generally low and insignificant between the two groups (7.3%; OR: 0.23, 95% CI: 0.02 – 1.9, P = 0.14).

Conclusion: Magnesium sulfate has proven to be a safe and effective drug in the prevention and treatment of eclamptic seizures, and standard regimens are associated with better feto-maternal outcome in our setting.

Key words: Magnesium sulfate, severe preeclampsia, eclampsia, toxicity, efficacy, maternal mortality.

RESUME

Contexte : Le sulfate de magnésium ($MgSO_4$) est l'anticonvulsivant de choix pour la prévention et le contrôle des crises éclamptiques . Cependant, l'utilisation de faibles doses suscite des inquiétudes, ainsi que sa toxicité.

Objectif : Cette étude visait à évaluer l'efficacité des doses sous-optimales et des doses standard de $MgSO_4$ dans la prise en charge de la prééclampsie sévère et de l'éclampsie , ainsi que de ses effets indésirables.

Méthodes : Nous avons mené une étude prospective analytique en milieu hospitalier dans deux hôpitaux tertiaires de Yaoundé incluant 123 femmes atteintes de prééclampsie et d'éclampsie sévères , recrutées par échantillonnage non probabiliste consécutif et exhaustif. Les sujets ont été divisés en deux groupes thérapeutiques : celles ayant reçu des doses incomplètes de $MgSO_4$ pour diverses raisons (groupe A, n = 41), et celles ayant reçu les doses standards (groupe B, n = 82).

Résultats : L'âge moyen des participantes était de 30,5 ± 7,3 ans et l'âge gestationnel moyen au moment du diagnostic était de 35,6 ± 4,1 semaines. Le taux de contrôle des convulsions avec $MgSO_4$ était de 92,7 % dans le groupe A et de 95,1 % dans le groupe B [AOR IC 95 %: 1,5 (0,3 – 7,2); P = 0,58]. Le taux de létalité était plus élevé dans le groupe A [14,6 %, AOR IC 95 %: 0,2 (0,1 – 0,9); P = 0,03], tandis que la prévalence des complications maternelles [46,3 % ; AOR IC 95 % : 3,1 (1,3 – 7,2); P = 0,01], des complications fœtales [59,8 %, AOR IC 95 % : 2,5 (1,2 – 5,6); P = 0,02], du taux d'accouchement par césarienne [66,7 % ; AOR IC 95 %: 2,6(1,2 – 5,5); P = 0,02] et des décès périnatals [32 % ; AOR IC 95 %: 1,3 (0,6 – 3,1); P = 0,49] étaient plus élevées dans le groupe B. La régression logistique multiple montre que le schéma posologique standard de $MgSO_4$ était associé à une diminution mortalité maternelle, taux d'admission en réanimation réduit et scores APGAR à la 5e minute plus élevés · La prévalence des effets indésirables était généralement faible et non significative entre les deux groupes [7,3 % ; AOR IC à 95 %: 0,23 (0,02 – 1,9) : P = 0,14].

Conclusion : Le sulfate de magnésium s'est avéré être un médicament sûr et efficace dans la prévention et le traitement des crises éclamptiques , et les schémas thérapeutiques standard sont associés à un meilleur résultat fœto -maternel dans notre contexte.

Mots clés : Sulfate de magnésium, prééclampsie sévère, éclampsie , toxicité, efficacité, mortalité maternelle.

CHAPTER 1 : INTRODUCTION

1.1 Background

Hypertensive disorders of pregnancy constitute one of the leading causes of maternal and perinatal mortality worldwide [1]. In Africa and in Cameroon they are the third cause of maternal mortality [2,3]. Preeclampsia/eclampsia are important entities among the hypertensive disorders of pregnancy. Preeclampsia (PE) is defined as a multisystem pregnancy-specific disorder of unknown etiology characterized by new-onset significant hypertension with proteinuria, or evidence of organ damage, after 20 weeks of gestation, in a previously normotensive nonproteinuric woman [1,4]. Globally, PE complicates 2 - 8% of pregnancies, and constitutes about 20% of cases of hypertension in pregnancy [1,5]. In Cameroon, the prevalence is between 4.9 and 8.2% [2,5,6]. Eclampsia, on the other hand, is the convulsive manifestation of PE and is among the more severe manifestations of the disease. It is defined by new-onset tonic clonic, focal, or multifocal seizures in the absence of other causative conditions such as epilepsy, cerebral arterial ischemia and infarction, intracranial hemorrhage, or drug use [1]. It is a dramatic complication of PE. Without appropriate prophylactic treatment, some 2 – 10% of preeclamptic women will develop eclampsia, with most seizures occurring in women with severe preeclampsia [7]. In developing countries, the risk of mortality with seizures is as high as 25 – 50% [7]. One study carried out in Cameroon in 2016 revealed that eclampsia was the cause of 17.5% of maternal deaths [2]. The maternal and fetal complications of the disease reported in our setting include: HELLP syndrome, retroplacental hematomas, prematurity, intrauterine fetal death and increased frequency of caesarean section [6,8].

Magnesium sulphate ($MgSO_4$) has been recommended by the world health organization (WHO) as the drug of choice for the prevention of seizures in women with severe preeclamptic (SPE), or prevention of recurrence of seizures in the eclamptic woman [9–11]. It is a low-cost drug and is safe to use. Even with the risk of side effects and toxicity, many studies have proven that $MgSO_4$ is much more superior in the treatment of eclampsia compared to other anticonvulsants [12]. It lowers the risk of recurrence of seizures in eclamptic women by 52% compared to diazepam, and by 67% when compared to phenytoin [10]. Also, women with severe pre-eclampsia given magnesium sulfate have a 58% lower risk of developing eclampsia compared to the placebo group [10].

Although the precise mechanism of action is not completely understood, $MgSO_4$ is thought to cause vasodilatation of cerebral vessels by blocking calcium receptors, thus reducing cerebral

ischemia. It also causes peripheral arteriolar dilatation thus reducing blood pressure. It may also protect the blood brain barrier and limit cerebral edema formation or it may have a central anticonvulsant action [13]. Pritchard showed that $MgSO_4$ concentration required for eclampsia prevention or treatment should be higher than normal serum level of 1.8 – 3 mgdl, and suggested that therapeutic concentration should be between 4 and 7 mEq/L (4.2 – 8.4 mg/dl) [10,14].

Adverse effects are rare and include loss of the patellar reflex (typically occurring at a serum concentration of 8 – 10 mEq/L) and respiratory depression (at >13mEq/L) [10]. Therefore close monitoring for the loss of deep tendon reflexes, respiratory rate <12 breathes/minute, urine output <30 mL/hour, and high plasma concentrations are of paramount importance [12]. Oliguria is an element of the disease process and can lead to reduced clearance by the kidneys, and not an adverse effect of $MgSO_4$. However, because magnesium sulfate is cleared by the kidneys, oliguria with urine output of less than 30 cc per hour is used as a threshold for withholding a scheduled dose, in order to avoid toxic levels [10]. In case of toxicity, calcium gluconate is used as an antidote.

1.2 Problem statement

Recent reproductive health data revealed that SPE/eclampsia are major causes of maternal deaths [8]. Eclampsia is one of the worst outcomes of hypertensive diseases of pregnancy because of its unpredictable evolution as well as its potentially severe complications [8]. In Cameroon, the prevalence of hypertensive disorders of pregnancy remains as high as 8.2%, with eclampsia complicating 0.96% of pregnancies [6,8]. Despite advances in the management of the disease, eclampsia and other hypertensive diseases of pregnancy, according to one study in Cameroon in 2015, were the first cause of maternal mortality, accounting for over 22.4% of maternal deaths [3]. Another study conducted in Cameroon in 2019 added that the maternal and neonatal mortality rates associated with the disease were 8.6% and 24.4% respectively [8].

While magnesium sulfate has been the drug of choice for the prevention and treatment of seizures associated with these conditions, there are variations in dosages and administration protocols, and a lack of consensus on the optimal dosages and administration protocols. One important factor affecting the use of $MgSO_4$ and thus its effectiveness is its availability at point of use [15]. In our setting, there are concerns about the use of incomplete (suboptimal) doses of magnesium sulfate for various reasons such as financial constraints or point of use unvailability. There are also concerns about potential adverse effects, including the nature, frequency, and severity. Current

literature provides conflicting evidence on the safety profile of $MgSO_4$, including concerns about maternal respiratory depression, neuromuscular blockade, and other complications. These warrant a thorough examination of its efficacy and safety as used in our services in the management of SPE and eclampsia. Finally, several studies have shown that low dose $MgSO_4$ regimens (suboptimal doses) are an effective tool in preventing maternal and perinatal morbidity and mortality [16–18], but there is paucity of data in Cameroon.

1.3 Significance of the study

The findings of this study can thus contribute to the development or modification of clinical practice guidelines, ensuring that healthcare providers are equipped with the latest evidence to optimize patient outcomes. In addition, enhancing the understanding of magnesium sulfate's efficacy and adverse effects can contribute to strategies aimed at reducing maternal and neonatal mortality associated with severe preeclampsia and eclampsia. Finally, this study can contribute in identifying gaps in the current knowledge base, which can further contribute in guiding future research efforts, by directing attention to areas that require further exploration and refinement.

1.4 Research goal

The goal of this study is to advance the knowledge and evidence base surrounding the use of magnesium sulfate in the management of severe PE and eclampsia needed to inform clinical practices, improve feto-maternal outcomes and reduce maternal morbidity and mortality.

1.5 Research questions

1.5.1 What are the sociodemographic, clinical and paraclinical profiles of women with severe preeclampsia and eclampsia at the Yaoundé Gyneco-obstetric hospital (YGOPH) and the Yaoundé Central Hospital (YCH)?

1.5.2 What are the maternal and fetal outcome between women with SPE and eclampsia treated with complete versus incomplete doses of $MgSO_4$?

1.5.3 What is the frequency of adverse effects of $MgSO_4$ associated with complete versus incomplete doses in severe preeclampsia and eclampsia?

1.6 Research hypothesis

Subtherapeutic doses of magnesium sulfate may significantly prevent and treat seizures among women with severe preeclampsia and eclampsia at the YGOPH and YCH, and there are few adverse effects of the drug in these settings.

1.7 Research objectives

1.7.1 General objective

To evaluate the efficacy of incomplete and complete magnesium sulfate regimens, and their adverse effects in the management of severe preeclampsia and eclampsia in two tertiary hospitals in Cameroon.

1.7.2 Specific objectives

1. To describe the socio-demographic, clinical and paraclinical characteristics of women with severe preeclampsia and eclampsia at the Yaoundé Gyneco-obstetric and pediatric hospital (YGOPH), and the Yaoundé Central Hospital (YCH).

2. To compare the maternal and fetal outcomes following treatment with suboptimal doses and complete doses of magnesium sulfate.
3. To assess the types and frequency of adverse effects of magnesium sulfate and their determinants in both treatment subgroups.

1.8 Research scope

The scope of this study is limited to recruiting at least 116 women irrespective of their ages, admitted at the YGOPH and YCH for the management of severe preeclampsia or eclampsia, in whom magnesium sulfate have been used as part of their treatment, and who must have given their informed consent to participate in the study. The recruitment period will last for a maximum of 6 months and will end when either 115 women would have been recruited or 6 months would have passed. An interviewer-administered questionnaire, alongside the patients' files will be used to evaluate the efficacy of magnesium sulfate and investigate its adverse effects.

1.9 Definition of terms and concepts

- **Efficacy**

Efficacy is the capacity to produce an effect; it is ability of an intervention or a drug to produce a desired effect in expert hands and under ideal circumstances. Effectiveness is the capability of producing a desired effect [19].

- **Adverse drug effect**

An adverse drug effect/reaction is a response to a drug which is noxious and unintended and which occurs at doses normally used for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function. In sum, an adverse drug effect is harm directly caused by the drug at normal doses, during normal use [20].

- **Preeclampsia**

Preeclampsia is defined as a multisystem pregnancy-specific disorder of unknown etiology characterized by new-onset significant hypertension and proteinuria, or evidence of organ damage, after 20th weeks of gestation, in a previously normotensive nonproteinuric woman [1,4]. Two forms

exist according to the severity: PE without severe features and severe PE. The features of severity are shown in table I.

- **Eclampsia**

Eclampsia is defined by new-onset tonico-clonic, focal, or multifocal seizures in the absence of other causative conditions such as epilepsy, cerebral arterial ischemia and infarction, intracranial hemorrhage, or drug use [1].

- **Oliguria**

Oliguria is defined as urinary output less than 400 ml per day or less than 30 ml per hour for an adult, and is one of the earliest signs of impaired renal failure. According to the Acute Dialysis Quality Initiative group, a patient with urinary output <0.3 ml/kg/hour for at least 24 hours can be defined to be oliguric [21].

- **Perinatal mortality rate**

This is the ratio of deaths of children within one week of birth (early neonatal deaths) plus fetal deaths of minimum gestation period 28 weeks or minimum fetal weight of 1000g, expressed per 1000 births [22].

- **Maternal mortality**

Maternal mortality is defined as the death of a woman while pregnant or during childbirth or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from unintentional or incidental causes [23].

- **Maternal mortality ratio (MMR)**

Maternal mortality ratio (MMR) is the number of maternal deaths during a given time period per 100 000 live births during the same time period [23].

- **Case fatality rate**

This is the proportion of people who die from a specified disease among all individuals diagnosed with the disease over a certain period of time. In this study the case fatality rate represents the

proportion of women with severe preeclampsia or eclampsia who died during the study period [24].

- **Intrauterine growth restriction (IUGR)**

IUGR is defined as a sonographic estimated fetal weight (EFW) or abdominal circumference (AC) below the 10^{th} percentile for gestational age [25].

- **Intrauterine fetal demise (IUFD)**

This is antepartum fetal death after age of viability (22 weeks gestation, or fetal weight of ≥500g, or crown-to-heel length of ≥25 cm according to WHO and the International Classification of diseases 10^{th} revision (ICD-10) [26].

- **Time-to-treatment initiation (TTI)**

This is the period between diagnosis and the start of definitive treatment [27]. In this study, the TTI referred to the time between the diagnosis of severe preeclampsia or eclampsia to the initiation of magnesium sulfate treatment.

- **Suboptimal dose**

Suboptimal dosing refers to dosing below therapeutic level [28]. In this study, suboptimal dose of magnesium sulfate (incomplete dose) was used to refer to a situation where either all, or one or more of the maintenance doses of $MgSO_4$ was not administered for some reasons.

CHAPTER 2 : LITERATURE REVIEW

2.1 Introduction

This chapter described the methods of literature review. An overview of the subject of preeclampsia and eclampsia has been elaborated including definition, epidemiology, risk factors, etiopathogenesis, pathophysiology and treatment. Magnesium sulfate in the management of preeclampsia is also described, historical aspects, treatment regimens, pharmacokinetics, pharmacodynamics, and its availability and training. Finally, a thorough review of literature on socio-obstetrical, clinical and para-clinical profile of preeclamptic and eclamptic patients, incidence of eclampsia and rate of control of seizures, toxicity of magnesium sulfate, and feto-maternal outcomes related to use of $MgSO_4$ has been elaborated.

2.2 Methods

A review of relevant literature was conducted using an internet search that included books, scientific journal articles, published thesis, newsletters, magazines, conference proceedings, and WHO data bases. Search engines like Google Scholar, Medline, PubMed and ChatGPT were used. Specific characteristics included hypertensive disorders of pregnancy, management of preeclampsia and eclampsia, socio-obstetrical profile of preeclamptic and eclamptic women, and efficacy of magnesium sulfate in the management of severe preeclampsia and eclampsia.

2.3 Overview of preeclampsia and eclampsia

2.3.1 Definition

2.3.1.1 Preeclampsia

Preeclampsia (PE) is defined as a multisystem pregnancy-specific disorder of unknown etiology characterized by new-onset significant hypertension and proteinuria, or evidence of organ damage, after 20th weeks of gestation, in a previously normotensive nonproteinuric woman (1,4). According to the American College of Obstetricians and Gynecologists (ACOG) 2020 the **diagnostic criteria for PE include** [1]:

Blood pressure

- Systolic blood pressure (SBP) of ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with previously normal blood pressure.
- SBP ≥ 160 mmHg or DBP ≥ 110 mmHg. (Severe hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy).

and

Proteinuria

- ≥ 300 mg per 24-hour urine collection (or this amount extrapolated from a timed collection) or
- Protein/creatine ratio of ≥0.3 mg/dl, or
- Urine dipstick reading of 2+ (used only if other quantitative methods not available)

Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following (evidence of end-organ damage):

- Thrombocytopenia (platelet count <100,000/µl)
- Impaired liver function: elevated blood concentrations of liver transaminases to twice normal concentration.
- Renal insufficiency: serum creatinine concentrations >1.1 mg/dL or doubling of the serum creatinine concentration in the absence of other renal disease.
- Pulmonary edema
- New-onset headache unresponsive to medication and not accounted for by alternative diagnoses or visual symptoms.

According to the severity of the disease it is classified in two categories: PE without severe features and severe PE as shown in the table below (table I):

Table I. Indicators of severe preeclampsia

Abnormality	Nonsevere	Severe
Diastolic BP	<110 mmHg	≥110 mmHg
Systollic BP	<160 mmHg	≥160 mmHg
Proteinuria	Absent	Present
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper abdominal pain	Absent	Present
Oliguria	Absent	Present
Convulsion (eclampsia)	Absent	Present
Serum creatinine	Normal	Elevated
Thrombocytopenia (<100,000/µl)	Absent	Present
Serum transaminase elevation	Minimal	Marked
Fetal-growth restriction	Absent	Present
Pulmonary edema	Absent	Present
Gestational age	Late	Early

Source: *Courtesy of Williams Obstetrics, 25th edition (2018)*[29].

2.3.1.2 Eclampsia

Eclampsia is defined by new-onset tonic-clonic, focal, or multifocal seizures in the absence of other causative conditions such as epilepsy, cerebral arterial ischemia and infarction, intracranial hemorrhage, or drug use [1,29]. The term PE implies that the natural history of patients with persistent hypertension and significant proteinuria during pregnancy is to have tonic-clonic seizures if no prophylaxis is instituted. Eclampsia often (78 – 83% of cases) is preceded by premonitory signs of cerebral irritation such as severe and persistent occipital and frontal headaches, blurred vision, photophobia, and altered mental status. Headaches are believed to reflect the development of elevated cerebral perfusion pressure, cerebral edema, and hypertensive encephalopathy. However, eclampsia can occur in the absence of signs or symptoms. Of note, a significant proportion of women (20 – 38%) do not demonstrate the classic signs of PE (hypertension or proteinuria) before the seizure episode. Thus, the notion that PE has a natural linear progression from PE without severe features, to PE with severe features and eventually to eclamptic convulsions is inaccurate [1].

2.3.1.3 Proteinuria

Proteinuria during pregnancy is defined as 300 mg/dL of protein or more in a 24-hour urine collection or protein to creatinine ratio of 0.30 or more. When quantitative methods are not available, a urine protein dipstick reading can be substituted. However, dipstick urinalysis has a high false positive and false-negative test results. A test result of 1+ proteinuria is false-positive in 71% of cases compared with 300 mg cutoff on 24-hour urine collection, and even 3+ proteinuria test results may be false positive in 7% of cases. Using the same 24-hour urine collection standard, the false-negative rate for dipstick urinalysis in 9%. If urinalysis is the only available means of assessing proteinuria then the overall accuracy is better using 2+ as the discriminant value [1,30].

2.3.1.4 HELLP syndrome

HELLP syndrome (hemolysis, elevated liver enzyme, low platelets) may be an outcome of severe PE, although some authors believe it to have an unrelated etiology. The syndrome has been associated with particularly high maternal and perinatal morbidity and mortality rates and may be present without hypertension or, in some cases, without proteinuria [31].

2.3.2 Classification of hypertensive disorders of pregnancy

As specified by the National High Blood Pressure Education Program (NHBPEP) Working Group, the classification is as follows:

2.3.2.1 Gestational hypertension

The characteristics include: BP ≥ 140/90 mmHg for the first-time during pregnancy; no proteinuria; BP returns to normal < 12 weeks' postpartum; and final diagnosis made only postpartum

2.3.2.2 Chronic hypertension

This is characterized by either (1) BP ≥ 140/90 mmHg before pregnancy or diagnosed before 20 weeks' gestation; not attributable to gestational trophoblastic disease or (2) hypertension first diagnosed after 20 weeks' gestation and persistent after 12 weeks postpartum.

2.3.2.3 Preeclampsia/eclampsia

Preeclampsia/eclampsia is characterized by a BP ≥ 140/90 mmHg after 20 weeks' gestation in a woman with previously normal BP and who has proteinuria (≥0.3 g protein in 24-h urine specimen). Eclampsia is defined as seizures that cannot be attributable to other causes, in a woman with preeclampsia.

2.3.2.4 Superimposed preeclampsia

This is characterized by (1) new-onset proteinuria (≥300 mg/24 h) in a woman with hypertension but no proteinuria before 20 weeks' gestation and (2) a sudden increase in proteinuria or BP, or a platelet count of <100,000/mm^3, in a woman with hypertension and proteinuria before 20 weeks' gestation.

2.3.3 Interest

2.3.3.1 Epidemiology

Globally, PE complicates 2 - 8% of pregnancies, and occurring in about 20% of hypertensive pregnant women [1,5]. The incidence of the disease is markedly influenced by race and ethnicity – and thus genetic predisposition. In one study by the Maternal-Fetal Medicine Units (MFMU) Network in 2012, the incidence of PE was 5% in white, 9% in Hispanic, and 11% in African-American women [29]. In sub-Saharan Africa, according to a meta-analysis conducted in 2023, the overall pooled incidence of PE was 13% [95% CI: 0.12-0.14], with an increasing trend of the disease from 2.22% in 2010 to 2.67% in 2018 [32]. Two randomized controlled trials indicate that eclampsia occurred in a small proportion of patients with PE (1.9%) or severe PE (3.2%)[1]. In

Cameroon, the prevalence of PE is between 4.9 – 8.2%, with eclampsia occurring in 151 out of 25680 deliveries (0.96%) [2,5,6].

2.3.4 Relevant anatomy and physiology

2.3.4.1 The endometrium

The uterus is made up of an external layer of smooth muscle called the **myometrium comprising most of the uterus,** and an internal layer called the **endometrium** which is the lining the uterine cavity. This endometrium is composed of an overlying epithelium, invaginating glands, and supportive, vascular stroma. The endometrium varies greatly throughout the menstrual cycle. Basically, it consists of two layers: a **functionalis layer**, which is sloughed with menses, and a **basalis layer**, which serves to regenerate the functionalis layer following each menses [29] (Figure I).

During pregnancy, the endometrium is termed **decidua** and undergoes dramatic hormonally driven alteration. The decidua parietalis is in turn is composed of three layers: **zona compacta** (surface layer), **zona spongiosa** (middle portion), and **zona basalis** (basal zone). **The zona compacta and spongiosa together form the zona functionalis**. The basal zone remains after delivery and gives rise to a new endometrium [29].

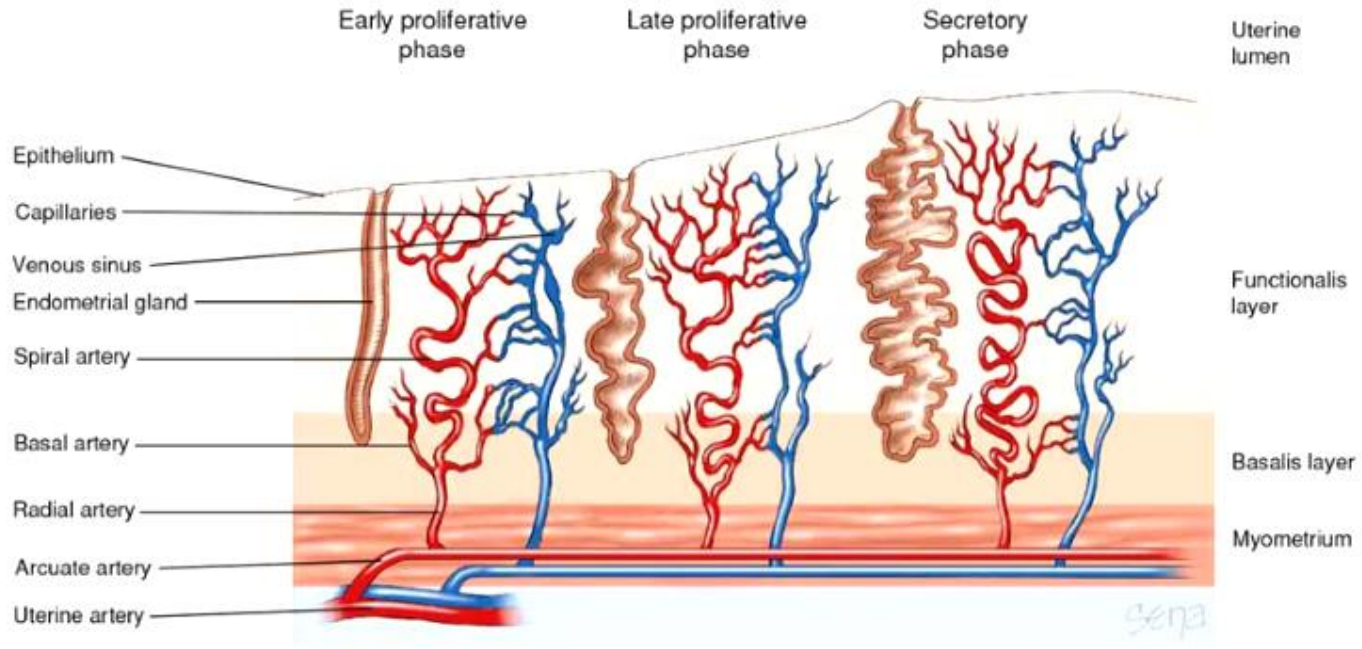

Figure I. The endometrium: layers and vascularization

Source: courtesy of Williams Obstetrics, 25th edition, 2018 [29].

The endometrial blood vessels form a vascular bed with a number of unusual properties. Unlike most vascular beds which maintain very constant structure and function throughout life, the endometrial vasculature alters dynamically. Blood supply to the endometrium arrives through the **radial arteries**, which arise from the **arcuate arteries** within the myometrium. After passing through the myometrial-endometrial junction the radial arteries split, to form the **smaller basal arterioles** that supply the basal portion of the endometrium and the **spiral arterioles** which continue up towards the endometrial surface (Figure I). The spiral arterioles which supply the functional layer of the endometrium, have a distinctive coiled appearance that becomes more pronounced during the secretary phase of the menstrual cycle. The spiral arterioles are unusual among resistance arterioles, in that they lack significant elastin within the internal lamina [33].

2.3.4.2 Hematological changes in pregnancy

Blood volume is markedly raised during pregnancy and the rise is progressive and inconsistent. All the constituents of blood are equally affected with this increased volume (table II). **The blood volume starts to increase from about 6th week**, expands rapidly thereafter to **maximum 40 – 50% above the nonpregnant level at 30 – 34 weeks**. The level remains almost static till delivery. Concerning the plasma volume, the rate of increase almost parallels that of blood volume but the maximum is reached to the extent of 50%. Total plasma volume increases to the extent of 1.25 liters, with a relatively greater increase in multigravida, multiple pregnancy and with large baby. The red blood cell (RBC) mass is increased to the extent of 20 – 30% with a total increase in volume of about 350 ml. The disproportionate increase in plasma and RBC volume produces a state of hemodilution (fall in hematocrit) during pregnancy. Thus, even though the total hemoglobin (Hb) mass increases during pregnancy to the extent of 18 – 20%, there is apparent fall in Hb concentration. At term, the fall is about 2g from nonpregnant value [4].

Concerning blood coagulation factors, pregnancy is a hypercoagulable state. Fibrinogen level is raised by 50% from 200 – 400 mg/dl in nonpregnant to 300 – 600 mg/dl in pregnancy. There is static or a slight fall to the extent of platelet count of 15% of prepregnant level. Recent studies show that gestational thrombocytopenia may be due to hemodilution and increased platelet consumption [4]. The levels of coagulation factors normalize 2 weeks postpartum.

Table II. Principal hematologic changes during pregnancy

Source: Courtesy DC Dutta's Obstetrics, 8th edition, 2015.

Parameters	Nonpregnant	Pregnancy near term	Total increment	Change
Blood volume (ml)	4000	5500	1500	+ 30 – 40%
Plasma volume (ml)	2500	3750	1250	+ 40 – 50%
Red Cell volume (ml)	1400	1750	350	+ 20 – 30%
Total Hb (g)	475	560	85	+ 18 – 20%
Hematocrit (whole body)	38%	32%		Diminished

2.3.4.3 Cardiovascular modifications of pregnancy.

Changes in cardiac function becomes apparent during the first 8 weeks of pregnancy [29]. Cardiac output (CO) starts to increase from 5th week of pregnancy and reaches its peak **40 – 50% at about 30 – 34 weeks** [4]. This is as a result of increased in blood volume (CO is a product of stroke volume (SV) and heart rate (HR)). CO is lowest in the sitting or supine position and highest in the right or left lateral or knee chest positions. It returns to pre-labor values by 1 hour following delivery and to the pre-pregnancy level by another 4 weeks' time. Concerning the blood pressure (BP), **there is a decrease in BP due to decrease in systemic vascular resistance (SVR)** owing to the smooth muscle relaxing effects of progesterone, nitric oxide (NO), prostaglandins and atrial natriuretic peptide (ANP) (i.e., BP = CO × SVR). There is an overall decrease in diastolic blood pressure (DBP) and mean arterial pressure (MAP) by 5 – 10 mm Hg.

The renin-angiotensin-aldosterone axis is intimately involved in blood pressure control via sodium and water balance. All components of this system show increased levels in normal pregnancy. Renin is produced by both maternal kidney and the placenta, and greater amounts of angiotensin are produced by both maternal and fetal liver and in part from augmented estrogen production during normal pregnancy.

2.4 Etiopathogenesis

2.4.1 Risk factors

A variety of risk factors have been associated with increased probability of PE and eclampsia [1,29]:

- Maternal age <20 years and ≥35 years
- Nulliparity
- Multifetal gestations
- Preeclampsia in previous pregnancy
- Chronic hypertension
- Pregestational diabetes
- Gestational diabetes
- Thrombophilia
- Systemic lupus erythematosus
- Prepregnancy body mass index (BMI) > 30 kgm^{-2}
- Antiphospholipid antibody (APA) syndrome
- Kidney disease
- Assisted reproductive technology
- Obstructive sleep apnea

In sub-Saharan Africa, other selected risk factors of PE include [8,34]:

- Maternal anemia in first trimester of pregnancy
- Low socio-economic status
- Family history of PE/eclampsia
- Lack of antenatal care (ANC) visits.

2.4.2 Etiology

Several imposing mechanisms have been proposed to explain the cause of PE. It is possible that a combination of some of these mechanisms may be responsible for triggering the clinical spectrum of PE. However, currently considered ones include [1,29]:

- Placental implantation with abnormal trophoblastic invasion of uterine vessel
- Other contributing factors:
  - Immune maladaptive tolerance between maternal, paternal (placental), and fetal tissues
  - Very low-density lipoprotein toxicity
  - Genetic imprinting including inherited predisposing genes and epigenetic influences
  - Increases trophoblastic apoptosis or necrosis
  - Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy.

Abnormal trophoblastic invasion

In normal pregnancy there is invasion of the cytotrophoblast into the wall of the spiral arterioles of the uteroplacental bed, which occurs in 2 waves: i) in the first trimester (10 – 12 weeks) with invasion up to decidual segments, and ii) in second trimester (16 – 20 weeks) with invasion up to myometrial segments. This invasion replaces the endothelial lining and the muscular arterial wall by fibrinoid formation, there by transforming the spiral arterioles into low resistance, low pressure, and high flow system (spiral arteriole remodeling). This is so because in normal pregnancy, soluble angiogenic factors like vascular endothelial growth factor (VEGF), placental growth factor (PlGF), and transforming growth factor beta (TGF-β) help the blood vessels to grow and keep the endothelium health.

In PE, the placenta releases two anti-angiogenic factors: *soluble fms-like tyrosine kinase 1 (sFLT-1)* and *soluble endoglin (sEng)* which are receptors for the angiogenic factors (VEGF, PlGF and TGF-β). They bind and block the angiogenic growth factors, thereby resulting in failure of the second wave of endovascular trophoblast migration, resulting in small-caliber vessels with high resistance to flow, thereby reducing the blood supply to the fetoplacental unit. Hence PE is characterized by widespread endothelial dysfunction and vasospasm.

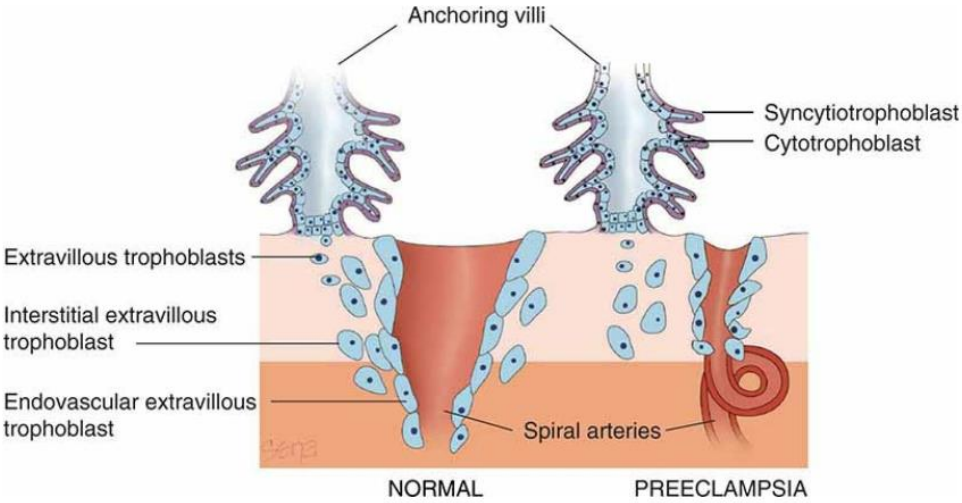

Figure II. Trophoblastic invasion in case of normal pregnancy and in case of preeclampsia
Source: courtesy of Williams Obstetrics 25th edition (2018)[29].

2.4.3 Pathophysiology

2.4.3.1 Pathophysiology of preeclampsia

PE is a multisystem disorder with poorly understood pathophysiology. It is considered as a "two-stage" disease: i.e., a systemic syndrome that originates in the placenta (stage 1) and characterized by maternal widespread endothelial dysfunction (stage 2). The underlying basic pathology is endothelial dysfunction and intense vasospasm. This results in vasoconstriction, resulting in ischemia of surrounding tissues and thus hemorrhage, necrosis and other pathological changes. The major organ system involved include the central nervous system, hematological system, hepatic system, renal system and the cardiovascular system. The clinical features depend on organ system involved as summarized in the table III below.

Table III. physiology of preeclampsia in major organ systems.

Source: Courtesy of Williams Obstetrics, 25th edition (2018)[29].

Organ system	Pathophysiology	Organ effect	Clinical features	Complications
CNS	Cerebral vasoconstriction when MAP>120 mmHg, cerebral autoregulation fails	Cerebral ischemia, infarctions, petechial hemorrhages	Head aches (occipital), mental confusion, drowsiness, dizziness, convulsions (eclampsia)	Cerebral edema, intracranial hemorrhage, pontine hemorrhage
Cardiovascular	Increased cardiac output, increased peripheral resistance	Hypovolemia	Weight gain, edema, hemoconcentration (Hb>12g/dl or creatinine > 0.8 mg/L	Left ventricular failure
Heart	Myocardial and sub-endocardial hemorrhage and necrosis		Dyspnea, edema, chest pain	Left ventricular failure
Lungs	Increased capillary permeability	Bronchopneumonia	Breathlessness	Pulmonary edema
Liver	Ischemia secondary to vascospasm coupled with fibrin deposition secondary to endothelial damage	Periportal hemorrhage, necrosis	Nausea, vomiting, epigastric pain, right hypochondriac tenderness	HELLP, subcapsular hemorrhage, rarely hepatic rupture
Kidneys	Damaged, swollen endothelial cells lining glomerular arterioles and arteriolar spasm results in decreased GFR; renal tubular necrosis leads to affection of permeability across renal tubules	Glomerulo capillary endotheliosis	Elevated serum levels of uric acid, urea and creatinine	Acute renal failure
Placenta	Atherosis of placental vessels i.e., endothelia damage by mononuclear cell infiltration, deposition of lipid and lipophages in arterial wall. End result is placental hypoperfusion.	Placental infarcts, chronic placental insufficiency	Oligohydramnios, chronic fetal distress	Intrauterine growth restriction, fetal demise, abruptio placentae.
Coagulation system	Platelets activation in microcirculation of the placenta, kidney and liver. Thrombocytopenia, increased fibrin production, decreased fibrinolytic activity	Increased fibrin and platelet deposition particularly in the placental, renal, hepatic arteries	Bleeding from different sites	DIC, HELLP syndrome

2.4.3.2 Pathophysiology of eclampsia

It is believed that in eclampsia there is abnormal cerebral blood flow in the setting of extreme hypertension. The regulation of cerebral perfusion is inhibited, vessels become dilated with increased permeability, and cerebral edema occurs, resulting in ischemia and encephalopathy. With increasing blood pressure, cerebral autoregulation is impaired resulting in regions of ischemia as well as microhemorrhage, each of which may initiate a seizure focus. In extreme hypertension, normal compensatory vasoconstriction may become defective. Several autopsy findings support this model and consistently reveal swelling and fibrinoid necrosis of vessel walls [31].

2.5 Clinical features

2.5.1 Clinical features of preeclampsia

Because the clinical manifestations of PE can be heterogenous, diagnosing PE may not be straightforward. PE without features of severity may be asymptomatic. Many cases are detected through routine prenatal screening.

2.5.1.1 Symptoms of preeclampsia

Patients with PE with sever features display end-organ effects and may complain of the following: headache; disturbed sleep; diminished urinary output; epigastric pain; dyspnea; eye symptoms (blurring of vision, scotomata, dimness of vision, blindness); weakness or malaise (may be evidence of hemolytic anemia) [4,31].

2.5.1.2 Signs of preeclampsia

- Elevation of blood pressure
- Abnormal weight gain
- Edema (pedal, ankle, vulvar)
- Altered mental status
- Pulmonary edema
- Evidence of placental insufficiency such as scanty liquor or intrauterine growth retardation

2.5.2 Clinical features of eclampsia

2.5.2.1 Symptoms eclampsia

Eclampsia always should be considered in a pregnant patient with a seizure episode. It can occur during the antepartum, intrapartum, and postpartum periods. Ninety (90) percent of eclamptic cases occur after 28 weeks' gestation [31].

Features of eclampsia include the following:

- Seizure or postictal state (100%)
- Headache (80%), usually frontal
- Generalized edema (50%)
- Vision disturbance (40%), such as blurred vision and photophobia
- Right upper quadrant abdominal pain with nausea (20%)
- Amnesia and other mental status changes.

The incidence of signs and symptoms before seizure include: headache (83%), hyperactive reflexes (80%), marked proteinuria (52%), generalized edema (49%), visual disturbances (44%), right upper quadrant pain or epigastric pain (19%) [31].

The relation of seizure to delivery is as follows: before delivery (>70%); before labor (antepartum) (25%); during labor (intrapartum) (50%); after delivery (postpartum) (25%) [31].

2.5.2.2 Physical signs

Findings on physical examination may include:

- Sustained SBP >160 mmHg or DBP > 110 mmHg
- Tachycardia
- Tachypnoea
- Rales
- Mental status changes
- Hypereflexia
- Clonus

- Papilledema
- Oliguria or anuria
- Localizing neurologic deficits
- Right upper quadrant or epigastric tenderness
- Generalized edema
- Small fundal height for estimated gestational age
- Apprehension

2.5.3 Complications

2.5.3.1 Maternal complications [4,35]

During pregnancy

- Eclampsia
- Accidental hemorrhage (placental abruptio)
- Acute kidney injury (oliguria and anuria)
- HELLP syndrome
- Cerebral hemorrhage
- Acute pulmonary edema
- Preterm labor
- Disseminated intravascular coagulation (DIC)

During labor

- Eclampsia
- Post-partum hemorrhage

puerperium

- Eclampsia (usually within 48 hours)
- Shock – puerperal vasomotor collapse is associated with reduced concentration of sodium chloride due to sudden fall in corticosteroid level.
- Sepsis – due to increased incidence of induction, operative interference, and low vitality.

2.5.3.2 Fetal complications [4]

- Intrauterine fetal death (IUFD) – due to spasm of uteroplacental circulation leading to accidental hemorrhage or acute red infarction.
- Intrauterine growth restriction (IUGR) – due to chronic placental insufficiency
- Asphyxia
- Prematurity – either due to spontaneous preterm onset of labor or due to preterm induction

2.5.3.3 Late complications [4]

- *Residual hypertension*

it may persist even after 6 months following delivery in about 50% cases. It is more related to familial diathesis and underlying thrombophilias (protein C, protein S deficiency, antiphospholipid syndrome.

- *Recurrent preeclampsia*

There is 25% chance of PE to occur in subsequent pregnancies. This too is related to familial diathesis, personal predisposition with underlying thrombophilias.

- *Chronic renal disease*

There is high incidence of glomerulonephritis in women with PE remote from term. This is more likely due to preexistent underlying renal disease.

2.6 Diagnosis

2.6.1 Positive diagnosis

All women who present with new-onset hypertension should have the following tests [4,29,31]:

- Full blood count (FB)
- Serum alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT)
- Serum creatinine
- Uric acid

- 24-Hour urine collection for protein and creatinine (criterion standard) or urine dipstick analysis

Additional studies to perform if HELLP syndrome is suspected are:

- Peripheral blood smear
- Serum lactate dehydrogenase (LDH) level
- Indirect bilirubin

Other procedures [31]

- Ultrasonography: transabdominal, to assess the status of the fetus and evaluate for growth restriction; umbilical artery Doppler ultrasonography, to assess blood flow
- Cardiotocography: The standard fetal nonstress test and the mainstay of fetal monitoring
- Fundoscopy: may reveal retinal edema, constriction of the arterioles, alteration of normal ratio of vein:
- Head CT scan if suspicion of intracranial hemorrhage in selected patients with either sudden severe headaches, focal neurologic deficits, seizures with prolonged postictal state, and atypical presentation for eclampsia

2.6.2 Differential diagnosis

2.6.2.1 Differential diagnosis of preeclampsia

- Gestational hypertension
- Nephropathy
- Hemolytic uremic syndrome

2.6.2.2 Differential diagnosis of eclampsia

Diseases associated with seizures and/or coma:

- Epilepsy
- Encephalitis
- Meningitis

- Intracranial tumors
- Metabolic disorders (hypoglycemia)
- Puerperal cerebral thrombosis
- Cerebral malaria in tropics
- Hysteria

2.7 Management of eclampsia and preeclampsia

2.7.1 Preventive

Preeclampsia is not a totally preventable disease, however, various strategies to prevent or modify the disease have been evaluated.

2.7.1.1 Screening tests

Although numerous screening tests for PE have been proposed, there is currently no predictably reliable, valid, and economical screening tests for preeclampsia. However, combinations of tests, some yet to be adequately evaluated, may be promising [4,29,31]:

Doppler ultrasound studies

High resistance index in the uterine artery in the second trimester is associated with sixfold increase in rate of PE [4]. Presence of a diastolic notch between 22 and 24 weeks' gestation in the uterine artery can predict the possible development of PE [4]. This, however, is reliable when combined with other maternal factors and biochemical indicators to identify high-risk population [36]. However, the screening efficacy of UAD for adverse perinatal outcomes seems poor in population at low risk; the findings have value for prediction of fetal growth restriction but not PE [29,37].

Development of renal dysfunction

Rise in the level of serum uric acid **(hyperuricemia)**, appearance of **microalbuminuria**, and isolated **gestational proteinuria** are observed to be predictors of PE [4,29]. Hyperuricemia likely results from reduced uric acid clearance from diminished glomerular filtration, increased tubular reabsorption, and decreased secretion [29].

Maternal serum levels of SFlt-1 and PlGF

SFlt-1 is increased in women with PE [4]. SFlt-1:PlGF ratio of ≤38 had a negative predictive value of 99.3% (95% CI, 97.9 – 99.9), suggesting an extremely unlikely development of PE or HELLP within 1 week, in women with clinical suspicion of PE or HELLP syndrome. Therefore, an sFlt-1:PIGF ration of ≤38 may have a potential role in predicting the short-term absence of PE in women in whom the syndrome is suspected [31].

Roll over test

An increase of 20 mmHg in diastolic BP from side (lateral) to back (supine) position between 28- and 32-weeks' gestation indicates a positive "roll over test" and about 33% of these women developed hypertension later. A negative test is of value [4].

2.7.1.2 Prophylactic measures

The following prophylactic measures to prevent and modify PE severity have been evaluated [4,29,31,38].

Regular antenatal checkup

For early detection of rapid weight gain or tendency of rising BP especially the diastolic one.

Dietary and lifestyle modifications

- Low-salt diet and regular exercise during pregnancy
- Antioxidants: vitamins C (1000mg daily), vitamin D (800 – 1200 IU daily), vitamin E (400 IU/day), magnesium, zinc, fish oil, statins and metformin.

Calcium supplementation 1.5 – 2g/day

Antithrombotic agents

- Low dose aspirin 50 – 150 mg daily before 15 weeks' gestation till 1 week before delivery
- Low-molecular weight heparin

2.7.2 Curative

2.7.2.1 Treatment objectives [4].

- Stabilize blood pressure
- Prevent and treat maternal and fetal complications
- Optimal delivery of health baby
- Restoration of health of mother in puerperium.

2.7.2.2 Means and methods

General measures

Admission in hospital, bed rest, salt restriction, and diet with adequate protein. The initial steps in the management of a woman with eclampsia are basic supportive measures such as calling for help, prevention of maternal injury, placement in lateral decubitus position, maintain oral airway to prevent of aspiration, administration of oxygen (10L/min), securing intravenous access (1 or 2 wide bore cannulas), insertion of Foley catheter with urometer and monitoring of vital sings including oxygen saturation (SPO_2>95%) [1,4].

Fluid therapy

Despite the presence of peripheral edema, patients with preeclampsia are intravascularly volume depleted [31]. Aggressive volume resuscitation may lead to pulmonary edema, a common cause of maternal morbidity and mortality. Controlled, conservative fluid administration is preferred and the total fluids (oral and intravenous) should generally be restricted to 80 ml/h (60 – 125 ml/h) or 1ml/kg/h [29,31,39]. If oliguria occurs, a trial of intravenous fluid bolus of 250 – 500 ml of isotonic fluid (normal saline or Lactated Ringer's) can be given [39].

Antihypertensives

Indications for antihypertensives include persistent rise blood pressure (usually BP >160/110 mmHg for ≥15 minutes). Intravenous hydralazine or labetolol and oral nifedipine are the three most commonly used agents [1]. Although parental antihypertensive therapy may be needed initially for acute control of BP, oral medications can be used as expectant management is continued (tables IV & V).

Table IV. Commonly used antihypertensives in the management of preeclampsia [4]

Drug	Mode of action	Dose
Methyl-dopa	Central and peripheral action	250 – 500 mg tid or qid
Labetolol	Adrenoceptor antagonists (α and β blockers)	100 mg tid or qid
Hydralazine	Vascular smooth muscle relaxant	10 – 25 mg bid
Nifedipine	Calcium channel blocker	10 – 20 mg bid

Table V. Commonly used antihypertensives in the management of hypertensive crises [4]

Drug	Onset of action	Doses schedule	Maximum dose	Maintenance dose
Labetolol	5 minutes	10-20 mg IV every 10 mins	300 mg IV	40 mg/h
Hydralazine	10 minutes	5 mg IV every 30 minutes	30 mg IV	10 mg/h
Nifedipine	10 minutes	10-20 mg oral, can be repeated in 30 minutes	240 mg/24 h	4 – 6 hours interval
Nitroglycerin sodium nitroprusside	0.5 – 5 minutes	5 µg/min IV 0.25-5 µg/kg/min IV	Short-term therapy only when the other drugs have failed	

Seizure prophylaxis and anticonvulsant

The aim is to control fits and to prevent its recurrence. Magnesium sulfate is the drug of choice (see section 2.8). Other regimens include: (1) Lytic cocktail using chlorpromazine, promethazine and pethidine; (2) Diazepam and (3) Phenytoin.

Obstetric measures

Termination of pregnancy is the only cure for preeclampsia [29]. All obstetric measures for delivery such as induction of labor, episiotomy, instrumental delivery, cesarean section can be employed.

2.7.2.3 Indications

Preeclampsia with severe features <24 weeks' gestation

Discuss medical termination of pregnancy due to high risk of adverse maternal outcome.

Preeclampsia with severe features >24 weeks' and <34 weeks' gestation

Expectant management may be considered if maternal and fetal conditions are stable. It involves fetal lung maturation and close maternal and fetal clinical monitoring, and serial laboratory testing (FBC, liver enzymes and serum creatinine) [1]. During this period, delivery is recommended at any time in case of maternal or fetal jeopardy. Maternal conditions include: uncontrolled BP, persistent headaches, epigastric or right upper quadrant pain unresponsive to analgesics, visual disturbances, stroke, HELLP syndrome, new or worsening renal dysfunction, pulmonary edema, eclampsia and suspected placental abruptio. Fetal conditions include: non-reassuring fetal status, fetal death, persistent reversed end-diastolic flow in umbilical artery doppler [1].

Preeclampsia with severe features >34 weeks' gestation

Delivery is recommended after maternal stabilization or with labor or prelabor rupture of membranes. Delivery should not be delayed for the administration of steroids in late preterm period [1].

Eclampsia

Women with eclampsia should be delivered in a timely fashion. Once the patient is stabilized, the method of delivery should depend, in part, on factors such as gestational age, and the findings of the cervical examination (eclampsia itself is not an indication for cesarean delivery)[1].

HELLP syndrome

Considering the serious nature of this entity, with increased rates of maternal morbidity and mortality, many authors have concluded that women with HELLP syndrome should be delivered regardless of their gestational age. Use of corticosteroids have no proven added benefits [1].

Mode of delivery

For gestational hypertension and preeclampsia without severe features, vaginal delivery is preferred. For preeclampsia with severe features, induction of labor has been proven reasonable and not harmful to low-birth infants compared to cesarean delivery. The decision to perform cesarean delivery should be individualized, based on anticipated probability of vaginal delivery

and on the nature and progression of preeclampsia disease [1]. Indications for cesarean section include: (1) when urgent termination is indicated and cervix is unfavorable; (2) severe preeclampsia with tendency of prolonged induction – delivery interval; (3) associated complicating factors such as elderly primigravidae, contracted pelvis, malpresentation, etc. [4].

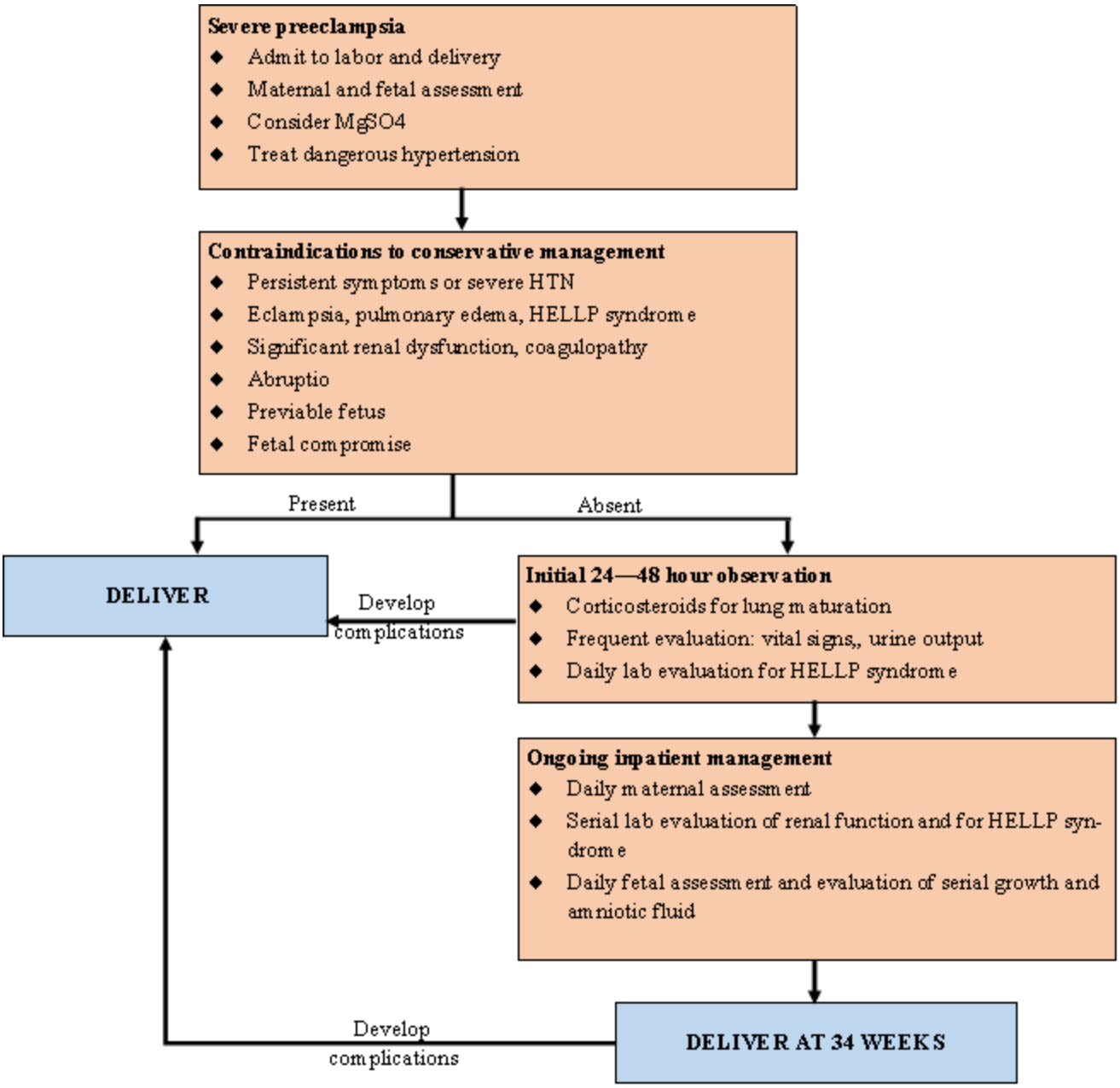

Table VI. Clinical algorithm for the management of severe preeclampsia[29].

2.7.2.4 Surveillance

The use of a progress chart should be employed

Maternal parameters

- Clinical evaluation of symptoms (headache, visual disturbance, epigastric pain, urine output) daily
- Blood pressure at least every 6 hours
- Signs of magnesium sulfate toxicity (respiratory depression, loss of deep tendon reflexes, oliguria) at least every hour.
- Edema and weight gain daily
- Fluid intake and urine output
- Proteinuria daily
- Blood hematocrit, platelet count, uric acid, creatinine, liver enzymes, coagulation profile at least once a week.

Fetal parameters

- Fetal well-being (biophysical profile)

2.7.2.5 Prognosis

Morbidity and mortality

Worldwide, preeclampsia and eclampsia are estimated to be responsible for approximately 14% of maternal deaths per year [31]. Once convulsion occurs, the prognosis becomes uncertain. Prognostic factors include existence of comorbidities (diabetes, nephropathies, neuropathies) and presence of complications (eclampsia, abruptio, HELLP, acute pulmonary edema etc.) [4]

Recurrence

In the general, the recurrence risk of preeclampsia in a woman whose previous pregnancy was complicated by preeclampsia near term is approximately 10%. In the case of preeclampsia with severe features or eclampsia, there is a 20% risk of developing PE in subsequent pregnancy [31].

2.8 Magnesium sulfate in preeclampsia and eclampsia

2.8.1 Historical aspects (the Magpie Trial)

Magnesium sulfate ($MgSO_4$) was first introduced to control convulsions in 1925, but it was the Collaborative Eclampsia Trial in 1955 that confirmed the efficacy of $MgSO_4$ in the treatment of severe preeclampsia and eclampsia [40]. The trial (also called the Magpie trial) was a randomized, placebo-controlled study that enrolled over 10,000 women in 33 countries and across a wide variety of clinical settings. Four centers in Nigeria – Ibadan, Sagamu, Port Harcout and Sokoto – participated in the study. Women treated with $MgSO_4$ had a 52% and 67% lower recurrence of convulsions than those treated with diazepam and phenytoin, respectively [10,40]. Use of $MgSO_4$ in patients with severe preeclampsia reduced the risk of progression to eclampsia by more than half and reduced maternal mortality. Magnesium sulfate also significantly improved the outcomes for newborns compared to phenytoin [40].

2.8.2 Regimens

The two standard regimens that are most commonly used for the management of severe preeclampsia and eclampsia are predominantly the IM **Pritchard regimen** and exclusively IV **Zuspan regimen.** The dosages for severe PE are the same as for eclampsia. Because labor and delivery is a more likely time for convulsions to develop, $MgSO_4$ is usually continued for 24 hours postpartum or after the last fit (whichever comes last) [29,40].

2.8.2.1 The Pritchard regimen

The Pritchard regimen involves administering two loading doses of magnesium sulfate ($MgSO_4.7H_2O$ USP), consisting of a slow IV dose of 4g (i.e., 20 ml injection of 20% $MgSO_4$ solution) over 5 – 10 minutes (or at a rate of 1g/min), immediately followed by an IM dose of 10g (i.e., 20 ml of 50% $MgSO_4$ solution) divided into 5g in each buttock (injected deeply into the upper outer quadrant of the buttock through a 3-inch-long, 20-gauge needle). This is then followed by maintenance dosing of 5g (i.e., 10 ml of 50% $MgSO_4$ solution) IM into alternate buttocks every 4

hours, but only after it was ascertained that *(1)* the knee jerk (patellar reflex) was present, *(2)* urine flow was ≥100 ml in the previous 4 hours, and *(3)* respirations were not depressed [12,14].

2.8.2.2 The Zuspan regimen

In the Zuspan regimen, a single loading dose of 4 – 6 g $MgSO_4$ diluted in 100 mL of IV fluid is administered as a slow IV infusion over 15 – 20 minutes, followed by an hourly maintenance infusion of 1 – 2g by a controlled infusion pump. Monitor for Mg toxicity: assess deep tendon reflexes periodically. Some measure Mg level at 4 – 6 hour and adjust infusion to maintain levels between 4 and 7 mEq/L (4.8 – 8.4 mg/dL). Measure serum Mg levels if serum creatinine ≥ 1.0 mg/dL. $MgSO_4$ is discontinued 24 hours after delivery. The serum concentrations of magnesium obtained from the Pritchard regimen fluctuate more often compared to the Zuspan regimen [12,29].

The $MgSO_4$ dosage regimens presented above and represented in table 2.4 below usually result in plasma magnesium levels as illustrated in figure 2.1 below. When $MgSO_4$ is given to arrest eclamptic seizures, 10 – 15% of women will have subsequent convulsion. If so, an additional 2g dose of $MgSO_4$ in a 20% solution is slowly administered intravenously [29].

Table VII. Magnesium sulfate dosage schedule for severe preeclampsia and eclampsia.

Source: courtesy of Williams Obstetrics 25 edition (2018) [29]**.**

Continuous Intravenous (IV) infusion
Give 4- to 6-g loading dose of magnesium sulfate diluted in 100 mL of IV fluid administered over 15 – 20 minutes. Begin 2g/hr in 100 mL of IV maintenance infusion. Some recommend 1g/hr. Monitor for magnesium toxicity: • Assess deep tendon reflexes periodically • Some measure serum magnesium level at 4 – 6 hr and adjust infusion to maintain levels between 4 and 7 mEq/L (4.8 to 8.4 mg/dL) • Measure serum magnesium levels if serum creatinine ≥ 1.0 mg/dL • Magnesium sulfate is discontinued 24 hours after delivery
Intermittent Intramuscular Injections
Give 4g of magnesium sulfate ($MgSO_4.7H_2O$ USP) as 20% solution intravenously at a rate not to exceed 1g/min. Follow promptly with 10 g of 50% magnesium sulfate solution, one half (5 g) injected deeply in the upper outer quadrant of each buttock through a 3-inch-long 20-gauge needle. (Addition of 1.0 mL of 2% lidocaine minimizes discomfort.) If convulsions persist after 15 minutes, give up to 2g more intravenously as a 20% solution at a rate not to exceed 1g/min. if the woman is large, up to 4 g may be given slowly. For every 4 hr thereafter, give 5g of a 50% solution of magnesium sulfate injected deeply in the upper outer quadrant of alternate buttocks, but only after ensuring that: • The patellar reflex is present • Respirations are not depressed, and • Urine output the previous 4 hours exceed 100 mL Magnesium sulfate is discontinued 24 hours after delivery.

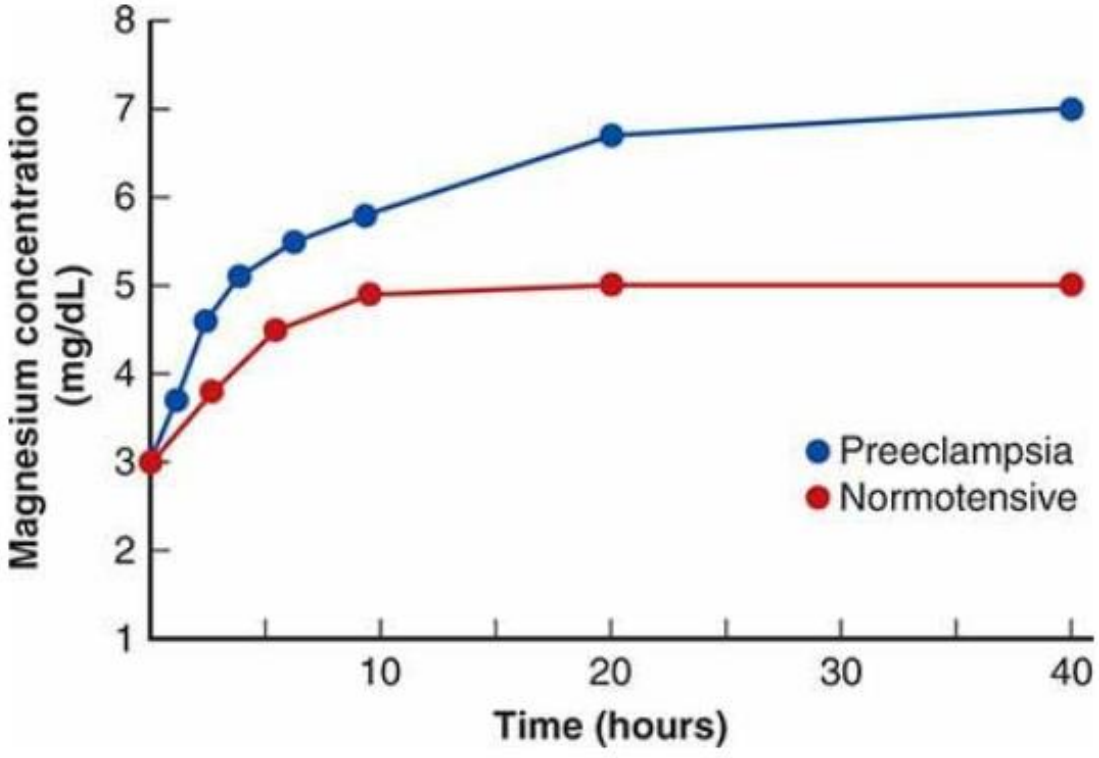

Figure III. Magnesium sulfate concentrations in normotensive and preeclamptic women following 4 g loading dose and 2g/h infusion pump

Source: Courtesy of Williams Obstetrics 25th edition (2018) [29].

2.8.2.3 Choice of regimen

The choice of which regimen to use depends on a number of factors such as availability of staff to monitor the drug or expertise of the staff. Most resource-constrained settings are consistent with the Pritchard regimen since it is given intramuscularly (could thus be administered by lower cadre of health workers). It, however, has the disadvantage of being very painful, a situation which is not desired for a patient on whom efforts are been made to lower the blood pressure. As such, I.M dose could be administered with about 2ml of 1% xylocaine in the same syringe [40].

Some workers have reported modifications in the above-mentioned regimens. For example, $MgSO_4$ has been used with reduced dose (loading dose of 4.5g IV and maintenance dose of 1.5g every 4 hours until 12 h after delivery or the last fit). In another, the loading dose was 10 g I.M followed by a maintenance dose of 2.5g I.M every 4 h for 24 h. the drug has been used as in Pritchard regimen, but the duration of its administration reduced to 12 h after the initial loading

dose. The feto-maternal outcome was similar to the two more famous regimens (Pritchard and Zuspan) [40].

2.8.3 Pharmacokinetics and pharmacodynamics of magnesium sulfate

2.8.3.1 Pharmacokinetics

After administration, about 40% of plasma magnesium becomes protein-bound, while the unbound ionized magnesium increases proportionately to the total serum concentrations of magnesium. The free magnesium ions (Mg^{2+}) diffuse into the extravascular space, into the bone, and across the placenta and fetal membranes to enter the fetus and amniotic fluid. Magnesium is eliminated almost exclusively by the maternal kidneys, with almost 90% of the dose excreted in the urine during the first 24 hours after an IV infusion.

Normal serum concentration of Mg^{2+} are 1.5 – 2.5 mmol/L (1.8 – 3 mg/dL) and a plasma concentration of 3.5. – 7 mmol/L (4.2 – 8.4 mg/dL) is advocated for the treatment of eclamptic seizures [41]**.** Pritchard IV loading of 4g increases the plasma concentrations to about 7 – 9 mEq/L, which falls to about 4 – 5 mEq/L over the next 45 minutes. The I.M loading dose of 10 g (i.e., 5g in each buttucks) typically stabilizes the plasma Mg level at about 4 – 7 mEq/L[14]. Okusanya and colleagues, in one systematic review conducted in Nigeria in 2016, found that baseline serum concentrations were consistently <1mmol/L and the IV loading dose of 4 and 6g was associated with doubling of this baseline concentration half an hour after injection. They added that the maintenance infusion of 1g/hour consistently produced concentrations well below 2 mmol/L, whereas that of 2g/hour and the Pritchard IM regimen had higher but inconsistent probability of producing concentrations between 2 and 3 mmol/L [42].

2.8.3.2 Pharmacodynamics

Though the specific mechanisms of action remain unclear, the effect of $MgSO_4$ in prevention of eclampsia is likely multi-factorial. Magnesium sulfate may act as a vasodilator, with actions in the peripheral or cerebral vasculature, to decrease vascular resistance or relieve vasoconstriction. Additionally, it may also protect the blood-brain barrier and limit cerebral edema formation, or it may act through central anticonvulsant action [41].

2.8.3.2.1 Magnesium-induced vasodilation

Magnesium is a unique calcium antagonist as it can act on most types of calcium channels (in this case, voltage-operated calcium channels (VOCC)) in vascular smooth muscle causing decrease in both intracellular and extracellular calcium. This leads to inactivation of calmodulin-dependent mysosin light chain kinase activity and decrease contraction, causing arterial relaxation that may subsequently lower peripheral and cerebral vascular resistance, relieving vasospasm, and decreasing arterial blood pressure [41]. It is also suggested to cause vasodilatation by stimulating prostacyclin 12 and nitric oxide synthesis in vascular endothelial cells. The end result is reduction in cerebral ischemia when used in the prophylaxis and treatment of eclampsia [12].

Vascular Effects of Magnesium Sulfate.

Cellular Target	Mode of Action	Possible Mechanism(s)
Smooth Muscle Uterine +++ Mesenteric +++ Aorta +++ Cerebral +	Relaxation ↓ Vasodilation ↓ Decreased Vascular Resistance	Calcium Antagonism Decreased Voltage-operated Calcium Channel (VOCC) Activity Decreased $[Ca^{+2}]_i$ Release From Sarcoplasmic Reticulum
Endothelium	Decreased Platelet Aggregation	Increased Prostaglandin I_2 (PGI_2)
	Vasodilation	Increased Nitric Oxide (NO, Gestation Dependent)

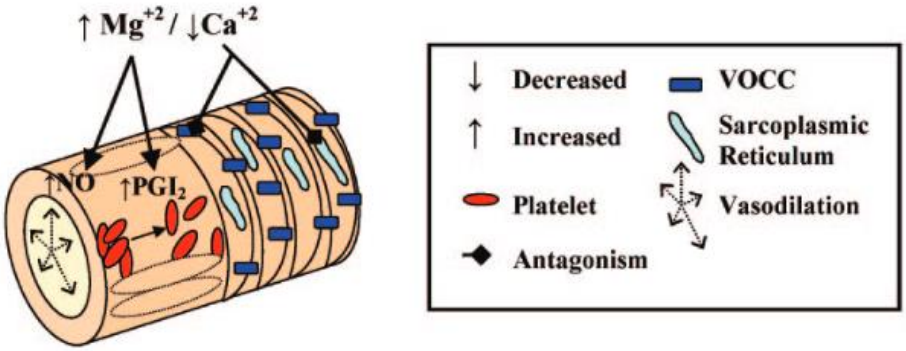

Figure IV. Vascular effects of magnesium sulfate

Source: Courtesy of Euser and Cipolla (2009)[41].

2.8.3.2.2 Effects on the blood-brain barrier and cerebral edema formation

The cerebral endothelium that forms the BBB has unique features compared to the peripheral endothelium including a lack of capillary fenestrations, a low basal rate of pinocytosis, and the presence of high electric resistance tight junctions between adjacent endothelial cells. Disruption of the BBB can result in vasogenic edema formation, an important component in the clinical picture of eclampsia [41].

Several mechanisms of actions have been proposed to explain the neuroprotective effects of $MgSO_4$. As a calcium antagonist, it may act directly on cerebral endothelial cell actin cytoskeleton opposing paracellular movement of solutes through tight junctions. Alternatively, as pinocytosis is induced by hypertension, $MgSO_4$ may therefore decreases pinocytosis, restricting movement of water and solutes into the brain by transcellular transport, thereby limiting edema formation and improving clinical outcomes in eclampsia [41].

2.8.3.2.3 Anticonvulsant activity

Seizures are thought to be mediated at least in part by stimulation of glutamate receptors such as N-methyl-D-aspartate (NMDA) receptor. Excessive glutamate can activate NMDA receptor, leading to massive depolarization of neuronal networks and bursts of action potentials. The possible anticonvulsant activity of magnesium may be related to its role as an NMDA receptor antagonist. Generalized CNS depression occurs via NMDA receptor blockade and NMJ blockade by decreasing calcium conductance, acetylcholine release, and motor endplate excitability to acetylcholine release. [12].

Anticonvulsant Activity of Magnesium Sulfate.

Cellular Target	Mode of Action	Possible Mechanism
Neurons	Increased Seizure Threshold	N-Methyl-D-Aspartate (NMDA) Receptor Antagonism ↓ Decreased Effect of Glutamate, Limiting Massive Neuronal Depolarization

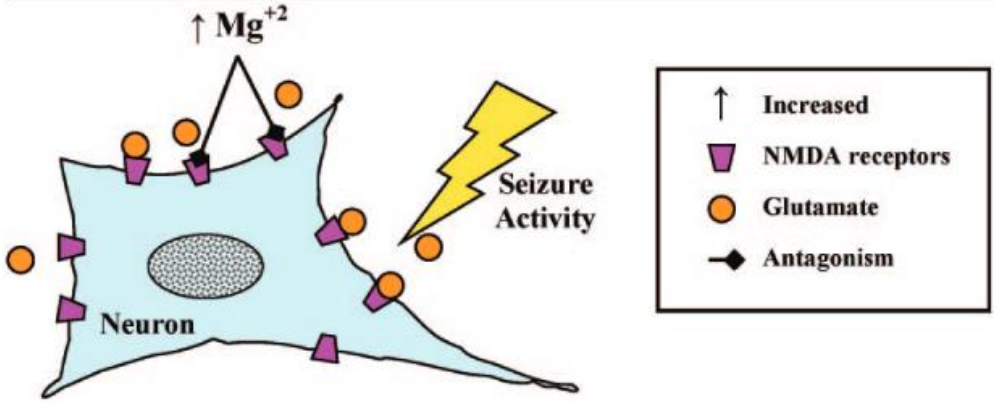

Figure V. Anticonvulsant activity of magnesium sulfate.
Source: Courtesy of Euser and Cipolla (2009) [41]

2.8.4 Magnesium sulfate toxicity

Magnesium levels up to at least 7 mEq/L are not accompanied by evidence of toxicity [14]. With the above-mentioned regimens, the expected serum range of Mg is 2 – 3.5 mmol/l.[40]. One study revealed that using the Pritchard regimen, a mean serum magnesium level of 2.1 mmol/l was found[40]. The first warning of imminent toxicity in the mother is the loss of the patellar reflex at concentrations between 3.5 and 5 mmol/L [40]. Respiratory paralysis occurs at supratherapeutic concentrations beyond 5 mmol/L (i.e., 5 – 6.5 mmol/l), cardiac conduction is altered at more than 7.5 mmol/l, while cardiac arrest occurs when serum Mg exceeds 12.5 mmol/l [40]. Therefore the parameters that need to be monitored are the knee jerk (should be present), respiratory rate (should be >16 breathes/min), and urine output (should be more than 30 ml/min)[12,40]. Should toxicity be detected, however, the antidote is calcium gluconate, administered as 1g (i.e., 10 ml) of 10% calcium gluconate IV slowly over 10 minutes [14,40].

2.8.5 Availability and Training on $MgSO_4$

On the basis of available evidence, The World Health Organization (WHO) has recommended $MgSO_4$ as the most effective, safe, and low-cost drug for the treatment of severe preeclampsia and eclampsia [40]. However, the drug still remained largely unavailable in several developing countries where it is incidentally needed the most. Leading advocates, researchers, non-governmental organizations (NGOs), representatives of WHO and national health ministries from all over the world have met to identify barriers to the use and availability of $MgSO_4$. Major themes that emerged were lack of guidelines on its use, wrong perception that the drug is meant for use only at the highest level of facilities, lack of training of health workers on its use, little incentive for pharmaceutical companies to commercialize the drug, and ready availability of prepacked forms of less effective drugs. [40].

The need has now emerged for refresher trainings for health workers in the use of $MgSO_4$. Clinical protocols are particularly useful in guiding such workers. In countries like Nigeria, there exists a national clinical service protocol for obstetric care which outlines the management of eclampsia and how $MgSO_4$ can be used and monitored. There is, however, need to distribute the protocol and train health workers, and need for a universal dosage regimen that will also help in uniform studies and research. Some workers have also reported the utilization of the protocol to suit the working environment in respect of the available facilities, staff, investigations, and even the regimen used [40].

2.9 Literature review on socio-obstetrical, clinical, and paraclinical profile of women with severe preeclampsia and eclampsia

Most studies have revealed that preeclampsia and eclampsia affect mostly young women between the ages of 19 and 30 years although. Alsiddig et al., (2017) in Sudan reported a modal age group of 25 – 34 years in their study [2,5,16,43–46]. Other risk factors reported in literature include obesity, family history of hypertension, family history of diabetes and twin pregnancy[43,44]. Generally, preeclampsia was more prevalent than eclampsia, and was more common in primiparous than multiparous women [2,5,9]. Concerning the complications of the disease, Kollu et al (2023) in India reported derangement of renal function test (RFT), liver function test (LFT)

and coagulation profile in 71.93%, 88.60% and 50.88% of their study population [43]. Maternal complications which have been reported include: eclampsia, retroplacental hematomas, HELLP syndrome, Disseminated Intravascular Coagulation (DIC), acute kidney injury (AKI), acute pulmonary edema (APE) and cerebrovascular accidents [5,45,46]. The fetal complications reported include: prematurity, intrauterine fetal death (IUFD), intrauterine growth restriction (IUGR), neonatal asphyxia [5,45] (table VIII).

Table VIII. Literature review on sociodemographic, clinical and praclinical profile of SPE and eclampsia women

Year	Author	Country	Title of study	Study design	Findings
2023	Kollu et al.,	India	Efficacy of $MgSO_4$ to prevent eclampsia in women with severe preeclampsia and impending eclampsia	Hospital-based prospective observational	Modal age group = 22-26 yrs (28.95%) Mean age = 28.17±4.69 yrs Mean SBP = 160.88 mmHg Mean DBP = 101.93 mmHg Deranged RFT = 71.93% Deranged LFT = 88.60% Deranged coagulation profile = 50.88%
2020	Rency et al.,	India	Assessment of socio-demographic and clinical factors associated with preeclampsia and eclampsia among primigravida attending tertiary care center in South India	Case control prospective study	Teenagers (< 19 yrs) = 3%, Young women (19 – 30 yrs) = 78%, Mean age 27.3 years modal gestational ages = < 37 weeks (74.1%), Obesity = 33.3% Family of HTN = 30.6% Family history of diabetes = 24.1% Place of residency (majority) = rural (66.7%) Level of education (majority) = literate (96.3%)
2019	Essome et al.,	Cameroon	Preeclampsia at Laquintinie hospital (Douala): Survey of prevalence and morbidity from 2010 to 2015	Retrospective descriptive	Preeclampsia was common in primiparous women (46.7%) in the age group 20 – 29 years. Pregnant women under the age of 20 were most affected by eclampsia. PE was frequently found in women with twin pregnancies (10.1%). Modal age group 20 – 29 years (554.5%), mostly primiparous (46.7%),

Year	Author	Country	Title of study	Study design	Findings
					gestation age group mostly involved 37-41 weeks (60.3%). Maternal complications: eclampsia (29.7%), retroplacental hematoma (3.6%), HELLP syndrome (1.6%), DIC (0.2%) Fetal: prematurity (19.5%), IUFD (9.4%), neonatal asphyxia (25.8%), IUGR (6.6%).
2017	Alsiddig et al.,	Sudan	Assessment of magnesium sulfate usage in preeclamptic and eclamptic women in Omdurman Maternity Hospital	Cross-sectional	Modal age group = 25-34 yrs (48%) Preeclampsia = 78% Eclampsia = 22%
2017	Tripti et al.,	India	Single loading dose $MgSO_4$: a simple, safe and effective alternative to Pritchard's regimen for Indian women	Prospective interventional comparative	Mean maternal age 23.7±4.57, primigravida (67.1%), mean gestational age 33.1±4.8 weeks, majority (70%) from rural location.
2016	Fouedjio et al.,	Cameroon	Predictors of eclampsia among preeclamptic patients: a case control study in Yaounde	Case control	Modal age = 20 – 25 yrs (34.9%) Level of education mostly attained = secondary (65.1%) Parity = majority (50.8%) primiparous.
2015	Priso et al.,	Cameroon	Trend in admissions, clinical features and outcome of preeclampsia and eclampsia as seen from the ICU of Douala General Hospial	Retrospective	Mean age 30 years, majority (61.8%) married. Mode of admission: majority (56.9%) were referred. Mean gestational age 34±3.9 weeks. Median (range) gravidity 3 (1 – 9), median (range) parity 2 (0 – 7). Median length of hospital-stay 3 (1-10).

Year	Author	Country	Title of study	Study design	Findings
					Complications of preeclampsia: Acute kidney injury (70%), Acute pulmonary edema (33.3%), HELLP syndrome (60.0%), placenta abruptio (0.0%), cerebrovascular accidents (0.0%); *Complications of eclampsia:* AKI (51.1%), APO (12.5%), HELLP (41.2%), placenta abruptio (4.2%), cerebrovascular accidents (8.3%).
2015	Prosun et al.,	India	Study of efficacy of low dose $MgSO_4$ (Dhaka Regimen) as compared to standard regimen (Pritchard) in the management of eclampsia	Prospective	Modal age group 21 – 25 years (72%); mean age 23.45±3.47 years; abnormal liver function (22.33%), abnormal renal function (14.33%), thrombocytopenia (11.67%).
2012	Ekechi et al.,	Nigeria	Benefits of using $MgSO_4$ for eclampsia management and maternal mortality reduction in Nigeria	Retrospective	Teenagers (15 – 19 years) = 52% Young women = 32% Primigravidae = 60.4% Grand multipara = 3.7% Literate = 13.6%m Illiterate (no schooling) = 74.1% Monogamous marriage = 71% Polygamous marriage = 28.8%.
2009	Ekele et al.,	Nigeria	Magnesium sulfate therapy in eclampsia: the Sokoto (ultrashort) regimen	Prospective cohort	No ANC = 79% Mean age = 21 years Primigravidae = 83%

2.10 Literature review on rate of control of seizures and associated factors among preeclamptic and eclamptic women on $MgSO_4$

According to Budhwani et al., (2017) the effectiveness of $MgSO_4$ is dependent on dosage and time of administration [47]. Generally, the incidence of eclampsia among preeclamptic women on prophylactic treatment with $MgSO_4$ was less than 3.5%, while the rate of control of seizure among eclamptic women was over 90% [9,12,16,43,46,48]. Kollu et al, (2023) in India reported an incidence of eclampsia of 1.75% among preeclamptic women on $MgSO_4$ prophylaxis while Tripti et al (2017) in same country reported 3.4%. In one study in USA by Pada et al., (2021) none of the 1,049 eclamptic women on $MgSO_4$ had repeat seizures, while Ekechi et al., (2012) in Nigeria had a recurrence of 7.5%. See table IX below.

2.11 Frequency of adverse effects of $MgSO_4$ on preeclamptic and eclamptic women

The toxic effects of $MgSO_4$ in the management of preeclampsia and eclampsia reported in literature include respiratory depression, oliguria, loss of deep tendon reflexes, pulmonary edema and atonic post-partum hemorrhage. Most cases of toxicity were treated by stopping $MgSO_4$ and administration of calcium gluconate [9,45,46,48]. In one study adverse effects was reported in about 2% of their study population, and the most reported adverse effect was the loss of tendon reflexes. See table X below.

2.12 Feto-maternal outcome associated with use of $MgSO_4$ in preeclampsia and eclampsia management

Use of magnesium was associated with a higher death rate in preeclamptic (RR for death with Mg use 6.5, CI 1.6-25.5). provision of Mg may not stop all maternal deaths, and its effectiveness is dependent on dosage and time of administration. Logistic regression of maternal mortality on Mg use and eclampsia status revealed a significant ($P<0.05$) positive interaction between these two variables. Performance of cesarean delivery did not alter the maternal mortality rate, before or after adjustment for eclampsia and Mg use.

Neonatal mortality rate among PE-E women 16/797 (2.0%). This was greater in offspring of eclamptic than of preeclamptic mothers (9.0 vs 0.46%; $p<0.001$). This difference was not found in the subgroup that received magnesium (N=105, p=0.3).

Table IX. Literature review on the rate of control convulsions among SPE and eclampsia women

Year	Author	Country	Title of study	Study design	Findings
2023	Kollu et al.,	India	Efficacy of $MgSO_4$ to prevent eclampsia in women with severe preeclampsia and impending eclampsia	Hospital-based prospective observational	Incidence of eclampsia after treatment with $MgSO_4$ (1.75%).
2021	Padda et al.,	USA	Efficacy of $MgSO_4$ on maternal mortality in eclampsia in USA	A review	Risk of eclampsia was reduced by 50% when compared to placebo (no anticonvulsant). None of the 1,049 eclamptic women had repeat seizures.
2017	Tripti et al.,	India	Single loading dose $MgSO_4$ regimen: a simple, safe and effective alternative to Pritchard's regimen for Indian women	Prospective interventional comparative	Prevention of convulsion (96.6%) Control of convulsions (97.6%)
2017	Alsiddig et al.,	Sudan	Assessment of $MgSO_4$ usage in preeclamptic and eclamptic women in Omdurman Maternity Hospital	Cross-sectional	Majority of patients (121: 93.1%) had controlled seizures. $MgSO_4$ was administered as loading dose in 39.2% patients, while most treated patients (98.5%) were administered maintenance dose.
2015	Prosun et al.,	India	Study of efficacy of low dose $MgSO_4$ regimen (Dhaka regimen) as compared to standard regimen (Pritchard) in the management of eclampsia.	Prospective	Number of convulsions before admission 5.1±2.85; number of MgSO4 doses 9.13±1.56, no. of MgSO4 doses omitted (0.25±0.66), total amount of MgSO4 given in grams (54.67±7.81 g), number of recurrent convulsions (0, n=150),
2012	Ekechi et al.,	Nigeria	Benefits of using $MgSO_4$ for eclampsia management and maternal mortality reduction in Nigeria	Retrospective	92.5% did not have recurrent fits after the loading dose of $MgSO_4$

Year	Author	Country	Title of study	Study design	Findings
2009	Ekele et al.,	Nigeria	Magnesium sulfate in eclampsia: the Sokoto (ultrashort) regimen	Prospective cohort	Recurrence of fits within 4 hours of loading dose (7.4%).
2008	Omu et al.,	Kuwait	Magnesium sulfate therapy in women with preeclampsia and eclampsia in Kuwait	Prospective descriptive	Recurrence of seizures (0.2%)

Table X. Literature review on the adverse effects of magnesium sulfate on severe preeclampsia and eclampsia women

Year	Author	Country	Title of study	Study design	Findings
2017	Alsiddig	Sudan	Assessment of $MgSO_4$ usage in pre-eclamptic and eclamptic women in Omdurman Maternity Hospital.	Cross-sectional	Respiratory paralysis 1/130 (0.77%)
2015	Prosun et al.,	India	Study of efficacy of low dose $MgSO_4$ regimen (Dhaka Regimen) as compare to standard regimen (Pritchard) in the management of eclampsia	Prospective	Oliguria (n=150, 10%), loss of knee jerk reflex (n=150, 8%), respiratory depression (0%), pulmonary edema (n=150, 10%), atonic PPH (14%).
2012	Ekechi et al.,	Nigeria	Benefits of using $MgSO_4$ for eclampsia management and maternal mortality reduction in Nigeria	Retrospective	About 2% of patients had clinical toxicity (loss of tendon reflex). All cases of clinical toxicity were treated by stopping $MgSO_4$ and administering 1g of 10% calcium gluconate.
2008	Omu et al.,	Kuwait	Magnesium sulfate therapy in women with preeclampsia and eclampsia in Kuwait	Prospective descriptive	Reduced tendon reflexes (3.1%).

Table XI. Literature review on feto-maternal outcomes associated with magnesium sulfate in the management of SPE and eclampsia

Year	Author	Country	Title of study	Study design	Findings
2021	Padda et al.,	USA	Efficacy of $MgSO_4$ on maternal mortality in eclampsia in USA	Review	Compared to placebo (no anticonvulsant) the mortality rate was reduced by 46%
2019	Essome et al.,	Cameroon	Preeclampsia at Laquintinie hospital (Douala): survey of prevalence and morbidity from 2010 – 2015	Retrospective descriptive	Modes of delivery: Caesarean (70.6%), vaginal (29.4%).
2017	Tripti et al.,	India	Single loading low dose $MgSO_4$ regimen: a simple, safe and effective alternative to Pritchard's regimen for Indian women.	Prospective interventional comparative	Vaginal delivery 46.2%, Cesarean section 50.8%, forceps delivery 1.5%, undelivered 1.5%, maternal morbidity 44.3%, maternal mortality 1.4% Live birth 73.4%, intrauterine fetal death 28.1%, early neonatal death 12.8%, perinatal death 37.5%, mean birth weight (kg) 2.1±0.65, mean APGAR at 5 mins (6.6±2.8).
2017	Budhwani et al.,	India	Examining the use of $MgSO_4$ to treat pregnant women with preeclampsia and eclampsia: results of a program assessment of emergency obstetric care (EmOC) training in India		Death rate in eclamptic women (5.1%) was higher than that in preeclamptic women (0.8%, $p<0.001$). $MgSO_4$ was associated with higher death rate in preeclamptic but not eclamptic women.
2015	Priso et al.,	Cameroon	Trend in admissions, clinical features and outcome of preeclampsia and eclampsia as seen from the ICU of Douala General Hospital, Cameroon	Retrospective	Mortality rate was 24.3%. factors associated with mortality include blood transfusion and presence of APO.

Year	Author	Country	Title of study	Study design	Findings
2015	Prosun et al.,	India	Study of efficacy of low dose $MgSO_4$ (Dhaka Regimen) as compared to standard regimen (Pritchard) in the management of eclampsia	Prospective	Maternal mortality 10 (6.67%), still birth 23 (15.33%), live birth 127 (84.67%). Modes of delivery: forceps assisted delivery (35.33%), LSCS (27%), vaginal delivery (31.33%), ventouse application (6.33%)
2012	Ekechi et al.,	Nigeria	Benefits of using $MgSO_4$ for eclampsia management and maternal mortality reduction in Nigeria	Retrospective	Drastic reduction in case fatality rates among eclamptic patients from 20.9% to 2.3% when baseline mortality rates were compared to the intervention period using $MgSO_4$ therapy.
2009	Ekele et al.,	Nigeria	Magnesium sulfate therapy in eclampsia: the Sokoto (ultrashort) regimen.	Prospective cohort	There were 12 maternal deaths giving a case fatality rate of 9.9%.
2008	Omu et al.,	Kuwait	Magnesium sulfate therapy in women with preeclampsia and eclampsia in Kuwait	Prospective descriptive	Days of ICU stay: ≤2 days (70.2%), 3-4 days (21.6%), 5-6 days (5.1%), >6 days (3.1%) Causes of long hospital say (≥4 days): persistent HTN, massive generalized edema, thrombocytopenia, wound hematoma, infection, transient blindness, DIC, recurrent seizures.

CHAPTER 3 : METHODOLOGY

3.1 Study design

The study was a prospective hospital-based analytic study.

3.2 Study duration

The study was conducted over a period of six (6) months from February 2024 to July 2024

3.3 Study site and setting

The study was conducted in two tertiary hospitals situated in Yaoundé: the Yaoundé Gyneco-Obstetrics and Pediatrics Hospital (YGOPH) and the Yaoundé Central Hospital (YCH). These hospitals are well accessible to patients in the region. The YGOPH and the Maternity Unit of the YCH are specialized in women's health services, offering comprehensive care in gynecology and obstetrics. Pediatric services are also a key focus at YGOPY, proving medical care for infants, children, and adolescents.

The hospitals are equipped with state-of-the-art facilities to support a wide range of gynecological, obstetric, and pediatric services. The various specialized units include the labor and delivery rooms, obstetrics and gynecological wards, operating theaters, maternal and neonatal Intensive Care Units (ICU), pediatric wards, family planning units, gynecological oncology units, and medical imagery units. The hospitals are equally staffed with skilled and specialized healthcare professionals, including obstetricians-gynecologists, pediatricians, anesthesiologists and reanimators, residents and interns, midwives, nurses and support staff.

YGOPH was created in September 24, 2001 and inaugurated in March 28, 2002 by the President of the Republic, H. E. Paul BIYA, as a result of the Sino-Cameroonian Corporation. It is public administrative establishment whose mission is first the improvement of the quality of health care for women, mothers and children in Cameroon. It has a team of eleven (11) Obstetricians-Gynecologists among whom include 1 professor and 2 associate professors. The hospital conducts an average of 200 to 250 delivers every month. The maternity unit of the Yaoundé Central Hospital is headed by a professor of obstetrics and gynecologist, assisted by a team of seven (7) other obstetrician-gynecologists and six (6) midwives.

These hospitals have been chosen for this study because they are among the major reference hospitals for obstetrics and gynecological emergencies in this region, thereby enlarging the

sampling frame for the research problem to be investigated and increasing the chance for case recruitment.

3.4 Study population

The target population of study consisted of all women admitted for the management of severe preeclampsia and eclampsia.

3.4.1 Inclusion criterion

- Women with severe preeclampsia and eclampsia who were administered $MgSO_4$ as prophylaxis or treatment of seizures.

3.4.2 Exclusion criteria

- All cases of SPE and eclampsia treated with anticonvulsants other than $MgSO_4$.
- Women with other comorbidities like renal or hepatic disease.
- Non-consenting women

3.5 Sampling method

A nonprobability consecutive and exhaustive sampling was employed. Every woman admitted for the management of SPE or eclampsia during the study period was considered for recruitment. This sampling method was chosen because it was inexpensive and accessible, and usually required less time to achieve. The main weakness of this method of sampling is the little opportunity it provided to control for bias [49].

3.6 Sample size

The minimum sample required for the study will be calculated according to the following formula [50]:

$$N = \frac{z^2\, pq}{d^2} \qquad (1)$$

N = minimum sample size required

Z = is standard normal variate or degree of precision (at 95% confidence interval ($p<0.05$) it is 1.96

p = The prevalence of severe preeclampsia in Cameroon based on previous studies (8.2%).

d = degree of accuracy desired (5% margin of error).

q = 1 – p

$$\text{Sample size} = \frac{1.96^2 \times 0.082\ (1 - 0.082)}{0.05^2} \qquad (2)$$

$$= \frac{3.84 \times 0.075}{0.0025} = 115.2 \qquad (3)$$

Therefore, the minimum sample size needed for the study will be **116 participants.**

3.7 Study procedure

3.7.1 Compliance with administrative requirements

After completion of the research proposal and internal validation by supervisors, an ethical clearance was requested from the Ethics Committee of the Faculty of Medicine and Biomedical Sciences (FMBS) of the University of Yaoundé 1. Thereafter, administrative authorizations were obtained from the Institutional Ethics Committee of Research on Human Health in the two hospitals – YGOPH and YCH.

3.7.2 Recruitment and training of research assistants

Four research assistants (two from each hospital), who were junior residents in Obstetrics and Gynecology, and who understood and spoke both French and English, were recruited and trained. Their principal role was to notify the principal investigator each time a case that met the inclusion criteria was encountered, and assisted in the data collection process.

3.7.3 Data collection tool

Data was collected with the use of an interviewer-administered questionnaire (appendices 3 and 4). The questionnaire was conceived internally in English, validated, pre-tested, adapted and then translated into a French version (appendix 4). The questionnaire was subdivided into six parts:

The first part was the cover page, containing a brief introduction of the aim of the study and the respondents' informed consent. **Section A** of the questionnaire contained the variables used to describe the sociodemographic, clinical and paraclinical profile of the participants. **Sections B** contained maternal outcome variables including modes of delivery (spontaneous vaginal delivery, assisted vaginal delivery, and caesarean section), admission to ICU, outcome from ICU (whether death or discharge), and duration of hospital stay. **Section C** contained the fetal outcome variables such as birth outcome (live birth, stillbirth or early neonatal death), 5th minute APGAR scores and birth weights. **Section D** contained variables used to evaluate the efficacy of magnesium sulfate in control of seizures. The indications for its use, its availability, time-to-treatment initiation (i.e., time from diagnosis to initiation of $MgSO_4$ treatment), dosage regimens, compliance to the regimen (incomplete versus complete doses), and the occurrence of convulsions even after a single loading dose of the substance, were all evaluated in this section. **Section E** contained variables used to identify and report the adverse effects of magnesium sulfate. Reasons for discontinuation of the substance, and whether or not an antidote (calcium gluconate) was administered were elaborated.

3.7.4 Data collection process

The questionnaire was administered by the principal investigator and the trained data collectors. During the study period all women admitted into the labour room or the obstetrics intensive care units (ICU) with severe pre-eclampsia or eclampsia, who met the selection criteria were recruited. Some women were seen upon admission in the labor rooms and during administration of $MgSO_4$, while others were seen after the administration of $MgSO_4$. Women with complete $MgSO_4$ doses were identified as those who received a loading dose and all maintenance doses as prescribed by the attending physician. Those with suboptimal treatment were those who received the loading dose only, or with incomplete maintenance doses as was prescribed by the attending physician for some reasons such as financial constraints,

unavailability of the drug, or side effects etc.

Specific objective I: Sociodemographic, clinical and paraclinical characteristics

Following obtention of informed written consents, data collection began with documentation of the sociodemographic characteristics (age, marital status, highest level of education, occupation, ethnicity), gravidity formula, gestational age, number antenatal contacts (ANC), mode of conception, medical history (diabetes or hypertension), history of preeclampsia or eclampsia, family history of diabetes or hypertension, mode of admission (referred, internal transfer, or from home), systolic and diastolic blood pressures on entry. Elements of the paraclinical profile including full blood count, liver enzymes (ASAT and ALAT), and kidney function tests (urea and creatinine), were also recorded within the course of hospitalization. Maternal complications such as acute kidney injury (AKI), acute pulmonary edema (APE), HELLP syndrome, neurological deficits, placenta abruptio etc., and fetal complications such as prematurity, fetal asphyxia, IUGR and IUFD, were equally investigated and documented within the course of hospitalization.

Specific objective II: Maternal and fetal outcome

Following the hospitalization course of the study participants, the following maternal outcome parameters were recorded: the occurrence or recurrence of convulsions for women with SPE and eclampsia respectively following initiation of $MgSO_4$ treatment, the modes of delivery (unassisted vaginal, assisted vaginal, caesarean section), admission into ICU, length of hospital stay and number of maternal deaths. The fetal outcome parameters included the number of live births, still births and early neonatal deaths, the APGAR scores at 5^{th} minute, and the birthweights.

After initiation of $MgSO_4$ therapy, monitoring sheets and nursing care charts for parameters such as BP, pulse and respiratory rate, urine output, and deep tendon reflexes, were studied. The various magnesium sulfate regimens used were gotten from the patients' files as prescribed by the attending physician, and an assessment of the degree of adherence to the regimen was done with the use of the nursing care monitoring charts. This included a recording of the level of completeness of dosages and potential determinants, as well as the modes and frequency of administration for each of the patients. Information about availability of magnesium sulfate,

the time to treatment initiation (i.e., time from diagnosis to administration of $MgSO_4$), number of omitted doses, and reasons for omission and discontinuation, were equally obtained directly from the patients' files and the immediate management team. The occurrence and/or recurrence of seizures within the time-to-treatment initiation, and after loading dose of magnesium sulfate was also investigated and recorded.

The modes of delivery, birth weights, APGAR scores, still births and early neonatal deaths were also gotten from the patients' files through study of delivery reports, post-operative reports and progress notes. Birth weights <2500g were considered as low birth weight (LBW), while APGAR scores <7 was considered as low. The number of days of hospitalization was equally obtained from the file following discharge notes. Prolonged hospital stay was considered > 3 days for post-partum and >7 days for caesarean section. The number and causes of maternal deaths were obtained from the maternal mortality registers. Case fatality rates was calculated as the proportion of women with SPE and eclampsia who died during the during the study period.

Specific objective III: Adverse effects of magnesium sulfate

Also, clinical signs of $MgSO_4$ toxicity notably hypotension, depressed deep tendon reflexes and respiratory depression (<16 breathes/min) were equally investigated from the monitoring sheets and documented. The of use of calcium gluconate and its dosage in cases of suspected MgSO4 toxicity were also investigated and recorded. The women and their babies were followed up until discharge and the length of hospital stay was recorded.

3.9 Pilot study

A pilot study was conducted to ensure the feasibility, validity, and reliability of the questionnaire: the questionnaire was pre-tested on five (5) subjects from the University of Yaoundé I Hospital Center. Attention was paid on the time taken to completely administer a questionnaire, the reliability in responding to the research questions, and the difficulties encountered by the participants in understanding or responding to the questions. The questionnaire was then revised and adopted based on the feedback from the subjects.

3.10 Data analysis

Data management and analysis was done using the IBM Statistical Package for the Social Science (SPSS) version 23 and Microsoft Excel software. Responses from the questionnaires were edited, coded, entered into, and cleaned in the MS Excel prior to exportation into the SPSS. The data file in IBM format was then created and saved in the personal PC and protected with a strong password.

Descriptive statistics such as means for continuous variables, and percentages for categorical variables, were used to summarize data. Such was employed in describing the socio-obstetrical and clinical characteristics of the respondents, the occurrence of seizures, the prevalence of stillbirths and early neonatal deaths, and the case fatality rates. Frequencies were generally presented in tables and bar charts.

The Pearson Chi-square test was used to test the relationship between variables, and a $P<0.05$ at 95% confidence interval (CI) was considered statistically significant. Bivariate analyses were employed to determine the strength of association between adherence to MgSO4 regimen (those with complete versus sub-optimal doses), and maternal mortality, MgSO4 toxicity, stillbirths, and early neonatal deaths.

3.11 Ethical considerations

3.11.1 Autonomy

Autonomy is the ability of a person to take his or her own decision. It is a principle of ethics that assumes a certain level of respect for persons and their ability to take actions that concern them [51]. It includes issues of informed consent, confidentiality of information and anonymity, honesty, and protecting rights of institutions.

- **Informed consent:** A consent form was attached at the front page of questionnaire. This was read and explained to the study participants allowing them to indicate their willingness to participate in, and rights to withdraw from the study through signing of the form.
- **Confidentiality and anonymity**: Signed consent forms and every other information

- provided by the participants was stored by the principal investigator in a safe and confidential manner, ensuring no disclosure to any third party, except the supervisors. Also, the data was collected on a one-to-one basis to maintain confidentiality. Anonymity was guaranteed by the use of questionnaire codes, rather than names. No photos of the participants were taken or included in the study.
- **Honesty:** Honesty was maintained in this study by properly explaining the methods that were in the study and relating the results accordingly. Documentary evidence was used to support all the steps involved in data collection and analysis. Scientific integrity was maintained by providing references to all sources of materials which was used for this study.

3.11.2 Justice

This is participants' right to fair treatment and their right to privacy [51]. Justice was maintained throughout this study by adhering to the criteria of selection of subjects and the sampling method, giving every participant the due fair chances to participate in the study. Discrimination during data collection was discouraged, and no one participant was considered super to another. This helped in eliminating biases in age, social class, or educational level etc., which might have interfered the with right to fair treatment. Also, a copy of the final research will be made available to the various institutions concerned – YGOPH, the YCH and the FMBS.

3.11.3 Beneficence and non-maleficence

Human research should be intended to produce benefits for participants (beneficence) and avoiding, preventing, or minimizing harm (non-maleficence) in the course of the study [51]. The respondents were informed of no direct immediate benefit in participating in the study. However, the data collection methods during the study were non-invasive thereby posing no harm to the subjects. Also, conducting the study offered an opportunity for the principal investigator to improve on his clinical skills in research methodology.

3.12 Resources needed

3.12.1 Human resources

- The principal investigator
- Four research assistants
- A supervisor and Co-supervisor
- A statistician

3.12.2 Material resources

- A personal PC
- An internet modem

3.13 Study limitations

An assessment of deep tendon reflexes as a sign of magnesium sulfate toxicity is clinical and is a subjective measure. A more objective measure would have been to measure the serum levels of magnesium but could not be done due to financial constraints given that the study was not funded. In addition, the quality of data collected depended on correct and accurate documentation of findings in patient files which is also subjective. There also could be possible biases with respect to entry of participants into either group A or B since it was not randomized.

3.14 Dissemination of findings

- Thesis defense
- Publication of article

CHAPTER 4 : RESULTS

4.1 Socio-demographic, clinical, and the paraclinical profile of participants

4.1.1 Sociodemographic characteristics

A total of 123 participants were included in the study after excluding 3 cases of eclampsia treated with other anticonvulsants. The study participants were further divided into two subgroups: based on the disease (SPE, n = 92 cases and eclampsia, n = 31 cases) and based on magnesium sulfate dose-completion (those who received suboptimal doses, n = 41, and those who received the complete doses, n = 82) (Figure VI).

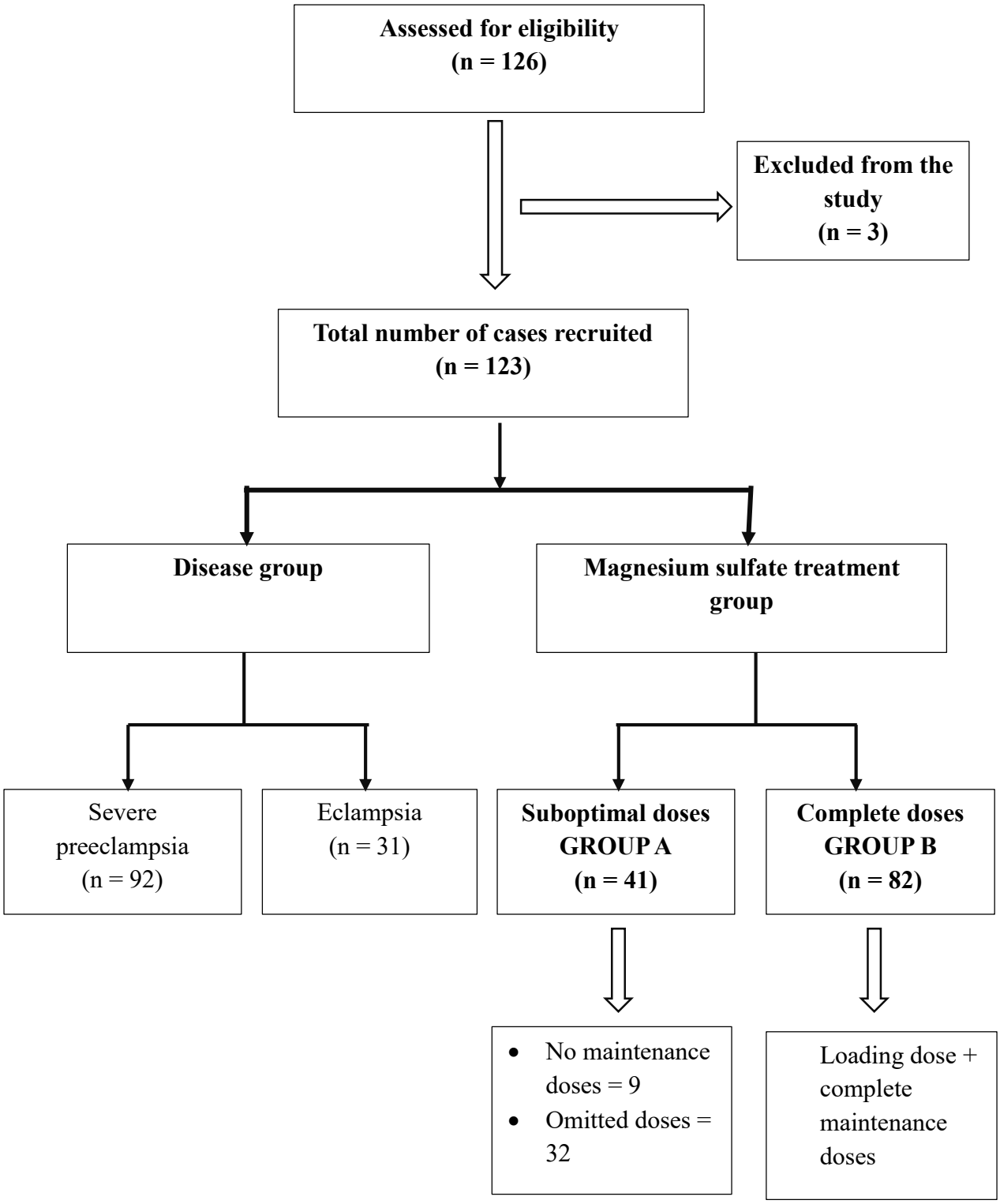

Figure VI. Distribution of study participants in terms of disease and level of completion of magnesium sulfate treatment.

Seventy-four (60.0%) participants were recruited from YCH while 49 (39.8%) from YGOPH. The mean maternal age was 30.5 ± 7.3 years (P <0.001) ranging between 17 – 54 years. Majority of the subjects 69 (57.5%) were single women, who were house wives 34 (30.1%),

and the highest level of education represented by a majority 76 (69.7%), was secondary education [Table XIII].

Table XII. Distribution of women as per sociodemographic characteristics.

Characteristics	SPE (n = 92)	Eclampsia (n = 31)	Total (N = 123)	P-value
Hospital n (%)				**0.26**
YCH	58 (63.0)	16 (51.6)	74 (60.2)	
YGOPH	34 (37.0)	15 (48.4)	49 (39.8)	
Age group (years) n (%)				**0.001**
15 – 19	2 (1.6)	5 (4.1)	7 (5.7)	
20 – 24	12 (13.0)	9 (29.0)	21 (17.1)	
25 – 29	19 (20.7)	9 (29.0)	28 (22.8)	
30 – 34	22 (23.9)	4 (12.9)	26 (21.1)	
≥35 yrs	37 (40.2)	4 (12.9)	41 (33.3)	
Mean age (mean ± SD years)	32.0 ± 7.0	26.2 ± 6.4	30.5 ± 7.3	**<0.001**
Marital status n (%)				**0.32**
Married/co-habiting	41 (34.2)	10 (8.3)	51 (42.5)	
Single	50 (41.7)	19 (15.8)	69 (57.5)	
Occupation n (%)				**0.11**
Student	12 (10.6)	8 (7.1)	20 (17.7)	
House wife	24 (21.2)	10 (8.8)	34 (30.1)	
Civil servant	14 (12.4)	1 (0.9)	15 (13.3)	
Private sector worker (formal)	11 (9.7)	2 (1.8)	13 (11.5)	
Self-employed	23 (20.4)	4 (3.5)	27 (23.9)	
Unemployed	2 (1.8)	2 (1.8)	4 (3.5)	
Highest level of education n (%)				**<0.001**
No schooling	0 (0.0)	3 (2.8)	3 (2.8)	
Primary	6 (5.5)	4 (3.7)	10 (9.2)	
Secondary	59 (54.1)	17 (15.6)	76 (69.7)	
Higher	20 (18.3)	0 (0.0)	20 (18.3)	

4.1.2 Clinical characteristics

The clinical characteristics of the women with SPE and eclampsia were generally comparable. Majority of the cases 104 (84.6%) were referred cases from other peripheral hospitals. Primiparas constituted about a third (33.6%, P = 0.39) of our study population, with a mean gestational age of 35.6 ± 4.1 weeks. The quality of antenatal care for majority of the subjects was poor with an overall mean of 3.3 ± 2.2 antenatal contacts. The means SBP and DBP on admission were 175±22.6 mmHg and 114.0±18.8 mmHg respectively. The diagnosis was made mostly in the antenatal period with only 8 (6.5%) cases diagnosed at postpartum (Table XIII). The most prevalent risk factor observed was primipaternity (40.2%) while the least was family history of diabetes (4.2%) [Figure VII]. The Pritchard regimen was the most commonly used (Table XIII), and financial constraints was the most common reason for not completing magnesium sulfate dosing schedules (18.6%) [Figure VIII]. The mean time-to-treatment initiation of $MgSO_4$ was 2.2±3.0 hours. The frequency of twin gestation was 13% (P = 0.89).

Table XIII. Distribution of women as per clinical characteristics.

Characteristics	SPE (n=92)	Eclampsia (n=31)	Total (N = 123)	P-value
Parity n (%)				**0.39**
Primipara	29 (31.5)	12 (40.0)	41 (33.6)	
Multipara	63 (68.5)	18 (60.0)	81 (66.4)	
Mean ± SD	3.10 ± 2.04	2.45 ± 2.17	2.93 ±2.08	
Gestational age at diagnosis n (%)				**0.94**
< 37 weeks	48 (52.7)	14 (51.9)	62 (52.5)	
≥37 weeks	43 (47.3)	13 (48.1)	56 (47.5)	
Mean ± SD	35.7 ± 4.2	36.0 ± 3.6	35.6 ± 4.1	
Twin gestation	10 (10.9)	3 (10.0)	13 (10.7)	**0.89**
Mean number of ANCs	3.5 ± 2.1	2.73 ± 2.2	3.3 ± 2.2	**0.12**
Primipaternity				**0.09**
Yes	33 (35.9)	16 (53.3)	49 (40.2)	
No	59 (64.1)	14 (46.7)	73 (59.8)	
Mode of admission				**0.09**
Referred	74 (80.4)	30 (96.8)	104 (84.6)	
Internal transfer	14 (15.2)	1 (3.2)	15 (12.2)	
From home	4 (4.3)	0 (0.0)	4 (3.3)	
Mean BP on admission				
SBP	177.6±22.0	169.3±23.6	175±22.6	
DBP	115.8±16.3	109.0±24.3	114.0±18.8	
Period at diagnosis				
Antenatal	90 (97.8)	25 (80.6)	115 (93.5)	
Postpartum	2 (2.2)	6 (19.4)	8 (6.5)	
Loading dose regimen				**0.08**
Pritchard	92 (100)	30 (96.8)	122 (99.2)	
Zuspan	0	1 (3.2)	1 (0.8)	
Maintenance dose regimen				**0.03**
I.M	65 (70.7)	14 (45.2)	79 (64.2)	
Infusion pump	22 (23.9)	13 (41.9)	35 (28.5)	
Time-to-treatment initiation (mean±SD) hours	2.2±3.3	2.2±1.6	2.2±3.0	**0.95**

ANC: antenatal contacts; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; SPE = severe preeclampsia

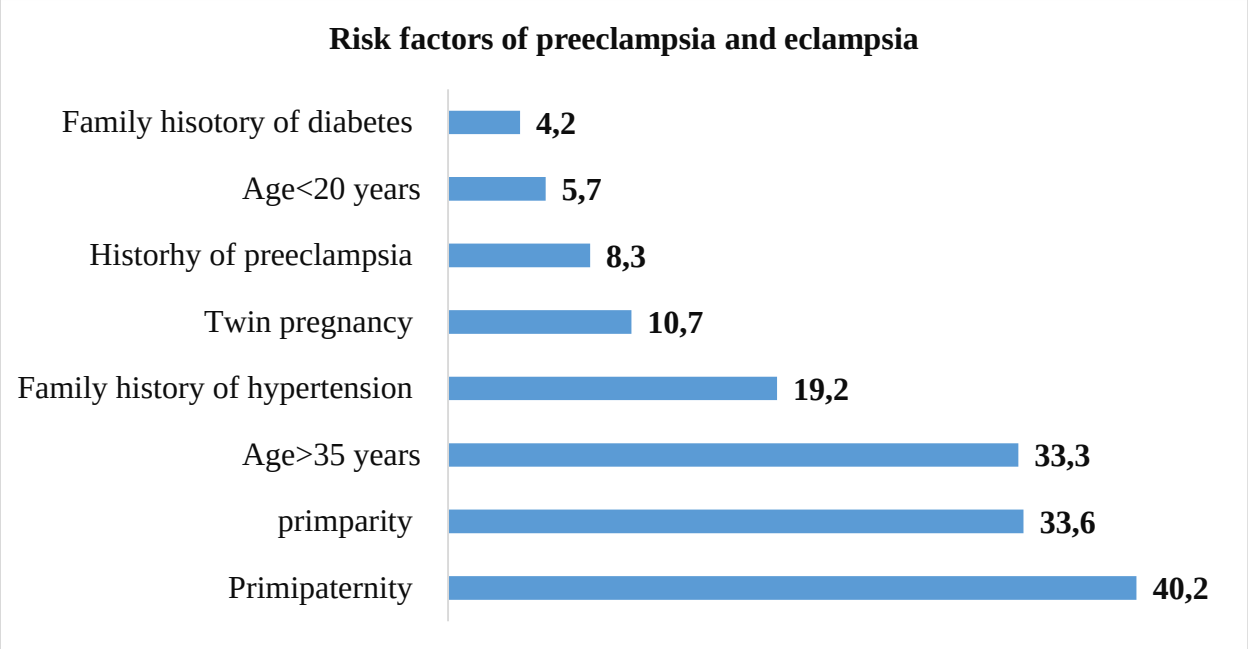

Figure VII. Distribution of risk factors of severe preeclampsia and eclampsia.

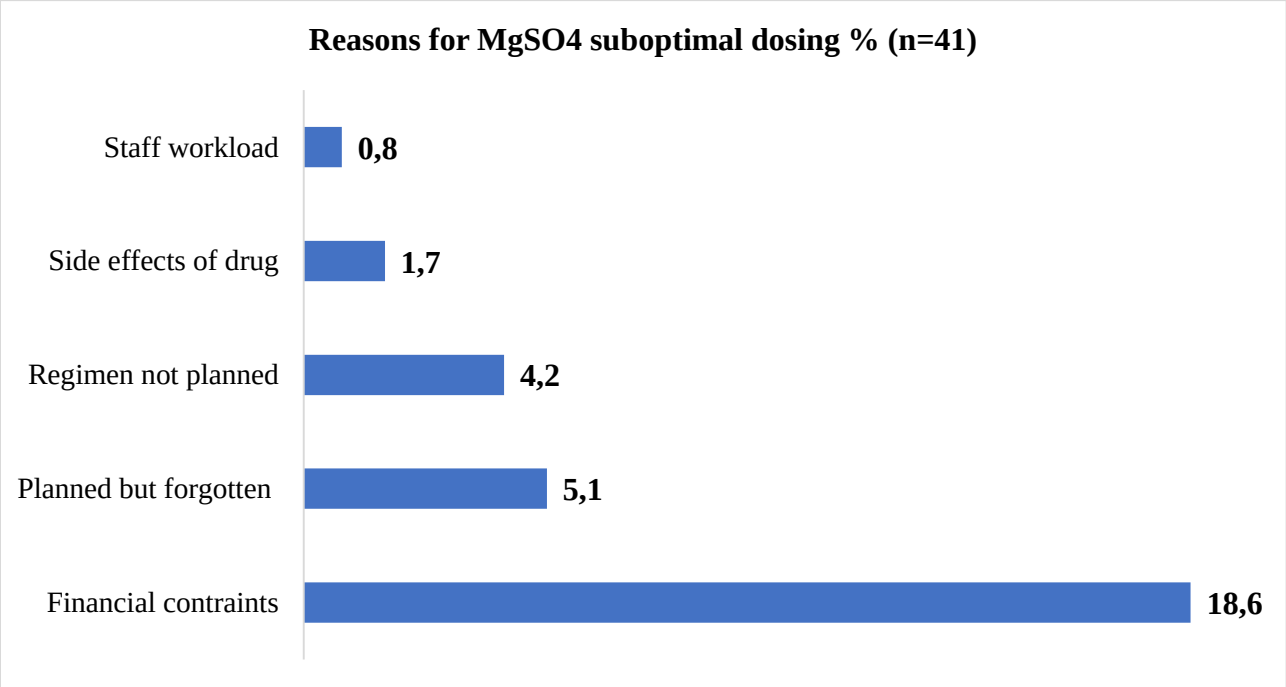

Figure VIII. Reasons for $MgSO_4$ suboptimal dosing.

4.1.3 Paraclinical characteristics of women with severe preeclampsia and eclampsia

Generally, the paraclinical profile of the women with SPE and eclampsia were comparable except for the liver enzymes (ASAT and ALAT) which were significantly more deranged (elevated) in women with eclampsia compared to those with SPE [Table XIV].

Table XIV. Distribution of women as per para-clinical characteristics.

Characteristics	SPE (n=92)	Eclampsia (n=31)	Total (N = 123)	P-value
WBC (10^3 cells/µl)	12,252±5,925	12,631±5,173	12,358±5,698	**0.784**
Hemoglobin (g/dl)				**0.46**
Low (<11)	9 (14.3)	5 (19.2)	11 (15.7)	
Normal (11-14)	43 (68.3)	15 (57.7)	58 (65.2)	
Hemoconcentration (>14)	11 (17.5)	6 (23.1)	17 (19.1)	
Mean ± SD	12.6±2.1	12.3±1.9	12.5±2.0	
Hematocrit (%)				
Elevated	5 (15.2)	1 (14.3)	6 (15.0)	**0.69**
Mean±SD	39.1±6.6	40.2±7.6	39.3±6.7	
Platelets (10^9/L)				
Low (<100)	6 (24.0)	18 (28.6)	24 (27.3)	**0.66**
Mean±SD	164±87	170±101	166±91	**0.75**
ASAT (U/L)				
Elevated	11 (21.6)	15 (75.0)	26 (36.6)	**0.07**
Mean±SD	73.2±125.1	167.1±178.7	99.7±147.2	**0.02**
ALAT (U/L)				
Elevated	11 (22.0)	12 (63.2)	23 (33.3)	**0.20**
Mean±SD	59.4±94.0	146.6±163.4	83.4±122.4	**0.01**
Urea (mg/dl)	87.4±147.3	74.1±159.1	83.3±150.0	**0.74**
Creatinine (mg/dl)				**0.94**
Elevated	6 (30.0)	17 (30.9)	23 (30.7)	
Mean±Sd	1.4±0.9	1.9±1.5	1.6±1.1	**0.10**

ASAT = aspartate transaminase; ALAT = alanine transaminase

4.2 Comparison of maternal and fetal outcomes between women treated with suboptimal and complete regimens of magnesium sulfate

4.2.1 Maternal outcomes

The overall rate of control of convulsion was 94.3% with no significant difference between the two treatment groups (OR: 1.5, 95% CI: 0.3 – 7.2, P = 0.58). There was a statistically significant difference in the prevalence of maternal complications, caesarean delivery rates, and case fatality rates between $MgSO_4$ treatment groups [Table XV]. The case fatality rate was relatively higher in group A (14.6%, OR: 0.2; 95% CI: 0.1 – 0.9; P = 0.03), while maternal complications (46.3%; OR: 3.1, 95% CI: 1.3 – 7.2; P = 0.01) and caesarean delivery rate (66.7%; OR: 2.6, 95% CI: 1.2 – 5.5; P = 0.02) were higher in group B. HELLP syndrome was the most prevalent maternal complication (24.4%; OR: 0.2, 95% CI: 0.1 – 0.6; P = 0.002), while DIC was the least prevalent complication (0.8%) [Table XVI & figure IX]. Of the nine maternal deaths recorded, the most prevalent cause was neurological deficits accounting for three (3) cases. There was one (1) case of maternal death from suspicion of magnesium sulfate toxicity [Figure X].

Table XV. Comparison of maternal outcome following magnesium sulfate therapy between treatment subgroups.

Parameter	Group A (n=41)	Group B (n=82)	Total (N=123)	OR 95% CI	P-value
Convulsions after treatment n (%)				1.5 [0.3 – 7.2]	0.58
Yes	3 (7.3)	4 (4.9)	7 (5.7)		
No	38 (92.7)	78 (95.1)	116 (94.3)		
Maternal complications n (%)	9 (22.0)	38 (46.3)	47 (38.2)	3.1 [1.3 – 7.2]	0.01
Admission into ICU n (%)	25 (61.0)	51 (62.2)	76 (61.8)	1.1 [0.5 – 2.3]	0.90
Admission into ICU ≥ 7 days n(%)	2 (5.1)	11 (13.6)	13 (10.8)	2.9 [0.6 – 13.8]	0.16
Mean duration in ICU days	1.9±2.1	3.6±4.2	3.1±3.6		0.02
Caesarean delivery n (%)	18 (43.9)	54 (66.7)	72 (59.0)	2.6 [1.2 – 5.5]	0.02
Maternal deaths	6 (14.6)	3 (3.7)	9 (7.3)	0.2 [0.1 – 0.9]	0.03

ICU = intensive care unit

Table XVI. Distribution of maternal complications among treatment subgroups.

Maternal complications	Group A (n=41)	Group B (n=82)	OR 95% CI	P-value
AKI	4 (9.8)	15 (18.3)	0.5 (0.1 – 1.6)	0.22
HELLP syndrome	3 (7.3)	27 (32.9)	0.2 (0.1 – 0.6)	0.002
APE	1 (2.4)	4 (4.9)	0.5 (0.1 – 4.5)	0.51
Neurological deficits	1 (2.4)	3 (3.7)	0.7 (0.1 – 6.5)	0.72
Placenta abruptio	2 (4.9)	4 (4.9)	6 (4.9)	1.0
DIC	0	1 (1.2)	1.5 (1.3 – 1.7) *	0.48
Cardiopathy	2 (4.9)	2 (2.4)	2.1 (0.3 – 15.1)	0.47

*Risk estimate for cohort group B subgroup; AKI = acute kidney injury; HELLP = hemolysis, elevated liver enzymes, low platelets; DIC = disseminated intravascular coagulation

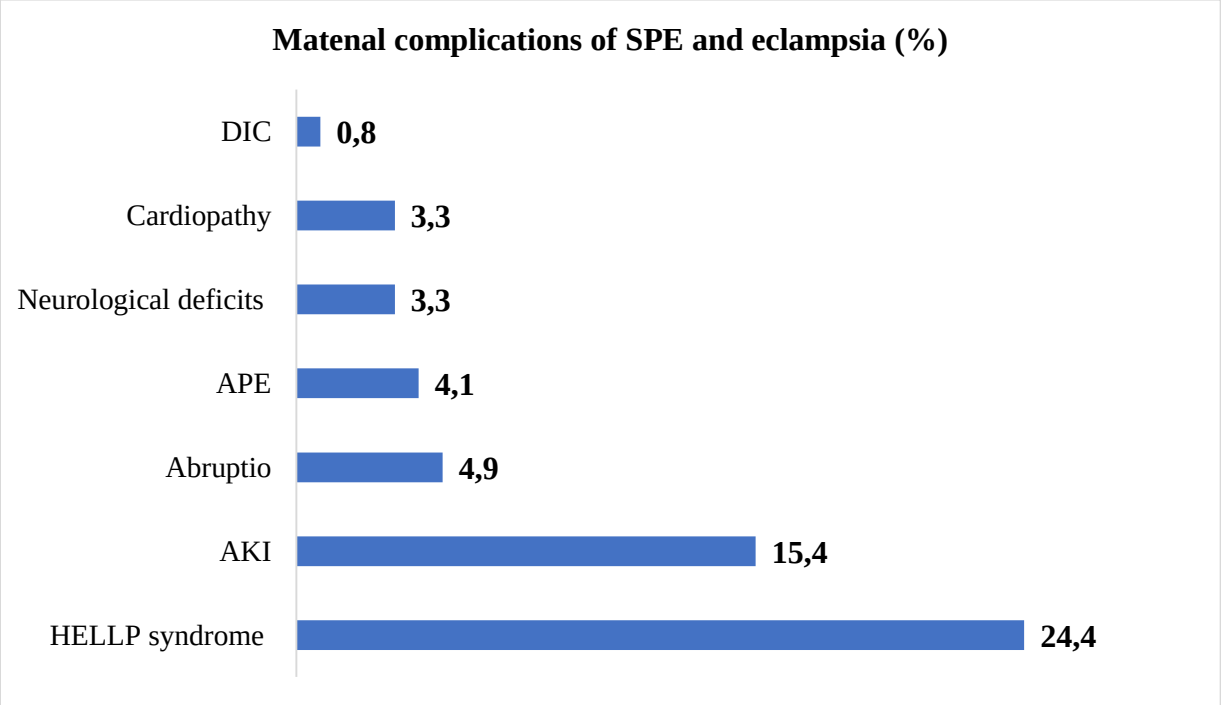

Figure IX. Distribution of maternal complications of SPE and eclampsia

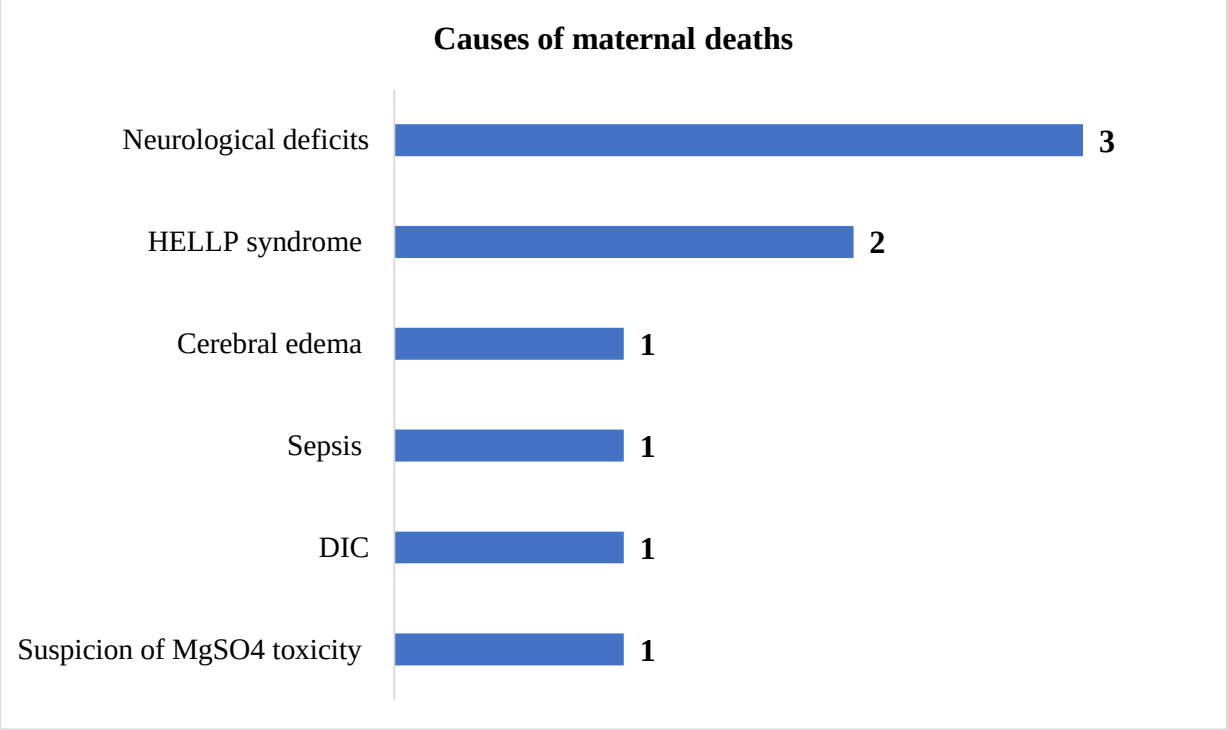

Figure X. Distribution of causes of maternal deaths following magnesium interventions.

4.2.2 Fetal outcomes

The prevalence of fetal complications (59.8%, OR: 2.5, 95 CI: 1.2 – 5.6; P = 0.02), perinatal deaths (32%; OR: 1.3, 95% CI: 0.6 – 3.1; P = 0.49), and low birth weight (<2500 g) (63.5%; OR: 0.4, 95% CI: 0.2 – 1.0; P = 0.04) were higher in group B when compared to group A. There was no significant difference in the 5th minute APGAR scores between the two groups [Table XVII]. Induced prematurity was the most prevalent fetal complication (35.8%), while asphyxia was the least prevalent (8.1%) [Figure XI].

Table XVII. Comparison of fetal outcome following magnesium sulfate therapy between treatment subgroups.

Fetal outcome parameter	Group A (n=41)	Group B (n=82)	OR 95% CI	P-value
Prevalence of fetal complications n (%)	15 (36.6)	49 (59.8)	2.5 [1.2 – 5.6]	0.02
Perinatal deaths n (%)	**11 (26.8)**	**26 (32.9)**	**1.3 [0.6 – 3.1]**	**0.49**
Still births n (%)	8 (19.5)	15 (18.3)		
Early neonatal deaths n (%)	3 (7.3)	11 (13.4)		
Low 5th minute APGAR (<7) n(%)	10 (24.4)	18 (22.5)	1.1 [0.5 – 2.7]	0.82
5th minute APGAR (mean±SD)	7.0 ± 3.8	6.8 ± 3.6		0.75
Low Birth weight (<2500 g) n (%)	17 (43.6)	47 (63.5)	0.4 [0.2 – 1.0]	0.04

APGAR = appearance, pulse, grimace, activity, respiration

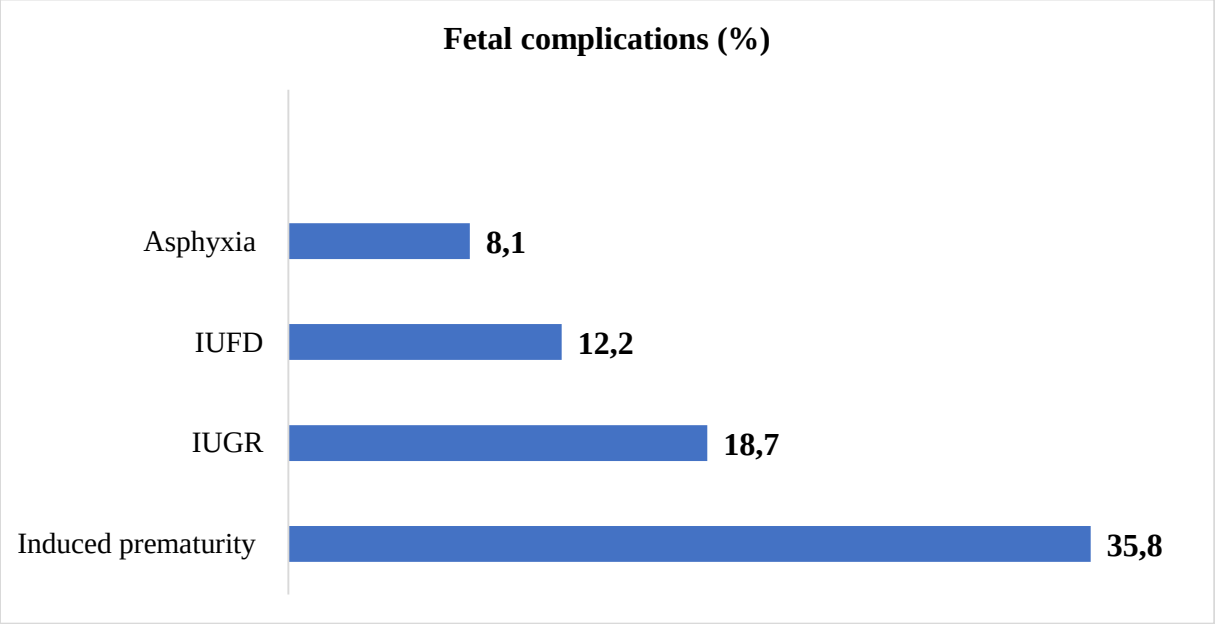

Figure XI. Distribution of fetal complications of following MgSO4 interventions

4.2.3 Association between MgSO4 dose-completion and feto-maternal outcomes

Ten (10) independent predictors associated with $MgSO_4$ dose-completion were tested as shown in table XVIII. Multiple logistic regression revealed that complete $MgSO_4$ dosing was associated with decreased maternal mortality (B = -0.361, P = 0.09), decreased rate of admission into ICU (B = -0.216, P = 0.09), and higher 5^{th} AGPGAR scores (B = 0.012, P = 0.62).

Table XVIII. Association between magnesium dose completion and feto-maternal outcomes.

Predictors	Coefficients		P-value
	B	Std. Error	
Constant	**0.498**	**0.346**	**0.15**
Maternal complications	0.089	0.114	0.44
Fetal complications	0.121	0.128	0.35
Recurrence convulsion rate	0.084	0.206	0.68
Caesarean delivery rate	0.199	0.101	0.05
Admission rate into ICU	**-0.216**	**0.125**	**0.09**
Duration in ICU	0.022	0.016	0.19
Prevalence of perinatal deaths	0.057	0.185	0.76
Case fatality rate	**-0.361**	**0.209**	**0.09**
5^{th} minute APGAR score	**0.012**	**0.023**	**0.62**
Birth weight	-<0.001	<0.001	0.67

Regression model $R^2 = 0.156$, P = 0.08

Chi-square: P<0.05 is statistically significant

4.2.4 Comparison of maternal mortality and caesarean section rates between the two hospitals.

Bivariate analysis shows that treatment of SPE and eclampsia at YGOPH was associated with lower maternal mortality (4.1%, OR: 2.5, 95% CI: 0.45–12.3; P = 0.26) and higher caesarean section rates (79.2%; OR: 4.5, 95% CI: 1.9 – 10.3, P = <0.001) than in YCH [Table XIX].

Table XIX. Comparison of maternal mortality and caesarean section rates between the two hospitals.

Variable	YCH n (%)	YGOPH n (%)	Corr. coefficient	Odds ratio 95% CI	P-value
Maternal mortality	7 (9.5)	2 (4.1)	0.10	2.5 [0.45–12.3]	0.26
Caesarian section rate	34 (45.9)	38 (79.2)	0.33	4.5 [1.9 – 10.3]	<0.001

4.3 Frequency of adverse effects of magnesium sulfate and their determinants among women with severe preeclampsia and eclampsia.

Generally, there was no significant difference in the prevalence of adverse effects of $MgSO_4$ between the two treatment groups, with an overall prevalence 7.3%. The various adverse effects observed were oliguria (3.3%) respiratory depression (1.6%), reduced tendon reflexes (3.3%), and hypotension (4.1%) [Table XX].

Table XX. Comparison of adverse effects of magnesium sulfate between the treatment subgroups.

$MgSO_4$ adverse effects	$MgSO_4$ Dose completion N (%)		Total N (%)	Odds ratio (95% CI)	P-value
	Group A	Group B			
Overall prevalence	1 (2.4)	8 (9.8)	9 (7.3)	0.23 [0.02-1.9]	0.14
Oliguria	1 (2.4)	3 (3.7)	4 (3.3)	0.66 [0.07-6.5]	0.72
Respiratory depression	0	2 (2.4)	2 (1.6)	-	0.31
Reduced/absent tendon reflexes	0	4 (4.9)	4 (3.3)	-	0.15
Hypotension	1 (2.4)	4 (4.9)	5 (4.1)	0.49 [0.05-4.5]	0.52

CHAPTER 5 : DISCUSSION

Severe preeclampsia and eclampsia are serious complications of pregnancy with potentially life-threatening consequences for both mothers and babies. While magnesium sulfate has been a widely used intervention for the prevention and treatment of seizures associated with these conditions, there are variations in dosages and administration protocols, concerns about its adverse effects, and paucity of clinical evidence in Cameroon. This study sought to advance the knowledge and evidence base surrounding its use in the management of SPE and eclampsia needed to inform clinical practices, improve feto-maternal outcomes and reduce maternal morbidity and mortality.

This was a hospital-based prospective and descriptive study with an analytical component, involving 123 participants, recruited through a nonprobability consecutive and exhaustive sampling method. All cases were followed up from admission to discharge. This study approach is inexpensive and well accessible and has been used by many authors from countries like India, Nigeria, Sudan, and Kuwait [16,45,46,48,52].

The following risk factors for preeclampsia/eclampsia were identified in this study primiparternity (40.2%), primiparity (33.6%), maternal age >35 years (33.3%), family history of hypertension (19.2%), twin pregnancy (10.7%), history of preeclampsia (8.3%)and family history of diabetes (4.2%), which are recognizable risk factors described in literature [1,44,53,54]. Primipaternity was the most prevalent risk factor.

The mean maternal age was 30.5 ± 7.3 years, similar so that of one study done in Kenya [55]. There was a significant difference in the mean ages of women with SPE (32.0 ± 7.0 years) and those with eclampsia (26.2 ± 6.4 years, P = <0.001). Studies from Cameroon and India have also revealed that young women between the ages of 19 and 30 years are mostly affected [2,5,16,43–46,53]. Primiparity is also an important risk factor which corroborates findings in most literature [2,5,9]. Primiparous women constituted about a third of our study population, majority of whom were affected by eclampsia (40.0%, P = 0.39). The prevalence of twin gestation among SPE and Eclampsia in our study was 10.7%, and similar findings were observed in other studies in Cameroon [5,54].

In our study as in many others, preeclampsia was more prevalent than eclampsia, mostly occurring in the antepartum period, and presents at preterm with gestational age (GA) of 35.6 ± 4.1 weeks (p <0.001) [16,17,53]. Most of the cases were referred cases from peripheral resource-limited facilities undermining the importance of adequate ANC, a primordial factor in management of [illegible] [45,47]. In this study we observed that the ANC of the subjects was

of poor quality as the mean number of ANC recorded was only 3.3 ± 2.2 instead of the minimum of 8 contacts as recommended by WHO. Blood pressures values at diagnosis usually exceed 160/100 mmHg, with a mean SBP of 175±22.6 mmHg and mean DPB of 114.0±18.8 mmHg observed in our study similar to that reported in some recent studies [43,54].

Concerning the paraclinical profile, liver enzymes (ASAT and ALAT) and platelet counts were the most deranged parameters in our study, consistent with findings from other studies [43,46]. Also, thrombocytopenia, elevated liver enzymes, elevated creatinine, were more prevalent in eclamptic women than those with SPE. This could be justified by the fact that as eclampsia is a complication of SPE indicating progression or worsening of the disease, one would expect to have more complications in the later than the former. Several studies have also revealed similar finding [4,35].

Concerning the feto-maternal outcomes, several studies have shown that low-dose regimens (LDR) of $MgSO_4$ are safe and effective for management of SPE and eclampsia, even at subtherapeutic serum concentrations with similar feto-maternal outcomes [16,46,52,56–58].

Several LDRs tried in several low-to-middle income countries (LMICs) have demonstrated an efficacy of >90% in the control and prevention of eclamptic convulsions, which is comparable to that of the standard Pritchard's regimen [9,12,16,43,46,48]. The overall rate of control of convulsions in our study was 94.3%, similar to other studies done in Nigeria and India [52,56,59]. There was no significant difference in the rates of control of convulsions between the two treatment subgroups, which corroborates the findings from many studies [16,58,60]. This means that despite subtherapeutic levels, the incomplete dosing regimen could effectively control eclamptic convulsions in 92.7% cases, almost as effective as the complete dosing regimen (95.1%, P = 0.58). Similar results were reported in other studies [16,17]. The recurrent convulsion rate of 5.7% observed in our study is similar to that reported by most other studies [52,56,59], but slightly higher than that for some other studies in India [16,61,62]. This difference could possibly be as a result of lower weight of women in their study. BMI is an important factor determining the efficacy and toxicity of $MgSO_4$. Also, the high prevalence of maternal complications in our study with a significant difference among the treatment subgroups (38.2%, P = 0.01), associated with deranged liver and renal function tests reflecting end-organ involvement, possibly altered the bioavailability of $MgSO_4$ in our study, thus accounting for this difference.

Studies have shown that low-dose regimens are associated with comparable maternal morbidity as in standard regimens [16,63]. This was not the case in our study where maternal complications were more prevalent in the complete dosing regimen group (46.3%; OR: 3.1, 95% CI: 1.3 – 7.2; P = 0.01) than in the incomplete dosing group. This difference could be explained by the complications of SPE and eclampsia, rather than $MgSO_4$ dose-dependency as most complications were diagnosed on entry, since most of them were referred cases. Also, other factors relating to the delay in initiation of treatment such financial constraints and untimely availability of $MgSO_4$ could possibly explain these findings. However, the prevalence of maternal complications in our study is similar to that reported by one study in India [16], but higher than one other report [63], explicable by the high turnover of referred unbooked cases with multiple high-risk factors, and usually presenting late to our tertiary hospitals. The maternal complications reported in this study were HELLP syndrome, acute kidney injury, placenta abruptio, acute pulmonary edema, and neurological deficits. HELLP syndrome was the most prevalent maternal complication (24.4%, P = 0.01), followed by acute renal failure (15.4%, P = 0.22). This result corroborates findings from other studies [5,35,45,54,55].

Majority of the women in group A delivered vaginally (56.1%, P = 0.024), while majority in group B delivered through cesarean section (CS) (66.7%, P = 0.024). The overall CS rate in our study was high (59.0%) when compared to other studies [52,56,58], but similar to findings from some studies [5,16,57]. It is well known that the definitive therapy for SPE and eclampsia is termination of pregnancy, and the seizure-to-delivery interval has to be minimized. Our hospitals, being tertiary care referral hospitals, received most cases that were either not in labor, with unfavorable cervix or with additional obstetric risk factors warranting prompt delivery thus favoring CS. However, the CS rate in group A was lower (43.9%; OR: 2.6, 95% CI: 1.2 – 5.5; P = 0.02) when compared to that of group B implying incomplete dosing regimen appears to alter labor outcomes or decrease the likelihood of CS compared to the standard Pritchard's regimen. Multiple regression analysis confirms a positive correlation between CS rate and complete $MgSO_4$ dosing, however, this association is weak (B = 0.199, P = 0.05). This finding is similar to one study done in Pakistan [58], but different from that reported in most literature [57,58,64]. This difference is as a result of difference in the protocols for management of SPE and eclampsia in the two hospitals in our setting. A higher prevalence of complete dosing regimen (mostly the Zuspan maintenance dose regimen) was observed in YGOPH (95.9%) where the CS rate was equally high (79.2%; OR: 4.5, 95% CI: 1.9 – 10.3, P = <0.001).

Concerning maternal mortality, there are variations in the overall case fatality rates from $MgSO_4$ interventions ranging from zero to up to 24.3% reported in most literature [16,45–47,52,59]. The overall case fatality rate in our study was 7.3%, with a relatively significant (P = 0.03) higher rate in group A (14.6%, OR: 0.2, 95% CI: 0.1 – 0.9, P = 0.03) when compared to that of group B (3.7%). Although some authors have reported maternal deaths with various low-dose regimens (LDRs) [16,46,52,56–58], the mortality rates are similar to those of conventional regimens (complete dosing regimens). Moreover, most of these deaths occur as a result of the complications of SPE and eclampsia or other high-risk obstetric conditions rather than $MgSO_4$ overdose. In our study, as in one other in Canada, only one out of the nine maternal deaths was attributed to "suspicion" of $MgSO_4$ toxicity [18].

Even though some authors argue that the effectiveness of $MgSO_4$ is dependent on dosage and time of administration [65], this was not the case in our study as there was no significant difference in the time-to-treatment initiation between the two treatment groups. A TTI >1 hour was considered high and we observed that the overall mean TTI was 2.2±3.0 hours. The various reasons for the delay in initiation of treatment observed in our study were staff workload, financial constraints, product not readily available at point of treatment, and other reasons such as delay in having laboratory results.

The fetal complications observed in our study include prematurity, IUGR, IUFD and asphyxia, with prematurity being the most prevalent (35.8%, P = 0.18). This finding is consistent with that reported in most literature [5,45,54]. The fetal complications were more prevalent in group B (59.8%, OR: 2.5, 95% CI: 1.2 – 5.6, P = 0.02) than in group A.

In this study and others [58], there were no significant differences in the 5th minute APGAR score and perinatal deaths between the two treatment subgroups thus emphasizing that LDR is not inferior to the standard regimen in preventing adverse perinatal outcomes, as depicted in other studies [16]. The overall prevalence of stillbirth was 18.7% and was similar among the two treatment subgroups. This is also similar to that reported by one study in India [46]. The prevalence of early neonatal death was 11.4% with no significant difference among the treatment subgroups (P = 0.45), comparable to findings from several other studies [16,42,56].

Generally, most studies have revealed that the toxic effects attributable to $MgSO_4$ are rare [18]. Lowering the dose virtually eliminated the risk of magnesium toxicity and thus increased the safety of the drug [56]. Various randomized control trials comparing low-dose regimen (LDR) to standard regimens have revealed that adverse effects are generally fewer in LDR

group [17,18,56,66]. From our study, the overall prevalence of adverse effects observed was 7.3%, relatively more in group B (9.8%), than in group A (2.4%) thereby corroborating the findings in literature. Signs of toxicity seen in our study were oliguria 4 (3.3%), reduced tendon reflexes 5 (3.3%), hypotension 4 (4.9%) and oliguria 4 (3.3%). One study in India reported toxicity of up to 12% in the group with complete dose [17]. Another study reported 4 cases of oliguria (n = 100) [66], which is similar to that of our study.

CONCLUSION

- Severe preeclampsia and eclampsia affected women at mean age of 30.5 ± 7.3 years, occurring mainly in the antenatal period (93.5%), at a mean gestational age of 35.6 ± 4.1 weeks, and affecting mostly multiparous women (66.4%). The most prevalent risk factor was primipaternity (40.2%). Liver enzymes and renal function test were deranged in over one-third of the cases.
- Magnesium sulfate effectively controlled convulsions in 94.3% cases. The case fatality rate was higher in women treated with suboptimal doses of $MgSO_4$ (14.6%, OR: 0.2; 95% CI: 0.1 – 0.9; P = 0.03) than those treated with complete doses, while maternal complications (46.3%; OR: 3.1, 95% CI: 1.3 – 7.2; P = 0.01), fetal complications (59.8%, OR: 2.5, 95 CI: 1.2 – 5.6; P = 0.02), caesarean delivery rate (66.7%; OR: 2.6, 95% CI: 1.2 – 5.5; P = 0.02), perinatal deaths (32%; OR: 1.3, 95% CI: 0.6 – 3.1; P = 0.49), and low birth weight (<2500 g) (63.5%; OR: 0.4, 95% CI: 0.2 – 1.0; P = 0.04) were higher in women treated with complete doses than those with suboptimal doses. HELLP syndrome was the most prevalent maternal complication (24.4%; OR: 0.2, 95% CI: 0.1 – 0.6; P = 0.002), while prematurity was most prevalent fetal complication (35.8%). Multiple logistic regression show that complete $MgSO_4$ dosing was associated with decreased maternal mortality, decreased rate of admission into the ICU, and higher 5^{th} minute APGAR scores.
- Adverse effects of the drug were generally low and insignificant between the two groups (7.3%; OR: 0.23, 95% CI: 0.02 – 1.9, P = 0.14). The various adverse effects were respiratory depression (1.6%), reduced tendon reflexes (3.3%) and hypotension (4.1%).

RECOMMENDATIONS

To pregnant women

- Continuous utilization and optimization of antenatal care services available in recognized health facilities.

To remote hospitals

- The training of health care providers on the identification and treatment of severe preeclampsia and eclampsia.
- Optimization of routine antenatal care (ANC) for all pregnant women.
- To ensure the consistent availability of magnesium sulfate

Tertiary hospitals

- To ensure the consistent availability of magnesium sulfate.
- To establish standardized and harmonized clinical guidelines/protocols for the administration of magnesium sulfate.
- To recruit more qualified personnel (nurses and midwives) so as to reduce workload and enhance emergency obstetric care services, especially in the management of preeclampsia and eclampsia .

To the Faculty of Medicine and Biomedical Sciences

- To promote further research in this subject which may facilitate the development and implementation of a consensus on optimal magnesium sulfate dosages in our setting.

REFERENCES

1. ACOG. Practice Bulletin Hypertension and Preeclampsia. ACOG. 2020;135:e135-60.

2. Fouedjio J, Foumane P, Fouogue J, Ndenga V, Fouelifack F, Bissene A, et al. Predictors of eclampsia among preeclamptic patients: a case control study in Yaounde, Cameroon. Int J Reprod Contracept Obstet Gynecol. 2016;2204–9.

3. Foumane P, Dohbit S, Ngo UM, NKada M, Ze M, Mboudou E. Étiologies de la Mortalité Maternelle à l'Hôpital Gynéco-Obstétrique et Pédiatrique de Yaoundé: Une Série de 58 Décès. Health Sci Dis. 2015;16:1–5.

4. Dutta D. DC Dutta's Textbook of Obstetrics including Perinatology and Contraception. 8th ed. Jaypee Brothers Medical Publishers (P) Ltd; 2015.

5. Essome H, Mve K, Ekono M, Essiben F, Boten M, Tocki TG, et al. Pre-Eclampsia at Laquintinie Hospital (Douala): Survey of Prevalence and Morbidity from 2010 to 2015. Health Sci Dis [Internet]. 2019;20. Available from: www.hsd-fmsb.org

6. Mboudou ET, Foumane P, Belley P, Ze M, Nkengafac WM, Doh AS. Hypertension au cours de la grossesse: Aspects clinique et épidemiologiques a l'Hopital Gynéco-Obstetrique et Pédiatrique de Yaounde, Cameroun. 2009;6:1087–93.

7. Goldenberg RL, Jones B. Reducing maternal mortality from preeclampsia and eclampsia in low-resource countries – what should work?

8. Félix E. Eclampsia in African Milieu, Yaounde-Cameroon: epidemiology, seasonal variations and treatment regimen. OGIJ. 2019;10:176–83.

9. Okereke E, Ahonsi B, Tukur J, Ishaku SM, Oginni AB. Benefits of using magnesium sulphate (MgSO4) for eclampsia management and maternal mortality reduction: lessons from Kano State in Northern Nigeria. BMC Res Notes. 2012;5:421.

10. Smith JM, Lowe RF, Fullerton J, Currie SM, Harris L, Felker-Kantor E. An integrative review of the side effects related to the use of magnesium sulfate for pre-eclampsia and eclampsia management. BMC Pregnancy Childbirth. 2013;13:34.

11. Long Q, Oladapo O, Leathersich J, Vogel J, Carroli G, Lumbiganon P, et al. Clinical practice patterns on the use of magnesium sulphate for treatment of pre-eclampsia and eclampsia: a multi-country survey. BJOG. 2017;1883–90.

12. Padda J, Khalid K, Colaco LB, Padda S, Boddeti NL, Khan AS, et al. Efficacy of Magnesium Sulfate on Maternal Mortality in Eclampsia. Cureus [Internet]. 2021 [cited 2023 Nov 11]; Available from: https://www.cureus.com/articles/65999-efficacy-of-magnesium-sulfate-on-maternal-mortality-in-eclampsia

13. Tahir S, Shafique N, Saleem S. Efficacy of Magnesium Sulphate In Prevension Of Fits In Severe Pre-Eclampsia. 2011;5.

14. Pritchard JA. Management of preeclampsia and eclampsia. Kidney International. 1980;18:259–66.

15. Eddy K, Vogel J, Zahroh R, Bohren M. Factors affecting use of magnesium sulphate for pre-eclampsia or eclampsia: a qualitative evidence synthesis. BJOG. 2022;129:379–91.

16. Nagaria T. Single Loading Low Dose MgSo4 Regimen: A Simple, Safe and Effective Alternative to Pritchard's Regimen for Indian Women. JCDR [Internet]. 2017 [cited 2023 Nov 11]; Available from: http://jcdr.net/article_fulltext.asp?issn=0973-709x&year=2017&volume=11&issue=8&page=QC08&issn=0973-709x&id=10453

17. Prasad A, Kumar A. Use of loading dose of magnesium sulphate versus standard regime for prophylaxis of severe Pre- Eclampsia- A comparative study. 2017;

18. Gordon R, Magee LA, Payne B, Firoz T, Sawchuck D, Tu D, et al. Magnesium Sulphate for the Management of Preeclampsia and Eclampsia in Low and Middle Income Countries: A Systematic Review of Tested Dosing Regimens. Journal of Obstetrics and Gynaecology Canada. 2014;36:154–63.

19. Onder G. Efficacy and Effectiveness models.

20. Adverse Drug Events, Adverse Drug Reactions. 2006; Available from: https://www.pbm.va.gov/PBM/vacenterformedicationsafety/tools/AdverseDrugReaction.pdf

21. Klahr S, Miller S. Acute Oliguria. N Engl J Med. 1998;338:671–5.

22. OECD O. Perinatal Mortality [Internet]. OECD Health Statistics; 2023. Available from: http://www.oecd.org/health/health-data.htm

23. World Health Organization. Maternal Mortlity [Internet]. OECD Publishiing; 2016. Available from: https://www.oecd-ilibrary.org/docserver/health_glance_ap-2016-12-en.pdf?expires=1709185698&id=id&accname=guest&checksum=C3D7397B3BCD090B391BF95BBC269DDF

24. Kim D-H, Choe YJ, Jeong J-Y. Understanding and Interpretation of Case Fatality Rate of Coronavirus Disease 2019. J Korean Med Sci. 2020;35:e137.

25. Martins JG, Biggio JR, Abuhamad A. Society for Maternal-Fetal Medicine Consult Series #52: Diagnosis and management of fetal growth restriction. American Journal of Obstetrics and Gynecology. 2020;223:B2–17.

26. Tavares Da Silva F, Gonik B, McMillan M, Keech C, Dellicour S, Bhange S, et al. Stillbirth: Case definition and guidelines for data collection, analysis, and presentation of maternal immunization safety data. Vaccine. 2016;34:6057–68.

27. Cone EB, Marchese M, Paciotti M, Nguyen D-D, Nabi J, Cole AP, et al. Assessment of Time-to-Treatment Initiation and Survival in a Cohort of Patients With Common Cancers. JAMA Netw Open. 2020;3:e2030072.

28. Farah D, Duncan H, Louise E, Tatiana L. Suboptimal dosing of opioid agonist treatments - a literature review. Heroin Addiction & Related Clinical Problems. 2022;1–9.

29. Gary C, Kenneth L, Steven B, Jodi D, Barbara H, Brian C, et al. Williams Obstetrics. 25th edition. Mc Graw Hill Education; 2018.

30. Phelan LK, Brown MA, Davis GK, Mangos G. A Prospective Study of the Impact of Automated Dipstick Urinalysis on the Diagnosis of Preeclampsia. Hypertension in Pregnancy. 2004;23:135–42.

31. Kee-Hak L, Guy S. Preeclampsia. Medscape [Internet]. 2022; Available from: https://emedicine.medscape.com/article/1476919-overview?&icd=login_success_email_match_fpf#a13

32. Jikamo B, Adefris M, Azale T, Alemu K. Incidence, trends and risk factors of preeclampsia in sub-Saharan Africa: a systematic review and meta-analysis. PAMJ-OH [Internet]. 2023 [cited 2024 Jan 20];11. Available from: https://www.one-health.panafrican-med-journal.com/content/article/11/1/full

33. Rogers P. Structure and function of endometrial blood vessels. Human Reproduction Update. 1996;2:57–62.

34. Meazaw MW, Chojenta C, Muluneh MD, Loxton D. Systematic and meta-analysis of factors associated with preeclampsia and eclampsia in sub-Saharan Africa. Spradley FT, editor. PLoS ONE. 2020;15:e0237600.

35. Konnur H, Modi S. Maternal complications in eclampsia and pre-eclampsia: an institutional study. Int J Reprod Contracept Obstet Gynecol. 2018;7:4992.

36. Tian Y, Yang X. A Review of Roles of Uterine Artery Doppler in Pregnancy Complications. Front Med. 2022;9:813343.

37. Eroğlu D, Yanik F, Başer E, Kuşcu E. The Value of The Uterine Artery Doppler at 22-24 Weeks Gestation In The Prediction of Adverse Perinatal Outcome In an Unselected Population.

38. World Health Organization. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia. 2011 [cited 2024 Aug 19]; Available from: https://iris.who.int/handle/10665/44703

39. Tom A, Holly C. Fluid Management. Califonia Maternal Quality Care Collaborative (CMQCC). 2013;

40. Tukur J. The use of magnesium sulphate for the treatment of severe pre-eclampsia and eclampsia. Ann Afr Med. 2009;8:76.

41. Euser AG, Cipolla MJ. Magnesium Sulfate for the Treatment of Eclampsia: A Brief Review. Stroke. 2009;40:1169–75.

42. Okusanya B, Oladapo O, Long Q, Lumbiganon P, Carroli G, Qureshi Z, et al. Clinical pharmacokinetic properties of magnesium sulphate in women with pre-eclampsia and eclampsia. BJOG. 2016;123:356–66.

43. Kollu BS, Talathi MA, Taralekar VS. Efficacy of MgSO4 to prevent eclampsia in women with severe pre-eclampsia and impending eclampsia. Int J Reprod Contracept Obstet Gynecol. 2023;12:1088–92.

44. Jaboi RM, S. V, . N. Assessment of socio-demographic and clinical factors associated with preeclampsia and eclampsia among primigravida attending tertiary care center in South India. Int J Reprod Contracept Obstet Gynecol. 2020;9:4486.

45. Priso EB, Njamen TN, Tchente CN, Kana AJ, Landry T, Niaga F, et al. Trend in admissions, clinical features and outcome of preeclampsia and eclampsia as seen from the intensive care unit of the Douala General Hospital, Cameroon. Pan Afr Med J [Internet]. 2015 [cited 2023 Nov 11];21. Available from: http://www.panafrican-med-journal.com/content/article/21/103/full/

46. Bera P, Bhoi NR, Khuntia P, Pradhan K, Mohanta C, Soren M, et al. STUDY OF EFFICACY OF LOW DOSE MAGNESIUM SULPHATE REGIMEN (DHAKA REGIMEN) AS COMPARED TO STANDARD REGIMEN (PRITCHARD) IN THE MANAGEMENT OF ECLAMPSIA. jemds. 2015;4:10609–18.

47. Budhwani H, Shivkumar P, Purandare CN, Cataldo NA, Desai S, Bhatt P, et al. Examining the Use of Magnesium Sulfate to Treat Pregnant Women with Preeclampsia and Eclampsia: Results of a Program Assessment of Emergency Obstetric Care (EmOC) Training in India. J Obstet Gynecol India. 2017;67:330–6.

48. Alsiddig Yousef B, Abdulmoniem Merghani A, Salah Abdulla W, Rifaat Binni R. Assessment of magnesium sulphate usage in pre-eclamptic and eclamptic women in Omdurman Maternity Hospital, 2017: A cross-sectional study. F1000Res. 2019;8:447.

49. Gray JR, Grove SK, Sutherland S. Burns and Grove's The Practice of Nursing Research: Appraisal, Synthesis, and Generation of Evidence.

50. Charan J, Biswas T. How to Calculate Sample Size for Different Study Designs in Medical Research? Indian Journal of Psychological Medicine. 2013;35:121–6.

51. Polit DF, Beck CT. Essentials of nursing research: appraising evidence for nursing practice. 7th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2010.

52. Ekele BA, Muhammed D, Bello LN, Namadina IM. Magnesium sulphate therapy in eclampsia: the Sokoto (ultra short) regimen. BMC Res Notes. 2009;2:165.

53. Tabassum S, AlSada A, Bahzad N, Sulaibeekh N, Qureshi A, Dayoub N. Preeclampsia and Its Maternal and Perinatal Outcomes in Pregnant Women Managed in Bahrain's Tertiary Care Hospital. Cureus [Internet]. 2022 [cited 2024 Sep 10]; Available from: https://www.cureus.com/articles/82149-preeclampsia-and-its-maternal-and-perinatal-outcomes-in-pregnant-women-managed-in-bahrains-tertiary-care-hospital

54. Henri-Leonard M, Junie MN, Ange NDM, Junette MM, Hector MC, Pascal F, et al. Maternal Complications and Prognostic Factors of Severe Pre-Eclampsia in Three University Hospitals of Yaoundé: A Study of 115 Cases. 2024;25.

55. Irene K, Amubuomombe PP, Mogeni R, Andrew C, Mwangi A, Omenge OE. Maternal and perinatal outcomes in women with eclampsia by mode of delivery at Riley mother baby hospital: a longitudinal case-series study. BMC Pregnancy Childbirth. 2021;21:439.

56. Jana N, Dasgupta S, Das AK, Santra D, Samanta B. Experience of a low-dose magnesium sulfate regimen for the management of eclampsia over a decade. Intl J Gynecology & Obste. 2013;122:13–7.

57. Gaur I, Kumar K. Comparison of low dose magnesium sulphate regime with standard Pritchard regime in severe preeclampsia and eclampsia: a tertiary centre experience. Int J Reprod Contracept Obstet Gynecol. 2022;11:1114.

58. Shoaib T, Khan S, Javed I, Bhutta SZ. Loading Dose of Magnesium Sulphate Versus Standard Regime for Prophylaxis of Pre-eclampsia. 2009;19.

59. Okereke E, Ahonsi B, Tukur J, Ishaku SM, Oginni AB. Benefits of using magnesium sulphate (MgSO4) for eclampsia management and maternal mortality reduction: lessons from Kano State in Northern Nigeria. BMC Res Notes. 2012;5:421.

60. Dasgupta S. Single Loading Dose of Magnesium Sulphate in Severe Preeclampsia and Eclampsia-Is it Effective? A Randomized Prospective Study. OGIJ [Internet]. 2015 [cited 2024 Sep 3];2. Available from: https://medcraveonline.com/OGIJ/single-loading-dose-of-magnesium-sulphate-in-severe-preeclampsia-and-eclampsia-is-it-effective-a-randomized-prospective-study.html

61. Kollu BS, Talathi MA, Taralekar VS. Efficacy of MgSO4 to prevent eclampsia in women with severe pre-eclampsia and impending eclampsia. Int J Reprod Contracept Obstet Gynecol. 2023;12:1088–92.

62. Omu AE, Al-Harmi J, Vedi HL, Mlechkova L, Sayed AF, Al-Ragum NS. Magnesium Sulphate Therapy in Women with Pre-Eclampsia and Eclampsia in Kuwait. Med Princ Pract. 2008;17:227–32.

63. Dasgupta S. Single Loading Dose of Magnesium Sulphate in Severe Preeclampsia and Eclampsia-Is it Effective? A Randomized Prospective Study. OGIJ [Internet]. 2015 [cited 2024 Sep 2];2. Available from: https://medcraveonline.com/OGIJ/single-loading-dose-of-magnesium-sulphate-in-severe-preeclampsia-and-eclampsia-is-it-effective-a-randomized-prospective-study.html

64. Mohanapu S, Raveendran S, Murugaiah Y, Sen M. A comparative study of low dose magnesium sulphate therapy with standard pritchard's regime in the management of eclampsia. Int J Reprod Contracept Obstet Gynecol. 2016;2939–43.

65. Budhwani H, Shivkumar P, Purandare CN, Cataldo NA, Desai S, Bhatt P, et al. Examining the Use of Magnesium Sulfate to Treat Pregnant Women with Preeclampsia and Eclampsia: Results of a Program Assessment of Emergency Obstetric Care (EmOC) Training in India. J Obstet Gynecol India. 2017;67:330–6.

66. Ranganna H, Saha SC, Thami MR, Kumar P. Prophylactic magnesium sulphate in severe preeclampsia- Loading dose only vs. conventional 24 hour therapy of modified Pritchard's regime- A randomised trial. iosrphr. 2014;4:39–47.

APPENDICES

Appendix 1: Ethical Clearance (Institutional Ethics Review Board, FMBS, University of Yaoundé I)

UNIVERSITÉ DE YAOUNDÉ I
FACULTÉ DE MÉDECINE ET DES SCIENCES BIOMÉDICALES
COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE
Tel/ fax : 22 31-05-86 22 311224
Email: decanatfmsb@hotmail.com

THE UNIVERSITY OF YAOUNDE I
FACULTY OF MEDICINE AND BIOMEDICAL SCIENCES
INSTITUTIONAL ETHICAL REVIEW BOARD

Ref. : N° 1204 /UY1/FMSB/VDRC/DASSR/CSD

CLAIRANCE ÉTHIQUE 10 SEPT 2024

Le COMITÉ INSTITUTIONNEL D'ÉTHIQUE DE LA RECHERCHE (CIER) de la FMSB a examiné
La demande de la clairance éthique soumise par :
M.Mme : OBASE MISONO RAOLPH Matricule: 20S1973

Travaillant sous la direction de :
- Pr MBU Robinson ENOW
- Dr EBONG Clifford

Concernant le projet de recherche intitulé : Evaluation of the efficacy and toxicity of magnesium sulfate in the management of severe preeclampsia and eclampsia in two tertiary hospitals in Yaoundé

Les principales observations sont les suivantes

Evaluation scientifique	
Evaluation de la convenance institutionnelle/valeur sociale	
Equilibre des risques et des bénéfices	
Respect du consentement libre et éclairé	
Respect de la vie privée et des renseignements personnels (confidentialité) :	
Respect de la justice dans le choix des sujets	
Respect des personnes vulnérables :	
Réduction des inconvénients/optimalisation des avantages	
Gestion des compensations financières des sujets	
Gestion des conflits d'intérêt impliquant le chercheur	

Pour toutes ces raisons, le CIER émet un avis favorable sous réserve des modifications recommandées dans la grille d'évaluation scientifique.
L'équipe de recherche est responsable du respect du protocole approuvé et ne devra pas y apporter d'amendement sans avis favorable du CIER. Elle devra collaborer avec le CIER lorsque nécessaire, pour le suivi de la mise en œuvre dudit protocole.
La clairance éthique peut être retirée en cas de non – respect de la réglementation ou des recommandations sus évoquées.
En foi de quoi la présente clairance éthique est délivrée pour servir et valoir ce que de droit

LE PRESIDENT DU COMITE ETHIQUE

Pr Mbana Ondoa
Obama Marie Thérèse

Appendix 2: <u>Administrative Authorization from YGOPH)</u>

REPUBLIQUE DU CAMEROUN
Paix-Travail-Patrie
MINISTERE DE LA SANTE PUBLIQUE
HOPITAL GYNECO-OBSTETRIQUE ET PEDIATRIQUE DE YAOUNDE
HUMILITE – INTEGRITE – VERITE – SERVICE

REPUBLIC OF CAMEROON
Peace-Work-Fatherland
MINISTRY OF PUBLIC HEALTH
YAOUNDE GYNAECO-OBSTETRIC AND PEDIATRIC HOSPITAL
HUMILITY – INTEGRITY – TRUTH – SERVICE

COMITE INSTITUTIONNEL D'ETHIQUE DE LA RECHERCHE POUR LA SANTE HUMAINE (CIERSH)

Arrêté n° 0977 du MINSANTE du 18 avril 2012 portant création et organisation des Comités d'Ethiques de la Recherche pour la santé Humaines. (CERSH).

AUTORISATION N° 682 /CIERSH/DM/2024

CLAIRANCE ETHIQUE

Le Comité Institutionnel d'Ethique de la Recherche pour la Santé Humaine (CIERSH) a examiné le 26 mars 2024 la demande d'autorisation et le Protocole de recherche intitulé « **evaluation of the efficacy and toxicity of Magnesium sulfate in the management of severe preeclampsia and eclampsia in two tertiary hospitals in Yaounde** » soumis par l'étudiant OBASE MUSONO RALPH.

Le sujet est digne d'intérêt. Les objectifs sont bien définis. La procédure de recherche proposée ne comporte aucune méthode invasive préjudiciable aux participants. Le formulaire de consentement éclairé est présent et la confidentialité des données est préservée. Pour les raisons qui précèdent, le CIERSH de HGOPY donne son accord pour la mise en œuvre de la présente recherche.

OBASE MUSONO RALPH devra se conformer au règlement en vigueur à HGOPY et déposer obligatoirement une copie de ses travaux à la Direction Médicale de ladite formation sanitaire.

Yaoundé, le 08 AVR 2024

LE PRESIDENT

Prof MBU Robinson
Directeur Général
HGOPY

N°1827 ; Rue 1564 ; Ngousso ; Yaoundé 5ème
BP : 4362 Tél. : 242 05 92 94 / 222 21 24 33 / 222 21 24 31 Fax : 222 21 24 30
E-mail : hgopy@hotmail.com / hgopy@hgopy.cm

Appendix 3: <u>Administrative Authorization from the Yaoundé Central Hospital</u>

REPUBLIQUE DU CAMEROUN
Paix-Travail-Patrie
****
MINISTERE DE LA SANTE PUBLIQUE
****
SECRETARIAT GENERAL
****
DIRECTION DE L' HOPITAL CENTRAL DE YAOUNDE
****
SECRETARIAT MEDICAL

N°2381/24 /AMS/DHCY/CM/SM

REPUBLIQUE DU CAMEROUN
Paix-Travail-Patrie
****
MINISTERE DE LA SANTE PUBLIQUE
****
SECRETARIAT GENERAL
****
DIRECTION DE L' HOPITAL CENTRAL DE YAOUNDE
****
SECRETARIAT MEDICAL

Yaoundé, le 10 MAI 2024

ACCORD DE PRINCIPE

Je soussigné **Professeur FOUDA Pierre Joseph**, Directeur de l'Hôpital Central de Yaoundé, marque mon Accord de principe à Monsieur **OBASE MUSONO Ralph**, Résident en 4ème Année de Gynécologie et Obstétrique à la Faculté de Médecine et des Sciences Biomédicales de l'Université de Yaoundé I , sous le thème « EVALUATION OF THE EFFICACY And TOXICITY OF MAGNESIUM SULFATE IN THE MANAGEMENT OF SEVERE PREECLAMPSIA AND ECLAMPSIA IN TWO TERTIARY HOSPITALS IN YAOUNDE» à l'Hôpital Central de Yaoundé sous la supervision du docteur EBONG Cliford .

Pour Le Directeur et par ordre
Le Conseiller Médical,

HOPITAL CENTRAL YAOUNDE – Le Conseiller Médical – MINISTERE DE LA SANTE PUBLIQUE

Pr. Alp Pierre Engole Ekoe

Ampliations :

- Conseiller Médical ;
- Chef service concerné ;
- Intéressé ;
- Archives /Chrono.

Appendix 4: Informed Consent Form

Hospital ID : 1) YCH ☐ 2) YGOPH ☐ **Questionnaire Code** : …… **Date:** ….....

CLINICAL RESERCH
INSTITUTION: DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, FMBS, UNIVERSITY OF YAOUND I

Research topic: THE EFFICACY AND TOXICITY OF MAGNESIUM SULFATE IN THE MANAGEMENT OF SEVERE PREECLAMPSIA AND ECLAMPSIA IN TWO TERTIARY HOSPITALS IN YAOUNDE.
As part of the requirements for the award of a specialization diploma (DES) in Obstetrics and Gynecology

The Researcher: OBASE MUSONO Ralph, 4th year resident in Obstetrics and Gynecology.
Tel : +237 673531182. E-mail : obaseralph@gmail.com

Supervisor : Pr. MBU Robinson ENOW (Professor of Obstetrics and Gynecology)
Co-Supervisors: Dr. EBONG Clifort (Senior Lecturer in Obstetrics and Gynecology)

Research goal: To advance the knowledge and evidence base surrounding the use of magnesium sulfate in the management of severe preeclampsia and eclampsia required in refining clinical practices, improving patient outcomes and reducing maternal morbidity and mortality.

Information to participant: This study has been approved by **the University of Yaounde 1**, the **Yaounde Gyneco-Obstetrics and Paediatrics Hospita**l, and the **Yaounde Central Hospita**l, and you have been randomly selected to participate in the study. You will be asked a series of questions which can last for about 30 to 45 minutes and you will undergo a clinical examination. Your medical file will also be reviewed to complete the data collection process. Your contribution will help in completing the research, and any information you provide will be used strictly for academic purposes. Your participation in the study is voluntary, and every information you provide will be kept confidential. No names or information about any individual will be shared or published. There will neither be any direct benefits nor harm in participating in this study.

Consent to participate
I, _____ confirm that the person asking my consent to take part in this research has told me about the nature, procedure, potential benefits and anticipated inconvenience of participation. I have read (or had explained to me) and understood the study as explained in the information sheet. I have had sufficient opportunity to ask questions and am prepared to participate in the study. I understand that my participation is voluntary and that I am free to withdraw at any time without penalty (if applicable). I am aware that the findings of this study will be processed into a research report, journal publications and/or conference proceedings, but that my participation will be kept confidential unless otherwise specified.
I agree to the recording of the questionnaire and to clinical examination.
I have received a signed copy of the informed consent agreement.

Yaounde the ……./ ……/ 2024

Participant's signature: …… Researcher's signature: ……

Appendix 5: Questionnaire (English)

SN	VARIABLE	RESPONSE	CODE
SECTION A: SOCIO-OBSTETRICAL AND PARA-CLCINICAL PROFILE			
1.	Age (years)		
2.	Marital status	[1] Married/cohabiting (monogamy) [2] Married (polygamy) [3] Unmarried	
3.	Highest level of education	[1]=No education, [2]=Primary, [3]=Secondary [4]=Higher	
4.	Occupation	[1]=Student, [2]=House wife [3]=Civil servant [4]=Formal private sector worker [5]=self-employed [6]=None	
5.	Region of origin	[1]=Center, [2]=West, [3]=Northwest [4]=South west, [5]=East, [6]=South, [7]=Adamawa [8]=North [9]=Far North [10]=Littoral	
6.	Tribe		
7.	Gravidity		
8.	Parity		
9.	Primipaternity	[1]=Yes [2]=No	
10.	Gestational age (in weeks) at diagnosis		
11.	Number of ANC		
12.	Mode of conception	[1]=natural, [2]=assisted reproductive technology	
13.	Number of gestations	[1]=singleton, [2]=multiple	
14.	History of gestational HTN or preeclampsia/eclampsia?	[1]=Yes, [2]=No	
15.	Personal history of chronic HTN?	[1]=Yes, [2]=No, [3]=don't know	
16.	Personal history of diabetes?	[1]=Yes, [2]=No, [3]=don't know	
17.	Family history of HTN?	[1] = Yes, [2] = No	
18.	Family history of diabetes?	[1] = Yes, [2] = No	
19.	Mode of admission	[1] = Referred, [2] = internal transfer, [3] = from home	
20.	SBP on admission (mmHg)		
21.	DBP on admission (mmHg)		
22.	Pre-pregnancy BMI (kg/m^2)		
23.	Diagnosis on admission	[1] = Severe preeclampsia [2] = Eclampsia	
Laboratory parameters			
24.	WBC (10^3 cell/µl)		
25.	Haemoglobin (g/dl)		
26.	Haematocrit (%)		
27.	Platelet count (10^3 /mm^3)		
28.	ASAT		
29.	ALAT		
30.	Urea		
31.	Creatinine		
32.	Maternal Complications	[1] = acute renal failure; [2]=HELLP syndrome; [3]=acute pulmonary edema; [4]=CVA, [5]=Placenta abruptio, [6] = DIC; [7]=Others (specify)	
33.	Foetal complications	[1] = Prematurity; [2] = IUFD; [3] = IUGR; [4] = fetal asphyxia [5] = others (specify)	
SECTION B: MATERNAL OUTCOME			

SN	VARIABLE	RESPONSE	CODE
34.	Antepartum maternal outcome *(What was the outcome of the pregnancy?)*	[1] = Delivered [2] = Undelivered (died)	
35.	Mode of delivery	[1] = vaginal delivery (unassisted) [2] = Forceps assisted delivery [3] = vacuum application [4] = Caesarean section	
36.	Admission to ICU?	[1] = Yes [2] = No	
37.	Reasons for admission into ICU	[1] = persistent HTN [2] = neurological deficit (coma) [3] = recurrent seizures [4] = thrombocytopenia/coagulopathy [5] = DIC [6] = massive generalized oedema [7] = infection [8] = Acute kidney injury [9] = Acute pulmonary edema [10] = Others (specify)	
38.	What was the outcome in the ICU	[1] = Discharged [2] = Died	
39.	If dead, what was the cause?	[1] = $MgSO_4$ toxicity [2] = Cardiac arrest [3] = Acute renal failure [4] = HELLP syndrome; [5] = Acute pulmonary edema; [6] = Cerebrovascular accident [7] = Hemorrhage [8] = DIC [9] = sepsis [10] = Others (specify)	
40.	Total number of days spent in ICU		
41.	Admission to postpartum ward?	[1] = Yes [2] = No	
42.	What was the outcome in postpartum ward?	[1] = discharged [2] = died	
43.	If dead, state the cause of death	[1] = $MgSO_4$ toxicity [2] = Cardiac arrest [3] = Acute renal failure [4] = HELLP syndrome; [5] = Acute pulmonary edema; [6] = Cerebrovascular accident [7] = DIC [8] = hemorrhage [9] = sepsis [10] = Others (specify)	
44.	Total number of days spent in postpartum ward		
SECTION C: FETAL OUTCOME			
45.	Foetal outcome	[1] = live birth [2] = still birth [3] = early neonatal death [4] = Others	
46.	If live birth. APGAR score at 5^{th} minute		
47.	Birth weight (g)		
SECTION D: EFFICACY OF MGSO4 IN CONTROL OF SEIZURES (*please check patient's file and nursing charting sheet, where necessary to complete this section)*			
48.	Indication of $MgSO_4$	[1] = Severe preeclampsia	

SN	VARIABLE	RESPONSE	CODE
		[2] = Eclampsia	
49.	If eclampsia, number of convulsions before initiation of $MgSO_4$		
50.	Was $MgSO_4$ readily available?	[1] =Yes, [2] = No	
51.	Where was $MgSO_4$ gotten?	[1] = from the maternity [2] = from the ICU [3] = from the hospital's pharmacy [4] = from a pharmacy out of the hospital	
52.	What was the delayed time of administration *(time from indication to administration of loading dose*) (hours)		
53.	If time > 1 hour, reason?	[1] = product not available [2] = financial constraints [3] = staff workload [4] = non-reassuring laboratory results [5] = Contraindications [6] = Others (specify)	
54.	What was the **LOADING DOSE**?	[1] = 4g IVL then 10g IM (given as 5g IM in each buttock) [2] = 4 – 6g of $MgSO_4$ diluted in 100mL IV fluid given as slow IV infusion over 15 – 20 minutes [3] = Others (specify)	
55.	Was there any convulsion after loading dose of MgSO4?	[1] = Yes; [2] = No	
56.	If yes, how many minutes or hours after?		
57.	Was the **MAINTENANCE DOSES** of $MgSO_4$ given?	[1] = Yes, [2] = No	
58.	What was the maintenance dose regimen?	[1] = 4g IM/ 4 hourly [2] = 4 g IM/ 6 hourly [3] = 5 g IM/ 4 hourly [4] = 5 g IM/ 6 hourly [5] = 1 – 2g IV infusion pump [6] = Others (specify)	
59.	Total number maintenance doses expected		
60.	Were there any omitted doses? *(an omitted dose is a dose of $MgSO_4$ that was prescribed but not administered by the time of the next scheduled dose)*	[1] = Yes [2] = No	
61.	If yes how many?		
62.	If omitted, what was the reason?	[1] = Financial constraints [2] = it was not planned [3] = It was planned but forgotten [4] = It was not readily available [5] = Work overload [6] = Others (specify)	
63.	Did patient require other anticonvulsants?	[1] Yes [2] No	
64.	If yes, specify	[1] Diazepam [2] Phenobarbital [3] Both [4] Others (specify)	
SECTION E: ADVERSE EFFECTS OF $MGSO_4$			
65.	Was there any reason to stop/discontinue $MgSO_4$ administration?	[1] = Yes [2] = No	

SN	VARIABLE	RESPONSE	CODE
66.	If yes, identify them?	[1] = Oliguria (urine output <400 ml/ 24 hour) or anuria [2] = respiratory depression (<12 breaths/min) [3] = absent/reduced tendon reflexes [4] = Hypotension [5] = Others (specify)	
67.	Was calcium gluconate administered?	[1] = Yes [2] = No	
68.	If "No" why was it not administered?	[1] = It was not readily available [2] = It was forgotten [3] = Didn't know it was supposed to be given [4] = Not indicated	

Appendix 6: Questionnaire (French)

SN	VARIABLE	RÉPONSE	CODE
SECTION A : PROFIL SOCIO-OBSTÉTRICAL ET CLCINIQUE			
1.	Années d'âge)		
2.	État civil	[1] Marié/cohabitant (monogamie) [2] Marié (polygamie) [3] Célibataire	
3.	Le plus haut niveau d'éducation	[1]= Aucune éducation, [2]=Primaire, [3]=Secondaire [4]=Supérieur	
4.	Profession	[1]= Étudiante, [2]=Femme au foyer [3]=Fonctionnaire [4]= Travailleur formel du secteur privé [5]= travailleur indépendant [6]= Aucun	
5.	Région d' origine	[1]= Centre, [2]=Ouest, [3]=Nord-Ouest [4]=Sud- ouest , [5]=Est, [6]=Sud, [7]=Adamawa [8]=Nord [9]= Extrême Nord [10]=Littoral	
6.	Gravidité		
7.	Parité		
8.	Primipaternité	[1]= Oui [2]= Non	
9.	Âge gestationnel (en semaines) au moment du diagnostic		
10.	Nombre de CPN		
11.	Mode de conception	[1]= naturel, [2]=technologie de procréation médicalement assistée	
12.	Nombre de gestation	[1]= singleton, [2]=multiple	
13.	Antécédents de HTN gestationnelle ou de prééclampsie/éclampsie ?	[1]= Oui, [2]=Non	
14.	Antécédents personnels d'HTN chronique ?	[1]= Oui, [2]=Non, [3]=ne sait pas	
15.	Antécédents personnels de diabète ?	[1]= Oui, [2]=Non, [3]=ne sait pas	
16.	Antécédents familiaux de HTN ?	[1] = Oui, [2] = Non	
17.	Antécédents familiaux de diabète ?	[1] = Oui, [2] = Non	
18.	Mode d'admission	[1] = Référé, [2] = transfert interne, [3] = de la maison	
19.	PAS à l'admission (mmHg)		
20.	PAD à l'admission (mmHg)		
21.	IMC (kg/m^2)		
22.	Diagnostic à l'admission	[1] = Prééclampsie sévère [2] = Éclampsie	
Paramètres de laboratoire			
23.	GB (10^3 cellules/ µl)		
24.	Hémoglobine (g/dl)		
25.	Hématocrite (%)		
26.	Numération plaquettaire ($10^3/mm^3$)		
27.	ASAT		
28.	ALAT		
29.	Urée		
30.	Créatinine		
31.	Complications maternelles	[1] = insuffisance rénale aiguë ; [2]= syndrome de HELLP ; [3]=œdème aigu pulmonaire ; [4]=AVC, [5]=Décollement placentaire, [6] = CIVD ; [7]=Autres (préciser)	
32.	Complications fœtales	[1] = Prématurité ; [2] = MFIU ; [3] = RCIU ; [4] = asphyxie fœtale [5] = autres (préciser)	

SN	VARIABLE	RÉPONSE	CODE
SECTION B : EFFICACITÉ DU MGSO4 DANS LE CONTRÔLE DES SAISIES (*veuillez vérifier le dossier du patient et le dossier infirmier fiche, si nécessaire pour compléter cette section)*			
33.	Indication du $MgSO_4$	[1] = Prééclampsie sévère [2] = Éclampsie	
34.	Si éclampsie, nombre de convulsions avant début du $MgSO_4$		
35.	Le $MgSO_4$ était-il facilement disponible ?	[1] = Oui, [2] = Non	
36.	Où a-t-on obtenu le $MgSO_4$?	[1] = de la maternité [2] = de l'USI [3] = de la pharmacie de l'hôpital [4] = d'une pharmacie hors de l'hôpital	
37.	Délai entre l'indication et l'administration (minutes)		
38.	Si durée > 10 minutes, raison ?	[1] = produit non disponible [2] = contraintes financières [3] = charge de travail du personnel [4] = résultats de laboratoire non rassurants [5] = Contre-indications [6] = Autres (préciser)	
39.	Quelle était la **DOSE DE CHARGE** ?	[1] = 4 g IVL puis 10 g IM (administrés sous forme de 5 g IM dans chaque fesse) [2] = 4 à 6 g de $MgSO_4$ dilué dans 100 ml de liquide IV administré en perfusion IV lente sur 15 à 20 minutes [3] = Autres (préciser)	
40.	Y a-t-il eu des convulsions après la dose de charge de MgSO4 ?	[1] = Oui ; [2] = Non	
41.	Si oui, combien de minutes ou d'heures après ?		
42.	La **DOSE D'ENTRETIEN** de $MgSO_4$ a-t-elle été administrée ?	[1] = Oui, [2] = Non	
43.	Quel était le schéma posologique d'entretien ?	[1] = 4 g IM/ 4 heures [2] = 4 g IM/6 heures [3] = 5 g IM/4 heures [4] = 5 g IM/6 heures [5] = 1 – 2 g de pouse syringue IV [6] = Autres (préciser)	
44.	Cette fréquence d'administration a-t-elle été respectée ?	[1] = Oui [2] = Non	
45.	A-t-il été poursuivi pendant 24 heures après la dernière convulsion ou après l'accouchement ?	[1] = Oui [2] = Non [3] = n'a pas été documenté	
46.	Nombre de doses d'entretien attendues		
47.	Nombre de doses d'entretien omises *(une dose omise est toute dose non administrée à l'heure prévue depuis la dose de charge jusqu'à 24 heures après la dernière convulsion ou l'accouchement)*		
48.	Si omis, quelle en était la raison ?	[1] = ce n'était pas prévu [2] = c'était prévu mais oublié [3] = il y avait des signes de toxicité du Mg [4] = Il n'était pas disponible [5] = autres raisons	
SECTION C : EFFETS INDÉSIRABLES DU MGSO 4			
49.	Y avait-il des raisons d'arrêter le $MgSO_4$?	[1] = Oui [2] = Non [3] = Je ne sais pas	
50.	Insuffisance rénale ?	[1] = Oligurie (débit urinaire <400 ml/ 24 heures) ou anurie	

SN	VARIABLE	RÉPONSE	CODE
		[2] = dépression respiratoire (<12 respirations/min) [3] = réflexes tendineux absents/diminués [4] = Hypotension [5] = Autres (préciser)	
51.	Si oui, du gluconate de calcium a-t-il été administré ?	[1] = Oui [2] = Non	
52.	Si non, pourquoi n'a-t-il pas été administré ?	[1] = il n'était pas facilement disponible [2] = Il a été oublié [3] = Je ne savais pas que c'était comme censé être donné [4] = Autres (préciser)	
SECTION D : RÉSULTAT MATERNELLE			
53.	Résultat maternel avant l'accouchement *(Quelle a été l'issue de la grossesse ?)*	[1] = Livré [2] = Non livré (décédé)	
54.	Mode de livraison	[1] = accouchement vaginal (sans assistance) [2] = accouchement assisté par forceps [3] = application ventouse [4] = Césarienne	
55.	Admission en soins intensifs ?	[1] = Oui [2] = Non	
56.	Raisons d'admission en REA	[1] = HTN persistant [2] = déficit neurologique (coma) [3] = crises récurrentes [4] = thrombocytopénie/coagulopathie [5] = CIVD [6] = œdème généralisé massif [7] = infection [8] = Lésion rénale aiguë [9] = Autres (préciser)	
57.	Quel a été le résultat à REA	[1] = Déchargé [2] = Décédé	
58.	S'il est mort, quelle en était la cause ?	[1] = toxicité du $MgSO_4$ [2] = Arrêt cardiaque [3] = Insuffisance rénale aiguë [4] = syndrome HELLP ; [5] = Œdème pulmonaire aigu ; [6] = Accident vasculaire cérébral [7] = décollement placentaire [8] = CIVD [9] = hémorragie [10] = septicémie [11] = Autres (préciser)	
59.	Nombre total de jours passés en REA		
60.	Admission en service post-partum ?	[1] = Oui [2] = Non	
61.	Quel a été le résultat dans le service post-partum ?	[1] = déchargé [2] = mort	
62.	En cas de décès, indiquez la cause du décès	[1] = toxicité du $MgSO_4$ [2] = Arrêt cardiaque [3] = Insuffisance rénale aiguë [4] = syndrome HELLP ; [5] = Œdème pulmonaire aigu ; [6] = Accident vasculaire cérébral [7] = décollement placentaire [8] = CIVD [9] = hémorragie [10] = septicémie [11] = Autres (préciser)	

SN	VARIABLE	RÉPONSE	CODE
63.	Nombre total de jours passés en service post-partum		
SECTION E : RÉSULTAT FŒTAL			
64.	Résultat fœtal	[1] = naissance vivante [2] = mort-né [3] = décès néonatal précoce	
65.	Si naissance vivante. APGAR marque à la 5ème minute		
66.	Poids à la naissance (g)		

Appendix 7: Timeline of study

Activity	Months of the Year 2024																	
	Jan		Feb		Mar		April		May		June		Jul		Aug		Sept	
Writing of research proposal																		
Correction of research proposal																		
Administrative procedures: • Ethical clearance and research authorization																		
Recruitment and training of data collectors																		
Pilot study																		
Data collection																		
Data entry, analysis and synthesis																		
Writing of dissertation																		
Revision of dissertation by supervisors																		
Defense of dissertation																		
Submission of final copy																		