"A RANDOMISED CONTROLLED TRIAL OF ORAL NIFEDIPINE VS ORAL LABETALOL IN MANAGEMENT OF HYPERTENSION IN PREGNANCY"

BY

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DECLARATION BY THE CANDIDATE

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ABBREVATIONS

BP	: Blood Pressure
PIH	: Pregnancy Induced Hypertension
WHO	: World Health Organization
HELLP	: Haemolysis, Elevated liver enzymes and Low platelet count
NICU	: Neonatal Intensive Care Unit
RDS	: Respiratory Distress Syndrome
IUD	: Intra Uterine Death
APTT	: Activated partial thromboplastin time
LMP	: last menstrual period
EDD	: expected date of delivery
Hb	: haemoglobin
IM	: intramuscular
IV	: intravenous
IUGR	: intra uterine growth restriction
LFT	: liver function test
NST	: non stress test
PIH	: pregnancy induced hypertension

PR : pulse rate

PT : prothrombin time

RFT : renal function test

SD : standard deviation

SGA : small for gestational age

USG : ultrasound

SBP : systolic blood pressure

DBP : diastolic blood pressure

RCT : randomized control trial

Vs : versus

Y : yes

N : no

ABSTRACT

INTRODUCTION:

Hypertensive disorders complicating pregnancy are common, and form a deadly triad, along with haemorrhage and infection. These hypertensive disorders contribute greatly to maternal morbidity and mortality. One in ten women will develop hypertension during pregnancy and preeclampsia complicates 2% to 8% of pregnancy.

AIM OF THE STUDY:

To compare the efficacy of oral Nifedipine Vs oral Labetalol in hypertension in pregnancy and to assess the adverse effects of the drugs along with maternal and perinatal outcome.

MATERIALS AND METHODS:

102 women, divided as 51 patients in two groups, with gestation more than 20 weeks and blood pressure greater than 140 mmHg systolic and/or greater than 90 mmHg diastolic were randomized to receive either oral Nifedipine or oral Labetalol at Shri. B.M.Patil Medical College hospital and Research centre, Bijapur. The time required to reduce the blood pressure to target value, the number of doses required and the adverse effects were measured. The statistical level of significance was taken as $p < 0.005$.

RESULTS:

The patients who came in the inclusion criteria were treated with either oral Nifedipine or oral Labetalol based on randomization and it was found that Nifedipine had 23.96% decline rate whereas Labetalol had 20.19% decline rate in reducing the blood pressure to reach the target value. The p value is 0.0001 which is highly significant, suggesting that Nifedipine requires short time to act than Labetalol.

This study also indicates that Nifedipine acts much quicker and also requires fewer doses than oral Labetalol to control blood pressure in hypertension in pregnancy.

Patients were also monitored for any side effects that may arise from the drugs. The adverse effects noted were hypotension, dizziness, sweating, flushing, nausea, vomiting, palpitations, headache and fetal tachycardia.

CONCLUSION:

Both oral Nifedipine and oral Labetalol were ultimately effective in reaching the therapeutic goal, but Nifedipine achieved the target blood pressure more rapidly and with fewer doses than Labetalol. Both drugs demonstrated similar adverse effects.

Thus the present study concludes that Nifedipine is the preferred drug to control blood pressure than Labetalol in pregnancy as it is more efficacious and can be used in the peripheral centres due to cost effectiveness and its ease of administration and storage.

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INTRODUCTION

Hypertensive disorders complicating pregnancy are common, and form a deadly triad, along with haemorrhage and infection. These hypertensive disorders contribute greatly to maternal morbidity and mortality [1] .One in ten women will develop hypertension during pregnancy and preeclampsia complicates 2% to 8% of pregnancy (WHO 1988) and contributes to 9% of maternal mortality in Asia and 12% in India [2, 3].

The spectrum of hypertensive disease that can complicate pregnancy is broad, ranging from "white coat" hypertension to gestational hypertension, chronic hypertension and preeclampsia to chronic hypertension with superimposed pre-eclampsia. Particularly challenging, however, is hypertension in pregnancy that becomes severe enough to qualify as a hypertensive crisis, bringing immediate risk to both the mother and fetus[4]. The risk may evolve over days or just few hours and may present as worsening blood pressure that may culminate into hypertensive emergencies.

The role of anti hypertensive therapy for pregnant women with mild to moderate hypertension is unclear. As there is no immediate need to lower BP, the rationale for treatment is that it will prevent or delay progression to more severe diseases, thereby benefiting the women or her baby or both, and reducing consumption of health service resources. As well as reducing BP, the belief has been that these drugs reduce the risk of preterm delivery and placental abruption and improve fetal growth. [5]

There is 5 fold increase in perinatal mortality [6] which is mainly due to iatrogenic prematurity .In women with gestational hypertension or pre-eclampsia, greater the severity of hypertension, greater the adverse perinatal outcome.

Recent studies have attributed the occurrence of fatal intra cranial haemorrhages to inadequate treatment of severe systolic hypertension (≥ 160mmHg) in preeclampsia and recommend urgent and effective antihypertensive treatment for such cases. It is important to stabilise the maternal hypertension prior to delivery to avoid dangerous fluctuations or exacerbations of blood pressure during labor.

Thus adequate and safe blood pressure control will allow definitive treatment of delivery of the baby to be carried out with minimal delay in many cases of severe hypertension in pregnancy .Delivery is the most appropriate therapy for the mother but may not be so for the fetus which is remote from term.

The obstetricians should aim not just for the diagnosis, but also for the prevention of complications of hypertensive disorders.

Maternal complications of acute hypertension in pregnancy include cerebrovascular accident, renal failure, hepatic dysfunction, HELLP syndrome and left ventricular failure. The fetus is also at risk of growth restriction, prematurity, asphyxia and intra uterine death due to placental abruption.

There is consensus that due to these risks the patients should be treated with anti hypertensive agents as an inpatient to achieve rapid control of hypertension.

There have been many drugs that have been described in control of preeclampsia, they include Hydralazine, Labetalol, Nifedipine .A few trials have been conducted on the above mentioned drugs, but no single drug has been identified as being superior to the other.

Labetalol, a beta blocker, has arteriolar vasodilating action that lowers peripheral resistance.

Calcium channel blockers include Nifedipine, Nicardine, Nimodipine and Verapamil. These drugs inhibit influx of calcium ions to vascular smooth muscles resulting in arterial vasodilatation.

Nifedipine has the advantage of being cost effective and can be administered orally, however it is known to cause sudden hypotension and respiratory embarrassment when used sublingually concomitant with magnesium sulphate. An interaction between Nifedipine and magnesium sulphate may be associated with profound muscle weakness and hypotension.

Nifedipine and magnesium sulphate both have tocolytic effect and can prolong the duration of labour.

In India, Nifedipine is the most commonly used antihypertensive because of ease of administration. It is however banned in countries like Australia in view of sudden unpredictable fall of blood pressure and cardiac side effects.

Very few studies comparing the efficacy of Nifedipine and Labetalol have been done so far, and there is no set protocol for therapy. As such, drug of choice for management of control of BP in hypertension in pregnancy has not yet been recognized.

Hence the need for a comparison between these 2 drugs Nifedipine and Labetalol, to recognize the superior drug is essential.

OBJECTIVES

PRIMARY OBJECTIVE:

To compare the efficacy of oral Nifedipine Vs oral Labetalol in reducing the BP to systolic 140 mm Hg and diastolic 90 mm hg or lower within the shortest interval of time, in hypertension in pregnancy.

SECONDARY OBJECTIVE:

To assess the adverse effects of the drugs along with the maternal and perinatal outcome.

REVIEW OF LITERATURE

In the year 2000, a RCT was conducted by Magee L and study on oral beta blockers for mild to moderate hypertension during pregnancy was done on 2500 women with hypertension in pregnancy and it was concluded that oral beta blockers decreases the risk of severe hypertension with placebo/ no beta blocker .[7]

In the year 2002, RCT was done on 126 women comparing Hydralazine and Nifedipine by Aali BS and it was concluded that Nifedipine is safe and more effective than Hydralazine in controlling BP in severe preeclampsia. It has the added advantage of being cheaper and more widely available than the latter and is easily available.[8]

In a systematic review of 46 trials (4282 women) conducted by Abalos E, Duley L et al [9] the primary aim was, to ascertain the maternal and fetal hazards of indicating antihypertensive agents for mild to moderate hypertension in pregnancy and secondary aim was to compare the effects of alternative agents. The results summarised were as follows:

a)Anti hypertensive agents have the risk of developing severe hypertension irrespective of the class of drug, type of hypertension or gestational age at the trial entry.(19 trials, 2409 women; RR 0.50;(95% CI 0.41 to 0.61); risk difference (RD) – 0.10;number needed to treat(NNT)10 (8 to 13).

b) There was no overall difference in risk of pre-eclampsia development, abruptio placenta or small for gestational age. No statistically significant difference in the risk of fetal or neonatal deaths. 22 trials (2702 women) RR 0.97; 95% CI 0.83 to 1.13.

The study conducted by Barton JR, O'brien JM, Bergauer Nk et al[10] described the prognostic signs in the natural course of mild gestational hypertension & pregnancy outcomes in women who were remote from term with mild gestational hypertension that was expectantly managed. A total of 748 women with mild gestational hypertension with singleton pregnancy between 24 & 35 weeks without proteinuria were studied. 46% ultimately had pre -eclampsia, with progression to severe disease in 9.6%. The development of proteinuria is associated with an earlier gestational age at delivery, lower birth weight & an increased incidence of small for gestational age new born. Gestational age of infants at delivery (36.5+/-2.4vs37.4+/-2.0weeks), birth weight (2752+/-767vs3038+/- 715g), incidence of small for gestational age newborns (24.8%vs13.8%), and duration of neonatal hospital stay (7.1+/-10vs5.0+/-9.3days) differed significantly in the patients with versus those without proteinuria ($p<0.001$ for all).

In an article on Nifedipine on maternal fetal binomial, more safety, efficacy and effectiveness were found with Nifedipine. Therefore Nifedipine can be used in antihypertensive treatment during pregnancy without serious complications.[11]

A prospective trial by C. A. Michael et al performed to evaluate the use of Diazoxide and Labetalol given intravenously in the management of severe hypertensive disease in pregnancy concluded that both drugs had an efficient hypotensive action. The reduction in blood pressure in the Labetalol group was better controlled and concluded that this may be a factor influencing perinatal outcome. Because of the freedom of maternal and fetal side-effects, Labetalol given by intravenous infusion is a more appropriate drug for use in the management of hypertensive crisis occurring in pregnancy and labor.[12]

Duley et al compared different antihypertensive drugs for very high blood pressure during pregnancy and concluded that, the choice of antihypertensive should depend on the clinician's experience and familiarity with a particular drug and on what is known about adverse effects. Exceptions are Diazoxide, Ketanserin, Nimodipine and Magnesium sulphate, which are probably best avoided.[13]

Tooke-Miller C, Allen JC [14], carried out a prospective observational study to research the cerebral hemodynamic effects of Labetalol in pregnant women with hypertension .It was concluded that Labetalol effectively reduces CPP (cerebral perfusion pressure), without affecting cerebral perfusion, primarily by a decrease in systemic blood pressure. This makes it an ideal agent for blood pressure control in hypertensive pregnant women.

IA Raheem, R Saaid, SZ Omar, PC Tan [15] conducted a double blinded randomized trial comparing oral Nifedipine with intra venous Labetalol in their rapidity of controlling hypertensive emergencies in pregnancy.

Main outcome measured was the time taken to achieve a blood pressure of ≤150/100 mmHg. The median time taken to achieve target blood pressure was 30 minutes versus 45 minutes for Nifedipine and Labetalol, respectively.

It was concluded that oral Nifedipine and intravenous Labetalol regimens are similarly effective in the acute control of severe hypertension in pregnancy.

Vigil-De Gracia P, Lasso M, Ruiz E conducted a randomized control trial on 200 women with severe hypertension in pregnancy to compare the safety and efficacy of intravenous Labetalol and intravenous Hydralazine for acutely lowering blood pressure in pregnancy. The primary end point was successful lowering of blood

pressure and maternal hypotension. The trial concluded that Labetalol and Hydralazine fulfil the criteria required for an antihypertensive drug to treat severe hypertension in pregnancy. [16]

Calcium antagonists generally constitute second line agents, usually administered late in pregnancy. A prospective cohort study suggests that calcium channel blockers (especially Nifedipine) do not represent a major teratogenic risk. Nifedipine has shown to result in a lower incidence of overshoot hypotension and to have a more rapid onset of action.[17]

Acute arterial hypertension in pregnancy causes cerebral haemorrhage and infarction, hence the control of blood pressure, and more specifically cerebral perfusion pressure, assumes greater importance in the management of pre eclamptic women at risk for eclampsia. Most of the drugs currently used to control severe hypertension in preeclampsia are:

1) Calcium channel blockers (Nifedipine, Nicardipine),

2) Sympathetic nervous system inhibition; α_2 agonist (α methyl dopa),

3) Peripherally acting adrenergic receptor agonist; α and β adrenergic receptor blocker (Labetalol) and

4) Arterial vasodilators (Hydralazine). [14, 18]

Magee LA et al in their systematic review of meta analysis of randomised controlled trials on assessing effectiveness of antihypertensive treatment for mild hypertension during pregnancy concluded that for mild chronic or mild to moderate

late hypertension in pregnancy , anti hypertensive treatment benefit the mother , but the overall benefit to the infant is unclear.

Early delivery of women with severe hypertension increase adverse neonatal outcomes related to prematurity, without providing benefit to the mother.[19]

A randomised controlled trial was conducted by Corine M Koopmans et al [20] to find out whether induction of labour in women with a singleton pregnancy complicated by gestational hypertension or mild pre-eclampsia reduces severe maternal morbidity.

The primary outcome was a composite measure of poor maternal outcome – maternal mortality, maternal morbidity (eclampsia, HELLP syndrome, pulmonary oedema, thromboembolic disease and placental abruption), progression to severe hypertension or proteinuria and major post partum haemorrhage (> 1000ml blood loss). 756 patients were allocated to receive induction of labour (n= 377 patients) or expectant monitoring (n=379). Of women who were randomised, 117 (31%) allocated to induction of labour developed poor maternal outcome compared with 166(44%) allocated to expectant monitoring (relative risk 0.71%, 95%. CI 0.59-0.86, $p<0.0001$). No cases of maternal or neonatal death or eclampsia were recorded.

Study concluded that, induction of labour is associated with improved maternal outcome and should be advised for women with mild hypertensive disease beyond 37 weeks gestation.

Sauden et al [21] in retrospective review of 416 patients with gestational hypertension, demonstrated that 15 % (62 patients) subsequently developed pre eclampsia . An altogether separate, but prospective, aim of the study involving a

cohort of 112 patients showed that 26% (29 patients) developed pre eclampsia. Patients in whom the initial diagnosis of gestational hypertension was made beyond 36 weeks gestation demonstrated a 10 % risk (much lower than the overall risk) of developing pre-eclampsia. Multiple logistic regression analysis of the data identified, previous miscarriage and early gestation of presentation as markers associated with an increased likelihood of developing pre-eclampsia.

A prospective study assessing the effect of maternal age on outcome in mild hypertension in a cohort of 379 mature women (>34 years old) by Barton et al [22] reported similar maternal outcomes but a higher still birth rate in women over 35 years of age compared with a cohort of women with less than 35 years years. Although this was statistically insignificant (p-0.63), the sample size was too small to detect a significant difference.

A further study from Barton et al [23] evaluated the influence of ethnicity on outcome in a prospective analysis of 1182 patients of Hispanic , African ,American & Caucasian ethnicity. They reported that Hispanics demonstrated a higher rate of progression to severe pre Eclampsia compared to Caucasians (<0.005) . The incidence of small for gestational age (SGA) was highest among the Hispanic newborns. The rates of progression to HELLP & eclampsia were similar among all the groups. An African Americans when compared to white patients demonstrated a lower gestational age at delivery as well as lower birth weights (< 0.005 for both parameters). In addition, Africans had a higher still birth & neonatal death incidence compared to other 2 ethnic groups.

A case control study by Huma Tasleem et al [24] studied the co-relation of pregnancy induced hypertension with placental abruption & effect of anti

hypertensive therapy. In this study patients who were on anti hypertensive therapy had no abruption & where as the women with PIH who were not on anti hypertensive therapy suffered from abruption (8%).

In a reproductive health library commentary by Fatima Paruk et al [25] the review states that the benefits and potential adverse effects of using anti hypertensive agents for mild to moderate hypertension in pregnancy are unclear. Inspite of this, the practice of using these drugs , particularly in under resourced regions , should not be abandoned until firm evidence becomes available to refute their role in the treatment of mild to moderate hypertension in pregnancy . In addition there is little evidence that any particular antihypertensive agent is better than others. The review suggests that women should make the decision regarding the use of an antihypertensive agent in pregnancy in consultation with their obstetricians.

A prospective multi centre cohort study by Laura A. Magee et al [26] studied the safety of calcium channel blockers in human pregnancy to examine the potential teratogenicity. They prospectively collected information and followed up 78 women with first trimester exposure to calcium blockers do not represent a major teratogenic risk.

A randomised multi centre clinical trial comparing Nifedipine , given between 12 to 34 gestational weeks to delivery and expectant management for mild to moderate hypertension in pregnancy by Renata Bortolus et al [27] studied the safety of use of calcium channel blocker Nifedipine in pregnancy , children were followed up to 18 months of age . Results suggest that the use of Nifedipine in pregnancy is safe with respect to the risks of malformation and Nifedipine or expectant management for

mild – moderate hypertension in pregnancy do not affect major impairment in development at 18 months of age.

Victoria M Allen et al [28] conducted a population based study on the effect of hypertensive disorders in pregnancy on small for gestational age and stillbirth. Study showed that, the women with any hypertension in pregnancy were 1.6 (95% CI 1.5-1.6) times more likely to have a live birth with SGA and 1.4 (95% CI 1.1-1.8) times more likely to have a still birth as compared with normotensive women. Analysis showed that women with gestational hypertension without proteinuria and with proteinuria were more likely to have infants with SGA (RR 1.5, 95% CI 1.4 -1.6 and RR 3.2.95% CI 2.8 -3.6, respectively). Women with pre existing hypertension were also more likely to give birth to an infant with SGA (RR 2.5.95% CI 2.2-3.0) or to have a still birth (RR 3.2, 95% CI 1.9 -5.4).

In the textbook of obstetrics and gynaecology by Arul Kumaran, Gita Arjun, Leonie Penna : The management of Labour 3rd edition[29] states that : In treating severe hypertension it is crucial that hypotension is avoided, for it may lead to decreased utero placental blood flow and hence fetal distress. Labetalol, intra venous hydralazine and oral Nifedipine are acceptable agents for this indication. Labetalol, a selective α_1 and a non selective β blocker decreases systemic vascular resistance, slows the heart rate, reducing myocardial oxygen demand. It doesn't reduce peripheral, renal, cerebral, coronary and utero placental blood flow.

In the textbook of Practical Guide to high risk pregnancy and delivery, 3rd edition by Fernando Arias [30] states that ; the most commonly used non selective β blocker agent is Labetalol, which can be used parenterally to treat severe hypertension and orally in less severe cases. Labetalol is different from other β blockers as it acts

by decreasing peripheral vascular resistance with little or no effect on cardiac output. One of its main obstetrical uses is for hypertensive emergencies with severe pre eclampsia.

In the textbook by James on High risk pregnancy management options 4th edition states that: Labetalol lowers blood pressure by blocking α_1 adrenoreceptors in peripheral vessels thereby reducing peripheral resistance, and the heart rate is reduced because of its β blocking effect. Labetalol has become popular for the treatment of hypertension in pregnancy and pre eclampsia. It has been used orally and intra venous for rapid blood pressure reduction. [31]

In the textbook of obstetrics and gynaecology by Mudaliar and Menon : Clinical Obstetrics 11th edition states that recently Labetalol (starting dose 100 mg BD , max dose 2.4 g/day) is being recommended as the best drug to control blood pressure in severe pre eclampsia. Intra venous Labetalol is very useful for rapid control of hypertension. [32]

A textbook by Ian Donald on Practical Obstetric problems 6th edition states that Labetalol lowers blood pressure smoothly but rapidly without the associated tachycardia characteristic of hydralazine. No adverse fetal or neonatal effects have been seen in relation to Labetalol. [33]

BACKGROUND

Hypertension is one of the most common medical disorders during pregnancy. Approximately 70 % of women diagnosed with hypertension during pregnancy will have gestational hypertension / pre-eclampsia .The exact incidence is unknown, estimates ranges from 2%-8% of all pregnancies.

The guideline by the Royal College of Obstetrics and Gynaecology provides the classification and describes about the management of hypertension in pregnancy. Drugs like Hydralazine, Labetalol and oral Nifedipine have been mentioned for the control of BP.[34.]

Women with gestational hypertension are at risk for progression to severe hypertension, pre-eclampsia or eclampsia [35]. The risks are increased with a lower gestational age at the time of diagnosis[36]. Worldwide, over half a million women die each year of pregnancy related causes and 99% of these deaths occur in the developing world[37]. In developing countries, hypertensive disorders complicating pregnancy rank second only to anaemia [38.]

High blood pressure is a sign, not a disease reflecting an increase in cardiac output or total peripheral resistance. These vascular changes can arise in a number of disorders that may have different effects on pregnancy outcome[38].

Preeclampsia is seen clinically as a syndrome ranging from indolent mild clinical hypertension and proteinuria to a severe form of rapid fulminant endothelial disease with multiorgan failure and death of mother and fetus[39]. Preeclampsia is associated with the release of anti-angiogenic factors, plasma volume is contracted and widespread effects on vascular endothelium lead to the maternal syndrome of preeclampsia.[40]

There is little evidence to suggest that any therapy alters the underlying pathophysiology of preeclampsia. Therapeutic efforts may be palliative, slow progression of the disorder and permit continuation of pregnancy but they have not been shown to reverse the underlying disorder.

When treatment is required, the ideal drug that reduces pressure to a safe level should act quickly, reduce pressure in a controlled manner, not lower cardiac output, reverse uteroplacental vascular constriction and result in no adverse maternal or fetal effects.[36]

Clinical management of severe hypertensive disorder of pregnancy is standardized and acceptable. But there is controversy in the optimal management of women with mild gestational hypertension or pre eclampsia before 37 weeks gestation. There is disagreement regarding the benefits of hospitalization, complete bed rest and use of anti hypertensive medications. Those who favour no treatment believe that most of these complications cannot be prevented by medication, that the risk of therapy is greater and that most of these patients have good perinatal outcome without treatment .[41]

In developing country like ours where in 80 % population resides in under resourced rural areas, lowering of blood pressure and prevention of complications by treating mild or moderate hypertension associated with pregnancy may prove beneficial if firm evidence is obtained by conducting scientific research.

Classification of the hypertensive disorders of pregnancy [36, 42]:

Pre eclampsia is a pregnancy specific syndrome of reduced organ perfusion related to vasospasm and activation of the coagulation cascade. The criteria used to identify remain subject to confusion and controversy. Several groups, including the American college of obstetricians and gynaecologists [42], the Australian society for the study of hypertension in pregnancy and the Canadian hypertension society have published classifications schemes and diagnostic criteria that differ from one document to the other. They include recommendations to eliminate oedema from diagnostic criteria, to abandon the use of changes in blood pressure as diagnostic [42, 43]., to use only diastolic blood pressures [43] and to add systematic changes to proteinuria as diagnostic markers.[44]

Modifications of the ACOG classification is slightly by adding the term gestational hypertension for the woman who has hypertension without proteinuria during pregnancy, reserving transient hypertension of pregnancy for a definitive diagnosis is made post partum.

Classification [36,42]

- Chronic hypertension
- Preeclampsia-eclampsia
- Pre eclampsia super imposed on chronic hypertension
- Gestational hypertension.

According to A COG :

Hypertension is defined as a blood pressure of ≥ 140/90mm Hg measured on at least two different occasions 6 hrs apart with the patient at rest in bed.

Proteinuria is defined as 300 mg or more of urinary protein per 24 hrs or 100mg/dl or more in at least two random urine specimens collected 6 or more hours apart. Severe hypertension is considered when the blood pressure ≥ 160/100 mm of Hg. But Blood pressure in not always a dependable indicator of severity. Other indicators like proteinuria, convulsion, visual disturbances etc are also important.

Gestational hypertension:

(1) Transient hypertension of pregnancy if pre eclampsia is not present at the time of delivery and blood pressure returns to normal by 12 weeks post partum (a retrospective diagnosis)

Chronic hypertension:

The diagnosis of chronic hypertension is based on a known history of hypertension in pre-pregnancy or an elevated blood pressure ≥140/90 mm Hg before 20 weeks gestation. Hypertension that is diagnosed for the first time during pregnancy and that does not resolve post partum is also classified as chronic hypertension.

The presence of mild pre-existing hypertension approximately doubles the risk of pre-eclampsia.

However, when chronic hypertension is severe (a diastolic blood pressure ≥ 110 mm Hg before 20 weeks gestation) the risk of pre-eclampsia is as high as 46% with resultant raised maternal and fetal risks.

Pre-eclampsia superimposed on chronic hypertension:

A diagnosis of superimposed Pre-eclampsia is made when the denovo proteinuria develops in the later half of pregnancy or when the hypertension accelerates greatly in the last trimester.

Superimposed Pre-eclampsia is diagnosed.

- When there is sudden increase in hypertension or proteinuria occurring after mid gestation, after an initial period of reasonably good blood pressure control
- As part of the HELLP syndrome (e.g., new onset thrombocytopenia, evidence of microangiopathic haemolytic anaemia, and elevation of alanine aminotransferase or aspartate aminotransferase levels).

Pre-eclampsia – Eclampsia

Pre-eclampsia usually occurs after 20 weeks gestation and is a multisystem disorder. It was classically defined as a triad of hypertension, edema and proteinuria, but a more modern definition of pre-eclampsia concentrates on a gestational elevation of blood pressure together with ≥ 0.3 g proteinuria per 24 hours.

Edema in no longer included because of the lack of specificity. Pre-eclampsia may also manifest, with few maternal symptoms and signs, as isolated intrauterine growth retardation (IUGR).

Eclampsia is defined as the occurrence of a grand mal seizure in association with pre eclampsia, although it may be the first presentation of the condition.

A. **Incidence**:

The incidence of pre eclampsia is very much influenced by the presence of existing hypertension, although other risk factors are recognized For Ex:

- Nulliparity
- Multiple pregnancy
- Family History of pre-eclampsia
- Chronic hypertension
- Diabetes
- Increased insulin resistance
- Increased body mass index
- Hypercoagulability (inherited thrombophilia)
- Renal disease even without significant impairment
- Low socioeconomic status
- Antiphospholipid syndrome (acquired thrombophilia)
- Previous pre-eclampsia
- Hydatidiform mole
- Black race.

B. Causes of pre eclampsia:

The exact cause is not known, but placental dysfunction seems to be integral to the development of the syndrome in most women.

The widespread endothelial dysfunction often manifests with primarily maternal effects and has the potential to cause dysfunction of multiple organ systems, including the brain, hepatic, pulmonary, renal, and haematological systems.

The endothelial damage leads to pathologic capillary leak that can manifest in the mother as rapid weight gain, edema of the face or limbs, pulmonary edema, and / or haemoconcentration resulting in haemoglobin greater than 12g / dL or creatinine greater than 0.8 mg/dL.

C. Signs and symptoms:

High blood pressure

Edema

Proteinuria

Blurred vision

Polyuria

Headache

Photophobia

Vomiting/nausea

Fatigue

Dyspnoea.

Table. PIH: Indications of severity.

Abnormality	**Mild**	**Severe**
Diastolic blood pressure	90-100	≥110mmHg
Proteinuria	Trace to 1+	Persistent 2 + or more
Headache	X	√
Visual disturbances	X	√
Upper abdominal pain	X	√
Oligouria	X	√
Convulsions	X	√
Serum Creatinine	Normal	Elevated
Thrombocytopenia	X	√
Hyperbilirubinemia	X	√
Liver enzyme elevation	Minimal	Obvious
Fetal Growth retardation	X	√
Pulmonary edema	X	√

√ :Symptoms observed

X : Symptoms not observed

D. Associated risks:

The risk associate with PIH can be divided into maternal and fetal risks.

a. **Maternal risks**:

Hypertensive disorders in pregnancy are among the leading causes of maternal mortality along with thrombosis, haemorrhage and non obstetric injuries. Severe maternal complication includes:

- Eclamptic seizures
- Intracerebral haemorrhage
- Pulmonary oedema due to capillary leak or myocardial dysfunction
- Acute renal failure due to vasospasm.
- Hepatic swelling with or without liver dysfunction.
- Disseminated intravascular coagulation and / or consumptive coagulopathy (rare).

b. **Fetal risks**:

Fetal complication include

- Abruptio placenta
- Intrauterine growth retardation **(**IUGR)
- Premature delivery
- Intrauterine fetal death **(**IUFD**).**

Pathophysiology:

Exact pathophysiology is unknown. Primary pathophysiology in preeclampsia is placental. In pre eclampsia trophoblastic implantation is abnormal, with reduced placental perfusion.As normal implantation is complete by around 20 weeks, this deficient implantation occurs weeks or months before the disease becomes clinically apparent. Early in gestation the spiral arteries are transformed from thick walled, muscular vessels to sac like flaccid vessels, which eventually accommodate a 10 fold increase in uterine blood flow. This transformation involves invasion of the spiral arteries by endovascular trophoblastic cells of the placenta. There is evidence that the trophoblastic invasion of the uterine spiral arteries is incomplete in women in whom pre- eclampsia eventually develops, with the vessels remaining thick walled and muscular.

The cause of this may be a failure of cytotrophoblast cells to express the adhesion molecules necessary for normal remodelling of the maternal spiral arteries. Failure of the spiral arteries to remodel is postulated as the morphologic basis for decreased placental perfusion in pre-eclampsia, which may ultimately lead to early placental hypoxia.

The secondary pathology in pre-eclampsia appears to be endothelial cell injury. The proposed model is that reduced blood supply to the placenta results in production of unknown factors which are released into the maternal circulation and act on endothelial cells, leading to endothelial dysfunction.

These results in vasospasm, with consequent reduction in plasma volume and activation of the coagulation cascade.These changes antedate other clinical findings[37].

Recently there has been interest in oxidative stress as the possible mechanism for this endothelial dysfunction[37].

Maternal manifestations of pre-eclampsia:

Blood pressure in pre eclampsia [36]:

Women with pre eclampsia do not usually demonstrate frank hypertension until the second half of gestation .High blood pressure is mainly due to a reversal of the vasodilatation characteristics of normal pregnancy, replaced by marked increase in peripheral vascular resistance.

There are changes in the ratio of vasodilator and vasoconstrictive prostanoids because there is evidence to suggest decrements and increments in the productions of prostacyclin and thromboxane respectively.

The Heart:

Usually unaffected in preeclampsia, with the decrements in cardiac performance representing a ventricle contracting normally against a markedly increased afterload. Cardiac decompensation may complicate this disorder; however, this is most often due to the presence of pre- existing heart disease .[45.]

The Kidney:

There is glomerular endotheliosis in pre-eclampsia [46]. Both glomerular filtration rate and renal blood flow is reduced leading to decrease in filtration fraction. The decrement is usually modest (25%), even when morphological changes are pronounced .

Because renal function normally rises 35% to 50 % during pregnancy, creatinine levels in women with pre-eclampsia may still be below the upper limits of normal for pregnancy (0.8 mg/dl). Renal insufficiency is rarely severe.

Fractional urate clearance decreases, producing hyperuricemia which is an important marker or pre eclapmsia.

There may be hypocalciuria & sometimes suppression of renin angiotensin system.

The Coagulation system:

There may be thrombocytopenia, elevated fibrin degradation products, reduced anti thrombin 3 levels and higher cellular fibronectin levels.

The Liver :

Pathologic changes include periportal haemorrhages, ischemic lesions , fibrin deposition, hepato-cellular necrosis, abnormalities in serum enzyme levels. There may be HELLP syndrome, with markedly elevated liver enzymes and sometimes even sub capsular bleeding or hepatic rupture. This syndrome represents serious disease and is associated with significant maternal morbidity [47].

The Central Nervous System :

Eclampsia remains a significant cause of maternal mortality. Manifestations include headache, visual disturbances, scotomata and rarely cortical blindness.

There may be varying degree of haemorrhages, petchiae, vasulopathy and fibrinoid necrosis , ischemic brain damage and microinfarcts.

Prediction and Prevention [48]:

At present there is no single screening test that is considered reliable and cost effective.

Testing related to [49]	Examples of predictive tests
Placental perfusion / vascular resistance	Roll over tests, angiotensin infusion , mid trimester mean arterial pressure, platelet angiotensin binding , renin, 24 hour ambulatory BP monitoring, Doppler velocimetry
Feto placental unit endocrine dysfunction	Human chorionic gonadotrophin, alpha feto protein, estradiol, pregnancy associated protein A, Inhibin A, Activin A, placental protein 13, corticotrophin releasing hormone
Renal dysfunction	Serum uric acid, microalbuminuria, urinary calcium, micro transferrinuria, N- acetyl b glucosaminidase
Endothelial dysfunction	Platelet count, fibronectin, endothelial adhesion molecules, prostaglandin, thromboxane, C reactive protein
Others	Anti thrombim 3, artrial natriuretic peptide

Maternal and Perinatal outcome:

Gestational hypertension:

Women with gestational hypertension are more likely to have higher rates of induction of labour , the increased rates of caesarean delivery in such women is mainly related to failed medical induction or dystocia [50]

Pre eclampsia: Outcome depends on:

- Gestational age at onset of pre Eclampsia
- Severity of disease
- Presence of pre existing medical conditions.

Management:

The treatment before 37 weeks is controversial.

Delivery is always appropriate therapy for the mother but may not be for the fetus.

Restricted activity is usual and reasonable, although its efficacy is not clearly established strict sodium restriction and diuretic therapy appear to have no role.

Fetal surveillance: Daily fetal movement assessment is a useful screening tool . NST & BPP performed periodically. USG to know the amniotic fluid volume and fetal weight. Doppler flow velocimetry in suspected IUGR.

Maternal surveillance: Goal is to recognise pre eclampsia early and prevent its complications. Regular blood pressure monitoring, watch for signs and symptoms of pre eclampsia. Laboratory testing for platelet count, renal function and liver enzymes. Quantification of a 12 to 24 hour urine sample for proteinuria.

Indications for delivery: Delivery is the only definitive treatment of pre-eclampsia.

Maternal:

- Gestational age >38 weeks
- Platelet count < 100,000 cells/ mm^3
- Progressive deterioration in hepatic or renal function
- Suspected abruption placenta
- Persistent severe headache, severe epigastric pain or vomiting.

Fetal :

- Severe growth restriction
- Nonreassuring fetal testing results.

Route of delivery:

Vaginal route is preferable. Labor induction should be carried out aggressively once the decision for delivery is made. Glucocorticoids in prematurity and when maternal condition is stable and permits pregnant to be prolonged for 48 hours. If vaginal delivery cannot be effected within a reasonable time, caesarean delivery should be considered and also performed for other obstetric indications.

Anti Convulant therapy:

Usually indicated in women with eclampsia or to prevent convulsions in impending eclampsia or severe pre eclampsia .There is no clear agreement regarding its role in mild pre eclampsia. Magnesium sulphate is the drug of choice.

Post partum counselling and follow up:

The women is re-evaluated during the immediate post partum period and also be counselled the risk in future gestation with the expectation that hypertension and other signs & symptoms will have remitted by the 6 week post partum examination , if abnormality persists , however, the patient should be re examined 6 weeks later when any persisting pathologic conditions will probably be chronic .Recurrence rates in future pregnancy are higher among multiparous women with preeclampsia than among nulliparous women with preeclampsia .

Anti hypertensive drug therapy:

Hydralazine, a potent arterial vasodilator, has long been the criterion standard of therapy for the management of hypertensive emergencies complicating pregnancy.

Less obvious, however, are alternative therapies for the management of this disorder. This question became even more important when intravenous Hydralazine was temporarily withdrawn from the market in the early 1990s. Alternative agents suggested from the literature include Nifedipine, a dihydropyridine (L-type) calcium channel blocker, and Labetalol hydrochloride, a unique alpha- and beta-adrenergic receptor blocker.

Both Nifedipine and Labetalol have demonstrated comparable efficacy and a lower risk of overshoot hypotension and fetal distress when compared with Hydralazine in randomized clinical trials.[51, 52]

Nifedipine:

Nifedipine is available as a capsule as well as a tablet.

Nifedipine belongs to a class of pharmacological agents, the calcium channel blockers. Nifedipine is 3,5-pyridinedicarboxylic acid, 1,4-dihydro-2, 6-dimethyl-4-(2-nitrophenyl)-, dimethyl ester, C17H18N2O6,

Nifedipine is a yellow crystalline substance, practically insoluble in water but soluble in ethanol. It has a molecular weight of 346.3. Nifedipine Capsules are formulated as soft gelatin capsules for oral and sublingual administration each containing 5 mg/10 mg Nifedipine.

Mechanism of action:

Nifedipine is a calcium ion influx inhibitor (slow-channel blocker or calcium ion antagonist) and inhibits the trans-membrane influx of calcium ions into cardiac muscle and smooth muscle. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels. Nifedipine selectively inhibits calcium ion influx across the cell membrane of cardiac muscle and vascular smooth muscle without changing serum calcium concentrations.

Pharmacokinetics and metabolism

Nifedipine is rapidly and fully absorbed after oral administration. The drug is detectable in serum 10 minutes after oral administration, and reaches peak blood levels in approximately 30 minutes. Bioavailability is proportional to dose from 10 to 30 mg; half-life does not change significantly with dose.

There is little difference in relative bioavailability when Nifedipine capsules are given orally and either swallowed whole, bitten and swallowed, or bitten and held sublingually.

However, biting through the capsule prior to swallowing does result in slightly higher plasma concentrations (27 ng/mL 10 minutes after 10 mg) than if capsules are swallowed intact. It is highly bound by serum proteins.

Nifedipine is extensively converted to inactive metabolites and approximately 80 percent of Nifedipine and metabolites are eliminated via the kidneys. The half-life of Nifedipine in plasma is approximately two hours.

Since hepatic biotransformation is the predominant route for the disposition of Nifedipine, the pharmacokinetics may be altered in patients with chronic liver disease. Patients with hepatic impairment (liver cirrhosis) have a longer disposition half-life and higher bioavailability of Nifedipine than healthy volunteers. The degree of serum protein binding of Nifedipine is high (92–98%). Protein binding may be greatly reduced in patients with renal or hepatic impairment.

Hemodynamics: Like other slow-channel blockers, Nifedipine exerts a negative ionotropic effect on isolated myocardial tissue. Nifedipine causes decreased peripheral vascular resistance and a fall in systolic and diastolic pressure, which is usually modest (5–10mm Hg systolic), but sometimes larger. There is usually a small increase in heart rate, a reflex response to vasodilatation.

Pregnancy:

Pregnancy Category C

Nifedipine has been shown to produce teratogenic findings in rats and rabbits, including digital anomalies similar to those reported for Phenytoin. On a mg/kg basis, all of the doses associated with the teratogenic, embryo-toxic or feto-toxic effects in animals were higher (3.5 to 42 times) than the maximum recommended human dose of 120 mg/day. On an mg/m^2 basis, some doses were higher and some were lower than the maximum recommended human dose but all are within an order of magnitude of it. The doses associated with placento-toxic effects in monkeys were equivalent to or lower than the maximum recommended human dose on a mg/m2 basis.

Non-teratogenic Effects: There are no adequate and well-controlled studies in pregnant women. Nifedipine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Dosage:

10mg is the initial dose give orally. Followed by 20 mg given every 20-30 minutes, until the total dose of 120 mg/day if needed.

Adverse effects:

Nifedipine has frequent adverse effects but generally not serious and rarely require discontinuation of therapy or dose adjustment. Sudden hypotension is one of the greatly feared adverse effects of Nifedipine. This is most commonly seen in sublingual use.

Other adverse effects like peripheral edema, dizziness or light-headedness, nausea, headache flushing, weakness, transient hypotension, palpitation, nasal and chest congestion, shortness of breath, diarrhoea, constipation, cramps, inflammation, joint stiffness, muscle cramps, shakiness, nervousness are noted.

Labetalol Hydrochloride:

Labetalol hydrochloride is an adrenergic receptor-blocking agent that has both selective alpha 1-adrenergic and non-selective beta-adrenergic receptor blocking actions in a single substance. In man, the ratios of alpha- to beta-blockade have been estimated to be approximately 1:3 and 1:7 following oral and IV administration, respectively.

Labetalol produces dose-related falls in blood pressure without reflex tachycardia and without significant reduction in heart rate, presumably through a mixture of its alpha- and beta-blocking effects.

Hemodynamic effects are variable, with small, nonsignificant changes in cardiac output seen in some studies but not others, and small decreases in total peripheral resistance. Elevated plasma renins are reduced.

Doses of Labetalol HCL that controlled hypertension did not affect renal function in mild to severely hypertensive patients with normal renal function.

Pharmacokinetics and Metabolism

Labetalol lowers blood pressure by blocking α_1 adrenoreceptors in peripheral vessels thereby reducing peripheral resistance, and the heart rate is reduced because of its β blocking effect.

Labetalol has become popular for the treatment of hypertension in pregnancy and pre eclampsia. It has been used orally and intra venous for rapid blood pressure reduction.

The plasma half-life of Labetalol following oral administration is about 6 to 8 hours. In patients with decreased hepatic or renal function, the elimination half-life of Labetalol is not altered; however, the relative bioavailability in hepatically impaired patients is increased due to decreased “first-pass” metabolism.

The metabolism of Labetalol is mainly through conjugation to glucuronide metabolites. The metabolites are present in plasma and are excreted in the urine and, via the bile, into the feces. Approximately 55% to 60% of a dose appears in the urine as conjugates or unchanged Labetalol within the first 24 hours of dosing.

Labetalol has been shown to cross the placental barrier in humans. Only negligible amounts of the drug crossed the blood-brain barrier in animal studies. Labetalol is approximately 50% protein bound. Neither hemodialysis nor peritoneal dialysis removes a significant amount of Labetalol HCL from the general circulation (<1%).

Pregnancy:

Pregnancy Category C

A teratology study performed with Labetalol in rabbits at IV doses up to 1.7 times the MRHD revealed no evidence of drug-related harm to the fetus. There are no adequate and well-controlled studies in pregnant women. Labetalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects:

Hypotension, bradycardia, hypoglycemia, and respiratory depression have been reported in infants of mothers who were treated with Labetalol HCL for hypertension during pregnancy.

Labor and Delivery:

Labetalol HCl given to pregnant women with hypertension did not appear to affect the usual course of labor and delivery.

Dosage

If the drug is given intravenously, 20 mg initial dose, followed by 40-80 mg every 10 minutes , until the therapeutic response is achieved . It can also be given in IV drip, dissolving 250 mg in 250 ml of normal saline and giving 20 ml/min (20mg/ hour) and adjusting the rate up or down according to the patient's response.

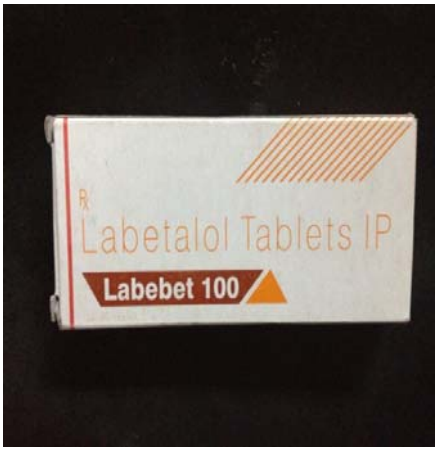
If given orally 75% of the drug is inactivated in the first liver pass. The initial dose is 100 mg twice daily. This dose may be increased according to the patient's response. The maintenance dose is usually 200- 400 twice daily.

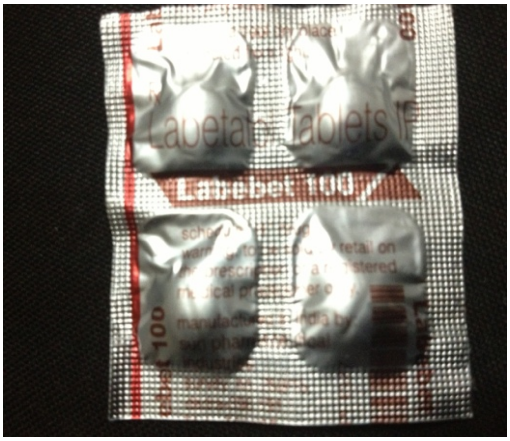
Adverse Reactions

Labetalol is usually well tolerated. Most adverse effects have been mild and transient. Symptomatic postural hypotension (incidence, 58%) is likely to occur if patients are tilted or allowed to assume the upright position within 3 hours of receiving Labetalol hydrochloride injection.

Moderate hypotension, Ventricular arrhythmia, dizziness tingling of the scalp, hypoesthesia (numbness) and vertigo, nausea, vomiting, dyspepsia and taste distortion and somnolence/yawning have been noted. Labetalol has been associated with hepatic injury in a limited number of patients.

Nifedipine capsules 10 mg





Labetalol tablets 100 mg

MATERIALS AND METHODS

The study got ethical approval by B.L.D.E UNIVERSITY'S, SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE BIJAPUR-586103, KARNATAKA.

Study Design: Randomized control trial.

Source of data

All women admitted with a systolic BP of more than 140mm Hg or more and diastolic BP of more than 90 mmHg during pregnancy at BLDE University's Shri.B. M. Patil Medical College, Hospital and Research Centre, Bijapur from Oct 2011 to June 2013.

Details of the study

Inclusion criteria

- Gestation more than 20wks.
- All women with a systolic BP of more than 140mm Hg or more and diastolic BP of 90mm Hg or more.

Exclusion Criteria

- Patient with cardiac disease
- Exposure to either study medication within 24hrs of enrollment
- Asthma
- Diabetes
- Chronic hypertension.

SAMPLE SIZE

Positive character (p) = 15 % (highest value of prevalence)

Then, q =100- p

i.e., 100-15 = 85%

Allowable error (L) = 10 %

Hence, estimate of sample size would be

$n = 4pq/ (L)^2$

Where, n =sample size

$n = 4(15 \times 85)/ (10)^2$

$= 4(1275)\ 100$

$=5100/100$

$=51$

Informed Consent: Women who presented to opd or labor room at Shri B.M.Patil medical college ,Bijapur, were screened for enrolment in the study using inclusion and exclusion criteria. Informed consent was obtained, a signature or left had thumb impression from the consented subject was obtained after reading the informed consent document. For illiterate participants, the consent document was read out. The patient and the relatives were explained the relative risks involved in the study. None of the participants were pressurized to enrol into the trial. No monitory benefit was offered to any of the participants enrolled in the study.

Method of data collection

Enrolled patients were randomized to receive either oral Nifedipine or oral Labetalol .Randomization was done by simple randomization method with no blind method .For equal allocations of patients we can take odd and even numbers to indicate treatment and grouped as A and B respectively. Once the patient was randomized to a group, a proforma regarding the basic details of the patient was entered.

A sphygmomanometer was used to record blood pressure manually. Blood pressure was checked in the right arm with the cuff covering at least 2/3 of the arm. Systolic pressure corresponded to the appearance of Korotkoff sounds and diastolic pressure corresponded to the disappearance of Korotkoff V sounds

Patients randomized to oral Nifedipine received 10mg stat and repeated every 4 to 6 hours depending on control of BP either with the same dosage or with reduced or increased dosage with maximum dosage of 120 mg. Nifedipine was never give sublingually.

Patients randomized to oral Labetalol received 100 mg stat and repeated every 8 to 12 hours either with same dosage or with increased or reduced dosage to a maximum of 2400 mg dosage depending on control of BP.

Bp was recorded every 4^{th} hourly or monitored according to control of BP.

For every woman the following data was recorded :

- Amount of drug administered
- Time needed to control blood pressure
- Number of doses administered
- Urinary output
- Adverse effects
- Maternal and perinatal outcome

For the admitted patients the following investigations was done :

- Hb % :
- TC :
- DC :
- ESR :
- Platelets :
- BT :
- CT :
- PT :
- aPTT :
- PT-INR :
- Peripheral Smear :
- Blood Grouping and Rh Typing :
- Urine Routine (albumin, sugar, microscopy) :
- RBS :

- HBs Ag :
- RVD :
- USG :
- RENAL FUNCTION TESTS :
- LIVER FUNCTION TEST :
- Fundoscopy:
- Any other investigations if done was noted :

Patients who remained hypertensive without complications (as evidenced by urine and blood investigations and sonology and reactive NST) belonging to both groups were observed in the hospital till spontaneous vaginal delivery occurred at term.

In both groups, if the gestational age was > 34 weeks with worsening of condition, termination of pregnancy was done.

If gestational age was 28- 34 weeks, 2 doses of betamethasone 12 mg, 24 hours apart was given for fetal lung maturity and then delivered after 48 hours.

For severe hypertension and severe pre eclampsia, magnesium sulphate was given as prophylactic anti convulsant .The magnesium sulphate prophylaxis regimen was given according to prichards regimen. Immediate termination was done preferably by vaginal delivery.

However LSCS was chosen for patients with obstetric indications like unfavourable indications like unfavourable cervix, nonprogression of labor, unfavourable lie, abnormal Doppler indices etc.

For induction, in primigravida, PGE2 gel & in multigravida PGE1 / oxytocin was used.

Patients were followed up in the intrapartum, post partum period for 1 week, for the maternal fetal as well as neonatal complications .

Once blood pressure has been lowered to a lower level the following dosage was used for long term treatment:

- Labetalol 200-400mg BID ,
- Nifedipine 10mg every 8^{th} hourly

The significance of these tests was calculated using various formulas. The significance was based on P-value.

The outcome was noted as:

- **Primary outcome:** The time taken in minutes, by either drug to reduce the blood pressure.
- **Secondary outcome**: The number of drugs required and the adverse effects.

RESULTS

Table 1: Distribution of cases according to age.

Age (years)	No Of Patients(n=51)		Percentage	
	Nifedipine Group	Labetalol Group	Nifedipine Group	Labetalol Group
15-20	19	12	37.25%	23.53%
21-25	21	24	41.18%	47.06%
26-30	9	11	17.65%	21.57%
31-35	2	3	3.92%	5.88%
36-40	0	1	0%	1.96%

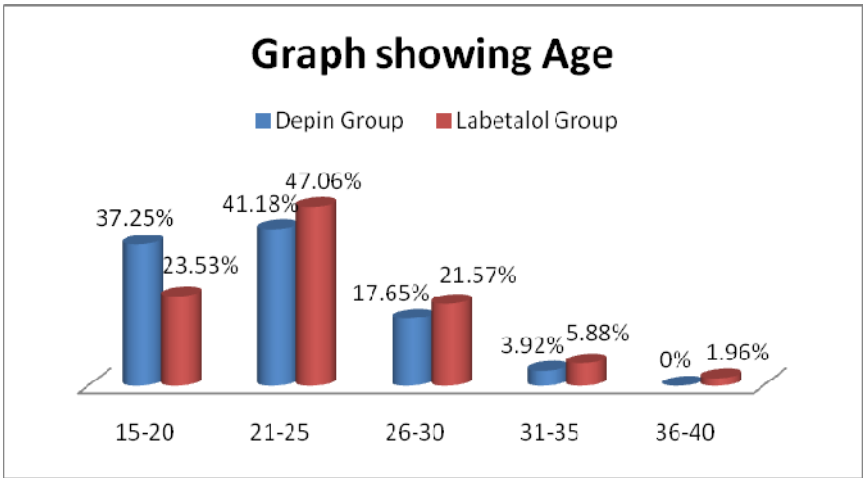


Fig 1: Distribution of cases according to age

The two groups were comparable regarding age distribution. The mean age for the Nifedipine group was 23 years and 6 months and for Labetalol group was 23 years and 9 months.

In the Nifedipine group : 19 patients (37.25 %) aged between 15 to 20 years , 21 patients (41.18%) aged between 21-25 years , 9 patients (17.65%) aged between 26-30 years and 2 patients (3.92%) aged between 31-35 years .

In the Labetalol group:12 patients (23.53%) aged between 15-20 years, 24(41.18 %) patients aged between 21-25 patients , 11 patients (21.57%) aged between 26-30 years, 3 patients (5.88%) aged between 31-35 years and 1 patient(1.96%) aged between 36-40 years .

Table 2: Parity

Parity	Nifedipine(n=51)	Percentage	Labetalol(n=51)	Percentage
G1	30	58.82%	28	54.90%
G2	15	29.41%	11	21.56%
G3	3	5.88%	8	15.68%
>G3	3	5.88%	4	7.84%

In the Nifedipine group 30 patients (58.8%) were primigravida, 15 patients were 2nd gravida (29.4%), and 3 patients were 3rd gravid (5.8 %) and 3 patients were more than 3rd gravida (5.8%).

In the Labetalol group 28 patients (54.9%) were primigravida, 11 patients (21.5%) were 2nd gravida, 8 patients (15.8%) were 3rd gravida and 4 patients (7.8%) were more than 3rd gravida

Fig 2: Parity

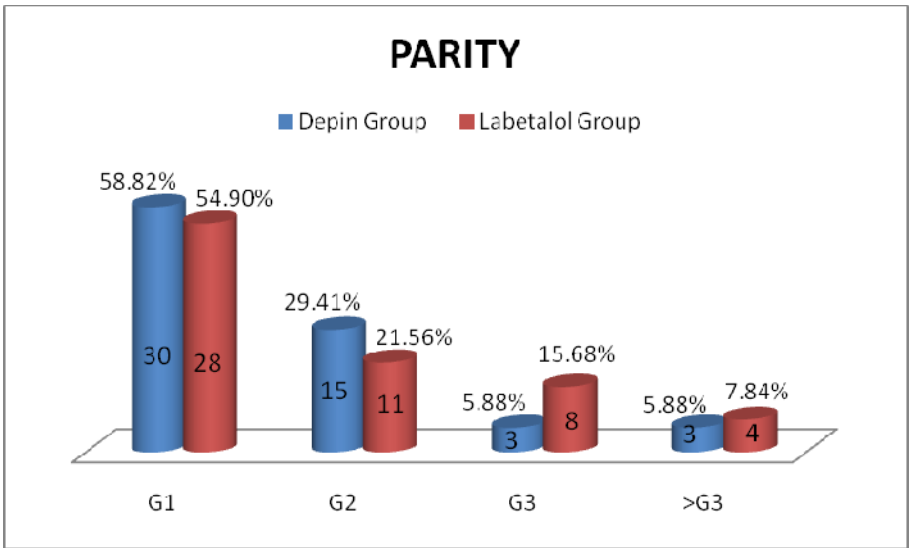


Table.3) Risk Factors.

Risk factors	Nifedipine(n=51)	Nifedipine%	Labetalol(n=51)	Labetalol%
Nil	28	54.90%	28	54.90%
h/o HTN in previous pregnancy	2	3.92%	7	13.72%
Anaemia	7	13.72%	6	11.72%
prev LSCS	3	5.88%	1	1.96%
PROM	5	9.80%	2	3.92%
Oligohydramnios	3	5.88%	2	3.92%
Placenta previa	1	1.96%	0	0.00%
Grand multi	1	1.96%	0	0.00%
Post dated	1	1.96%	1	1.96%
IUGR	0	0.00%	3	5.88%
Rh negative	0	0.00%	1	1.96%

The risks factors were comparable in both the groups . Majority of the patients did not have any risk factors .

Fig 3 : Risk Factors

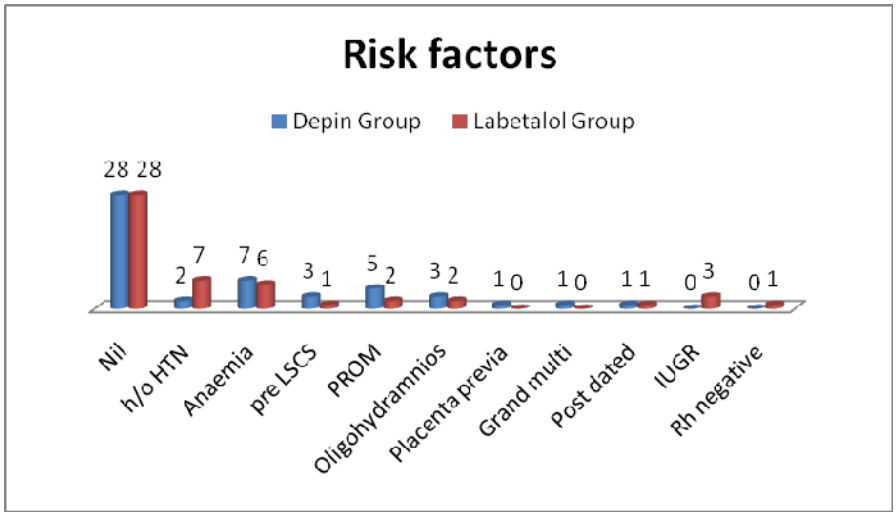


Table.4) Urine albumin

Urine albumin	Nifedipine(n=51)	Labetalol(n=51)
1+	8	8
2+	11	9
3+	6	9
4+	7	10
Traces	5	5
Nil	14	10
Total	51	51

The urine albumin in the patients were as follows :

In Nifedipine group : 8 patients had 1+, 11 patients had 2+, 6 patients had 3+, 7 patients had 4+, and traces was seen in 5 patients and in 14 patients urine albumin was nil.

In the Labetalol group : 8 patients had 1+, 9 patients had 2+, 9 patients had 3+, 10 patients had 4+, traces was seen in 5 patients , and it was absent in 10 patients .

Fig 4:- Urine albumin

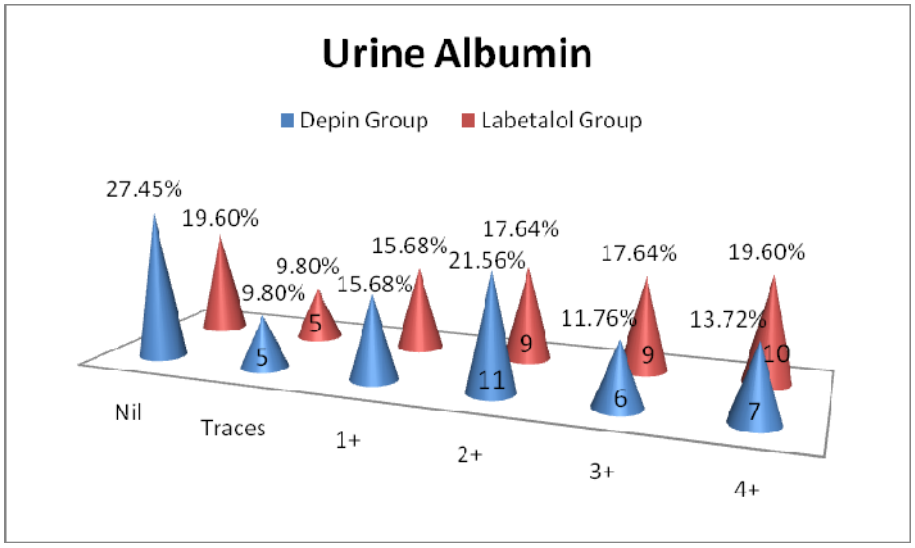


Table no. 5) Statistical measures of SBP (Pre) and SBP (post)

	Nifedipine (n=51)			Labetalol(n=51)		
Measures	**SBP(pre)**	**SBP(post)**	**Decline Rate**	**SBP(pre)**	**SBP(post)**	**Decline Rate**
Mean	**165.02**	**126.27**	**23.63%**	**165.49**	**132.74**	**20%**
SD	**12.70**	**12.15**		**16.28**	**8.50**	
Max	**220**	**140**		**240**	**140**	
Min	**150**	**100**		**150**	**110**	

The mean systolic BP before the treatment in Nifedipine group was 165.02 with a SD of 12.70, which was reduced to 126.27 with SD of 12.15. Maximum pre SBP was 220 mmHg and minimum was 150 mmHg. And following treatment with Nifedipine the maximum measure was reduced to 140mm Hg and minimum measure to 100 mmHg following treatment.

In the Labetalol group the mean Systolic Blood Pressure before treatment was 165.49 with SD of 16.28 and following treatment it was reduced to 132.74 with SD of 8.50. The maximum measured BP before treatment was 240 mm Hg which was reduced to 140 mmHg and minimum measure BP of 150 mmHg was reduced to 110 mmHg.

The Nifedipine group had a decline rate of 23. 63 % when compared to 20 % in the Labetalol group.

Fig .5:- Measure of Systolic blood pressure

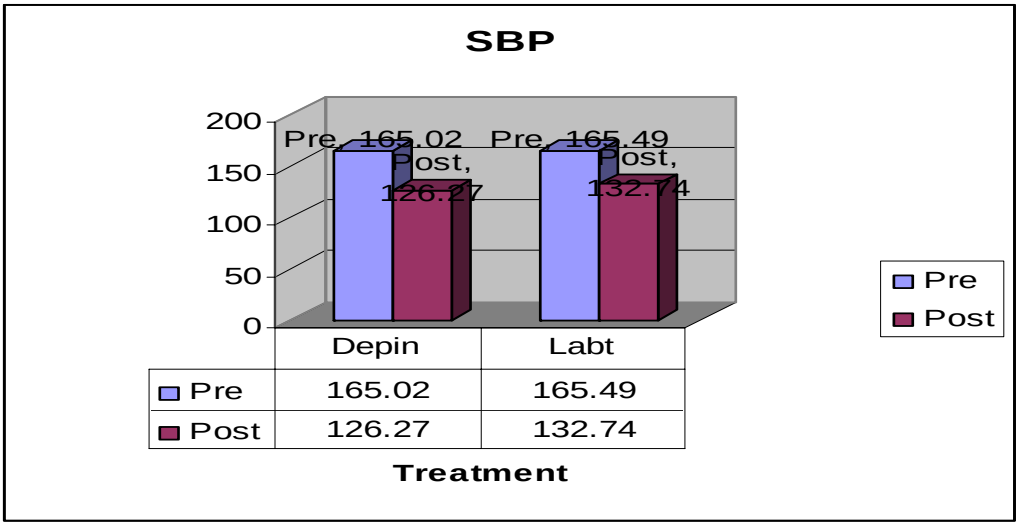


Table . 6 : Statistical measures of DBP (Pre) and DBP (post)

	Nifedipine (n=51)			Labetalol(n=51)		
Measures	**DBP(pre)**	**DBP(post)**	**Decline Rate**	**DBP(pre)**	**DBP(post)**	**Decline Rate**
Mean	**107.53**	**81.56**		**103.25**	**82.15**	
SD	**10.23**	**9.02**	**24.3%**	**8.59**	**8.78**	**20.38%**
Max	**140**	**100**		**130**	**90**	
Min	**90**	**60**		**90**	**50**	

The mean diastolic blood pressure before the treatment in Nifedipine group was 107.53 with a SD of 10.23, which was reduced to 81.56 with SD of 9.02 .Maximum pre DBP was 140 mmHg and minimum was 100 mmHg. And following treatment with Nifedipine the maximum measure was reduced to 100mm Hg and minimum measure to 60 mmHg.

In the Labetalol group the mean diastolic Blood Pressure before treatment was 103.25 with SD of 8.59 and following treatment it was reduced to 82.15 with SD of 8.78. The maximum measured BP before treatment was 130 mm Hg which was reduced to 90mmHg and minimum measure BP of 90 mmHg was reduced to 50 mmHg.

The Nifedipine group had a decline rate of 24. 3 % when compared to 20.38% in the Labetalol group.

Fig . 6) Measure of Diastolic blood pressure

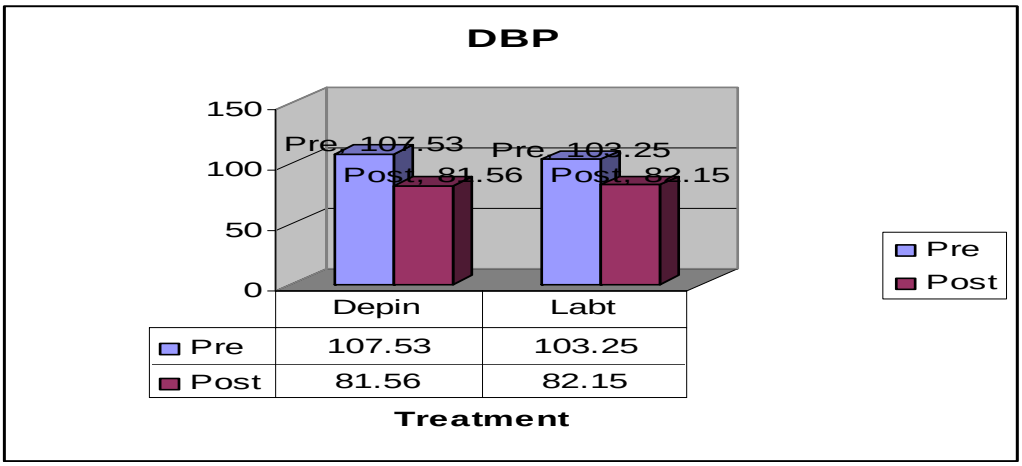


Table 7: Test of Significance between "Time taken" for decline in BP

Time taken(min)	Nifedipine(n=51)	Labetalol(n=51)	Z-Test value	P-value
Mean	**181.27**	**687.64**	**9.38**	**0.0001 (HS)**
SD	**176.22**	**342.72**		
Max	**600**	**1560**		
Min	**30**	**120**		

The mean time taken to reduce the BP to target value in Nifedipine group was 181.27 minutes with SD of 176.22 when compared to 687.64 minutes in Labetalol group with SD of 342.72.

The maximum time taken was 600 minutes in Nifedipine group and minimum of 30 minutes in Nifedipine group when compared to maximum of 1560 minutes in Labetalol group and minimum of 120 minutes. The p value is 0.0001 which is highly significant.

Fig no. 7: Time taken for decline in BP

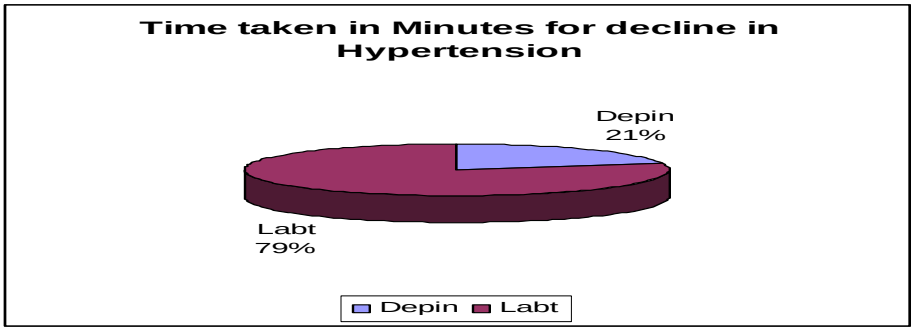


Table 8: Test of Significance between "Dose level" for decline in BP

Dose	Nifedipine (n=51)	Labetalol(n=51)	Z-Test value	P-value
Mean	**1.35**	**1.84**	**2.84**	**0.001**
SD	**0.72**	**1.02**		
Max	**4**	**6**		
Min	**1**	**1**		

The Nifedipine group required mean of 1 dosage to reduce the BP whereas Labetalol required 2 dosages. The p value is 0.001 which is significant

Table 9. Adverse effects of the drugs

Adverse effects	Nifedipine(n=51)	Labetalol(n=51)	Nifedipine %	Labetalol %
Nil	28	36	54.90%	70.58%
Hypotension	2	1	3.92%	1.96%
headache	9	4	17.65%	7.84%
Sweating	1	2	1.96%	3.92%
Nausea/ vomiting	5	3	9.80%	5.88%
Palpitation	3	4	5.88%	7.84%
Fetal tachycardia	7	1	13.72%	1.96%

The side effects of the drugs were noted. In the Nifedipine group 28 patients did not have any side effects when compared to 36 patients in Labetalol group. 2 of the patients had hypotension in Nifedipine group and 1 patient in Labetalol. 9 patients had headache in Nifedipine group whereas 4 patients had headache in Labetalol. Sweating was seen in 1 patient in Nifedipine group and 2 patients in Labetalol group. 3 patients and 4 patients in Nifedipine and Labetalol respectively had palpitation. 7 fetuses in Nifedipine had tachycardia and 1 in Labetalol.

Fig 8 .Adverse effects

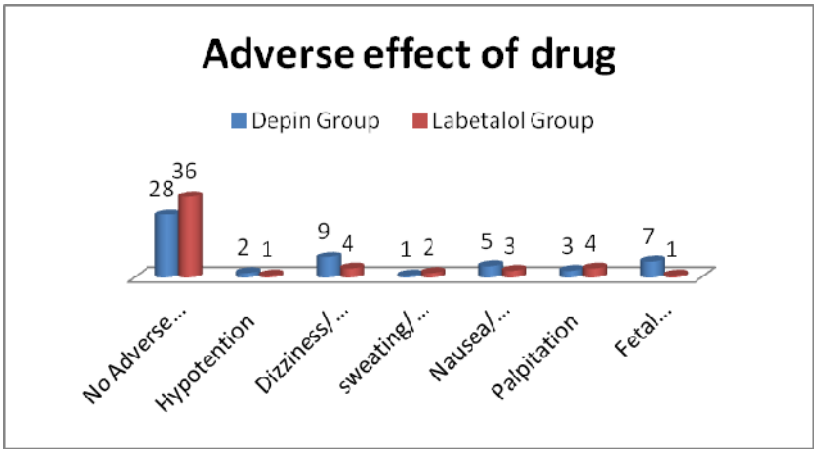


Table 10) Complications due to PIH

	Nifedipine (n=51)	Labetalol(n=51)	Nifedipine Group %	Labetalol Group %
Eclampsia	**12**	**10**	**23.53%**	**19.60%**
Abruption	**9**	**10**	**17.65%**	**19.60%**
HELLP	**4**	**2**	**7.84%**	**3.92%**
Renal failure	**0**	**2**	**0%**	**3.92%**
CVA	**0**	**1**	**0%**	**1.96%**
Pulmonary edema	**1**	**1**	**1.96%**	**1.96%**
Mortality	**1**	**0**	**1.96%**	**0%**

12 patients (23.53 %) in Nifedipine group had eclampsia where as 10 patients(19.64 %) in Labetalol group had eclampsia. Abruption was seen in 9 patients (17.65 %) in Nifedipine group and in Labetalol group 10 patients had abruption (19.60%). HELLP syndrome was seen in 4 patients (7.84 %) in Nifedipine group and 2 patients (3.92%) in Labetalol group.2 patients (3.92 %) in Labetalol group had renal failure and none(0%) in Nifedipine group. Cerebrovascular accident was seen in 1 patient (1.96 %) in Labetalol group. 1 patient (1.96 %) in Nifedipine group and 1 patient (1.96%) in Labetalol group had pulmonary edema and there was 1 maternal mortality(1.96%) in Nifedipine group.

Fig 9.) Complications due to PIH.

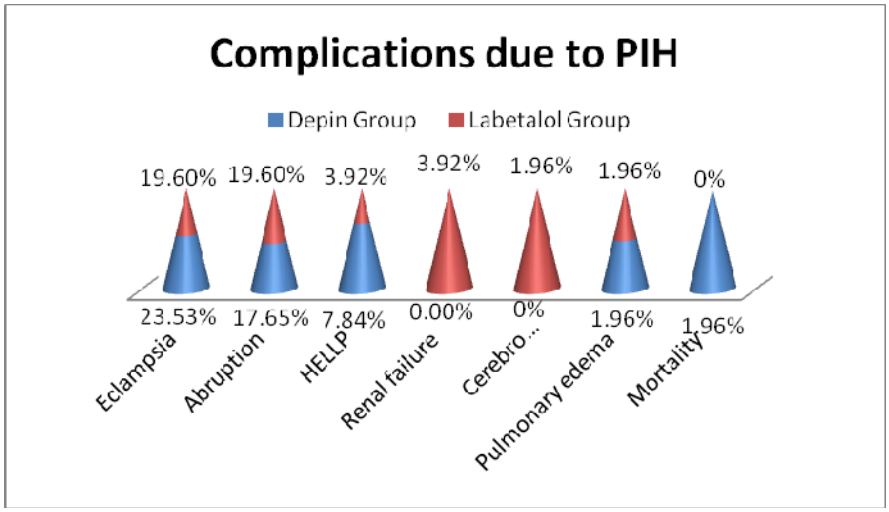


Table 11: Mode of delivery

	Nifedipine (n=51)	Labetalol(n=51)	Nifedipine %	Labetalol %
Normal	**22**	**26**	**43.14%**	**50.98%**
Instrumental	**4**	**2**	**7.84%**	**3.92%**
LSCS	**25**	**23**	**49.01%**	**45.09%**

The mode of delivery in both the groups were as follows :

In the Nifedipine group 22 patients had normal delivery, 4 had instrumental delivery and 25 patients had cesarean section .

In the Labetalol group 26 patients had normal delivery , 2 patients had instrumental delivery and 23 patients underwent cesarean section.

Fig 10 : Mode of delivery

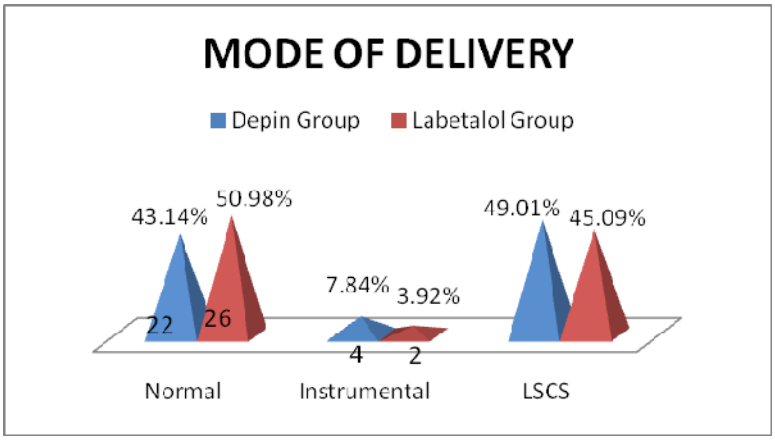


Table 12: LSCS due to PIH

Type	Nifedipine (n=51)	Labetalol(n=51)
Total pts	25	28
No	17	9
Yes	9	14
Total	51	51

Among 25 patients who underwent LSCS

In Nifedipine group 9 cesarean section were done due to PIH and among 28 patients in Labetalol group 14 patients underwent LSCS due to PIH .

Fig 11: LSCS due to PIH

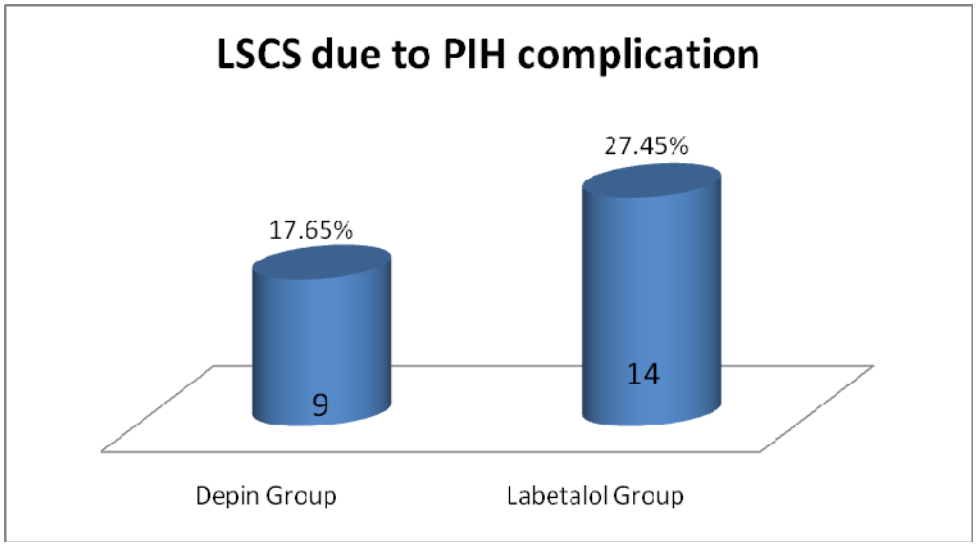


Table 13: Patients with term and preterm pregnancy

	Nifedipine Group(n=51)	Labetalol Group(n=51)	Nifedipine %	Labetalol %
Term	**33**	**31**	**64.71%**	**60.78%**
Preterm	**18**	**20**	**35.29%**	**39.22%**

Among 51 patients in both the groups 33 patients were term in Nifedipine group and 31 patients in Labetalol group . 18 patients had preterm delivery in depin group and 20 patients in Labetalol group.

Fig 12: No. of patients with term and pre term pregnancy.

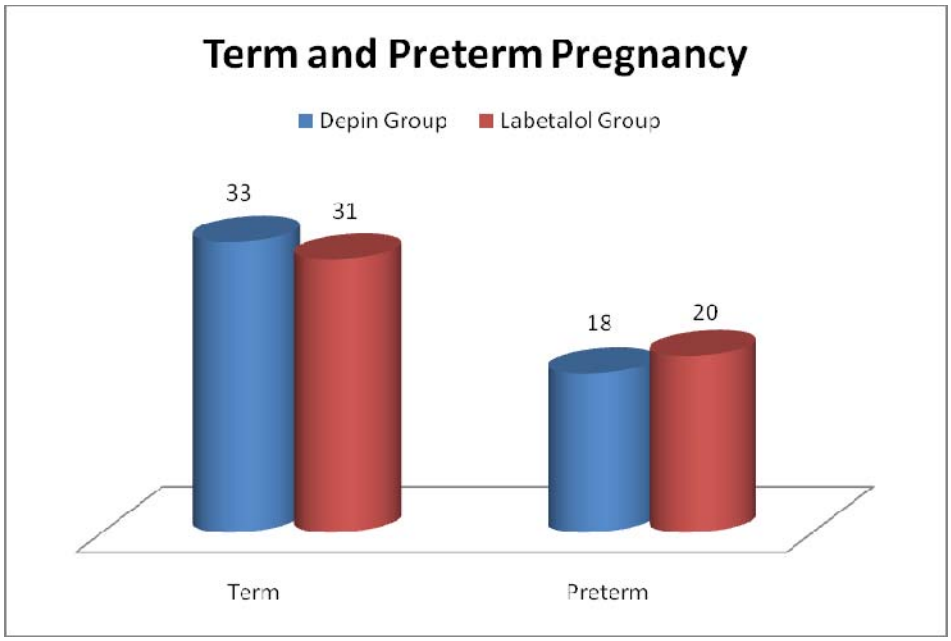


Table 14: NICU Admissions

Nifedipine Group (n=51)	**20**	**39.22%**
Labetalol Group(n=51)	**24**	**47.06%**

Among 51 deliveries in both the groups : In Nifedipine group 20 babies (39.22 %) had NICU admission and 24 babies (47.06 %) in Labetalol group .

Fig 13 : NICU Admissions

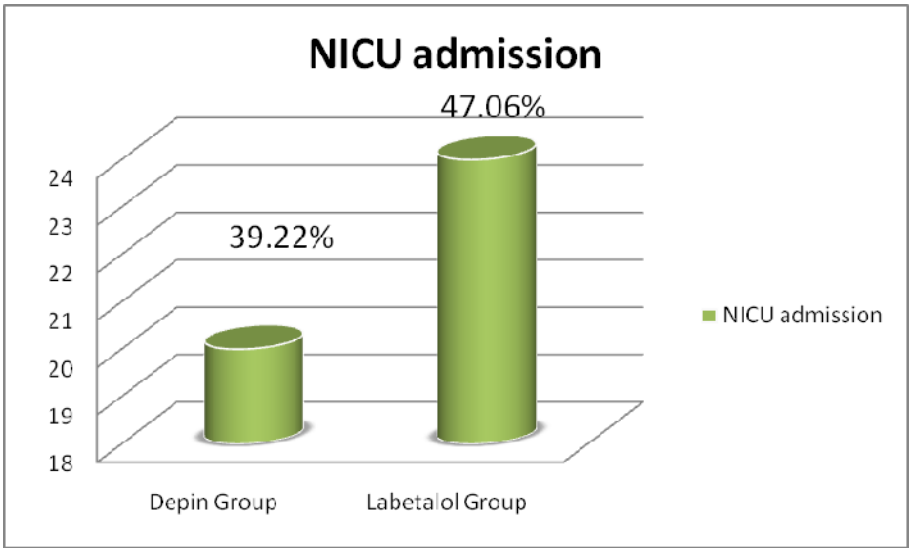


Table 15: Neonatal Complications

	Nifedipine (n=51)	Labetalol(n=51)	Nifedipine Group %	Labetalol Group %
Nil	**29**	**31**	**56.86%**	**60.78%**
Hyperbilirubinemia	**9**	**7**	**17.65%**	**13.73%**
RDS	**7**	**9**	**13.73%**	**17.65%**
IUD	**6**	**4**	**11.76%**	**7.84%**

Among 51 deliveries in each group, 29 babies (56.86 %) had no neonatal complications in Nifedipine group and 31 babies(60.78 %) in Labetalol group had no neonatal complications . 9 babies(17.65 %) had hyperbilirubenemia in Nifedipine group compared to 7 babies(13.73 %) in Labetalol group. RDS was observed in 7 babies (13.73 %) in Nifedipine group and 9 babies (17.65 %) in Labetalol group. There were 6 IUD's (11.74 %) in Nifedipine group and 4 (7.84 %) in Labetalol group.

Fig 14. Neonatal complications

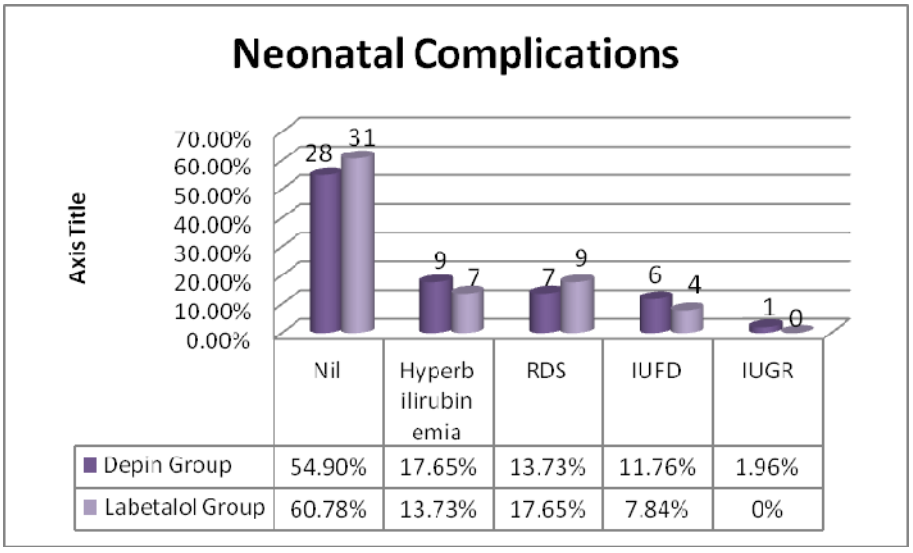


Table 16. Apgar score:-

Apgar score at 5 min	Nifedipine Group(n=51)	Labetalol Group(n=51)
<9	35.29%	47.06%
>9	64.71%	52.94%

The Apgar score at 5 minutes <9 was 35.29 % in Nifedipine group and 47.06 % in Labetalol group. The Apgar score > 9 was 64.71 % in Nifedipine group and 52.94% in Labetalol group

Fig 15. Apgar score

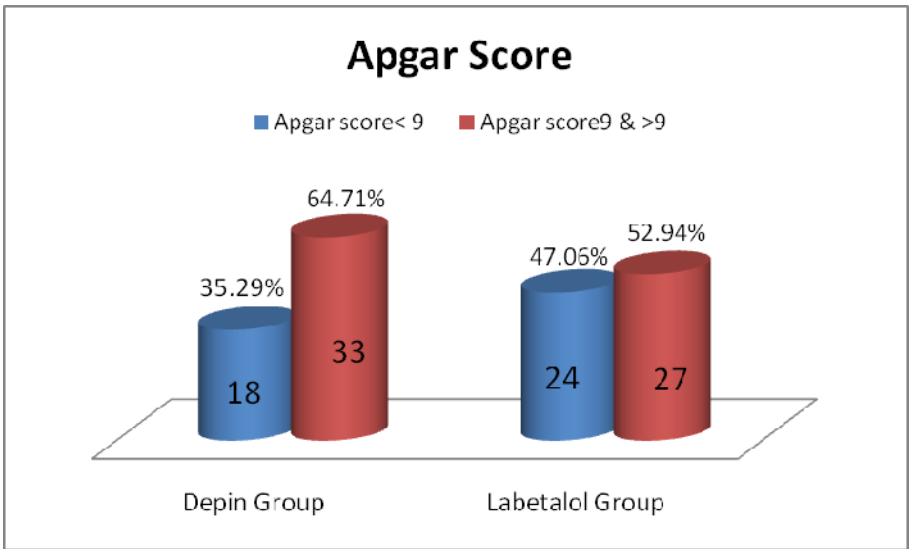


Table 17: Condition of Babies at discharge.

S.No	Status	Under Nifedipine (n=51)	Under Labetalol(n=51)
1	FSB	2	1
2	Good	43	45
3	IUD	6	4
4	Expired	0	1
5	Total	51	51

At the time of discharge: In the Nifedipine group there were 2 FSB , and 43 babies had no complications , 6 IUD's had happened .

In the Labetalol group: there was 1 FSB and 45 babies had no complications and 4 patients had IUD's and there was 1 neonatal mortality

Table 18: Conditions of Mothers at Discharge.

Status	Under Nifedipine (n=51)	Under Labetalol(n=51)
No complications	**37**	**38**
Recovered	**13**	**13**
Expired	**1**	**0**
Total	**51**	**51**

Conditions of the mother at the time of discharge in the Nifedipine group were as follows: 37 mothers had no complications and 13 patients had recovered from severely hypertensive status , and there was 1 maternal mortality (due to cardiopulmonary arrest)

In the Labetalol group 38 mothers had no complications and 13 patients had recovered well and there was no mortality in this group.

DISCUSSION

This randomized controlled study, compares the efficacy of two anti-hypertensive drugs, oral Nifedipine and oral labetalol.102 patients were included in the trial of which, 51 were randomized to Nifedipine and 51 were randomized to Labetalol.

Both groups were similar in terms of age, parity, weight and period of gestation. The mean age of a subject in the Nifedipine group was 23 years and 6 months and the average age in the Labetalol group was 23 years 9 months. The mean period of gestation in both groups was similar. The risk factors assessed and the urine albumin done in both the groups were comparable.

Decline rate for control of blood pressure :

Many studies have shown that both Nifedipine and Labetalol can be used successfully in treating hypertension in pregnancy. The present study reveals that oral Nifedipine reduces the blood pressure at a significantly faster rate than oral Labetalol. The mean systolic blood pressure before the treatment in Nifedipine group was 165.02 with a SD of 12.70, which was reduced to 126.27 with SD of 12.15. Maximum pre SBP was 220 mmHg and minimum was 150 mmHg. And following treatment with Nifedipine the maximum measure was reduced to 140mm Hg and minimum measure to 100 mmHg following treatment.

In the Labetalol group the mean Systolic Blood Pressure before treatment was 165.49 with SD of 16.28 and following treatment it was reduced to 132.74 with SD of 8.50. The maximum measured BP before treatment was 240 mm Hg which was reduced to 140 mmHg and minimum measure BP of 150 mmHg was reduced to 110 mmHg. Nifedipine group had a decline rate of 23. 63 % when compared to 20 % in the Labetalol group.

The mean diastolic blood pressure before the treatment in Nifedipine group was 107.53 with a SD of 10.23 , which was reduced to 81.56 with SD of 9.02 .Maximum pre DBP was 140 mmHg and minimum was 100 mmHg and following treatment with Depin the maximum measure was reduced to 100mm Hg and minimum measure to 60 mmHg .

In the Labetalol group the mean diastolic Blood Pressure before treatment was 103.25 with SD of 8.59 and following treatment it was reduced to 82.15 with SD of 8.78. The maximum measured BP before treatment was 130 mm Hg which was reduced to 90mmHg and minimum measure BP of 90 mmHg was reduced to 50 mmHg. The Nifedipine group had a decline rate of 24. 3 % when compared to 20.38% in the Labetalol group.

The randomized controlled study done earlier comparing these two drugs had similar results where in Nifedipine reduced blood pressure in a significantly shorter duration when compared to the Labetalol group[39].

Time required to achieve the target BP:

The mean time taken to reduce the BP to target value in Nifedipine group was 181.27 minutes with SD of 176.22 when compared to 687.64 minutes in Labetalol group with SD of 342.72.

The maximum time taken was 600 minutes in Nifedipine group and minimum of 30 minutes in Nifedipine group when compared to maximum of 1560 minutes in Labetalol group and minimum of 120 minutes. Z test value was 9.38. The p value is 0.0001 which is highly significant.

This indicates that Nifedipine acts faster than Labetalol in reaching the target value.

Number of doses required:

The study also compared the dosage required for the drugs to reduce the BP. The mean value for the dose level required in Nifedipine group was 1.35 with SD 0.72 whereas Labetalol had mean value of 1.84 with SD of 1.02.

The Nifedipine group required mean of 1 dosage to reduce the BP whereas Labetalol required 2 dosages. Z test value was 2.84.The p value is 0.001 which is significant.

A randomized controlled trial done on the same drugs had similar results where a significantly smaller dose was required by Nifedipine to control blood pressure[52].

Adverse effects:

The most common adverse effect includes hypotension, dizziness, flushing, nausea, vomiting, palpitation, headache, and fetal tachycardia.

The side effects of the drugs were noted.

In the Nifedipine group 28 patients (54.9 %) did not have any side effects when compared to 36 patients (70.58 %) in Labetalol group.

2 of the patients (3.92%) had hypotension in Nifedipine group and 1 patient (1.96%) in Labetalol.

9 patients (17.65 %) had headache in Nifedipine group whereas 4 patients (7.84%) had headache in Labetalol. Since High blood pressure can present with headache, it is difficult to attribute it to the adverse effects of any of the drugs.

Sweating was seen in 1 patient (1.96 %) in Nifedipine group and 2 patients (3.92%) in Labetalol group.

3 patients (5.88%) and 4 patients (7.84%) in Nifedipine and Labetalol respectively had palpitation.

7 fetuses (13.72%) in Nifedipine had tachycardia and 1 in Labetalol (1.96%).

Comparison done for both the groups did not show statistical significant value. . Similar studies done earlier also indicate that the side effects of the above mentioned were of a very minor degree and did not harm either the mother or the baby.

Complications due to High Blood pressure:

The complications were attributed to severe preeclampsia and not related to the study drugs.

Eclampsia recorded in this study occurred prior to admission. There were no incidences of eclampsia after therapy was started.12 patients (23.53 %) in Nifedipine group had eclampsia where as 10 patients (19.64 %) in Labetalol group had eclampsia.

Abruption was seen in 9 patients (17.65 %) in Nifedipine group and in Labetalol group 10 patients had abruption (19.60%).

HELLP syndrome was seen in 4 patients (7.84 %) in Nifedipine group and 2 patients (3.92%) in Labetalol group.

2 patients (3.92 %) in Labetalol group had renal failure and none (0%) in Nifedipine group.

Cerebrovascular accident was seen in 1 patient (1.96 %) in Labetalol group.

1 patient (1.96 %) in Nifedipine group and 1 patient (1.96%) in Labetalol group had pulmonary edema.

And there was 1 maternal mortality (1.96%) in Nifedipine group due to cardio pulmonary arrest.

There was no statistically significant difference in the two study groups regarding the complications.

Mode of delivery :

In the Nifedipine group 22 patients (43.14 %) had normal delivery, 4 (7.84%) had instrumental delivery and 25 patients (49.01%) had cesarean section.

In the Labetalol group 26 patients (50.98%) had normal delivery, 2 patients (3.92%) had instrumental delivery and 23 patients (45.09%) underwent cesarean section.

Among 25 patients who underwent LSCS in Nifedipine group 9 cesarean section were done due to PIH and among 28 patients in Labetalol group 14 patients underwent LSCS due to PIH.

Incidence of preterm and term gestation :

Among 51 patients in both the groups,

33 patients (64.71 %) were term in Nifedipine group and 31 patients (60.78 %) in Labetalol group.

18 patients (35.29 %) had preterm delivery in Nifedipine group and 20 patients (39.22%) in Labetalol group.

Neonatal complications:

18 patients (35.29 %) had preterm delivery in Nifedipine group and 20 patients (39.22%) in Labetalol group.

Among 51 deliveries, 20 babies (39.22 %) in Nifedipine group and 24 babies (47.06 %) in Labetalol group required NICU admission.

Among 51 deliveries: 29 babies (56.86 %) in Nifedipine group and 31 babies (60.78 %) in the Labetalol group had no neonatal complications. 9 babies(17.65 %) had hyperbilirubinemia in Nifedipine group compared to 7 babies (13.73 %) in Labetalol group.

RDS was observed in 7 babies (13.73 %) in Nifedipine group and 9 babies (17.65 %) in Labetalol group. There were 6 IUD's (11.74 %) in Nifedipine group and 4 (7.84 %) in Labetalol group .The higher incidence of RDS in the study group can be explained by the higher incidence of preterm deliveries.

The IUD's was due to complication of high BP and not because of drugs.

The apgar score at 5 minutes <9 was 35.29 % in Nifedipine group and 47.06 % in Labetalol group. The apgar score > 9 was 64.71 % in Nifedipine group and 52.94% in Labetalol group.

Condition of Babies at discharge:

In the Nifedipine group there were 2 FSB's, 6 IUD's and 43 babies had no complications .

In the Labetalol group: there was 1 FSB, 4 IUD's and 1 neonatal mortality (due to congenital anamoly) after 24 hours of birth and 45 babies had no complications.

Conditions of Mothers at Discharge:

In the Nifedipine group : 37 mothers had no complications and 13 mothers had recovered from severely hypertensive status , and there was 1 maternal mortality (due to cardio pulmonary arrest) .

In the Labetalol group: 38 mothers had no complications and 13 patients had recovered well from severely hypertensive status and there was no mortality in this group.

There have been many studies comparing antihypertensive drugs. The present study was a randomized controlled trial. There was no bias in selecting patients to a particular study group. Both groups were similar in most aspects, in terms of age, weight and period of gestation, parity and blood pressure.

One of the main objective in treating women with mild to moderate hypertension in pregnancy is to prevent or delay progression to eclampsia. The present study contains only a small population. Hence the interpretation may be misleading. There is need for large scale multicenter trial to know the benefits of antihypertensive therapy in mother and baby taking into the consideration all the outcomes measures proposed in this study. The absolute levels of BP at which antihypertensive therapy becomes meaningful also needs to be determined by trials. In this study there may be inter- observer variability as the blood pressure was manually checked for each patient. The newborns have to be followed up to their childhood to know the effects on infant and child development.

Our study measured the time interval for action, dosage, adverse effects and the maternal and perinatal outcome, so we can conclude that Nifedipine was a superior drug than Labetalol in treatment for hypertension in pregnancy.

SUMMARY

This study was done to assess the effectiveness of two anti hypertensives : oral Nifedipine and oral Labetalol in cases of hypertension in pregnancy , for the prevention of progression and complications of the diseases and better maternal and fetal outcome .

This was a randomized case controlled study.

Study was conducted on 102 patients divided as 51 patients in 2 groups, at Shri B.M.Patil medical college, Bijapur, who fulfilled the inclusion criteria. After taking the informed consent the patients were categorized into 2 groups after randomization.

Patients with systolic blood pressure of 140 mmHg or more and/or diastolic blood pressure of 90 mmHg or more were treated with either oral Nifedipine or oral Labetalol.

The primary objective of the study was to calculate the time required to reduce the blood pressure to the target level of <140 mmHg systolic or less and 90 mmHg diastolic or less.

The secondary outcome was to calculate the number of doses required to achieve the target blood pressure and the adverse effects of the drugs.

The patients who came in the inclusion criteria were treated with either Nifedipine or Labetalol based on their randomization number.

Antihypertensives in pregnant ladies in hypertension in pregnancy produced a significant control in the absolute mean value of systolic BP and Diastolic BP. The mean systolic blood pressure before the treatment in Nifedipine group was 165.02 with a SD of 12.70, which was reduced to 126.27 with SD of 12.15.

In the Labetalol group the mean Systolic Blood Pressure before treatment was 165.49 with SD of 16.28 and following treatment it was reduced to 132.74 with SD of 8.50. The Nifedipine group had a decline rate of 23. 63 % when compared to 20 % in the Labetalol group.

The mean diastolic blood pressure before the treatment in Nifedipine group was 107.53 with a SD of 10.23, which was reduced to 81.56 with SD of 9.02. In the Labetalol group the mean diastolic Blood Pressure before treatment was 103.25 with SD of 8.59 and following treatment it was reduced to 82.15 with SD of 8.78.

The Nifedipine group had a decline rate of 24. 3 % when compared to 20.38 % in the Labetalol group .

The mean time taken to reduce the BP to target value in Nifedipine group was 181.27 minutes with SD of 176.22 when compared to 687.64 minutes in Labetalol group with SD of 342.72.

The maximum time taken was 600 minutes and minimum of 30 minutes in Nifedipine group when compared to maximum of 1560 minutes in Labetalol group and minimum of 120 minutes. Z test value was 9.38. The p value is 0.0001 which is highly significant.

This indicates that Nifedipine acts faster than Labetalol in reaching the target value

It was also found that Nifedipine requires fewer doses than Labetalol to achieve the same goal. Oral Nifedipine required one dose of 10 mg to reduce blood pressure where as oral Labetalol required 2 doses, a total of 200 mg to reduce blood pressure to the target level. The p-value calculated was <0.001. Indicating the difference was highly significant.

Patients were also monitored for any side effects that may arise from the drugs. The adverse effects noted were, hypotension, dizziness, sweating, flushing, nausea, vomiting, palpitations, headache and fetal tachycardia. Adverse effects observed were very few and of minor degree.

There was no statistical difference noted in the adverse effects in both group.

Complications arising from the raised Blood pressure such as, eclampsia, abruption, HELLP, stroke, renal failure, cerebrovascular accidents were noted.

The complications that were noted were not attributable to the drugs. These complications were due to High blood pressure secondary to preeclampsia.

Perinatal morbidity and mortality was also noted. The incidence of NICU admission, preterm and complications like hyperbilirubinemia , RDS, low apgar score were noted . The results were comparable in both the groups.

There was 1 maternal death in Nifedipine group which was due to cardio pulmonary arrest, this patient had HELLP syndrome and was in renal failure.

And there was 1 neonatal death after 24 hours of birth in Labetalol group which was due to congenital anamoly of the baby .

These complications were due to hypertension in pregnancy and not due to the effects of the drugs.

This study proved that Nifedipine is the choice of drug in cases of hypertension in pregnancy. Nifedipine acts faster, at a lesser dose and has equal side effects to that of Labetalol and similar maternal and perinatal outcome as of Labetalol. Nifedipine has the added advantage of being easily available, and cheap.

CONCLUSION

In the present study, both oral Nifedipine and oral Labetalol were ultimately effective in reaching the therapeutic goal, but Nifedipine achieved the target blood pressure more rapidly and with fewer doses than Labetalol.

Both drugs demonstrated a similar adverse effects profile.

Nifedipine is also cheaper, easier to store, easier to administer, where as oral Labetalol is more expensive and requires more dosage than Nifedipine.

Thus the present study concludes that Nifedipine is the preferred drug in case of hypertension in pregnancy to control blood pressure as it is more efficacious and can be used in the peripheral centers due to cost effectiveness and its ease of administration and storage.

BIBLIOGRAPHY

1. Cunningham FG, Hauth JC, Leveno KJ, Gilstrap L, Bloom SL, Wenstrom KD. William's obstetrics 23rd ed. McGraw Hill publishers; 2010,706
2. Khan KS et al, WHO analysis of causes of maternal death: a systematic review. Lancet 2006;367:1066-74.
3. Kausar R, Maternal Mortality in India: Magnitude, Causes and Concerns. Indmedica. 2005-06;Vol.2, No.2.
4. Repke J. Management of obstetric hypertensive emergencies; OBG management. July 2005;Vol 17, No 7.
5. Abalos E ,Duley l, Steyn Dw.Antihypertensive drug therapy for mild to moderate hypertension during pregnancy .Cochrane Database of systemic Review 2007,Issue 1,ArtNo.: CD002252.
6. Guler Sahin, Gulmezoglu AM. Incidence, morbidity and mortality of pre eclampsia and eclampsia. Geneva foundation for medical education and research
7. Magee L, Duley L.Oral Beta Blockers For Mild To Moderate Hypertension During Pregnancy. Cochrane Database of Systemic Reviews.2003 ;(3):CD002863.
8. Aali BS,Nejad SS.Nifedipne or Hydralazine as a first line agent to control hypertension in severe pre-eclampsia. Acta Obstet Gynaecol Scand 2002 Jan ;81(1) : 25-30

9. Abalos E ,Duley l, Steyn Dw.Antihypertensive drug therapy for mild to moderate hypertension during pregnancy .Cochrane Database of systemic Review 2007,Issue 1,ArtNo.: CD002252.
10. Barton Jr, O'brien Jm, Bergauer Nk, Jacques Dl,Sibai Bm. Mild gestational hypertension remote from term : progression and outcome. Am J Obstet Gynecol. April 2001; 184(5): 979 – 83.
11. DeSouza AR,Amorim MR, Costa AR.Nifedipine antihypertensive treatment effects in pre-eclampsia. Acta Med Port 2008 jul-aug; 21 (4): 351-8. Epub 2008 Oct 24
12. Williams H. Frishman, MD, Megan Veresh BS, Pathophysiology and Medical Management of Systemic Hypertension in Preeclampsia, Curr. Hypertens Rep; 2006, 8:502-511.
13. Williams obstetrics 23rd edition; 34:706-709.
14. Belfort MA, Tooke-Miller C, Allen JC Jr, et al.: Labetalol decreases cerebral perfusion pressure without negatively affecting cerebral blood flow in hypertensive gravidas. Hypertens Pregnancy 2002, 21:185–197.
15. Raheem IA, Saaid R, Omar S Z. Oral nifedipine versus intravenous labetalol for acute blood pressure control in hypertensive emergencies of pregnancy: a randomized trial: BJOG 2011; DOI: 10.1111/j.1471-0528.2011.03151.x(E pub ahead of print)
16. Vigil-De Gracia P, Lasso M, Ruiz E. Severe hypertension in pregnancy: hydralazine or labetalol. A randomized clinical trial. Eur J Obstet Gynecol Reprod Biol. 2006 Sep-Oct;128(1-2):157-62
17. Rosenthal T and Oparil S, 2002, "The effect of antihypertensive drugs on the fetus", Journal of Human Hypertension, 16, 293-298.

18. Podymow T, August P . Upate on the use of anti hypertensive drugs in pregnancy. Hypertens.2008;51:960-69
19. Magee La, Ornstein Mp, Von Dadelszen P.Management of hypertension in pregnancy. BMJ 1999; 318: 1332-1336
20. Corine M Koopmans , Denise Bijlenga , Henk Groen , Sylvia MC Vijgen, Jan G Aarnoudse et al.Induction of labour Versus Expectant Monitoring for Gestational Hypertension or Mild Pre-eclampsia after 36 Weeks ' Gestation (HYPITAT): A Multicentre,Open –label Randomised Controlled Trial .BMC Pregnancy and childbirth 2007; 14: 2393-7
21. Saudan P, Brown MA,Buddle ML,Jones M. Does Gestational hypertension become Pre Eclampsia ? Br J Obstet Gynecol 1998;1177-1184
22. Barton JR, Bergaur NK, Jaques DL et al. Does advanced maternal age affect pregnancy outcome in women with mild hypertension remote from term? Am J Obstet Gynecol 1997; 176: 1236-1243
23. Barton CJ, Barton JR, O' Brien JM et al. Mild Gestational hypertension : differences in ethinicity are associated with altered outcomes in women who undergo outpatient treatment .Am J Obstet Gynecol 2002; 186: 896-898
24. Huma Tasleem , Samina Tasleem, Malik Muhammed Adil, Mahfooz Siddique, Khalida Waheed .Co-relation of Pregnancy induced Hyperyension with Placental Abruption & Effect of Antihypertensive therapy.Rawal Med J 2005; 30: 104-109.
25. Paruk F,Moodley J.RHL commentary on Cochrane Review : 'Antihypertensive drug therapy for mild-to-moderate hypertension during pregnancy '. The WHO Repoductive Health Library No .5.Geneva : WHO, 2002.

26. Laura A.Magee,Betsy Schick Rn,Alan E.Donnenfeld,Suzanne R.Sage RN,Beth Conover Rn et al. The safety of calcium channel blockers in human pregnancy : A prospective, multicenter cohort study . Am J obstet Gynecol 1996;174 (3): 823-829.
27. Renata bortolus , Elena Ricci, Liliane Chatenoud , Fabio Parazzini . Nifedipine administered in pregnancy : effect on the development of children at 18 months . Br J Obstet Gynecol 2000; 107: 792-794
28. Victoria M Allen; KS Joseph ; Kellie E Murphy ; Laura A Magee; Arne Ohlsson. The Effect of Hypertensive Disorders in Pregnancy on small for Gestational Age And Stillbirth: A Population Based Study . BMC Pregnancy and Childbirth 2004; 4(17): 297-290
29. Arulkumaran S S, Gita A, Penna L K. The management of labour 3rd ed.2011;463,471
30. Arias F , Daftary S N, Bhide A G. Hypertensive disorders in pregnancy. Practical guide to high risk pregnancy and delivery 3rd ed. 2011; 401-07
31. James D, Steer J P, Weiner P C. Hypertension. High risk pregnancy and management options 4th ed. 2011;615
32. Sarala G, Jain V. Hypertensive disorders of pregnancy. Mudaliar and Menons' Clinical Obstetrics 11th ed.2011;179
33. Renu M. Ian Donald's Practical Obstetrics Problems 6th ed.2007;299
34. Zamroski MA, Green LA. NHBPEP report on High Blood Pressure in Pregnancy: A Summary For Family Physicians. American Family Physician July 15, 2001/Vol 64, No 2

35. Steven G.Gabbe , Jennifer R.Niebyl ,Joe Leigh Simpson . Hypertension. Obstetrics- Normal & Problem Pregnancies. 5th edn.China: Churchill Livingstone; 2007:p.863-912
36. Report of the National High Blood Pressure Education Program. Working group report on high blood pressure in pregnancy . Am J Obstet Gynecol 2000;183:S1-22
37. Leila Duley . Pre-eclampsia and the hypertensive disorders of Pregnancy . British Medical Bulletin 2003; 67:161-176
38. Ian Donald . Practical Obstetric Problems. 6th edn. New Delhi : BI Publications; 2007: p280-309
39. Scardo JA, Vermillion ST, Newman RB, Chauhan SP and Hogg BB, 1999, "A randomized, double blind, haemodynamic evaluation of nifedipine and labetalol in preeclamptic hypertensive emergencies", Am J Obstet Gynecol, 181,4, 858-861.
40. Khalil A, Jauniaux E and Harrington K, 2009, "Antihypertensive therapy and central haemodynamics in women with hypertensive disorders in pregnancy", Obstet Gynecol, 113, 646-654.
41. Fernando Arias , Shirish N Daftary, Amarnath G Bhide. Hypertensive Disorders in Pregnancy. 3rd edn. New Delhi: Elsevier; 2008 :p 397-439
42. American college of Obstetricians and Gynecologists . Hypertension in pregnancy . ACOG Technical Bulletin No.: 219. Washington , DC: The College; 1996.p.1-8
43. Helewa ME, Burrows RF, Smith J, Williams K, Brain P, Rabkin SW. Report of the Canadian Hypertension society Consensus

Conferences:1. Definitions, evaluation and classification of hypertensive disorders in pregnancy. CMAJ 1997; 157: 715-25

44. Brown MA, Hague WM, Higgins J, Lowe S, Mcowan L, Oates J, et al. The detection , investigation and management of hypertension in pregnancy , full consensus statement of recommendation from the Council of the Australian Society for the Study of Hypertension in Pregnancy (ASSHP) . Aust N Z J Obstet Gynaecol 2000; 40: 139-56
45. Lang RM, Pridjian G, Feldman T, Neumann A, Lindheimer M,Borow KM. Left ventricular machanics in preeclampsia. Am Heart J 1991; 121: 1768-75.
46. Lindheimer MD, Katz AI. Renal Physiology , diseases in pregnancy in the kidney. In : Seldin DW, Giebisch G, editors. The kidney: physiology and pathophysiology . 2nd ed, vol 3 . New York: Raven Press; 1992, 3371-3429.
47. Weinstien L. Syndrome of hemolysis, elevated liver enzymes , and low platelet count: a severe consequences of hypertension in pregnancy. Am J Obstet Gynecol 1982; 142: 159-67
48. Baha M. Sibai. Diagnosis and Management of Gestational Hypertension and preeclampsia . Obstet Gynecol 2003; 102: 181-92.
49. Cunningham GF, Leveno CJ, Steven LB. Williams obstetrics . 23rd edn . USA: MCGraw Hill; 2010. 706-756
50. Hauth JC , Ewell MG, Levine RL, Esterlitz JR, Sibai BM, Curet LB. Pregnancy outcomes in healthy nulliparas women who

subsequently developed hypertension . Obstet GYnecol 2000; 95: 24-8.

51. 6 Fenakel K, Fenakel G, Appelman Z, Lurie S, Katz Z, Shoham Z. Nifedipine in the treatment of severe preeclampsia. Obstet Gynecol 1991; 77:331-7.
52. Mabie WC, Gonzalez AR, Sibai BM, Amon E. A comparative trial of labetalol and hydralazine in the acute management of severe hypertension complicating pregnancy. Obstet Gynecol 1987; 70:328-33.

ANNEXURE 1 : PROFORMA DESIGNED FOR THE STUDY

Name	:	Ipno:
Age	:	case.no
Address	:	Occupation
DOA	:	DOD
Time of admission	:	
Chief complaints	:	
History of present pregnancy	:	
Antenatal history	:	
booked/unbooked	:	
immunised/unimmunised	:	
1st trimester	:	
2nd trimester	:	
3rd trimester	:	
Obstetrics history	:	
married life	:	
obstetric score	:	
Details of previous pregnancies	:	
Menstrual history		
LMP	:	
EDD	:	POG
Past history	:	
Family history	:	
Personal history	:	

General physical examination

Build and nourishment	:	Respiratory rate	:
Height	:	Breast	:
Weight	:	Thyroid	:
Temp	:	Spine	:

pallor / icterus / cyanosis / clubbing / edema / lymphadenopathy.

Systemic examination

CVS :

RS :

Per abdomen :

Per speculum examination :

Per vaginal examination :

Vitals on admission

PR

BP

Vitals before starting treatment

PR

BP

Whether patient put on prophylactic magnesium sulphate : y/n

Time of initation of treatment

BP recordings 4th hourly or monitored according to control of BP.

Time (hours)	PR(bpm)	BP(mm hg)	U/O If catherized

Number of drugs required for achievement of target BP:

Adverse effects

1)Hypotension (min BP) : Y/N

2)Dizziness/headache : Y/N

3)Sweating/flushing : Y/N

4)Nausea/vomiting : Y/N

5)palpitations : Y/N

6) Fetal tachycardia : Y/N

Maternal outcome:

POG:

Mode of delivery : normal/instrumental/cesarean

Eclampsia : Y/N

Abruption : Y/N

HELLP : Y/N

Renal failure : Y/N

Cerebro vascular

accident :Y/N

Pulmonary edema/

Left ventricular failure : Y/N

Mortality : Y/N

Perinatal outcome:

POG:

Birth weight:

Apgar score

Nicu admission : Y/N

RDS/hyperbilirubinemia : Y/N

Pre-term : Y/N

IUD : Y/N

Neonatal mortality : Y/N

Investigations

HB % :

BLOOD GROUPING AND RH TYPING :

URINE ROUTINE :

RBS :

HBS AG :

RVD :

USG :

BT :

CT :

PT :

PLATELETS :

TC :

DC :

ESR :

RENAL FUNCTION TESTS

SERUM CREATININE

BLOOD UREA

URIC ACID

LIVER FUNCTION TEST :

PERIPHERAL SMEAR

APTT

SERUM ELECTROLYTES

PT-INR

ANY OTHER INVESTIGATIONS IF DONE :

II. ETHICAL CLEARANCE

Ethical Committee
BIJAPUR-586103
OUT WARD
No 271/2011
Date 21-10-11
Shri B. M. PATIL Med. Col

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 20-10-2011 *at* 10-30 am *to scrutinize the Synopsis/Research projects of postgraduate/undergraduate student/Faculty members of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis/Research project has been accorded Ethical Clearance.*

Title "A Randomised controlled trail of oral nifedepine Vs oral labetapol in management of hypertension in pregnancy"

Name of P.G./U.G. student/Faculty member Dr. Ashwini. V.
Dept of OBG.

Name of Guide/Co-investigator Dr. S. R. Bidri, Assoc prof of OBG

DR.M.S.BIRADAR,
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.
Chairman
Ethical Committee
BLDEA'S Shri. B.M. Patil
Medical College
Bijapur-586103

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

III. CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Study: A randomised controlled trial of oral Nifedepine vs oral Labetalol in management of hypertension in pregnancy.

Principal investigator: Dr.Ashwini V. postgraduate

Guide : Dr. Shailja R. Bidri , prof

We request you to be a participant in above said research to be conducted at BLDEU 's Shri. B.M. Patil medical college hospital from oct 2011 to june 2013 conducted by Dr. Ashwini V, postgraduate student in the Dept. Of obstetrics and gynaecology at Shri B.M. Patil Medical College, Bijapur .

Your participation in this study is your voluntary decision whether or not to participate will not affect your current or future relationship with the at Shri B.M. Patil Medical College, Bijapur

Procedure involved:

If you agree in this research we would subject you to either of the two study drugs and measure the efficiency of the drugs to control blood pressure. The outcome will be measured by regular blood pressure monitoring.

Risk and benefits:

There are no additional risks involved in this procedure, as they are getting the same conventional treatment that they would receive, if they were not part of the trial. If any complications arise during the procedure then the patients will be treated with best of our knowledge. There will be no compensation or payment for such medical treatment.

If you attain any complication during the procedure you may contact Dr.Shailja R. Bidri professor and and Dr.Ashwini V, postgraduate in the dept. of obstetrics and gynaecology.

During the course of study you will be informed of any significant new findings such as changes in risks and benefits resulting from participation in the research.

Privacy and confidentiality:

The only people who will know that you are a research participant are members of the research team. No information about you or provided by you, during the research will be disclosed to others without your written consent. When the results of the research are published or discussed the conferences, no information will be disclosed that would reveal your identity. Any information obtained in connections with this study and that can be identified with you remain confidential and will be disclosed only with your permission.

Voluntary participation:

Your participation in this study will help us identify a superior drug amongst the two that will help us treat the future patients with the same drug. You are free to discontinue the participation in the study at any time for any reasons and you will not be paid any reimbursement for participation in the research.

Statement of consent:

To voluntarily agree to take part in this study i must sign on the line below: if you chose to take part in this study i may withdraw at any time i am not giving up any of my legal rights, by signing this form. My signature below indicates that i have read or have read to me this entire consent form including the risks and benefits and had all questions answered, i will be given a copy of this consent form.

Signature of the subject:

Name: date:

Signature of the authorized representative:

Name: date:

Relation to the subject:

Signature of the witness:

Name: date:

Signature of the investigator:

Name: date:

MASTER CHART

V. KEY TO MASTER CHART

- S. No : serial number
- IP No: Hospital inpatient number
- Parity :
    - G : gravida,
    - P: para
    - L: living
    - A: abortion
    - D: death
- POG : Period of gestation, W: weeks, D: days
- Risk factors :
        - PROM : premature rupture of membranes
        - PIH : pregnancy induced hypertension
        - Prev LSCS : previous lower segment caesarean section
        - HTN : hypertension
- Wt (Kg) : weight in kilograms
- Pre SBP : pre systolic blood pressure
- Pre DBP : pre diastolic blood pressure
- Time taken : Hr: hours ,Min : minutes
- Post SBP: post systolic blood pressure

- Pre DBP : post diastolic blood pressure
- ADR : adverse effects
- Complications due to PIH : HELLP : haemolysis, elevated liver enzymes and low platelet count
- MOD : mode of delivery
    - LSCS : lower segment cesarean section
    - Severe PE : severe pre eclampsia
    - SVD : Spontaneous vaginal delivery
    - VD -M: vaginal delivery-Misoprost induced
    - VD-C: vaginal delivery –Cerviprime induced
    - VD- O: vaginal delivery –oxytocin induced
    - VD-I(V) : vaginal delivery –instrumental- vaccum assisted
    - VD-I(F) : vaginal delivery – instrumental –forceps assisted
    - VBAC: Vaginal birth after caesarean section
- Patients' with term and preterm pregnancy : T: term, PT: preterm
- Sex of the baby :
    - M: male
    - F: female

- Neonatal complications :
    - IUGR :intrauterine growth restriction
    - RDS : respiratory distress syndrome
- Condition of babies at discharge :
    - IUD : intrauterine death,
    - LBW : low birth weight
    - FSB : fresh still born
- Y: yes
- N: no
- 0: NIL

MASTER CHART NIFEDIPINE GROUP (n=51)

sl no	NAME	AGE	IP NO	PARITY	POG	RISK FACTORS	WT (KG)	URINE ALBUMIN	PRE SBP	PRE DBP	TIME TAKEN	POST SBP	POST DBP	DOSES REQUIRED	ADVERSE EFFCETS	COMPLICATIONS DUE TO PIH	MOD	LSCS DUE TO PIH	TERM/PRETERM	BIRTH WT	SEX OF BABY	APGAR SCORE at 5 min	NICU ADMISSION	NEONATAL COMPLICATION	CONDITION OF MOTHER AT DISCHARG	CONDITION OF BABY AT DISCHARGE
1	Kaveri	24	190	G1	39W+1	Nil	60	traces	162	104	7hr	130	90	4	Sweating+ nausea	N	LSCS(failure to progress)	N	T	2.67	M	9	N	N	good	good
2	Bibijan	20	1996	G1	41W+4d	Nil	70	4+	182	120	2hr+20min	140	90	4	headache	eclmapsia	LSCS(antepartum eclampsia	Y	T	1.85	F	9	Y	IUGR	recovered	good(term IUGR)
3	Bhuvaneshwari	27	2014	G4P2L1D1A1	35W+1d	h/o PIH in 2nd pregnancy	72	1+	170	100	8hr+40 min	110	90	1	N	N	LSCS(severe PE)	Y	PT	1.7	M	9	Y	Hyperbiliruminemia)	good	good
4	Reshma	25	2456	G1	33W+3d	Nil	63	2+	160	108	1hr+30 min	120	90	1	N	Abruption	SVD	0	PT	1.5	M	7	Y	RDS	good	good
5	Mallamma	20	14959	G1	37	moderate anaemia	58	3+	170	120	1hr+30min	100	90	1	N	Eclampsia	LSCS(poor bishops score with	Y	T	2.3	M	9	N	N	recovered	good
6	Boramma	25	14893	G6P5L3D2	37W+2d	grand multi	68	1+	160	120	6hr+10 min	110	80	2	N	Eclampsia, Abruption	LSCS(Poor maternal bearing	Y	T	2	F	0	0	0	recovered	IUD
7	Shilpa	25	16432	G2P1L1	30w+1d	prev ,LSCS	72	3+	170	110	30min	110	100	1	headache	N	VD-M	0	PT	1	M	5	Y	Hyperbiliruminemia)	good	good
8	Yallawwa	30	15894	G2P1L1	38w+6d	prom	79	nil	160	100	30 min	120	90	1	N	N	LSCS(threatened scar ruptur	N	T	2.9	F	9	N	N	good	good
9	Laxmi	20	15852	G1	36w+4d	Nil	64	2+	170	100	1hr+30 min	100	70	1	N	N	LSCS(antepartum eclampsia	Y	PT	2.3	F	9	N	N	recovered	good
10	Durgawwa	25	15541	G1	37	PROM	65	2+	180	120	2hr+30 min	100	90	1	tachycardia	N	LSCS(severe PE)	Y	T	2.6	F	9	N	N	GOOD	GOOD
11	Parvathi	21	15654	G1	38W+4d	Severe anaemia	54	1+	150	110	2hr+30 min	140	80	1	Hypotention	N	LSCS(breech)	N	T	2.2	F	9	N	N	good	good(LBW)
12	Swapna	24	20094	G1	38	Nil	67	2+	160	100	1hr	120	80	1	N	N	LSCS(fetal distress, non react	N	T	2.7	F	9	Y	Y	good	good
13	Mala	18	20203	G1	36	Nil	90	nil	170	100	30 min	140	90	1	Dizziness/ headache	N	LSCS(failure to progress)	N	PT	2.7	M	9	N	N	good	good
14	Sangeetha	30	20500	G2A1	39W+3d	Nil	70	nil	160	100	2hr	130	80	1	headache	N	LSCS(failure to progress)	N	T	3.6	M	9	N	N	good	good
15	Ameerin	22	27905	G1	28w+2d	nil	54	4+	170	140	3hr+30 min	140	70	2	vomiting	Eclampsia, Abruption	VD-C	0	PT	0.75	M	0	0	0	recovered	IUD
16	Channamma	28	26158	G2P1L1	36w+5d	moderate anaemia	60	nil	150	110	4hr	140	80	1	hypotension	N	VD-M	0	T	1.9	M	9	Y	Hyperbiliruminemia)	good	good
17	Roopa	22	203	G2A1	35w+1d	Nil	62	nil	150	110	2hr	130	80	1	N	N	VD-M	0	T	2.2	M	9	N	N	good	good
18	Savitha	22	556	G1	39w+5d	PROM	50	nil	152	104	1hr	130	70	1	Palpitation	N	VD-O	0	T	3.2	M	8	N	N	good	good
19	Kusuma	20	483	G1	34+2d	Nil	54	4+	190	120	7hr	140	90	2	tachycardia	N	VD-C	0	PT	1.2	F	9	Y	RDS/ Hyprebiliruminemia	good	good
20	Neelawwa	20	586	G2P1L1	32	Nil	64	2+	160	120	2hr+45 min	130	90	2	N	Eclampsia, HELLP	VD-M	0	PT	1.2	M	5	Y	RDS	recoverd	good
21	Sangawwa	20	609	G1	39w+6d	Moderte anaemia	65	nil	170	120	30min	120	70	1	N	N	LSCS(fetal distress)	N	T	2.7	M	9	Y	N	good	good
22	Kalavathi	35	840	G3P2L2	37	h/o HTN in 1st pregnancy	70	3+	160	110	30 min	140	80	1	N	abruption+eclapmsia	VD-O	0	T	2.8	M	0	0	0	recovered	FSB
23	Roopa	22	1366	G2A1	37w+5d	Nil	57	traces	170	104	3hrs	130	80	1	N	N	LSCS(breech)	N	T	2.37	M	9	N	N	good	good
24	Rekha	22	1873	G1	40w+3d	severe anaemia +PROM	63	traces	180	100	40 min	140	80	1	Fetal tachycardia	N	LSCS(fetal distruss)	N	T	2.8	F	6	Y	N	good	good
25	Sujatha	21	4946	G1	37w+4d	Nil	65	traces	170	110	1hr+30 min	130	70	1	N	N	VD- I(V)	0	T	3.06	F	9	Y	RDS	GOOD	GOOD
26	Kusuma	20	2431	G4P3L3	24	Nil	68	4+	160	104	30min	120	70	1	headache	HELLP	VD-M	0	PT	750	M	0	0	0	recovered	IUFD
27	Sumithra	25	11697	G2P1L1	37w+3d	severe anaemia	72	3+	160	100	8hrs	140	90	2	tachycardia	Abruption, HELLP	VD-C	0	T	2.43	M	7	Y	RDS	good	good
28	Mahalaxmi	28	10926	G1	39w+3d	Nil	44	nil	150	110	30min	140	80	1	N	N	LSCS(CPD with thick MSL)	N	T	2.48	F	9	N	N	good	good
29	Shantabai	20	14127	G1	34w	nil	78	1+	180	120	1hr	130	70	1	N	Pulmonary edema	LSCS(obstructed labour)	N	PT	2.1	F	7	Y	RDS	recovered	good
30	Jayashree	25	18427	G3P1L1A1	40w	prev lscs	58	1+	180	100	30 min	130	90	1	N	N	LSCS(pre- LSCS with CPD)	N	T	3	M	9	N	N	good	good
31	Goundamma	25	23211	G2P1L1	36w	oligohydarmnios	60	nil	160	90	1hr	130	80	1	Headache	Abruption	VD-O	N	T	2	M	7	Y	N	good	good
32	Deepa	32	23322	G2A1	39w	oligo	70	nil	160	100	30 min	120	80	1	N	N	LSCS(severe oligohydramnios	N	T	2.05	F	9	Y	Hyperbiliruminemia)	good	good
33	Shashikala	30	24549	G2A1	39w	placenta previa	82	3+	150	100	5hrs	140	80	1	N	Abruption	LSCS(Placenta Previa)	N	T	3	M	0	0	0	good	IUD
34	Renuka	28	24808	G2A1	40w	PROM	73	2+	160	100	7hrs	130	90	2	Nausea	N	VD-O	0	T	3	M	9	N	N	GOOD	GOOD
35	Jyothi	20	17705	G1	35w	Nil	80	nil	160	100	1hr	120	90	1	N	N	VD-C	0	PT	1.86	F	9	Y	Hyperbiliruminemia)	good	good
36	Sangeetha	25	17815	G1	37w+1d	Nil	76	nil	170	100	3hr	130	80	1	N	N	VD-M	0	T	2	F	9	N	hyperbilirubinemia	good	good
37	Gayathri	22	18196	G1	38w	Nil	74	4+	150	110	9hr	140	80	2	N	N	SVD	0	T	2.4	M	9	N	N	good	good
38	Jahida	25	18911	G1	34w+2d	Nil	68	2+	170	110	4hr	130	90	2	N	eclampsia	LSCS(failure to progress, feta	Y	PT	1.26	F	8	Y	RDS	recovered	good
39	Ayesha	25	14390	G1	33w	Nil	72	1+	180	100	10hr	120	80	2	headache	abruption	VD-C	0	PT	1.2	M	0	0	0	good	IUD
40	Geetha	25	23916	G1	25W+2d	severe anaemia	73	4+	170	110	5hrs	140	80	1	Vomiting	Abruption	LSCS(abrupto placenta)	Y	PT	1.2	F	0	0	0	recovered	IUD
41	Amhika	20	25265	G1	36w	Nil	80	2+	160	90	30 min	120	90	1	N	Eclampsia	VD-M	0	PT	2.6	F	0	0	0	recovered	FSB
42	Rekha	22	26093	G1	41w+5d	podt dated	74	nil	150	100	30 min	110	70	1	N	N	VD -I(F)	0	T	3.4	F	9	N	N	good	good
43	Iramma	30	26557	G3P2L2	38w	oligohydarmnios	75	nil	170	100	3hrs	110	90	1	N	N	LSCS(severe oligohydramnios	N	T	1.8	M	9	Y	Hyperbiliruminemia)	good	good
44	Rani	20	26905	G2P1L1	37w+3d	prev LSCS	60	1+	160	110	30 MIN	110	70	1	tachycardia	N	VBAC	0	T	2.75	F	9	N	N	good	good
45	Chandrakala	19	27431	G1	40w	PROM	73	tracre	160	100	2hrs	130	90	1	Headache	N	VD- I(F)	0	T	3.5	F	9	N	N	good	good
46	Nagamma	22	1818	G1	38w	Nil	80	2+	160	110	1hr+30 min	130	60	1	N	Eclampsia	LSCS(antipartum eclampsia)	Y	T	2.52	M	9	N	N	good	good
47	Nasima	20	2355	G1	33w	Nil	78	3+	150	100	1hr	120	90	1	N	Eclampsia	VD-C	0	PT	1.3	F	9	Y	Hyperbiliruminemia	recovered	good
48	Bharathi	20	2845	G1	35w	Nil	80	2+	160	110	3hrs	140	80	1	N	N	VD-O	0	PT	2.5	F	9	Y	N	good	good
49	Parvathi	30	3319	G2P1L1	39w	Nil	64	2+	150	110	14hrs	120	60	2	Vomiting	Eclampsia	SVD	0	T	2.52	F	9	N	N	good	good
50	Roopa	20	6522	G2A1	40w+5d	Nil	70	1+	170	100	2hrs+30 min	110	70	1	Headache,palpitations	N	LSCS(breech)	N	T	3.67	M	9	N	N	good	good
51	Sunanda	20	6727	G1	35w+1d	nil	77	4+	220	140	18hrs	140	90	3	tachycardia	HELLP	VD-I(F)	0	PT	1.9	M	0	0	0	expired (cardiopulmo	

MASTER CHART LABETALOL GROUP (n=51)

sl no	NAME	AGE	IP NO	PARITY	POG	RISK FACTORS	WT (KG)	URINE ALBUMIN	PRE SBP	PRE DBP	TIME TAKEN	POST SBP	POST DBP	DOSES REQUIRED	ADVERSE EFFCETS	COMPLICATIONS DUE TO PIH	MOD	LSCS DUE TO PIH	TERM/PRETERM	BIRTH WT	SEX OF BABY	APGAR SCORE at 5 min	NICU ADMISSION	NEONATAL COMPLICATION	CONDITION OF MOTHER AT DISCHARGE	CONDITION OF BABY AT DISCHARGE
1	Tayawwa	35	23741	G3P2L2	23W	previous h/o PIH	70	1+	170	100	15hrs	140	80	2	nil	nil	VD-C	0	PT	900 gm	F	0	0	0	Good	Abortus
2	Rekha	21	22479	G4P3L2D1	34W	h/o antepartum eclamps	62	2+	160	100	20 hrs	140	80	3	nil	nil	VD-M	0	PT	1.93	M	9	Y	hyperbiliruminemia	Good	Good
3	Mahadevi	25	22046	G1	36W	severe anemia	56	2+	160	90	12 hrs	120	70	2	nil	nil	VD-M	0	PT	2.5	M	5	Y	RDS(anamalous bat	Good	expired)after 1 day)
4	Basamma	20	22410	G1	32w+2d	IUGR	70	3+	160	110	14hrs	140	90	2	Drowsiness	abruption	VD-M	0	PT	1.25	F	7	Y	RDS	Good	Good
5	Rajeshwari	22	17608	G1	24W+3D	nil	51	3+	240	120	26 hrs	130	90	6	Vomiting	Renal Failure	VD-M	0	PT	650 gm	F	0	0	0	Recovered	Abortus
6	Rajama	20	5104	G1	39W+5D	nil	60	1+	200	100	16hrs	110	90	3	nil	nil	SVD	0	T	2.7	M	9	N	N	Good	Good
7	Basalingamma	24	6713	G3P2L2	41W	h/o PIH in previous 2 pre	60	T	150	110	8hrs	140	70	1	nil	nil	VD-O	0	T	2.7	F	9	N	N	Good	Good
8	Parvathi	23	5135	G1	38W+5D	NIL	70	1+	160	120	10 hrs	120	90	1	nil	nil	LSCS(Fetal distres		T	3.4	M	9	Y	Hyperbilirubenemia	Good	Good
9	Shridevi	25	13831	G2A1	39W+1D	Moderate anaemis	64	Nil	160	100	8hrs	110	80	1	Fatigue	abruption	VD-C	0	T	3	F	7	Y	N	Good	Good
10	Sangeetha	20	19402	G1	41W	mild anaemia	64	Nil	150	100	4hrs	130	90	1	nil	nil	SVD	0	T	3.4	F	9	Y	N	Good	Good
11	Bharathi	23	18119	G2P1L1	39W+4D	prev LSCS	70	Nil	150	110	16 hrs	140	90	2	nil	nil	LSCS(prev LSCS wi		T	2.2	M	8	Y	N	good	good
12	Shridevi	23	1878	G1	40W+5D	post dated	67	Nil	170	110	13 hrs	130	90	2	nil	nil	LSCS(prev LSCS wi		T	2.8	F	9	N	N	good	good
13	Sujatha	26	24860	G1	35W+5D	nil	64	1+	150	100	10hrs	120	80	1	nil	abruption	LSCS(fetal distress		PT	3.3	F	8	Y	N	good	good
14	Sangeetha	27	26575	G1	38W+1D	oligohydarmnios	63	Traces	150	110	15 hrs	130	80	2	nil	nil	LSCS(severe oligo		PT	2.05	M	7	Y	RDS	good	good
15	Asma	28	27511	G1	34W+6D	nil	74	2+	160	110	7hrs	140	90	1	Palpitations	Renal Failure,Pulm	LSCS(non progres		PT	2	F	6	N	N	recovered	good
16	Suvarna	19	603	G2A1	41W+3D	nil	65	4+	160	100	10 hrs	130	80	2	nil	nil	LSCS(fetal distress		T	2.6	M	9	Y	N	good	good
17	Bharthi	25	21022	G3P1L1A1	39W	h/o PIH in 1st pregnancy	68	3+	160	106	5hrs	140	70	1	nil	nil	LSCS(prev LSCS wi		T	2.04	F	9	N	N	good	good
18	Savitha	22	22170	G1	40W	PROM	70	2+	160	100	8hrs	140	90	1	Nausea	eclampsia	LSCS(CPD)		T	2.89	M	9	N	N	recovered	good
19	Sunitha	34	21525	G4P3L3	26W+5D	NIL	72	3+	180	100	12hrs	130	90	2	nil	Eclampsia,Abruptio	VD-M	0	PT(IUD)	750g	F	0	0	0	good	IUD
20	Kadambari	21	20796	G2A1	36W+3D	Rh neg	63	Traces	160	100	8hrs	120	50	1	Hypotension	nil	VD-C	0	T	2.2	M	6	Y	hyperbiliruminemia	good	good
21	Netra	28	20867	G3A2	33w+2d	h/o PIH in previous 2 abo	82	4+	200	120	25 hrs	120	80	3	Headache	nil	LSCS(PIH)		PT	1.8	F	9	Y	hyperbiliruminemia	good	good
22	Kavitha	36	17942	G3P1L1A1	40W	IUGR	54	3+	170	100	1Ohrs	140	80	2	nil	HELLP	VD-M	0	T	3.7	M	6	Y	RDS	recovered	good
23	Laxmi	20	21223	G3P2L1D1	35W	h/o PIH in 1st pregnancy	74	4+	160	90	4hrs	130	80	1	nil	nil	VD-O	0	PT	1.2	F	9	Y	RDS	Good	good
24	Siddamma	22	22822	G2A1	33W+4D	nil	68	2+	160	100	5hrs	130	90	1	nil	nil	SVD	0	PT	1.6	F	9	Y	RDS	Good	good
25	Ameena	30	23219	G1	36W	nil	67	4+	160	100	16 hrs	140	80	3	nil	Abruption	VD-M	0	PT(IUD)	2.5	F	0	0	0	good	IUD
26	Mallamma	22	23351	G1	38	NIL	86	2+	160	100	8hrs	130	70	1	nil	Eclampsia	LSCS(antipartum e		T	2.5	M	7	Y	N	recovered	good
27	Shantabai	35	24234	G3P2L2	40	moderate anaemia	63	1+	160	90	5 hrs	140	90	1	nil	nil	VD-O	0	T	2.24	F	9	Y(thin MS	Y(septicemia)	good	recovered
28	Bhagyashree	29	24607	G1	37W+1D	nil	60	Nil	160	90	5hrs	130	80	1	nil	nill	VD-I(F)	0	T	2.44	F	9	N	N	Good	good
29	Tarabai	22	24606	G4P3L2D1	37W	severe anaemia	59	1+	170	100	14hrs	140	90	2	nil	nil	VD-O	0	T	2	M	9	N	N	Good	good
30	Meenakshi	30	24691	G4P3L2D1	30W	nil	60	Trace	150	100	20hr	140	90	3	Palpitation	Eclampsia	VD-C	0	PT	1	F	6	Y	RDS	Recovered	good
31	Vaishali	23	23702	G1	37w+6d	IUGR	49	Nil	170	130	16hrs	130	90	3	nil	nil	VD-O	0	T	2.1	F	8	N	N	good	good
32	Ambika	22	23963	G2A1	39W+4D	nil	105	Nil	170	110	10hrs	140	80	2	nil	nil	VD-I(V)	0	T	3.4	M	9	N	N	good	good
33	Reshma	20	24130	G2P1L1	38W+1D	h/o PE in 1st preg	75	4+	150	100	6hrs	130	80	1	nil	Eclampsia	LSCS(prev LSCS wi		T	3	M	9	N	N	recovered	good
34	Ankitha	26	17033	G3P2L2	36W+5D	Oligohydramnios	84	1+	160	110	10hrs+30	140	80	2	nil	nii	LSCS(fetal distress		T	2.1	F	9	N	N	good	good
35	Deepa	25	17484	G2P1L1	29W	nil	70	4+	160	120	12 hrs	130	70	2	Sweating	Abruption	VD-C	0	PT	650	F	0	0	O	Good	FSB
36	Surekha	20	17747	G1	36W	NIL	62	4+	180	110	10hrs	140	80	2	Palpitation	Eclampsia	LSCS(antepartum		PT	2.75	M	9	N	N	Recovered	good
37	Shreedevi	26	18337	G2A1	39W	nil	55	Nil	180	100	8hrs	130	70	1	nil	nil	LSCS(fetal distress		T	2.18	M	9	N	N	Good	good
38	Rabina	28	18453	G1	39w+2d	nil	68	4+	150	100	2hrs	140	90	1	nil	Eclampsia	SVD	0	T	2.5	F	8	N	N	recovered	good
39	Mahadevi	25	19392	G1	37W	nil	70	2+	150	100	3hrs	140	90	1	nil	nil	LSCS(immenans e		T	2.95	M	9	N	N	good	good
40	Ayesha	25	14390	G1	33W	nil	55	4+	180	100	8hrs	130	90	1	nil	Eclampsia, Abrupti	VD-O	0	PT	1.2	M	0	0	0	recovered	IUD
41	Mangala	22	14428	G1	32W	NIL	70	3+	150	100	20hrs	130	90	4	nil	Abruption	LSCS(Abrupto pla		PT	1.7	F	7	Y	hyperbiliruminemia	good	good
42	Dundawwa	20	19441	G1	37w+5d	nil	62	3+	150	110	15hrs	140	90	2	nil	Eclampsia,Abruptio	LSCS(antipartum e		T	3.5	M	9	Y	N	recovered	good
43	Danamma	20	25867	G1	37W	nil	64	4+	170	90	20hrs	140	80	3	nil	Eclampsia	LSCS(fetal distress		T	2.12	M	7	Y	RDS	recovered	good
44	Yashodha	20	934	G1	32W	nil	60	2+	180	100	8hrs	140	90	1	Headache	nil	LSCS(severe preec		PT	1.32	M	8	Y	RDS	good	good
45	Shekubai	25	2419	G1	38W	nil	70	1+	160	100	6hrs	140	90	1	nil	nil	VD-O	0	T	2.6	M	9	N	N	good	good
46	Manjula	21	2341	G2A1	35W	nil	80	3+	180	100	12 hrs	130	70	2	Headache	nil	LSCS(fetal distress		PT	2.1	M	8	Y	Hyperbilirubinemia	good	good
47	Sandhya	20	4519	G1	37W	nil	70	2+	160	100	11hrs	140	80	1	nil	nil	VD-M	0	T	3.15	M	9	N	N	good	good
48	Malakshi	21	5560	G1	38W	mild anaemia	57	nil	160	90	8hrs	140	70	1	Fetal tachycard	nil	LSCS(fetal distress		T	2.2	F	9	Y	N	good	good
49	Geetha	29	6068	G1	40W	PROM	60	3+	190	110	24hrs	140	90	4	nil	abruption	LSCS(severe PIH)		T	2.75	M	7	Y	N	good	good
50	Geetha	22	7780	G2P1L1	39W+2D	NIL	64	Traces	160	100	15hrs	120	80	2	Vomiting	Cerebro vascular A	VD-O	0	T	2.3	M	9	N	N	Recovered	good
51	Bharati	22	7983	G1	40W	nil	76	Nil	170	100	12hrs	120	70	2	Sweating	nil	SVD	0	T	3.4	M	9	N	N	good	good