

**EFFECT OF MAGNESIUM SULPHATE IN MOTHERS SUFFERING FROM
TOXEMIA OF PREGNANCY AND THEIR NEONATES**

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A Dissertation submitted in partial fulfillment of the Requirements for the Award of the Degree of Master of Pharmacy in Clinical pharmacy in the School of Pharmacy, University of Nairobi.

November, 2014

DECLARATION

This Dissertation is my Original Work and has not been presented for a degree award in any other University.

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DEDICATION

To every healthcare worker dealing with maternal- child health.

ACKNOWLEDGEMENTS

The Almighty God for His blessings upon my life.

PRIME-K linked award for funding the research.

The administration of Pumwani Maternity hospital where the study was carried out.

The nursing and laboratory staff of Pumwani Maternity hospital for helping collect the data.

The University of Nairobi Paediatric department laboratory where the analysis of the samples was done.

My supervisors Dr Karimi, and Dr Wandolo for their advice, guidance, critiquing and corrections all through from the conceptual stage of the study till its completion.

My colleagues from the Clinical pharmacy class of 2011/2012 for their advice and encouragement.

My husband Manasseh for his advice & support.

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ABBREVIATIONS

NHBPEP -National High Blood Pressure Education Program

MgSo₄ -Magnesium Sulphate

BP- Blood pressure

BBB Blood brain barrier

NMDA-N-Methyl-D-Aspartate

CNS-Central nervous system

ECG-Electroencephalogram

HELLP-Haemolysis, elevated liver enzymes, low platelet count

PET Preeclampsia

MAGPIE-Magnesium sulphate for prevention of eclampsia trial

APGAR-Activity Pulse Grimace Appearance Respiration

OPERATIONAL DEFINITION OF TERMS

Mild pre-eclampsia: The presence of hypertension (BP \geq 140/90 mm Hg) on 2 occasions, at least 6 hours apart, but without evidence of end-organ damage in the patient.

Severe pre-eclampsia: The presence of 1 of the following symptoms or signs in the presence of preeclampsia:

- SBP of 160 mm Hg or higher or DBP of 110 mm Hg or higher on 2 occasions at least 6 hours apart
- Proteinuria of more than 5 g in a 24-hour collection or more than 3+ on 2 random urine samples collected at least 4 hours apart
- Pulmonary edema or cyanosis
- Oliguria (< 400 mL in 24 h)
- Persistent headaches
- Epigastric pain and/or impaired liver function
- Thrombocytopenia

❖ **Eclampsia:** Pre-eclampsia associated with seizures.

ABSTRACT

Background

About 10% of all pregnancies are complicated by hypertension especially the first pregnancies of women older than 35 years or those with multiple foetuses and this can be fatal in severe cases due to convulsions especially when accompanied by disseminated intravascular coagulation and multiple organ failure. Magnesium Sulphate the drug of choice for management of severe preeclampsia and eclampsia has been shown to cross the placental barrier from maternal circulation into the foetal blood.

Objective: The main objective was to determine the levels of serum magnesium in exposed neonates and correlate the findings with the levels in non-exposed neonates. The specific objectives were to determine the serum urea, electrolyte and magnesium levels achieved in mothers treated with magnesium sulphate and to measure the serum levels in their neonates.

Methodology: A quasi-experimental study design was used and the study area was Pumwani Maternity hospital. The test group comprised mothers diagnosed with severe eclampsia and treated with magnesium sulphate and their neonates while the control group comprised mothers who had preeclampsia but were treated using other drugs i.e. nifedipine and methyl dopa. Sampling was done using simple random technique. The study consisted of a total of 54 mothers and 54 neonates. Blood samples were obtained from both mothers and neonates and the test group results compared to the control group. The neonates' APGAR scores, serum urea and electrolytes and magnesium levels of both neonates and their mothers were determined and compared. The data obtained was analyzed using descriptive and inferential statistics.

Results: There were statistically significant differences in serum sodium ($p = 0.015$), urea ($p = 0.043$) and creatinine ($p = 0.008$) levels between the maternal test and control groups. Serum sodium was higher in the control group (mean 138.4, SD 3.6 versus 135.9, SD 3.8) while creatinine (mean 89.8 versus 71.5) and urea (mean 3.3 versus 2.6) were higher in the test group.

Maternal serum levels of potassium ($p = 0.495$), chloride ($p = 0.371$) and calcium ($p = 0.629$) did not show significant differences between the test and control groups.

There were also significant differences between neonatal test and control groups in levels of serum urea ($p = 0.007$) and chloride ($p = 0.017$). Urea levels were significantly higher in test compared to control groups (mean = 4.0 versus 2.9), while chloride levels were higher in the control group (mean = 99.4 versus 97.2). The calcium and potassium levels were elevated in the test group but not to significant levels.

There was a positive correlation between maternal and neonatal serum magnesium levels in both groups. The correlation was stronger in the test group ($r = 0.56$, $p = 0.003$) as compared to the control group ($r = 0.35$, $p = 0.087$).

The mean maternal serum magnesium in the test group (mean = 2.9, SD = 0.9) was significantly higher than the control group (mean = 2.3, SD = 0.6), $p = 0.008$. The mean neonatal serum magnesium in the test group (mean = 3.0, SD = 1.0) was significantly higher than the control group (mean = 2.3, SD = 0.6), $p = 0.008$.

There was a statistically significant difference between the two groups in the birth weight of the neonates Mann Whitney test p value = 0.003 . The median birth weight in the treatment group was 2.2 kg (IQR 1.8 to 3.0) compared to a median of 3 kg (IQR 2.3 to 3.6) in the control group.

The infant birth weight was not significantly associated with neonatal serum magnesium sulphate levels after adjusting for treatment group. The mean serum magnesium level was 0.66 mmol/L higher in neonates in the treatment compared to control group ($p = 0.008$).

Conclusion: Serum creatinine and urea levels were significantly elevated in the test group as compared to the control group. Maternally administered magnesium sulphate during management of severe preeclampsia and eclampsia does affect serum urea and electrolyte levels but not all electrolytes are affected significantly.

CHAPTER ONE: INTRODUCTION

1.1 Background

Pre-eclampsia also referred to as toxemia of pregnancy, is defined as the development of hypertension accompanied by proteinuria and oedema during the third trimester of pregnancy. In a patient with pre-existing essential hypertension, it is diagnosed if the systolic blood pressure increases by 30mmHg or the diastolic increases by 15mmHg. Almost 10% of all pregnancies are complicated by hypertension especially the first pregnancies of women older than 35 years and in women with multiple fetuses^[1, 2]. In severe cases, convulsions may appear and the condition is thus termed eclampsia.

Eclampsia can be fatal especially when accompanied by disseminated intravascular coagulation and multiple organ failure. Severe pre-eclampsia is one of the major causes of high maternal mortality rate in both developed and developing countries. It also contributes to high neonatal morbidity and mortality rates and is strongly associated with foetal growth restriction^[2]. Complications may arise from the disease itself or from the drugs used for the management of the condition.

Pre-eclampsia may be classified as mild or severe. Mild hypertension is a BP greater than 140/90 mmHg on more than one occasion, six hours apart but with no evidence of end-organ damage.

Severe hypertension refers to presence of any of the following signs in a patient with pre-eclampsia: BP of 160/110 mmHg or higher on more than one occasion at least six hours apart, a proteinuria of more than 5g in a 24-hr urine collection sample or more than 0.3g in two random samples collected at least four hours apart, oliguria (less than 400ml/24hours), cyanosis, pulmonary oedema, persistent headaches, thrombocytopenia, epigastric pain, elevated liver enzymes, albumin creatinine ratio (greater than 35.5mg/mmol) decreased foetal growth, oligohydramnios or placenta abruption^[1,3,4].

The NHBPEP classifies hypertension in pregnancy into four classes: chronic hypertension, gestational hypertension, preeclampsia eclampsia and superimposed preeclampsia on chronic hypertension^[5].

1.2 Pathophysiology of preeclampsia

Preeclampsia is not primarily a hypertensive disease but a disorder induced by factors due to the presence of the placenta. It is a syndrome of endothelial dysfunction leading to the release of toxins like cytokines and others, vasoconstriction and platelet activation producing complications associated with the vascular system^[6]. Borzychowski AM. et al^[7] divide preeclampsia into two stages the first of which begins with poor placentation thus reduced blood supply that results in placental hypoxia. This initial stage is silent and is followed by the release of several mediators. That is inflammatory cytokines, growth factors and their soluble receptors, products of placental oxidative stress and placental debris. These mediators lead to the systemic inflammatory syndrome and endothelial cell dysfunction that cause the manifestations of the second stage of preeclampsia. Evidence suggests that an imbalance of pro-angiogenic and anti-angiogenic factors that the placenta produces plays a role in endothelial dysfunction^[8, 9]. According to Cunningham FG et al^[10], factors implicated in the etiology of preeclampsia include: maternal immunological intolerance, cardiovascular and inflammatory changes, abnormal placenta implantation and environmental, genetic and nutritional factors.

1.3 Maternal and foetal impact of severe preeclampsia and eclampsia

Hypertensive women and those who develop hypertension during pregnancy have an increased risk of developing complications pre-partum, intra -partum and post-partum. Inadequate maternal blood flow to the placenta leads to ischemia and infarction of the placenta thus releasing various complement factors that result in abnormalities in production of vasodilators. This produces complications associated with the vascular system i.e. disseminated intravascular coagulation, bleeding and hepatic and renal organ failure due to poor perfusion. The HELLP syndrome may develop, which alongside preeclampsia accounts for the high maternal mortality rate associated with hypertension^[11]. Preeclampsia also increases the risk of development of long term cardiovascular disease^[12]. Harskamp and Zeeman noticed an association between preeclampsia and an increase in risk of later developing chronic hypertension with increase in morbidity and mortality^[13].

The major consequences of preeclampsia on the foetus are intrauterine growth restriction, foetal distress, thrombocytopenia, increased risk of developing chronic lung disease^[14, 15, 16, 17, 18], high

perinatal mortality rates and because of preterm delivery advocated for in the definitive management of preeclampsia, high neonatal morbidity^[19, 20]. The perinatal outcome is influenced by maternal disease severity i.e. hypertension degree, presence of HELLP syndrome and increase in proteinuria. Poor outcome is associated with placental abruption, utero-placental insufficiency and low gestational age^[21, 22, 23]. A population based study that followed a million children exposed to preeclampsia over a period of 27 years showed an increase in risk of nutritional, endocrinal and metabolic derangements from adolescence to early adulthood^[24]. There is evidence also that such neonates exposed to preeclampsia have an increased risk of cardiovascular and diabetes morbidity in adulthood^[25].

1.4 Mode of action of magnesium sulphate

Magnesium is a calcium antagonist that acts on the calcium channels in the vascular smooth muscles thus decreasing intracellular calcium^[26]. As a result of the decreased intracellular calcium, there is inactivation of calmodulin-dependent myosin light chain kinase activity and decreased contraction leading to arterial relaxation that lowers peripheral and cerebral vascular resistance, relieves vasospasm and decreases arterial BP. Disruption of the BBB can lead to vasogenic oedema formation which occurs in eclampsia^[27]. There have been studies done that show the effectiveness of MgSo₄ in decreasing BBB permeability in response to acute hypertension in 3rd trimester pregnant rats^[28].

Seizures are postulated to consist of an excessive release of excitotoxic neurotransmitters like glutamate through mediation (at least in part) of stimulation of glutamate receptors i.e. NMDA receptor^[29, 30]. Magnesium anti-convulsant activity is thought to be through its role as an NMDA receptor antagonist. Studies in rats have shown treatment with systemic magnesium to result in resistance to electrically stimulated and NMDA induced hippocampal seizures^[31, 32]. Magnesium increases the seizure threshold thus limiting the effect of glutamate. To elicit a central anti-convulsant effect, magnesium ions have to cross the BBB which has been demonstrated in animals^[31]. The same study shows seizure activity to increase this movement.

Depression of neuromuscular transmission by MgSo₄ that is dose-related has been shown^[33]. There has been concern that this may mask the outward signs of convulsions without treating the CNS cause of the convulsion. Studies show there is minimal to no change in the ECGs done during MgSo₄ treatment and very few signs of CNS depression in both eclamptic and normal

patients^[34]. However evidence demonstrates the efficacy of MgSo4 over traditional anti-convulsant drugs like phenytoin and diazepam in the prevention and management of eclamptic seizures^[35, 36].

1.5 Treatment of severe preeclampsia/eclampsia

The goals of management of preeclampsia and eclampsia are to prevent progression to eclampsia thus preventing convulsions, to control the blood pressure by stabilizing the diastolic pressure to between 90- 100 mmHg and to prevent untoward effects in the foetus.

The first-line option for the treatment and prevention of eclamptic seizures is magnesium sulfate^[36, 37, 38, and 39]. There is evidence to support its effectiveness in the prevention and treatment of eclamptic seizures^[37, 40]. In the magnesium sulphate for prevention of eclampsia (MAGPIE) trial, it was found that women with pre-eclampsia had a lower risk of progression to eclampsia and a lower mortality rate when treated with magnesium sulphate. For prophylaxis in women with preeclampsia, MgSo4 was shown to be superior to diazepam, phenytoin, nimodipine and placebo^[40, 41, and 42]. It was shown to reduce the risk of recurrent seizures in women with eclampsia by 52% when compared to diazepam and by when compared to phenytoin by 67% in the multinational Collaborative Eclampsia Trial^[42].

MgSo4 is given as a 4g intravenous loading dose, immediately followed by 10g IM and then by 5g every 4 hours in alternating buttocks or a loading dose of 4g followed by a maintenance infusion of 1 to 2 g/h by controlled infusion pump. The clinical effect and the toxicity of MgSo4 depend on its serum levels. For treatment of eclamptic seizures, a concentration of 1.8 – 3.0 mmol/L should be achieved. Magnesium is excreted mainly by the kidney with the half-life being 4.66 hours^[43].

When carefully administered and monitored, toxicity is rare. At levels between 3.5 -5 mmol/L, there is loss of the patellar reflex in the mother indicating impending toxicity and at 5 – 6.5 mmol/L, respiratory paralysis occurs. CNS depression which may range from drowsiness to coma also begins. At concentrations > 7.5 mmol/L cardiac conduction is altered and when 12.5 mmol/L is exceeded cardiac arrest occurs.

1.6 Treatment options in severe hypertension.

Severe hypertension refers to persistent elevated BP >160/110 mmHg. The goal is to lower the BP so as to prevent cardiac and cerebrovascular complications while maintaining utero-placental blood flow. Recommended drugs include nifedipine, labetalol and hydralazine. Atenolol, ACE inhibitors, diuretics and ARBs are not recommended. Beta blockers other than labetalol are associated with inhibition of foetal growth especially if used before 28 weeks gestation age. ACE inhibitor and ARB use in pregnancy has been associated with foetal renal failure, oligohydramnios, hypotension and intra-uterine foetal death. If pregnancy occurs while on ACE inhibitor or ARB therapy, they should be discontinued preferably in the first trimester. Diuretics have the potential to reduce the circulatory volume further in women with pre-eclampsia.^[44]

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter details various studies done to investigate the superiority of magnesium sulphate over other anti-convulsants in managing eclamptic seizures and effects on both the mother and neonate.

2.2 Recommended management of preeclampsia

For prophylaxis in women with preeclampsia, MgSo₄ was shown to be superior to diazepam, phenytoin, nimodipine and placebo^[40, 41, 42]. It was shown to reduce the risk of recurrent seizures in women with eclampsia by 52% when compared to diazepam and by 67% when compared to phenytoin in the multinational Collaborative Eclampsia Trial^[43].

2.3 Placental transfer of magnesium sulphate

After MgSo₄ is administered, 40% is protein bound. The free magnesium diffuses into the extra cellular space, bone and across the placenta and foetal membranes into the amniotic fluid and the foetus. Hallak and Cotton demonstrated in a study with rats the transfer of magnesium from maternal circulation into the foetal blood^[45]. Studies have shown an increase in magnesium serum levels in both mother and foetus after administration^[46].

2.4 Hypermagnesemia and its effects on the neonate

Dangman and Rosen showed in their study that in both the full-term and premature neonate the elevated levels persist for up to seven days with an elimination half – life of 43.2 hours^[47].

Neonates born to mothers treated with MgSo₄ for severe preeclampsia and eclampsia may be born with significant high levels of magnesium concentration ranging from 3 – 11 mmol/L^[48].

Lipsitz P.J. and English I.C in a study on hypermagnesemia in the newborn infant showed that the signs and symptoms of hypermagnesemia in the infant are similar to those in the adult with hypermagnesemia^[49]. Such neonates at birth would be expected to have severe asphyxia with low APGAR scores and absent or feeble reflexes. Pruett K.M et al showed that treatment with MgSo₄ did not lead to low APGAR scores in neonates of mothers with eclampsia though the mean cord level of magnesium, was equal to the mean maternal serum level^[50]. MacIntyre et al in their study gave evidence that a rise in serum magnesium levels inhibits secretion of parathyroid hormone which results in increased urinary excretion of calcium^[51]. In a study of

five newborn infants whose mothers had been treated with IV magnesium sulfate for periods ranging from 5 to 14 weeks, Lamm CI et al noted radiographic bony abnormalities in two of the infants^[52].The investigators came to the same conclusion as MacIntyre et al that the foetal hypermagnesemia due to long term treatment with magnesium depressed parathyroid hormone release resulting in foetal hypocalcaemia. Savory J and Monif GRG reported in their study of mothers treated with magnesium a mild decrease in cord calcium concentrations^[53].So did Cruikshank DP et al in their study on effects of magnesium sulfate treatment on perinatal calcium metabolism^[54].In contrast, Donovan EF et al reported high cord calcium levels following magnesium therapy. No neonatal symptoms were associated with either calcium levels^[55].Mina A.G. et al in a study of more than six thousand women spanning over nine years showed an association between several neonatal complications and high maternal serum magnesium levels^[56].Green KW et al in their study comparing newborns of magnesium-treated mothers with newborns of untreated mothers found no differences in neurological behavior between the two study groups except that the magnesium exposed infants had a decrease in active tone of the neck extensors on the first day after birth^[57].During the Collaborative Perinatal Project in which around fifty thousand mother-child pairs were monitored, in around a hundred pairs who had exposure to magnesium sulfate during pregnancy there was no evidence found to suggest any links between the exposure and congenital malformations^[58].In a study of several thousands of neonates of mothers treated with MgSo₄ for preeclampsia. Stone SR and Pritchard JA noted no adverse effects from the therapy in both the foetuses and the neonates^[59].

A study done by Savory J and Monif GRG reported two neonates with serum magnesium levels above 8mg/dL who were severely depressed at birth. There was a remission of hypermagnesemia symptoms after 12 hours in one neonate while the second had residual effects of anoxic encephalopathy^[53].In another investigation head lag, suck reflex, ventral suspension and cry response which all require sustained muscle contraction were impaired up to 48 hours after birth in utero magnesium exposed neonates^[60].Brady JP and Williams HC in their study reported a hypertensive woman who when treated with 11g of magnesium sulfate within 3 ½ hours of delivery gave birth to a depressed neonate without spontaneous respirations, reflexes or movements which was reversed with an exchange transfusion performed at 24 hours^[61].Brazy JE et al in their investigation reported hypotonia, decreased gastrointestinal motility, ileus and patent ductus in neonates of mothers with severe pre-eclampsia.^[62]

2.5 Hypermagnesemia in mothers suffering from preeclampsia

Rodis JF et al reported maternal hypothermia with bradycardia and also foetal bradycardia in a woman being treated for preeclampsia when the magnesium sulfate infusion was increased from 2g/hour to 3g/hour. Serum magnesium levels were 6.6mg/Dl. Upon discontinuation of the infusion, within 6 hours all signs and symptoms returned to baseline values^[63]. L'Hommedieu CS et al reported a drug interaction between magnesium and gentamicin whereby a woman who had received MgSo4 a day pre-partum gave birth to a neurologically depressed infant who was given gentamicin every twelve hours for presumed sepsis. The neonate developed respiratory arrest after the second dose which resolved when the antibiotic was stopped^[64]. In a study done by YP Bansal at Pumwani maternity hospital, out of 23,084 births analyzed for a year, the incidence of preeclampsia was found to be 3.7% i.e. around 800 cases with 31 cases being severe preeclampsia. Around 22% of the neonates born to the mothers with preeclampsia were underweight as compared to 4% in mothers with normal uncomplicated pregnancies. 5% were stillborn as compared to nil in the controls, 26% had an APGAR score of less than 8 while in the controls only 8% scored less than 8^[65].

2.5 Problem statement

Studies done at Pumwani Maternity hospital have shown neonates born to mothers with preeclampsia and eclampsia were underweight at birth and had low APGAR scores. This could be attributed to in utero magnesium sulphate exposure used for the management of preeclampsia and eclampsia in their mothers. Hypermagnesemia in the neonate has been shown to be associated with asphyxia and decreased serum calcium levels on long term use. Neonatal neurological depression may occur with respiratory depression, loss of reflexes and muscle weakness. This may result in low APGAR scores. In view of the above, the study aims to find out whether there is a link between the low birth weights and low APGAR scores in neonates of mothers with preeclampsia/eclampsia and the in utero magnesium sulphate exposure when mothers were treated with magnesium sulphate.

2.6 Significance of the study

The study will help determine whether in utero magnesium sulphate exposure in neonates of mothers being treated for severe preeclampsia and eclampsia contributes to longer hospital-bed stay days thus increasing morbidity during the immediate postnatal period. This will help towards the achievement of Kenya Millennium Development Goal 4 which aims to reduce by two thirds the mortality rate among children under five.

2.7 Research question

1. What is the effect of MgSO₄ in mothers suffering from toxemia of pregnancy and their neonates?

2.8 Study hypothesis

2.8.1 Null Hypothesis

Magnesium Sulphate used during management of severe preeclampsia and eclampsia has no effect on mothers suffering from toxemia of pregnancy and their neonates.

2.8.2 Alternative hypothesis

Magnesium sulphate has an effect on mothers suffering from toxemia of pregnancy and their neonates.

2.9 Objectives

2.9.1 Main Objective

To correlate the serum level of magnesium in neonates born to mothers treated with magnesium Sulphate during management of severe pre-eclampsia and eclampsia with the serum magnesium levels of neonates born to mothers treated with other drugs.

2.9.2 Specific objectives:

1. To determine the serum levels of Magnesium in the mothers treated with magnesium sulphate and those treated using other drugs.
2. To determine the serum magnesium levels in neonates exposed to Magnesium Sulphate in utero and those treated with other drugs.

3. To determine the electrolyte and urea levels in mothers and neonates exposed to magnesium sulphate in utero and those not exposed.
4. To determine the effect of MgSO₄ on APGAR scores of exposed and non-exposed neonates,
5. To determine the neonatal birth weight of neonates born to mothers suffering from toxemia of pregnancy.

CHAPTER THREE: METHODOLOGY

3.1 Introduction

This chapter describes the research design, sampling, inclusion and exclusion criteria, data collection, reliability and validity of the collection tool and the analysis of the data.

3.2 Research design

The research design was a quasi-experimental study. It was chosen because the study involved collection of blood samples from both the test and control groups. The serum levels of magnesium in mothers treated with magnesium sulphate for severe preeclampsia and eclampsia and the prevalence of hypermagnesemia in their neonates was determined. This was compared to serum magnesium levels of neonates whose mothers had preeclampsia but were treated with other drugs other than Magnesium Sulphate.

3.3 Study area

The study was conducted at Pumwani Maternity hospital. The facility is located 2km east of the CBD in Nairobi and is the biggest government maternity hospital in East and Central Africa catering for both low and middle income earners. It is located in Eastleigh in Kamukunji constituency of Nairobi County. There is one labor ward, two ante-natal wards and 5 post-natal wards. Pumwani maternity hospital has an average of 70 deliveries per day, 30,000 per year.

3.4 Target population

The target population comprised of mothers admitted to Pumwani Maternity hospital for delivery. The test population was made up of neonates of mothers who had been treated with magnesium sulphate for severe preeclampsia. These were compared to the controls who were neonates of mothers who had preeclampsia but were treated with other drugs other than magnesium sulphate such as nifedipine, hydralazine and methyldopa.

3.5 Sampling

3.5.1 Sample size determination

Sample size was calculated using the Karl Fischer's method. According to a study done on public health perspectives of preeclampsia in developing countries, the prevalence of preeclampsia in developing countries was found to be 1.8% [66].

$$N = \frac{1.96^2 * P(1 - P)}{D^2}$$

$$D^2$$

$$= \frac{3.8416 * .018(1 - 0.018)}{0.0025}$$

$$0.0025$$

$$= 27$$

Where n= sample size

1.96 = Standard normal deviate at 5% level of significance.

P = prevalence of severe pre-eclampsia in developing nations

The test sample size was 27 mothers treated with magnesium sulphate and their neonates. For the controls, 27 mothers with preeclampsia but treated with other drugs other than magnesium sulphate were chosen.

3.5.2 Sampling method

Sampling was by convenient sampling method due to the limited number of patients presenting with severe pre-eclampsia and eclampsia. Any patient presenting with severe preeclampsia and eclampsia in the labour ward was included in the study. Out of 77 mothers enrolled for the study, 23 were dropped as either samples could not be obtained from the neonate or the sample obtained gave erroneous results.

3.6 Inclusion/exclusion criteria

The inclusion criteria was:

- Patients diagnosed with severe preeclampsia and eclampsia and on magnesium sulphate therapy.
- Babies born to mothers treated with MgSo₄ for preeclampsia/eclampsia.
- The control group consisted of neonates born to mothers who have preeclampsia but were treated with other drugs other than magnesium sulphate.
- Patients who had given consent

Exclusion criteria

- Patients who did given consent.
- Patients receiving magnesium for treatment of any other ailments.
- Patients suffering from the following conditions which might present with symptoms similar to hypermagnesemia. Adrenal insufficiency, renal failure, hypocalcaemia, hypokalemia, hypoparathyroidism, hypothyroidism and rhabdomyolysis which may precipitate hypermagnesemia.
- Patients from whom samples could not be obtained for both mother and baby.

3.7 Data collection

Patient's particulars were filled in a data collection form by the investigators after consent had been obtained. Data was collected using a data form (Appendix 1).The signs and symptoms used to diagnose the patient were also noted from the patient file and confirmed with the patient. The patients were observed for any signs like increase or decrease of seizures, urine output, presence or absence of deep tendon reflexes indicating toxicity.

With assistance from the nurses in the labour ward, blood samples were drawn from the mothers 30 minutes after a loading dose of magnesium sulphate had been given. The procedure is indicated in appendix 2. Blood samples were also collected from the neonate at birth to measure the levels of magnesium transferred to the neonate. The samples were then centrifuged and the serum obtained analysed.

3.8 Pilot study/pre-testing

After Ethical approval was obtained from the KNH/UoN Ethical committee, a pilot study was carried out beforehand to determine whether the data collection tool was adequate and whether any modifications needed to be done on the instrument. It was found impossible to get more than one blood sample from the neonates as most of them were underweight and obtaining the first sample was difficult. The nurses also felt pricking the neonates for a second sample would be traumatizing for them.

3.9 Reliability

The reliability of the research tool was tested during the pilot study to ensure its usability to collect the right data. The same questions were put to a number of respondents to see if they gave the same required response.

3.10 Validity

The questionnaire was given to a few respondents to see whether the questions were simple and easy to understand. All aspects of quality assurance were adhered to. From the specimen collection to the handling and laboratory analysis, standard operating procedures were followed. For external quality assurance, controls were run and compared to reagents from South Africa National hospital laboratory services. Study samples were run only if the controls were within acceptable limits.

3.11 Data analysis

The drugs used for management of severe preeclampsia/eclampsia and the dosages used were compared against the recommended WHO guidelines. The serum urea and electrolyte levels were measured and reference made to the normal ranges. The serum levels of magnesium in mothers treated with magnesium sulphate were compared to the recommended serum levels needed to elicit a therapeutic response. The mean magnesium levels were determined and the deviation from reference ranges determined. The serum magnesium levels in the exposed neonates were measured and compared to serum magnesium in neonates not exposed to MgSo₄. The APGAR scores for the neonates exposed were compared to APGAR scores for normal healthy neonates. The mean magnesium serum levels in the neonates was determined and the

deviation from the normal values determined. The standard deviation from which levels became toxic were determined.

3.12 Ethical considerations

Permission was sought from the Kenyatta National Hospital Ethics Committee and the Pumwani Maternity Hospital administration before commencing the study. Each of the respondents was given information on the rationale of the study and its objectives. They were then allowed to voluntarily opt to participate. Confidentiality of the respondents as well as of all records evaluated was observed. They were asked to sign a consent form (attached as Appendix 4) if they agreed to participate and a copy was given to them to keep. All patients with pre-eclampsia and eclampsia were adequately treated. Neonates with hypermagnesemia at birth were adequately managed by ensuring they received the right treatment such that their serum magnesium levels were stabilized before discharge.

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter entails the results of the study and their interpretation. The analysis was done at 0.05 level of significance

4.2 Characteristics of study participants

4.2.1 Maternal age

The mean age of mothers in the test group was 25.3 years (SD 4.6) compared to a mean age of 25.7 years (SD 4.7) years among controls. Figure 1 shows age distribution by group. The modal age group in the test group was 21- 25 years (n ==11) and the modal age group in the control group was 26-30 years (n = 10). There was no significant difference in the mean age of mothers in the two groups ($t = 0.29$; $p = 0.76$).

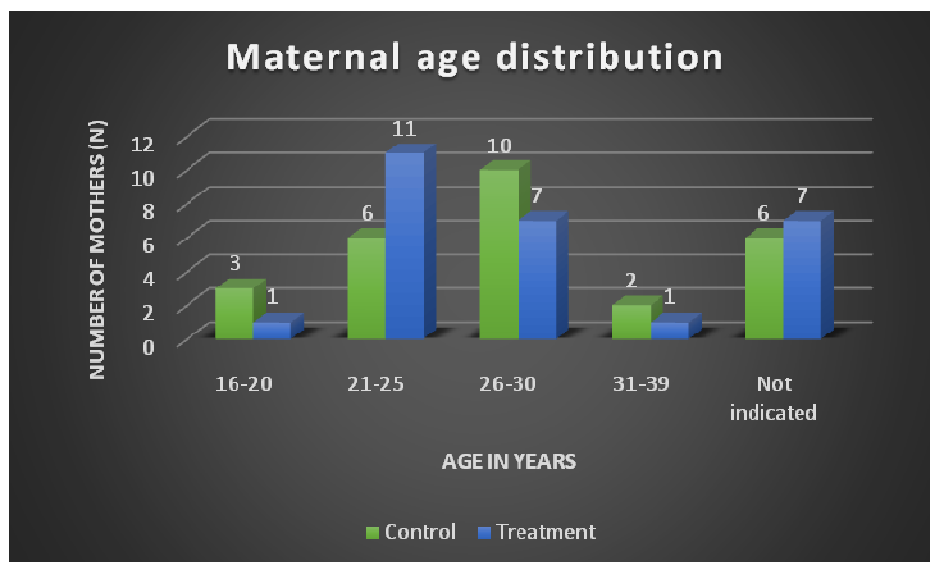


Figure 1: Age distribution of mothers in the study

4.2.2 Gestational age

The median gestation age in the test group was 38 weeks and the range was 34 to 40 weeks while the median gestation and range of the control group was 39 weeks and 36 to 41 weeks respectively, Table 1 shows the distribution of participants' gestation age at delivery according to treatment. Mothers receiving magnesium sulphate treatment were mostly delivered during week 37-38 (48.2%) while most (48.2%) mothers in the control group delivered at 39-41 weeks.

Table 1: Gestation age of mothers by group

	Controls	Tests
Gestation		
34-36 weeks	2(7.4%)	6(22.2%)
37-38 weeks	9(33.3%)	13(48.2%)
39-41 weeks	13(48.2%)	4(14.8%)
Not indicated	3(11.1%)	4(14.8%)
Total	27(100%)	27(100%)

4.2.3 Maternal hypertension

The mean diastolic blood pressure among mothers in test group was 115.4 mmHg (SD 12.1) compared to a mean blood pressure of 98.3 mmHg (SD 5.7) in the control group (Fig 2). The difference was statistically significant ($p < 0.001$). Seventeen mothers in test group had severe hypertension, while there was a bimodal distribution of blood pressure measurement in the control group; with patients equally likely to have mild hypertension ($n = 11$) or normal blood pressure ($n = 11$).

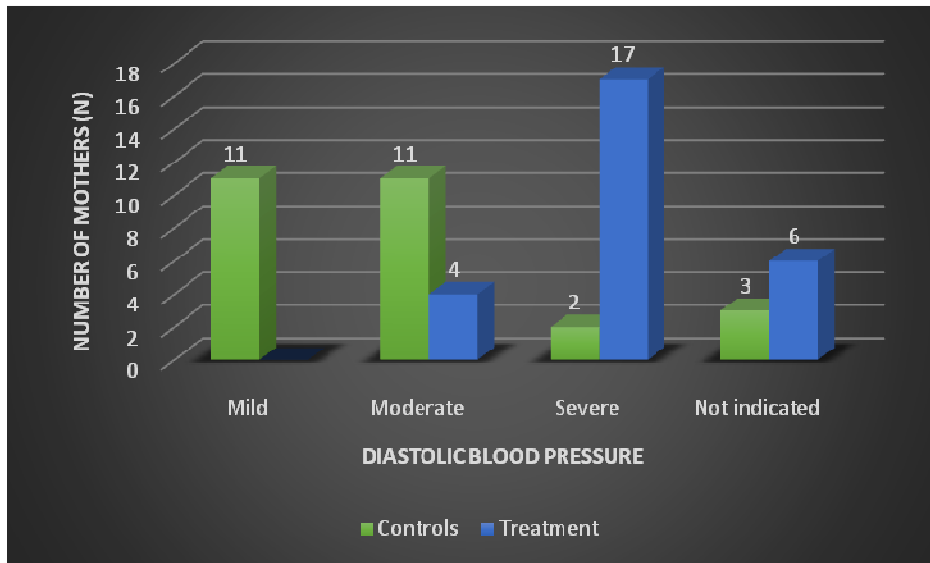
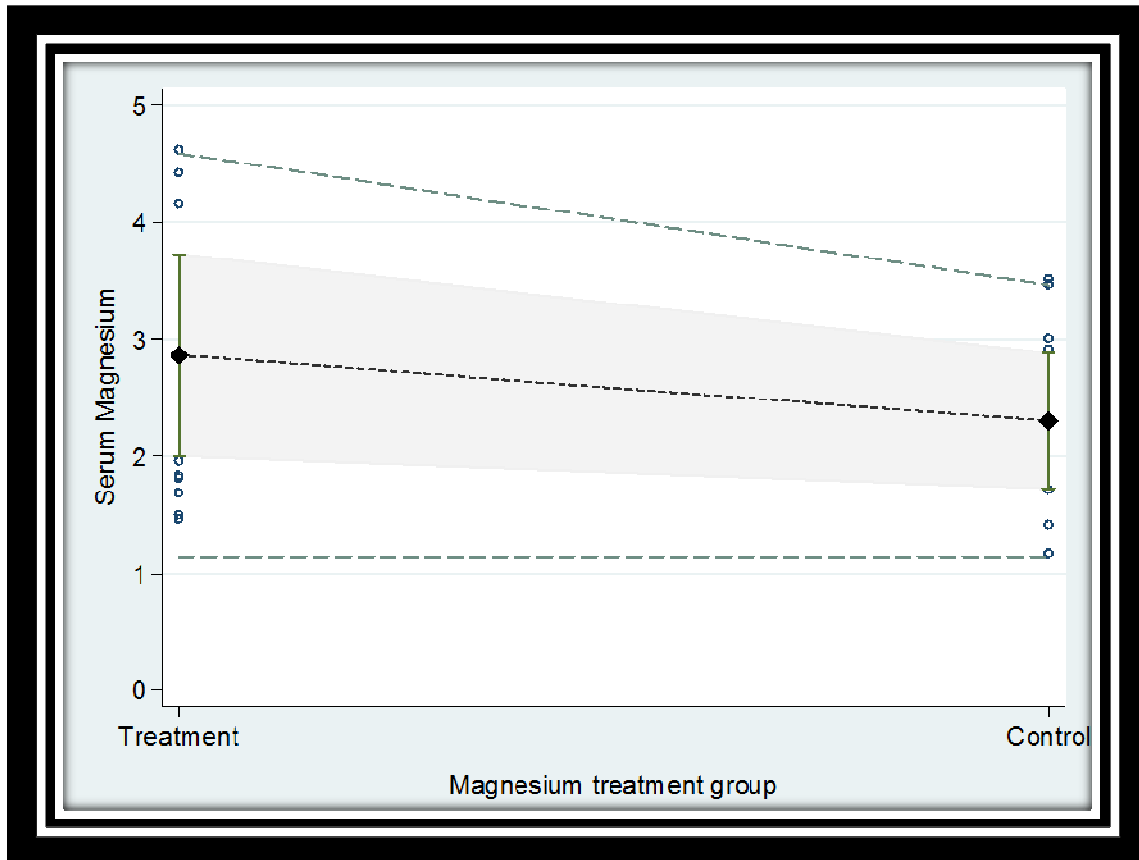


Figure 2: Diastolic blood pressure measurements.

4.3 Maternal serum magnesium

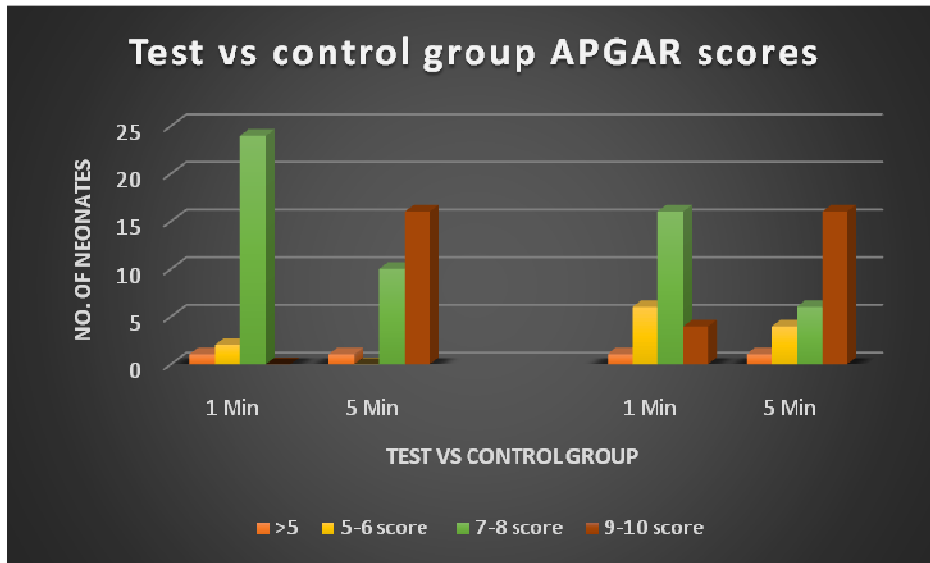
Figure 3 compares mean (SD) maternal serum magnesium levels in test and control groups. The mean serum magnesium in the test group (mean = 2.9, SD = 0.9) was significantly higher than the control group (mean = 2.3, SD = 0.6, $p = 0.008$).



4.4 Neonatal characteristics.

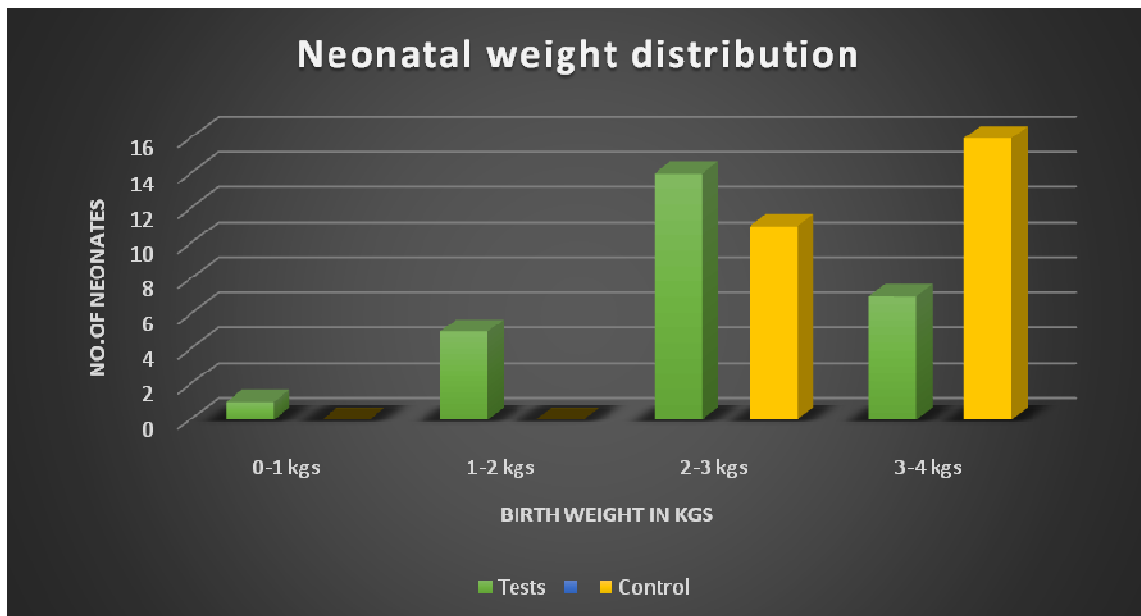
4.4.1 Neonatal Apgar scores

There was no significant difference between the APGAR scores of the neonatal test and control groups. 89 % of the neonates in the test had a score of 7-8 at 1 minute and at 5 minutes 59% had a score of 9-10. In the control group, 59% had a score of 7-8 at 1 minute while at 5 minutes, 59 % had a score similar to that of the test group.



4.4.2 Neonatal birth weight

Most of the neonates in the test group were born with a birth weight of 2-3 kg while the most of the neonates in the control group were born with a birth weight of 3-4 Kgs.

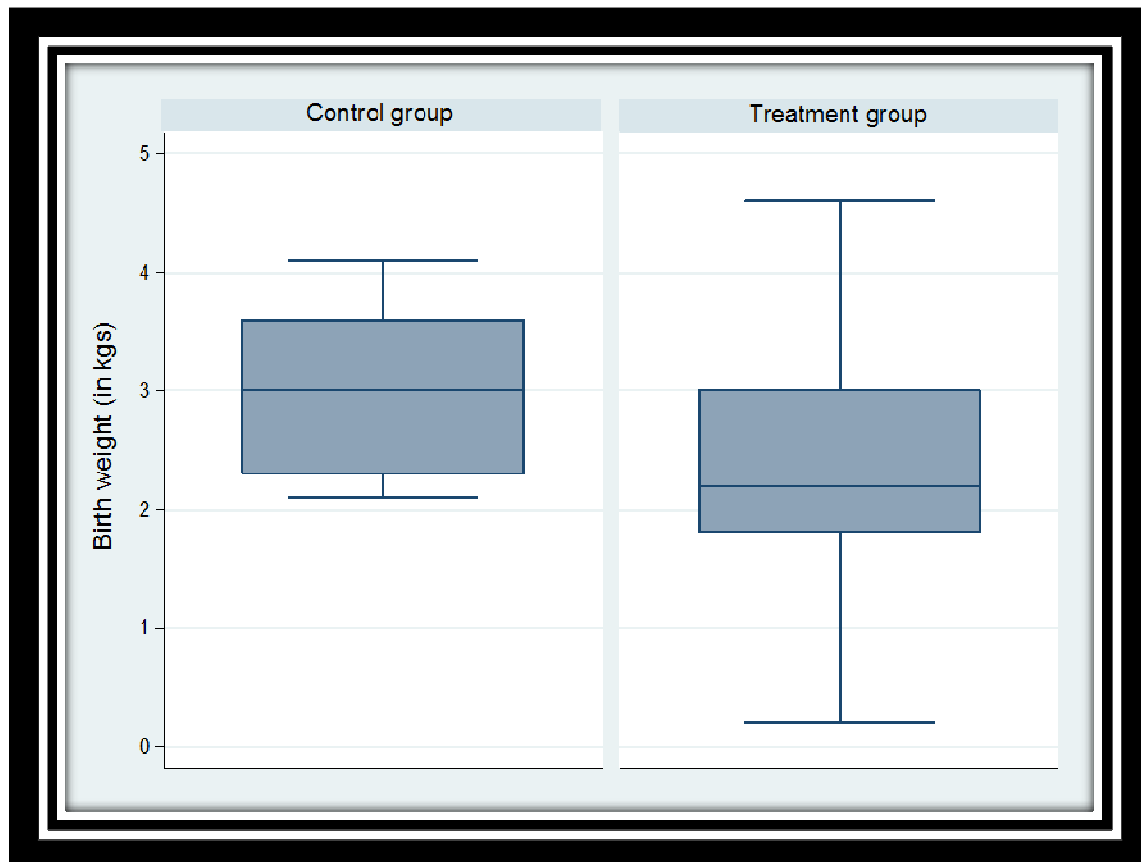


74% of the neonates in the test group were under weight with only 19% being of normal birth weight. In the control group, only 41% were underweight with 52% being of normal birth weight. 7% of neonates in both groups were overweight.

	Under weight(<3 Kg)	Normal weight (3-4 Kg)	Overweight(>4 Kg)
Test group weight	20 (74%)	5 (19%)	2 (7%)
Control group weight	11 (41%)	15 (52%)	2 (7%)

The median birth weight in the test group was 2.2 kg (IQR 1.8 to 3.0) compared to a median of 3 kg (IQR 2.3 to 3.6) in the control group. There was a statistically significant difference in birth weight of neonates in the test and intervention groups, Mann Whitney test p value = 0.003 .

Box and whisker diagram showing difference in weight between the test and control group.



4.5 Neonatal serum magnesium

Figure 4 compares mean (SD) neonatal serum magnesium levels in test and control groups. The mean serum magnesium in the test group (mean = 3.0, SD = 1.0) was significantly higher than the control group (mean = 2.3, SD = 0.6, $p = 0.008$).

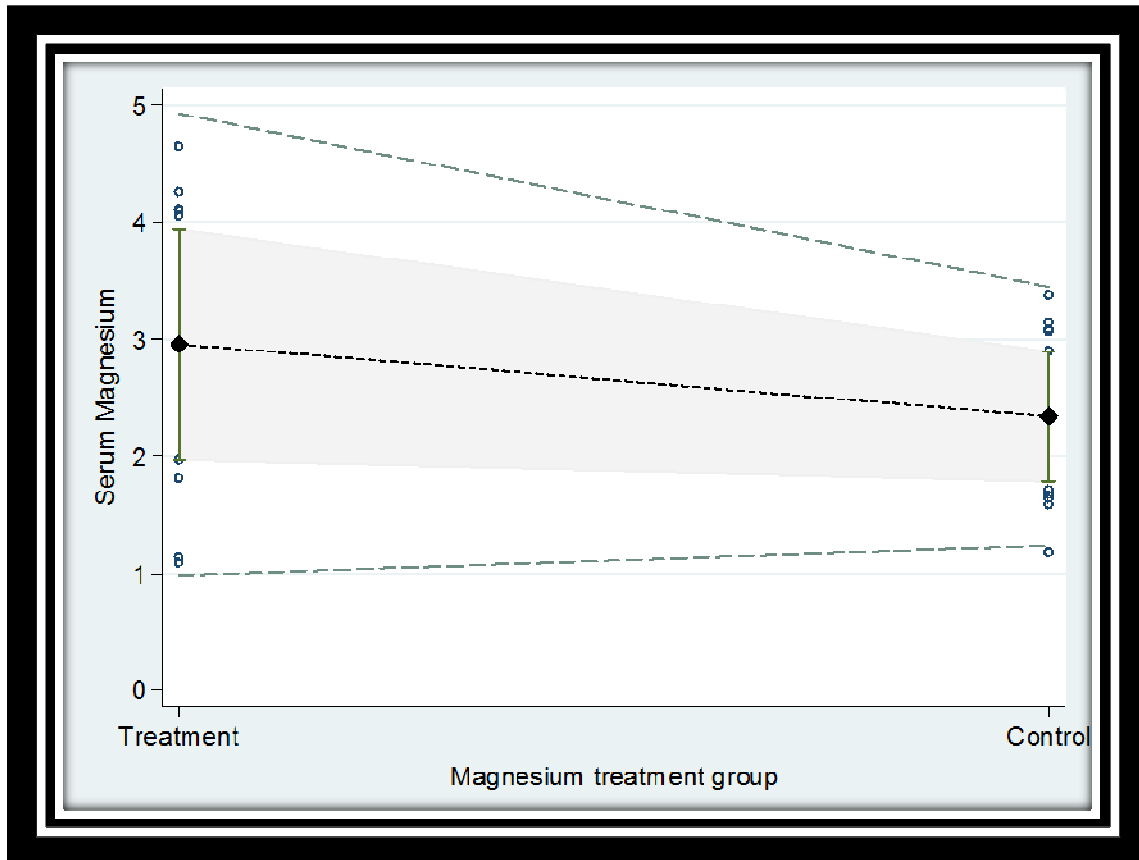


Figure 4: Mean (SD) serum magnesium levels in neonates delivered by mothers receiving magnesium sulphate treatment compared to controls.

4.6 Maternal urea and electrolytes levels

The comparison of mean serum levels of urea and electrolytes between mothers in the test and control groups are shown in Table 2. There were statistically significant differences in serum sodium ($p = 0.015$), urea ($p = 0.043$) and creatinine ($p = 0.008$) levels in the test and control groups. Serum sodium was higher in control group (mean 138.4, SD 3.6 versus 135.9, SD 3.8) while creatinine (mean 89.8 versus 71.5) and urea (mean 3.3 versus 2.6) were higher in the test group. Maternal serum levels of potassium ($p = 0.495$), chloride ($p = 0.371$) and calcium ($p = 0.629$) did not show significant differences between the test and control groups.

Table 2: Maternal urea and electrolytes in treatment and control groups

	Tests		Controls		P value
	Mean	SD	Mean	SD	
Sodium	135.9mmol/L	3.8	138.4mmol/L	3.6	0.015
Potassium	4.5mmol/L	1.6	4.3mmol/L	0.8	0.495
Chloride	99.6mmol/L	3.8	98.8mmol/L	2.3	0.371
Urea	3.3mmol/L	1.7	2.6mmol/L	0.8	0.043
Creatinine	89.8µmol/L	24.7	71.5µmol/L	23.0	0.008
Calcium	2.0mmol/L	0.4	1.9mmol/L	0.3	0.629

4.7 Neonatal urea and electrolytes levels

Table 3 compares neonatal serum electrolytes for neonates born to mothers on magnesium sulphate treatment and controls. There were significant differences between tests and controls in levels of serum urea ($p = 0.007$) and chloride ($p = 0.017$). Urea levels were significantly higher in test group as compared to the control group (mean = 4.0 versus 2.9), while mean chloride levels were 99.4 for the test group versus 97.2 for the control group.

Table 3: Neonatal urea and electrolytes in test and control groups

	Tests		Controls		P value
	Mean	SD	Mean	SD	
Calcium	2.4mmol/L	0.4	2.3mmol/L	0.3	0.241
Creatinine	99.0µmol/L	27.6	82.1µmol/L	37.0	0.067
Urea	4.0mmol/L	1.8	2.9mmol/L	1.0	0.007
Chloride	99.4mmol/L	3.2	97.2mmol/L	3.2	0.017
Potassium	5.1mmol/L	1.6	4.9mmol/L	0.7	0.689
Sodium	138.6mmol/L	6.0	138.4mmol/L	4.4	0.883

4.8 Correlation between the neonatal serum magnesium levels and birth weight

Table 4 shows that infant birth weight was not significantly associated with neonatal serum magnesium sulphate levels after adjusting for the test group. The mean serum magnesium level was 0.66 mmol/L higher in neonates in the test compared to control group ($p = 0.008$). The neonatal magnesium serum levels increased by 0.07 mmol/L for each additional kilogram of birth weight but this increase was not significant ($p = 0.605$).

Table 4: Linear regression analysis of the effect of birth weight and magnesium sulphate treatment on levels of neonatal magnesium sulphate

	Coefficient	Standard error	T statistic	P value	95 % CI	
					Tests	Control
Magnesium sulphate treatment	0.66	0.24	2.76	0.008	0.18	1.14
Birth weight (in Kgs)	0.07	0.13	0.52	0.605	-0.20	0.33
Intercept	2.13	0.43	4.95	<0.001	1.27	3.00

4.9 Correlation between maternal and neonatal serum magnesium levels

There was a positive correlation between maternal and neonatal serum magnesium levels in both the test and control groups as shown in Figure 5. The correlation was stronger in the test group ($r = 0.56$, $p = 0.003$) compared to the control group ($r = 0.35$, $p = 0.087$).

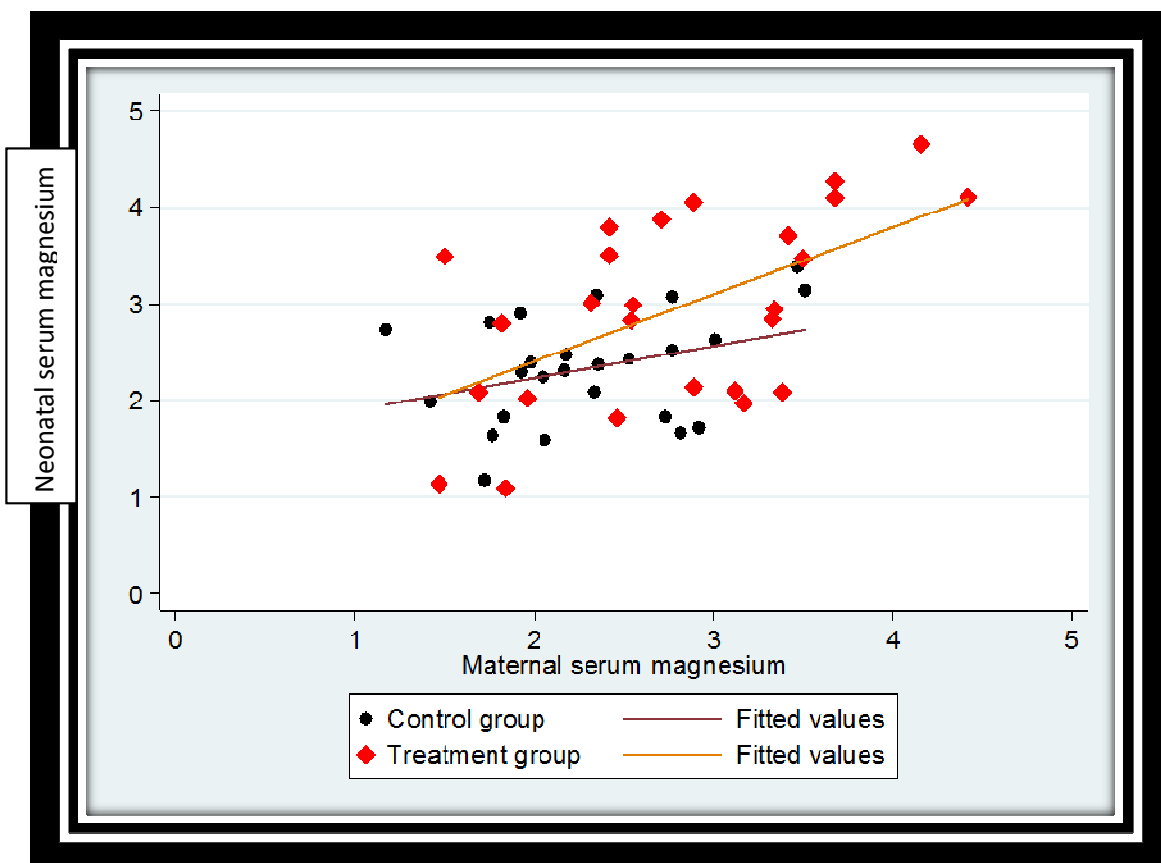


Figure 1: Correlation between maternal and neonatal serum magnesium according to treatment group

CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Introduction

This chapter will entail a comparison of the results obtained from this study and results from other studies that have been done before. The conclusions drawn from the study and further recommendations will also be included.

5.2 Discussion

The first-line option for the treatment and prevention of eclamptic seizures is magnesium sulfate. [36, 37, 38, 39] Evidence supports its effectiveness in the prevention and treatment of eclamptic seizures. [37, 40]

Accordingly, in our study, patients presenting with severe preeclampsia (headache, oedema, blurred vision, confusion and a diastolic BP above 110)^[1,3,4] were first given a loading dose of 4g of magnesium sulphate then an infusion of 1g /hour as a maintenance dose. This is in line with the recommended guidelines.

70% of the mothers in the test group presented and delivered at a gestation age below 38 weeks as compared to 11% in the control group. This is in line with studies that recommend delivery as the definitive treatment for severe preeclampsia after 34 weeks. [68,69,70]

The serum magnesium levels were found to be significantly high in the test group as compared to the control group. The clinical effect and the toxicity of MgSo₄ depend on its serum levels. For treatment of eclamptic seizures, a concentration of 1.8 – 3.0 mmol/L should be achieved. Magnesium is excreted mainly by the kidney with the half-life being 4.66 hours. [43]

When carefully administered and monitored, toxicity is rare. At levels between 3.5 -5 mmol/L, there is loss of the patellar reflex in the mother indicating impending toxicity and at 5 – 6.5 mmol/L, respiratory paralysis occurs. CNS depression which may range from drowsiness to coma also begins. At concentrations > 7.5 mmol/L cardiac conduction is altered and when 12.5 mmol/L is exceeded cardiac arrest occurs. In this study the serum level of magnesium were well within the recommended levels for treatment and not elevated to toxic levels.

In our study, maternal serum urea and creatinine were found to be elevated in the mothers in the test group. Serum creatinine levels are used as a marker for kidney injury. This is significant because MgSO₄ the recommended treatment option in severe preeclampsia and eclampsia is excreted through the renal route ^[43] and in view of the damage caused to the kidney by the disease, magnesium toxicity could occur. A systematic review and meta-analysis found an increased risk for development of kidney injury after preeclampsia and eclampsia.^[71]

Sibai BM, Anderson GD and McCubbin JH observed that in eclampsia, abnormalities in blood urea nitrogen and serum creatinine among other findings are statistically significant and recommended serum creatinine tests in eclamptic patients.^{[72][73]}

Serum calcium levels in the controls were lower than in the test group. This is in line with the findings of Mason B.A et al who in his study found low calcium levels in pre-eclamptic women not on treatment with MgSO₄ sulphate. After magnesium therapy the levels were raised and the study concluded that ionized calcium levels appeared to be tightly regulated in the presence of elevated serum magnesium levels.^[74]

In this study the potassium levels were slightly elevated in the maternal test group as compared to the control group. Iglesias MH et al reported in their study a case of a woman who when given MgSO₄ first for eclampsia prophylaxis then for treatment of eclampsia, developed hyperkalemia without severe renal failure or any other explanation. They recommended close monitoring of serum electrolytes during management of severe preeclampsia and eclampsia with MgSO₄.^[75]

There was no significant difference in the APGAR scores of the neonatal test and control groups. Lipsitz P.J. and English I.C in a study on hypermagnesemia in the newborn infant showed that the signs and symptoms of hypermagnesemia in the infant are similar to those in the adult with hypermagnesemia.^[49] Such neonates at birth would be expected to have severe asphyxia with low APGAR scores and absent or feeble reflexes. Pruett K.M et al showed that treatment with MgSO₄ did not lead to low APGAR scores in neonates of mothers with eclampsia though the mean cord level of magnesium, was equal to the mean maternal serum level.^[50]

The neonatal serum magnesium levels in our study correlated with the maternal serum magnesium levels. The levels in the neonatal test group were higher than in the control group. Hallak and Cotton demonstrated in a study with rats the transfer of magnesium from maternal circulation into the foetal blood^[45]. Studies have shown an increase in magnesium serum levels in both mother and foetus after administration^[46]. Newborns of mothers exposed to MgSo4 have been shown to have elevated serum magnesium levels ranging from 3-11 mmol/L.^[48]

The serum levels of all electrolytes were elevated in the neonatal test group as compared to the levels in the control group. The urea levels were significantly elevated. The high electrolyte levels could be explained by the fact that at birth, renal blood flow is low and the immature kidney has limited adaptability in case of excess administration of drugs and thus a higher risk of toxicity. In preterm neonates born at 26- 34 weeks gestation age, the increase in the glomerular filtration rate is limited because of incomplete nephrogenesis. And thus clearance of drugs from the circulation is limited resulting in elevated serum levels.^[76]

In our study the serum creatinine was found to be elevated in the test group. Creatinine levels are used as a marker for kidney function. Serum creatinine has been shown to be elevated in the first days of life reflecting maternal creatinine and a low intrinsic glomerular filtration rate. The lower the gestation age at birth, the more elevated is the serum creatinine. Because the neonates in the test group were born before term, this could explain the elevated serum creatinine levels.

The neonatal serum calcium levels in both groups of our study were higher than the maternal serum calcium levels. Studies have shown active transfer of calcium from the mother to the neonate during the last trimester of pregnancy whereby the cord calcium levels are higher than the maternal serum calcium levels.^[77] In our study, neonatal serum calcium levels in the test group were slightly higher than in the control group but not significantly different. MacIntyre et al in their study gave evidence that a rise in serum magnesium levels inhibits secretion of parathyroid hormone which results in increased urinary excretion of calcium.^[51] In a study of five newborn infants whose mothers had been treated with IV magnesium sulfate for periods ranging from 5 to 14 weeks, Lamm CI et al noted radiographic bony abnormalities in two of the

infants^[52]. The investigators came to the same conclusion as MacIntyre et al that the foetal hypermagnesemia due to long term treatment with magnesium depressed parathyroid hormone release resulting in foetal hypocalcaemia Savory J and Monif GRG reported in their study of mothers treated with magnesium a mild decrease in cord calcium concentrations^[53]. So did Cruikshank DP et al in their study on effects of magnesium sulfate treatment on perinatal calcium metabolism.^[54] In contrast, Donovan EF et al reported high cord calcium levels following magnesium therapy. No neonatal symptoms were associated with either calcium levels.^[55]

The neonatal serum potassium levels in both groups were found to be higher than the maternal serum potassium levels while the serum sodium levels were found to be lower in the neonates. A study was done showing physiological hyponatremia and hyperkalemia in healthy newborns which was highly suggestive of functional hypoaldosteronism.^[78] This was postulated to be due to the adaptive process from intrauterine aquatic environment where renal sodium reabsorption is dispensable, to life outside the uterus where strict sodium control by the kidney is essential. In our study the serum potassium levels in the test group were slightly higher than in the control group. Nader PJ et al demonstrated higher aldosterone and potassium levels in preterm newborns as compared to term healthy newborns.^[79, 80, 81]

There was a statistically significant difference in birth weight of neonates in the treatment and intervention groups in our study. A premature baby with an extremely low birth weight of 990g was found to have severe hypermagnesemia^[82]. But there was no correlation between the birthweight and the serum magnesium levels which implies that the low birth weight was more of a function of the disease than the effect of administered magnesium sulphate.

5.3 Conclusion.

Maternally administered magnesium sulphate during management of severe preeclampsia and eclampsia does affect serum urea and electrolyte levels but not all electrolytes are affected significantly.

5.4 Recommendations

5.4.1 Recommendations for practice and policy

Due to the elevated serum urea and electrolyte levels in both mother and neonate, the study recommends that in cases whereby magnesium sulphate is administered, serum urea and electrolyte levels be closely monitored.

5.4.2 Recommendations for research

The study recommends further research be done in following up the mothers treated with MgSO₄ and their newborns for a period of time and testing their serum urea and electrolyte levels to find out whether the findings of this study persist or they resolve.

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APPENDIX 1: ACKNOWLEDGEMENT OF FUNDING

The funding is from the Linked-Strengthening Maternal, Newborn and Child Health Research Training in Kenya. The grant is linked to Partnership for Innovative Medical Education in Kenya (PRIME-K). The project described was supported by Award Number 5R24TW008907 from the US National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the US National Institutes of Health.

PPENDIX 2: QUESTIONNAIRE

Tests

(A)MOTHER'S DETAILS
S.no of patient(mother)	
Age in years
Weight
Gestation age
Signs & tests used to diagnose preeclampsia	Headache[] Thrombocytopenia[] Blurred vision [] Deranged LFTs [] Proteinuria []
Signs and tests used to diagnose eclampsia	Headache[] Thrombocytopenia[] Blurred vision [] Deranged LFTs [] Proteinuria []Convulsions[]
BP
RR
Temp.
Loading Dose of MgSo4
Serum Mg levels after loading dose of MgSo4
Serum Mg levels at delivery.
(B)EXPOSED NEONATE'S DETAILS	
Weight of baby at birth	
APGAR score	
Mg serum levels at birth	

(c) Questionnaire for controls

(a) S.no of patient(mother)
BP:
Drug managed with:
Serum magnesium levels:
NEONATE'S DETAILS	
(b) Weight of baby at birth
APGAR score
Mg serum levels at birth
Mg levels after 12 hrs	

APPENDIX 3:LABORATORY PROCEDURE

The venous blood was drawn from the patients from the arm away from that receiving the infusion and transferred into vacutainers. It was then taken to the Pumwani hospital laboratory where it was centrifuged to obtain the serum. The sample was marked with the patient's serial number and time of collection, put in a safe bag or cool box and transferred to the university of Nairobi clinical chemistry laboratory for analysis. 1ml of serum was then transferred into a serum vial for chemical analysis using the photometric method. The principle of the test is that magnesium ions in alkaline medium form a coloured complex with xylydyl blue at a wavelength of 520nm. The absorbance is proportional to the magnesium concentration in the sample.

APPENDIX 4: APGAR SCORING FOR NEWBORNS

The neonates will be scored for APGAR scores at birth.

APGAR Scoring for Newborns

A score is given for each sign at 1 minute and 5 minutes after the birth. If there are any problems with the baby, an additional score is given at 10 minutes. While a score of 7-10 is considered normal, 4-7 might require some resuscitative measures, and a baby with Apgars of 3 and below requires immediate resuscitation.

	Sign	0 Points	1 Point	2 Points
A	Activity (Muscle Tone)	Absent	Arms and Legs Flexed	Active Movement
P	Pulse	Absent	Below 100 bpm	Above 100 bpm
G	Grimace (Reflex Irritability)	No Response	Grimace	Sneeze, cough, pulls away
A	Appearance (Skin Color)	Blue-gray, pale all over	Normal, except for extremities	Normal over entire body
R	Respiration	Absent	Slow, irregular	Good, crying

Adopted from America Academy of Pediatrics

APPENDIX 5: CONSENT FORM FOR PATIENTS USING MAGNESIUM SULPHATE

To be read and explained in a language the respondent best understands.

Study title: Assessment of the utilization of magnesium sulphate in management of severe preeclampsia and eclampsia at Pumwani maternity hospital.

Introduction

I am Dr Faith Rachel a student from University of Nairobi. I am requesting you to participate in a study I am carrying out. This study will involve obtaining blood samples from both you and your newborn.

Purpose

The purpose of this study is to determine the serum level of magnesium in both you and your newborn baby.

Consent: Your participation in this study is voluntary. You will not be penalized for failure to participate.

Procedure to be followed: With your permission, blood samples will be drawn from you to measure the levels of the drug being used to treat you in the blood thirty minutes after the drug is administered and just before delivery. With your permission blood samples will also be drawn from your baby immediately after birth and twelve hours after birth.

Risks: There will be minimal risks involved in the procedure. Care will be taken to minimize pain and any infection. This will be achieved by using aseptic techniques and qualified personnel to obtain the blood samples.

Benefits: The blood magnesium levels will be determined and compared to the normal therapeutic values. If the level is low information will be conveyed to the clinician to ensure that the appropriate therapeutic levels are achieved. If the magnesium levels are high in the neonate measures will be taken to avoid harm. The results of the study will be used in subsequent dosing of magnesium sulphate among other patients.

Confidentiality: Your name will not be recorded in the data collection instrument. Data obtained will be confidential and only the investigator will have access to it during the entire study period. Your identity will only be revealed through your permission or through a legal process.

Contacts:In case of any enquiries please contact any of the following.

- **The investigator:**Faith RachelTel no. 0718-486-375
- **ERC:** Prof A.N.Guantai, Chairperson KNH/UoN-Ethics Review Committee P.O BOX 20723-00100, Nairobi.Tel.no. 2726300/2716450 .Ext 44355.
- **Supervisors:** Dr P.N Karimi, Department of Pharmaceutics and Pharmacy Practice, Dr Wandolo: Department of Pathology ;Clinical chemistry unit
- **Institution:**Department of Pharmaceutics and Pharmacy Practice,School of Pharmacy; University of Nairobi. P.O BOX 30197-0400 Nairobi.

Ethical approval:The study has been approved by the Ethics and Research Committee of Kenyatta National Hospital/University of Nairobi P.O BOX 20723-00100,Nairobi.Tel.no. 2726300/2716450.Ext 44355.Attached is a copy of the same.

Patient consent

I have read the above consent form and understood it.The nature of the study has been explained to me by Dr Faith Rachel. I voluntary agree to participate in the study.

Name of participant.....

Signature of participant.....

Date.....

APPENDIX 6: CONSENT FORM FOR PATIENTS NOT USING MAGNESIUM SULPHATE

To be read and explained in a language the respondent best understands.

Study title: Assessment of the utilization of magnesium sulphate in management of severe preeclampsia and eclampsia at Pumwani maternity hospital.

Introduction

I am Dr Faith Rachel a student from University of Nairobi. I am requesting you to participate in a study I am carrying out. This study will involve obtaining blood samples from both you and your newborn.

Purpose

The purpose of this study is to determine the serum level of magnesium in both you and your newborn baby.

Consent: Your participation in this study is voluntary. You will not be penalized for failure to participate.

Procedure to be followed: With your permission, blood samples will be drawn from you to measure the levels of the drug being used to treat you in the blood thirty minutes after the drug is administered and just before delivery. With your permission blood samples will also be drawn from your baby immediately after birth and twelve hours after birth.

Risks: There will be minimal risks involved in the procedure. Care will be taken to minimize pain and any infection. This will be achieved by using aseptic techniques and qualified personnel to obtain the blood samples.

Benefits: The serum magnesium levels will be determined and compared to the normal therapeutic values. If not found to be normal, measures will be taken to facilitate treatment. The results of the study may also be used in subsequent studies.

Confidentiality: Your name will not be recorded in the data collection instrument. Data obtained will be confidential and only the investigator will have access to it during the entire study period. Your identity will only be revealed through your permission or through a legal process.

Contacts:In case of any enquiries please contact any of the following.

- **The investigator:**Faith Rachel Tel no. 0718-486-375
- **ERC:** Prof A.N.Guantai, Chairperson KNH/UoN-Ethics Review Committee P.O BOX 20723-00100,Nairobi.Tel.no. 2726300/2716450 .Ext 44355.
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Patient consent

I have read the above consent form and understood it. The nature of the study has been explained to me by Dr Faith Rachel. I voluntary agree to participate in the study.

Name of participant.....

Signature of participant.....

Date.....