

COMPARISON OF EFFICACY OF LABETALOL VERSUS ALPHA METHYL DOPA IN THE MANAGEMENT OF PRE ECLAMPSIA

Dissertation submitted to

The Tamil Nadu Dr. M.G.R. Medical University

in partial fulfilment for the award of the Degree of

M.D. (OBSTETRICS AND GYNECOLOGY)

BRANCH-II



**THE TAMIL NADU Dr. M. G. R. MEDICAL UNIVERSITY
INSTITUTE OF SOCIAL OBSTETRICS,
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APRIL 2012

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled “ **COMPARISON OF EFFICACY OF LABETALOL VERSUS ALPHA METHYL DOPA IN THE MANAGEMENT OF PRE ECLAMPSIA** ” is the bonafide work done by **Dr. PREETHI. B**, Post Graduate in Obstetrics and Gynaecology under my over all supervision and guidance in the Institute of Social Obstetrics, Kasturba Gandhi Hospital, Madras Medical College Chennai, in partial fulfillment of the requirements of The Tamil Nadu Dr.M.G.R.Medical University for the award of M.D DEGREE in Obstetrics and Gynaecology BRANCH - II.

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CERTIFICATE OF APPROVAL

To
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Dear Dr. Preethi .B

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the project / proposal / clinical trail entitled " Compare the efficacy of oral labetolol with routinely used regimen of oral anti hypertensive tablet alpha methyl dopa in management of pre eclampsia" No. 04102010.

The following members of Ethics Committee were present in the meeting held on 22.10.2010 conducted at Madras Medical College, Chennai -3.

- | | |
|---|---------------------|
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We approve the Proposal to be conducted in its presented form.

Sd / . Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report


Member Secretary, Ethics Committee

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INTRODUCTION

Pre Eclampsia is a multi-system disorder of unknown etiology, unique to pregnancy characterized by occurrence of Gestational Hypertension along with proteinuria after the 20th week of pregnancy in a previously normotensive and non-proteinuric patient. Gestational Hypertension is defined as Systolic blood pressure of 140 mm of Hg or more and Diastolic blood pressure of 90 mm of Hg or more on two occasions, measured at least 6 hours apart but within 7 days. Proteinuria is defined as excretion of 0.3 g or more of protein in a 24 hour urine sample or >1+ on dipstick in a random sample after excluding urinary tract infection.

Pre Eclampsia complicates 2-8% of pregnancies. Pre Eclampsia can affect virtually every organ system in the body and is a major cause of maternal and perinatal mortality and morbidity. Pre Eclampsia, when not controlled or left untreated can lead to catastrophes like Eclampsia, Abruption placenta, HELLP syndrome, fetal growth restriction, and intrauterine fetal death. Though the definitive treatment of Pre Eclampsia is termination of pregnancy, aggressive treatment is necessary to ameliorate the disease progression in order to carry on the pregnancy till adequate fetal maturity is obtained.

Oral anti hypertensive drugs have a major role in the management of Pre Eclampsia. A comparison is made here between Labetalol and the commonly used drug Alpha methyl dopa in the management of Pre Eclampsia.

REVIEW OF LITERATURE

Preeclampsia, a disorder with genetic and immunological components, occurs in approximately 3% of patients – a figure mirrored worldwide. It is possible that unmanaged preeclampsia could proceed to Eclampsia in a large proportion of cases.

Though Eclampsia was known for centuries and attempts were made to find out the cause of Eclampsia, the concept of preeclampsia was discovered much later. It was only in the 19th century, the link between Eclampsia and preeclampsia was made. Rayer's landmark contribution (1839-1841) provided evidence for renal involvement with the observation of protein in the urine of pregnant, edematous women. Lever (1843), of Guy's Hospital in London, published a paper on a series of cases of puerperal convulsions and reported finding proteinuria in Eclampsia and observed the disappearance of proteinuria after delivery of the child. Lever's work led to the belief that Eclampsia was a renal disease, a form of nephritis.

Blood pressure measurements began in 1910, which was when preeclampsia became distinguished from Eclampsia.

Preeclampsia and Eclampsia still account for 20% of maternal deaths worldwide; the current annual worldwide mortality can be estimated to be about 150, 000 women. The principal causes of death in the UK remain pulmonary complications and cerebral haemorrhage. It became clear earlier on in the 20th century that Eclampsia was a preventable disease and some of the

improvement seen during this time has been due to the development of antenatal care with the early recognition of signs of preeclampsia and immediate treatment.

Methyldopa and labetalol have for many years been primary agents used for control of blood pressure in pregnancy.

Mahmoud TZ, Bjornsson S, Calder AA (1993) prospectively studied the effects of oral labetalol therapy in patients with moderate to severe pregnancy induced hypertension (PIH). The outcome variables were blood pressure control, effect on umbilical artery flow velocity waveforms (UAFVW) and fetal outcome. Forty-two patients were recruited, all had moderate to severe PIH. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) on entry were 154 +/- 7 mmHg and 104 +/- 5 mmHg, respectively. All had significant proteinuria. After 1 week on labetalol therapy, 85% of patients had their blood pressure controlled. The reduction in both SBP and DBP was statistically significant. There were no significant changes in UAFVW, Resistance Index (RI), uric acid or platelets. The mean birth weight was 2712 +/- 609 g. No perinatal mortality occurred in this study. Labetalol is an effective drug in controlling blood pressure and does not adversely affect the UAFVW. No neonatal problems were attributed directly to the drug. Fetal outcome was satisfactory despite the 12 fetuses that were growth-retarded. Labetalol allows safe prolongation of pregnancies complicated by PIH.

Richards et al., (1979) Prichard et al., (1975) established that the dual alpha- and beta-adrenoceptor blocking properties of labetalol in normal subjects and

hypertensive patients lead to a similar pattern of circulatory effects. Following acute intravenous administration in the supine position, significant reductions in blood pressure occur without a fall in heart rate or cardiac output. After continuous oral administration to patients, small reductions in resting heart rate are usually found (Lund-Johansen, 1979), although individual changes are influenced by the degree of resting sympathetic drive. Marked reductions in resting heart rate after labetalol may follow intravenous administration (Cumming et al., 1979; Marx & Reid, 1979). Cardiac output at rest does not usually change much after labetalol treatment (Koch, 1976; Edwards & Raftery, 1976; Mehta & Cohn, 1977).

Mabie and coworkers (1987) compared bolus intravenous labetalol with intravenous hydralazine in the acute treatment of severe hypertension. They found that labetalol had a quicker onset of action and did not result in reflex tachycardia. In terms of fetal effects, blood pressure reduction with labetalol does not result in fetal distress (Mahmoud and co-workers, 1993) unlike acute blood pressure reduction with hydralazine where 15% of fetuses will exhibit distress frequently requiring immediate cesarean section for delivery. Studies of uteroplacental blood flow indicate that no decrease in perfusion occurs despite the reduced maternal blood pressure (Lunell and co-workers, 1982). As with all beta-blockers, labetalol has been associated with hypoglycemia, bradycardia and hypotension but neonatal outcome is uniformly good and ACOG currently recommends labetalol as one of the first line antihypertensive medications for preeclampsia (ACOG, 1996).

Labetalol has some interesting, and potentially, important non-antihypertensive effects that may be beneficial in preeclampsia. Among these are an anti-platelet aggregation action, a thromboxane reducing effect (Greer and co-workers, 1985), and a fetal lung maturation accelerating influence (Micheal and co-workers, 1980).

A prospective placebo controlled study done in Nottingham (1992) included 144 women (86 primigravidae) who developed PIH after 20 weeks gestation. They were treated with either oral labetalol up to 600 mg daily or placebo. Main outcomes measured included the number of days spent as an antenatal inpatient; the development of proteinuria; the perceived need for induction of labour or elective caesarean section; and gestation age at delivery. According to the study, Labetalol significantly lowered the blood pressure and reduced the incidence of proteinuria. However, neither the number of days spent as an antenatal inpatient, nor the perceived need for induction of delivery or elective caesarean section, nor the gestation age at delivery differed significantly between the two treatment groups. The placebo treated early-onset group seemed to have more patients with severe hypertension ($> 150/110$ mmHg) and a greater requirement for additional antihypertensive therapy prior to labour than the group treated with labetalol.

PRE ECLAMPSIA

Preeclampsia is best described as pregnancy-specific syndrome that can affect virtually every organ system. Although preeclampsia is much more than

simply gestational hypertension with proteinuria, appearance of proteinuria remains an important objective diagnostic criterion. Proteinuria is defined by 24-hour urinary protein excretion exceeding 300 mg, a urinary protein:creatinine ratio of ≥ 0.3 or persistent 30 mg/dl (1+ dipstick) in random urine samples (Lindheimer and colleagues, 2008 a). Some women may have atypical preeclampsia with all aspects of the syndrome, but without hypertension or proteinuria, or both (Sibai and Stella, 2009).

Eclampsia

The onset of generalized convulsions in a woman with preeclampsia that cannot be attributed to epilepsy or other causes is termed Eclampsia. Eclampsia is a preventable condition. Adequate prenatal care, early detection of preeclampsia and its adequate control can prevent Eclampsia; hence the need to treat preeclampsia aggressively.

Indicators of Severity of Preeclampsia

Pre Eclampsia is divided into mild and severe. Severe Pre Eclampsia is characterized by one or more of the following:

1. Severe hypertension (BP 160/110 mm of Hg or more)
2. Proteinuria (>5 g/24 hours or 3+ or more on random samples)
3. Oliguria (<500 ml /24 hours)
4. Elevated serum creatinine level
5. Pulmonary oedema
6. Thrombocytopenia ($<1, 00,000$ /cumm)

7. Microangiopathic hemolysis
8. Elevated liver enzymes
9. Symptoms of end-organ involvement like headache, blurring of vision and epigastric pain
10. Fetal growth restriction.
11. HELLP Syndrome

RISK FACTORS

1. Age – Pre Eclampsia is more likely to occur at both extremes of age, but is greatest in women younger than 20 years of age.
2. Parity – Pre Eclampsia is believed to be a disease of primigravidae. The incidence of pre Eclampsia in multiparous women is lower than primipara women.
3. Obstetric factors – Pre Eclampsia occurs most commonly in pregnancies associated with a large placenta, such as multiple pregnancies, molar pregnancies and hydrops fetalis. Hydramnios and history of Pre Eclampsia in previous pregnancy are also predisposing factors.
4. Pre existing medical disorders – like Hypertension, Gestational Diabetes, Renal disease, Obesity, Thrombophilias (both inherited and acquired) such as Antiphospholipid antibody syndrome, Factor 5 Leiden deficiency, Activated protein C resistance, and hyperhomocysteinaemia.

5. Family history – Women with Pre Eclampsia are more likely to have family history of female relatives (mothers or sisters) affected by preeclampsia.

AETIOPATHOGENESIS

The exact etiology of Pre Eclampsia remains unknown. Several theories have been proposed over the years. As Boyd stated Pre Eclampsia remains “die krankheit der theorien” – the disease of theories. Any satisfactory theory concerning the etiology and pathogenesis of Pre Eclampsia must account for the observation that Pre Eclampsia is more likely to develop in women who:

- Are exposed to chorionic villi for the first time
- Are exposed to a superabundance of chorionic villi, as with twins or hydatidiform mole
- Have preexisting renal or cardiovascular disease
- Are genetically predisposed to hypertension developing during pregnancy.

Thus, presence of a fetus is not a requisite for preeclampsia, although chorionic villi are essential. The chorionic villi need not be located within the uterus. Worley and associates (2008) reported a 30-percent incidence of preeclampsia in women with an extrauterine pregnancy exceeding 18 weeks gestation.

Preeclampsia as a Two- Stage Disorder

Observations that abnormal interfaces between maternal, paternal and fetal tissues may cause preeclampsia have led to hypothesis that the syndrome is a two-stage disorder. According to Redman and colleagues (2009), stage 1 is caused by faulty endovascular trophoblastic remodeling that downstream causes the stage 2 clinical syndrome. Importantly, stage 2 is susceptible to modification by preexisting maternal conditions that include cardiac or renal disease, diabetes, obesity, or hereditary influences. Thus, although such compartmentalization is helpful to classify the syndrome for research purposes, preeclampsia is clinically a continuum of worsening disease.

ETIOLOGY

Instead of being simply ‘one disease,’ preeclampsia appears to be a culmination of factors that likely involves a number of maternal, paternal and fetal factors. Those currently considered important include:

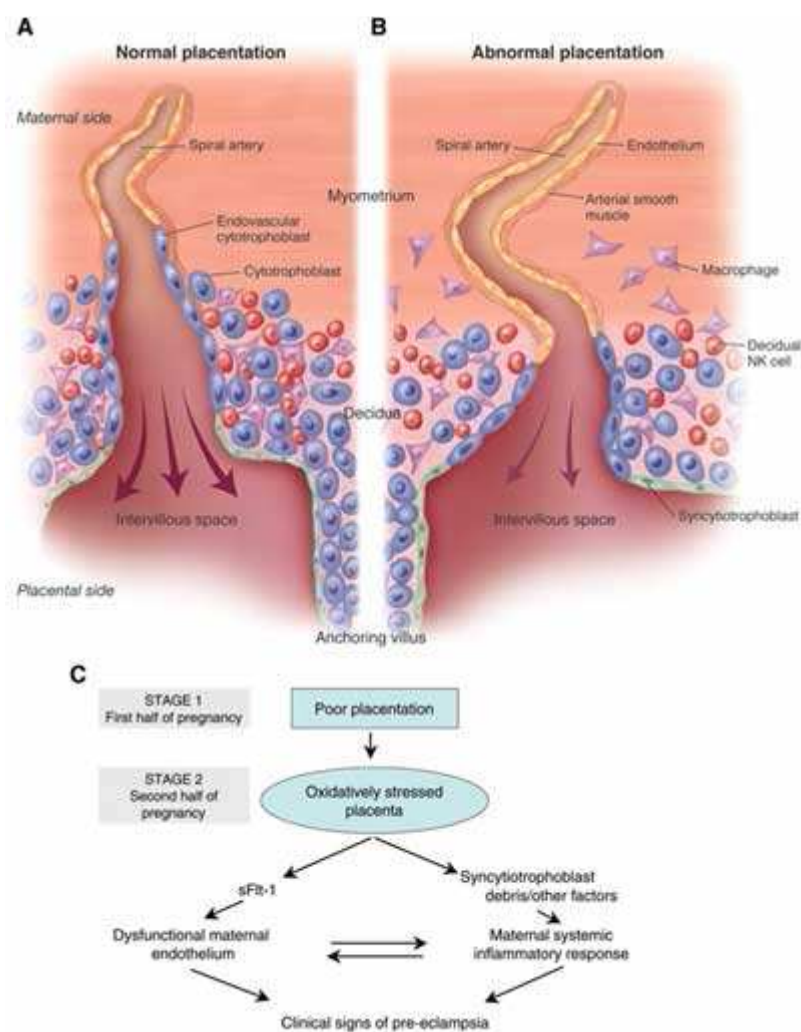
1. Placental implantation with abnormal trophoblastic invasion of uterine vessels
2. Immunological maladaptive tolerance maternal, paternal (placental) and fetal tissues
3. Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy
4. Genetic factors including inherited predisposing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

Abnormal Trophoblastic Invasion

The inciting organ in Pre Eclampsia is essentially the placenta. Abnormal placentation, in particular lack of dilatation of the uterine spiral arteries leading to placental ischaemia, seems to be the common denominator in the genesis of Pre Eclampsia. Optimal placental development in normal pregnancy involves a process of controlled trophoblastic invasion extending from the deciduas up to the inner third of myometrium. The endothelial lining and the muscular layer of the spiral arteries are disrupted and replaced by cytotrophoblasts, in turn converting the small caliber muscular arteries into large capacity low resistance spaces. The process commences around 10-12 weeks and is completed by 18-20 weeks. In women destined to develop Pre Eclampsia, there is incomplete trophoblastic invasion. With such shallow invasion, decidual vessels, but not myometrial vessels become lined with endovascular trophoblasts. The deeper myometrial arteries do not lose their endothelial lining and musculoelastic tissue. Thus, the mean external diameter of these vessels is only half that of vessels in normal placentas (Fisher and colleagues, 2009), resulting in reduced uteroplacental blood flow.

The ensuing placental ischaemia and hypoxia leads to an aberrant expression of genes which encode for certain cytokines and vasoactive molecules, inciting a systemic inflammatory response that contributes to the pathophysiology of Pre Eclampsia. Using electron microscopy, De Wolf and co-workers (1980) examined arteries taken from the implantation site. They

reported that early preeclamptic changes included endothelial damage, insudation of plasma constituents into vessel wall, proliferation of myointimal cells and medial necrosis. Lipid first accumulated in myointimal cells and then within macrophages. Such lipid-laden cells and associated findings were referred to as atherosclerosis by Hertig (1945). Typically the vessels affected by atherosclerosis develop aneurismal dilatation (Khong, 1991).



Immunological factors

Loss of maternal immune tolerance to paternally derived placental and fetal antigens, or perhaps its dysregulation, is another theory cited to account

for preeclampsia syndrome. The histological changes at the maternal-placental interface in preeclampsia are suggestive of acute graft rejection (Labrere, 1988). Tolerance dysregulation might also explain an increased risk when the paternal antigenic load is increased, that is, with two sets of paternal chromosomes – a “double dose”. For example, women with molar pregnancies have a high incidence of early-onset preeclampsia.

Redman and colleagues (2009) recently reviewed the possible role of immune maladaptation in the pathophysiology of preeclampsia. Early in a pregnancy destined to be preeclamptic, extravillous trophoblasts express reduced amounts of immunosuppressive human leukocyte antigen G (HLA-G). This may contribute to defective placental vascularisation in stage 1.

Endothelial Cell Dysfunction

Endothelial cell dysfunction in Pre Eclampsia occurs in response to placental factors released secondary to ischaemic changes, setting a cascade of events in motion. Briefly, cytokine such as tumour necrosis factor (TNF-alpha) and the interleukins (IL) may contribute to the oxidative stress associated with preeclampsia. This is characterized by reactive oxygen species and free radicals that lead to formation of self propagating lipid peroxides (Manten and associates, 2005). These in turn generate highly toxic radicals that injure endothelial cells, modify their nitric oxide production, and interfere with prostaglandin balance. Other consequences of oxidative stress include

activation of microvascular coagulation manifest by thrombocytopenia and increased capillary permeability manifest by oedema and proteinuria.

Genetic factors

Preeclampsia is a multifactorial, polygenic disorder. In their comprehensive review, Ward and Lindheimer (2009) cite an incident risk for preeclampsia of 20-40 percent for daughters of preeclamptic mothers; 11-37 percent for sisters of preeclamptic women; and 22-47 percent in twin studies. From their recent review, Ward and Lindheimer (2009) found that more than 70 genes have been studied for their possible association with preeclampsia. This hereditary predisposition is likely the result of hundreds of inherited genes. From their recent review, Ward and Lindheimer (2009) found that more than 70 genes have been studied for their possible association with preeclampsia.

PATHOGENESIS

Endothelial Cell Activation

During the past two decades, endothelial cell activation has become the centerpiece in understanding the pathogenesis of preeclampsia. Unknown factors – likely placental in origin – are secreted into the placental circulation and provoke activation and dysfunction of the vascular endothelium. The clinical syndrome of preeclampsia is thought to result from these widespread endothelial cell changes. Grundmann and associates (2008) have reported that

circulating endothelial cell – CEC – levels are significantly elevated fourfold in the peripheral blood of preeclamptic women. Intact endothelium has anticoagulant properties, and endothelial cells blunt the response of vascular smooth muscle to pressor agents by releasing nitric oxide. Damaged and activated endothelial cells may produce less nitric oxide and increase sensitivity to vasopressors and secrete substances that promote coagulation.

Prostaglandins

A number of prostanoids are thought to be central to the pathophysiology of preeclampsia syndrome. Specifically, the blunted pressor response in normal pregnancy is at least partially mediated by endothelial prostaglandin synthesis. Compared with normal pregnancy, endothelial prostacyclins (PGI₂) production is decreased in preeclampsia, thromboxane A₂ secretion by platelets is increased and the prostacyclin: thromboxane A₂ ratio decreases. These actions are mediated by phospholipase A₂. The net result favors increased sensitivity to infused angiotensin 2, and ultimately, vasoconstriction. Chavarria and co-workers (2003) have provided that these changes are apparent as early as 22 weeks in women who later develop preeclampsia.

Endothelins

These 21-amino acid peptides are potent vasoconstrictors, and endothelin-1 is the primary isoform produced by human endothelium. Plasma

ET-1 levels are increased in normotensive pregnancies, but women with preeclampsia have even higher levels. According to Taylor and Roberts (1999), endothelins arise from systemic endothelial activation and not from placental source.

Angiogenic and Antiangiogenic Proteins

Angiogenic imbalance in preeclampsia is used to describe excessive amounts of antiangiogenic factors that are hypothesized to be stimulated at the uteroplacental interface by worsening hypoxia. Trophoblastic tissue of women destined to develop preeclampsia overproduces at least two antiangiogenic peptides that enter the maternal circulation:

1. Soluble Fms-like tyrosine kinase 1 (sFlt-1)
2. Soluble endoglin (sEng)

PATHOPHYSIOLOGY

Placenta - Placentae from preeclamptic pregnancies have shown an increased incidence of infarcts, haematomas, congested chorionic villi, proliferative endarteritis and degeneration, although the changes are not specific to preeclampsia. Microscopy reveals increased syncytial knots, cytotrophoblastic cellular proliferation, fibrinoid necrosis, endothelial proliferation and calcified and hyalinised villous spots.

Kidney – Preeclampsia appears to have a characteristic renal lesion termed as ‘glomerular capillary endotheliosis’. The glomeruli are diffusely enlarged and avascular. Electron microscopy reveals endothelial cell hyperplasia and exudation of foamy macrophages, lymphocytes and polymorphonuclear leukocytes within the capillary lumen and mesangium. The capillary walls show hypertrophied endothelial cells, subendothelial fibrinoid and granular deposits and interposition of mesangial cells resulting in reduced glomerular filtration. However, these lesions resolve completely after pregnancy.

Liver – The pathological changes in the liver include periportal haemorrhages, ischaemic lesions and fibrin deposition. Liver damage may vary from mild hepatocellular necrosis to severe lung injury with marked increase in liver enzymes, subcapsular rupture and rarely even liver rupture.

Brain – The brain may show cortical and subcortical petechial hemorrhages, subcortical oedema, multiple areas of softening throughout the brain and gross intracerebral haemorrhage in the basal ganglia or pons, often with rupture into the ventricles. The classical microscopic lesions consist of fibrinoid necrosis of the arterial wall and perivascular microinfarcts and haemorrhages.

Other organs – Subendocardial petechial haemorrhages may be present in the myocardium. The lungs may demonstrate pulmonary oedema. Haemorrhages and necrosis of the adrenal glands are likely to occur.

COMPLICATIONS

Maternal

1. Eclampsia
2. HELLP syndrome
3. Abruption placenta
4. Acute left ventricular failure with pulmonary oedema
5. Acute renal failure
6. Cerebrovascular accidents

Fetal

1. Intrauterine death
2. Intrauterine growth restriction
3. Prematurity
4. Antepartum and intrapartum asphyxia

MANAGEMENT

The only definitive cure of preeclampsia is termination of pregnancy. Hence, management is directed towards early detection and amelioration of its progression, the goal being to prolong the pregnancy to achieve fetal maturity and prevent maternal complications. Management is determined by the period of gestation and the maturity and growth of the foetus. If the pregnancy is 37 weeks or more, elective induction of labour should be performed. When hypertension develops earlier, the aim is to continue pregnancy upto 37 weeks

if possible, with close maternal and fetal monitoring to ensure adequate growth and maturity of the baby.

The management of severe preeclampsia at various gestational ages is as follows:

- <=24 weeks - stabilize the patient and terminate pregnancy
- 25 – 33 weeks - expectant management with intensive maternal and fetal surveillance. Deliver if maternal or fetal indication
- >= 34 weeks - stabilize the patient, strict fetal surveillance and deliver

Antihypertensive therapy plays a very important role in preeclampsia. Antihypertensive agents reduce the blood pressure and thereby allow continuation of pregnancy and reduce the need to terminate the pregnancy prematurely. The commonly used antihypertensives include

Methyldopa:

Methyldopa is a centrally acting agent (alpha-adrenergic receptor blocker) and remains the drug of first choice for treating hypertension in pregnancy. It has been the most frequently assessed antihypertensive in randomized trial and has the longest safety track record. Treatment does not seem to have adverse effects on utero-placental or on foetal haemodynamics. Long term use has not been associated with fetal or neonatal problems and there are safety data for children exposed in utero up to 7.5 years follow up available, the children exhibited intelligence and cognitive development similar

to control subjects. Dose of methyldopa is 250 mg (thrice or four times daily), not exceeding 3 gm/day. Side effects are consequence of central alpha-2 agonism or decrease peripheral sympathetic tone and include decreased mental alertness and impaired sleep leading to fatigue and depression in some patients, increased liver enzymes (in 5% cases) and a positive coomb's test (rare).

Labetalol:

Labetalol is an adrenergic receptor blocking agent possessing both alpha-1 (Post synaptic) and beta₁ receptor blocking activity (4 times more potent action on beta-receptors than on alpha₁ receptors). It lowers blood pressure by partially blocking alpha-adrenoceptors in the peripheral arterioles, thus causing vasodilatation and resulting reduction of peripheral resistance. At the same time, blocking of beta-adrenoceptors in the myocardium prevents reflex tachycardia and subsequent elevation of blood pressure. Recommended initial dose 100 mg twice daily, maximum dose is 2,400 mg daily. The peak effects of single oral doses of labetalol occur within 2 to 4 hours. The duration of effect depends upon dose, lasting at least 8 hours following single oral doses of 100 mg and more than 12 hours following single oral doses of 300 mg. The maximum, steady-state blood pressure response upon oral, twice-a-day dosing occurs within 24 to 72 hours. The metabolism of labetalol is mainly through conjugation to glucuronide metabolites. These metabolites are present in plasma and are excreted in the urine, and via the bile, into the faeces. Adverse effects are consequence of alpha₁ receptor block and include fatigue, lethargy,

and exercise intolerance due to alpha 2 blocking effect in skeletal muscle vasculature, peripheral vasoconstriction, sleep disturbances, and bronchospasm. Labetalol should not be used in women with asthma or having history of obstructive airway diseases, uncontrolled CCF, 2nd or 3rd degree AV block, severe peripheral arterial disease and hepatic impairment.

Nifedipine:

Nifedipine is a calcium channel blocker, used in preeclampsia as first-line therapy or in combination with other antihypertensives. Nifedipine is available as 5 mg and 10 mg tablets. The dose is 10-20 mg three or four times daily, with a maximum dose of 120 mg/ day.

Hydralazine:

Hydralazine acts directly on the arterial smooth muscle to cause vasodilatation. It is given orally in a dose of 25 to 100 mg three or four times daily with a maximum daily dose 300 mg.

AIM OF THE STUDY

This study compares the efficacy of oral Labetalol versus oral Alpha methyl dopa in the management of Pre Eclampsia in terms of reducing the blood pressure, need for labour induction, mean birth weight, APGAR score and rate of neonatal admissions.

MATERIALS AND METHODS

STUDY DESIGN:

Prospective case control study

SETTINGS:

This randomized prospective comparative study was conducted at Institute of Social Obstetrics and Govt. Kasturba Gandhi Hospital for Women and Children, Triplicane, Chennai, on hundred patients, diagnosed as preeclampsia and admitted in the Eclampsia ward.

DURATION OF STUDY:

From September 2010 to August 2011

METHODOLOGY:

The patients included in this study were assigned to two groups at random of 50 patients in each group.

GROUP 1:

Tablet Alpha methyl dopa (Aldomet) 250 mg was given thrice daily.

GROUP 2:

Tablet Labetalol 100 mg was given twice daily.

INCLUSION CRITERIA

All patients with Gestational Hypertension (more than 20 weeks of gestation till term)

- Systolic Blood Pressure of 140 mm of Hg or more
- Diastolic Blood Pressure of 90 mm of Hg or more
- Proteinuria (0.3 g in 24 hours or more/ 1+ dipstick or more)

EXCLUSION CRITERIA

- Chronic Hypertension
- Renal Disease
- Liver Disease
- Bronchial Asthma
- GDM
- Cardiac Disease
- Imminent symptoms :
 - ❖ Headache
 - ❖ Blurring
 - ❖ Epigastric pain
 - ❖ Oliguria(<500 mg/24 hrs)

- Complications –
 - ❖ Acute LVF
 - ❖ Coagulation failure
 - ❖ Intracerebral Hemorrhage
 - ❖ HELLP Syndrome
- Eclampsia

PROCEDURE

Informed consent was obtained from these patients before administration of the drugs. Blood Pressure was recorded every 12th hourly. The treatment was continued till delivery if the blood pressure is controlled. If the blood pressure was not controlled within 48 hours, the dose of drugs was doubled. Blood pressure was measured by a mercury sphygmomanometer over the right arm in the sitting position after a period of rest for 15 minutes. Korotkoff phase 5 was used to define diastolic blood pressure. Proteinuria was detected using the sulphosalicylic acid test. The period of study was 1 year. The change in BP after 48 hours, need for induction, and mode of termination of pregnancy, birth weight, Apgar score and neonatal admissions were recorded.

RESULTS AND ANALYSIS

This study was commenced with 100 women and the outcome was analyzed using various parameters. The results were subjected to statistical analysis using the t test and chi square test.

AGE GROUP:

TABLE 1:

AGE IN YEARS	LEGEND		GROUP 1 ALPHA METHYL DOPA	GROUP 2 LABETALOL	Total
< 20	1	Count	6	6	12
		% within GROUP	12.0%	12.0%	12.0%
21-25	2	Count	21	19	40
		% within GROUP	42.0%	38.0%	40.0%
26-30	3	Count	17	20	37
		% within GROUP	34.0%	40.0%	37.0%
>30	4	Count	6	5	11
		% within GROUP	12.0%	10.0%	11.0%
	Total	Count	50	50	100
		% within GROUP	100.0%	100.0%	100.0%

The above table shows the prevalence of preeclampsia in each age group.

Most of the patients in both Groups were in the age group of 21-25 yrs. 42% of cases in Group 1 and 38% of cases in Group 2 were in the age group of 21-25 yrs. However, this was not statistically significant (p value = 0.933)

Bar Chart

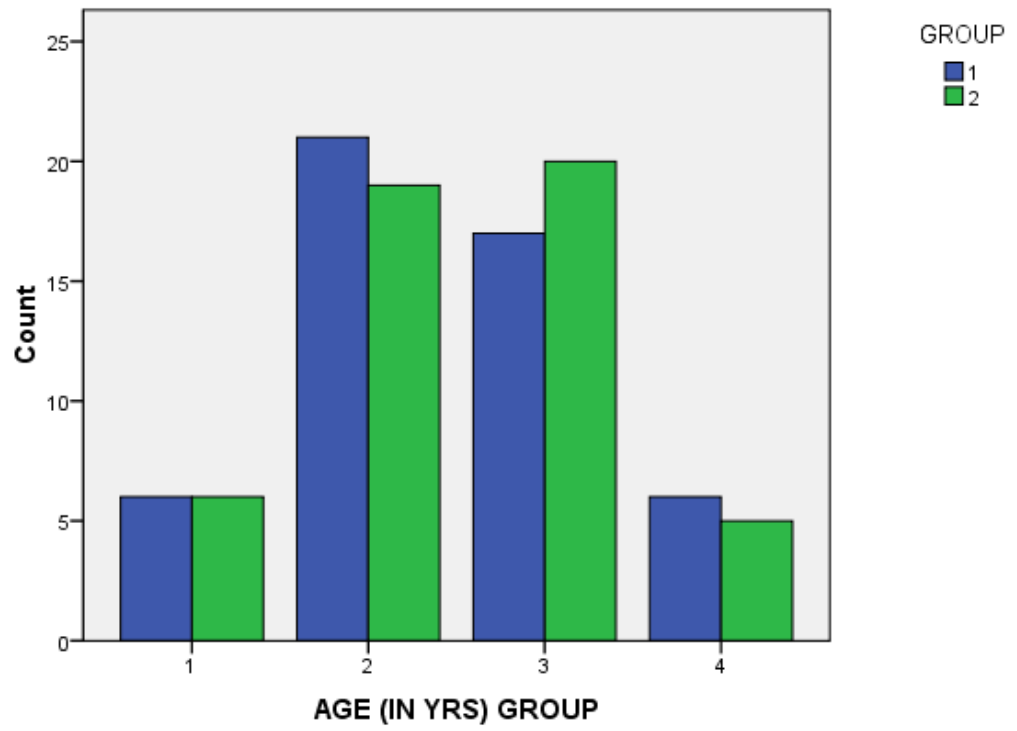


TABLE 2:

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
AGE (IN YRS)	1	50	25.50	3.808	.539
	2	50	25.82	4.443	.628

The above table shows the mean ages of the patients in both the Groups.

The difference between the mean ages between the two Groups is not statistically significant (p value = 0.700).

PARITY:**TABLE 3:**

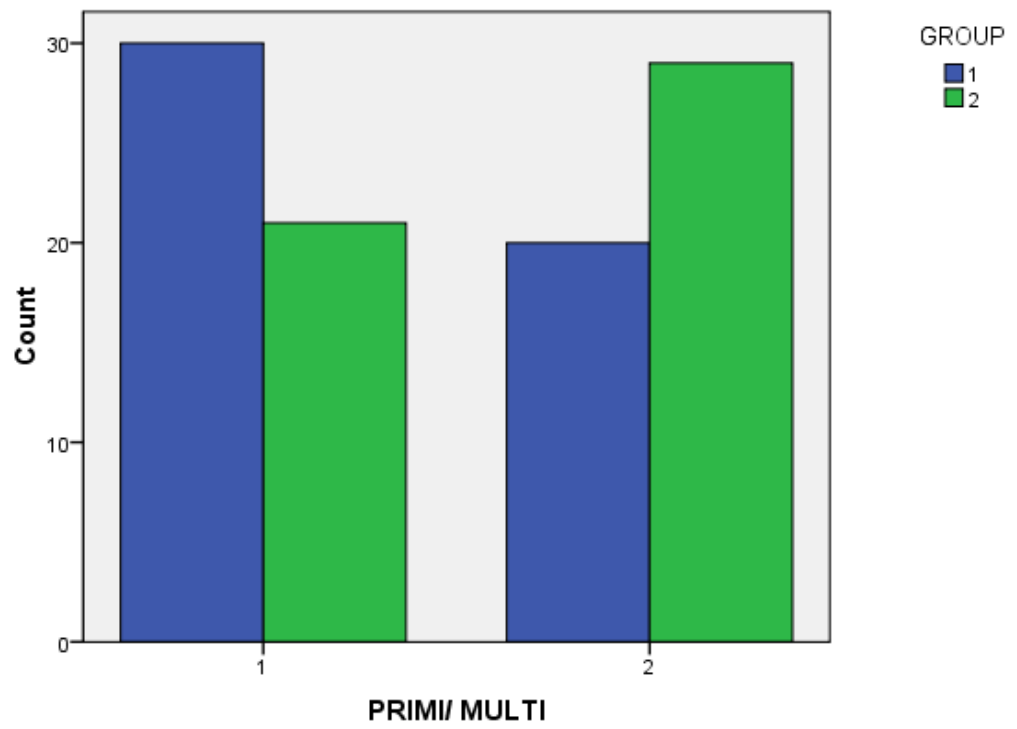
PARITY	LEGEND		GROUP 1 ALPHA METHYL DOPA	GROUP 2 LABETALOL	Total
PRIMI	1	Count	30	21	51
		% within GROUP	60.0%	42.0%	51.0%
MULTI	2	Count	20	29	49
		% within GROUP	40.0%	58.0%	49.0%
	Total	Count	50	50	100
		% within GROUP	100.0%	100.0%	100.0%

p value = 0.072

60% of women in Group 1 and 40% of women in Group 2 were primigravidae.

40% of women in Group 1 and 58% of women in Group 2 were multigravidae.

Bar Chart



GESTATIONAL AGE:**TABLE 4:**

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
GESTATION AGE (IN WEEKS)	1	50	37.90	1.930	.273
	2	50	37.94	1.596	.226

The above table shows the mean gestational age in both the Groups. The difference between the mean gestational ages between the two Groups is not statistically significant (p value = 0.910).

BODY MASS INDEX:**TABLE 5:**

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
BODY MASS INDEX	1	50	27.0076	3.28910	.46515
	2	50	27.3086	3.76136	.53194

The above table shows the mean BMI in both the Groups. The difference between the mean BMI between the two groups is not significant (p value = 0.671).

BLOOD PRESSURE:

TABLE 6:

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
SYSTOLIC BLOOD PRESSURE IN MM OF HG	1	50	150.60	8.668	1.226
	2	50	150.20	8.204	1.160
DIASTOLIC BLOOD PRESSURE IN MM OF HG	1	50	103.40	4.785	.677
	2	50	102.40	4.314	.610

The above table shows the mean systolic and diastolic blood pressures in both the Groups. There is no statistically significant difference between the mean systolic blood pressures between the two Groups (p value = 0.813). Also there is no statistically significant difference between the mean diastolic blood pressures between the two Groups (p value =0.275)

BP AFTER 48 HOURS:

TABLE 7:

BP AFTER 48 HRS	GROUP	N	Mean	Std. Deviation	Std. Error Mean
SYSTOLIC BLOOD PRESSURE IN MM OF HG	1	50	146.20	8.303	1.174
	2	50	144.60	8.621	1.219
DIASTOLIC BLOOD PRESSURE IN MM OF HG	1	50	95.00	7.354	1.040
	2	50	91.20	6.273	.887

The above table shows the mean systolic and diastolic blood pressures in both the Groups 48 hrs after administration of the drug. There is no statistically significant difference between the mean systolic blood pressures between the two Groups (p value = 0.347). However, there is a statistically significant difference between the mean diastolic blood pressures between the two Groups (p value =0.007)

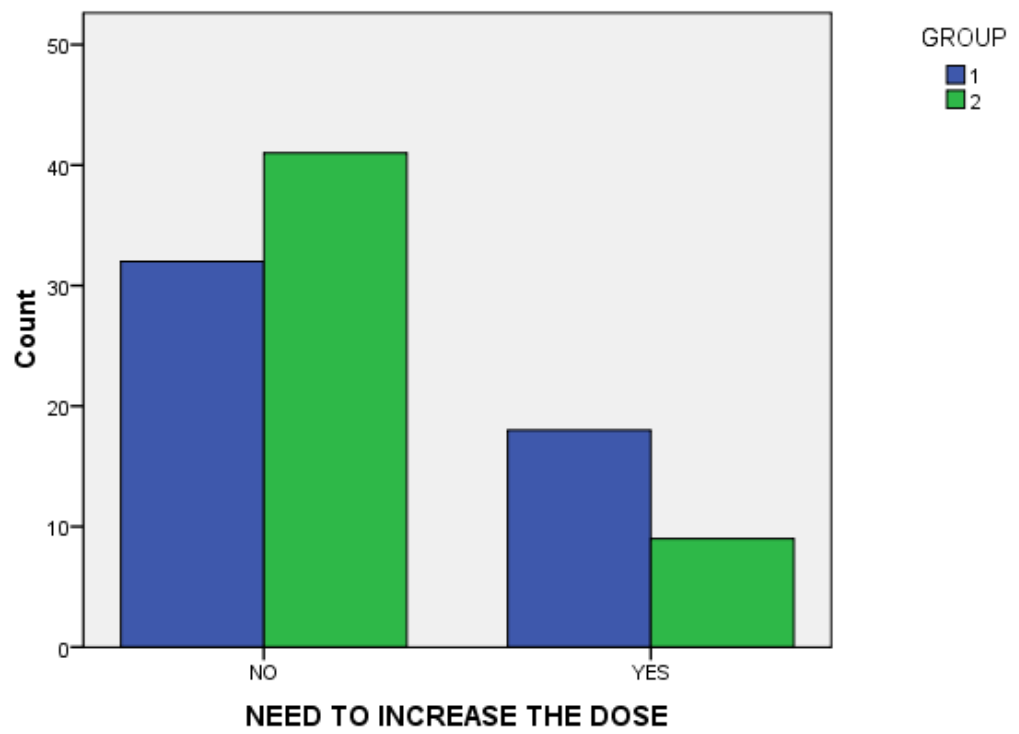
NEED TO INCREASE THE DOSE:

TABLE 8:

NEED TO INCREASE THE DOSE		GROUP 1 ALPHA METHYL DOPA	GROUP 2 LABETALOL	Total
NO	Count	32	41	73
	% within GROUP	64.0%	82.0%	73.0%
YES	Count	18	9	27
	% within GROUP	36.0%	18.0%	27.0%
Total	Count	50	50	100
	% within GROUP	100.0%	100.0%	100.0%

This table shows the need to increase the dose after 48 hrs in both the groups. 36% of the cases in Group 1 needed an increase in the dose when compared to 18% in Group 2. There is a statistically significant need to increase the dose after 48 hrs in Group 1 when compared to Group 2 (p value = 0.043).

Bar Chart



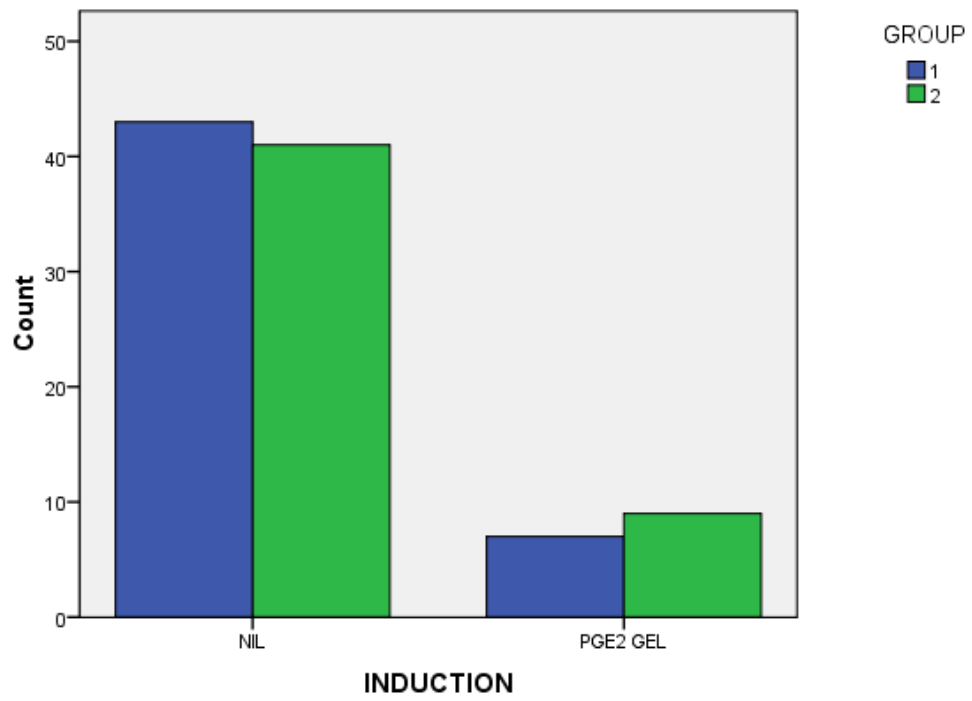
NEED FOR INDUCTION:

TABLE 9:

INDUCTION		GROUP 1 ALPHA METHYL DOPA	GROUP 2 LABETALOL	Total
NIL	Count	43	41	84
	% within GROUP	86.0%	82.0%	84.0%
PGE2 GEL	Count	7	9	16
	% within GROUP	14.0%	18.0%	16.0%
Total	Count	50	50	100
	% within GROUP	100.0%	100.0%	100.0%

The above table shows the need for induction in both the Groups. 14% in Group 1 and 18% in Group 2 were induced with PGE2 gel. However, this is not statistically significant (0.585)

Bar Chart



MODE OF DELIVERY:

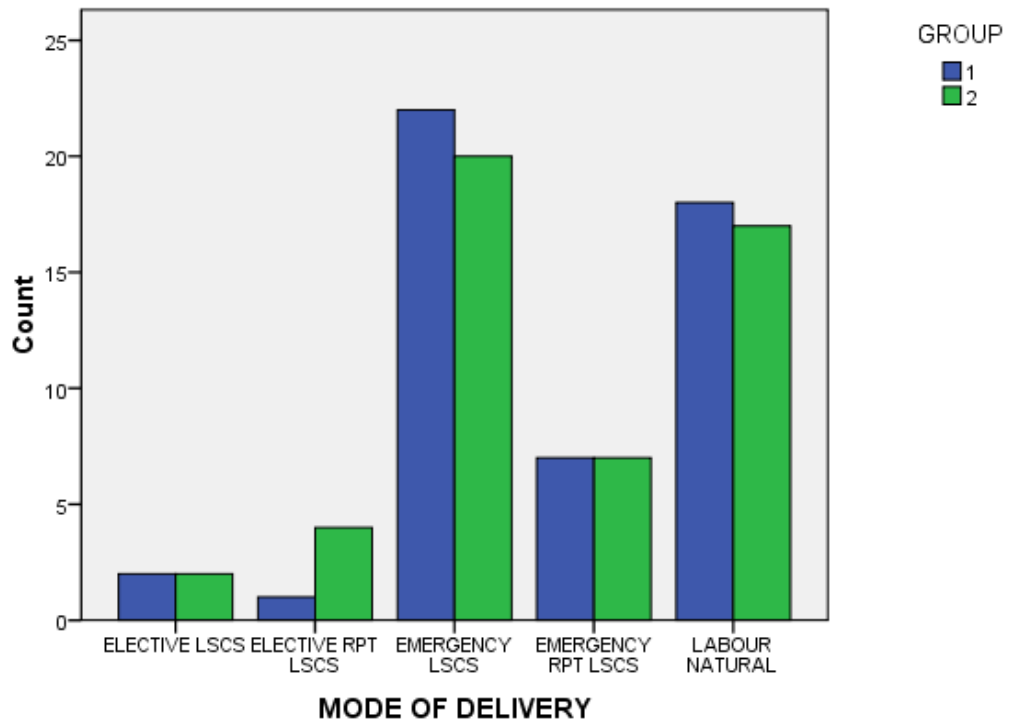
TABLE 10:

MODE OF DELIVERY		GROUP 1 ALPHA METHYL DOPA		Total
			GROUP 2 LABETALOL	
ELECTIVE LSCS	Count	2	2	4
	% within GROUP	4.0%	4.0%	4.0%
ELECTIVE RPT LSCS	Count	1	4	5
	% within GROUP	2.0%	8.0%	5.0%
EMERGENCY LSCS	Count	22	20	42
	% within GROUP	44.0%	40.0%	42.0%
EMERGENCY RPT LSCS	Count	7	7	14
	% within GROUP	14.0%	14.0%	14.0%
LABOUR NATURAL	Count	18	17	35
	% within GROUP	36.0%	34.0%	35.0%
Total	Count	50	50	100
	% within GROUP	100.0%	100.0%	100.0%

p value = 0.750

The above table shows the mode of delivery in both the Groups. 44% of cases in Group 1 and 40% of cases in Group 2 underwent Emergency LSCS. 36% of cases in Group 1 and 34% of cases in Group 2 were delivered by Labour natural.

Bar Chart



BP AT THE TIME OF DELIVERY:

TABLE 11:

BP AT THE TIME OF DELIVERY	GROUP	N	Mean	Std. Deviation	Std. Error Mean
SYSTOLIC BP IN MM OF HG	1	50	143.00	9.530	1.348
	2	50	139.40	9.982	1.412
DIASTOLIC BP IN MM OF HG	1	50	91.60	7.918	1.120
	2	50	89.40	6.197	.876

The above table shows the mean systolic and diastolic blood pressures in both the Groups at the time of delivery. There is no statistically significant difference between the mean systolic blood pressures between the two Groups (p value = 0.068). Also there is no statistically significant difference between the mean diastolic blood pressures between the two Groups (p value =0.125)

BIRTH WEIGHT:**TABLE 12:**

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
BIRTH WEIGHT	1	50	2.67736	.604872	.085542
	2	50	3.11936	.611578	.086490

The above table shows the mean birth weight in both the Groups. The difference between the mean birth weights between the two groups is 442 g, which is statistically significant (p value = 0.000 < 0.01).

APGAR:**TABLE 13:**

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
APGAR	1	50	8.24	1.318	.186
	2	50	8.64	1.064	.151

The above table shows the mean APGAR scores in both the Groups. The difference between the mean APGAR score between two groups is 0.4, which is not statistically significant (p value = 0.090)

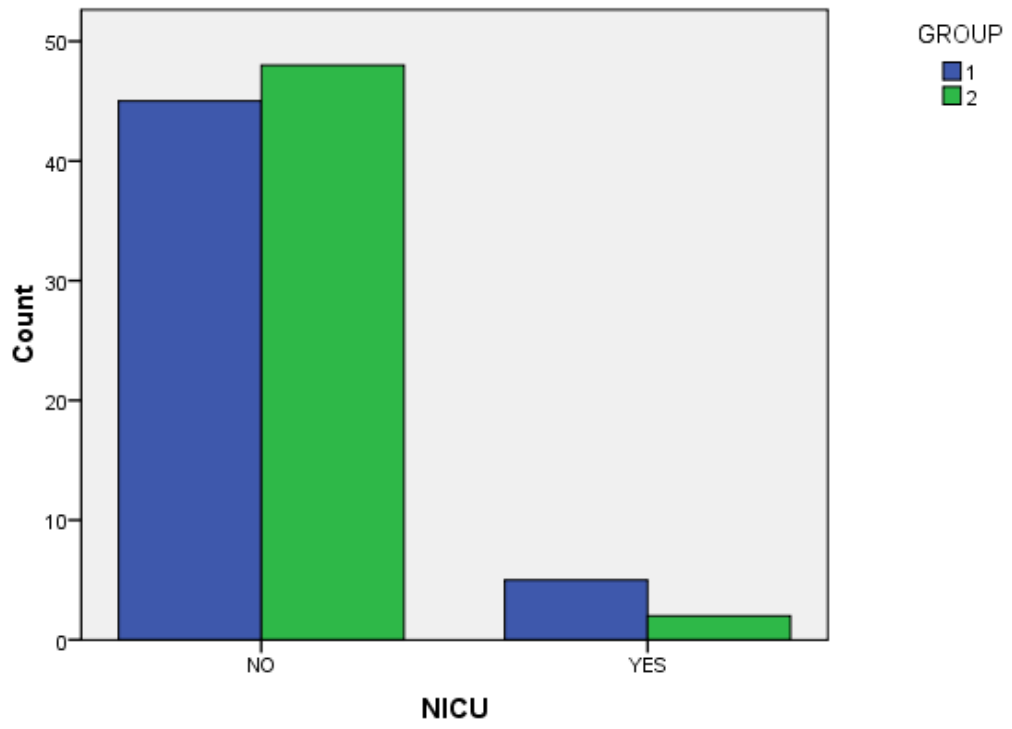
NICU ADMISSION:

TABLE 14:

NICU ADMISSION		GROUP 1 ALPHA METHYL DOPA	GROUP 2 LABETALOL	TOTAL
NO	Count	45	48	93
	% within GROUP	90.0%	96.0%	93.0%
	% of Total	45.0%	48.0%	93.0%
YES	Count	5	2	7
	% within GROUP	10.0%	4.0%	7.0%
	% of Total	5.0%	2.0%	7.0%
Total	Count	50	50	100
	% within GROUP	100.0%	100.0%	100.0%
	% of Total	50.0%	50.0%	100.0%

The above table shows the need for NICU admission in both the Groups. 10% of babies delivered in Group 1 and 4% of babies delivered in Group 2 needed NICU admission. However, this difference is not statistically significant (p value = 0.240).

Bar Chart



DISCUSSION

This randomized prospective study compares the efficacy of oral labetalol versus oral alpha methyl dopa in the management of preeclampsia.

Preeclampsia is an important cause of maternal mortality and perinatal mortality and morbidity. Oral antihypertensive drugs have played a major role in controlling the disease progression, preventing Eclampsia and other dreaded complications, prolonging pregnancy, and reducing fetal pre maturity.

Though methyl dopa has been used routinely because of its safety profile, several controlled trials have suggested labetalol to be a better drug in controlling hypertension with the least side effects.

A prospective study was carried out at City Hospital, Nottingham, UK in 1979. Nineteen patients with Pregnancy Induced Hypertension whose Mean arterial pressure were >103.3 mm of Hg were selected. They were randomly allocated to two groups. They were given either Labetalol 400 mg or Alpha methyl dopa 750 mg daily. This dose was doubled 3 days later if satisfactory BP control had not occurred. Significant falls in BP only occurred in the group treated with labetalol, and daily BP control was better in this group. There was a higher incidence of spontaneous labour in the labetalol group and a significant difference in the Bishop score of the cervix between the two groups. There were no apparent detrimental effects on the foetus antenatally, during labour or postpartum.

In our study, the initial daily dose of labetalol was 200 mg and the initial daily dose of alpha methyl dopa was 750 mg. The dose was increased after 48 hrs if satisfactory BP control had not occurred. Statistically significant fall occurred only in the diastolic blood pressure in the labetalol group after 48 hrs ($p = 0.007$). There was no statistically significant difference between the need for PGE2 induction between alpha methyl dopa and labetalol groups. 86% of cases in alpha methyl dopa group and 82% of cases in labetalol group went in for spontaneous labour. Only 5% of babies born in alpha methyl dopa group and 2% of babies born in labetalol group required NICU admission. This difference was also not statistically significant (p value = 0.240)

A prospective study (2005) was carried out at Al-Jahra Hospital, Jahra, Kuwait to assess the efficacy and safety of labetalol compared with methyldopa in the management of mild and moderate cases of pregnancy-induced hypertension (PIH). One hundred four primigravidae with PIH were randomly allocated to receive either labetalol (group A) or methyldopa (group B). The dose of the drugs was doubled every 48 h to maintain a mean arterial blood pressure ≤ 103.6 mmHg. Ten patients in group B (18.5%) developed significant proteinuria whereas none developed proteinuria in group A. Labetalol was quicker and more efficient at controlling blood pressure, having a beneficial effect on renal functions and causing fewer side effects compared with methyldopa. The rate of induction of labor and rate of caesarean section for uncontrolled PIH was less in group A (48% and 1%, respectively) compared with group B (63.0% and 5.6%, respectively). Moreover a higher Bishop score

at induction of labor was noticed in group A. Conclusions: Labetalol is better tolerated than methyldopa, gives more efficient control of blood pressure, and may have a ripening effect on the uterine cervix.

In our study, 44% of cases in alpha methyl dopa group and 40% of cases in labetalol group delivered by Emergency LSCS; 36% of cases in alpha methyl dopa group and 34% of cases in labetalol group delivered by Labour Natural.

In a Randomized controlled trial (1988), labetalol was compared with methyldopa in a randomized controlled trial involving 176 pregnant women with mild to moderate hypertension. Diastolic blood pressure below 86 mmHg was obtained in a similar proportion of women given labetalol or methyldopa. Intrauterine death occurred in four women treated with methyldopa, and the one neonatal death on day 1 occurred in the labetalol group. The average birth weight and the proportion of preterm or small-for-gestational-age babies were similar in both groups. Heart rate, blood pressure, blood glucose, respiratory rate, and Silverman score of the babies did not differ between the two treatment groups, whether the comparison was made for all the infants or only for those that were preterm or small-for-gestational-age. These data indicate that maternal beta blockade with labetalol is as safe as methyldopa for the fetus and the newborn.

In our study, there were no reports of intrauterine deaths. There was a statistically significant increase in the mean birth weight in the labetalol group

when compared to alpha methyl dopa group (3.11 kg and 2.67 kg respectively,
p value = 0.00)

SUMMARY

- This is a study comparing the efficacy of oral Labetalol and Alpha methyl dopa in the management of preeclampsia, carried out in ISO KGH.
- The time duration of the study was from September 2010 to August 2011.
- 100 patients diagnosed as preeclampsia and admitted to ISO KGH were included in this study.
- Inclusion criteria included those who came under the definition of preeclampsia.
- Exclusion criteria included those who had pre-existing medical disorders, those who had features of imminent Eclampsia, Eclampsia and those who developed complications of preeclampsia like acute left ventricular failure and HELLP syndrome.
- These 100 patients were assigned to two groups at random of 50 patients in each group. Group 1 was started on tablet Alpha methyl dopa 250 mg thrice daily and Group 2 was started on tablet Labetalol 100 mg twice daily. Blood Pressure and proteinuria was recorded every 12th hourly.
- The treatment was continued till delivery if the blood pressure is controlled. If the blood pressure was not controlled within 48 hours, the dose of drugs was doubled.
- The relationship of age, parity, gestational age and body mass index to prevalence of preeclampsia in both the groups has been analyzed. Also

the fall in BP after 48 hrs, need to increase the dose of the drugs, need for labour induction, method of delivery, blood pressure at the time of delivery, birth weight, APGAR score and neonatal admissions in each group has been analyzed.

CONCLUSION

- This is a study comparing the efficacy of Labetalol and Alpha methyl dopa in the management of preeclampsia, in which 50 patients were started on oral Labetalol and 50 patients were started on oral Alpha methyl dopa.
- Significant fall in the diastolic blood pressure after 48 hrs occurred only in the labetalol group ($p = 0.007$).
- In the Alpha methyl dopa group, there was a significant need to increase the dose of the drug after 48 hrs ($p = 0.043$)
- There appears to be no significant difference in the rate of induction between the two groups ($p = 0.585$)
- The mean birth weight was significantly higher ($p = 0.00$) in the labetalol group (3.11 kg) compared to the alpha methyl dopa group (2.67 kg).
- There was no significant difference in the APGAR scores ($p = 0.090$) and rate of neonatal admissions ($p = 0.240$) in both the groups.

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PROFORMA

NAME:

AGE:

IP NO:

ADDRESS:

OBSTETRIC SCORE:

GESTATION AGE:

HEIGHT:

WEIGHT:

BODY MASS INDEX:

BLOOD PRESSURE AT THE TIME OF ADMISSION:

URINE ALBUMIN AT THE TIME OF ADMISSION:

DRUG ADMINISTERED: Alpha methyl dopa / Labetalol

BLOOD PRESSURE AFTER 48 HRS:

URINE ALBUMIN AFTER 48 HRS:

NEED TO INCREASE THE DOSE: Yes / No

INDUCTION WITH PGE2 GEL: Yes / No

MODE OF DELIVERY:

1. Elective LSCS
2. Elective Repeat LSCS
3. Emergency LSCS
4. Emergency Repeat LSCS
5. Labour Natural

BP AT THE TIME OF DELIVERY:

URINE ALBUMIN AT THE TIME OF DELIVERY:

BIRTH WEIGHT:

APGAR SCORE:

NICU ADMISSION: Yes / No

Master Chart

S.NO	GROUP	NAME	AGE (IN YRS)	OBSTETRIC SCORE	GESTATION AGE (IN WEEKS)	HEIGHT (IN CM)	WEIGHT (IN KG)	BODY MASS INDEX	BLOOD PRESSURE (IN MM OF HG)	URINE ALBUMIN	DRUG GIVEN	BP AFTER 48 HRS	URINE ALBUMIN AFTER 48 HRS	NEED TO INCREASE THE DOSE	INDUCTION	BP AT THE TIME OF DELIVERY	URINE ALBUMIN AT DELIVERY	MODE OF DELIVERY	BIRTH WEIGHT	APGAR	NICU
1	1	ROSEMARY	35	G3P1L1 A1	38	151	64	28.06	160/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	PGE2 GEL	140/90	NIL	LABOUR NATURAL	2.92	9	NO
2	1	RAJESWARI	24	PRIMI	37	148	62	28.3	150/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	140/80	NIL	EMERGENCY LSCS	2.25	9	NO
3	1	SATYA	27	G2P1L1	36	166	58	21.04	160/110	3+	ALPHA METHYL DOPA	150/110	1+	YES	NIL	150/100	NIL	LABOUR NATURAL	2	6	YES
4	1	SARASWATHY	24	PRIMI	38	149	70	31.53	160/100	1+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	150/90	NIL	EMERGENCY LSCS	3.25	8	NO
5	1	KALPANA	28	PRIMI	39	144	80	38.58	140/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	140/90	NIL	LABOUR NATURAL	2.92	9	NO
6	1	DEVI	29	G2P1L1	40	148	71	32.41	150/100	1+	ALPHA METHYL DOPA	140/100	NIL	YES	NIL	130/80	NIL	LABOUR NATURAL	2.1	9	NO
7	1	SARASWATHY	26	PRIMI	37	156	75	30.81	150/110	2+	ALPHA METHYL DOPA	160/100	2+	YES	NIL	160/110	1+	EMERGENCY LSCS	2.56	9	NO
8	1	BHUVANESHWARI	28	PRIMI	38	151	60	26.31	140/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	130/90	NIL	LABOUR NATURAL	2.025	7	NO
9	1	ANURADHA	20	PRIMI	39	150	54	24	160/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	140/80	NIL	LABOUR NATURAL	2.39	8	NO
10	1	UMA MAHESHWARI	29	G2P1L1	38	157	58	23.53	160/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	150/90	NIL	ELECTIVE RPT LSCS	3.135	8	NO
11	1	JENITHA	21	PRIMI	38	149	53	23.87	150/110	2+	ALPHA METHYL DOPA	150/100	1+	YES	NIL	150/100	NIL	EMERGENCY LSCS	3.24	8	NO

12	1	DEVAKI	32	G3A2	38	152	69	29.86	140/100	1+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	150/90	NIL	ELECTIVE LSCS	2.53	9	NO
13	1	HAJIRA	27	PRIMI	37	166	80	29.03	150/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	120/80	NIL	EMERGENCY LSCS	2.31	9	NO
14	1	AARIFA	22	PRIMI	36	159	70	27.68	160/110	3+	ALPHA METHYL DOPA	150/100	1+	YES	PGE2 GEL	150/100	NIL	LABOUR NATURAL	2	9	NO
15	1	NISHANTHI	23	PRIMI	39	142	56	27.77	140/100	2+	ALPHA METHYL DOPA	130/90	NIL	NO	NIL	130/90	NIL	EMERGENCY LSCS	2.21	8	NO
16	1	CHITRA	25	PRIMI	40	148	54	24.65	150/100	1+	ALPHA METHYL DOPA	150/90	NIL	NO	PGE2 GEL	150/80	NIL	EMERGENCY LSCS	2.75	9	NO
17	1	ANANDHI	25	PRIMI	38	149	70	31.53	150/110	2+	ALPHA METHYL DOPA	150/110	1+	YES	NIL	150/100	NIL	EMERGENCY LSCS	2.163	7	NO
18	1	ZARINA BEGUM	30	G3P1L1 A1	39	167	78	27.96	140/110	2+	ALPHA METHYL DOPA	150/100	1+	YES	NIL	140/90	NIL	EMERGENCY LSCS	2.81	9	NO
19	1	NANCY	25	PRIMI	40	164	59	21.93	140/100	1+	ALPHA METHYL DOPA	130/90	NIL	NO	NIL	130/90	NIL	EMERGENCY LSCS	3.201	9	NO
20	1	ROSEMATHY	20	PRIMI	39	168	60	21.25	140/110	2+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	130/90	NIL	EMERGENCY LSCS	3.332	9	NO
21	1	VASANTHI	29	G2P1L1	39	156	60	24.65	140/100	1+	ALPHA METHYL DOPA	140/100	NIL	YES	NIL	140/90	NIL	EMERGENCY RPT LSCS	3.102	9	NO
22	1	USAINA	24	G2P1L1	37	163	59	22.2	150/100	1+	ALPHA METHYL DOPA	150/100	NIL	YES	NIL	150/90	NIL	EMERGENCY RPT LSCS	2.81	9	NO
23	1	SANGEETHA	26	PRIMI	37	157	60	24.34	150/110	2+	ALPHA METHYL DOPA	150/100	1+	YES	NIL	150/90	NIL	EMERGENCY LSCS	3.225	8	NO
24	1	MINNALKODI	32	G3P1L1 A1	37	158	61	24.43	160/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	150/90	NIL	LABOUR NATURAL	3.615	9	NO

25	1	RASHEELA BEE	29	G3P1L1 A1	38	166	64	23.22	160/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	150/90	NIL	EMERGENCY RPT LSCS	3.402	9	NO
26	1	SANGEETHA	23	PRIMI	40	154	68	28.67	140/100	1+	ALPHA METHYL DOPA	130/90	NIL	NO	NIL	130/90	NIL	LABOUR NATURAL	3.155	9	NO
27	1	MANJULA	22	PRIMI	39	152	60	25.97	150/100	1+	ALPHA METHYL DOPA	140/100	1+	YES	NIL	140/90	NIL	EMERGENCY LSCS	2.275	9	NO
28	1	INDIRAJI	25	G3A2	37	149	54	24.32	140/100	2+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	140/90	NIL	ELECTIVE LSCS	2.85	9	NO
29	1	SHAILAJA	19	PRIMI	40	141	58	29.17	140/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	140/80	NIL	LABOUR NATURAL	3.075	8	NO
30	1	MAHESWARI	32	G3P2L1	37	161	64	24.69	150/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	150/90	NIL	EMERGENCY RPT LSCS	2.235	9	NO
31	1	PERIYANAYAKI	29	G2P1L0	36	160	67	26.17	150/110	2+	ALPHA METHYL DOPA	150/110	2+	YES	NIL	150/110	1+	EMERGENCY LSCS	2.4	8	NO
32	1	PREMA	23	PRIMI	40	158	69	27.64	150/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	PGE2 GEL	140/90	NIL	EMERGENCY LSCS	2.695	9	NO
33	1	NANDHINI	20	PRIMI	32	162	68	25.91	150/110	2+	ALPHA METHYL DOPA	160/110	2+	YES	NIL	150/110	3+	LABOUR NATURAL	0.89	4	YES
34	1	CHITRA	20	PRIMI	38	163	77	28.98	160/110	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	150/90	NIL	LABOUR NATURAL	2.968	9	NO
35	1	PRINCY	28	G2P1L1	39	166	62	22.5	170/110	3+	ALPHA METHYL DOPA	160/110	4+	YES	NIL	160/100	3+	EMERGENCY LSCS	1.67	5	YES
36	1	HEMALATHA	26	G2P1L1	37	165	74	27.18	160/110	3+	ALPHA METHYL DOPA	160/100	3+	YES	NIL	150/100	1+	LABOUR NATURAL	2.651	9	NO
37	1	MOHANA	24	PRIMI	40	154	66	27.83	140/100	1+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	120/80	NIL	LABOUR NATURAL	2.84	9	NO

38	1	MUMTAZ	31	G2P1L1	38	161	68	26.23	150/110	2+	ALPHA METHYL DOPA	150/110	1+	YES	NIL	150/100	NIL	EMERGENCY RPT LSCS	3.35	9	NO
39	1	DHANALAKSHMI	28	G2P1L1	39	156	64	26.3	150/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	140/90	NIL	EMERGENCY RPT LSCS	2.963	9	NO
40	1	SHARMILA	23	PRIMI	39	149	62	27.93	160/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	PGE2 GEL	140/90	NIL	EMERGENCY LSCS	3.562	9	NO
41	1	KAVITHA	24	PRIMI	40	148	66	30.13	150/100	2+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	140/90	NIL	LABOUR NATURAL	2.969	8	NO
42	1	GAYATHRI	26	PRIMI	38	150	57	25.33	150/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	150/90	NIL	EMERGENCY LSCS	2.659	9	NO
43	1	SHAHINA	20	PRIMI	38	146	56	26.27	150/100	1+	ALPHA METHYL DOPA	140/90	NIL	NO	NIL	140/90	NIL	LABOUR NATURAL	2.106	8	NO
44	1	PRIYA	25	PRIMI	39	160	72	28.13	140/100	1+	ALPHA METHYL DOPA	130/90	NIL	NO	NIL	130/90	NIL	EMERGENCY LSCS	2.352	7	NO
45	1	VIJAYALAKSHMI	31	G2P1L1	38	155	66	27.47	150/100	1+	ALPHA METHYL DOPA	150/100	1+	YES	NIL	150/100	NIL	EMERGENCY RPT LSCS	3.265	8	NO
46	1	HEMAVATHY	22	PRIMI	34	149	70	31.53	170/110	3+	ALPHA METHYL DOPA	160/90	NIL	NO	PGE2 GEL	160/90	NIL	EMERGENCY LSCS	1.986	5	YES
47	1	KARPAGAM	25	G2P1L1	39	165	84	30.85	150/110	3+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	3.456	9	NO
48	1	SAIBUNISHA	26	G3P2L1	30	152	60	25.97	170/110	3+	ALPHA METHYL DOPA	160/110	3+	YES	PGE2 GEL	150/110	4+	LABOUR NATURAL	0.98	4	YES
49	1	SUMATHY	22	PRIMI		149	65	29.28	150/100	2+	ALPHA METHYL DOPA	150/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	3.111	9	NO
50	1	KAMATCHI	21	PRIMI	39	154	64	26.99	140/100	1+	ALPHA METHYL DOPA	130/90	NIL	NO	NIL	130/80	NIL	LABOUR NATURAL	3.155	9	NO

51	2	SUMATHY	28	PRIMI	37	154	88	37.1	150/100	1+	LABETALOL	150/100	1+	YES	NIL	140/90	NIL	ELECTIVE LSCS	2.21	9	NO
52	2	MANJULA	33	G3A2	37	160	56	21.87	150/100	1+	LABETALOL	150/90	NIL	NO	NIL	150/90	NIL	ELECTIVE LSCS	3.5	9	NO
53	2	SHANTHI	32	G2P1L0	38	155	53	22.06	140/100	2+	LABETALOL	140/90	NIL	NO	NIL	130/80	NIL	EMERGENCY LSCS	2.85	9	NO
54	2	BEULA	28	G2P1L1	30	155	62	25.8	160/110	4+	LABETALOL	160/100	4+	YES	PGE2 GEL	160/100	3+	LABOUR NATURAL	1.214	3	YES
55	2	VENNILA	27	G2P1L1	38	158	69	27.63	140/100	1+	LABETALOL	130/90	NIL	NO	NIL	130/90	NIL	LABOUR NATURAL	2.85	9	NO
56	2	JAMEELA BANU	22	G2P1L1	38	166	63	22.86	150/100	2+	LABETALOL	150/90	NIL	NO	NIL	150/90	NIL	ELECTIVE RPT LSCS	2.8	9	NO
57	2	VIJAYALAXMI	26	PRIMI	40	160	80	31.25	140/100	1+	LABETALOL	130/80	NIL	NO	PGE2 GEL	130/80	NIL	EMERGENCY LSCS	2.79	9	NO
58	2	AMMU	24	PRIMI	38	156	70	28.76	150/100	1+	LABETALOL	140/90	NIL	NO	PGE2 GEL	140/90	NIL	LABOUR NATURAL	2.355	9	NO
59	2	JOTHI	36	G2P1L1	38	157	65	26.37	150/100	1+	LABETALOL	140/90	NIL	NO	NIL	140/90	NIL	LABOUR NATURAL	3.13	9	NO
60	2	THENMOZHI	29	PRIMI	39	147	84	38.87	150/100	1+	LABETALOL	140/90	NIL	NO	PGE2 GEL	130/90	NIL	EMERGENCY LSCS	3	9	NO
61	2	VARALAXMI	26	PRIMI	37	154	78	32.88	140/100	1+	LABETALOL	130/80	NIL	NO	NIL	120/80	NIL	LABOUR NATURAL	2.305	8	NO
62	2	MADHUMITHA	22	PRIMI	38	142	60	29.75	140/110	2+	LABETALOL	140/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	4.07	8	NO
63	2	NEELAVATHY	24	G2A1	39	153	66	28.19	160/100	2+	LABETALOL	150/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	3.7	9	NO
64	2	DHANALAXMI	20	PRIMI	37	155	63	26.22	150/100	1+	LABETALOL	150/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	2.523	9	NO
65	2	DEVI	29	G2P1L1	38	160	89	34.76	150/100	1+	LABETALOL	150/90	NIL	NO	NIL	120/80	NIL	LABOUR NATURAL	3.325	9	NO
66	2	KAMATCHI	29	G3P2L1	37	148	54	24.65	150/110	2+	LABETALOL	150/100	2+	YES	PGE2 GEL	140/100	1+	EMERGENCY LSCS	3.75	9	NO
67	2	SAMUNDESHWAR I	19	PRIMI	38	155	55	22.89	140/100	1+	LABETALOL	140/90	NIL	NO	NIL	120/80	NIL	EMERGENCY LSCS	3.78	9	NO
68	2	INDARANI	26	G2P1L1	38	163	59	22.2	150/100	1+	LABETALOL	140/80	NIL	NO	NIL	140/80	NIL	EMERGENCY RPT LSCS	3.05	7	NO
69	2	PITCHAIAMMAL	22	G2P1L0	38	154	68	28.67	140/100	1+	LABETALOL	140/90	NIL	NO	NIL	130/90	NIL	ELECTIVE RPT LSCS	4.015	9	NO

70	2	SUMATHY	36	G3P1L1 A1	39	153	56	23.92	150/100	1+	LABETALOL	150/10 0	NIL	YES	NIL	140/90	NIL	EMERGENCY RPT LSCS	3.455	9	NO
71	2	FAIZ JAHAN	28	G2P1L1	37	149	71	31.98	150/100	2+	LABETALOL	150/10 0	1+	YES	NIL	150/100	NIL	EMERGENCY RPT LSCS	3.37	9	NO
72	2	KAVITHA	24	PRIMI	40	159	66	26.1	150/100	1+	LABETALOL	140/90	NIL	NO	NIL	140/80	NIL	EMERGENCY LSCS	3.625	9	NO
73	2	REBECCA	21	PRIMI	36	144	56	27	160/110	3+	LABETALOL	150/90	NIL	NO	PGE2 GEL	150/90	NIL	LABOUR NATURAL	2.78	9	NO
74	2	SEETHA	29	G2P1L1	38	166	66	23.99	170/110	4+	LABETALOL	160/11 0	3+	YES	PGE2 GEL	160/100	2+	EMERGENCY LSCS	2.955	9	NO
75	2	BHAVANI	28	PRIMI	39	147	66	30.54	140/100	1+	LABETALOL	130/90	NIL	NO	NIL	120/80	NIL	EMERGENCY LSCS	3.22	9	NO
76	2	CHITRA	25	PRIMI	38	148	59	26.93	150/110	2+	LABETALOL	150/10 0	1+	YES	NIL	150/100	NIL	EMERGENCY LSCS	3.19	9	NO
77	2	VANESHREE	25	G3P1L1 A1	38	167	68	24.38	150/110	1+	LABETALOL	140/90	NIL	NO	NIL	140/80	NIL	ELECTIVE RPT LSCS	4.125	9	NO
78	2	SABEERA BEGUM	22	PRIMI	40	155	66	27.47	140/100	1+	LABETALOL	130/90	NIL	NO	PGE2 GEL	130/90	NIL	EMERGENCY LSCS	2.955	8	NO
79	2	NITHYAVATHI	29	G2P1L1	38	164	64	23.79	150/100	2+	LABETALOL	140/90	NIL	NO	NIL	140/80	NIL	LABOUR NATURAL	2.69	8	NO
80	2	SASIKALA	22	G2P1L1	39	168	78	27.63	150/110	1+	LABETALOL	150/90	NIL	NO	NIL	150/100	NIL	LABOUR NATURAL	3.27	9	NO
81	2	ARIFA BEE	24	G2A1	39	157	60	24.34	140/100	1+	LABETALOL	140/90	NIL	NO	NIL	130/90	NIL	EMERGENCY LSCS	3.711	9	NO
82	2	KOTTEESWARI	30	PRIMI	37	153	57	24.34	160/110	3+	LABETALOL	160/90	NIL	NO	NIL	150/90	NIL	EMERGENCY LSCS	4	9	NO
83	2	TAMILSELVI	29	G3P1L1 A1	38	165	79	29.02	140/100	1+	LABETALOL	140/80	NIL	NO	NIL	140/90	NIL	ELECTIVE RPT LSCS	3.25	9	NO
84	2	SHANAZ BEGUM	18	PRIMI	39	151	59	25.88	140/100	1+	LABETALOL	130/90	NIL	NO	NIL	130/90	NIL	LABOUR NATURAL	3.285	9	NO
85	2	RAJESWARI	27	G2P1L1	37	151	71	31.14	160/100	1+	LABETALOL	150/90	NIL	NO	NIL	150/90	NIL	EMERGENCY RPT LSCS	2.925	9	NO
86	2	MANIMEGALAI	36	G4P1L1 A2	39	161	65	25.08	150/110	2+	LABETALOL	150/90	NIL	NO	NIL	140/90	NIL	LABOUR NATURAL	3.25	8	NO
87	2	SAINA	19	PRIMI	40	144	59	28.45	160/100	2+	LABETALOL	150/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	3.152	8	NO

88	2	PRABAVATHY	24	PRIMI	37	152	73	31.6	160/100	2+	LABETALOL	150/90	NIL	NO	PGE2 GEL	150/90	NIL	LABOUR NATURAL	2.97	9	NO
89	2	ALMAS	21	PRIMI	38	160	70	27.34	160/100	2+	LABETALOL	150/90	NIL	NO	NIL	150/90	NIL	EMERGENCY LSCS	3.845	9	NO
90	2	KOKILA	25	PRIMI	38	155	59	24.56	160/100	2+	LABETALOL	150/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	3.2	9	NO
91	2	MEHERNISHA	30	G2P1L1	40	162	66	25.15	140/100	1+	LABETALOL	140/90	NIL	NO	NIL	130/90	NIL	LABOUR NATURAL	3.1	9	NO
92	2	MAHALAKSHMI	29	G3P1L1 A1	38	152	60	25.97	160/100	1+	LABETALOL	150/90	NIL	NO	NIL	140/90	NIL	EMERGENCY RPT LSCS	3.212	9	NO
93	2	KALAIARASI	29	G2P1L1	39	164	65	24.17	140/100	2+	LABETALOL	140/80	NIL	NO	NIL	130/80	NIL	LABOUR NATURAL	2.563	9	NO
94	2	SEETHA	24	PRIMI	34	165	60	22.04	160/100	2+	LABETALOL	160/100	2+	YES	NIL	150/100	3+	LABOUR NATURAL	1.243	5	YES
95	2	SAIRA BANU	19	PRIMI	39	145	58	27.59	150/100	2+	LABETALOL	140/90	NIL	NO	NIL	130/90	NIL	EMERGENCY LSCS	2.856	9	NO
96	2	SATYA	23	G2A1	38	153	68	29.05	140/100	1+	LABETALOL	130/90	NIL	NO	NIL	130/90	NIL	LABOUR NATURAL	2.658	9	NO
97	2	SHAKIRA	20	G2A1	37	150	70	31.11	160/110	3+	LABETALOL	160/110	1+	YES	NIL	150/100	NIL	EMERGENCY RPT LSCS	3.985	9	NO
98	2	PARVATHY	26	G2P1L1		163	78	29.36	160/110	2+	LABETALOL	150/90	NIL	NO	NIL	140/90	NIL	LABOUR NATURAL	3.252	9	NO
99	2	UMADEVI	23	G3P1L1 A1	39	159	64	25.32	150/100	1+	LABETALOL	140/90	NIL	NO	NIL	150/90	NIL	EMERGENCY RPT LSCS	3.673	9	NO
100	2	RAHIMA	24	G2P1L1		154	65	27.41	160/100	2+	LABETALOL	140/90	NIL	NO	NIL	140/90	NIL	EMERGENCY LSCS	2.986	9	NO