A COMPARATIVE STUDY OF INTRAVENOUS VERSUS INTRAMUSCULAR MAGNESIUM SULPHATE IN SEVERE PRE-ECLAMPSIA AND ECLAMPSIA IN GOVT RAJAJI HOSPITAL, MADURAI

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CERTIFICATE

This is to certify that the dissertation entitled **"A COMPARATIVE STUDY OF INTRAVENOUS VERSUS INTRAMUSCULAR MAGNESIUM SULPHATE IN SEVERE PRE-ECLAMPSIA AND ECLAMPSIA IN GOVT RAJAJI HOSPITAL, MADURAI**" is a bonafide work done by **Dr. ASHMITAA .S** in the institute of Madurai medical college, Madurai in partial fulfilment of the university rules and regulations for ward of MS degree in Obstetrics and Gynaecology under my guidance and supervision during the academic year 2019-2020.

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CERTIFICATE FROM DEAN

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DECLARATION

I, **DR ASHMITAA.S** solemnly declare that this dissertation entitled **"A COMPARATIVE STUDY OF INTRAVENOUS VERSUS INTRAMUSCULAR MAGNESIUM SULPHATE IN SEVERE PRE-ECLAMPSIA AND ECLAMPSIA IN GOVERNMENT RAJAJI HOSPITAL, MADURAI"** was done by me at the Department of Obstetrics and Gynaecology, Govt. Rajaji Hospital, Madurai medical college, Madurai during 2019-2020 under the guidance and supervision of **Prof. Dr. N. SUMATHI M.D, DGO.,** This dissertation is submitted to the Tamil Nadu Dr.M.G.R Medical University towards the partial fulfilment of requirements for the award of M.S Degree in Obstetrics and Gynaecology (Branch III)

Place: Madurai

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CONTENTS

ABBREVATIONS

1.MgSO4	Magnesium sulphate
2.IV	Intravenous
3.IM	Intra muscular
4.SBP	Systolic Blood Pressure
5.DBP	Diastolic Blood Pressure
6.NMDA	N –Methyl D-aspartate
7.PGE_1	ProstaglandinE_1
8.PGE_2	ProstaglandinE_2
9.$PGF_2\alpha$	Prostaglandin$F_2\alpha$ (Prostodin)
10.HELLP	Hemolysis, Elevated liver enzymes, Low platelets
11.PIGF	Platelet Inhibiting Growth Factor
12.VEGF	Vascular Endothelial Growth Factor
13.TGF	Transforming Growth Factor
14.NO	Nitric Oxide
15.PRES	Posterior Reversible Encephalopathy Syndrome

INTRODUCTION

Hypertensive disorders are one of the most common medical complications of pregnancy and contributes significantly to maternal and perinatal morbidity and mortality. Approximately, 5,00,000 or more women die of complications due to pregnancy every year and 95% of these women are from Asia & Africa.[1]

Hypertensive disorder of pregnancy is the foremost cause of maternal deaths in developed countries and the third most common cause of maternal deaths in developing countries.

Eclampsia alone accounts for 50,000 maternal deaths worldwide annually.[2]

Anticonvulsants have been advocated for prevention of eclampsia in pre-eclamptic patients.[3]

Diazepam being cheap and readily available is still being used for the control of convulsions. In the 1980s, Phenytoin was found to have theoretical advantage of controlling convulsions while avoiding sedation.[4]

However, collaborative eclamptic trial in 1995 conclusively proved that Magnesium Sulphate (MgSO4) is the preferred treatment for eclamptic fits rather than Diazepam or Phenytoin. It reduced the incidence of

maternal death from 7% to 4% and the recurrence rate of convulsions was found to be reduced by 52% and 67% when compared to Diazepam and Phenytoin, respectively.[5]

The two standard regimens are Zuspan's (intravenous) and Pritchard's regimen (supposedly 'high dose' intramuscular).

Pritchard's is commonly preferred in developing countries, although it is derived with the Western population as the standardized BMI. On the other hand, Indian population have lower BMI, majority of them being malnourished and hence a low dose of magnesium therapy would more likely reduce the dose related complications of magnesium toxicity all the while being more compliant and patient friendly, provided adequate monitoring is possible.

The objective of this study is to determine the efficacy and safety of Zuspan regimen among patients admitted at Government Rajaji Hospital, Madurai.

REVIEW OF LITERATURE

DEFINITION:

Pre-eclampsia is defined as a multisystem disorder of unknown etiology characterized by Blood pressure more than 140/90mmHg or more after 20 weeks with proteinuria; urinary excretion of more than 0.3g protein/24hrs or more than or equal to +2(1g/L), in a previously normotensive and non proteinuric woman.

It is associated with maternal complications like eclampsia, acute renal failure, acute haemorrhage, pulmonary oedema, Disseminated Intravascular Coagulation (DIC), Haemolysis, Elevated Liver Enzymes and Low Platelet (HELLP) syndrome.

Eclampsia is defined as a convulsive episode or any other sign of altered consciousness arising in a setting of pre-eclampsia, and which cannot be attributed to a pre-existing neurological condition.

Risks of intrauterine death, intrauterine growth restriction, asphyxia, perinatal death, preterm birth and admission to Neonatal Intensive Care Unit (NICU) are also more frequent in pre-eclampsia.

Pre-eclampsia is clinically classified as mild (blood pressure more than 140/90 mmHg but less than 160/90mmHg) and severe pre-eclampsia: persistent systolic blood pressure more than 160mmHg or diastolic pressure above 110mmHg, proteinuria of more than 5g/24 hrs, oliguria (<400ml/24hrs), platelet count less than 1,00,000/mm^3 and HELLP syndrome.

Prophylactic magnesium sulphate therapy lowers the risk of eclampsia and feto-maternal morbidities (MAGPIE trial)[3]. The aim is to control seizures and prevent its recurrence.

INCIDENCE:

In India, the incidence of preeclampsia is reported to be 8-10% among the pregnant women.[6]

RISK FACTORS FOR PREECLAMPSIA: [7.8.9]

- Chronic hypertension
- Pre-gestational diabetes
- Multifetal pregnancy
- Pre-pregnancy BMI >30
- Previous stillbirth
- Nulliparity
- Maternal age >40
- Long inter-pregnancy interval (>5 years)
- Low socioeconomic status
- Previous pre-eclampsia
- Antiphospholipid antibody syndrome
- Systemic lupus erythematosus
- Chronic renal disease
- Assisted reproduction

ETIOLOGY:

The pathophysiology of remains poorly understood but it eventually resolves once the placenta is removed. Hence, in terms of pathogenesis it is primarily a placental disorder.

1. Placental implantation with abnormal trophoblastic invasion of uterine vessels
2. Immunological maladaptive tolerance between maternal (placental), and fetal tissues
3. Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy
4. Genetic factors including inherited predisposing genes and epigenetic influences.

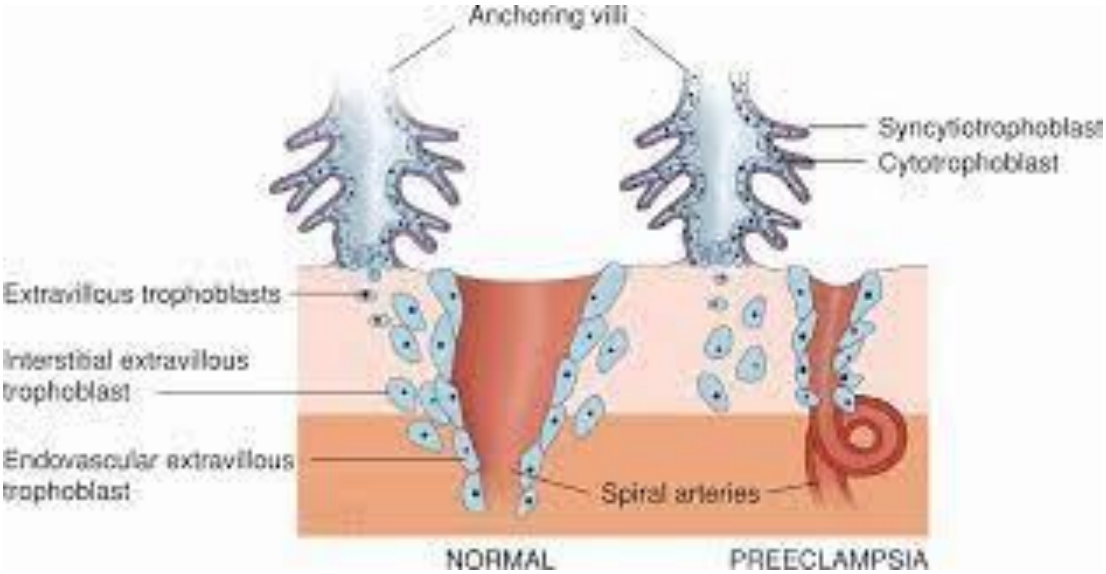


Figure 1 : Abnormal trophoblast implantation in pre-eclampsia

Defective implantation is characterized by incomplete invasion of the spiral arteriolar wall by extravillous trophoblasts which results in a small-calibre vessel with high resistance to flow. These causes the blood to be supplied to villi in jet like spurts and this turbulent flow damages the villi.[10]

ROLE OF PLACENTA:

Factors released from the placenta into the systemic circulation during stress are considered to result in pre-eclampsia.[11]

Oxidative stress of the syncytiotrophoblast, the epithelial covering of the placental villi in contact with maternal circulation, releases a complex mix of factors, including pro-inflammatory cytokines, exosomes, anti-angiogenic agents, and cell-free foetal DNA, into the maternal circulation. [12,13]

These disrupt maternal endothelial function resulting in a systemic inflammatory response. (Lee, 2012; Redman, 2012)[11,14]

In early onset pre-eclampsia, there is uteroplacental malperfusion secondary to defective remodelling of the uterine spiral arteries. (Khodzhaeva, 2016)[15]

In late onset cases, there is an increasing mismatch between normal maternal perfusion and the metabolic demands of the placenta and fetus.[16]

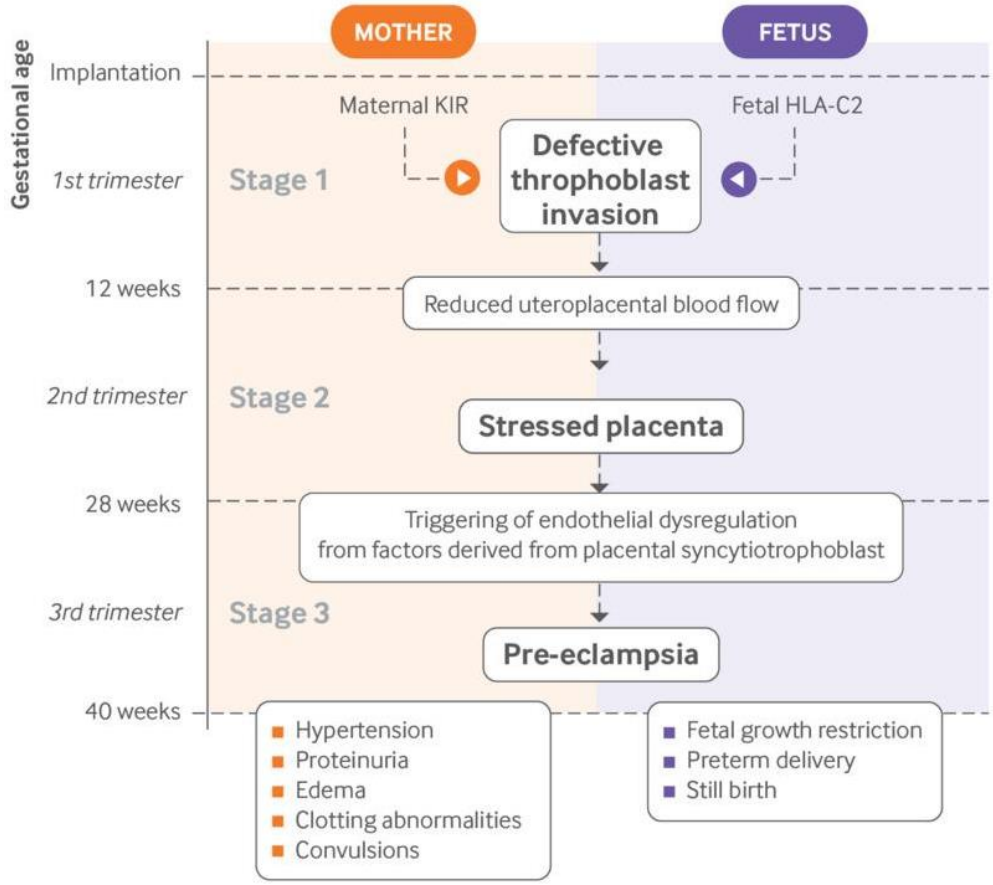


Figure 2: Pathophysiology of pre-eclampsia

The magnitude of defective trophoblastic invasion correlates with the severity of the hypertensive disorder (Madazli, 2000)[10]

IMMUNOLOGICAL FACTORS:

Loss of tolerance to paternally derived placental and fetal antigens can cause pre-eclampsia (Erlebacher, 2013)[17]

Likewise, increased load of parenteral antigens in cases such as molar pregnany predispposes the women to preeclampia

A second pregnancy with a different partner has also shown to increase the risk of preeclampsia. (Mostello, 2002)[18]

A woman with a Trisomy 13 fetus also has a 30 to 40% increased risk of preeclampsia due to a gene called *soluble fms-like tyrosine kinase 1* (sFlt-1) which is present in Chromosome 13. (Bdolah, 2006)[19]

ENDOTHELIAL CELL ACTIVATION:

Placental ischemia leads to release of various oxidative particles usch as free oxygen radicals, cytokines, tumor necrosis factor-α (TNF-α) and interleukins which lead to systemic enothelial activation or dysfunction. (Davidge, 2015)[20]

These oxidants and angiogenic agents contributes to the systemic oxidative stress by causing activation of lipid peroxides and thus lead to atherosis. (Manten, 2005)[21]

It also causes the production of lipid laden macrophages seen in atherosis which leads to activation of the systemic microvascular coagulation causing thrombocytopenia and increased systemic vascular permeability leading to proteinuria and oedema.

GENETIC FACTORS:

Hundreds of genes have been studied for their possible association with preeclampsia (Buurma, 2013; Sakowicz, 2016; Ward, 2015)[22,23,24]. Some of these include MTHRF, F5(Leiden), ACE, F2, HLA, LPL etc.

Glu298Asp polymorphism in the eNOS gene could be an individual's risk factor and may modulate progression to eclampsia in patient with preeclampsia in the Turkish population. [25]

COVID-19 AND PRE-ECLAMPSIA:

Mendoza and colleagues presented data that support a link between SARS-CoV-2 infection and the occurrence of a preeclampsia-like syndrome. [26]

PATHOGENESIS:

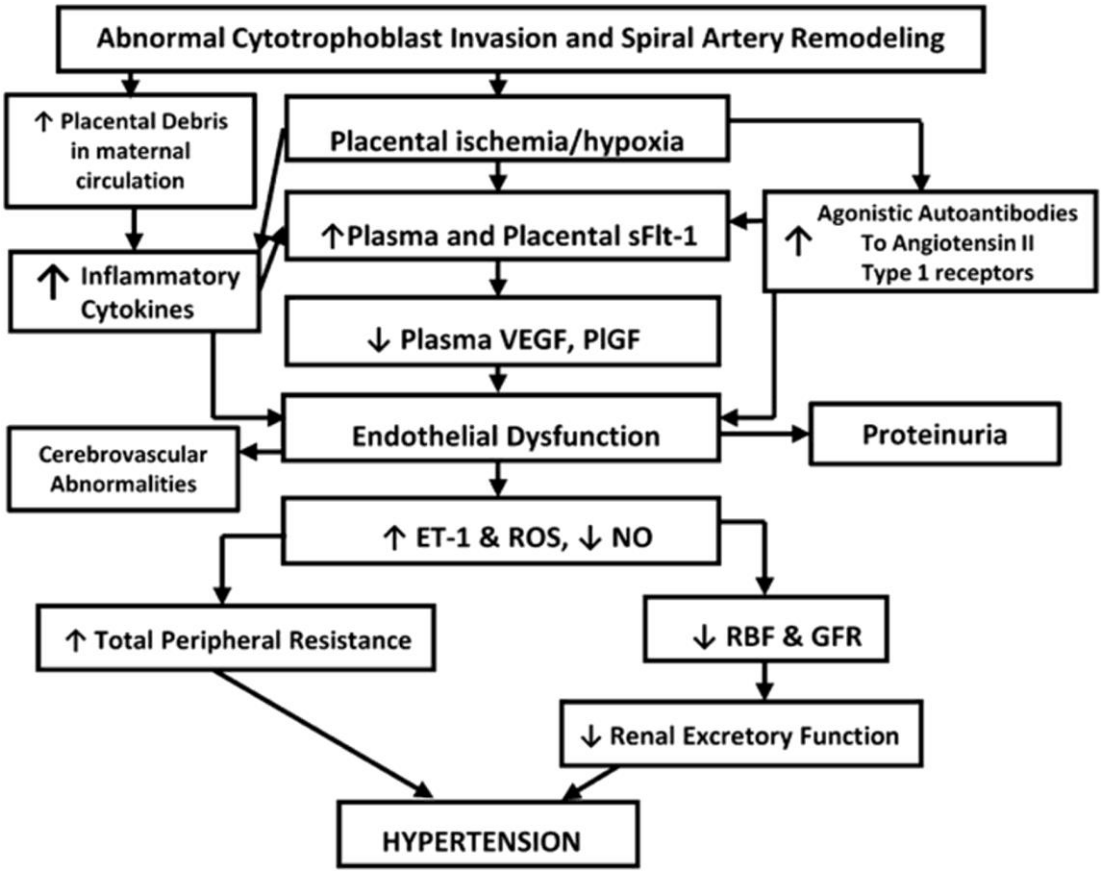


Figure 3: Pathogenesis of Pre-eclampsia

VASOSPASM:

Endothelial activation leads to vasospasm which in turn leads to increase in resistance and hypertension.

Vasospasm also leads to necrosis due to defective blood supply and this causes damage to end organs. (Zeeman, 2009).[27]

ENDOTHELIAL CELL INJURY:

Endothelium layer has anticoagulant property. Also, the systemic endothelial layer produces substances like Nitrous Oxide and therefore help in antagonizing the pressor action on the vessels.

Endothelial injury or activation causes release of placental protein factors that promote coagulation, increase the pressor response of the systemic vasculature. This is evident by the presence of capillary leaks, oedema and changes to the glomerular capillaries in the kidney.[20]

INCREASED PRESSOR RESPONSE:

Prostacyclin (PGI2) levels are low and thromboxane A2 level is higher. The prostacyclin/Thromboxane ratio falls leading to increased sensitivity to angiotensin II and hence, vasoconstriction. (Davidge, 2015)[20]

Nitrous oxide synthase is not produced adequately at the endothelial layer. Therefore, nitrous oxide cannot blunt the action of vasopressors leading to vasospasm, elevated blood pressure and lowers heart rate.[20]

Endothelin (ET-1) is a 21 amino acid protein and a potent vasoconstrictor. Its level is elevated in a patient with pre-eclampsia. (Ajne, 2003)[28] Interestingly, magnesium sulphate seems to lower the Endothelin concentration. (Sagsoz, 2003)[29]

ANGIOGENIC AND ANTI-ANGIOGENIC FACTORS:

An imbalance between the angiogenic and anti-angiogenic factor can predispose to preeclampsia. This occurs due to hyoxia at the uteroplacental surface.

Overproduction of two main anti-angiogenic peptides play a vital role: soluble fms-like tyrosine kinase 1 (sFlt-1) and soluble endoglin (sEng) (Karumanchi, 2016a)[30]

Elevated maternal sFlt-1 levels inactivate and reduce circulating free placental growth factor (PlGF) and VEGF concentrations, leading to endothelial dysfunction (Maynard, 2003).[31]

Soluble endoglin (sEng), inhibits various transforming growth factor beta (TGF-β) isoforms from binding to endothelial receptors which diminishes endothelial nitric oxide-dependent vasodilatation. (Haggerty, 2012)[32]

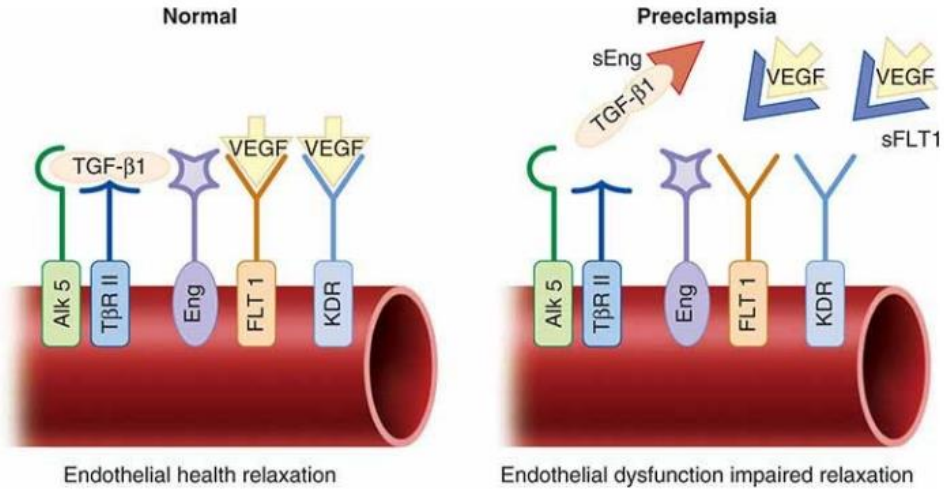


Figure 4:Receptor blocking action of sFlt-1 (soluble fms like tyrosine kinase 1) and soluble endoglin (sEng)

PATHOPHYSIOLOGY:

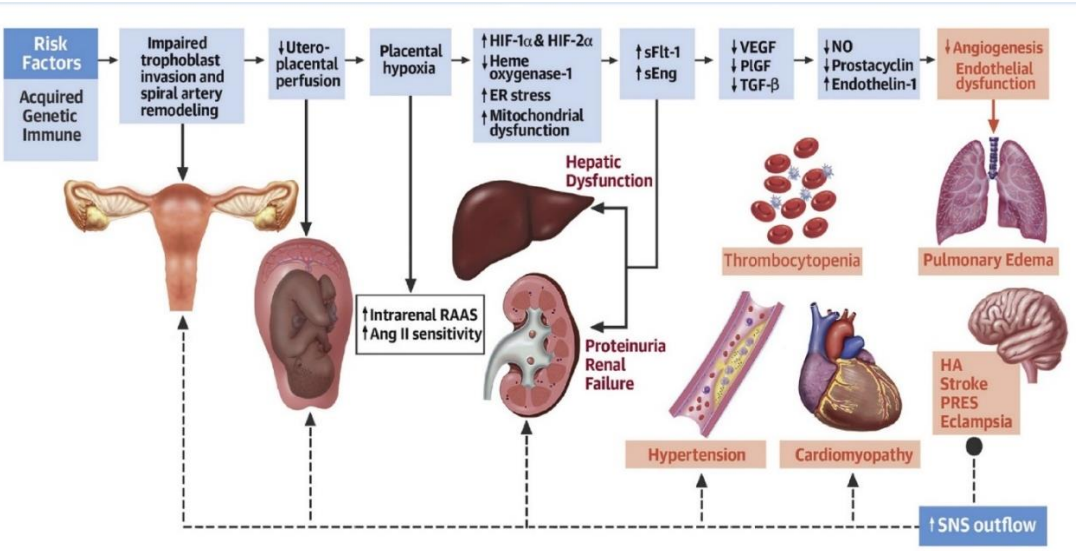


Figure 5: Pathophysiology of pre-eclampsia

CARDIOVASCULAR SYSTEM:

Greater cardiac afterload leads to decreased cardiac output.

Ventricular function is normal in most women or slightly hyperdynamic.

Serial echocardiographic studies document diastolic dysfunction in 40 to 45 percent women. (Guirguis, 2015; Melchiorre, 2012) [33, 34]. High levels of antiangiogenic proteins may be contributory (Shahul, 2016).[35]

Haemoconcentration may be present as evidenced by Zeeman and colleagues in 2009.[27] The frequency and intensity of thrombocytopenia vary and are dependent on the severity and duration of the preeclampsia syndrome (Heilmann, 2007; Hupuczi, 2007) [36, 37]. It usually reaches the normal level within 3 to 5 days after delivery.

Coagulation changes include elevated factor VIII consumption, increased levels of fibrinopeptides A and B and of D-dimers, and reduced levels of regulatory proteins—antithrombin III and proteins C and S. These changes are mild and are not clinically significant (Kenny, 2015; Pritchard, 1984).[38, 39]

ENDOCRINOLOGICAL CHANGES:

Levels of serum ANP (Luft, 2009) [40] and its precursor—proatrial natriuretic peptide—are increased in preeclampsia (Sugulle, 2012).[41]

ELECTROLYTE ALTERATION:

There is not much electrolyte alteration when compared with those of normal pregnant women. However, following an eclamptic convulsion, the serum pH and bicarbonate concentration are lowered due to lactic acidosis and compensatory respiratory loss of carbon dioxide.

KIDNEY:

Reduced renal perfusion and glomerular filtration rate due to high renal afferent arteriolar resistance. (Conrad, 2015; Cornelis, 2011) [42, 43]

Increased serum creatinine up to 1mg/ml which normalizes after delivery within 10 days. (Lindheimer, 2008a)[44] (Cornelis, 2011; Spaan, 2012a).[42, 45]

Increased serum uric acid due to reduced filtration and increased tubular reabsorption. (Chesley, 1945) [46]

Increased serum calcium levels due to increased tubular reabsorption. (Taufield, 1987) [47]

Abnormal protein excretion is defined by 24-hour urinary excretion exceeding 300 mg; a urine protein: creatinine ratio ≥0.3; or persistent protein values of 30 mg/dL (1+ dipstick) in random urine samples. In one report, 17 percent of eclamptic women did not have proteinuria by the time of seizures (Zwart, 2008).[48]

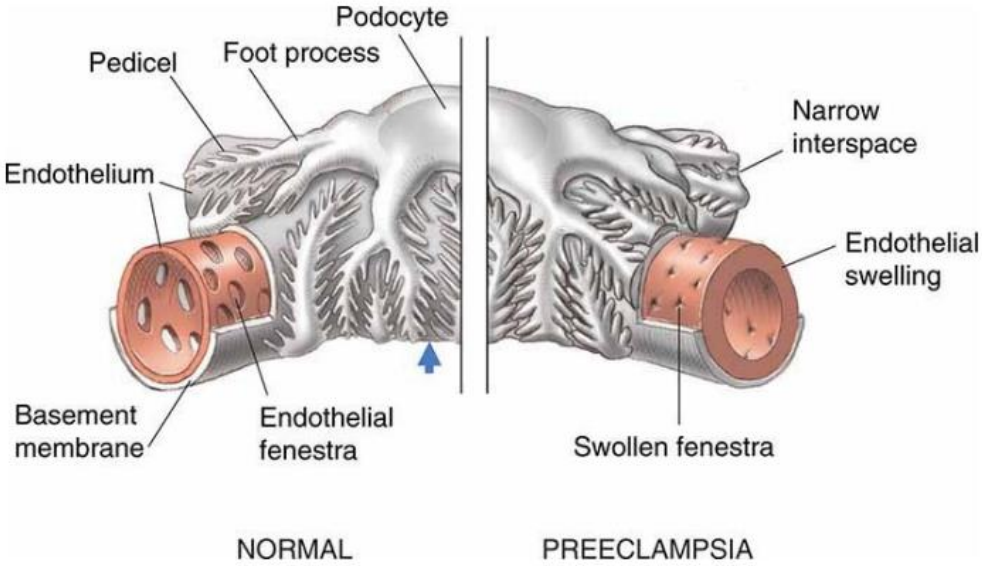


Figure 5: Glomerular capillary endotheliosis in pre-eclampsia

LIVER:

Periportal haemorrhage in the liver periphery are characteristic changes. (Hecht, 2017)[49]

Elevation of serum aspartate transaminase (AST) or alanine transaminase (ALT) levels is a marker for severe pre-eclampsia and normalize within 3 days following delivery.

Haemorrhagic infarction leads to subcapsular haematoma formation which may rupture. It stretches the Glisson's capsule and causes pain. This is more common in HELLP syndrome.

CENTRAL NERVOUS SYSTEM:

In response to acute and severe hypertension, cerebrovascular overregulation leads to vasospasm (Trommer, 1988).[50] This leads to ischaemia, cyototoxic edema and infarction. Sudden elevations in systemic blood pressure exceed the normal cerebrovascular autoregulatory capacity (Schwartz, 2000).[51]

At the capillary level, disruption of end-capillary pressure causes increased hydrostatic pressure, hyper-perfusion, and extravasation of plasma and red cells through endothelial tight-junction openings. This leads to vasogenic oedema.

These manifest as the posterior reversible encephalopathy syndrome (PRES) which appear as hyperintense T2 lesions in the subcortical and cortical regions of the parietal and occipital lobes. (Fugate, 2015)[52]

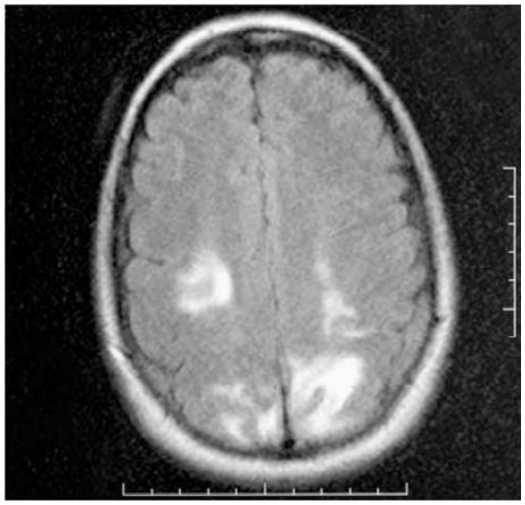


Figure 6: Posterior reversible encephalopathy syndrome (PRES) in MRI brain

Eclampsia occurs when cerebral hyper-perfusion forces capillary fluid interstitially because of endothelial damage. This leak leads to perivascular oedema characteristic of the preeclampsia syndrome. (Zeeman, 2004b)[53]

Up to 75 percent of women have headaches, and 20 to 30 percent have visual changes preceding eclamptic convulsions (Zwart, 2008).[48]

Convulsions are due to excessive release of excitatory neurotransmitters—especially glutamate; massive depolarization of network neurons; and bursts of action potentials (Meldrum, 2002).[54]

Oedema of the occipital lobes or diffuse cerebral oedema may cause symptoms such as blindness, lethargy, and confusion (Cunningham, 2000).[55] Occipital blindness is also called amaurosis. Vision is usually regained within 4–6 weeks following delivery.

The eye symptoms are due to spasm of retinal vessels (retinal infarction-Purtscher retinopathy), occipital lobe damage (vasogenic oedema) or serous retinal detachment. Reattachment of the retina occurs following subsidence of oedema and normalization of blood pressure after delivery. If blindness is caused by retinal artery occlusion, vision may be permanently impaired.

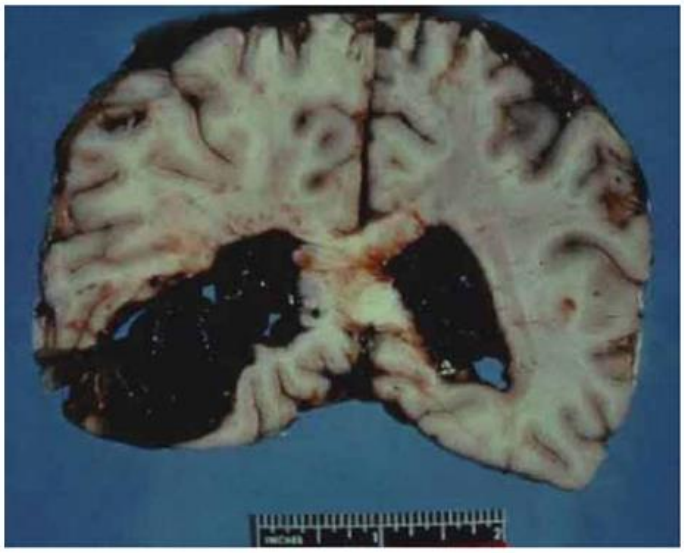


Figure 7: Fatal intracerebral haemorrhage

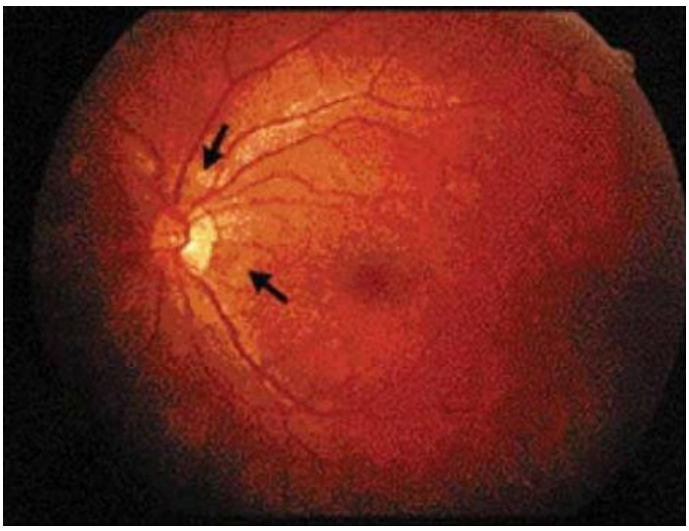


Figure 8: Purtscher Retinopathy

PREDICTORS OF PRE-ECLAMPSIA:

- Hyperuricemia
- Microalbuminuria
- Doppler ultrasound of high resistance index in the uterine artery in second trimester.

- Presence of diastolic notch at 24 weeks' gestation in the uterine artery.
- Absence of end-diastolic frequencies or reverse diastolic flow patterns in the umbilical artery indicates poor perinatal outcome.
- Average mean arterial pressure (MAP) in second trimester > 90 mm Hg may predict the onset.
- Increased serum level of SFlt-1.
- Proteomics, metabolomics and transcriptomic markers are currently being studied.
- Roll over test: This screening test is done between 28 and 32 weeks. An increase of 20 mm Hg in diastolic pressure from side to back position indicates a positive "roll over test". About 33% of women with positive "roll over test" developed hypertension later.
- Cell-free DNA (cf-DNA).

PREVENTION:

Staff [56] in 2015 evaluated some of the methods that could prevent preeclampsia:

a) Dietary modification: low-salt diet, calcium or fish oil supplementation
b) Exercise: physical activity, stretching
c) Cessation of smoking
d) Cardiovascular drugs—diuretics, antihypertensive drugs

e) Antioxidants—ascorbic acid (vitamin C), α-tocopherol (vitamin E), vitamin D

f) Antithrombotic drugs—low-dose aspirin, aspirin/dipyridamole, aspirin + heparin, aspirin + ketanserin. Low dose Aspirin inhibits thromboxane synthesis thus altering the balance in favour of PGI

g) Control of Hypertension in women having chronic hypertension

h) Control of sugar levels in women having Diabetes pre-pregnancy

i) Calcium supplementation: it reduces parathyroid and renin release thereby reducing intracellular calcium and smooth muscle contractility, the ideal patient is the one who is obese with raised BP at booking visit.

Evidence from the latest Cochrane review does not support routine antioxidant administration during pregnancy to reduce the risk of preeclampsia.[57]

A 17% reduction in the risk of preeclampsia associated with the use of antiplatelet agents has been reported. [58, 59]

CLINICAL PRESENTATION:

- Headaches, tinnitus, phosphene signals, visual disorders, brisk tendon reflexes, and vigilance disorders are related to cerebral oedema.
- Oliguria relates to acute renal failure.
- Uterine contraction, vaginal bleeding relates to placental abruption.
- Vomiting relates to hepatic subcapsular haemorrhage.
- Bandlike epigastric pain to subcapsular hepatic hematoma.

- Dyspnoea to cardiac failure.
- Eclampsia
- Eye symptoms—there may be blurring, scotomata, dimness of
- vision or at times complete blindness

CLINICAL SIGNS:

- Abnormal weight gain of more than 0.5 kg per week.
- Abrupt increase in blood pressure.
- Initially it begins as swelling of the ankles, followed by swelling of legs and in severe cases can progress to swelling of the vulva, face, abdomen wall and the whole body.
- Neurologic findings such as papilledema and hyperreflexia must be addressed quickly, as they can herald the onset of eclampsia.
- Petechiae and bruising could suggest coagulopathy.
- Right upper quadrant or mid epigastric tenderness develops as a result of hepatocellular necrosis.
- Pulmonary oedema.

INVESTIGATIONS:

i. Blood grouping and typing

ii. Complete blood count with platelets

iii. Renal Function Test (Urea > 40 mmol/l or >11 mg/dl • Creatinine>1 mg/dl • Serum uric acid levels >6.3 mg/dl)

iv. Liver Function Test (AST or ALT >50 IU/L • Biluribin >25 IU/L)

v. Urine albumin: Proteinuria 2+ or higher is significant

vi. Urine spot PCR (Protein:Creatinine ratio)

vii. Coagulation profile

viii. Lactate dehydrogenase

ix. 24-hour proteinuria

x. Prothrombin, activated thrombin time, and fibrinogen (microangiopathic haemolytic anaemia)

xi. Ophthalmological examination to assess fundal status

xii. Cardiological examination including Echocardiography

xiii. Ultrasound: Confirmation of normal foetal. The following are noted:

- Foetal biometry (AC, HC, BPD, FL)
- Amniotic Fluid Index
- Estimated foetal weight
- Placental localization
- Doppler velocimetry
- Screening test in first trimester to detect changes in spiral arteries and is considered abnormal if there is an early diastolic notch or high RI.

xiv. Foetal monitoring: Daily kick count, Biophysical profile, Cardiotocography

MANAGEMENT OF PRE-ECLAMPSIA:

Termination of the pregnancy is the definitive treatment.

A Dutch study—HYPITAT-II by Broekhuijsen [60] in 2015 concluded that immediate delivery reduced the risks for adverse maternal outcome. However, it increased the risk for neonatal respiratory distress syndrome.

While Hospital admission is advised, outpatient management is not contraindicated but various studies have shown that these outpatient women have an increased chance of developing severe preeclampsia and termination at earlier weeks (Turnbull, 2004) [61]

If the pre-eclampsia features are under control and the pregnancy is remote from term, expectant management is done till 34 wks.

If it's more than 37wks pf gestation, delivery is done without delaying.

If the patient has uncontrolled blood pressure in spite of antihypertensives, have imminent symptoms such as epigastric pain, vomiting, headache, blurring of vision or present as HELLP syndrome, immediate termination of pregnancy irrespective of gestation age is done. Glucocorticoids are given for lung maturity.

ANTIHYPERTENSIVES:

Table 1: Commonly Used drugs in the Management of Preeclampsia

DRUG	MODE OF ACTION	DOSAGE
Labetalol	Adrenoceptor antagonist (α and β blockers)	100 mg tid or qid
Nifedipine	Calcium channel blocker	10–20 mg bid
Hydralazine	Vascular smooth muscle relaxant	10–25 mg bid
Methyl-dopa	Central and peripheral antiadrenergic action	250–500 mg tid or qid

GLUCOCORTICOIDS FOR FETAL LUNG MATURITY:

Administration of Betamethasone 12mg IM every 24 hrs for 2 days or Dexamethasone 6mg IM every 12hrs for 2 days is found to reduce the incidence of respiratory distress, intraventricular haemorrhage and death in preterm babies. (Amorim, 1999) [62]

INDICATION OF IMMEDIATE DELIEVRY IN SEVERE PRE-ECLAMPSIA:

- Persistent symptoms of Severe Preeclampsia
- Pulmonary oedema/hypoxia (PaO2<95%)
- Hepatocellular injury: Increased AST, ALT

- Oliguria <500 mL/24h
- Abnormal coagulation profile
- Non-reassuring foetal status
- Eclampsia

MODE OF DELIVERY:

Depending if the cervix is favorable or not, labor is induced either by mechanical induction using Foley's catheter or by using Prostaglandin gel (PGE2)

If the patient is in active phase, labor is accelerated with amniotomy (if membranes were present) and oxytocin infusion.

Cesarean section is indicated when the cervix is unfavorable, or for obstetric indications such as contracted pelvis, elderly primi, malpresentation etc.

MANAGEMENT DURING LABOUR:

- Blood pressure monitoring.
- Urine Input and Output monitoring.
- Fetal heart rate monitoring.
- Prophylactic Magnesium Sulphate if Systolic BP >160 mmHg and Diastolic BP >110mmHg, or MAP >125mmHg.

- Labour is cut short by early Artificial Rupture Of Membrane. (ARM) and syntocinon acceleration. Second stage is cut short using Venthouse or Forceps.
- Intravenous Ergometrine is avoided as it shoots up Blood Pressure.

ECLAMPSIA:

Eclampsia is preeclampsia complicated by generalized tonic-clonic convulsions The hospital incidence in India ranges from 1 in 500 to 1 in 30. It is more common in primigravidae (75%), five times more common in twins than in singleton pregnancies and occurs between the 36th week and term in more than 50% cases.

The incidence of eclampsia is decreased in recent years due to improved access to prenatal care, earlier detection of antepartum preeclampsia, and prophylactic use of magnesium sulfate (Chames, 2002).[63]

HISTORY OF ECLAMPSIA:

Ancient accounts of eclampsia and childbirth are available in medical writings of Egyptian, Indian, Chinese, and Greek civilizations.

The term “eclampsia” was used by ancient Greeks. Prior to the 18th century, the term “eclampsia” was used to refer to the visual phenomenon associated with this disorder.

Mauriceau, a noted French obstetrician, in 1673 gave a detailed description of the subject in his book, and he believed that eclampsia improved after delivery.[64, 65]

The discovery of proteinuria in eclampsia was made by LC Lever of London and JY Simpson of Scotland in 1843. Lever recommended periodic testing of urine for proteinuria in pregnancy.

Georg Schmorl, in 1893, first demonstrated the presence of fetal cells in the maternal body and emphasized the importance of the placenta in eclampsia.[66]

Until the middle of the 19th century, treatment of eclampsia was mostly by physical methods and expediting the delivery. Physical methods were bleeding by venesection, blistering, immersion in hot water, and hot compress in kidney regions.

As early as 1906, magnesium sulphate was injected intrathecally to prevent eclamptic seizures by Horn.

Because of reports that intramuscular magnesium sulphate–controlled convulsions associated with tetanus, a similar regimen was used by Lazard and Dorsett in 1926 to prevent recurrent seizures in women with eclampsia.

In 1933, the drug was given intravenously to hundreds of women with preeclampsia and eclampsia at the Los Angeles General Hospital.[64,67]

CAUSES OF ECLAMPSIA:

The cerebral irritation can occur due to

- Cerebral oedema
- Increases release of neurotransmitters
- Anoxia due to cerebral vasospasm

TYPES OF ECLAMPSIA:

- Antepartum Eclampsia (38% to 53%),
- Intrapartum eclampsia (18% to 36%)
- Post-partum Eclampsia (11% to 44%)[68]: occurs either before or within 48 hours of delivery.
- Late postpartum eclampsia: Eclampsia occurring more than 48 hours, but less than 4 weeks.

CLINICAL FEATURES OF ECLAMPSIA:

There are 4 stages of eclampsia:

a) PREMONITORY STAGE: (30 seconds)

The patient becomes unconscious.

There is twitching of the muscles of the face, tongue and limbs.

Eye ball roll or are turned to one side.

b) TONIC STAGE: (30 seconds)

The whole body goes into a tonic spasm - the trunk-opisthotonus, limbs are flexed and hand clenched.

Respiration ceases and the tongue protrudes between the teeth.

Cyanosis appears. Eye balls become fixed.

c) CLONIC STAGE: (1 to 4 minutes)

All the voluntary muscles undergo alternate contraction and relaxation.

Tongue bite occurs.

Cyanosis gradually disappears.

d) STAGE OF COMA: (varies in duration)

Following the fit, the patient passes on to the stage of coma.

If the convulsions occur recurrently, it is called as Status Eclampticus which might need sedation and general anaesthesia.

COMPLICATIONS OF ECLAMPSIA:

MATERNAL COMPLICATIONS:

- HELLP syndrome (3 %)
- Disseminated Intravascular Coagulopathy (DIC) (3 %)
- Acute Kidney Injury (4 %)
- Adult respiratory distress syndrome (3 %)
- Cerebrovascular haemorrhage (< 2 %)
- Permanent CNS damage.
- Death (1.8 %)
- Liver failure and subcapsular haemorrhage
- Injuries: Tongue bite, injuries due to fall from bed, bed sore.

FETAL COMPLICATIONS:

- Intrauterine growth restriction (IUGR).
- Prematurity.
- Infant respiratory distress syndrome.
- Intrauterine foetal death.
- Placental abruption.
- Perinatal death
- Hypoxic neurological injury

MANAGEMENT OF ECLAMPSIA:

GENERAL MANAGEMENT: This includes the following:

1.SUPPORTIVE CARE:

- To prevent maternal injuries from fall, she is kept in a railed cot. A tongue blade is given to prevent tongue bite.
- To prevent aspiration, she is kept in the left decubitus position
- Frequent suctioning is done to remove the oral secretion and the vomit.
- Nasal O2 using a face mask at 8 to 10litres/minute is given to prevent respiratory
- Arterial blood gas analysis if the saturation falls to less than 92%.

2. DETAILED HISTORY:

- A detailed history s obtained from the relatives including the number of fits, its duration and treatment history.

3.EXAMINATION:

- After stabilization, a quick general and systemic examination is done. Obstetric exanimation is done to see if the cervix is favourable and viability of the fetus is checked for.
- A self-retaining Folay's catheter is introduced and the urine is tested for protein. This also helps in monitoring the urinary output.

4.MONITORING:

- Half hourly pulse, respiration rate and blood pressure monitoring
- Hourly urinary output monitoring.
- Uterine contractions are checked for the progress of labour.
- Careful foetal heart rate monitoring. Foetal bradycardia after a fit is transient and not uncommon.

5. FLUIDS IN ECLAMPSIA:

- Crystalloid solution (Ringer's solution) is the fluid of choice.
- Total fluids should not exceed the previous 24 hours urinary output plus 1000 mL
- Dextrose and colloids tend to cause circulatory overload and can cause pulmonary oedema.

6. ANTIBIOTICS:

- To prevent infection.

SPECIFIC MANAGEMENT:

1. ANTICONVULSANTS:

The Eclamptic Trial Collaborative Group in 1995 showed that magnesium sulphate given intramuscularly or intravenously is superior to phenytoin or diazepam in reducing recurrent eclamptic seizures. [5]

Another study revealed that magnesium was superior to phenytoin for prophylaxis against eclamptic seizures.[69]

In a Cochrane review, authors found that magnesium sulphate, rather than phenytoin, reduces the risk ratio of recurrence of seizures, risk of maternal death, and improves outcome for the baby.[70] They concluded that MgSo4 should be the drug of choice and phenytoin to be abandoned.

In another Cochrane review, magnesium sulphate was found to be more effective than diazepam for treatment of eclampsia (LEAN REGIEMN) [71]

Diazepam or lorazepam does stop or shorten seizures, but there is risk of maternal apnoea and/or cardiac arrest.

In a later review, the same group of authors compared magnesium sulphate compared with lytic cocktail (comprised of chlorpromazine, promethazine and pethidine). It was concluded that the use of lytic cocktail should be abandoned. (MENON REGIMEN) [72]

Magnesium sulphate is more effective than nimodipine for prophylaxis against seizures in women with severe preeclampsia.[73]

Magnesium sulphate was found to be the most effective agent in relation to a number of measures maternal and perinatal morbidity (MAGPIE Trial).[3] Women treated with magnesium had a 52% lower risk of recurrent convulsions than those treated with diazepam and a 67% lower risk than those treated with phenytoin.

In patients with eclampsia, Magnesium sulphate remains the agent of choice for treatment of posterior reversible encephalopathy syndrome when compared to Mannitol.[74]

Magnesium sulphate also plays a neuroprotective role in preterm babies as evidenced by PREMAG Trials. (Marret et al, 2007).[75]

In Parkland hospital in the year 1955, Pritchard used both IV & IM of MgSO4 regimen.

MAGNESIUM SULPHATE:

Magnesium sulphate (MgSO4) is the first anticonvulsant of choice to prevent and control eclamptic events.

Severe preeclampsia should be treated with magnesium to prevent progression to eclampsia.

The mechanism of action of magnesium sulfate is thought to trigger cerebral vasodilation, thus reducing ischemia generated by cerebral vasospasm during an eclamptic event.

The substance also acts competitively in blocking the entry of calcium into synaptic endings, thereby altering neuromuscular transmission. Being a

calcium antagonist, its effect on vascular smooth muscle to promote relaxation and vasodilation may have a role in lowering total peripheral vascular resistance.

$MgSO_4$ treatment significantly decreased circulating levels of angiotensin-converting enzyme. These actions may attenuate the endothelial dysfunction associated with pre-eclampsia.

In addition, $MgSO_4$ may have an effect on the cerebral endothelium to limit vasogenic edema by decreasing stress fiber contraction and paracellular permeability via calcium-dependent second messenger systems. [76]

Lastly, $MgSO_4$ may also act centrally to inhibit NMDA receptors, providing anticonvulsant activity by increasing the seizure threshold.[76]

PHARMACOLOGICAL ASPECT:

- The chemical formula of MgSO4 is $MgSO_4.7H_2O$
- 1 gm of MgSO4 has 98mg of elemental Magnesium.
- Ph is 6.0 (5.5 to 7.0)
- The Osmolarity of 50% MgSO4 is 4.06 mosm/ml.
- It should be stored in room temperature.

PLASMA LEVELS AND DISTRIBUTION:

40% is protein bound and the remaining 60% of magnesium diffuse into extravascular compartment like the extracellular space. It crosses the placenta, into the fetus and liquor.

The volume of distribution reaches constant levels in the 4th hour after administration.

PHARMACOKINETICS:

There are 2 phases: A Rapid Distribution phase and Slow phase of Elimination.

EXCRETION:

Primarily by kidneys. 50% of the dose is excreted after 4 hours and 90% of the total dose is excreted with in a period of 24 hrs.

DRUG INTERACTIONS:

The following group of drugs affect the binding capacity of magnesium sulphate:

- Diuretics
- Aminoglycosides
- Cyclosporine

THERAPEUTIC LEVELS:

Therapeutic levels of serum magnesium: 4 -7 mEq/L (4.8 – 8.4gm/dL)

Magnesium toxicity and serum Mg is seen as

- Loss of deep tendon reflex > 7mEq/L
- Respiratory depression > 10 mEq/L
- Cardiac arrest >25mEq/L

Duley at al [77] showed that there is no need to measure the Serum Magnesium level. Serum magnesium measurement is used only for the patients who develop magnesium toxicity symptoms.

American College of Obstetricians and Gynecologists (2002)[78] a; Royal College of Obstetricians and Gynecologists (2006)[79] has recommended that it is not needed to measure the plasma magnesium level in all cases routinely.

MAGNESIUM TOXICITY:

1g of 10% Calcium gluconate or calcium chloride intravenously over 15 minutes.

Along with this magnesium sulphate is stopped to reverse the toxic effect of respiratory depression.

For severe respiratory depression or respiratory arrest mechanical ventilatory support becomes necessary.

MONITORING MAGNESIUM SULPHATE THERAPY:

Pulse, blood pressure, respiratory rate and patellar reflexes are checked before and after the loading dose.

While the maintenance infusion is running, observe for any adverse effects.

4 hourly blood pressure, hourly pulse rate monitoring, hourly respiratory rate, hourly patellar reflexes,4th hourly urine output monitoring and fetal heart rate are monitored.

Strict urine input and output chart is maintained.

The woman should be reviewed and discontinuation of the infusion should be considered if

- Respiratory rate is less than 12 breaths per minute
- Absent patellar reflexes
- Hypotension
- Urine output is less than 100 ml over 4 hours.

OTHER EFFECTS:

- Tocolytic effect used for uterine relaxation.
- Neuroprotective dose in preterm babies.

Nelson assessed the neuro protective effects.[80]

Doyle and associates concluded that gross motor dysfunction was reduced in the babies of mothers treated with MgSO4.[81]

ADVERSE EFFECTS:

Vasodilatory effects:

- Feeling of warmth/ Flushing
- Lethargy
- Facial flushing
- hypotension

Other side effects:

- Sweating
- Diminished reflexes
- Confusion, Drowsiness
- Intense thirst
- Nausea
- Respiratory depression

CONTRAINDICATIONS:

- myasthenia gravis [82]
- heart block
- renal disease
- recent myocardial infarction [83]

MAGNESIUM SUPLHATE REGIMENS:

The various Magnesium sulphate regimens are:

1. Pritchard Regimen
2. Zuspan Regimen
3. Sibai Regimen
4. Padhar Regimen
5. Dhaka Regime
6. Sokkotto Regimen

Flower [84] et al adjusted doses according to body weight. In 2003 Sardesai Suman[85] et al studied low dose MgSO4 in Indian women. He reported 90% control of eclampsia and safety and efficacy of low dose MgSO4 inferred.

In Dhaka regimen there was 98% control of eclampsia.

PRITCHARD REGIMEN:

- Loading dose of 4 gm MgSO4 (20 ml of 20%-8ml of MgSO4 + 12 ml of Normal Saline) IV over 3 to 5 minutes which was immediately followed by 10 gm IM (50% MgSO4), 5 gm in each buttock)
- Maintenance dose of 5 gm (10 ml of 50% MgSO4) was given 4th hourly IM in alternate buttocks till 24hrs after delivery or after last convulsion, whichever was later.

ZUSPAN REGIMEN (1964):

- Loading dose of 4 gm MgSO4 (20 ml of 20% - 8ml of MgSO4 + 12 ml of Normal Saline) IV over 15 to 20 minutes
- Maintenance dose of 1gram MgSO4/ hour (10 ml i.e. 5g of MgSO4 + 40 ml of Normal Saline at the rate of 10ml/hr) via infusion pump till 24hrs after delivery or after last convulsion, whichever was later.

SIBAI REGIMEN: [86]

- Loading dose of 6 gm of 20% MgSO4 IV.
- Maintenance dose of IV infusion of 20% MgSO4 for 24 hours after the fit.

PADHAR REGIMEN: [87]

- Loading dose of 6 gm of 50% MgSO4 IV
- Maintenance dose: IM administration of 4 gm of 20% MgSO4.

In a Prospective study conducted in Padhar hospital, India, out of 95 eclampsia cases only one woman had recurrent fits. She was given 5 gm as IM maintenance.

DHAKA REGIMEN (1998):

- Loading dose of 4 gm of 20% MgSO4 IV at a rate not exceeding 1 gm per minute. IM 6 gm of 50% MgSO4 as deep IM, 3gm in each buttock.
- Maintenance dose of 2.5gm of 50% MgSo4 IM on alternate buttock every 4 hours.

This prospective study was done in in Dhaka Medical college hospital in March to June 1998. Out of 65 eclamptic patients only one developed recurrent fit that occurred 3 hours after the loading dose. It was treated with diazepam and intramuscular maintenance dose. It was concluded that half the dose will be enough to control the fits.

SOKOTTO REGIMEN: [88]

- Ultra-Short Dose of IV administration of 4 grams of 20% MgSO4 followed by intramuscular administration of 10 gms of 50% MgSO4.

At Sokkotto, capital city of Nigeria, a study was conducted in the year july 2007 to june 2008 to study the efficacy of the ultra-short regimen in

antepartum, intrapartum, postpartum eclamptic patients. There was 7.4% of recurrent seizures within 4 hours of loading dose in this study. Out of 121 patients, 12 mothers died. Thus, case fatality rate was 9.9% in that study. Thus, it was concluded that the efficacy of Sokkoto's regimen was 92.6% in that study.

OTHER LITERATURES:

- Tripti et al concluded that the single loading low dose MgSo4 regimen is an effective and safe alternative to the Pritchard's regimen, especially tailored to the small built Indian women. [89]
- Singh et al studied the efficacy of Pritchard, Sibai and Zuspan regimen in Eastern India and concluded that Magnesium sulphate was equally effective in controlling seizures in the three groups. [90]
- Jeremy.J.Pratt et al reviewed various studies on different regimens of magnesium sulphate and concluded that lower-dose and loading dose-only regimens could be as safe and efficacious as standard regimens.[91]
- Sipra Singh et al compared the safety and efficacy of intravenous versus intramuscular MgSO4 and concluded that both IM and IV regimen are equally effective in controlling the recurrence of eclamptic fits. IM Magnesium Sulphate had a higher incidence of toxicity as evidenced by significantly higher incidence of loss of knee jerk reflux. [92]
- Shailey Agarwal et al compared Pritchards, Zuspan and Dhaka regimen and found higher incidence of signs of impending toxicity such as loss of patellar reflex, oliguria, respiratory rate depression more Pritchard's as

compared to other groups. There were no significant differences in other measures of feto-maternal complications. They concluded that Zuspan and Dhaka (Low dose regimens) have similar efficacy in controlling and prevention of convulsions & potentially have less side effects. [93]

TABLE 2: Comparison Of Various $Mgso_4$ Regimen

REGIMEN	RECURRENCE	MATERNAL MORTALITY	AUTHOR
Single Dose MgSo4	9.16%	3.3%	Joshi & Veerendrakumar [94]
Pritchard	12%	0.4%	Prichard et al [95]
Low Dose MgSo4	7.8%	2.6%	Suman Sardesai et al [85]
Eclampsia trial group	5.3–13.2 %	3.8-5.2%	Eclampsia trial group[5]
Dhaka regimen	1.53%	8.6%	Begum et al [96]
Padhar regimen	1.05%	NIL	Mahajan [87]
Low dose maintenance	2%	3.3-5%	Chowdhury [97]

2. ANTIHYPERTENSIVES:

First line of antihypertensive drugs are: labetalol and hydralazine (ACOG-2011).

Target level of BP is SBP; 140–160 mm Hg and DBP: 90–100 mm Hg.

In case of pulmonary oedema, Frusemide is given at dosage of 20 – 40mg.

HYPERTENSIVE CRISIS:

Following JNC 7 definitions, a hypertensive crisis occurs when systolic BP (SBP) rises above 180 mmHg or a diastolic BP (DBP) above 120 mmHg.

Table 3: Commonly Used drugs in the Management of Hypertensive Crisis

DRUG	ONSET OF ACTION	DOSE SCHEDULE	MAXIMUM DOSE	MINIMUM DOSE
Labetalol	5 min	10–20 mg IV every 10 minute	300 mg IV	40 mg/h
Hydralazine	10 min	5 mg IV every 30 minute	30 mg IV	10 mg/h
Nifedipine	10 min	10–20 mg oral, can be repeated in 30 minute	240 mg/ 24 hr	4–6 hours interval
Nitroglycerin Sodium nitroprusside	0.5–5 min	5 µg/minute IV 0.25–5 µg/kg/minute IV		Short-term therapy only when the other drugs have failed

STATUS ECLAMPTICUS:

Thiopentone sodium 0.5 g dissolved in 20 mL of 5% dextrose is given intravenously very slowly by anaesthetist.

TREATMENT OF COMPLICATIONS:

- Pulmonary oedema: Inj Frusemide 40mg followed by Inj Mannitol 20mg reduces pulmonary oedema.
- Heart failure: Diuretic, Digitalis, Oxygenation and other anti-failure measures are done.
- Anuria: Most commonly anuria resolves after delivery. Dopamine infusion at rate of 1mcg/kg may be needed.
- Hyperpyrexia: Tepid sponging and Anti-pyretics may be given.
- Psychosis: Chlorpromazine or Trifluoperazine is given

OBSTETRIC MANAGEMENT:

Immediate termination of pregnancy and acceleration of labour after stabilization of the patient. In case of prematurity, delivery in a Tertiary care centre is mandatory.

Vaginal delivery is attempted in a patient with a favourable Bishop score.

The second stage of labour should be cut short and outlet forceps can be used.

The third stage of labour should be treated actively to prevent Post-Partum Haemorrhage. Eclamptic patients have decreased blood volume when compared to normal pregnant patients and hence cannot withstand postpartum haemorrhage.

This is done by Active Management of Third Stage of Labour by giving Inj. oxytocin 10 units IM immediately after the delivery of anterior shoulder.

Post-partum haemorrhage is managed by uterine massage, Inj.Carboprost (PGF2α analogue) 250μg as intramuscular injection or Tab.Misoprostol (PGE1 analogue) 600 to 800μg kept per rectally. Methyl erogometrine is contraindicated as it can shoot up the blood pressure. Blood transfusion is given for the required cases.

Indications for caesarean section:

- Uncontrolled fits in spite of therapy.
- Unconscious patient and poor prospect of vaginal delivery.
- Obstetric indications.

FOLLOW UP AND PROGNOSIS:

Fluids should be administered carefully to avoid a volume overload state.

Anti-hypertensives are tapered slowly.

Patient should be followed up in the postnatal clinic by 6 weeks. Further pregnancy should be deferred till blood pressure is under control.

RECURRENCE:

Recurrence risk varies between 2% and 25%. The risk of preeclampsia and eclampsia to the daughter of an eclampsia patient is about 25% and 3%, respectively.

LONG TERM CONSEQUENCES OF PRE-ECLAMPSIA SYNDROME:

CARDIOVASCULAR:

- Chronic hypertension
- Ischemic heart disease
- Atherosclerosis
- Coronary artery calcification
- Cardiomyopathy
- Thromboembolism

NEUROVASCULAR:

- Stroke
- Retinal detachment
- Diabetic retinopathy

METABOLIC:

- Type 2 diabetes
- Metabolic syndrome
- Dyslipidemia
- Obesity

RENAL:

- Glomerular dysfunction

- Proteinuria

CENTRAL NERVOUS SYSTEM:

- White-matter lesions
- Cognitive dysfunction
- Retinopathy

ATYPICAL PRE-ECLAMPSIA:

It is defined as the development of preeclampsia/eclampsia without fulfilling the standard definition or criteria.

The common presentations are:

- Early onset preeclampsia/ eclampsia less than 20 weeks.
- Late postpartum preeclampsia/ eclampsia more than 48 hours postpartum.

They should be treated as if they have severe preeclampsia. They are also treated with parenteral MgSO4.

HELLP SYNDROME:

HELLP Syndrome stands for Hemolysis (H), Elevated Liver enzymes (EL) (70 IU/L, LDH >600 IU/L) and Low Platelet count (LP)

Bilirubin is elevated (>1.2 mg/dL)

There may be subcapsular hematoma formation and abnormal peripheral blood smear. Eventually liver may rupture to cause sudden hypotension, due to hemoperitoneum.

Definitive treatment of HELLP syndrome is immediate termination of pregnancy, transfusion of blood and blood products and other supportive measures.

Various trials were out to find out the efficacy of Steroids in managing HELLP syndrome but none were definitive. (Pourrat, 2016) [98]

RECENT ADVANCES:

HDP-Gestosis score:

It is an effective and feasible prediction policy.

This score involves all the existing and emerging risk factors in the pregnant woman.

Score 1, 2 and 3 is allotted to each clinical risk factor as per its severity in development of preeclampsia.

The score is assessed on very visit to the Antenatal clinic.

When the total score is =/> 3; the pregnant woman should be marked as 'At risk for Preeclampsia' and started with Aspirin 75-150 mg.[99]

Along with aspirin, calcium 1-1.5 gm daily (in low calcium intake group) is to be started.[100]

LOW RISK FACTORS:
(1 POINT FOR EACH)

1. Maternal age > 35 years
2. Maternal age <19 years
3. Obesity (BMI >30 kg/m2)
4. Woman born as SGA
5. Nulligravida
6. Short duration of paternity(coinhabitation)
7. Maternal anemia
8. PCOS
9. Chronic vascular disease(dyslipidemia)
10. Interpregnancy interval > 7 years
11. Excessive maternal weight gain during pregnancy
12. MAP >/= 85 mmHg
13. ART Pregnancy (IVF/ ICSI)
14. Family history of cardiovascular disease

MODERATE RISK FACTORS
(2 POINTS FOR EACH)

1. Gestational diabetes mellitus
2. Obesity (grade 3) (BMI>40 kg/m2)
3. Multiple pregnancy
4. Hypertensive disorders during previous pregnancy
5. Maternal hypothyroidism
6. Family history of pre-eclampsia

HIGH RISK FACTORS
(3 POINTS EACH)

1. Pregestational diabetes mellitus
2. Chronic hypertension
3. Mental disorders (schizophrenia)
4. Inherited or acquired thrombophilia
5. Maternal chronic kidney disease
6. Autoimmune (SLE, APLA)
7. ART (donor oocyte)

SCREENING TECHNIQUES

Maternal Factors + Mean Arterial Pressure + Uterine artery PI (raised) + Pregnancy Associated Plasma Protein -A (PAPP-A < $5^{th)}$ + Placental Growth Factor (PlGF reduced) = 93 to 95% sensitivity

PIERS MODEL (Pre-eclampsia Integrated Estimate of Risk)

The PIER score is a recently designed tool which assesses maternal signs, symptoms, and laboratory findings to generate a valid and reliable algorithm for predicting maternal and perinatal outcome in patients with preeclampsia.

The **fullPIERS** calculator includes gestational age at diagnosis, the symptom complex of chest pain and/or dyspnoea, oxygen saturation by pulse oximetry, and laboratory estimation of platelet count, serum creatinine, and aspartate transaminase.[101] It was was able to predict adverse maternal outcomes in women admitted with early-onset preeclampsia within 48 hours of admission and up to 7 days.

Because there is a shortage of health care workers who are adequately trained in many Low- and middle-income countries (LMIC), the researchers developed **miniPIERS**, a clinical risk prediction model for adverse outcomes among women with hypertensive disorders of pregnancy suitable for use in community and primary health care facilities.[102]The miniPIERS model included parity, gestational age, headache/visual disturbances, chest pain/shortness of breath, vaginal bleeding with abdominal pain, systolic blood pressure, and proteinuria detected using a dipstick.

It had a good discriminatory ability with an accuracy of 85.5% [102]

AIMS AND OBJECTIVE OF THE STUDY

The main purpose of the study is to compare the efficacy and safety of intravenous MgSo4 (Zuspan regimen) versus intramuscular MgSo4 (Pritchard's regimen) in severe pre-eclampsia and eclampsia patients in GRH,Madurai.

- PRIMARY OUTCOME: Safety of Zuspan regimen in terms of development of adverse effects and the need to withhold MgSO4 regimen. Efficacy in terms of comparison of serum magnesium levels with the therapeutic levels.
- SECONDARY OUTCOME: Maternal morbidities (recurrence of convulsion, HELLP, DIC, pulmonary oedema, Postpartum haemorrhage, intracranial haemorrhage) and feto-maternal outcome (low birth weight, still birth, neonatal death).

MATERIALS AND METHOD

SOURCE OF DATA:

The study is conducted in 100 Antenatal mothers with severe pre-eclampsia and eclampsia admitted in GRH Madurai.

METHODS OF COLLECTION OF DATA:

Study design: Prospective interventional study

Study period: 1 year.

Sample design: Simple Random Sampling

Sample size:100

INCLUSION CRITERIA:

- Antenatal mothers diagnosed as severe pre-eclampsia and imminent eclampsia irrespective of their age, parity, gestational age and booking status
- All types of eclampsia – antepartum, intrapartum, postpartum

EXCLUSION CRITERIA:

- Non-severe pre-eclampsia
- Chronic hypertension
- Other causes of convulsion: Epilepsy/ Cerebrovascular accidents/meningitis

- Patients treated outside with MgSO4
- Maternal renal failure/ Chronic kidney disease
- Myasthenia gravis
- Cardiac conduction defects
- HELLP syndrome

METHODOLOGY

The study was conducted in 100 Antenatal mothers with severe pre-eclampsia, imminent eclampsia and eclamptic mothers admitted in labour ward at GRH, Madurai for a period of 1 year after obtaining ethical clearance.

The patients were randomly assigned into two groups (group A and group B) by using random numbers.

Informed and written consent were obtained from all the patients or the next of kin if the patient was not conscious or oriented. Counseling about the needs and methods of study was done.

Detailed history taking, Blood pressure recording, general examination, per abdomen, pelvic examination and routine investigations is taken.

Totally about 152 eclampsia cases were admitted in the study period of which 52 patients were excluded according to exclusion criteria.

History taking and General examination:

History regarding her age, parity, booking status, gestational age, whether she was a known case of pregnancy induced hypertension, whether she

is on anti-hypertensive drugs, presence of edema, existence of imminent symptoms like head ache, vomiting, blurring of vision were all elicited thoroughly.

General examination included pulse, blood pressure, pallor, icterus and edema.

Systemic examination included respiratory system examination, cardiovascular system examination, obstetric pelvic examination, neurological examination and fundal examination.

Obstetric examination:

Per abdomen examination of uterine fundus height, presence of contractions and the viability of the fetus was done. Per vaginal examination done under strict aseptic precautions. Favorability of the cervix assessed by Modified Bishop's score.

Blood samples were sent for Complete blood count, Renal Function Test and Liver Function Test.

The patient was catheterized with Foley's indwelling catheter and urine output noticed immediately and monitored every hour. Urine sample was sent for estimation of proteinuria.

GROUP A

- Group A was administered Zuspan regimen
- Loading dose of 4 gm MgSO4 (20 ml of 20% - 8ml of MgSO4 + 12 ml of Normal Saline) IV over 15 to 20 minutes

- Maintenance dose of 1 gram MgSO4/ hour (10 ml i.e. 5g of MgSO4 + 40 ml of Normal Saline at the rate of 10ml/hr) via infusion pump till 24hrs after delivery or after last convulsion, whichever was later.
- Total dose: 28 grams/24 hrs

GROUP B

- Group B was administered Pritchard's regimen
- Loading dose of 4 gm MgSO4 (20 ml of 20%-8ml of MgSO4 + 12 ml of Normal Saline) IV over 3 to 5 minutes which was immediately followed by 10 gm IM (50% MgSO4), 5 gm in each buttock)
- Maintenance dose of 5 gm (10 ml of 50% MgSO4) was given 4th hourly IM in alternate buttocks till 24hrs after delivery or after last convulsion, whichever was later.
- Total dose: 44 grams/24 hrs

In both these groups, if convulsions persisted after 15 minutes of administering the loading dose, 2 gm of MgSO4 was given IV over 5 minutes. If the patient seizes despite magnesium therapy, midazolam 1-2mg IV is given.

Side effects include nausea, vomiting, flushing, dizziness, loss of patellar reflex, blurred vision, respiratory depression, oliguria, eclamptic seizures.

Serum Magnesium was checked after 4 hours from administration the loading dose.

MONITORING MAGNESIUM SULPHATE:

Pulse, blood pressure, respiratory rate and patellar reflexes are checked before and after the loading dose.

While the maintenance infusion is running, observe for any adverse effects.

4 hourly blood pressure, hourly pulse rate monitoring, hourly respiratory rate, hourly patellar reflexes,4^{th} hourly urine output monitoring and fetal heart rate are monitored.

Strict urine input and output chart is maintained.

The woman should be reviewed and discontinuation of the infusion should be considered if

- Respiratory rate is less than 12 breaths per minute
- Absent patellar reflexes
- Hypotension
- Urine output is less than 100 ml over 4 hours.

MANAGEMENT FOR MAGNESIUM TOXICITY:

Injection calcium gluconate 10ml (10% solution) slowly by intravenous route.

MANAGEMENT OF BLOOD PRESSURE:

Hypertension is treated with Tab Labetalol 100mg, Tab Nifedipine 10mg and IV Labetalol.

OBSTETRIC MANAGEMENT: -

Mode of delivery was decided according to the Modified Bishop scoring, Gestational age and the viability of fetus.

Antenatal corticosteroids were given for fetal lung maturity in preterm patients.

Labor was induced either by mechanical induction using Foley's catheter or by using Prostaglandin gel (PGE2)

If the patient is in active phase, labor was accelerated with amniotomy (if membranes were present) and oxytocin infusion. Careful fetal heart rate monitoring and partograph was plotted.

Cesarean section (or) Hysterotomy was performed in patients with unfavorable cervix, obstetric indication and for failed induction.

Weight of the baby, APGAR score and neonatal outcome were recorded.

FOLLOW UP AFTER DELIVERY:

Complete blood count and Renal function test were repeated after administrating MgSo4.

Post discharge management:

Home BP monitoring by self or a visiting Healthcare Worker should be regularly practiced and OPD review must be within 3-5 days or earlier if symptoms persist or recur.

Postpartum Care:

Every patient of preeclampsia should be monitored closely for 3 months with advice regarding antihypertensive medicines and regular visits.

They should be encouraged to use contraception at least for a period of 2-3 years. The preferred method would be an IUCD.

Long term surveillance:

Every mother should be advised long term surveillance as preeclampsia increases long-term risk of chronic hypertension, IHD, cerebrovascular disease, kidney disease, Diabetes Mellitus, thromboembolism, hypothyroidism and impaired memory.

RESULTS AND ANALYSIS

This study was done in hundred pre-eclampsia patients, who were admitted in labour ward. The data collected from the both groups were analysed and statistically verified by non-parametric Chi square (X^2) test. A p value of < 0.05 was taken as statistically significant.

AGE IN DISTRIBUTION:

Age distribution in both the study groups varied to a certain extent but was not statistically significant.

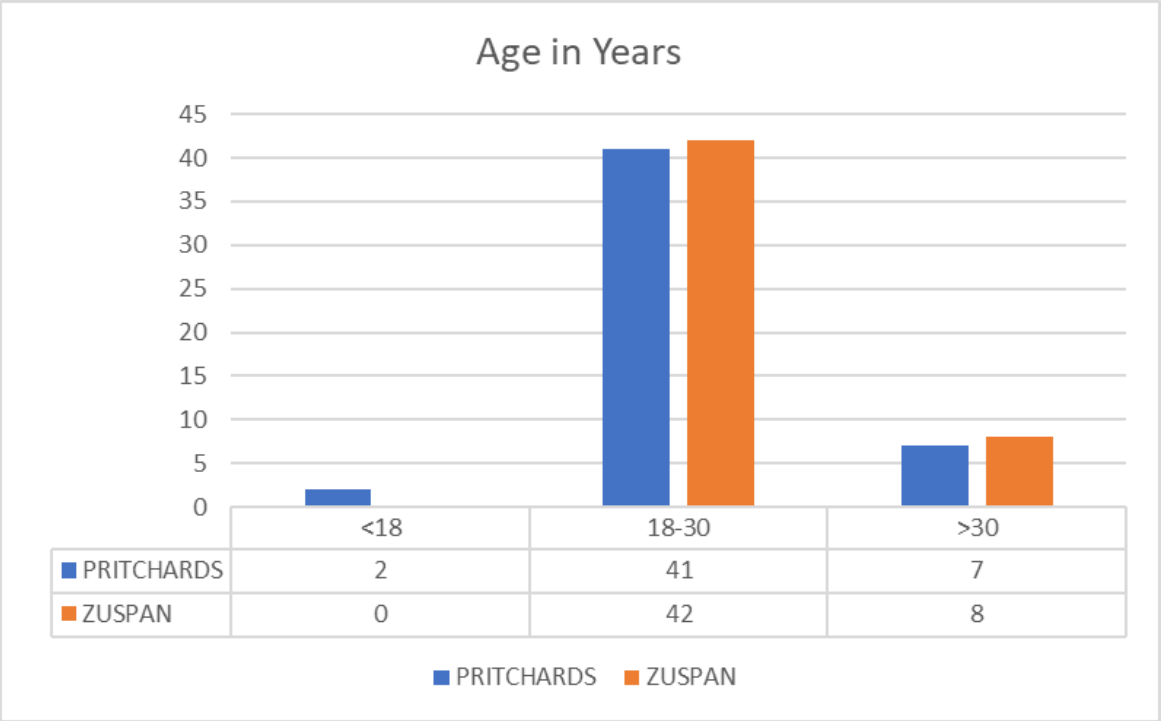
Table 4: Distribution in Age

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
AGE GROUP	<18 YEARS	2	0
		4.0%	.0%
	18-30 YEARS	41	42
		82.0%	84.0%
	>30 YEARS	7	8
		14.0%	16.0%
Total		50	50
		100.0%	100.0%

Table 5: Statistical Analysis

	MGSO4 REGIMEN	**N**	**Mean**	**Std. Deviation**	**P value**
AGE	PRITCHARD	50	25.40	5.447	0.354
	ZUSPAN	50	25.38	5.795	Not significant

Figure 8: Distribution in Age



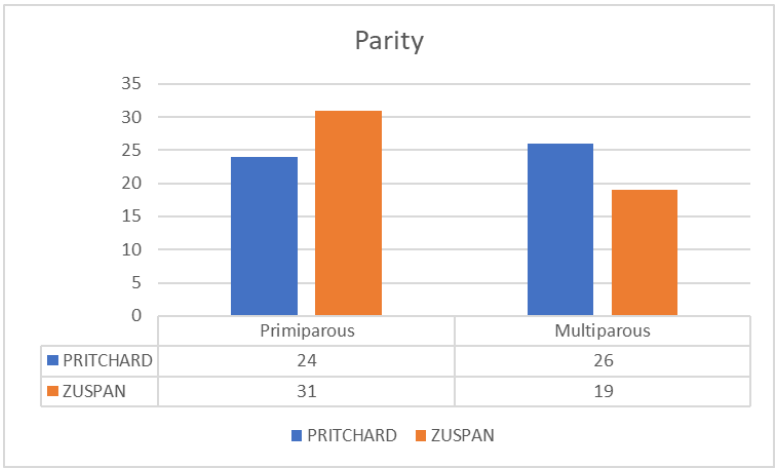
PARITY:

As seen from the table and graph,the number of primigravidas and multigravidas were slighty different in both the groups with the number of primiparous women on the higher side.

Table 6: Distribution in Parity

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
OBSTETRIC H/O	PRIMI	24	31
		48.0%	62.0%
	MULTI	26	19
		52.0%	38.0%
TOTAL		50	50
		100.0%	100.0%
P value		0.159	Not significant

Figure 9: Distribution in Parity



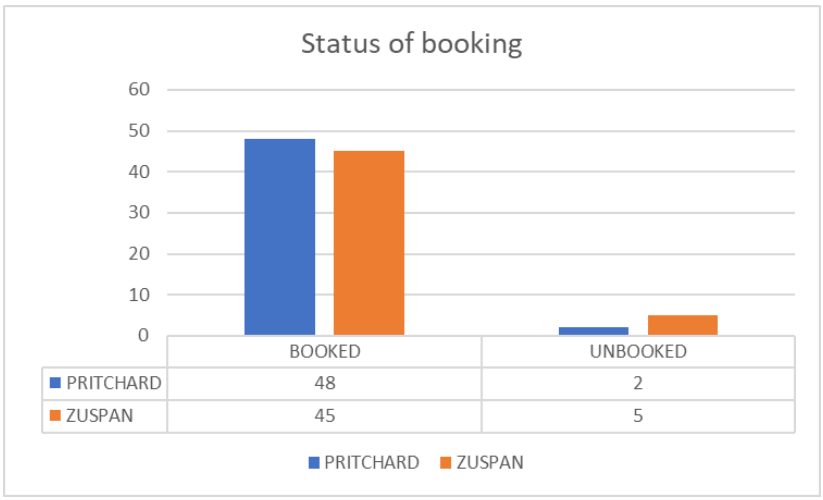
STATUS OF BOOKING:

There was no significance between the booking status of the patients in both the groups.

Table 7: Distribution in Booking status

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
BOOKED / NOT BOOKED	BOOKED	48	45
		96.0%	90.0%
	UNBOOKED	2	5
		4.0%	10.0%
TOTAL		50	50
		100.0%	100.0%
P value		0.240	Not significant

Figure 10: Distribution in booking status



GESTATIONAL AGE:

The mean gestational age among the Pritchard group was 35.47 weeks and among the Zuspan group was 34.82 weeks. The p value was 0.230.

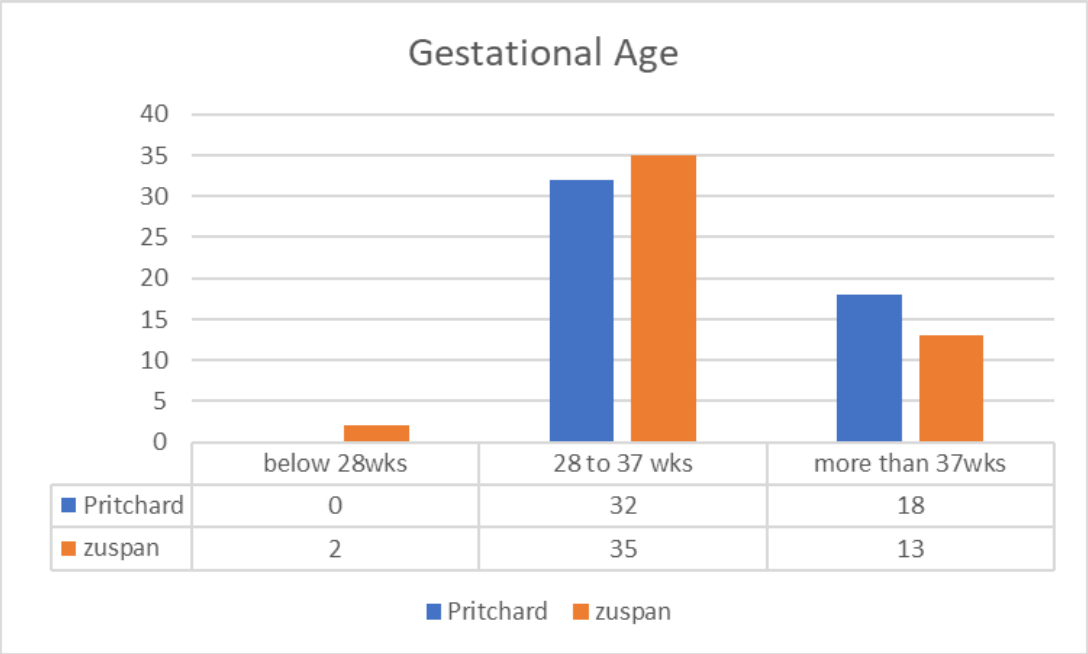
Table 8: Distribution in Gestational Age

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
GESTATIONAL AGE	BELOW 28 WEEKS	0	2
		.0%	4.0%
	28 - 37 WEEKS	32	35
		64.0%	70.0%
	MORE THAN 37 WEEKS	18	13
		36.0%	26.0%
TOTAL		50	50
		100.0%	100.0%

Table 9: Statistical Analysis

	MGSO4 REGIMEN	N	Mean	Std. Deviation	P value
GA	PRITCHARD	50	35.476	3.1832	0.230
	ZUSPAN	50	34.826	3.6081	Not significant

Figure 11: Distribution in Gestational Age



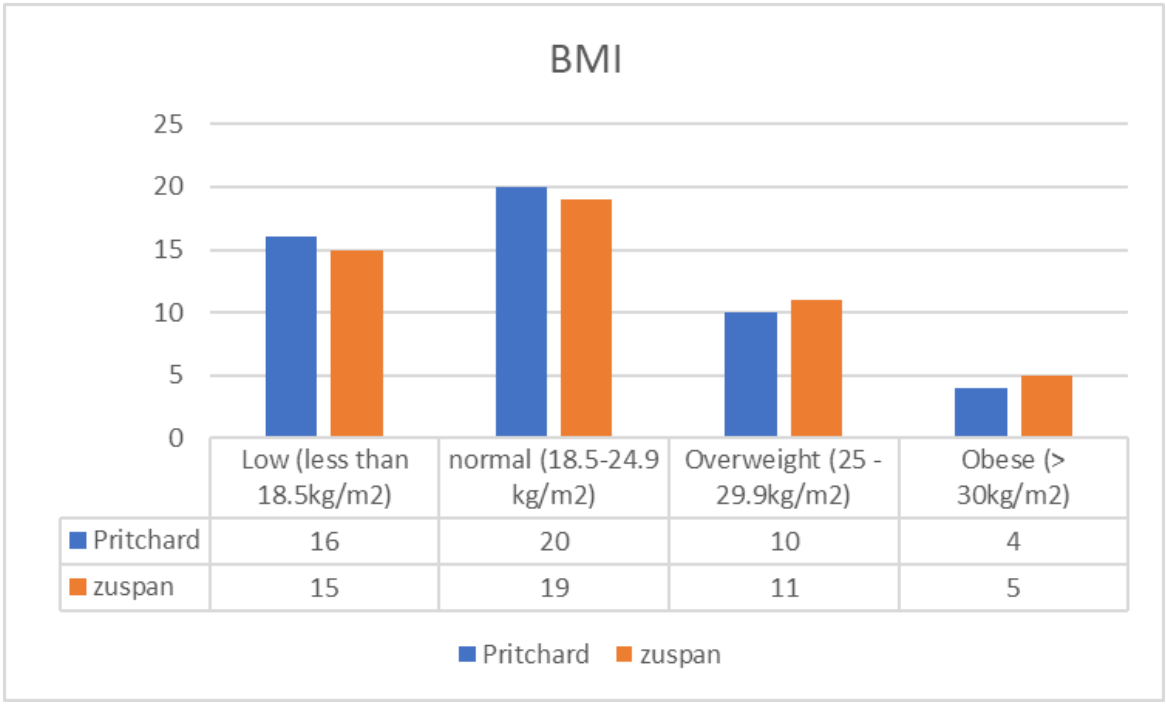
BODY MASS INDEX:

There were only 4 obese patients treated in Pritchard group and 5 obese patients treated in Zuspan group whereas majority were of normal weight. p value was 0.975.

Table 10: Distribution in BMI

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
BMI	UNDER WEIGHT	16	15
		32.0%	30.0%
	NORMAL	20	19
		40.0%	38.0%
	OVERWEIGHT	10	11
		20.0%	22.0%
	OBESE	4	5
		8.0%	10.0%
TOTAL		50	50
		100.0%	100.0%
P value		0.975	Not significant

Figure 12: Distribution in BMI



SYSTOLIC BLOOD PRESSURE:

In Pritchard regimen,15 patients had systolic BP above 161mmHg ,7 patients had below 140 mmHg. The mean systolic BP was 159.20 mmHg. In patients treated under Zuspan, 13 had systolic BP above 161 mmHg. 4 were below 140 mmHg. The mean systolic BP was 158.20 mmHg. The p value is 0.504 and it is insignificant.

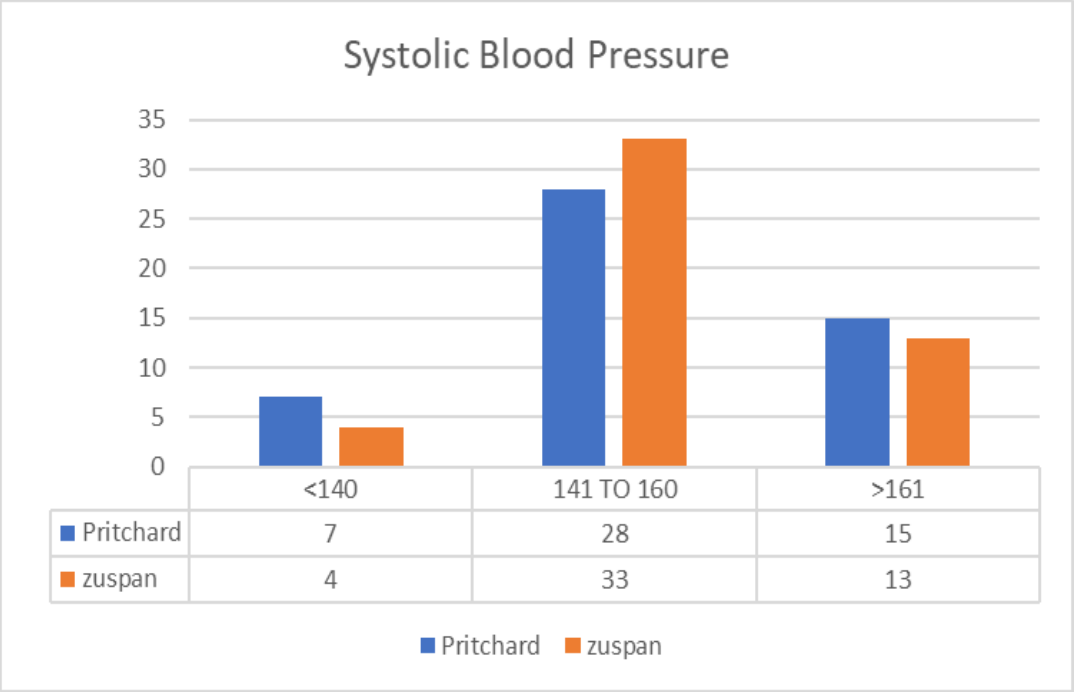
Table 11: Distribution in Systolic BP

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
SYSTOLIC BP	<140	7	4
		14.0%	8.0%
	141 TO 160	28	33
		56.0%	66.0%
	>161	15	13
		30.0%	26.0%
TOTAL		50	50
		100.0%	100.0%

Table 12: Statistical Analysis

	MGSO4 REGIMEN	N	Mean	Std. Deviation	P value
SYSTOLIC BP	PRITCHARD	50	159.20	11.753	0.504
	ZUSPAN	50	158.20	11.726	Not significant

Figure 13: Distribution in Systolic BP



DIASTOLIC BLOOD PRESSURE:

6 patients under Pritchard regimen had more than 110 mmHg diastolic BP. The mean value is 104.60 mmHg. In Zuspan regimen, 6 patients had diastolic BP more than 110 mmHg. The mean value is 103.80 mmHg. P value was 0.507.

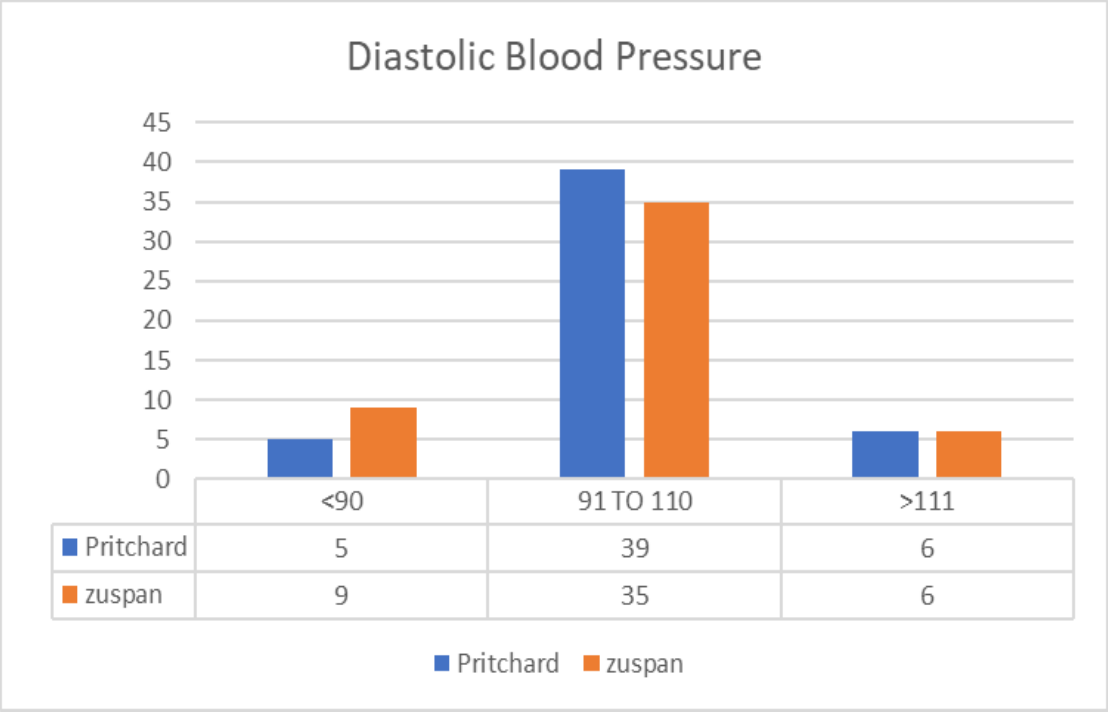
Table 13: Distribution in Diastolic BP

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
DIASTOLIC BP	< 90	5	9
		10.0%	18.0%
	91 TO 110	39	35
		78.0%	70.0%
	>111	6	6
		12.0%	12.0%
TOTAL		50	50
		100.0%	100.0%

Table 14: Statistical Analysis

	MGSO4 REGIMEN	N	Mean	Std. Deviation	P value
DIASTOLIC BP	PRITCHARD	50	104.60	8.381	0.507
	ZUSPAN	50	103.80	9.234	Not significant

Figure 14: Distribution in Diastolic BP



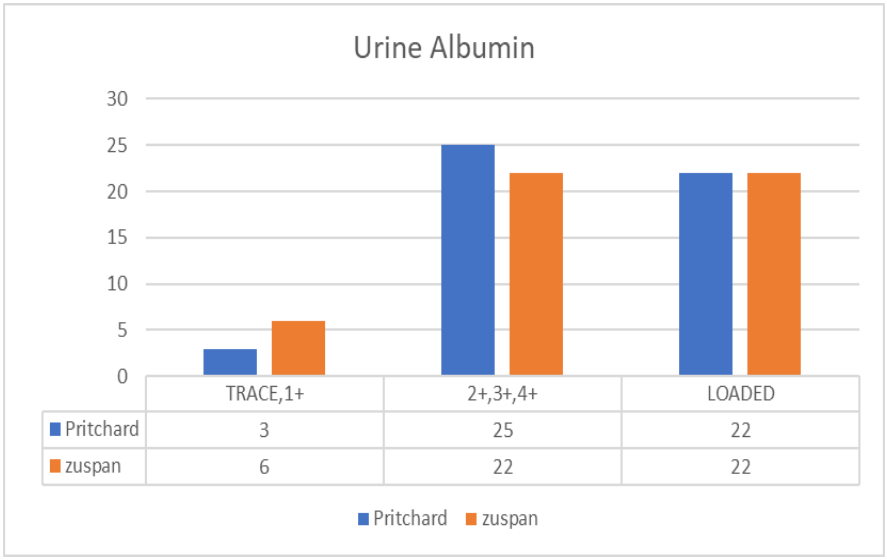
URINE ALBUMIN:

There urine albumin among both the groups were compared. p value was 0.551 and insignificant.

Table 15: Distribution in Urine Albumin

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
URINE ALBUMIN	TRACE, 1+	3	6
		6.0%	12.0%
	2+,3+,4+	25	22
		50.0%	44.0%
	LOADED	22	22
		44.0%	44.0%
TOTAL		50	50
		100.0%	100.0%
P value		0.551	Not significant

Figure 15: Distribution in Urine albumin



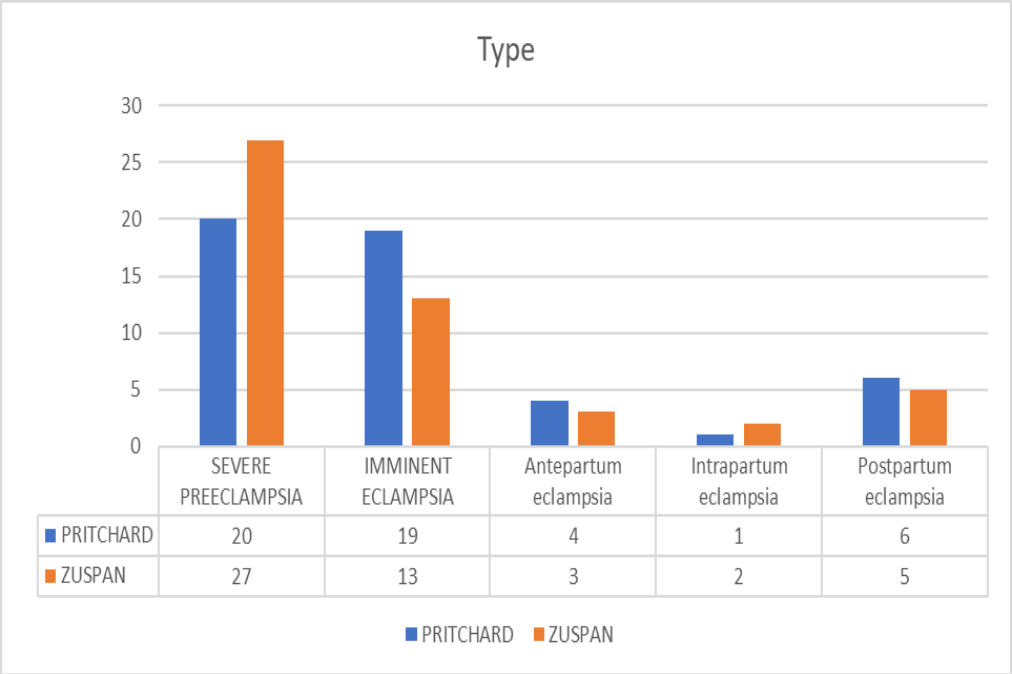
TYPES OF PRE-ECLAMPSIA:

Among the Pritchard regimen, 40% were severe pre-eclampsia, 38% were Imminent Eclampsia, 12% were postpartum eclampsia, 8% were Antepartum eclampsia and 2% were intrapartum eclampsia. Among the Zuspan regimen, 54% were severe pre-eclampsia, 26% were Imminent Eclampsia, 10% were postpartum eclampsia, 6% were Antepartum eclampsia and 4% were intrapartum eclampsia. P value was not significant.

Table 16: Distribution based on the Types of Pre-eclampsia

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
DIAGNOSIS	ANTEPARTUM ECLAMPSIA	4 8.0%	3 6.0%
	IMMINENT ECLAMPSIA	19 38.0%	13 26.0%
	INTRAPARTUM ECLAMPSIA	1 2.0%	2 4.0%
	PP ECLAMPSIA	6 12.0%	5 10.0%
	SEVERE PREECLAMPSIA	20 40.0%	27 54.0%
TOTAL		50 100.0%	50 100.0%
P value		0.464	Not significant

Figure 16: Distribution based on the Types of Pre-eclampsia



RENAL FUNCTION TEST - CREATININE

Serum Creatinine among the study groups were compared. Mean S.creatinine among the Pritchard regimen was 0.82 and among the Zuspan Regimen was 0.844 and were not statistically significant. P value was 0.749.

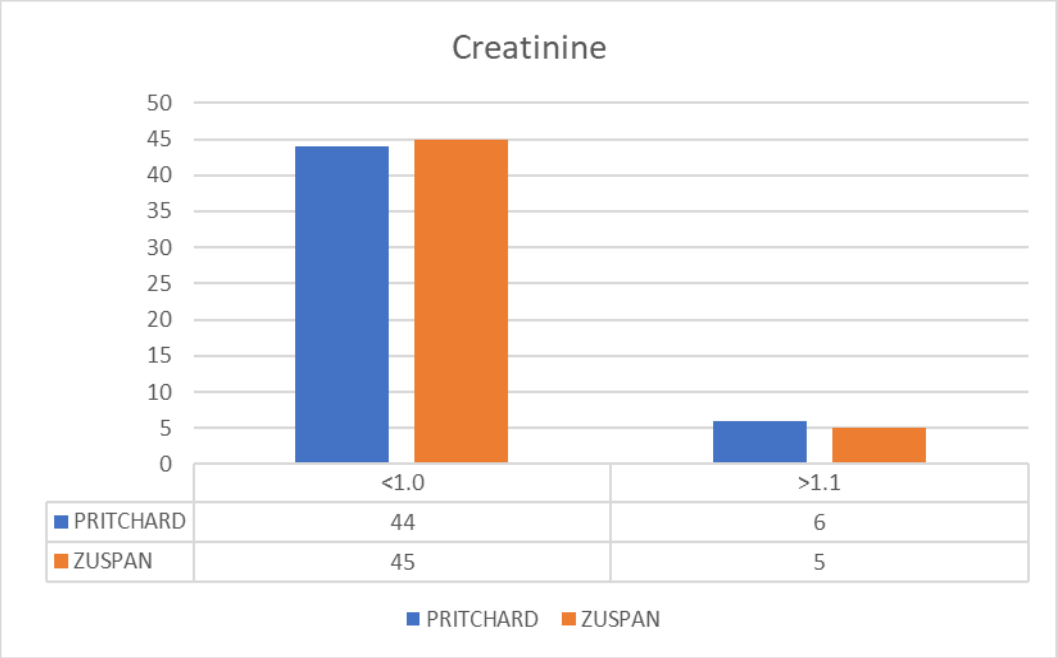
Table 17a: Distribution based on serum creatinine

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
RFT CREATININE	<1.0	44	45
		88.0%	90.0%
	>1.1	6	5
		12.0%	10.0%
TOTAL		50	50
		100.0%	100.0%

Table 17b: Statistical Analysis

	MGSO4 REGIMEN	N	Mean	Std. Deviation	P value
RFT CREATININE	PRITCHARD	50	.826	.2155	0.749
	ZUSPAN	50	.844	.2251	Not significant

Figure 17: Distribution based on serum creatinine



SERUM MAGNESIUM LEVELS:

The mean serum magnesium levels between the groups were 7.4mEq/L among Pritchard regimen and 6.08mEq/L among the Zuspan regimen. P value was significant.

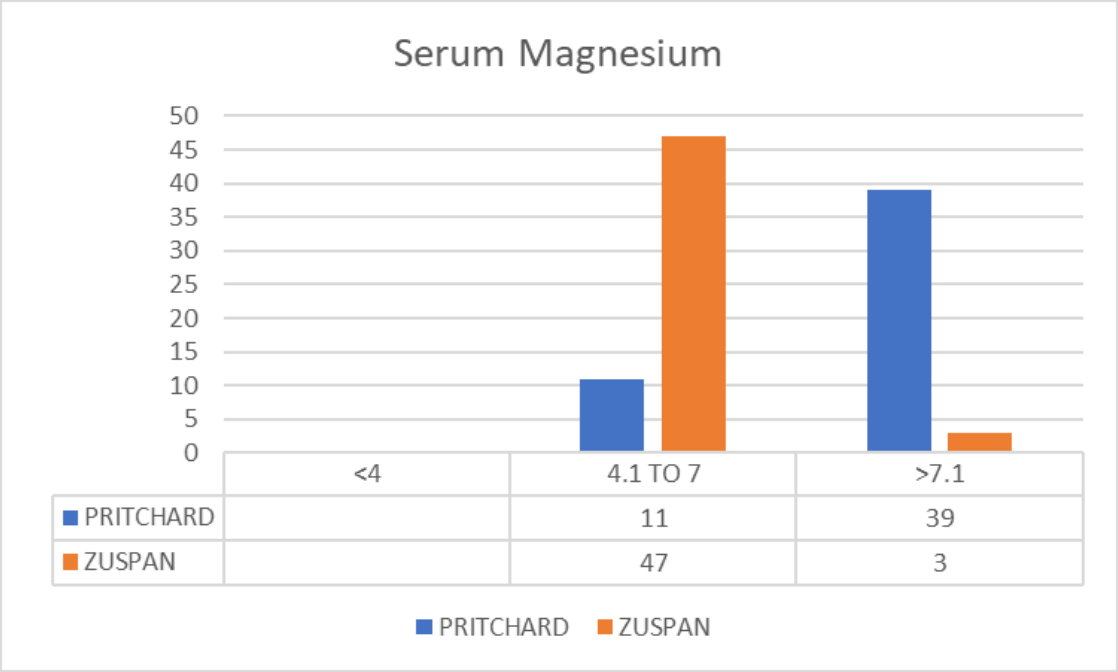
Table 18a: Distribution based on serum magnesium levels

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
S. MAGNESIUM LEVEL (AFTER 4 HRS) mEq/L	4.1 TO 7	11	47
		22.0%	94.0%
	>7.1	39	3
		78.0%	6.0%
TOTAL		50	50
		100.0%	100.0%

Table 18b : Statistical Analysis

	MGSO4 REGIMEN	N	Mean	Std. Deviation	P value
S. MAGNESIUM LEVEL (AFTER 4 HRS)	PRITCHARD	50	7.436	.7515	0.00
	ZUSPAN	50	6.088	.6811	significant

Figure 18: Distribution based on serum magnesium levels



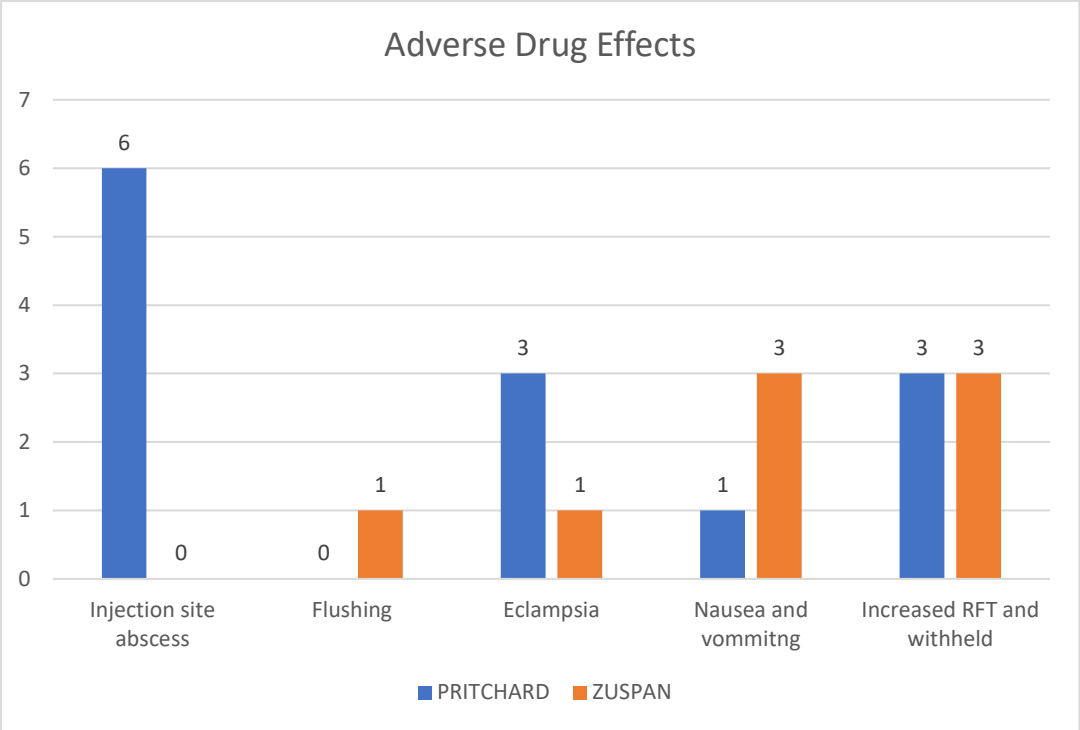
ADVERSE DRUG EFFECTS:

The various adverse effects among the two study groups were compared and was found to be statistically insignificant with a p value of 0.097.

Table 19: Distribution based on the adverse effects

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
COMPLICATIONS / ADVERSE EFFECT	INJECTION SITE ABSCESS	6	0
		12.0%	.0%
	FLUSHING	0	1
		.0%	2.0%
	ECLAMPSIA	3	1
		6.0%	2.0%
	NAUSEA	1	3
		2.0%	6.0%
	WITHHELD	3	3
		6.0%	6.0%
	NIL	37	42
		74.0%	84.0%
TOTAL		50	50
		100.0%	100.0%
P value		0.097	Not significant

Figure 19: Distribution based on the adverse effects



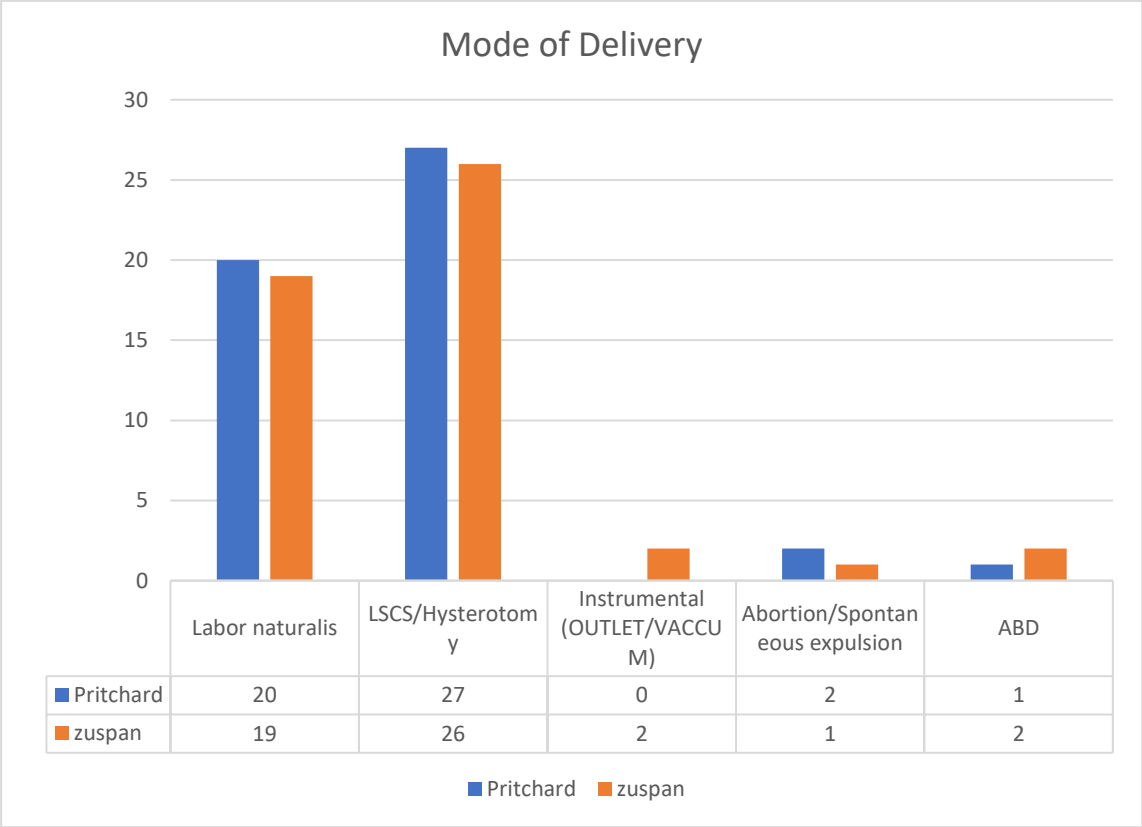
MODE OF DELIVERY:

Among the Pritchard group, 20 patients delivered by Labor Naturalis, 27 were taken up for cesarean section, 2 underwent spontaneous expulsion and 1 patient was delivered by Assisted breech delivery. Among the Zuspan group, 19 patients delivered by Labor Naturalis, 26 were taken up for cesarean section, 2 had instrumental delivery, 1 patient underwent spontaneous expulsion and 2 were delivered by Assisted breech delivery.

Table 20 : Distribution based on Mode of delivery

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
MODE OF DELIVERY	LN	20	19
		40.0%	38.0%
	LSCS	27	26
		54.0%	52.0%
	OUTLET FORCEPS	0	2
		.0%	4.0%
	SPONTANEOUS EXPULSION	2	1
		4.0%	2.0%
	ABD	1	2
		2.0%	4.0%
TOTAL		50	50
		100.0%	100.0%
p value		0.607	Not significant

Figure 20: Distribution based on Mode of delivery



APGAR:

There was no significant difference between the groups with regards to APGAR score at both 1 minute and 5 minute.

Table 21a : Distribution based on APGAR score at 1 minute

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
APGAR 1 MIN	<5	9	2
		20.0%	4.5%
	6	8	12
		17.8%	27.3%
	7	22	19
		48.9%	43.2%
	>8	6	11
		13.3%	25.0%
TOTAL		45	44
		100.0%	100.0%

Table 21b: Statistical Analysis

	MGSO4 REGIMEN	N	Mean	Std. Deviation	P value
APGAR 1 MIN	PRITCHARD	45	6.31	1.474	0.074
	ZUSPAN	44	6.89	0.841	Not significant

Figure 21: Distribution based on APGAR score at 1 minute

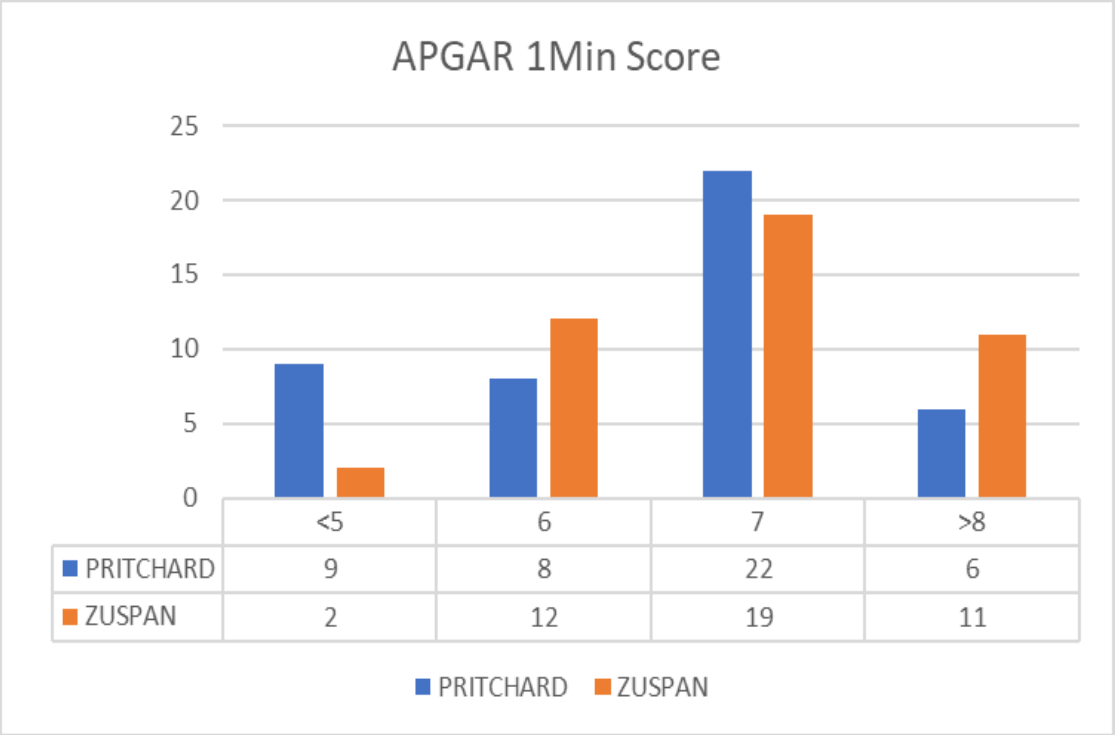


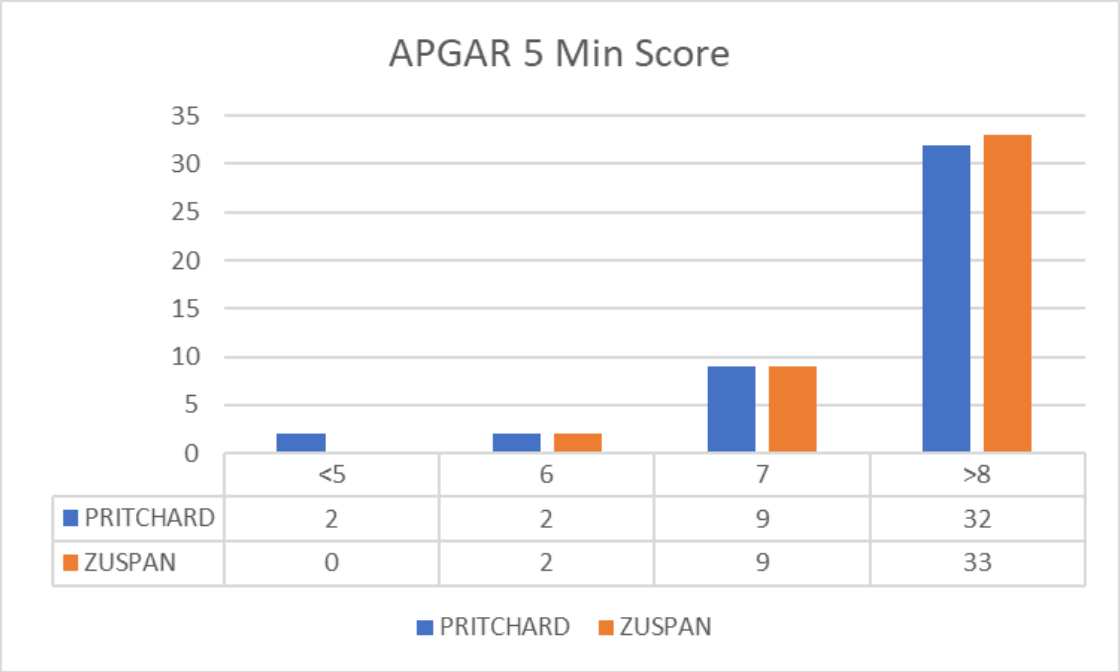
Table 22a: Distribution based on APGAR score at 5 minutes

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
APGAR 5MIN	<5	2	0
		4.4%	.0%
	6	2	2
		4.4%	4.5%
	7	9	9
		20.0%	20.5%
	>8	32	33
		71.1%	75.0%
Total		45	44
		100.0%	100.0%

Table 22b : Statistical Analysis

	MGSO4 REGIMEN	N	Mean	Std. Deviation	P value
APGAR 5MIN	PRITCHARD	45	7.93	1.250	0.571
	ZUSPAN	44	8.20	.930	Not significant

Figure 22: Distribution based on APGAR score at 5 minutes



BIRTHWEIGHT:

There was no significant difference in birth weight of newborn between the two groups.

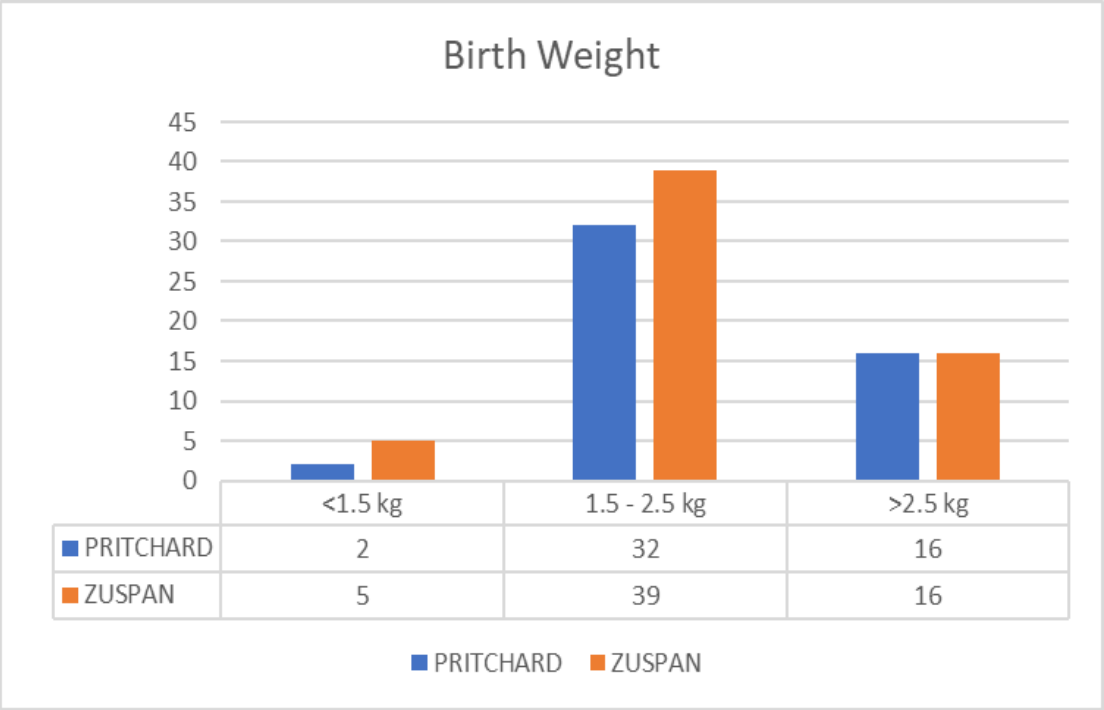
Table 23a: Distribution based on neonatal birth weight

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
NEONATAL BIRTH WEIGHT	<1.5 kg	2	5
		4.0%	10.0%
	1.5 - 2.5 kg	32	29
		64.0%	58.0%
	>2.5 kg	16	16
		32.0%	32.0%
TOTAL		50	50
		100.0%	100.0%

Table 23b: Statistical Analysis

	MGSO4 REGIMEN	**N**	**Mean**	**Std. Deviation**	**P value**
NEONATAL BIRTH WEIGHT	PRITCHARD	50	2.28	.536	0.488
	ZUSPAN	50	2.22	.616	Not significant

Figure 23: Distribution based on neonatal birth weight



FOETAL OUTCOME:

There were 4 perinatal mortality among the Pritchard group and 1 among the Zuspan group. P value was 0.169 and not significant.

Table 24a: Distribution based on Perinatal Mortality Rate (PNMNR)

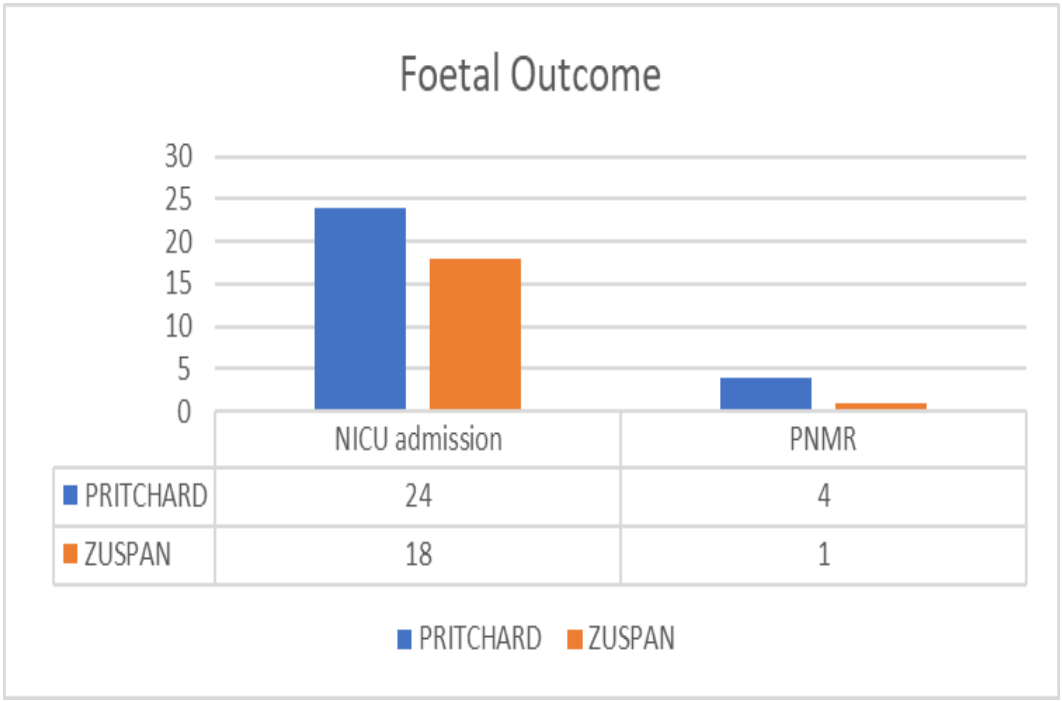
		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
PNMR	YES	4	1
		8.0%	2.0%
	NO	46	49
		92.0%	98.0%
TOTAL		50	50
		100.0%	100.0%
P value		0.169	Not significant

24 babies required admission/observation among the Pritchard group and 18 babies among the Zuspan group.

Table 24b: Distribution based on NICU admission

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
NICU ADMISSION	YES	24	18
		54.5%	40.9%
	NO	20	26
		45.5%	59.1%
TOTAL		44	44
		100.0%	100.0%
P value		0.200	Not significant

Figure 24: Distribution based on foetal outcome



MATERNAL COMPLICATIONS:

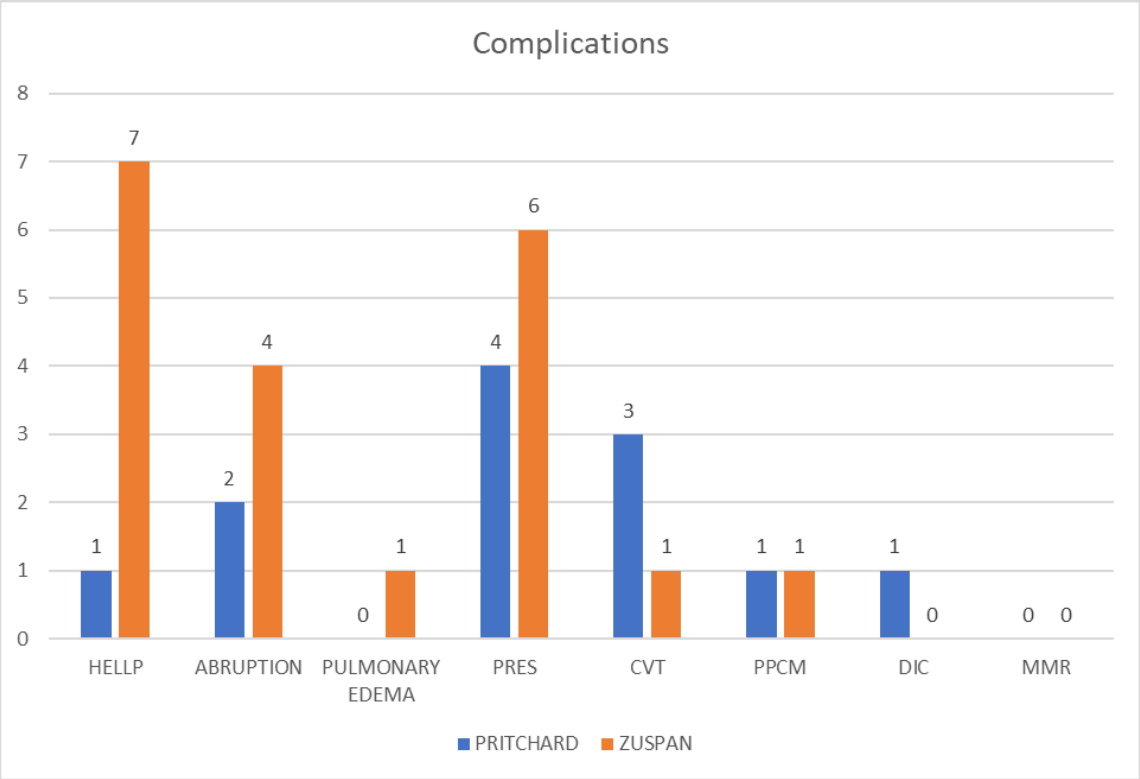
The various associated maternal complications are compared in the following table and graph. Out of 50 patients, 30 patients among Pritchard regimen and 28 patients among Zuspan regimen were found to be uneventful. There were no maternal mortality in this study.

Table 25: Distribution according to Maternal Complication

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
COMPLICATIONS	HELLP	1 2.2%	7 14.0%
	ABRUPTION	2 4.3%	4 8.0%
	PULMONARY EDEMA	0 .0%	1 2.0%
	PRES	4 8.7%	6 12.0%
	CVT	3 6.5%	1 2.0%
	DIC	1 2.2%	0 .0%
	PPCM	1 2.2%	1 2.0%
	DVT	1 2.2%	0 .0%
	PNMR	2 4.3%	1 2.0%

	PRES/ABRUPTION	0 .0%	1 2.0%
	PRES/CVT	1 2.2%	0 .0%
	UNEVENTFUL	30 65.2%	28 56.0%
TOTAL		46 100.0%	50 100.0%
P value		0.377	Not significant

Figure 25: Distribution according to Maternal Complication



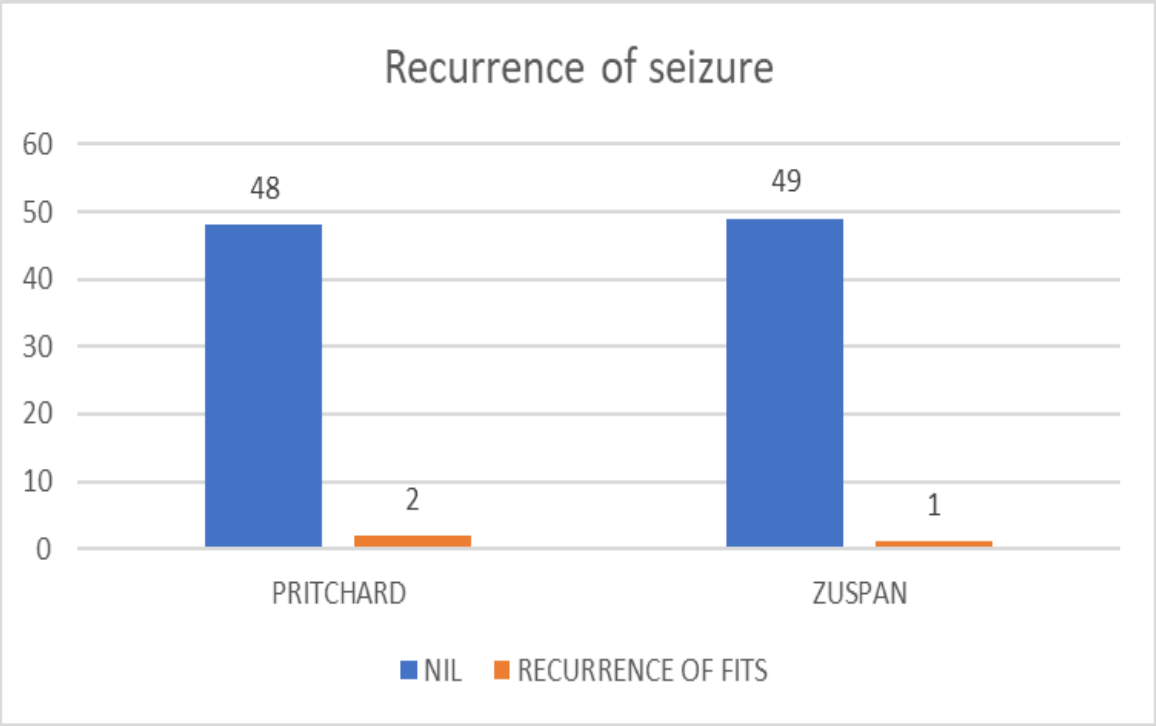
RECURRENCE OF SEIZURES:

Among the 50 patients in each group, 2 patients has a recurrence of seizures among the Pritchard group and 1 patient had a recurrence among the Zuspan group which was managed accordingly. There was no status eclampticus in both the regimen. P value was 0.558.

Table 26: Distribution based on recurrence of seizures

		MGSO4 REGIMEN	
		PRITCHARD	**ZUSPAN**
RECURRENCE OF FIT	YES	2	1
		4.0%	2.0%
	NO	48	49
		96.0%	98.0%
Total		50	50
		100.0%	100.0%
P value		0.558	Not significant

Figure 26: Distribution based on recurrence of seizures



DISCUSSION

Eclampsia is a life-threatening complication of hypertensive disorders of pregnancy. It is a major cause of maternal mortality, perinatal mortality and morbidity. The incident rate in this study is high as this was conducted in a tertiary care centre and also the referral cases are higher. During the study period, there were 21 cases of eclampsia of which 7 were antepartum, 3 were intrapartum and 11 were postpartum eclampsia. 33 patients were diagnosed as imminent eclampsia and 47 patients as severe preeclampsia.

In this study, the maximum number of patients belonged to 18-30 years age group where 82% patients belonged to the age group 18-30 years and there were only 16% patients above 30 years and only 2% patients were below 18 years age. This low age indicates that girls are still married at an early age particularly in low socio-economic status. The mean age of incidence was 25.6 years similar to Kauser U et al study where 22% of the eclamptic patients were between 26 to 30 years.

In regards to the booking status, 93% of the patients were booked and a 7% of the cases were not booked. This was similar to a study by S Singh and A Behera.[90] This depicts the lack of vigorous screening for the antenatal cases at the rural areas and the ignorance and unawareness of the importance of antenatal visits among the community.

The mean gestational age of incidence 35.47 weeks among the Pritchard regimen and 35.02 weeks among the Zuspan regimen. Overall, only 2% of the patients presented at less than 28 weeks of gestation wheras 31% were term gestation. Gestational age of the patients is comparable with collaborative eclampsia trial.[5]

The total number of primigravidas were 55 (55%) indicating that hypertensive disorders of pregnancy are more common among the primigravidas rather than multigravidas(45%). In Collaborative Eclampsia Trial (1995) primi were 64% and multi were 36%.[5]

In this study, the distribution with regards to Body Mass Index was also studied to analyse the effect of comparatively lower dose of the Zuspan regimen versus the higher does of Pritchard regimen. 31% of the patients were underweight and only 9% were obese thus, reflecting the poor nutrition status and lower BMI among Asian women in comparison to that of the Western standards as concluded by Tript et al study.[89] Hence a seemingly lower dose of Magnesium sulphate would suffice for the developing countries.

The mean systolic blood pressure (SBP) was 158.50 mmHg and the mean diastolic blood pressure (DBP) was 103.70 mmHg. Around 28% of the patients had an SBP of more than 161 mmHg and a majority (61%) remained between 141 to 160 mmHg. With respect to the Diastolic blood pressure, 12% had DBP of more than 111 mmHg and 74% were between 91 to 110 mmHg in contrast to Collaborative Eclampsia Trial group study (1995) where patients with diastolic BP of more than 110 mm Hg were 53% .[5]

Urine dipstick was done for all the patients and were graded as Trace (9%), 2+ to 4+ (47%) and loaded (44%). The landmark WHO sponsored Eclampsia Trial Collaborative Study established the superiority of magnesium sulphate in preventing eclamptic seizures. Some studies have suggested that a lower total dose or even a loading dose-only regimen may be as effective as the standard regimen for managing preeclampsia and eclampsia. The patients were randomly started on either intravenous Zuspan or the intramuscular Pritchard regimen in this study. Majority of the patients (89%) were found to have normal renal function tests as evidenced by serum creatinine levels.

In order to compare the efficacy of the two regimens among the current study population, serum magnesium was taken which is otherwise not routinely recommended unless the patients suffer from renal damage. The mean serum magnesium levels between the groups were 7.4mEq/L among Pritchard regimen and 6.08mEq/L among the Zuspan regimen. This was statistically significant as the patients receiving Pritchard's regimen were having an upper limit most of the time and therefore in more risk of toxicity from magnesium sulphate. The adverse effects between both the groups were almost similar with the exception of injection site abscess among Pritchard regimen. In 6% of the patients, it was withheld due to elevated renal parameters. This was in concordance with S Singh[89], Pratt J[91] and Kauser U studies.

47% of the patients had a vaginal delivery (labor naturale/ instrumental/ spontaneous expulsion) whereas 53% underwent either cesarean section or

hysterotomy in view of obstetric indications. This is comparable to a similar study by Alexander et al.

The mean birth weight was 2.24kg with an average APGAR score of 6.7 at 1 minute and 7.9 at 5 minutes. Around 42% of the neonates required either observation or admission at the Neonatal Intensive Care Unit (NICU). The Perinatal Mortality Rate (PNMR) was around 5% with majority the babies being low birth weight, preterm or Intrauterine growth restriction. Shika seth et al reported 69% live birth, 31% perinatal death in patients treated under Pritchard regime and 75% live birth and 25% perinatal death in patients treated under low dose regime.

Around 58% of the mothers had an uneventful period. The most common complication was Posterior Reversible Encephalopathy Syndrome (PRES) accounting for 31%, followed by HELLP (25%) and Placental Abruption (19%) which is much less than that described by Chabbra and Kakani.

2 patients among the Pritchard regimen group and 1 among the Zuspan regimen group had recurrence of seizures. Similar results were found in the study of Vaibhav Kanti et al.

There was no maternal mortality in this study, similar to Begum et al and in Bangal et al studies.[96]

CONCLUSION

- Both the Intramuscular MgSO4 (Pritchard regimen) and Intravenous MgSO4 regimen (Zuspan regimen) are equally effective in controlling maternal and fetal side effects which were equally low.
- Most of the Indian women considered to be of low to normal BMI and lower dose magnesium sulphate (Zuspan -28g; Pritchard – 44g) is sufficient for them.
- Intramuscular injection of MgSO4 is painful and the compliance of intramuscular MgSO4 is lower in comparison to intravascular infusion of MgSO4.
- The risk of toxicity is also lower in Zuspan regimen.

SUMMARY

In this present study 100 patients of pre eclamptic women irrespective of the type (Severe/ Imminent /Antepartum eclpamsia/ Intrapartum eclampsia/ Postpartum eclampsia) were included.

50 patients were treated under Zuspan regimen. Another 50 eclamptic patients were treated under Pritchard regime. And the two group of patients were observed for the adverse effects, magnesium toxicity, recurrence of fits, maternal morbidity, mortality as well as for perinatal outcome. Thus, the safety and efficacy of low dose intravenous magnesium sulphate was compared with Pritchard's regimen.

The adverse effects between both the groups were almost similar except for adverse effects related to the route of drug administration. The patients getting Pritchard regimen complained of pain which led to greater maternal discomfort in addition to complications such as injection site hematoma and abscess. This was not seen in Zuspan regimen.

The need for an infusion pump or gravity assisted infusion using Zuspan makes it difficult to be practiced in a low resource setting whereas Pritchard's was easy to administer.

With respect to seizure recurrence, 1 patient from Zuspan and 2 from Pritchard regime had recurrent fit. The recurrent seizure patients were treated with additional dose of 2g of 20% $MgSO_4$ Intravenously.

There were no symptoms of Magnesium toxicity in both the patients.

In both study and control groups, totally 100 patients were discharged in a healthy state. There was no maternal mortality. Perinatal outcome of patients treated in the two different regimens are comparable. The perinatal outcome does not differ significantly in both Zuspan and Pritchard regimen groups.

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PROFORMA

NAME: AGE: IP NO

DOA: BOOKED / NOT BOOKED

DATE OF DELIVERY: LMP:

DOD: EDD:

PHONE NUMBER: GA:

ADDRESS:

PAST H/O:

MENSTRUAL H/O:

MARITAL H/O:

OBSTETRIC H/O

HEIGHT: WEIGHT: BMI:

VITALS: TEMP: PR: BP: SPO2:

SYSTEMIC EXAMINATION:

PER ABDOMINAL EXAMINATION:

PER VAGINAL EXAMINATION:

DIAGNOSIS:

RFT: UREA: CREATININE: URINE ALBUMIN:

MGSO4 REGIMEN:

S. MAGNESIUM LEVEL (AFTER 4 HRS):

COMPLICATIONS / ADVERSE EFFECT:

MODE OF DELIVERY:

NEONATAL OUTCOME:

APGAR: 1” 5”

NICU ADMISSION: YES/ NO

POSTPARTUM STAY:

CONSENT FORM

Research title: "**A COMPARATIVE STUDY OF INTRAVENOUS VERSUS INTRAMUSCULAR MAGNESIUM SULPHATE IN SEVERE PRE-ECLAMPSIA AND ECLAMPSIA IN GOVT RAJAJI HOSPITAL, MADURAI"**

Research Station: Government Rajaji Hospital, Madurai

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I understand that I am free to withdraw at any time without giving any reason. I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study. I consent voluntarily to participate as a participant in this research.

Name of Participant

Signature of Participant

Date

Thumb print of participant

Name of witness

Signature of witness

Date

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:

1.Intravenous or Intramuscular magnesium sulphate.

2.S. Magnesium from venous sample.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Name of Researcher/person taking the consent

Signature of Researcher /person taking the consent

Date

ஆராய்ச்சிஒப்புதல்படிவம்

பெயர்: தேதி:

வயது: நோயாளிஎண்:

ஆராய்ச்சி சேர்க்கை எண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கபட்டது.

எனக்கு விளக்கபட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது முழுமனதுடன் சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் பின் வாங்கலாம் என்றும் அதனால் எந்த பாதிப்பும் எனக்கு ஏற்படாது என்பதையும் புரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழுசுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் பங்கு கொள்ள சம்மதிக்கிறேன்.

PATIENT'S INFORMATION FORM

Research title: "**A COMPARATIVE STUDY OF INTRAVENOUS VERSUS INTRAMUSCULAR MAGNESIUM SULPHATE IN SEVERE PRE-ECLAMPSIA AND ECLAMPSIA IN GOVT RAJAJI HOSPITAL, MADURAI"**

Research Station: Government Rajaji Hospital, Madurai

Respected Madam,

We request you participate in this study where we are planning to compare the safety and efficacy of intravenous magnesium sulfate regimen in comparison with the intramuscular Pritchard regimen.

Hypertensive disorders are one of the most common medical complications of pregnancy and contributes significantly to maternal and perinatal morbidity and mortality.

Prophylactic magnesium sulphate therapy lowers the risk of eclampsia and feto-maternal morbidities. The aim is to control seizures and prevent its recurrence. The two standard regimens are Zuspan's (intravenous) and Pritchard's regimen (supposedly 'high dose' intramuscular).

What are the risks and the side-effects?

Includes allergic reactions, loss of reflexes, decreased urine output, respiratory depression. Side effects such as vomiting, flushing and giddiness can rarely occur. You will be monitored hourly in regards to occurrence of any slight side effects in a well-equipped facility.

Why this study?

Pritchard's is commonly preferred in developing countries, although it is derived with the Western population as the standardized BMI. On the other hand, Indian population have lower BMI, hence a low dose of magnesium therapy would more likely reduce the dose related complications of magnesium toxicity all the while being more compliant and patient friendly.

SNO	AGE	BOOKED / NOT BOOKED	GA	OBSTETRIC H/O	BMI	SYSTOLIC BP	DIASTOLIC BP	DIAGNOSIS	RFT UREA	RFT CREATININE	URINE ALBUMIN	MGSO4 REGIMEN	S. MAGNESIUM LEVEL (AFTER 4 HRS) gm/Dl	COMPLICATIONS / ADVERSE EFFECT	MODE OF DELIVERY	NEONATAL BIRTH WEIGHT	APGAR 1" 5"	APGAR 1 MIN	APGAR 5MIN	NICU ADMISSION YES/ NO	COMPLICATIONS	RECURRENCE OF FIT	MATERNAL DEATH
1	37	Booked	33.5	1	1	160	110	SEVERE PREECLAMPSIA	17	0.6	2	1	7.8	6	1	2.5	8.9	8	9	No	12	2	2
2	22	Booked	40.1	1	2	150	90	IMMINENT ECLAMPSIA	16	0.8	6	2	6.1	6	2	3.05	8,9	8	9	No	12	2	2
3	21	Booked	38	1	2	160	110	IMMINENT ECLAMPSIA	42	1.3	2	1	8.2	5	2	1.75	7,8	7	8	Yes	12	2	2
4	35	Booked	39	2	3	150	100	SEVERE PREECLAMPSIA	26	0.7	5	1	8.3	6	2	1.95	7,9	7	9	Yes	12	2	2
5	23	Booked	39.2	1	2	160	120	IMMINENT ECLAMPSIA	27	0.9	3	2	6.2	6	1	2.4	7,9	7	9	No	12	2	2
6	28	Booked	37	2	2	160	110	IMMINENT ECLAMPSIA	23	0.8	5	1	7.9	6	2	2.6	7,9	7	9	Yes	5	2	2
7	27	Booked	33.4	1	2	150	100	IMMINENT ECLAMPSIA	20	0.7	5	2	5.7	4	2	2.2	IUD				2	2	2
8	20	Booked	32.5	1	2	140	100	IMMINENT ECLAMPSIA	26	0.9	3	2	4.9	6	5	1.2	6,7	6	7	Yes	9	2	2
9	25	Booked	39	1	2	160	90	ECLAMPSIA	33	1	5	1	8	6	1	2	6,7	6	7	Yes	12	2	2
10	25	Booked	29.4	1	3	160	100	IMMINENT ECLAMPSIA	29	1.3	2	1	7.8	5	5	1	7,9	7	9	Yes	9	2	2
11	19	Booked	36.6	1	4	160	120	SEVERE PREECLAMPSIA	27	0.8	2	2	6.7	6	2	2	7,9	7	9	Yes	12	2	2
12	25	Booked	39.2	2	1	150	110	SEVERE PREECLAMPSIA	18	0.7	2	2	7	6	1	3	7,9	7	9	No	12	2	2
13	20	Booked	38.2	2	1	150	110	PP ECLAMPSIA	22	0.7	2	2	6.4	4	2	2.5	7,9	7	9	No	4	2	2
14	28	Booked	34.6	2	1	160	120	INTRAPARTUM ECLAMPSIA	23	0.8	5	1	6.8	6	2	2.6	7,9	7	9	Yes	12	2	2
15	21	Booked	37.4	2	2	150	90	IMMINENT ECLAMPSIA	18	0.8	6	2	5.4	6	2	1.35	7,9	7	9	Yes	2	2	2
16	29	Booked	27	1	2	160	100	IMMINENT ECLAMPSIA	23	0.8	2	2	5.2	6	1	0.95	5,6	5	6	Yes	1	2	2
17	18	Booked	30.6	1	2	170	100	IMMINENT ECLAMPSIA	19	0.9	6	1	7.2	4	1	1.4	4,5	4	5	Yes	12	2	2
18	23	Booked	38.2	2	4	160	100	SEVERE PREECLAMPSIA	31	1.4	3	1	7.9	5	2	2.9	7,9	7	9	No	12	2	2
19	34	Booked	33.4	2	2	150	100	ANTEPARTUM ECLAMPSIA	18	0.7	5	2	5	6	2	2	7,9	7	9	Yes	4	2	2
20	20	Booked	38	1	4	170	110	PP ECLAMPSIA	20	0.5	1	2	6.3	6	2	2.5	7,9	7	9	No	4	1	2
21	27	Booked	32.1	1	2	160	110	IMMINENT ECLAMPSIA	15	0.8	2	1	8.1	1	1	1.8	6,7	6	7	Yes		2	2
22	27	Booked	39	1	1	150	120	SEVERE PREECLAMPSIA	19	1.1	3	1	8	6	2	2.6	7,9	7	9	No	12	2	2
23	20	Booked	36.6	1	3	170	100	IMMINENT ECLAMPSIA	27	1	5	2	5.7	6	3	2.1	7,8	7	8	Yes	12	2	2
24	19	Booked	34.5	1	3	160	100	SEVERE PREECLAMPSIA	22	0.6	5	2	5.4	6	3	2	7,8	7	8	Yes	12	2	2
25	19	Booked	30.1	1	2	160	120	SEVERE PREECLAMPSIA	23	0.7	5	1	7.4	6	4	2.5	IUD	I	D		12	2	2
26	27	Booked	38.3	1	4	180	110	ANTEPARTUM ECLAMPSIA	28	0.9	5	1	7.9	6	2	3.1	6,9	6	9	Yes	12	2	2
27	37	Booked	31.1	1	4	160	110	ANTEPARTUM ECLAMPSIA	26	1.3	5	2	6.1	5	2	1.8	6,7	6	7	Yes	1	2	2
28	27	Booked	36.4	1	1	160	120	IMMINENT ECLAMPSIA	19	0.5	4	2	5.8	6	2	2.1	7,9	7	9	No	12	2	2
29	29	Booked	31.4	2	3	170	100	IMMINENT ECLAMPSIA	27	0.9	5	1	8.1	6	1	1.9	IUD				2	2	2
30	27	Booked	39	2	2	160	100	PP ECLAMPSIA	23	1	5	2	5.7	2	2	3.1	7,9	7	9	No	3	2	2
31	29	Booked	36.4	2	2	160	100	CHRONIC HTN WITH SUPERIMPOSED	21	0.7	5	1	8.4	1	2	1.5	7,9	7	9	Yes		2	2
32	21	Not Booked	29.1	2	2	180	110	SEVERE PREECLAMPSIA	23	0.6	4	1	7.7	3	4	2	IUD				4	2	2
33	20	Booked	33.3	1	1	170	110	SEVERE PREECLAMPSIA	26	0.6	3	2	6.9	6	2	1.5	7,8	7	8	Yes	1	2	2
34	28	Booked	35.4	1	1	160	100	IMMINENT ECLAMPSIA	19	0.7	2	1	8.2	6	2	2.2	7,9	7	9	No	12	2	2
35	35	Booked	36	2	3	170	100	SEVERE PREECLAMPSIA	21	0.9	5	1	5.8	6	1	2.1	1,8	1	8	Yes	12	2	2
36	27	Booked	35.5	1	3	160	120	SEVERE PREECLAMPSIA	22	0.8	4	2	7.1	6	2	2.78	8,9	8	9	No	12	2	2
37	30	Booked	39.3	1	1	140	100	ANTEPARTUM ECLAMPSIA	18	0.6	3	1	7.2	6	2	2.6	8,9	8	9	No	11	2	2
38	28	Booked	36.1	2	3	140	100	SEVERE PREECLAMPSIA	12	0.7	5	1	8.3	6	2	2.9	6,7	6	7	Yes	12	2	2
39	20	Booked	32.5	1	2	160	100	SEVERE PREECLAMPSIA	23	0.9	3	1	5.4	6	1	2.2	4,7	4	7	Yes		2	2
40	33	Booked	29.3	1	3	170	100	IMMINENT ECLAMPSIA	22	0.8	4	2	5.3	4	1	1.9	IUD				1	2	2
41	24	Booked	34.3	2	2	180	100	ANTEPARTUM ECLAMPSIA	22	0.7	5	1	7.9	3	2	2.4	7,8	7	8		4	1	2
42	25	Booked	39.2	2	1	150	90	PP ECLAMPSIA	42	1.4	2	2	6	5	1	2.8	8,9	8	9	No	12	2	2

43	19	Booked	31.6	1	1	160	100	SEVERE PREECLAMPSIA	19	0.9	2	2	6.3	6	1	2.6	8,9	8	9	No	12	2	2
44	21	Booked	32.6	2	1	170	100	SEVERE PREECLAMPSIA	22	0.7	2	1	8	6	1	1.9	7,8	7	8	No	1	2	2
45	23	Booked	39.1	1	1	150	90	IMMINENT ECLAMPSIA	19	1	6	2	5.9	6	1	3	8,9	8	9	No	12	2	2
46	26	Booked	34.5	2	1	160	110	SEVERE PREECLAMPSIA	22	0.9	5	1	6.9	1	1	2.1	4,6	4	6	Yes	9	2	2
47	19	Booked	31.1	1	3	150	90	IMMINENT ECLAMPSIA	27	0.7	4	2	5.5	6	5	2.2	IUD				12	2	2
48	27	Booked	39.5	2	3	140	90	IMMINENT ECLAMPSIA	19	0.8	1	1	7.6	6	1	3	8,9	8	9	No	12	2	2
49	29	Booked	32	2	2	150	90	SEVERE PREECLAMPSIA	20	1	2	2	6.3	6	1	2	7,8	7	8	Yes	12	2	2
50	19	Not Booked	30.1	1	2	140	100	IMMINENT ECLAMPSIA	22	0.9	1	2	6.7	6	1	1.8	6,7	6	7	Yes	12	2	2
51	24	Booked	37.2	1	4	150	100	ANTEPARTUM ECLAMPSIA	21	1	5	1	7.2	6	2	2.6	7,8	7	8	No	12	2	2
52	43	Not Booked	27.5	2	3	170	110	ANTEPARTUM ECLAMPSIA	19	0.8	5	2	6.9	6	4	0.85	IUD				2	2	2
53	20	Booked	38	1	1	160	100	SEVERE PREECLAMPSIA	22	0.9	2	1	8	6	1	2.2	7,9	7	9	No	12	2	2
54	24	Booked	39.1	2	2	170	100	IMMINENT ECLAMPSIA	33	1	5	1	7.4	6	1	2.9	7,9	7	9	No	12	2	2
55	20	Booked	31.5	1	2	160	110	IMMINENT ECLAMPSIA	24	0.7	6	2	6	6	2	1.7	6,7	6	7	Yes	12	2	2
56	27	Booked	31.6	2	4	150	90	IMMINENT ECLAMPSIA	25	0.9	2	2	5.7	6	2	2.1	6,7	6	7	No	12	2	2
57	20	Booked	33.3	2	3	160	110	PP ECLAMPSIA	22	0.9	5	1	6.1	6	1	2.2	6,7	6	7	Yes	5	2	2
58	25	Booked	34.2	1	3	120	110	IMMINENT ECLAMPSIA	19	0.6	5	2	5.9	6	1	2.6	6,7	6	7	Yes	12	2	2
59	22	Booked	34.3	1	3	170	100	INTRAPARTUM ECLAMPSIA	22	0.7	5	2	5.6	6	2	2.5	6,7	6	7	Yes	4	2	2
60	20	Booked	38.4	2	2	150	90	IMMINENT ECLAMPSIA	23	0.6	6	1	7.3	6	2	2.4	7,8	7	8	No	12	1	2
61	23	Booked	35.2	1	2	150	90	IMMINENT ECLAMPSIA	21	0.8	5	2	5.5	6	1	2.2	6,8	6	8	No	12	2	2
62	24	Booked	39.5	1	1	160	110	SEVERE PREECLAMPSIA	35	1.5	5	2	7	5	2	3.1	7,9	7	9	No	4	2	2
63	31	Booked	32	2	1	160	100	SEVERE PREECLAMPSIA	19	0.7	2	1	6.9	6	1	2.1	4,7	4	7	Yes	12	2	2
64	30	Booked	34.3	2	2	170	110	PP ECLAMPSIA	20	0.5	2	1	7.4	6	2	1.9	07-May	4	3	Yes	12	2	2
65	28	Booked	38.6	2	1	180	120	AP ECLAMPSIA	22	0.9	5	2	7	6	1	2.8	7.8	7	8	No	5	2	2
66	23	Booked	37.4	1	1	150	100	IMMINENT ECLAMPSIA	18	0.6	2	1	7.5	6	1	3	8,9	8	9	No	12	2	2
67	26	Booked	39.1	2	1	170	110	SEVERE PREECLAMPSIA	19	0.7	5	2	6.9	6	2	3	7,8	7	8	No	12	2	2
68	26	Booked	39.6	1	1	160	110	SEVERE PREECLAMPSIA	22	1	5	1	6.6	6	2	3.1	6,8	6	8	Yes	8	2	2
69	27	Booked	39.4	2	3	150	120	IMMINENT ECLAMPSIA	23	1.1	2	1	7.9	6	2	2.5	IUD				4	2	2
70	22	Booked	35.2	2	1	140	100	IMMINENT ECLAMPSIA	20	1	5	1	7.7	6	1	2.1	7,8	7	8	No	2	2	2
71	34	Booked	32.6	2	3	150	110	IMMINENT ECLAMPSIA	17	0.8	5	2	7.4	6	2	2.2	IUD				2	2	2
72	29	Booked	35.2	2	1	170	110	INTRAPARTUM ECLAMPSIA	28	0.6	5	2	7.2	6	2	2.4	7,8	7	8	No	7	2	2
73	19	Booked	38.5	2	1	180	120	AP ECLAMPSIA	23	0.7	5	1	6.1	1	1	3	7,8	7	8	No	4	2	2
74	27	Booked	33.4	1	2	160	100	IMMINENT ECLAMPSIA	23	0.6	2	2	7	6	1	2.1	6,8	6	8	Yes	12	2	2
75	24	Booked	33	1	2	160	110	SEVERE PREECLAMPSIA	41	1.3	2	1	8	6	2	2.5	4,7	4	7	Yes	12	2	2
76	27	Booked	38.5	1	2	150	110	IMMINENT ECLAMPSIA	21	0.5	3	1	7.6	6	1	2.7	8,9	8	9	No	7	2	2
77	30	Booked	34.1	2	1	170	110	SEVERE PREECLAMPSIA	18	0.8	2	1	7.7	1	2	2	6.9	6	9	Yes	12	2	2
78	21	Booked	38.4	2	4	180	100	IMMINENT ECLAMPSIA	16	0.9	3	2	6	3	2	2.8	8,9	8	9	No	12	2	2
79	24	Booked	37.5	1	1	160	100	IMMINENT ECLAMPSIA	19	1	5	2	4.9	6	1	2.9	8,9	8	9	No	12	2	2
80	20	Booked	38.1	1	2	160	90	SEVERE PREECLAMPSIA	24	0.7	5	1	5	1	1	2.6	7,8	7	8	No	12	2	2
81	24	Booked	40	1	1	140	90	IMMINENT ECLAMPSIA	28	0.6	5	1	7.9	6	2	2.5	7,8	7	8	No	5	2	2
82	32	Booked	35.4	2	2	140	100	PP ECLAMPSIA	18	0.5	5	2	5.2	6	2	2	6,8	6	8	No	4	2	2
83	34	Booked	33.1	2	2	160	110	SEVERE PREECLAMPSIA	15	1	3	1	7.4	3	2	2.1	5,7	5	7	Yes	6	2	2
84	28	Booked	37.6	1	2	160	110	SEVERE PREECLAMPSIA	19	0.9	5	2	6.5	6	1	2.9	7,9	7	9	No	12	2	2
85	17	Booked	31.5	1	3	170	110	IMMINENT ECLAMPSIA	22	0.6	4	1	7.2	6	1	2.2	4,6	4	6	Yes		2	2

86	27	Booked	40.1	2	3	170	100	IMMINENT ECLAMPSIA	21	0.8	3	2	6.4	6	2	4.1	8,9	8	9	No	12	2	2
87	32	Not Booked	28.2	2	1	150	110	SEVERE PREECLAMPSIA	18	0.9	5	2	6.6	6	2	1.4	IUD				10	2	2
88	21	Not Booked	30	1	1	150	90	IMMINENT ECLAMPSIA	44	1.4	5	2	7	6	1	1.8	6,7	6	7	Yes	12	2	2
89	36	Booked	34.4	2	4	170	100	IMMINENT ECLAMPSIA	32	1	2	1	6.9	6	2	2	7,8	7	8	No	12	2	2
90	40	Not Booked	29.4	2	1	150	110	IMMINENT ECLAMPSIA	20	1	5	2	4.9	6	2	2	5,6	5	6	Yes	1	2	2
91	18	Booked	32.5	1	2	160	100	IMMINENT ECLAMPSIA	17	0.9	5	2	5.3	6	2	1.9	6.7	6	7	Yes	12	2	2
92	22	Booked	37.6	1	2	150	110	AP ECLAMPSIA	27	0.8	4	1	7.4	6	2	2.5	8,9	8	9	No	12	2	2
93	38	Not Booked	34.1	2	2	130	100	IMMINENT ECLAMPSIA	21	0.6	5	1	7.3	6	2	2.2	6,7	6	7	Yes	12	2	2
94	16	Booked	33.1	1	1	140	100	IMMINENT ECLAMPSIA	22	0.7	2	1	8	6	2	2	7,8	7	8	Yes	12	2	2
95	23	Booked	36.3	1	2	160	110	SEVERE PREECLAMPSIA	29	1.1	3	2	6.3	6	1	2.3	8,9	8	9	No	1	2	2
96	23	Booked	37.4	1	2	160	120	SEVERE PREECLAMPSIA	26	1	2	2	5.9	6	1	2.9	8,9	8	9	No	12	2	2
97	19	Booked	29.4	1	3	170	120	SEVERE PREECLAMPSIA	21	0.6	2	1	7.9	6	2	1.8	IUD				12	2	2
98	18	Booked	36.6	1	2	180	100	IMMINENT ECLAMPSIA	22	0.5	3	2	5.8	6	1	2.1	8,9	8	9	No	1	2	2
99	19	Booked	38.6	2	2	170	100	SEVERE PREECLAMPSIA	28	0.7	5	1	6.6	6	2	2.9	7,8	7	8	No	12	2	2
100	30	Booked	35.4	2	3	180	100	IMMINENT ECLAMPSIA	21	0.9	4	2	5.9	6	2	2	7,8	7	8	No	12	2	2

INSTITUTIONAL ETHICS COMMITTEE
MADURAI MEDICAL COLLEGE & GOVT. RAJAJI HOSPITAL, MADURAI
CDSCO:Reg.No.ECR/1365/Inst/TN/2020 &
DHR Reg.No.EC/NEW/INST/2020/484

Study Title	:	**A Comparative study of intravenous verus intramuscular magnesium sulphate in severe pre-eclampsia and Eclampsia in govt rajaji hospital ,Madurai**
Principal Investigator	:	**Dr.S.Ashmitaa.,**
Designation	:	**PG in MS. O&G (2019 – 2022)**
Guide	:	Dr.N.Sumathy,MD.,DGO., Professor and HOD Department of Obestrics and Gynecology , Govt.Rajaji Hospital & Madurai Medical College, Madurai
Department	:	**Department of Obestrics and Gynecology, Govt. Rajaji Hospital & Madurai Medical College, Madurai.**

The request for an approval from the Institutional Ethics Committee (IEC) was considered on the IEC meeting held on 08.02.2021 at Auditorium, Govt. Rajaji Hospital, Madurai at 10.00 AM.

The Members of the committee, the Secretary and the Chairman are pleased to inform you that your proposed project mentioned above is **Approved.**

You should inform the IEC in case of any changes in study procedure, methodology, sample size investigation, Investigator or guide or any other changes.

1. You should not deviate from the area of work for which you had applied for ethical clearance.

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4. You should complete the work within the specific period and if any extension is required, you should apply for the permission again for extension period.

5. You should submit the summary of the work to the ethical committee on completion of the study.

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This is to certify that the dissertation work titled "**A COMPARATIVE STUDY OF INTRAVENOUS VERSUS INTRAMUSCULAR MAGNESIUM SULPHATE IN SEVERE PRE-ECLAMPSIA AND ECLAMPSIA IN GOVT RAJAJI HOSPITAL, MADURAI**" of the candidate **Dr ASHMITAA,** with the registration number **221916102** for the award of **M.S Degree** in the branch of **Obstetrics and Gynaecology**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **15%** of plagiarism in the dissertation.

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