THE EFFICACY OF SECOND-TRIMESTER SERUM BETA HCG LEVELS IN THE PREDICTION OF PREGNANCY INDUCED HYPERTENSION: A PROSPECTIVE STUDY

By

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ABSTRACT

BACKGROUND: Hypertensive disorders of pregnancy complicate up to 10% of pregnancies worldwide, In spite of improvement in maternal and neonatal care, PIH and its sequel are a dreaded complication of pregnancy. If prediction becomes possible, prevention will follow naturally.

OBJECTIVES: The main aim of the study is to test the hypothesis that pregnant women with raised serum beta hCG in second trimester have risk of developing PIH**.**

MATERIALS AND METHODS: Study was done in 163 pregnant women who had antenatal care at Shri B.M.Patil Medical College Hospital And Research Centre between December 2020 to December 2022 at 16weeks to 20 weeks and they are followed up till delivery. Assessment of serum beta hCG and its predictability for development of pregnancy induced hypertension were done and results analysed statistically with Chi-square test, receiver operating charaecteristic(ROC) and relevant predictive boundary values were identified .

RESULTS: This study was conducted among 163 pregnant women, 114 women did not have hypertension while 49 women had pregnancy induced hypertension. The mean value of β-hCG of the normotensive group is 55,666mIU/mL, while in hypertensive group it was 1,00,124mIU/,mL there is an statistical significance(<0.05).Serum beta hCG data were used as testing parameters to obtain the boundary values for PIH prediction at as values 67,641 (sensitivity-91.8%, specificity-70.2%), 73,951(sensitivity-83.7%, specificity-83.3%), 77,817 (83.7% sensitivity, 92.1% specificity). In the overall population, with the use of 77,817 mIU/mL of β-hCG as cutoff value, the sensitivity of β hCG as a screen for development of pregnancy induced hypertension was 83.7% and specificity of 92.1%. Area under the curve (AUC) showed highest correlation (0.924) for beta HCG in detecting PIH

CONCLUSION: One of the main causes of maternal morbidity and death during pregnancy is hypertensive disorders. It is still difficult to find the optimum illness predictor, whose use might considerably change the related morbidity and death. Serum beta-hCG can be used to predict PIH, the tests with accepted level of sensitivity and sensitivity. If this test is made available to women who have PIH risk factors, it would be beneficial.

KEYWORDS: serum beta hCG, pre-eclampsia, eclampsia, pregnancy induced hypertension

ABBREVATIONS

GHT	Gestational Hypertension
LDH	lactate Dehydrogenase
DIC	Disseminated Intravascular Coagulation
APTT	Activated Partial Thromboplastin Time
ALT	Alanine Transaminase
AST	Aspartate Transaminase
DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
ACOG	American College of Obstetricians and Gynecologists
RCOG	Royal College of Obstetricians and Gynecologists
HT	Hypertension
DM	Diabetes Mellitus
IV	Intra Venous
IM	Intra muscular
MM	Millimeter
PG	Prostaglandins
dL	Deciliter
OPD	Out Patient
DNA	Deoxy Ribonucleic Acid
mL	Milliliter
IGF	Insulin like Growth Factor
IGFBP	Insulin Like Growth Factor Binding Protein

MG	Microgram
IUGR	Intra Uterine Growth restriction
HCG	Human Chorionic Gonadotrophin
LBW	Low Birth Weight
NICE	National Institute of Health and Clinical Excellence
FSH	Follicular Stimulating Hormone
LH	Luteinizing Hormone
TGFβ	Transforming Growth Factor Beta
TSH	Thyroid Stimulating Hormone
HLA-G	Human Leukocyte Antigen-G
TH1	'T' Helper Cells 1
TH2	'T' Helper Cells 2
IL	Interleukin
PIH	Pregnancy Induced Hypertension
SLE	Systemic Lupus Erythematosus
BP	Blood Pressure
BMI	Body Mass Index
AA	Amino acids
PE	Pre-eclampsia

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INTRODUCTION

The health of the mother and the unborn child must be given the highest consideration during pregnancy. Unfavourable situations might endanger both the mother and the unborn child's lives. Gestational diabetes, obesity, and pregnancy-induced hypertension are just a few of the illnesses and side effects connected to pregnancy.[1-4]

According to National Health Portal, Approximately 10% of pregnant women worldwide experience hypertensive disorders of pregnancy. 3-5% of pregnancies are affected by preeclampsia. In addition to preeclampsia, gestational hypertension, eclampsia, and chronic hypertension are all illnesses that fall under the category of hypertensive disorders of pregnancy. Nearly 10% of all maternal fatalities in Asia and Africa are linked to hypertensive disorders during pregnancy.[5]

Pregnancy-related hypertensive diseases are among the world's top causes of maternal and perinatal death. Preeclampsia is a condition that affects pregnant women and is characterised by newly developed hypertension. It often develops after 20 weeks of pregnancy and commonly close to term. According to ACOG, After 20 weeks of pregnancy, a woman with a previously normal blood pressure is said to have gestational hypertension if her systolic blood pressure is 140 mm Hg or higher, her diastolic blood pressure is 90 mm Hg or higher, or both.[6]

The prevalence of many infections and disorders has significantly decreased due to recent improvements in maternal and newborn health, but PIH is still a deadly condition in many areas of the world.[7]

An obstetrician must use considerable caution while diagnosing and forecasting PIH in a pregnant patient. The ability to predict PIH is important for preventing treatment-related problems and follow-up visits.[8]

RATIONALE OF THE STUDY:-

For the prediction of PIH, several testing facilities have been offered. Unfortunately, a lot of these tests have a poor predictive value and don't seem to be very important in the early detection of PIH. According to studies, immunological variations in trophoblasts during pregnancy might cause secretory responses, which further increase beta HCG levels.[9-10]

CLASSIFICATION OF HYPERTENSION IN PREGNANCY[30-34]

1. **Gestational Hypertension**

- First-time readings of blood pressure of 140/90 mm Hg or higher after 20weeks period of gestation but lack proteinuria.
- Preeclampsia subsequently develops in 50 percent of afflicted patients.
- Ignoring an increase in blood pressure that is significant simply because proteinuria has not yet established poses a risk to both the mother and the foetus.
- “10 percent” of eclampsia seizures develop before overt proteinuria can be detected.
- GTN is reclassified as transient hypertension if preeclampsia does not develop and BP returns to normal by 12 weeks postpartum.

2. **Pre-eclampsia Syndrome:-**

- Pregnancy-specific syndrome that can affect virtually every organ system.
- Gestational hypertension with proteinuria.

- Preeclampsia can be divided into
    i. early onset <34weeks,
    ii. late onset >/= 34 weeks,
    iii. preterm onset <37 weeks
    iv. term onset >/= 37 weeks
- Multiorgan involvement present as thrombocytopenia, renal dysfunction, hepatocellular necrosis, central nervous system perturbations, or pulmonary oedema.
- Pre-eclampsia is categorised into severe and non-severe ACOG(2020)

Table no 1: Hypertension Associated with Pregnancy: Classification and Diagnosis

Condition	Criteria required
Gestational hypertension	BP>140/90 mm Hg after 20weeks in previously normotensive women
Preeclampsia : Hypertension plus Proteinuria	>/=300mg/24hr, or Urine protein:creatinine ratio >/=0.3 or Dipstick +1 persistent **(or)**
Thrombocytopenia	Platelets <100,000/µL
Renal insufficiency	Creatinine >1.1 mg/dl or doubling of baseline
Liver involvement	Serum transaminase levels twice normal
Cerebral symptoms	Headache, visual disturbances, convulsions
Pulmonary edema	--

Table no 2: Gestational hypertension indicators of severity

Abnormality	**Non severe**	**Severe**
DBP	<110 mmHg	>/= 100mmHg
SBP	<160mmHg	>/= 160mmHg
Proteinuria	None to positive	None to positive
Headache	Not Present	Present
Vision disturbances	Not Present	Present
Upper Abdominal Pain	Not Present	Present
Oliguria	Not Present	Present
Convulsions	Not Present	Present
Serum Creatinine	Normal	Elevated
Thrombocytopenia	Not Present	Present
Serum Transaminase Elevation	Slight	Marked
Fetal-growth Restriction	Not Present	Present
Pulmonary edema	Not Present	Present
Gestational age	Late	Early

3. Chronic Hypertension Superimposed by Preeclampsia

- Chronic hypertension is diagnosed when before becoming pregnant, or before to 20 weeks of pregnancy or both, blood pressure readings more than or equal to 140/90 mm Hg.
- After 24 weeks of pregnancy, blood pressure normally rises to clearly abnormal levels in 20 to 50% of women with chronic hypertension.

- Superimposed preeclampsia can be identified if there is new-onset proteinuria, deteriorating baseline HT, or any of the other abnormalities mentioned above. (ACOG, 2019a).
- Superimposed PE frequently appears during pregnancy earlier than "pure" PE.
- It typically has a greater severity and is more frequently associated by foetal growth restriction.

Incidence[35,36]:-

- 5 to 8 % of all pregnancies
- Nulliparous 3%-10%
- Multiparous 2%-5%

Factors at risk[37]:

- early age
- Nulliparous
- Age of mother more than 35 years
- Environmental elements
- Molar pregnancies
- Multifetal pregnancy
- At 18-24 weeks Uterine artery Doppler abnormality

Factors of high risk[37]:-

- Prior PE

- APLA syndrome
- Patients with SLE
- CKD
- Pre-existing diabetes mellitus and/or Hypertension

Factors of moderate risk:-

- Multifetal pregnancy
- Prim gravida
- BMI of more than 35 kg/m2
- History of PE in family
- Interval between pregnancy is more than 10 years.
- Age of mother more than 40 years

Etio-Pathogenesis[38]:-

The following traits make women more susceptible to developing gestational hypertension disorders:

- Exposure to chorionic villi for the first time.
- Being exposed to an excess of chorionic villi, such as in twins or a molar pregnancy
- Existing diseases linked to inflammation or endothelial activation
- Genetic predisposition to hypertension developing during pregnancy

Phenotypic Expression – Pre-eclampsia

"Two-stage disorder" theory of pre-eclampsia[39]

- stage I—the placental syndrome is caused by faulty endovascular trophoblastic remodelling that downstream causes stage II—the maternal syndrome
- Stage II can be modified by maternal conditions like chronic hypertension, renal disease, obesity, immunological or connective tissue disorders, and diabetes.

Aetiology[40]:

a. An aberrant trophoblastic invasion of the uterine vessels together with placental implantation
b. Immunoregulatory tolerance between maternal, paternal, and foetal tissues that is defective
c. Maladaptation of the mother to the inflammatory or cardiovascular changes that are typical with pregnancy
d. Genetic aspects.

Stage I—Placental Syndrome

Trophoblastic invasion abnormality[41]:

• Normal: Endovascular trophoblasts replace the muscular and vascular endothelial cells.

• Abnormality: Endovascular trophoblasts line decidual vessels, but not myometrial vessels, causing a high resistance flow and a narrow diameter vessel.

This defective endovascular remodelling may also be brought on by soluble antiangiogenic growth factors.

• Women who have a defective placentation are more susceptible to placental abruption, gestational hypertension, preeclampsia syndrome, preterm births, and foetus growth restriction**.**

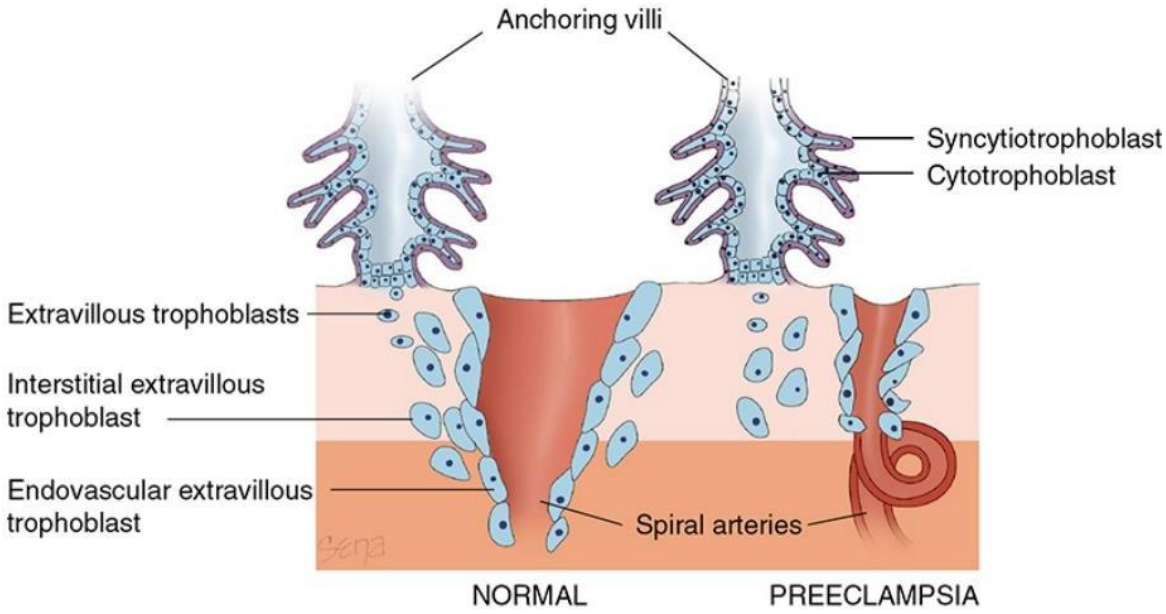


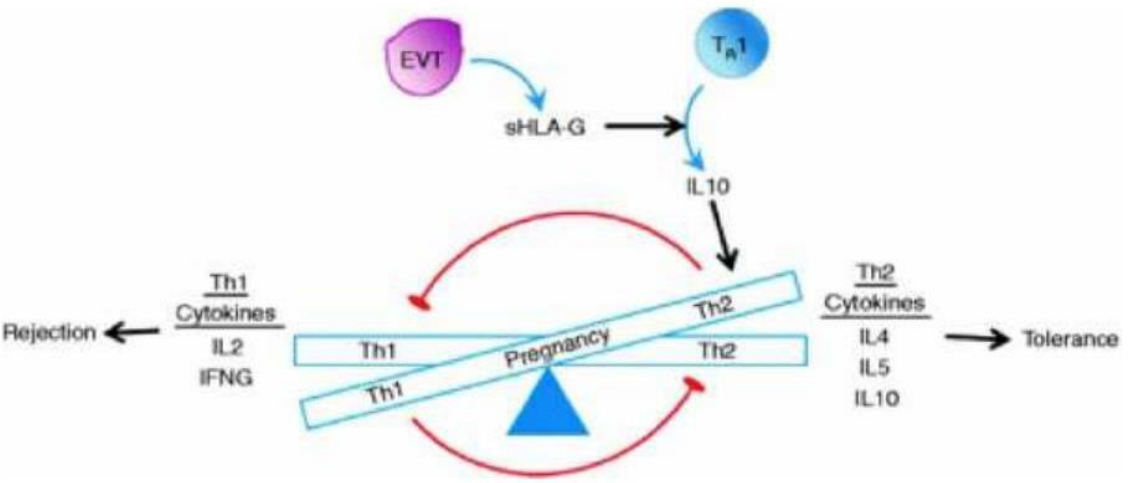
Figure no 1 : Placental implantation

Immunological Factors

- Acute graft rejection.
- Tolerance dysregulation seen when the paternal antigenic load is increased.
- Preeclampsia affects pregnant women with trisomy 13 foetuses with a 30- to 40% frequency.
- There is a rise in serum antiangiogenic factor, which might harm the placenta and is encoded by the soluble tyrosine kinase 1 gene on chromosome 13. Therefore, preeclampsia is a serious concern for women carrying Trisomy 13 foetuses[42].

- Women may be "immunised" against preeclampsia if they have previously been exposed to paternal antigens.
- Preeclampsia risk is higher in multiparas who become pregnant with a new partner[43].
- Preeclampsia-prone women have lower levels of the immunosuppressive gene human leukocyte antigen G (HLAG).
- Th2 (anti-inflammatory cytokines) and Th1 (pro-inflammatory cytokines) lymphocyte activity is altered. Observed in women who develop preeclampsia in the first trimester or the second trimester.
- CD4 cells produce Th1 cells when IL 12 is present.
- Th1 cells are generated from CD4 cells when IL 12 is present. In the rejection of allografts, Th1 cells play a key role.
- In the presence of "IL4 and IL10", CD4 cells produce Th2 cells. The allergic reaction involves th2 cells. Soluble HLA-G is produced by extra villous trophoblast, which induces regulatory type Tg1 cells. Maternal tolerance is promoted by IL10 produced from Tg1 cells.

FIGURE NO 2 : Immunological Factors



Genetic Factors

- Preeclampsia is a multifactorial, polygenic disorder
- There is increase in risk of preeclampsia in daughters of preeclampsia mothers; sisters of preeclampsia women; and twins[44].
- Ethno racial factors like in African American women.
- The genetic propensity to preeclampsia is caused by the combination of maternal and paternal inherited genes.
- Candidate genes include FAS polymorphism, the protein HIF-1 α, IL-1 β, Lymophotoxin -α, TGF-β.

Stage II—Maternal Syndrome

- Vasoconstriction: Hypertension is caused by an increase in vasoconstriction and flow resistance in response to endothelial activation.

- Increased responsiveness to vasopressor: Normally pregnant women start to become resistant to the vasopressors. Individuals who are susceptible to preeclampsia have higher sensitivity to vasopressors.
- Prostaglandins: In individuals prone to preeclampsia, prostacyclin (PGI2) levels decline and thromboxane A2 levels rise, this enhances susceptibility to vasopressor infusions.
- Nitric oxide: Nitric oxide synthesis suppression causes the heart rate to decrease and the mean arterial pressure to rise, mimicking the features of preeclampsia.
- Endothelin :
    - ❖ Endothelin-1 levels are higher in preeclampsia patients than they are in normal pregnant women.
    - ❖ Before the appearance of clinical features, levels of sFlt-1 and sEng start to rise.
    - ❖ Treatment with magnesium sulphate reduces ET-1 levels.

PATHOPHYSIOLOGY:-

CVS[45]:-

- Cardiac output is lowered and peripheral resistance is elevated
- Normal or hyper dynamic ventricular function.
- An alveolar endothelial leak that causes pulmonary oedema and a decrease in oncotic pressure because of low serum albumin.

Blood Volume[46]:-

- Gestational hypertension, the blood volume is at a normal level;
- In preeclampsia, the blood volume decreases

Disorders of Coagulation[47,48]:-

- Reduced platelet levels
- There are increased LDH levels.
- The peripheral blood may show schistocytosis, spherocytosis, or reticulocytosis.
- Increased liver enzyme levels.
- Fibronectin - Elevated.

Liver [49]:-

- Right epigastric discomfort and pain are caused by liver haemorrhage and infarction.
- Hepatic hematoma formation may be possible. This could develop into a sub capsular hematoma and grow further[26].

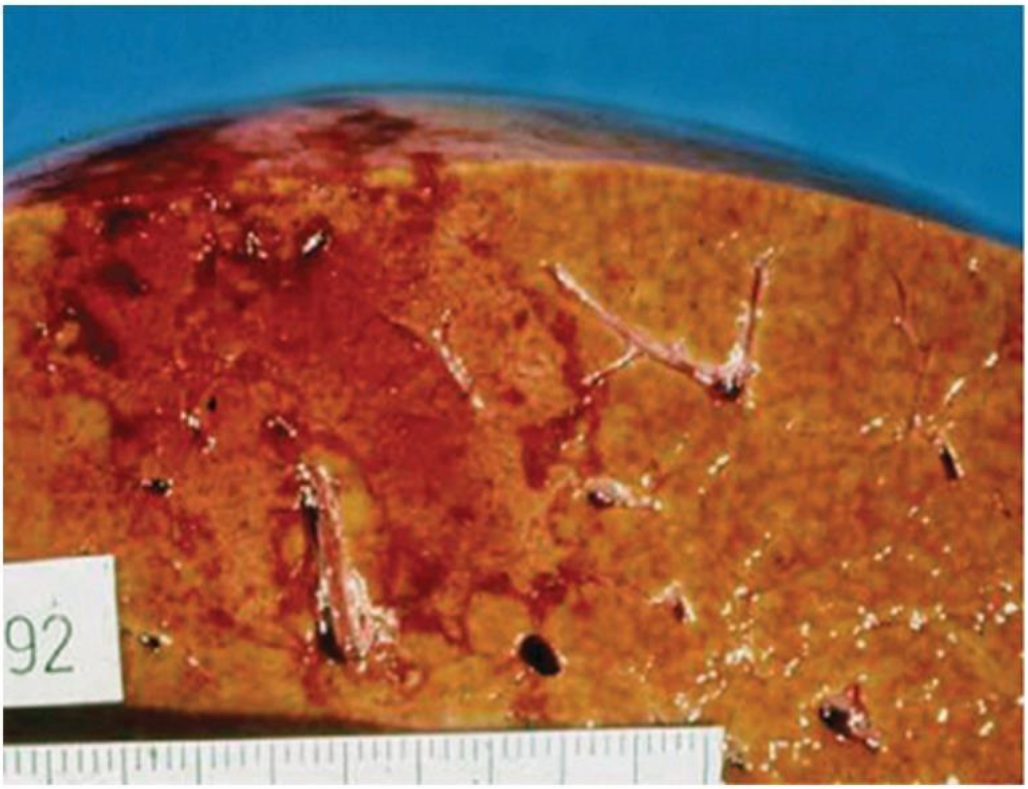


FIGURE NO 3: Areas of ischemia and infarction, periportal haemorrhage

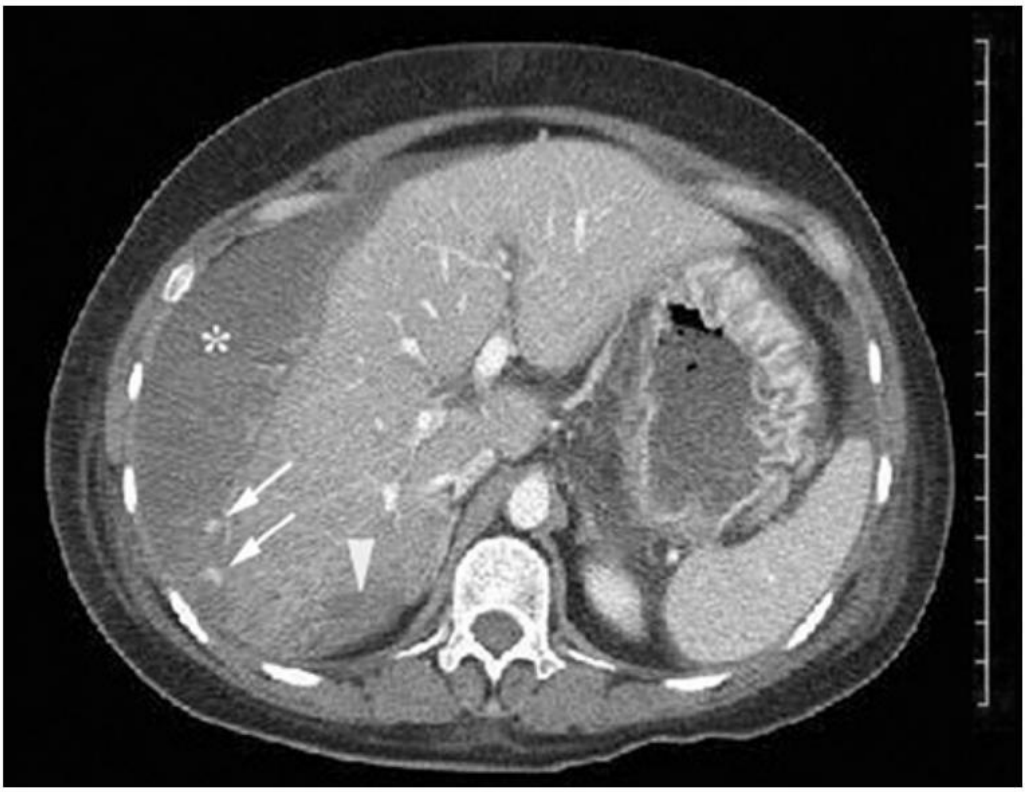


FIGURE NO 4: Abdominal CT showing a large subcapsular hematoma

Kidney[50,51]**:-**

- Glomerular endotheliosis results in higher serum creatinine concentrations because it reduces filtration.
- There is an increase in urine sodium concentration and a decrease in urine calcium.
- The level of plasma uric acid rises.
- A rise in urine protein excretion.

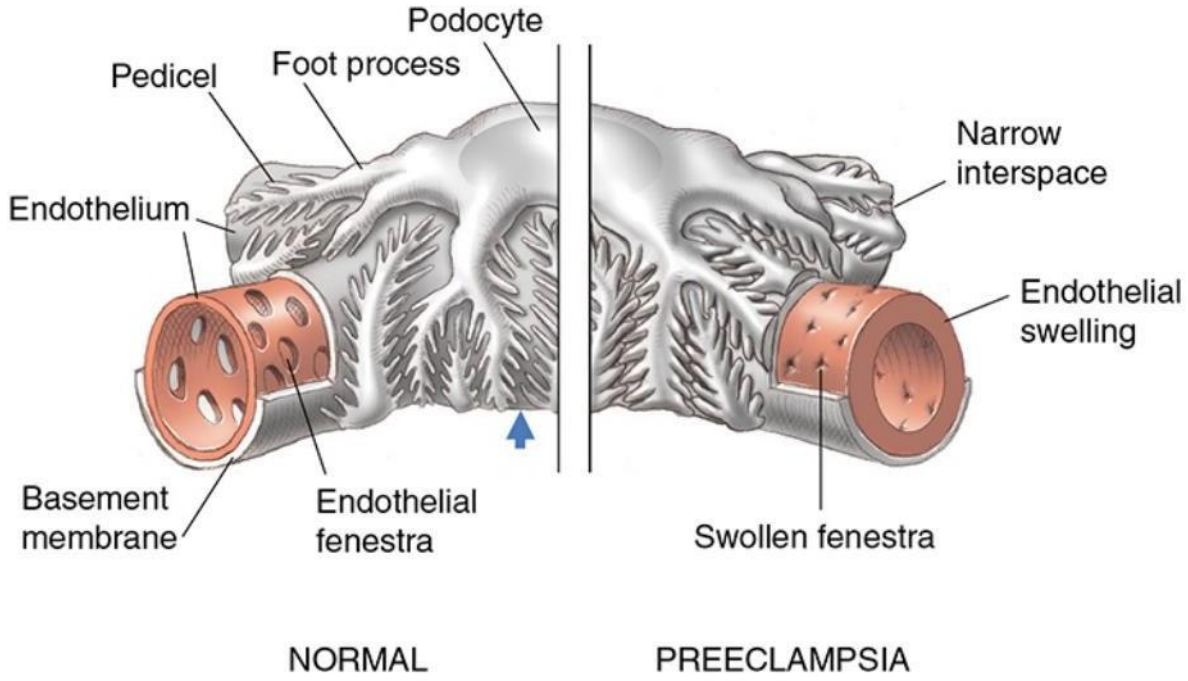


FIGURE NO 5: Diagram displaying the endotheliosis of the glomerular capillaries.

Wide endothelial fenestrations can be seen in the capillaries of the healthy glomerulus on the left side, the pedicels coming from the podocytes are widely spread shown by arrow mark. The right-hand figure shows glomerulus with "preeclampsia syndrome-induced" alterations. The pedicels that are now touching one another, the endothelial cells, and their fenestrae have all swelled and narrowed.

Placenta[52a,b]:-

- Chorionic villi congestion and proliferative endarteritis in the placenta
- An increase in infarcts and haemorrhages
- Increased syncitial knots and proliferation of cytotrophoblastic cells.

Brain[53,54]:-

- Cytotoxic oedema is brought on by cerebral vasoconstriction brought on by autoregulation. when this fails, it causes vascular permeability and vasogenic oedema..
- There may be visible infarction foci.
- Eclampsia and chronic hypertension increase the risk of cerebral hemorrhage.
- When a pregnant woman has significant hypertension with complications, an MRI should be done[55].

Management:-

Pre conception care:

- Due to their teratogenic effects, ACE-I, Atenolol, Statin's, Thiazide's should be stopped using.

Evaluation[56]:-

- Thorough examination, including daily monitoring for headache, vision changes, or epigastric pain;
- Daily weight measurement to detect rapid weight gain;
- Readings of blood pressure every four hours;

- Increasing haemoglobin percentage.
- A urine test for proteinuria
- Dropped platelet count
- Schistiocytes on the peripheral smear;
- Elevated INR and APTT (in DIC)
- Aberrant LDH.
- Raised Serum creatinine levels
- Raised transaminases, bilirubin levels
- A lower level of albumin
- A fundus examination
- An assessment of foetal size, health, and amnionic fluid index.

Prenatal Care: - Per NICE45b recommendations

- From the 12th week of pregnancy until delivery, Women should take low dose aspirin daily if they have at least "1 severe or 2 moderate risk factor" for preeclampsia.
- They should also limit their physical activity
- Undergo weekly or biweekly antenatal visits for blood pressure checks and anti-hypertensive therapy.
- Women with preeclampsia who also have complications are also advised to stay in the hospital.

Criteria for managing mild preeclampsia at home:-

- Systolic of less than 150 mm Hg, Diastolic of less than 100 mm Hg
- Normal lab findings and no maternal symptoms

- 1 g or less of protein in the urine in 24 hours
- Reassuring foetal condition with sufficient growth;

Intrapartum management[57,58]:

- The goal of intrapartum treatment is to keep diastolic and systolic blood pressure at or below 110mmHg and 160mmHg, respectively.
- Start giving antihypertensive if you have mild hypertension and a serious illness or organ malfunction.
- Patients with mild to severe hypertension and a co-morbid disease are advised to receive antihypertensive treatment.
- monitoring the foetal heart rate continuously
- Eclampsia prophylaxis provided to women with severe preeclampsia or imminent eclampsia
- Vaginal delivery recommended unless there are obstetric indications.
- If the bishop score is low, prostaglandins should be used for induction.
- Avoid using ergometrine
- Practise active management of the third stage of labour (AMTSL).

Timing of Delivery (ACOG)

- Patients with well controlled HT (With drugs) :- 37 to 39 period of gestation.
- When mild preeclampsia is present, the result of labour induction after 37 weeks is superior to expectant treatment.
- When Hypertension is severe can terminate at 36 - 37 weeks.

MANAGEMENT OF GESTATIONAL HYPERTENSION

SUPPORTIVE CARE:

- Most of the day should be spent with less physical activity; complete bed rest is not required. (prolonged bed rest is associated with venous stasis and risk of thromboembolism, muscle disuse atrophy)
- Calorie and protein intake should be adequate but not excessive, and sodium and hydration intakes shouldn't be restricted or mandated.
- Gestational hypertension without risk factors patients are instructed how to perform daily foetal movement counts
- They should have clinical visits every week for the assessment of maternal and foetal well being
- Gestational hypertension with risk factors should be managed as severe preeclampsia and admitted to the hospital to complete her evaluation and start medical treatment.
- Initial evaluation includes full blood count with platelets , LDH and liver enzymes , urea and electrolytes
- Ultrasound for foetal growth , amniotic fluid volume and umbilical and cerebral Doppler every 2 weeks and weekly CTG
- They require treatment with antihypertensive agents.
- The objective of the treatment is to avoid potential complications like ischaemic or haemorrhagic stroke, congestive heart failure, myocardial infarction, renal injury , pulmonary oedema .
- Gestational hypertension by itself is not an indication for caesarean section except in severe cases unresponsive to treatment or with FGR

- If cervix is ripe , vaginal delivery is the best option ; but if cervix is unripe and the cervical length is >2.5cm caesarean delivery may often be Indicated to avoid a prolonged induction
- Induction can still be an option with unripe cervix if the BPs are well controlled .

MANAGEMENT OF MILD PREECLAMPSIA

- Close supervision of the pregnant woman is need for this hospitalization is needed , once the blood pressure is under control weekly antenatal visits or twice in a week is needed
- Goal in management of mild preeclampsia is to prevent it progression to severe PE and also organ dysfunction, continuing pregnancy till < 37 weeks of gestational age.
- Measurement of BP at least “4 times” a day
- Measurement of weight every alternate day
- Daily urinary “dipstick evaluation for protein” in the first urine voided every morning
- CBC for platelet count, AST & ALT weekly/two times a week. Coagulation profile is not required when the platelet count is normal.
- The patient should be questioned about any concerning symptoms, such as a severe headache, discomfort in the right upper quadrant, or frequent nausea and vomiting.
- Daily foetal movement count with NST and weekly/biweekly amniotic fluid evaluation
- Antihypertensive treatment

According to NICE clinical guidelines (2010, amended 2019)

Should be started at BP 150/100 mmHg

First line -

Oral therapy used like

1. Labetalol given orally 100 - 400 mg every 8 - 12 hours

- Alternately Methyldopa or Nifedipine can be given
- If BP below 150/100 mmHg no immediate need for antihypertensives unless markers of severe disease are present
- Persistent high levels >160/110 mm Hg is most common indication for delivery in women with sever preeclampsia.

2. Hydralazine (10 - 25mg twice a day)

- Commonly used for rapid lowering of elevated blood pressure
- Acts directly on arteriolar smooth muscles to reduce PVR
- Most frequent side effects are decreased uteroplacental perfusion andhyperdynamic circulation indicated by late decelerations in patients with previously normal FHR tracing

3. Methyldopa (250 – 500 mg tid or qid)

- Central and peripheral antiadrenergic action

Role of Glucocorticoids[14]

- If birth likely prior to 34 weeks, 2 doses of betamethasone 12 mg intramuscularly 24 hours apart is recommended
- Significantly reduces neonatal complications like RDS, intraventricular haemorrhage and death .

Delivery

- Induction of labour should be attempted in women with mild preeclampsia once pregnancy reaches 37 weeks.(ACOG 2020)
- Frequent monitoring of blood pressure done hourly.
- In suspected situations of foetal growth restriction, continuous electronic foetal monitoring should be carried out.
- 3rd stage of labor managed with oxytocin or prostaglandins to prevent postpartum haemorrhage

MANAGEMENT OF SEVERE PERECLAMPSIA

≥ 34 weeks

- Treat with magnesium sulfate for prevention of seizures
- Antihypertensive administration
- Deliver after stabilization of patient

Indications for Delivery in Women less than 34 weeks who are managed expectantly:

- **Prompt delivery after maternal stabilisation and after single dose corticosteroid therapy**
    - Uncontrolled severe hypertension
    - Persistent headache, refractory to treatment
    - Persistent epigastric pain
    - Eclampsia

- HELLP syndrome
- Pulmonary edema
- Placental abruption
- DIC
- Stroke
- Myocardial infraction
- Nonreassuring fetal status
- Fetal demise

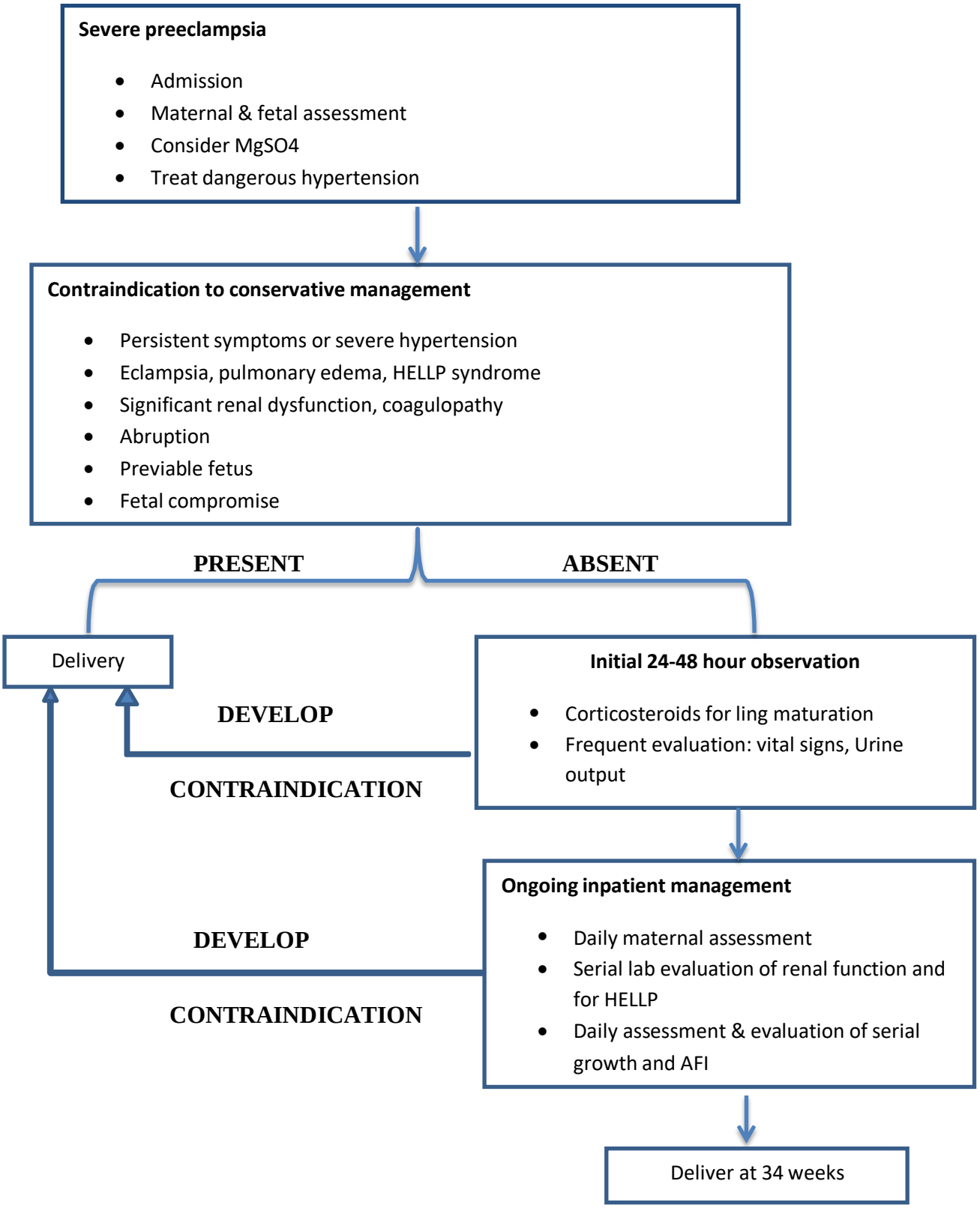
➢ **Delay delivery 48hr if possible to allow corticosteroid for lung maturation :**

- PPROM
- FGR
- Oligohydramnios
- "Reversed end-diastolic Doppler flow" seen in Umbilical artery
- Worsening "renal parameters"

≤ 34 weeks

- Keep in high risk antepartum area for intensive fetal and maternal monitoring is needed for blood pressure and urine output, cerebreal status is done.
- Symptoms like Epigastric pain/tenderness, Shortness of breath are monitored.
- Antihypertensive administered with an aim to lower SBP between 140 - 155 mmHg and DBP between 90 -105 mmHg.
- Corticosteroids will be administered (12 mg betamethasone IM two doses 24hours apart).
- Delivery should be done at least if possible 12 - 24 hours after second steroid dose

FIGURE NO 6: An algorithm for treating severe preeclampsia at less than 34 weeks



Eclampsia

- Eclampsia is defined as the onset of seizures in a pre-eclamptic woman during pregnancy or puerperium that cannot be attributed to other factors and/or an inexplicable comatose state.
- In Eclampsia, maternal mortality ranges from 1 to 5% and about 5–12% of instances involve perinatal death.

Impending Eclampsia:-

It is advised for women who show the signs / symptoms listed below.

- Headaches (occipital/frontal)
- Vision blurriness
- Vomiting and nausea.
- Pain in the right upper quadrant and/or in the epigastrium
- Reduced urine output
- Test results showing DIC

Management[59,60a,b,c]**:-**

- MgSO4 is used as a treatment and a preventative measure.
- Oral suctioning, airway clearing, and oxygen administration
- Blood pressure management
- Baby delivery

MGSO4 REGIMENS

Pritchard Regimen

- 4 gm of 20% mgso4 i.v over not less than 3 minutes

- 20 ml syringe + 4 ampoules of mgso4 + add to 12 ml of NS
- Immediately followed by 10 gm of 50% gmso4 IM (5g in each buttock)
- Maintenance dose → 5 gm of 50% mgso4 IM 4rth hourly in alternate buttocks

Zuspan Regimen

- Loading dose 4 g IV (administered over 5 to 10 mins)
- Maintenance dose 1 -2 g/ hour by controlled infusion pump up to 24 hours after last seizure

Sibai Regimen

- 6gm MgSo4 over 20 mins followed by 2 gm MgSo4 IV infusion
- Continuous IV regimen
- 4 -6 g LD of MgSo4 in 100 ml IVF slowly over 15 to 20 mins followed by 1 - 2 gm/ hr in 100 ml of IV infusion as maintenance.

Low dose regimen of SARDESAI

- Loading dose of 4 gm (20 ml in 20% solution) of mgso4 was given IV 4 -6 minutes
- Maintenance does is 2gm of 20% w/v every 3 hours
- Can be given IM route as well

Other anticonvulsants

- Levetiracetam
- Phenobarbitone
- Phenytoin regime
- Diazepam regime
- Lytic cocktail regime

Antihypertensive for urgent control of severe hypertension (ACOG -2020a)

1. **Hydralazine :**

   5mg IV or IM → 10mg (15-20 minutes apart) - Maximum upto 3 doses

   (or)

   Constant infusion 0.5-10mg/hr

   - Side effects – tachycardia, headache, hypotension

2. **Labetalol :**

   10mg→20mg→40mg→80mg (at 10-15 minutes interval)

   (or)

   Constant infusion 1-2 mg/min

   - Side effects – asthma precipitation, bradycardia, hypotension

3. **Nifidipine** : 10mg→20mg at 20 minutes interval for 2 doses

   - Side effects – tachycardia , headache

4. **Diuretics** :

- Use of diuretics in the antepartum period should be limited to eclamptic women with concomitant pulmonary oedema.
- They may form an integral part of the postpartum care.
- Placental perfusion is compromised with the use of diuretics.
- Women with severe preeclampsia and eclampsia usually have an acute expansion of intravascular volume during delivery due to the substantial amount of IV fluids that they receive. The auto transfusion that follows the contraction of the uterus during delivery adds additional volume to the intravascular space. Finally, following delivery large amounts of fluid accumulated in the interstitial space start to mobilise towards

the intravascular space. This is a perfect setup for congestive heart failure and pulmonary oedema particularly in women with renal function impairment.

- Therefore, before delivery “diuretics are not used to lower blood pressure” .
- Furosemide or similar drugs are used before delivery solely to treat pulmonary oedema.
- Furosemide 20–40 mg IV every 10–12 hours can be initiated shortly after vaginal or caesarean delivery and continued orally for several days after the patient is able to tolerate oral intake.

DELIVERY

- Delivery is the only definitive treatment for eclampsia
- The mode of delivery depends, on multiple factors like period of gestation, presenting part & cervical examination findings
- Cervix - favourable, options include ARM or labour induction using Prostaglandins/oxytocin.
- Cervix - unfavourable with alive fetus, options like caesarean can be considered.
- Caesarean delivery may be indicated in the presence of prolonged fetal bradycardia, unripe cervix, gestational age less than 30 weeks

HELLP SYNDROME

This is a complication of pre-eclampsia characterised by the development of thrombocytopenia (<1lakh/mm^3) with elevated liver enzymes and hemolysis

Diagnosis:

- About 82%–85% of patients with HELLP have mild-to-severe hypertension and 85% have significant proteinuria.

- HELLP may have an atypical onset or features with about 15% lack either hypertension or proteinuria.
- "HELLP SYNDROME DIAGNOSIS CRITERIA":

1. Hemolysis
    - Peripheral blood smear showing abnormality like burr cells, schistocytes.
    - Increased bilirubin levels "≥ 1.2 g/dl"
    - Reduced "serum haptoglobin" levels
    - Elevated LDH more than "twice the upper limit of normal (>600 U/L)"
2. Elevated liver enzymes
    - Elevated AST, ALT "≥ twice the upper limit of normal (≥72 IU/L)"
3. Reduced platelet count (<1lakh/mm^3)

Table no 3: Mississippi classification of HELLP syndrome[61]

Class	Severity of thrombocytopenia	Platelet count/mm^3
I	Severe	<50,000
II	Moderate	50,000 to 1,00,000
III	Mild	100,000 to 150,000

Maternal complications[62]:

- Abruptio placentae with DIC,
- Acute renal failure
- Pulmonary oedema

Perinatal complications[62]:

- Prematurity(can lead to RDS, intracranial haemorrhage, necrotising enterocolitis and bronchopulmonary dysplasia)
- Growth restriction and
- Abruptio placentae

Hepatic rupture

- The signs and symptoms are those of significant circulatory collapse, and it can happen either antepartum or postpartum.
- Intraabdominal bleeding - signs of peritoneal irritation and progressive hypovolaemia will be seen.
- The pregnancy must be terminated immediately.
- At the time of the laparotomy, the laceration is almost always found on the diaphragmatic aspect of the right lobe of the liver. It frequently coexists with subcapsular petechiae and subcapsular haematomas.
- The prognosis for pre-eclamptic patients with liver rupture is ominous.
- Usually Attempts at surgical repair or excision → extension of the laceration →more bleeding, consumption coagulopathy and ultimately death.
- Least manipulation of the hepatic tissue have better results. The bleeding hepatic surface should be covered with Avitene, Oxycel or Gelfoam and then packed with surgical sponges placed above the haemostatic agent. One of the sponges is brought outside the abdominal incision to facilitate removal on the second or third postoperative day.

Management

- The clinical course of HELLP syndrome is frequently characterised by a gradual, occasionally rapid, deterioration in the status of the mother and foetus.
- Pregnant Women should be "delivered regardless of their gestational age" because of the dangerous nature of this condition and the elevated rates of maternal morbidity and mortality.
- It few studies it has been shown that corticosteroids due to their anti-inflammatory action and immunosuppressive action it might modify the proinflammatory condition of pre-eclampsia with severe features and may favourably change the clinical course. There was no difference in the risk of maternal death, severe maternal morbidity or perinatal or infant death. The only effect of treatment on individual outcomes was improved platelet count. The data is inadequate to support the use of corticosteroids for diminution of the disease process in HELLP syndrome.
- Investigations should be done at least at "12-hour intervals".
- AST > 2,000 IU/L or LDH > 3,000 IU/L suggest of increased risk of mortality.
- Platelet count: - Generally decreases at an regular rate of nearly "40% per day", and liver enzymes levels increased. The lowermost platelet count mostly occurs after delivery at a mean of 23 hours.
- HELLP syndrome might achieve peak condition in the first 2 days following delivery, with a descending trend in haematocrit values.
- If the platelet count continues to drop with increasing liver enzymes after 4 days of delivery, the initial diagnosis of HELLP syndrome should be reassessed.
- Supportive care alone, 90% of patients will have platelet count > 1,00,000 /mm^3 and a reduction in liver enzymes values <7 days following delivery.
- Women with HELLP syndrome are also at increased risk of pulmonary oedema, acute RDS and renal failure.

- Immediate delivery : -
    - If gestational age is ≥34 weeks (or)
    - At any weeks of gestation if there is uncontrollable hypertension, acute renal failure, pulmonary oedema, non-reassuring foetal status, abruptio placenta, severe liver parameters abnormality , bleeding is present.
- All other cases require administration of magnesium sulphate, steroids for the prevention of intraventricular bleed and RDS in the foetus and delivery within 24 hours after the second steroid dose.
- Delivery should not be delayed further even if there is some apparent improvement in the patient situation during the time required for steroid administration.
- Vaginal delivery - only if the cervix is ripe, the gestational age is >/=32 weeks of gestation, reactive FHR without any indications for caesarean delivery. Labour should proceed rapidly and cervical changes should be seen shortly after the initiation of induction. If vaginal delivery is not foreseen within 12 hours after the onset of induction, it is better to perform caesarean section.
- Platelets are given when the platelet count is below 50,000/mm3 and particularly if the patient shows signs of altered haemostasis. The platelet count is raised approximately 10,000/mm^3 by each unit of pooled platelets.
- An upward trend in platelet count and a downward trend in LDH should be apparent by the fourth postpartum day in patients recovering without complications.
- Plasmapheresis -For deteriorating patients despite the conventional therapy.
- A double-blind, placebo-controlled clinical trial with adequate number of subjects demonstrated that “dexamethasone treatment does not improve the outcome in women with HELLP syndrome”. Outcomes assessed included are “duration of hospitalisation, recovery time of abnormal lab results and complications such as ARF, pulmonary

oedema, eclampsia and death". In the same study, an unplanned subgroup analysis suggested a beneficial effect in platelet count recovery in women with severe HELLP (platelet count <50,000mm^3)

- At present, corticosteroids are not recommended for the treatment of HELLP.

Complications of pre-eclampsia:

Pulmonary oedema

- Pulmonary oedema is a rather common complication of severe preeclampsia and eclampsia, affecting approximately 3% of these patients.
- Mostly due to increased use of crystalloid solutions (for intravascular volume expansion).
- Usually occurs in the postpartum period and is characterised by deep respiratory distress, significant fall in oxygen saturation and on auscultation of chest diffuse rales are seen.
- Treatment include propped up position, administering oxygen by nasal prongs or a rebreathing mask, restriction of intravenous and oral fluids and furosemide 20–40 mg IV every 6 hours. Central haemodynamic monitoring (central venous pressure of Swan– Ganz catheter) has been recommended by the ACOG (2002a) only in severely pre-eclamptic women with accompanying severe cardiac disease, renal disease or both or in cases of refractory hypertension, oliguria and pulmonary oedema.

Acute renal failure

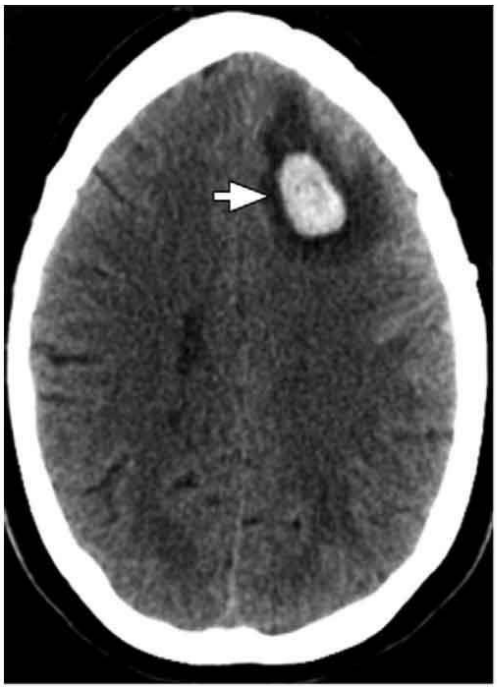
- In severe pre-eclampsia Oliguria is mostly due to prerenal in origin.

- The majority develop oliguria are volume depleted and they usually respond to an increase in the rate of intravenous fluid administration. Occasionally, some patients do not respond to the fluid challenge and it is necessary to make a rapid assessment of the pathophysiology of the process.
- In patients with uncontrolled hypertension with raised haematocrit reflecting haemo concentration need aggressive treatment with vasodilators to effect afterload reduction and decrease renal artery vasospasm.
- Normotensive or mildly hypertensive women with low haematocrit values have expanded intravascular volume and need aggressive diuresis.
- In older and obese patients, there is large increase in plasma volume with normal or decreased cardiac output. These women are at significant risk of pulmonary oedema and require fluid restriction and aggressive preload reduction with diuretics.
- In other patients, there is a contracted intravascular volume due to low plasma oncotic pressure and endothelial cell damage with leaking of serum into the interstitial space. These women usually respond to interruption of pregnancy and expansion of intravascular volume.
- Rarely, oliguria is of renal origin and commonly due to ATN that occur in pre-eclampsia setting complicated with severe abruption, DIC.many patients may require dialysis. The remote prognosis of properly managed ATN in patients with pre-eclampsia is good. Establishment of adequate urinary output is an important priority because the longer the low urinary output persists, the greater the possibility that the patient will develop severe or irreversible renal damage.
- If vaginal delivery cannot be anticipated to occur in a few hours, it is better to perform a caesarean section.

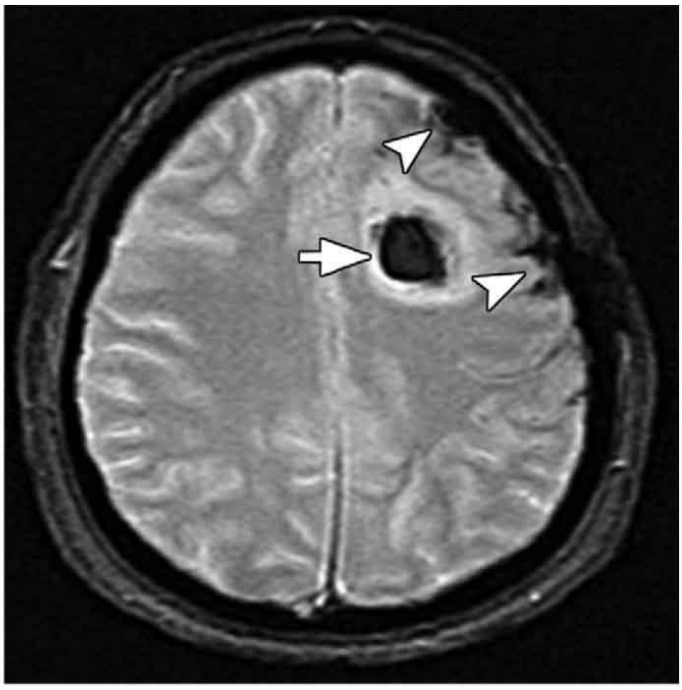
- Usually delivery is followed by disappearance of the renal vasospasm and brisk diuresis.

Intracranial bleeding

- It is the foremost cause of mortality in pre-eclampsia.
- Underestimation of severity of the disease, extended outpatient treatment, failure to use antihypertensive drugs to treat extreme elevations of BP and discharge from the hospital before obtaining adequate control of the hypertension is the most frequent cause of deaths.
- An important clinical observation from the analysis of 28 women who sustained a stroke in association with pre-eclampsia and eclampsia was that the main correlation of this event was the systolic, not the diastolic BP[63]. This suggests that antihypertensive therapy may be indicated when the systolic BP reaches 150, not 160 mm Hg, in pre-eclamptic women.
- The diagnosis is suggested by a deepening stupor and sensorimotor deficits and becomes highly probable if focal neurologic signs, such as unilateral pupil dilation, are present.
- By CT or MRI scan the diagnosis is confirmed.
- Recovery is more of an exception than the norm, and the prognosis is very bad.
- In most cases, coma becomes more profound, respiratory paralysis appears and finally the electroencephalogram shows loss of electrical activity.
- Severe occipital and temporal headaches are important symptoms in pregnant patients because they are frequently harbingers of convulsions.
- These headaches are usually secondary to inadequate BP control and they are an indication for aggressive treatment with hypotensive agents



CT showing intracranial haemorrhage with surrounding edem in left frontal lobe



MRI showing

Arrow – frontal lobe hemorrhage

Arrowheads - SAH

FIGURE NO 7

Visual disorders[38]

- Blindness may happen in patients with severe PE and eclampsia and may persist for several days, although quick recovery after delivery is the rule.
- In most cases, examination of the optic fundi does not show severe retinopathy, since the problem is usually caused by multiple micro haemorrhages and micro infarcts occurring in the occipital lobe.
- Cortical blindness is equivalent to a seizure, and patients with these symptoms should be treated as having eclampsia.
- The funduscopic examination of patients with pre-eclampsia usually does not reveal more than focal or generalised vasospasm and, in some cases, retinal oedema, which

frequently is missed in the examination because it begins in the periphery of the retina.

- Papilloedema in pre-eclampsia is highly unusual and demands a reevaluation to rule out the possibility of an intracranial tumour or bleeding.
- Diplopia is a symptom that may occur, and it is caused by functional impairment of the sixth cranial nerve paralysis. This finding requires a CT scan to rule out a tumour in the brainstem area. Like most lesions caused by pre-eclampsia, the sixth nerve paralysis improves after delivery and eventually disappears several weeks later.

Abruptio placentae

- About 7% of all patients with eclampsia will have abruption.

PREECLAMPSIA SCREENING TESTS FOR PREDICTION AND PREVENTION

I. Modification of the placental perfusion and vascular resistance functions

- Doppler ultrasonography,
- The rollover test, and mean arterial blood pressure
- Testing for angiotensin ii binding,
- Isometric exercise testing,
- Angiotensin infusion tests
- Serum renin levels
- The response of platelet calcium to argipressin,
- Monitoring of ambulatory BP for 24 hours

II. Changes in the foetalplacental unit function

- Inhibin A levels,
- The Alpha fetoprotein (AFP), and
- HCG
- Reduction in plasma protein A related with pregnancy
- Serum Estriol levels

III. Renal parameter changes

- Raised Serum U.A;
- elevated microalbuminuria levels.
- Urinary presence of kallikrein
- Increased microtransferrinuria levels.

IV. Changes in endothelial and oxidative stress function

- Raised Fibronectin levels
- Raised Homocysteine
- Raised Endothelin
- Thromboxane is raised

The different predictors can be broadly divided into two categories: non-laboratory approaches and laboratory approaches.

NON-LABORATORY APPROACHES:

1. History :- "High risk factors for PE" include

- Primi gravida
- Maternal age extremes

- Overweight or obese
- Preeclampsia-complicated prior pregnancy;
- Multifetal pregnancy;
- Ethnic group

2. Provocative Pressor tests include:

a. **Test with Angiotensin II infusion** -

- Between 28 and 30 weeks, this test is performed.
- Preeclampsia is predicted by angiotensin infusion test with sensitivity of 90%, specificity of 87%, and 78% PPV in high-risk individuals when the diastolic blood pressure rises by more than 20 mmHg.
- Drawback:
  - ❖ Difficult to complete as a mass screening technique
  - ❖ Costly
  - ❖ Time-taking
  - ❖ Not dependable

b. **Roll over Test:**-

- Performed between 28 to 32 weeks period of gestation
- With the patient in the left lateral posture, the blood pressure is first measured. A positive test is considered to occur when the patient's diastolic blood pressure rises by more than 20 mmHg when lying supine.
- Sensitivity is <88%, Specificity is of 5-95% and Positive predictive value is <93%.
- The substantial range in results makes this test useless for clinical usage.

c. **Isometric handgrip test**[64]:-

- Performed between 28 to 32 weeks period of gestation
- Patient is advised to squeeze a hand ball for about 3 minutes, it is suggested that their diastolic blood pressure threshold rises by 20 mmHg.
- Has Sensitivity of 81% and Specificity of 96% with Positive predictive value of 81%

d. **Mean Arterial pressure**:-

- Patients who have mean arterial pressure in the second trimester greater than 90 mmHg are at increased risk for pre-eclampsia.
- "The predictive value varies widely".

USG Doppler:-

- Pre-eclampsia can be detected as early as 18 weeks in a pregnancy using uterine and umbilical artery Doppler velocimetry.
- In patients who are at risk of developing pre-eclampsia, the diastolic waveform notches characteristically, indicating higher peripheral resistance as a result of inadequate trophoblastic invasion of spiral arterioles.
- It has Sensitivity of 78% and Positive predictive value of 28%

LABORATORY APPROACHES[20]**:-**

1. **Foetal placental unit: – indicating endocrine dysfunction**
    - Placental protein 13,
    - Alpha Fetoprotein(AFP),

- Estriol levels
- Pregnancy associated plasma protein A
- Inhibin A and
- Activin A levels
- Corticotrophin-Releasing Hormone(CRH)
- hCG.

2. Endothelium dysfunction indicators

a. S.Fibronectin levels

b. Inhibitors of plasminogen activator,

c. Cell adhesion molecules,

d. Serum thrombomodulin,

e. Endothelin-1

f. Coagulation factors, platelets

g. Uric acid levels

h. Atrial natriuretic peptide,

i. Haematocrit

3. Urinary Tests:

a. Microalbuminuria: - sensitivity of 7%-90% and specificity of 29%-97%.

b. calcium excretion[65]

c. urine $\frac{calcium}{creatinine}$[66]

d. $\frac{allikrien}{creatinine}$

e. Fasting urinary albumin and creatinine ratio

4. Angiogenic factors:-

a. Decreased levels of VEGF and placental growth factors, which are proangiogenic factors
b. An increase in the antiangiogenic molecules “sFlt-1 and sEng”

5. **Cell free fetal DNA**
    - Maternal plasma may contain cell-free DNA (cfDNA) from the placenta. Apoptosis of cytotrophoblasts is thought to be increased in preeclampsia, which releases cfDNA.
    - The overall cfDNA levels and preeclampsia prediction were not correlated, according to an MFMU Network study.
6. **Others :-**
    - Other markers under investigation include first-trimester estimated placental volume, serum cystatin-c levels, and glycosylated haemoglobin A1c.
    - Serum and urine proteins as well as cellular metabolites can be studied using proteomic, metabolomic, and transcriptomic technologies. preliminary research shows they have potential predicting ability

PLATELETS:-

- Preeclampsia includes thrombocytopenia and platelet dysfunction as essential symptoms. Platelet activation results in increased destruction of the cells and decreased blood levels. Platelet volume increases as a result of immaturity. Preeclampsia has been said to be early predicted by platelet volume.

SERUM URIC ACID:

- Because of reduced clearance, preeclampsia has higher serum uric acid content. The severity of the illness and the prognosis for the foetus are related to serum level. The increase in serum levels happens somewhat late in the disease's progression. As a result, unreliable as a predictor.
- Specificity ranged from 77 to 95%, and sensitivity from 0 to 55%.
- Raised serum uric acid is generally better understood as a sensitive sign of decreased renal function rather than a predictive, diagnostic, or unique feature of preeclampsia.

SERUM FIBRONECTION LEVELS[38]:

- The glycoprotein known as fibronectin is crucial for "cellular adhesions, migration, phagocytosis, and homeostasis". It is found in connective tissue as well as the basement membrane. Endothelial cells and extracellular matrix release it into the bloodstream after endothelial damage. It has been suggested that cellular fibronectin levels greater than "3.8 ug/mL within 22 to 26 weeks of gestation" may aid in the early diagnosis of preeclampsia in primigravida. There were discrepancies in the sensitivity, specificity, and positive and negative predictive values between investigations. According to a systemic review, "neither cellular nor total fibronectin were clinically helpful in predicting PIH".

RAISED HOMOCYSTEINE LEVELS:

- Homocysteine is reported to be increased in preeclampsia and causes oxidative stress, endothelial cell dysfunction, and other problems. Although there was a 3–4 fold increased risk of preeclampsia in pregnant women with elevated levels "at 14–16 weeks", the findings have not been consistent.

SERUM INHIBIN-A and ACTIVIN-A:

- It's unclear how they contribute to the development of preeclampsia. They are produced by the placenta's trophoblast cells, and their levels reach their peak at 8 weeks before dropping off till term. They exhibit placental bed formation with trophoblast invasion. Patients who later develop preeclampsia experience an increase in maternal serum levels between 13 and 18 weeks.

ALPHA-FETOPROTEIN (AFP):-

- AFP in the maternal serum rises up until 30 weeks of pregnancy. Numerous studies have proven that there is a link between increased maternal AFP and hypertensive disorders of pregnancy. At 12 weeks of gestation, AFP peaks at 3 mg/ml and then starts to fall

ANGIOGENIC & ANTI-ANGIOGENIC FACTORS:-

- The formation of placental vascular tissue involves a number of proangiogenic and antiangiogenic components. In preeclampsia, factors like placental growth factor (PLGF) and vascular endothelial growth factor (VEGF) are diminished. Early pregnancy doesn't typically show this distinction. A study showed that placental growth factor is a poor predictor of the development of severe preeclampsia later on. “Worsening hypoxia at the uteroplacental interface stimulates excessive levels of antiangiogenic factors”. At least two antiangiogenic peptides are overproduced by the trophoblastic tissue of pregnant women who will eventually develop preeclampsia.

i. Soluble Fms-like tyrosine kinase (sFlt-1) functions as a receptor for vascular endothelial growth factor (VEGF) and placental growth factor (PLGF).

ii. Endoglin is a TGFβ co-receptor. Endothelial nitric oxide dependent vasodilatation is reduced as a result of the inhibition of TGFB binding to endothelial receptors. There is still no known reason for the placental overproduction of antiangiogenic proteins.

iii. Before the development of a clinical condition, "soluble endoglin and soluble fms like tyrosine kinase 1 (SFlt-1) are elevated". Their clinical effectiveness is not advised until it is more clearly demonstrated.

Prevention:-

Preeclampsia prevention is a topic with a large body of literature. Instead than focusing on preventing preeclampsia's sequelae, there is some debate about whether or not preventing preeclampsia per se is a worthwhile objective.

Primary Avoidance:

- Primary avoidance, while ideal, is lone feasible when the precise aetiology is understood. By changing some of the risk variables, primary prevention is somewhat attainable.
- Better To have children at an "age when the endothelium is still able to handle the inflammatory stress associated with the pregnancy state".
- It is advised to have pregnancies with "low risk men", more common in "nulliparous" women and to stay with the same partner because the disease process more common in "mutliparous women with change of partners".
- Preeclampsia may occur less frequently if obesity is prevented and/or effectively controlled.

- Women with conditions including “diabetes, chronic hypertension, renal disease, and others” should have their underlying illness under control before trying to get pregnant.

Secondary prevention:

Secondary prevention's fundamental criteria are

a. comprehension of pathophysiological processes
b. The accessibility of screening techniques
c. Techniques for modifying and intervening with pathophysiology

Non-pharmacological methods of interventions

a. Bed rest;
b. alterations in lifestyle
c. Consistent physical activity

Dietary Modifications

a. Limiting salt in the diet
b. Nutritional protein and energy intake
c. Management of obesity
d. A alteration in food habits
e. Omega-3 fatty acids found in fish oil have been demonstrated in few trials to be helpful in preventing preeclampsia. Fish oils are unlikely to be helpful in preventing preeclampsia, according to a trial (FOTIP).
f. Consumption of alcohol.
g. Supplementing with arginine was reported to be advantageous, however the research was limited.

h. Toki-shakuyuku-san (TS), a Japanese herbal remedy, possibly will be helpful in management and prevention of PE.

Pharmaceutical Involvements

a. Hypertension medications.
b. Diuretics like furosemide
c. Supplementing with zinc.
d. Magnesium Sulphate
e. There is no evidence to support the benefits of folic acid or any other B vitamin in preventing preeclampsia.
f. Low-dose aspirin:
    - Treatment with “low-dose aspirin (50–150 mg/day)” during pregnancy reduces the production of platelet TX-A2 with only minor effects on prostacyclin.
    - ACOG (2020) recommendations : low-dose aspirin should be given between 12 and 28 week period of gestation to help prevent preeclampsia in:-
        - ❖ Women with one or more of the following high risk features:
        - Previous preeclampsia
        - chronic hypertension
        - overt diabetes mellitus
        - any renal disorders,
        - autoimmune diseases,
        - Multifetal pregnancy.
        - ❖ Supplementation can be considered in women with >1 of these qualities:

          -Nulliparity

-Age > 35 years,

- Obese women

- Family history of PE

- Vulnerable sociodemographic,

- Previous low-birthweight or growth-restricted baby.

- The CLASP (collaborative low dose aspirin) research is the largest trial to date. Overall, there was a 12% decrease in the incidence of preeclampsia when low dose aspirin was used (non-significant). Women who use aspirin have a slightly greater risk of placenta abruption (Statistically Not Significant). Antiplatelet medications used to prevent preeclampsia did not vary from the control group in a meta-analysis. The outcomes of the current trials do not support the usual therapeutic or preventive use of aspirin therapy for pregnant who are deemed to be at risk for PE. Women who face the risk of developing preeclampsia with early onset are the only population in which low dose aspirin may be indicated.

g. Only women with antiphospholipid antibody syndrome should take heparin and low-dose aspirin; they should not be recommended on a regular basis.

h. Calcium supplement: Calcium consumption and the likelihood of preeclampsia are inversely correlated. Levin d's study, which involved supplementing with 2g/day, revealed no advantages. The Cochrane study did find a slight decrease in preeclampsia, with the benefit being highest in high-risk mothers who consume little calcium.

i. Nitric oxide donors – preeclampsia affects Nitric oxide production, Data on how NO donors affect preeclampsia prevention are scarce and contradictory.

j. Antioxidants like Vitamin - C, E, lycopene, selenium, NAC, and garlic, have been utilised in numerous trials with positive outcomes. Antioxidant supplements, however, may not have an impact on the risk of preeclampsia or clinical outcomes, according to a 2008 Cochrane analysis.

Exercise

Cardiovascular medications:

a. Diuretic drugs
b. antihypertensive.

Anti-oxidants like Vitamins C, E, and D[67,68].

Anti-thrombotic medications[69,70]:

a. "low-dose aspirin"
b. "Aspirin with Dipyridamole or heparin or ketanserin"

HUMAN CHORIONIC GONADOTROPIN

- HCG is a glycoprotein, which is made up of a peptide frame with carbohydrate side chains attached.
- 24 to 36 hour half-life
- HCG is made up of two components.
    - ❖ Alpha have 92 amino acids
    - ❖ Beta component have 145 AA
- The alpha and beta subunits are connected by disulphide bond.

Fig No 8: Structure of hCG

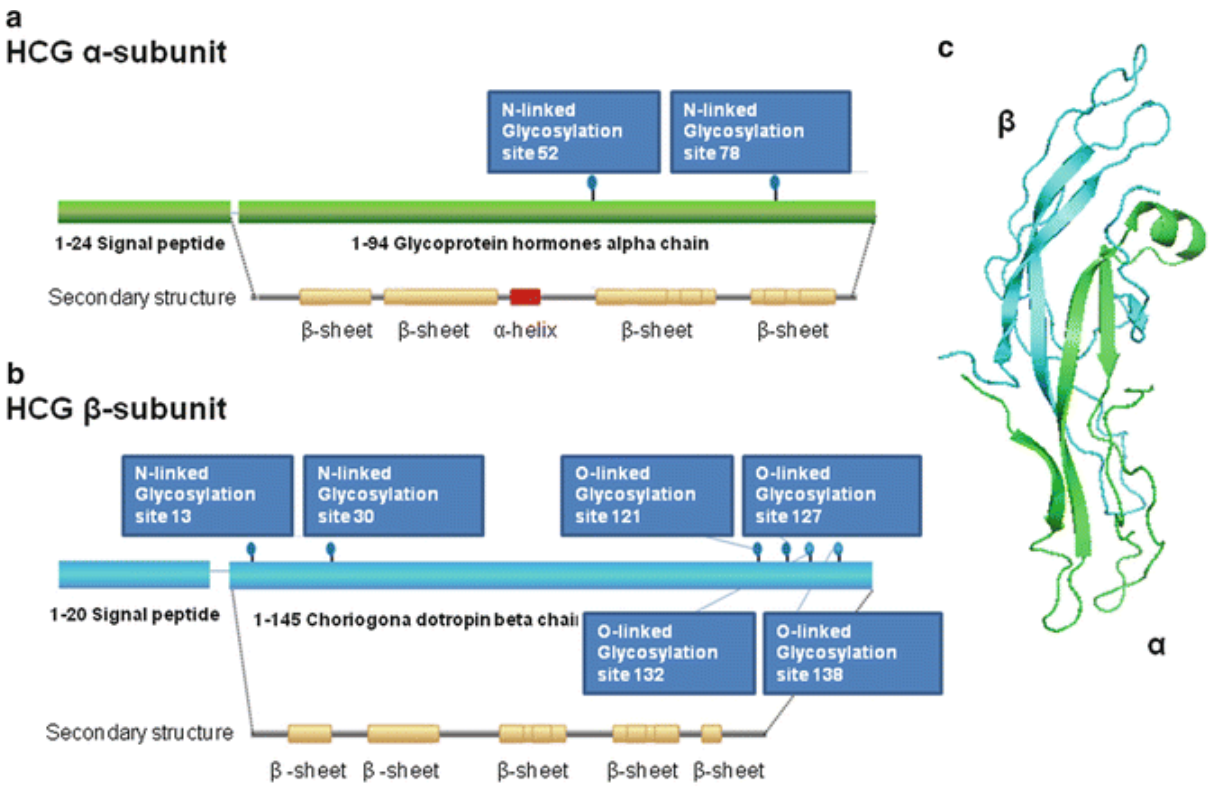
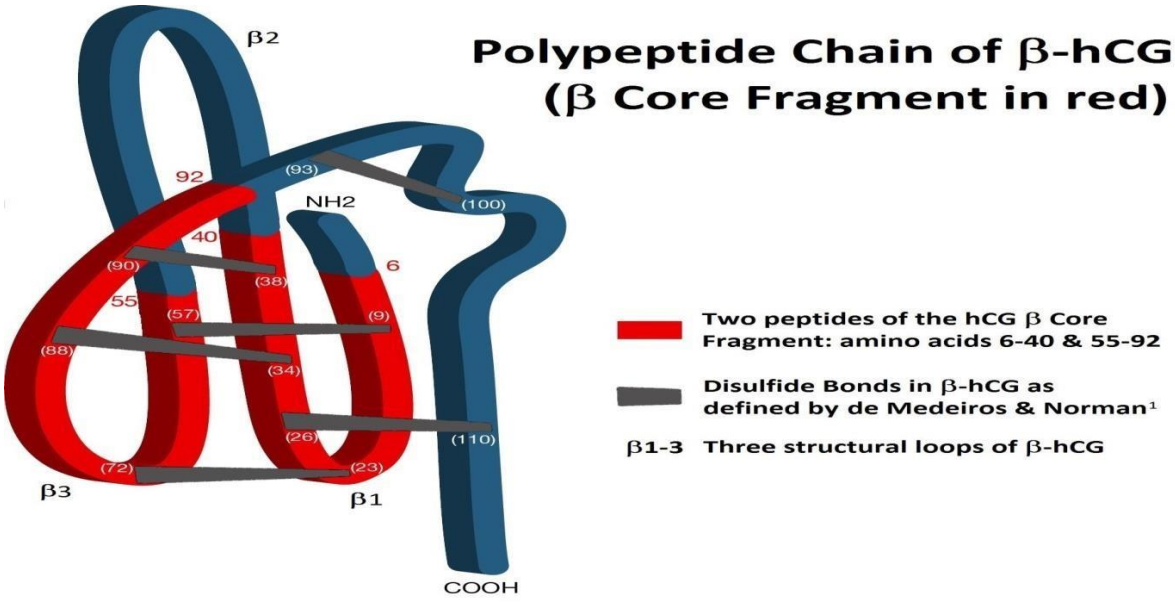
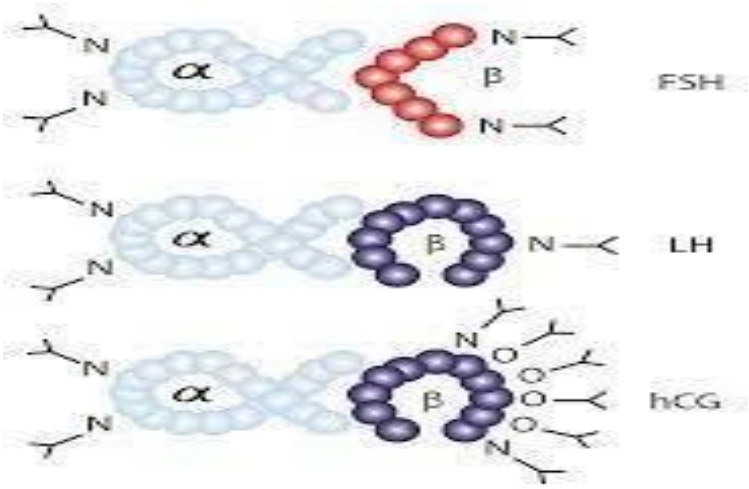


Fig No 9: Structure of beta subunit of hCG



- TSH, FSH AND LH have similar structure to alpha component.
- The specificity of the immunoassay is related to carbohydrate variations in the beta component, which makes it distinct.
- The beta subunit contains a distinctive carboxy terminal with 23 AA that enables the development of incredibly precise immunology testing.
- 36,000–40,000 Dalton molecular weight

Fig No 10: Structural similarities and differences between FSH,LH and hCG



HCG biosynthesis[32]:

- Only one gene on chromosome 6 gives rise to alpha subunit.
- On chromosome 19, there are 8 distinct genes that code for the beta subunits of several glycoprotein hormones.
- Produced by trophoblasts**.**
    - ❖ Syncytiotrophoblasts and cytotrophoblasts produce HCG prior to week 5. Thereafter formed only by syncytiotrophoblasts.
- It works through LH-HCG receptors on the plasma membrane**.**

HCG Synthesis Regulation:

- HCG Secretion is likely controlled by
    a. Placental GnRH and CRH
    b. Inhibin, Endorphin, and Activin
    c. Butylated cyclic- AMP
    d. IL 1, IL 6
    e. Transforming growth factor –β (TGF β)
    f. The Fibroblast growth factor
    g. Tumour necrosis factor(TNF).
- The precise process of regulation is unknown.

Clearance of HCG:

- 30% of HCG clearance is due to renal clearance.
- Liver metabolism is likely to remove any leftovers.
- There are many HCG molecular forms in plasma and urine.
    - ❖ Intact HCG.
    - ❖ Hyper - glycosylated hCG
    - ❖ Nicked hCG
    - ❖ As Free components.

Level of hCG in serum:

- The hCG level is roughly hundered IU/L at the time of the “anticipated but missing menstrual period”.

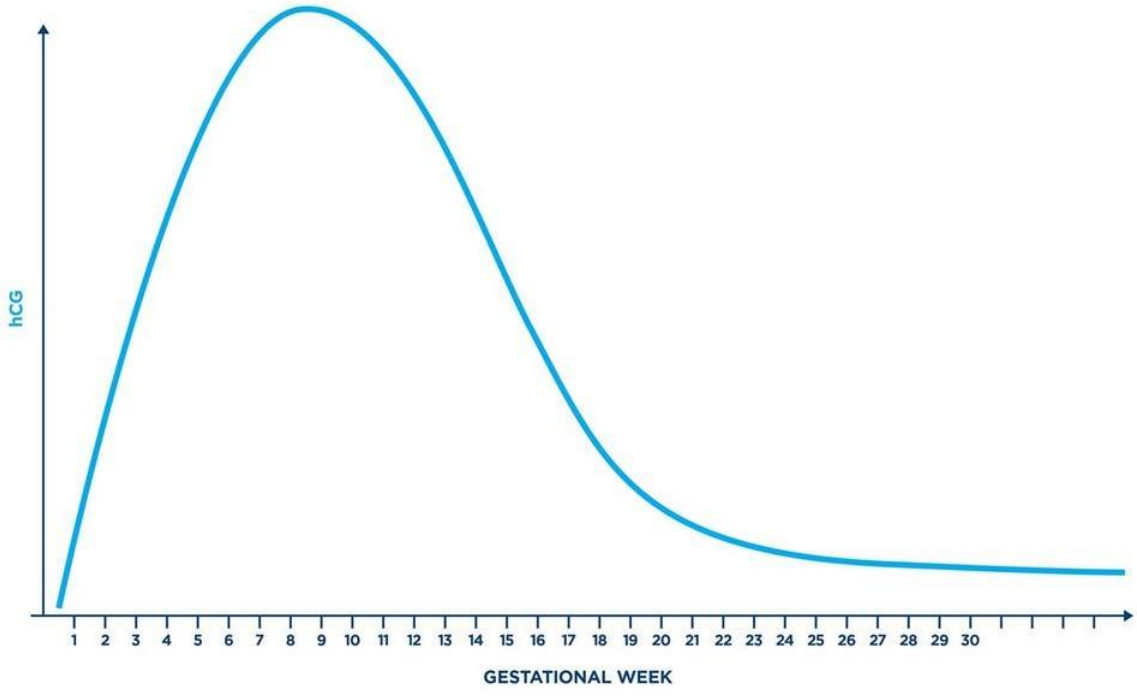
- At 18 to 20 weeks of gestation, hCG levels fall to roughly between 10,000 to 20,000 IU/L and remains there until birth.
- The duration to double is roughly three days (1.4 to 3.5 days)
- In most normal pregnancy at hCG level below 1200mIU/ml levels usually doubles every 48-72 hours and normally increases by at least 60% every two days. In early pregnancy, a 48 hours increase of hCG by 35% can still be considered normal.
- Between 1200-6000 mIU/ml serum hCG level usually takes 72-96 hours to double. After 6000 mIU/ml it takes over four or more days to double.
- When it reaches 7200mIU/ml a yolk sac and in 10,800mIU/ml or greater than that a visible embryo with heart beat should be seen
- Normal hCG levels in: -
    a. nonpregnant state:- 5mIU/ml ,
    b. pregnant state:- >25 IU/ml
    c. postmenopausal women:- up to 14 IU/ml
- Multiple pregnancies, foetuses with Down syndrome, and gestational trophoblastic illness all have higher levels.
- Ectopic pregnancy and impending miscarriage both exhibit decreased levels.

TABLE NO 4: Serum HCG levels during a normal pregnancy[71]

Weeks from LMP	hCG (mIU/ml)
3 weeks	5-50 m IU/ml
4 weeks	5-426 m IU/ml
5 weeks	18-7340 m IU/ml

6 weeks	1080-56500
7-8 weeks	7650 -229,000
9-12 weeks	25700-2,88,000
13-16 weeks	13,300-2,54,000
17-19 weeks	4,060 -1,65,400
25-40 weeks	3640-117,000

Fig No 11: hCG levels during pregnancy.



- In Non-pregnant females levels are less than 5 m IU/ml
- Several distinct tests (radio-immunoassay, enzyme immunoassay, fluorescent immunoassay), each with a unique methodology, sensitivity, and specificity, have been developed for the quantitative determination of HCG.

Conditions in which hCG levels is raised are:

- Multifetal pregnancy
- Molar pregnancy
- Choriocarcinoma
- Germ cell tumors of ovary and testes.

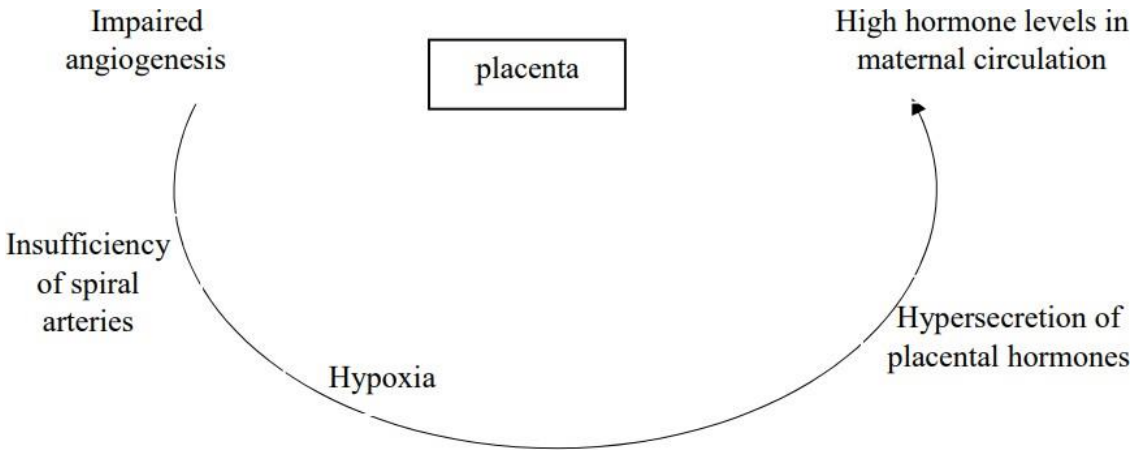
Conditions in which hCG levels is reduced are:

- Error in calculation of pregnancy dates.
- An ectopic pregnancy.
- Anembryonic pregnancy.
- Miscarriage.

Preeclampsia and HCG:

HCG is primarily produced by the placenta, and measuring plasma levels of HCG have shown to be a useful screening technique for pregnancies with impaired placental function.

FIGURE NO 12: relation of HCG and pre-eclampsia



Trophoblast cells hyperplasia

During typical pregnancy:

- first trimester have low oxygen tension →TGF β-mediated inhibition of the invasive phenotype of trophoblast
- At 10 to 12 weeks: There is natural rise in oxygen tension → the differentiation of trophoblast into a more invasive variety→ which decreases TGF-Beta.

In patients with preeclampsia:

TGF-β l continue to be high

↓

The development of immature trophoblasts

↓

A hyper secretory condition develops in response to hypoxia

↓

Higher placental hormone levels

↓

Prior to the onset of preeclampsia, placental hormones are increased.

ELISA:-

- It can be used to quantify incredibly minute levels of beta-HCG.
- The ELISA test binds the HCG in the sample using monoclonal antibodies that are attached to a solid phase substrate. To sandwich the beta-HCG test sample, a second antibody is introduced. An enzyme like alkaline phosphatase is connected to the second antibody. The colour turns blue when the enzyme's substrate is added. Its intensity is related to quantity of enzyme and, thus, to the quantity of 2nd antibody bound. This in turn depends on how much beta-HCG is present in the test sample.
- The test's sensitivity ranges from 25 to 50 mU/ml.

AIMS AND OBJECTIVES

AIM

Present Study was done to study the efficacy of second-trimester serum beta HCG levels in the prediction of pregnancy-induced hypertension

OBJECTIVES

Primary objective

1. To study the efficacy of second-trimester serum beta HCG levels in prediction of pregnancy induced hypertension.

Secondary objectives

1. To know the mean cut-off levels of beta HCG levels among the second-trimester pregnant women in the diagnosing of hypertensive disorders of pregnancy.

REVIEW OF LITERATURE

Huma Z et al.[11] (2022) did a Cross-sectional analytical study among 150 pregnant females to determine the diagnostic accuracy of high beta HCG levels of 13-20 weeks of gestation in predicting pregnancy induced hypertension. Beta HCG levels > 71000 mIU/ml were seen in Almost 70% cases of PIH in their study which suggests that PIH was associated with increased level of beta HCG.

Yasmin S et al.[12] (**2022)** did a s prospective observational study was to find out the role of early 2nd trimester β hCG levels in the prediction of Hypertensive disorders. 12.7% (23 Out of 180) got hypertensive disorders of pregnancy. Twelve of these 23 individuals had moderate hypertension, while eleven had a severe form of the condition. When compared to pregnant women with normotensive blood pressure, they found that the serum hCG levels in women with HTN disorder of pregnancy were considerably higher.

A prospective study done by **Rathore N et al.[13]** (**2021**) in 13 -20 weeks gestational aged women showed 21.5% incidence of PIH. Which had higher levels of β-hCG? The study comes to the conclusion that elevated blood -hCG levels in second-trimester pregnant women suggest an increased risk of preeclampsia and GTN, and that elevated -hCG levels are linked to illness severity.

A case-controlled study of **Wang R et al.[14]** (2021) showed Higher circulating β-HCG level was correlated with pregnancy-induced hypertension. Significant independent contributions to severe pregnancy-induced hypertension were made by oxidative stress variables like

thiobarbituric acid reactive substance and total antioxidant capacity as well as inflammatory factors like interleukin-6, tumour necrosis factor, and interferon. In individuals with pregnancy-induced hypertension in the perinatal period, the connection between circulating -HCG levels and inflammatory and oxidative stress markers was statistically significant.

Murmu S et al.[15] (2020) study was aimed at assessing the serum lipid profile and serum beta-hCG in early (14–18 weeks) and late trimesters (24–28 weeks) in predicting PIH and its time of onset. The incidence of PIH in our study was 14.67% with the late-onset PIH predominance. In both the early and late second trimesters, PIH patients' blood levels of cholesterol, triglycerides, and very low-density lipoprotein significantly increased. Their research demonstrated the value of blood beta-hCG levels and lipid profiles in the second trimester for identifying women at risk for PIH, preeclampsia, or eclampsia.

In another study **done** by **Sheba Rosatee Victor et al.[16] (2019)** also showed amplified risk of developing PIH in cases with higher β -HCG values in 13-20 weeks. From their study, it was found, "women who have elevated βHCG values in 13-20 weeks were at increased risk of developing PIH". HCG has a sensitivity of 71.4% and a specificity of 87.1% in this investigation. HCG readings are increased in preeclampsia patients when compared to people with normal blood pressure.

Md Mansor M et al.[17] (2018) did a similar study to assess the ability of serum hCG levels during early 2nd trimester to predict PIH and obstetric outcome at later gestation. 8.8% had late onset PIH. Receiver operator characteristic curve was poor (AUC = 0.398) in predicting

PIH by second trimester hCG Levls, But there was no significant association of hCG level and pregnancy outcome.

Women with high serum β-hCG in early 2nd trimester (12 and 24 weeks) have 1.67 times added risk of developing PIH and poor maternal and perinatal outcome in a study done in 400 antenatal women by **Dawle SS et al[18] (2018).** According to this study, elevated maternal serum β -hCG in the first trimester of the second trimester is a reliable non-invasive indicator of PIH. The amount of serum β -hCG was inversely correlated with the maternal and perinatal outcome.

According to **Revankar VM et al.[19]** study (**2017**), Serum β-hCG had 92.6% sensitivity and a 94.9% specificity to predict hypertension, respectively. The predictive values for the favourable and negative outcomes were 78.1% and 98.5%, respectively. Women who later developed hypertension had considerably higher serum levels of the pregnancy hormone hCG. Serum -hCG may be utilised as a predictor of hypertensive illnesses that complicate pregnancy, according to the researchers' study. Dyslipidemia was discovered not to be an effective marker.

Soundararajan P et al.[20] did a prospective study on 100 patients of 14-20 weeks of gestational age cases attending the op of the Obstetrics and Gynaecology of the Raja Mirasudar hospital. Studies comparing individuals who stay normotensive (group I) and those who develop pregnancy-induced hypertension were done on blood levels of hCG and the serum lipid profile (group II). Between those who stay normotensive (group I) and those who acquired pregnancy-induced hypertension, comparative examinations of blood hCG and

serum lipid profile were conducted (group II). According to the findings of this study, maternal lipid profiles and beta-hCG levels in the second trimester are excellent noninvasive tests that may be used to predict pregnancy-induced hypertension before it manifests clinically.

In order to evaluate the claim that women who have high blood beta-HCG levels in the early stages of pregnancy are more likely to develop PIH, **Kaur G et al.**[21] (**2012**) conducted a research. In their study 12.36 % cases developed PIH. The sensitivity was 90.91 %, specificity was 97.44 % and positive predictive value was 83.33 %. According to the study's findings, mid-trimester serum beta HCG estimate (13–20 weeks) is a reliable indicator of PIH, and greater levels of beta HCG are linked to PIH that is more severe with the sensitivity of 90% and specificity of 97%.

Based on the levels of maternal serum free ß-hCG, the prevalence of several unfavourable pregnancy outcomes like miscarriage, pregnancy-induced hypertension (both proteinuric and non-proteinuric), intrauterine foetal death, foetal growth restriction, spontaneous preterm birth, oligohydramnios, and placental abruption by **Yaron Y et al.**[22] **(2002)** in 1,622 consecutive patients with singleton pregnancies. Although it is a poor indicator of other pregnancy problems, low free ßhCG is linked to a greater likelihood of spontaneous miscarriage in their study.

METHODOLOGY

STUDY DESIGN: - This current study is a Hospital based prospective observational study.

TIME FRAME TO ADDRESS THE STUDY: - The study is conducted from January 2021 to January 2023 for a period of 2 years.

Table no 5: GANTT CHART

TIME PERIOD	2021	2022	2023 JANUARY
Review of literature			
Development of interview schedule & pilot testing			
Data collection			
Data compilation & analysis			
Thesis writing			

SOURCE OF DATA: - All pregnant women with 16-20 weeks period of gestation who visited Department of Obstetrics and Gynaecology in B.L.D.E (DEEMED TO BE UNIVERSITY) Shri B. M. Patil's Medical College, Hospital and Research Centre, Vijayapura.

STUDY POPULATION:-

INCLUSION CRITERIA:

Primigravidae/multigravida with singleton pregnancy with gestational age of 16 to 20 weeks as determined by last menstrual period or by ultrasonography who are previously normotensive.

EXCLUSION CRITERIA:

- Patients with Gestational age of <16 weeks or>20 weeks
- Chronic hypertension
- Diabetes Miletus
- Multifetal pregnancies
- Antenatal women with congenital anomalies/Down's syndrome and Gestational trophoblastic diseases in current or previous pregnancy
- Not willing to participate

SAMPLE SIZE

- With anticipated Proportion of developed GH among women with primi gravida/ multi gravida singleton pregnency14.8% [(73)], the study would require a sample size of minimum 135 patients with 95% level of confidence and 6% absolute precision.
- The formula used $n=z^2 p*q/ d^2$

Where Z= Z statistic at α level of significance

d^2= Absolute error

P= Proportion rate

q= 100-p

Dropout rate of 20%= 135+27= 162

Sample size= Minimum 162

STATISTICAL ANALYSIS

- Data was entered in MS-excel 2007. Nominal data analysis (were presented in numbers & percentages. Continuous data were expressed as mean & standard deviation. Appropriate statistical tests were applied, (Chi-square , T test, ANOVA test,

Bonferroni Post Hoc Analysis, Receiver Operating Characteristic Curve-ROC/AUC, sensitivity and specificity) and < 0.05 p values considered as significant.

METHODS:

Ethical committee approval

↓

Patient satisfying inclusion criteria

↓

Informed consent obtained

↓

Data collected

↓

Data entered into excel sheet

↓

Data compilation

↓

Statistical Analysis

↓

Conclusion

1. All the subjects were informed about the study, and consents are taken in accordance with the declaration of Helsinki.

2. Women are subjected to a detailed history, which includes age, parity, height, weight, Family history, past obstetric history, past medical history, smoking habits, medical history of first-degree family members taken.

3. Systemic examination in particular reference to blood pressure is recorded with sphygmomanometer in sitting position.

4. Gestational age is calculated from reliable last menstrual history and early USG scan.

5. Venous blood will is collected, and the estimation of serum beta HCG is done.

6. All patients were followed up in antenatal clinic and examined every fourth week till 28 weeks, fortnightly up to 34 weeks and after that weekly till delivery. At every visit blood pressure is recorded.

7. Patient showing hypertension were followed more frequently depending on severity and test for proteinuria, LFT and RFT were done and are admitted indoor as applicable.

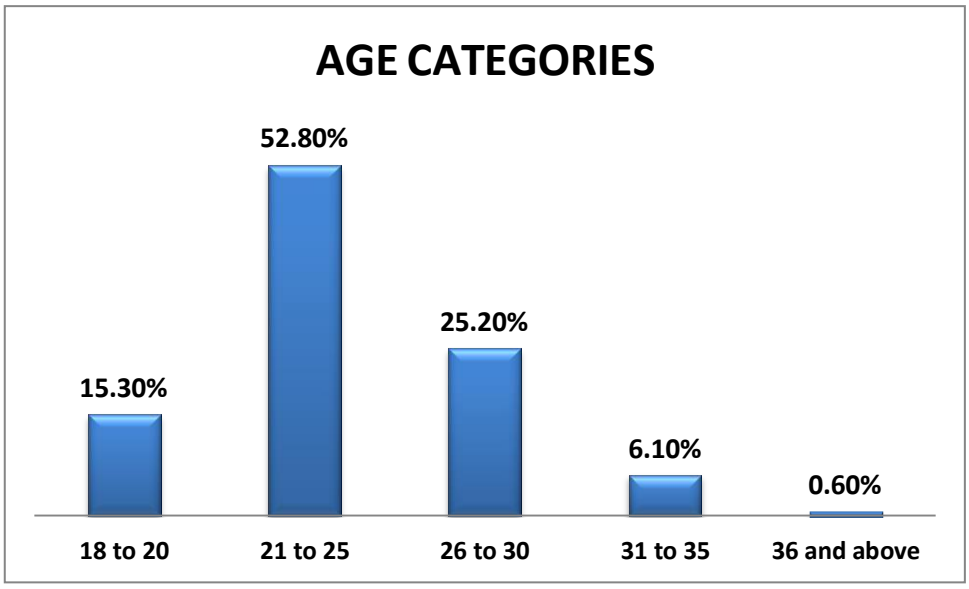
8. At the end of the study, subjects were divided into two groups depending on the evolution of pregnancy- Group A – who developed hypertension, Group B – who didn’t develop hypertension.

RESULTS

TABLE NO.6 AGE CATEGORIES

AGE CATEGORIES (YEARS)	N	N %
18 to 20	25	15.3%
21 to 25	86	52.8%
26 to 30	41	25.2%
31 to 35	10	6.1%
36 and above	1	0.6%
Total	163	100.0%
MEAN AGE IN YEARS	24 ± 4	

FIGURE NO.13 AGE CATEGORIES

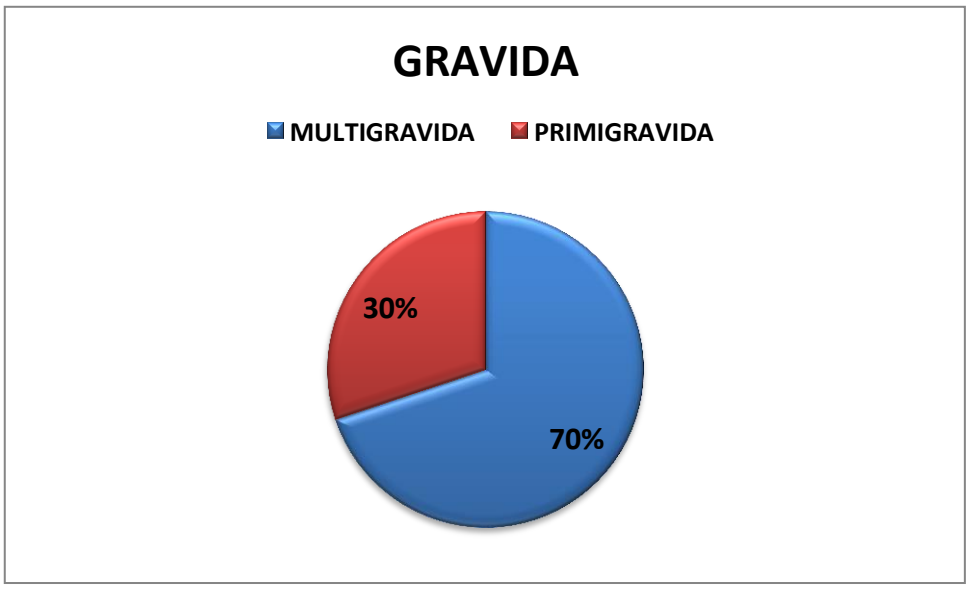


In present study, majority study population was in 21 to 25 years age group. Mean age of the study population was 24 + 4 years

TABLE NO.7 GRAVIDA TYPE

GRAVIDA	N	N %
MULTIGRAVIDA	114	69.9%
PRIMIGRAVIDA	49	30.1%
Total	163	100.0%

FIGURE NO.14 GRAVIDA TYPE

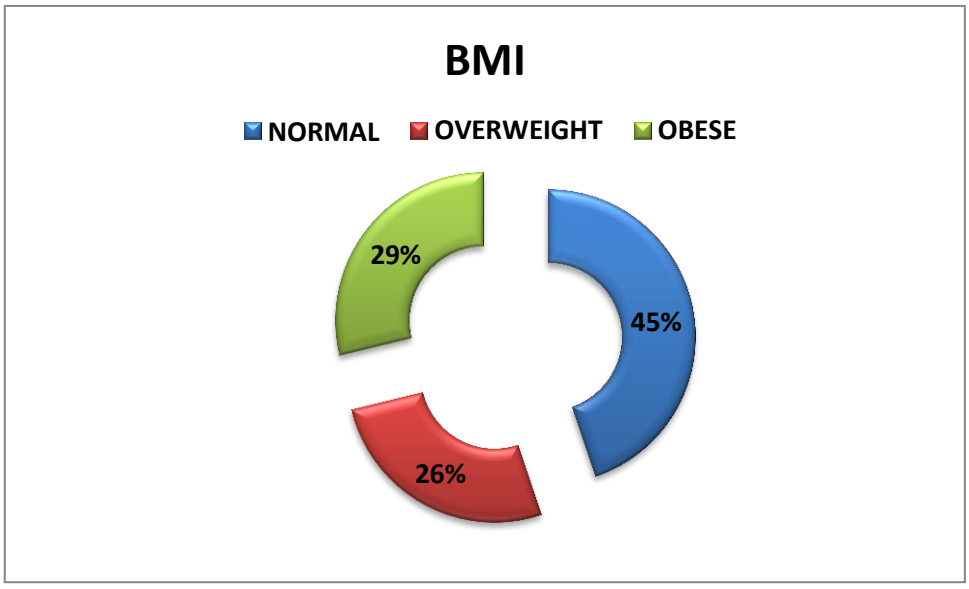


In present study, majority study population belonged to Multigravida (69.9%)

TABLE NO.8 BODY MASS INDEX

ASIAN BMI		N	N %
NON OBESE	NORMAL	73	44.80%
	OVERWEIGHT	43	26.40%
OBESE		47	28.80%
Total		163	100.00%
MEAN		23.7 ± 2.6	

FIGURE NO.15 BODY MASS INDEX

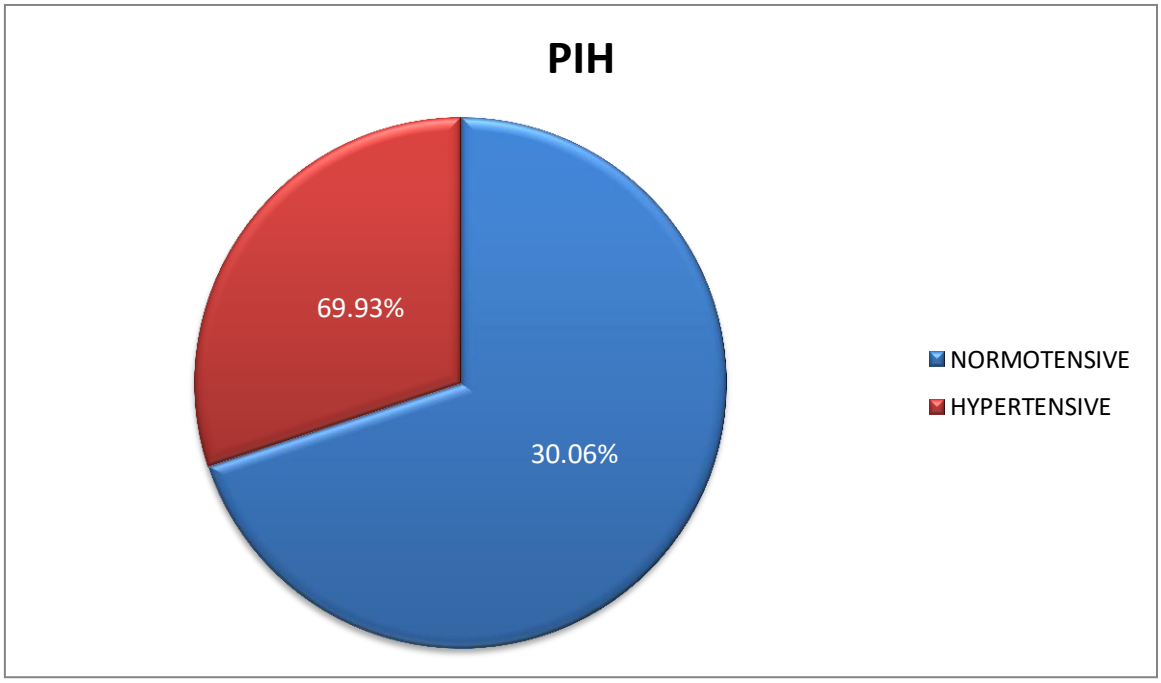


The current study is conducted using the WHO Asian BMI classification, majority study population was in Non-Obese category (73.6%) among 26% of them were overweight.Mean BMI of the study population was 23.7 ± 2.6

Table No. 9 CATEGORISATION OF STUDY GROUP

CATEGORY	N	N %
NORMOTENSIVE	114	69.9%
HYPERTENSIVE	49	30.1%
Total	163	100.0%

FIGURE NO 16. CATEGORISATION OF STUDY GROUP

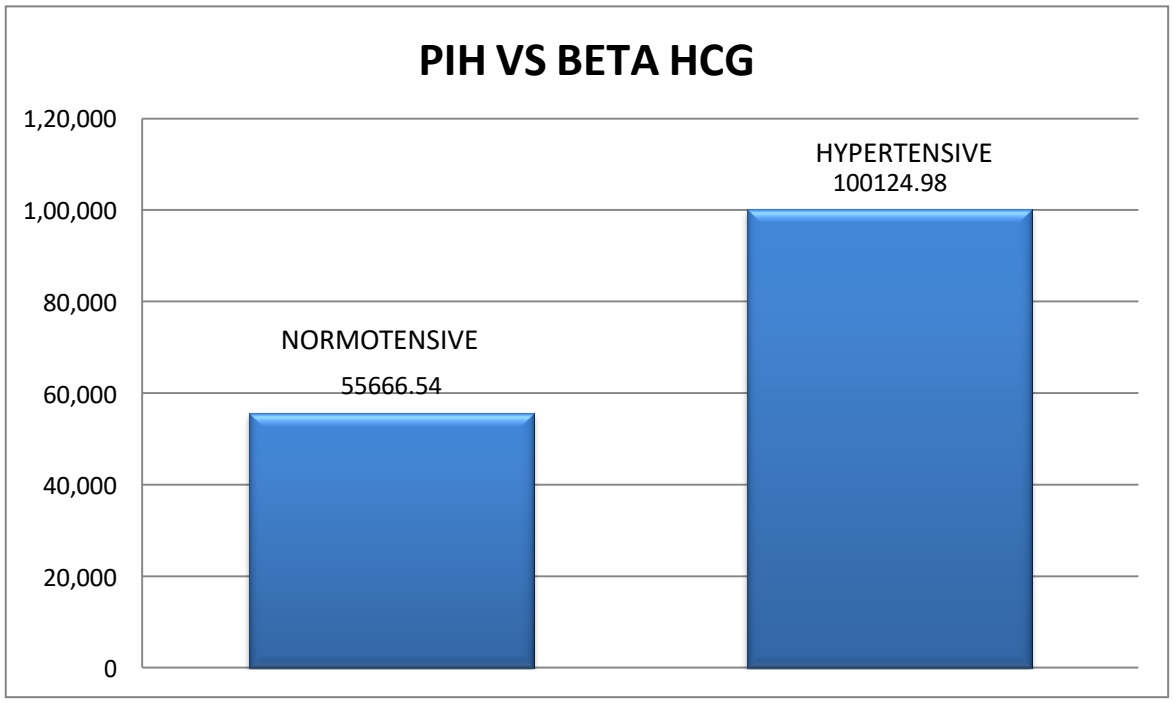


In this present study total number of patients with PIH is 49 (30.06%) among 49 patients preeclampsia was seen in 16 (9.8%) patients , and gestational hypertension in 33 (20.2%) patients of study population.

TABLE NO.10 PREGNANCY INDUCED HYPERTENSION vs BETA HCG

INDEPENDENT T TEST							
BETA HCG		N	Mean	SD	SEM	T VALUE	P VALUE
PIH	NOT PRESENT	114	55666.54	19034.302	1782.726	-11.6	**<0.05**
	PRESENT	49	100124.98	28760.994	4108.713		

FIGURE NO.17 PREGNANCY INDUCED HYPERTENSION vs BETA HCG

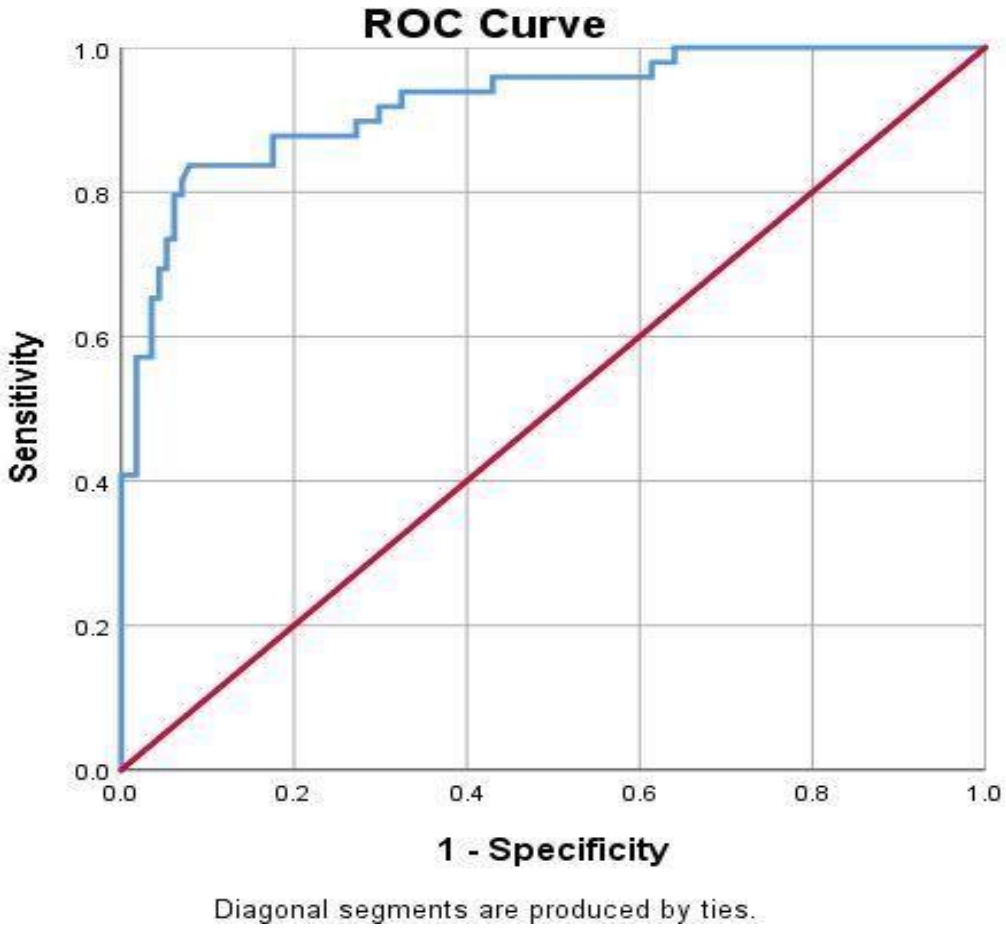


In present study, mean beta HCG level of total study population With no PIH was 55666 and with PIH was 100124. The difference between the groups was found to be statistically significant (p value <0.05).

TABLE NO. 12 **RECEIVER OPERATING CHARACTERISTIC CURVE IN DETECTING PIH with BETA HCG LEVELS.**

Area Under the Curve				
Test Result Variable(s):				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.924	0.023	0.00000	0.878	0.970
The test result variable(s): Primigravida has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.				
a. Under the nonparametric assumption				
b. Null hypothesis: true area = 0.5				

FIGURE NO. 18 **ROC- AREA UNDER THE CURVE -PIH with BETA HCG LEVELS**



Upon constructing ROC curve , Area under the curve (AUC) showed highest correlation with 0.924

TABLE NO 13. PIH with beta HCG levels in range

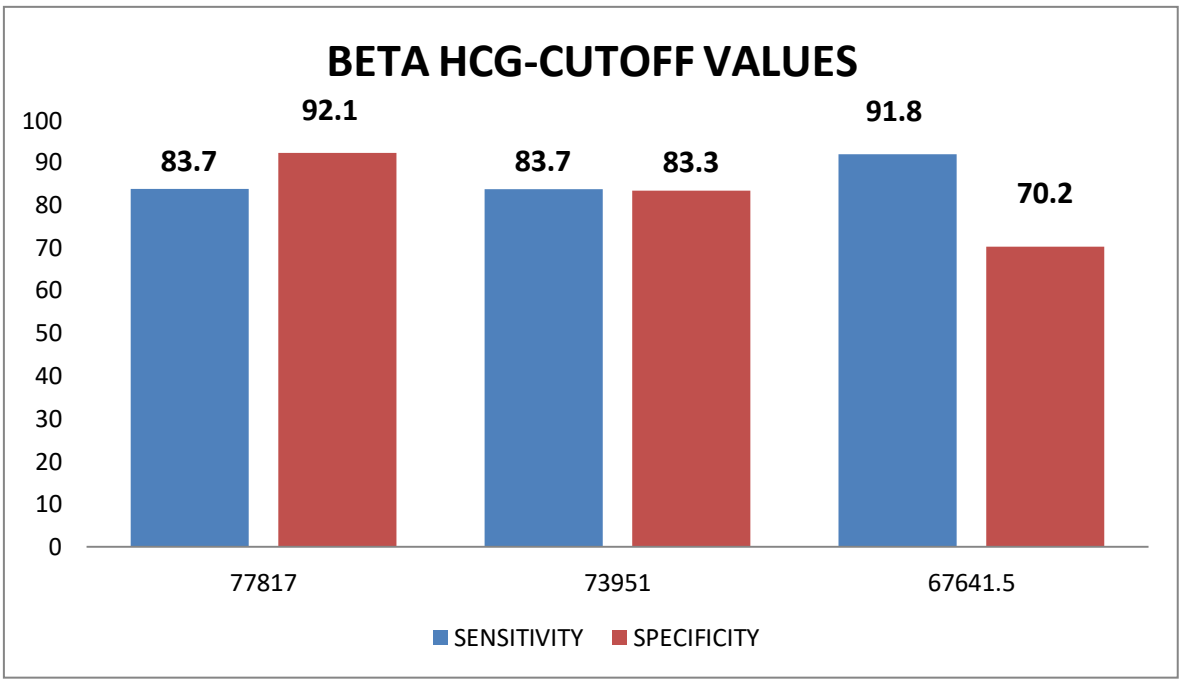
hCG Range	Total no of patients	No of patients with PIH
<60,000	64	2
61,000 to 65,000	17	2
66,000 to 70,000	12	2
71,000 to 75,000	12	1
>76,000	58	42
TOTAL	163	49

Above table shows the total number of patients with different ranges of beta hCG levels. There is an increased probability of PIH in patients whose beta Hcg levels are more than 76,000.

TABLE NO. 14 BETA-HCG LEVEL CUT-OFF VALUES IN DETECTING PIH

POSITIVE IF GREATER THAN OR EQUAL TO BETA-HCG LEVEL (CUT-OFF VALUE)	SENSITIVITY	SPECIFICITY
77817	**83.7**	**92.1**
73951	83.7	83.3
67641.5	**91.8**	**70.2**

FIGURE NO. 19 BETA-HCG LEVEL CUT-OFF VALUES IN DETECTING PIH



Beta HCG cut-off value of 77817 showed 83.7% of sensitivity, and 92.1% of specificity.

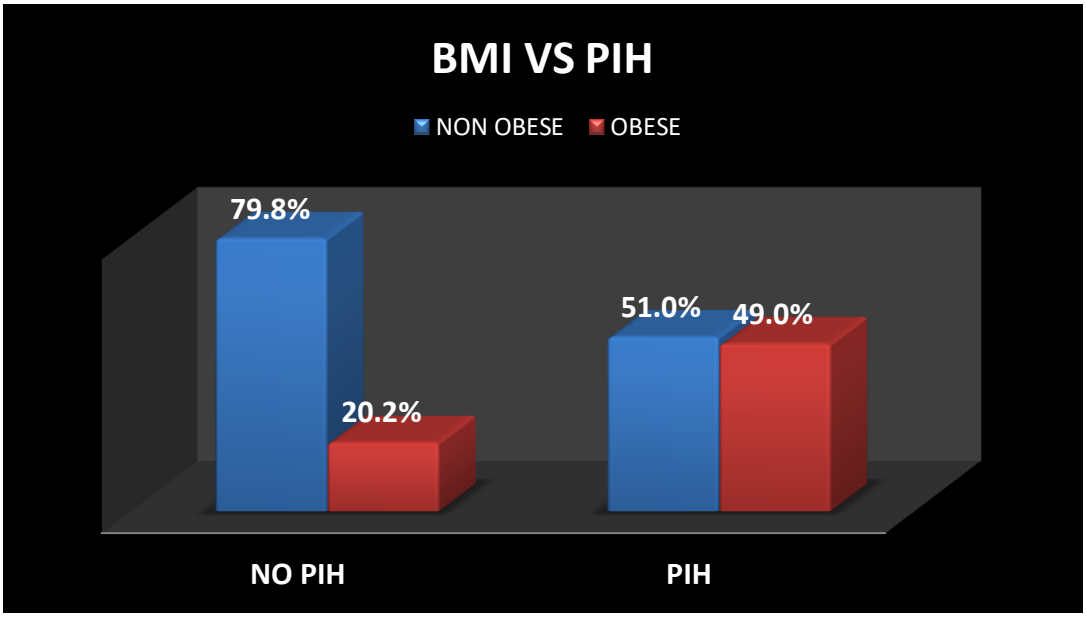
Beta HCG cut-off value of 73951, showed 83.7% of sensitivity and 83.3% of specificity.

Beta HCG cut-off value of 67641.5, showed 91.8% of sensitivity and 70.2% of specificity.

TABLE NO. 15 BMI CATEGORIES VS PREGNANCY INDUCED HYPERTENSION

BMI CATEGORIES	PREGNANCY INDUCED HYPERTENSION			
	NOT PRESENT		PRESENT	
	N	N %	N	N %
NORMAL	91	79.8%	25	51.0%
OBESE	23	20.2%	24	49.0%
Total	114	100.0%	49	100.0%
Chi-square value 13.8 p value-0.0002				

FIGURE NO. 20 BMI CATEGORIES VS PREGNANCY INDUCED HYPERTENSION

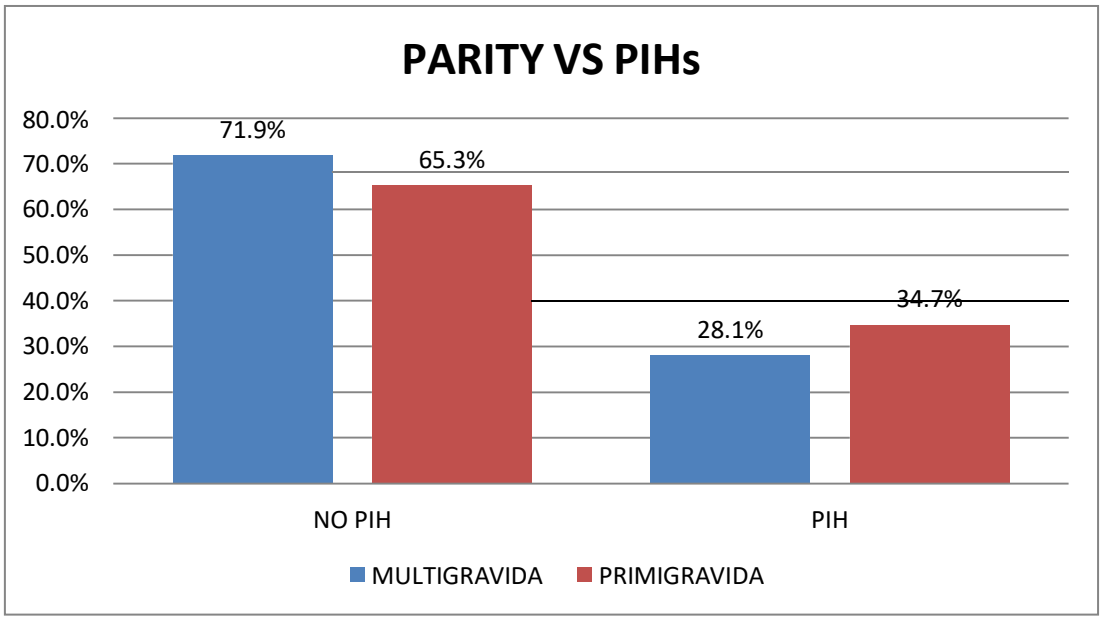


In present study, among normal no PIH category majority were having non obese BMI, on the other hand among PIH category obese and non obese population were almost equally distributed. The difference between the groups was found to be statistically significant (p value < 0.05).

TABLE NO. 16 PARITY VS PIH

PARITY	PIH			
	NOT PRESENT		PRESENT	
	N	ROW N %	N	ROW N %
MULTIGRAVIDA	82	71.9%	32	28.1%
PRIMIGRAVIDA	32	65.3%	17	34.7%
Total	114	69.9%	49	30.1%
Chi-square value .7 p value-0.3				

FIGURE NO 21: PARITY VS PIH



In present study, among primigravida 34.7% had PIH, whereas only 28.1% in Multigravida, though the difference was not found to be significant.

DISCUSSION

The majority of pregnancy-related medical issues, pre-eclampsia, which belongs to the PIH illness group, have an incidence of 5-7%. Although the indications and symptoms of this ailment are widely understood, the aetiology is still a mystery, making disease prevention impossible. Despite the fact that pre-eclampsia often develops in the late second to third trimester. Preeclampsia continues to be a leading cause of maternal and new-born morbidity and death despite advancements in prenatal and neonatal treatment.

The increased interest in this study to incorporate Beta hCG investigations in the early second trimester as early predictors of pregnancy-induced hypertension is due to a range of biological, biochemical, and biophysical indicators implicated in the pathogenesis of pre-eclampsia during the previous 20 years.

Preventive and therapeutic measures can be implemented in time to avoid or postpone issues related to pregnancy-induced hypertension if at-risk women are identified early. Maternal hCG levels in the second trimester are abnormally elevated due to aberrant alterations in placenta development in PIH. Therefore, it could contribute to the prediction of PIH.

In order to reduce maternal and foetal morbidity and mortality, the current study was conducted to assess the accuracy of second-trimester blood beta HCG levels in the prediction of pregnancy-induced hypertension.

This current study is a Hospital based prospective observational study conducted from January 2021 to January 2023 for a period of 2 years. All pregnant (Primigravida/Multigravida with singleton pregnancy) with gestational age of 16 to 20 women with 16-20 weeks period of gestation were included in the study. 163 cases were qualified for the present study.

Most of the participants in the current study were between the ages of 21 and 25 comprising abou 52.8% o(mean age of 24 years). **Murmu S et al.**[15] did a prospective observational study was carried out in Jamshedpur, India's Tata Main Hospital's Department of Obstetrics and Gynecology among 200 antenatal women also showed About 54.34% of the research population, or patients, were between the ages of 20 and 25.

According to latest statistics, majority of the Indians mean age of getting pregnant is 21 to 25years (Married women surveyed in India were first pregnant when they were about 21 years old.) [24] which supports presents study.

In present study, majority study population belonged to Multigravida (69.9%), among primigravida 34.7% had PIH, whereas only 28.1% in Multigravida, though the difference was not found to be significant.

Hernández-Díaz S et al.[25] did a study to investigate whether pre-eclampsia is more common in first pregnancies solely because fewer affected women, who presumably have a higher risk of recurrence, go on to have subsequent pregnancies, showed having pre-eclampsia in one pregnancy is a poor predictor of subsequent pregnancy but a strong predictor for recurrence of pre-eclampsia in future gestations and it is a disease of first pregnancy.

Preeclampsia is thought to affect 5–14% of all pregnancies worldwide[26]. According to reports, the condition is more common in underdeveloped countries (4–18%) [26], Preeclampsia is reported to affect 8–10% of expecting mothers in India.,[5] whereas in present study, preeclampsia was seen in 9.8% of study population which coincides with above data.

In present study, majority study population was in Non-Obese category (73.6%) among 26% of them were overweight. .Mean BMI of the study population was 23.7 $\pm$ 2.6.

In the current study, the bulk of the study population (73.6%) fell into the non-obese category, with 26% of them being overweight. The research population's mean BMI was 23.7. The non-PIH group included a majority of people with non-obesity, whereas the half of the PIH category had obesity. According to **Walsh SW[27]** study, obese women may have a higher chance of having preeclampsia when they get pregnant and are subjected to the additional stresses of pregnancy if their vasculature is inflamed.

In the current study, mean beta HCG levels were 69031 of total study group, 100124 for PIH patients. The mean beta HCG level of the entire study population was lower than the population with PIH. There was a statistically significant difference between the groups.

TABLE NO 17: Co-relation with different studies

STUDY	PLACE	YEAR	MEAN BETA HCG AMONG PIH CASES
Murmu S et al.[15]	INDIA	2020	HIGH
Huma Z et al.[11]	PAKISTAN	2021	HIGH
Yasmin S et al.[12]	PAKISTAN	2022	HIGH
Rathore N et al.[13]	INDIA	2021	HIGH
Sheba Rosatee Victor et al.[16]	INDIA	2019	HIGH
Kaur G et al.[21]	INDIA	2012	HIGH
Dawle SS et al[18]	INDIA	2018	HIGH
Soundararajan P et al.[20]	INDIA	2016	HIGH
PRESENT STUDY	INDIA	2022	HIGH

Our findings show that there is a higher risk of developing pregnancy-related hypertension when second-trimester [beta-hCG] are raised. A potentially cost-effective technique for identifying women at risk for preeclampsia would be second-trimester serum hCG testing. A

screening scheme like this would enable closer monitoring and potential aspirin or calcium supplement interventions.

Above studies, also supports our study findings except a study done in Finland by **Räty R et al.**[23] and another study done in india by **Suman K et al.**[28] , whrere mean beta-hCG levels were equally distributed among both preeclampsia and normal population.

Sorensen et al.[29] showed that women with higher second-trimester hCG levels had a greater risk of preeclampsia and proposed that a second-trimester screening programme may be created to identify women who might be at risk for pregnancy-induced hypertension. Typically, hCG is used in maternal blood screening in the second trimester for foetal aneuploidy and neural tubal abnormalities.

According to ROC curve analysis, the sensitivity and specificity for the current research were 83.7% and 92.1%, respectively, for an early second-trimester beta-hCG concentration over 77817 mIU/ml. Area under the curve (AUC) showed highest positive correlation (0.924).

TABLE NO 18: BETA HCG LEVELS FROM VARIOUS STUDIES

BETA HCG LEVEL VS PIH			
STUDY	SENSITIVITY	SPECIFICITY	CUT OFF (mIU/ml)
Murmu S et al.[15]	51.85%	88.54%	>67750
Suman K et al.[44]	42%	76%	NA
Huma Z et al.[11]	86.5%	96.8%	>100000
Rathore N et al.[13]	82%	93.2%	NA
Sheba Rosatee Victor et al.[16]	90.91%	97.4%	NA
Revankar VM et al.[19]	92.6%	94.9%	>71142
PRESENT STUDY.	83.7%	92.1%	>77817

In present study, Beta HCG cut-off value of 77817 showed 83.7% of sensitivity, and 92.1% of specificity. **Revankar VM et al.[19]** showed almost similar sensitivity and specificity at a cutoff value at >71142 mIU/ml. **Murmu S et al.[15]**showed almost lesser sensitivity but almost equal specificity at lesser cutoff value at >67750mIU/ml. all the above studies supports present study findings.

SUMMARY

1. Majority study population was in 21 to 25 years age group. (Mean age 24 ± 4 years).
2. Majority study population belonged to Multigravida (69.9%).
3. Majority study population was in Non-Obese category (73.6%) among 26% of them were overweight.
4. Mean beta HCG level of total study population was 69031,PIH patients was 1,00,124.
5. Mean beta HCG level among PIH cases were higher than non PIH population.
6. Area under the curve (AUC) showed highest correlation (0.924) for beta HCG in detecting PIH
7. Beta HCG cut-off value of 77817 showed 83.7% of sensitivity, and 92.1% of specificity.

CONCLUSION

One of the main causes of maternal morbidity and death during pregnancy is hypertensive disorders. It is still difficult to find the optimum illness predictor, whose use might considerably change the related morbidity and death. Serum beta-hCG can be used to predict PIH, the tests with accepted level of sensitivity and sensitivity. If this test is made available to women who have PIH risk factors, it would be beneficial.

RECOMMENDATION

The results of our study will aid in the early detection and management of pregnant women who have high blood pressure. Hence lowering the possibility of complication Given that pregnancy-induced hypertension is strongly correlated with increased levels of beta HCG, screening for all cases of ANC may be utilized as a routine, effective screening method for detecting this condition and averting future difficulties.

LIMITATIONS

1. Small sample size: - The small sample size for this study makes it necessary to conduct additional, extensive research when taking into account the significance of -hCG in PIH prediction.
2. Element of bias: - subjective bias, machinery errors in measuring beta HCG levels.
3. The fact that the study was limited to a particular location (single center) may have caused some statistical bias.

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ANNEXER-I

ETHICAL CLEARANCE

B.L.D.E. (DEEMED TO BE UNIVERSITY) IEC/NO-09/2021 Date-22/01/2021

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: The efficacy of second – trimester serum beta HCG levels in the prediction of pregnancy induced hypertension: A Prospective study.

Name of PG student: Dr Kada Vishnu Priya.
Department of Obst/Gynaec

Name of Guide/Co-investigator: Dr Shailaja.R.Bidri, Professor of Obst/Gynaec

DR S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

4

ANNEXER-II

CONSENT FORM

B.L.D.E. (DEEMED TO BE UNIVERSITY)

SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTER

VIJAYAPUR-586103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

I, the undersigned,_____, D/O W/O_____, aged____years, ordinarily resident of_____do hereby state/declare that Dr KADA VISHNU PRIYA of Shri. B. M. Patil Medical College Hospital and Research Centre has examined me thoroughly on_____at_____(place) and it has been explained to me in my own language that I am suffering from_____disease (condition) and this disease/condition mimic following diseases. Further Dr KADA VISHNU PRIYA informed me that he/she is conducting dissertation/research titled "THE EFFICACY OF SECOND-TRIMESTER SERUM BETA HCG LEVELS IN THE PREDICTION OF PREGNANCY INDUCED HYPERTENSION: A PROSPECTIVE STUDY" Under the guidance of Dr SHAILAJA R. BIDRI requesting my participation in the study. Apart from routine treatment procedure, the preoperative, operative, post-operative and follow-up observations will be utilised for the study as reference. The further doctor has informed me that my participation in this study would help in the evaluation of the results of the study, which is a useful reference to the treatment of other similar cases in the near future. Also, I may be benefited in getting relieved of suffering or cure of the disease I am suffering.

The Doctor has also informed me that information given by me, observations made photographs video graphs taken upon me by the investigator will be kept secret and not assessed by the person other than my legal hirer or me except for academic purposes. The Doctor did inform me that though my participation is purely voluntary, based on the information given by me, I can ask any clarification during the course of treatment / study related to diagnosis, the procedure of treatment, result of treatment or prognosis. At the same time, I have been informed that I can withdraw from my participation in this study at any time if I want or the investigator can terminate me from the study at any time from the study but not the procedure of treatment and follow-up unless I request to be discharged. After understanding the nature of dissertation or research, diagnosis made, mode of treatment, I the undersigned Smt_____under my full conscious state of mind agree to participate in the said research/dissertation.

Signature of the patient: Signature of doctor:

Date:

Place:

ANNEXER-III

CASE PROFORMA

SHRI B.M PATIL MEDICAL COLLEGE, HOSPITAL AND. RESEARCH CENTRE, VIJAYAPURA-586103

NAME:

IP No:

Age: Case no:

Address: Occupation:

DO study: Contact No:

1.Obstetric History:

Obstetric score:

Gestational age:

2.Past History:

History of Hypertension: YES. NO

FAMILY HISTORY:

1. HYPERTENSION YES. NO

2. HISTORY OF HYPERTENSION IN FAMILY. YES. NO

3. BLOOD PRESSURE ON ADMISSION

4. Any Other Complications:

GENERAL PHYSICAL EXAMINATION:

PULSE: BLOOD PRESSURE:

TEMPERATURE:

HEIGHT: WEIGHT:

PALLOR: ICTERUS:

CYANOSIS: CLUBBING:

LYMPHADENOPATHY: EDEMA:

CARDIOVASCULAR SYSTEM:

RESPIRATORY SYSTEM:

PER ABDOMEN:

INVESTIGATIONS:

CBC

BLOOD GROUP

URINE ROUTINE

HIV

HbsAG

hCG

USG SCAN

ANNEXER-IV

MASTER CHART

SL NO	Name	Age	GRAVIDA	Gestational age in weeks	BMI	BMI2	Systolic BP	Diastolic BP	Hcg
1	Rani rajamane	21	MULTIGRAVIDA	19	24.56	OVERWEIGHT	110	80	12398
2	Geeta pattar	28	MULTIGRAVIDA	19	20.68	NORMAL	120	80	15416
3	Parvati	19	MULTIGRAVIDA	20	19.47	NORMAL	110	80	19470
4	Prerna Hirolli	22	MULTIGRAVIDA	18	24.88	OVERWEIGHT	110	70	20382
5	Shobha Biradar	24	MULTIGRAVIDA	18	26.4	OBESE	116	70	21480
6	Galpana Manjunath	24	MULTIGRAVIDA	17	21.3	NORMAL	110	76	21690
7	Vidya	22	PRIMIGRAVIDA	19	20.06	NORMAL	116	70	22764
8	Akshata	31	MULTIGRAVIDA	18	26.14	OBESE	126	70	23306
9	Renuka	21	PRIMIGRAVIDA	16	23.74	OVERWEIGHT	110	70	23740
10	Triveni	20	PRIMIGRAVIDA	19	26.9	OBESE	110	70	26848
11	Savitri	20	MULTIGRAVIDA	16	20.96	NORMAL	120	70	27330
12	Arati	18	PRIMIGRAVIDA	19	23.73	OVERWEIGHT	100	70	27440
13	Nagamani	34	MULTIGRAVIDA	16	21.64	NORMAL	110	80	28114
14	Meenaxi	25	MULTIGRAVIDA	18	26.02	OBESE	120	70	30057
15	Vijayalaishmi Dayanand	20	MULTIGRAVIDA	19	27.1	OBESE	100	60	30700
16	Muskar	20	MULTIGRAVIDA	17	24.69	OVERWEIGHT	110	80	31668
17	Jayashree	28	MULTIGRAVIDA	17	20.24	NORMAL	120	90	32571
18	Swati	20	MULTIGRAVIDA	17	21.1	NORMAL	124	80	32608
19	Laxmi chavan	20	MULTIGRAVIDA	20	21.5	NORMAL	106	70	34490
20	Vijayalakshmi Amit Kumar	23	MULTIGRAVIDA	18	24.75	OVERWEIGHT	114	70	35004
21	Kashibai	22	MULTIGRAVIDA	19	20.81	NORMAL	110	70	35290
22	Laxmi	25	MULTIGRAVIDA	18	26.2	OBESE	114	70	35,845
23	Saraswati shivasharan	25	MULTIGRAVIDA	17	24.6	OVERWEIGHT	116	70	38243
24	Savitri	28	MULTIGRAVIDA	16	22.3	NORMAL	110	70	38396
25	Sneha	21	PRIMIGRAVIDA	16	25.54	OBESE	120	82	38430
26	Aayisha	29	MULTIGRAVIDA	18	20.96	NORMAL	114	80	38716
27	Kanchamma	30	MULTIGRAVIDA	19	21.5	NORMAL	120	80	39204
28	Sana	21	MULTIGRAVIDA	19	18.55	NORMAL	100	60	39469
29	Shridevi Chavan	25	PRIMIGRAVIDA	18	23.31	OVERWEIGHT	110	70	39480
30	Ashwini Magond	24	PRIMIGRAVIDA	18	18.83	NORMAL	100	64	39820
31	Mallamma Banari	24	MULTIGRAVIDA	17	24.44	OVERWEIGHT	110	70	41111
32	Rekha	18	MULTIGRAVIDA	20	21.91	NORMAL	130	70	43661
33	Preeti kambale	21	MULTIGRAVIDA	19	19.31	NORMAL	108	60	43761
34	Shobha	21	PRIMIGRAVIDA	20	27.98	OBESE	106	64	43980
35	Chanabasamma	25	MULTIGRAVIDA	18	22.1	NORMAL	110	70	45007
36	Sanjana	27	MULTIGRAVIDA	14	23.27	OVERWEIGHT	116	70	45066
37	Shilpa Sachin	22	MULTIGRAVIDA	18	24	OVERWEIGHT	116	70	45820
38	Uma Kamble	22	PRIMIGRAVIDA	20	23.5	OVERWEIGHT	116	70	45930
39	Shivani Mane	22	MULTIGRAVIDA	19	19.8	NORMAL	126	80	46382
40	Geetha Mahesh	21	PRIMIGRAVIDA	16	22.39	NORMAL	124	80	46905
41	Renuka bandivaddar	26	MULTIGRAVIDA	19	23.4	OVERWEIGHT	124	66	47336
42	Shilpa	21	MULTIGRAVIDA	20	25.96	OBESE	110	70	47881
43	Neelamma	28	MULTIGRAVIDA	16	27.06	OBESE	120	80	51904
44	Sowmya salagundhi	23	MULTIGRAVIDA	18	21.3	NORMAL	110	70	52600
45	Shruti	29	MULTIGRAVIDA	18	21.7	NORMAL	116	70	52780
46	Javeriya	28	MULTIGRAVIDA	19	28.95	OBESE	128	84	54106
47	Sanjana	26	MULTIGRAVIDA	19	26.04	OBESE	106	60	54630
48	Priya	25	MULTIGRAVIDA	16	19.38	NORMAL	130	70	54792
49	Ayisha	28	PRIMIGRAVIDA	16	25.72	OBESE	1116	80	55714
50	Pooja Banatri	20	PRIMIGRAVIDA	17	22.65	NORMAL	110	70	56088
51	Mahadevi Satpur	24	MULTIGRAVIDA	16	23	OVERWEIGHT	100	60	56094
52	Bina Rathod	25	MULTIGRAVIDA	17	21.48	NORMAL	120	70	56246
53	Laxmi	23	MULTIGRAVIDA	19	20.35	NORMAL	124	76	56942
54	Rohini Pawar	21	PRIMIGRAVIDA	18	27.88	OBESE	120	70	57066

54	Rohini Pawar	21	PRIMIGRAVIDA	18	27.88	OBESE	120	70	57066	NO
55	Shilpa Santosh	22	PRIMIGRAVIDA	19	22.5	NORMAL	116	70	57108	NO
56	Vijayalaxmi	26	MULTIGRAVIDA	17	22.83	NORMAL	106	70	57302	NO
57	Deepa Chandra	27	MULTIGRAVIDA	20	24	OVERWEIGHT	126	70	57430	NO
58	Geeta	19	PRIMIGRAVIDA	20	22.1	NORMAL	110	70	57464	NO
59	Laxmi Kumbar	23	MULTIGRAVIDA	17	23.26	OVERWEIGHT	110	70	58094	NO
60	Nagamma Balavant	25	MULTIGRAVIDA	19	19.6	NORMAL	110	70	58404	NO
61	Nagamma kudari	28	MULTIGRAVIDA	18	22.6	NORMAL	124	80	58950	NO
62	Vaishali Kungadali	18	PRIMIGRAVIDA	19	24.03	OVERWEIGHT	110	70	59040	NO
63	Vijayalaxmi Kadagol	25	MULTIGRAVIDA	19	22.47	NORMAL	130	74	59906	NO
64	Kaveri Jaideep	28	MULTIGRAVIDA	18	23.68	OVERWEIGHT	120	70	59906	NO
65	Renuka Adavi	23	MULTIGRAVIDA	18	22.63	NORMAL	120	74	61908	NO
66	Rajashree Chanappa	22	MULTIGRAVIDA	19	25.42	OBESE	114	80	62408	NO
67	Savita Pujari	20	MULTIGRAVIDA	17	23.5	OVERWEIGHT	110	70	63450	NO
68	Sujata	20	MULTIGRAVIDA	20	18.32	NORMAL	126	72	63701	YES
69	Renuka	22	MULTIGRAVIDA	18	23.74	OVERWEIGHT	116	70	63704	NO
70	Rukamini Algali	25	MULTIGRAVIDA	19	21	NORMAL	110	80	63720	NO
71	Prabhavati biradar	28	MULTIGRAVIDA	19	22.6	NORMAL	110	70	63920	NO
72	Shruthi	23	MULTIGRAVIDA	38	23.94	OVERWEIGHT	110	76	64088	NO
73	Renuka bandivaddar	26	MULTIGRAVIDA	19	22	NORMAL	124	70	64370	NO
74	Bhagyasri	24	MULTIGRAVIDA	20	22	NORMAL	110	80	64721	NO
75	Sowmya Pattar	23	PRIMIGRAVIDA	18	21.8	NORMAL	118	80	64830	NO
76	Mallamma Hullur	25	MULTIGRAVIDA	16	22.83	NORMAL	128	70	65074	NO
77	Laxmi kore	21	MULTIGRAVIDA	17	22.7	NORMAL	110	64	65080	NO
78	Saraswati Piranji	20	PRIMIGRAVIDA	19	22.58	NORMAL	110	60	65094	NO
79	Sukanya balage	19	MULTIGRAVIDA	18	21	NORMAL	134	80	65273	NO
80	Saraswati shivasharan	24	MULTIGRAVIDA	17	22.4	NORMAL	120	84	65317	NO
81	Sneha	21	PRIMIGRAVIDA	18	28.3	OBESE	130	80	65521	YES
82	Sonali Kodahonna	22	MULTIGRAVIDA	16	25.07	OBESE	120	76	66590	NO
83	Shilpa Nagasure	28	MULTIGRAVIDA	19	25.41	OBESE	110	60	67097	NO
84	Anuradha	26	PRIMIGRAVIDA	16	25.72	OBESE	100	70	67481	NO
85	Devaki	19	MULTIGRAVIDA	20	27.06	OBESE	126	80	67802	YES
86	Geeta Lanagi	30	MULTIGRAVIDA	19	24.23	OVERWEIGHT	120	70	68035	NO
87	Mahadevi Hennappa	35	MULTIGRAVIDA	16	22.65	NORMAL	120	70	68044	NO
88	Kanchava Vittal	21	PRIMIGRAVIDA	18	25.74	OBESE	114	70	68046	NO
89	Prema	25	MULTIGRAVIDA	19	22.36	NORMAL	130	84	68992	YES
90	Laxmi	19	PRIMIGRAVIDA	18	24	OVERWEIGHT	114	80	68994	NO
91	Shruti Bajantri	28	MULTIGRAVIDA	18	21.72	NORMAL	100	60	69250	NO
92	Anjum Hawaldai	26	MULTIGRAVIDA	18	24.36	OVERWEIGHT	106	70	69304	NO
93	Shilpa Jadhav	22	MULTIGRAVIDA	16	19.8	NORMAL	124	70	69730	NO
94	Bhagya Walker	23	MULTIGRAVIDA	18	23.74	OVERWEIGHT	140	70	71340	NO
95	Swati Anil	24	MULTIGRAVIDA	18	21.36	NORMAL	100	60	72004	NO
96	Gausiya Darga	26	MULTIGRAVIDA	16	22	NORMAL	110	66	72068	NO
97	Laxmi Billu	28	MULTIGRAVIDA	19	21	NORMAL	110	70	72410	NO
98	Savita	32	MULTIGRAVIDA	19	22.84	NORMAL	114	70	72447	NO
99	Laxmi	19	PRIMIGRAVIDA	16	19.5	NORMAL	110	76	72490	NO
100	Shivaleela Kali	23	MULTIGRAVIDA	18	21.45	NORMAL	110	70	73306	NO
101	Bharati	25	MULTIGRAVIDA	16	20.6	NORMAL	130	70	73763	YES
102	rajini	36	MULTIGRAVIDA	16	20.6	NORMAL	130	70	73763	YES
103	Jyothi Handagi	22	MULTIGRAVIDA	20	25.63	OBESE	130	70	73809	NO
104	Jasmeen	25	PRIMIGRAVIDA	19	23	OVERWEIGHT	110	60	74093	NO
105	Kanchana Suthar	21	PRIMIGRAVIDA	18	23	OVERWEIGHT	110	74	74094	NO
106	Kashibai	28	MULTIGRAVIDA	19	24.37	OVERWEIGHT	114	70	75092	NO
107	Jayashree	25	PRIMIGRAVIDA	19	25.72	OBESE	120	80	76110	NO
108	Kashibai kotyal	36	MULTIGRAVIDA	19	25.3	OBESE	136	74	76278	NO

109	Pratibha Mucchandi	22	PRIMIGRAVIDA	18	22.4	NORMAL	110	70	76404	NO
110	Shivaleela Chalawadi	27	PRIMIGRAVIDA	18	22.27	NORMAL	110	70	76811	NO
111	Mahadevi Satpur	35	MULTIGRAVIDA	16	21.06	NORMAL	112	78	77063	NO
112	Neelamma Nellagi	20	PRIMIGRAVIDA	18	25	OBESE	116	70	77406	NO
113	Laxmi Chavan	21	MULTIGRAVIDA	17	19.98	NORMAL	120	70	77530	NO
114	pooja	24	PRIMIGRAVIDA	17	23.7	OVERWEIGHT	136	80	78104	YES
115	rani	37	PRIMIGRAVIDA	17	23.7	OVERWEIGHT	136	80	78104	NO
116	Sujata	27	PRIMIGRAVIDA	19	28.05	OBESE	130	86	78447	YES
117	Nagamma	21	MULTIGRAVIDA	18	21.99	NORMAL	120	74	79102	NO
118	priyanka	22	PRIMIGRAVIDA	16	29.3	OBESE	140	90	79106	YES
119	sudha	35	MULTIGRAVIDA	17	21.72	NORMAL	130	84	79115	YES
120	Geeta	23	MULTIGRAVIDA	18	20.93	NORMAL	140	80	79460	YES
121	Drakshayani chalawadi	22	PRIMIGRAVIDA	16	22.45	NORMAL	110	60	80604	NO
122	Syrita	23	PRIMIGRAVIDA	19	28.3	OBESE	140	78	80814	YES
123	neela	24	MULTIGRAVIDA	17	25.73	OBESE	130	86	81806	YES
124	Bharathi	28	MULTIGRAVIDA	17	22.41	NORMAL	104	80	82404	NO
125	Sana	30	MULTIGRAVIDA	16	21.63	NORMAL	130	90	83044	YES
126	Kanchana	21	MULTIGRAVIDA	18	24.06	OVERWEIGHT	134	86	83604	YES
127	Mehisha Chavan	21	PRIMIGRAVIDA	19	24.88	OVERWEIGHT	110	70	85390	NO
128	Savitri Shinde	24	MULTIGRAVIDA	19	23.82	OVERWEIGHT	130	86	86005	YES
129	Vanita	22	PRIMIGRAVIDA	16	27.43	OBESE	146	94	86124	YES
130	Laxmi	26	MULTIGRAVIDA	17	26.34	OBESE	130	84	86304	YES
131	Nagamma	28	MULTIGRAVIDA	17	22.53	NORMAL	130	90	86742	YES
132	Megha	20	PRIMIGRAVIDA	19	20.32	NORMAL	110	70	87040	NO
133	Akshata	21	MULTIGRAVIDA	18	21.83	NORMAL	100	70	87430	NO
134	Sonali	22	MULTIGRAVIDA	18	24	OVERWEIGHT	110	70	88053	YES
135	Faranaz	26	MULTIGRAVIDA	18	20.57	NORMAL	130	80	91247	YES
136	Savitri Malli	33	MULTIGRAVIDA	19	24	OVERWEIGHT	130	90	92076	YES
137	Bhagyashree	25	PRIMIGRAVIDA	20	24.23	OVERWEIGHT	134	86	96018	YES
138	priyanka	22	PRIMIGRAVIDA	16	28.03	OBESE	140	80	96427	YES
139	Kanchan	26	MULTIGRAVIDA	17	24.3	OVERWEIGHT	136	94	96632	YES
140	Savita	31	MULTIGRAVIDA	19	29.6	OBESE	140	80	96994	YES
141	Kaveri	22	MULTIGRAVIDA	20	24.46	OVERWEIGHT	128	80	97451	YES
142	Geeta	25	MULTIGRAVIDA	19	27.94	OBESE	130	70	97920	NO
143	Geeta	25	MULTIGRAVIDA	19	27.94	OBESE	130	70	97920	NO
144	Pavitra	23	MULTIGRAVIDA	20	26.37	OBESE	130	96	100124	YES
145	Rakshita dadamani	20	PRIMIGRAVIDA	19	23.8	OVERWEIGHT	138	94	100567	YES
146	Afsha	27	MULTIGRAVIDA	17	23.96	OVERWEIGHT	130	90	100748	YES
147	Umashree godehar	25	PRIMIGRAVIDA	19	22.55	NORMAL	110	70	104007	YES
148	Laxmi	20	MULTIGRAVIDA	16	26.9	OBESE	126	70	110450	YES
149	Veena	19	PRIMIGRAVIDA	17	30.2	OBESE	120	86	112306	YES
150	Ratna	27	MULTIGRAVIDA	16	24.3	OVERWEIGHT	138	90	115306	YES
151	Choudamma	23	PRIMIGRAVIDA	18	29.41	OBESE	148	100	115380	YES
152	shobha	26	MULTIGRAVIDA	19	26.3	OBESE	134	90	124905	YES
153	Geeta	23	PRIMIGRAVIDA	18	29.82	OBESE	140	96	125508	YES
154	Roopa	23	MULTIGRAVIDA	18	24.4	OVERWEIGHT	110	70	127030	YES
155	Nagamma	21	MULTIGRAVIDA	20	27.9	OBESE	130	84	132987	YES
156	bhavani	22	PRIMIGRAVIDA	17	26.71	OBESE	138	94	134504	YES
157	Kavita Pratap	28	MULTIGRAVIDA	20	25.56	OBESE	146	100	135906	YES
158	Prabhavati	28	PRIMIGRAVIDA	18	22.8	NORMAL	130	80	144802	YES
159	jyothi	31	MULTIGRAVIDA	19	29.04	OBESE	140	88	149302	YES
160	Bismilla	31	PRIMIGRAVIDA	16	21.36	NORMAL	130	90	154737	YES
161	Sonika	20	PRIMIGRAVIDA	17	25.4	OBESE	120	86	156405	YES
162	Mamata	29	MULTIGRAVIDA	18	23.69	OVERWEIGHT	144	90	156703	YES
163	sunita	30	MULTIGRAVIDA	20	28.07	OBESE	152	96	165345	YES