PREDICTION OF PREGNANCY INDUCED HYPERTENSION AND ITS SEVERITY BY ELEVATED SERUM BETA HCG LEVEL IN SECOND TRIMESTER OF PREGNANCY

Dissertation submitted to

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In partial fulfilment of the requirements for the award of the degree of

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APRIL 2015

DECLARATION

I solemnly declare that this dissertation titled **"Prediction of Pregnancy Induced Hypertension and its Severity by Elevated Serum Beta HCG Level in Second Trimester of Pregnancy"** was prepared by me in the Institute of Obstetrics and Gynaecology, Egmore, Chennai-600008 Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai under the guidance and able supervision of Prof. Dr.Usharani, M.D., D.G.O, DNB (O&G), Professor ,Institute of Obstetrics and Gynaecology, Egmore, Chennai - 600 008.This dissertation is submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfilment of the university requirements for the award of the degree of M.S (OG) Obstetrics and Gynaecology.

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CERTIFICATE

This is to certify that the dissertation titled **"Prediction of Pregnancy Induced Hypertension and its Severity by Elevated Serum Beta HCG Level in Second Trimester of Pregnancy"** submitted by Dr.Preetha.G appearing for M.S (OG) degree examination in April 2015, is a bonafide record of work done by her under my guidance and supervision in partial fulfilment of requirement of the Tamil Nadu Dr.M.G.R.Medical University, Chennai. I forward this to the Tamil Nadu Dr.M.G.R.Medical University, Chennai.

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INTRODUCTION

Pregnancy induced hypertension commonly affects 10-15 % of pregnant women.So the constant endeavour for obstetricians to identify the risk factors and its complications.So it is important to predict the preeclampsia then prevention will follow routinely.Abnormal placentation with impaired trophoblastic invasion is the initiating factor[18].In the mid trimester due to the immunological changes in the trophoblasts cause secretory response leads to rise in beta HCG levels.

In the first trimester there is a drop in blood pressure because of the active vasodilatation,and the normal physiological change in blood pressure during pregnancy is mediated through the action of local mediators like prostacyclin and nitric oxide.The fall in blood pressure primarily affects the diastolic pressure and reduction of 10 mm Hg is usual by 13–20 weeks gestation. Blood pressure continues to drop until 22–24 weeks till the nadir level then there is a gradual rise in blood pressure until term when pre-pregnancy levels are attained.Soon after delivery, blood pressure usually drops then rises over the first five days of

postnatal period.Even women whose blood pressure was normal throughout pregnancy may have transient rise in blood pressure in the early post partum period because of the vasomotor instability.

HYPERTENSION IN PREGNANCY

It is diagnosed by an absolute rise in blood pressure or from a relative rise above the blood pressure at the time of booking. The convention for the absolute value is a systolic blood pressure 140 mm Hg or a diastolic blood pressure 90 mm Hg. However it should be accepted that blood pressure is gestation related. A diastolic blood pressure of 90 mm Hg is 3 standard deviations above the mean for mid pregnancy, 2 SD at 34 weeks, and 1.5 SD at term.

The relative increase in blood pressure point out that a increase in systolic pressure of 30 mm Hg or increase in diastolic pressure of 15 mm Hg above blood pressure at the time of initial examination. Blood pressure must be increased on at least two occasions and the blood pressure should be taken with the woman seated measured 6 hours gap with the proper cuff size. Late in the second trimester and in the third

trimester, venous return may be blocked by the enlarged uterus and for the supine position blood pressure should be measured with the woman in left lateral side[15].

Preeclampsia complications affect about 4-5%of pregnancies, and other hypertensive disease present about 8-10 % of pregnancies. Hypertensive disorders in pregnancy leads on to higher rates of perinatal mortality, and severe morbidity mainly in patients with severe preeclampsia, eclampsia, haemolysis, increased liver function test and low platelet count.

Preeclampsia is a pregnancy specific hypertensive disorder related with significant perinatal mortality and morbidity.With the increasing kind of the disease process many complications as well as the perinatal mortality have declined over the past few years. In the developing countries, the rates of mortality and morbidity still at a higher level .Hence diagnosis of the disease process at correct time helps to prevent the disease progression and its mortality. Since prevention is better than cure, the prediction of PIH at earlier pregnancy period helps to prevent the progression of preeclampsia and its morbidity and mortality.

Prevention of disease has three aspects and primary prevention by avoiding the occurrence of a disease, secondary prevention by breaking of the disease process before emergence of obvious clinical disease and tertiary prevention by avoidance of complications caused by disease process and is almost similar to the treatment.

PRIMARY PREVENTION

Primary prevention is by the modification of risk factors and identifying underlying medical diseases like chronic hypertension, diabetes, renal disease, obesity (BMI>35kg/m^2),maternal low birth weight, polycystic ovarian syndrome, migraine, collagen vascular diseases, uncontrolled hyperthyroidism, factor V leiden deficiency, activated proteinC defiency and antiphospholipid antibodies. Although it is recommended to modify the risk factors for preeclampsia it would be possible only in a small number of cases.

But the relative risk of preeclampsia in high risk situations as suggested by Duckitt and Harrington, the early diagnosis of preeclampsia with timely referral for the higher institute care using PRECOG guidelines will help in their

appropriate management and prevent them going to severe preeclampsia and its complications.

SECONDARY PREVENTION

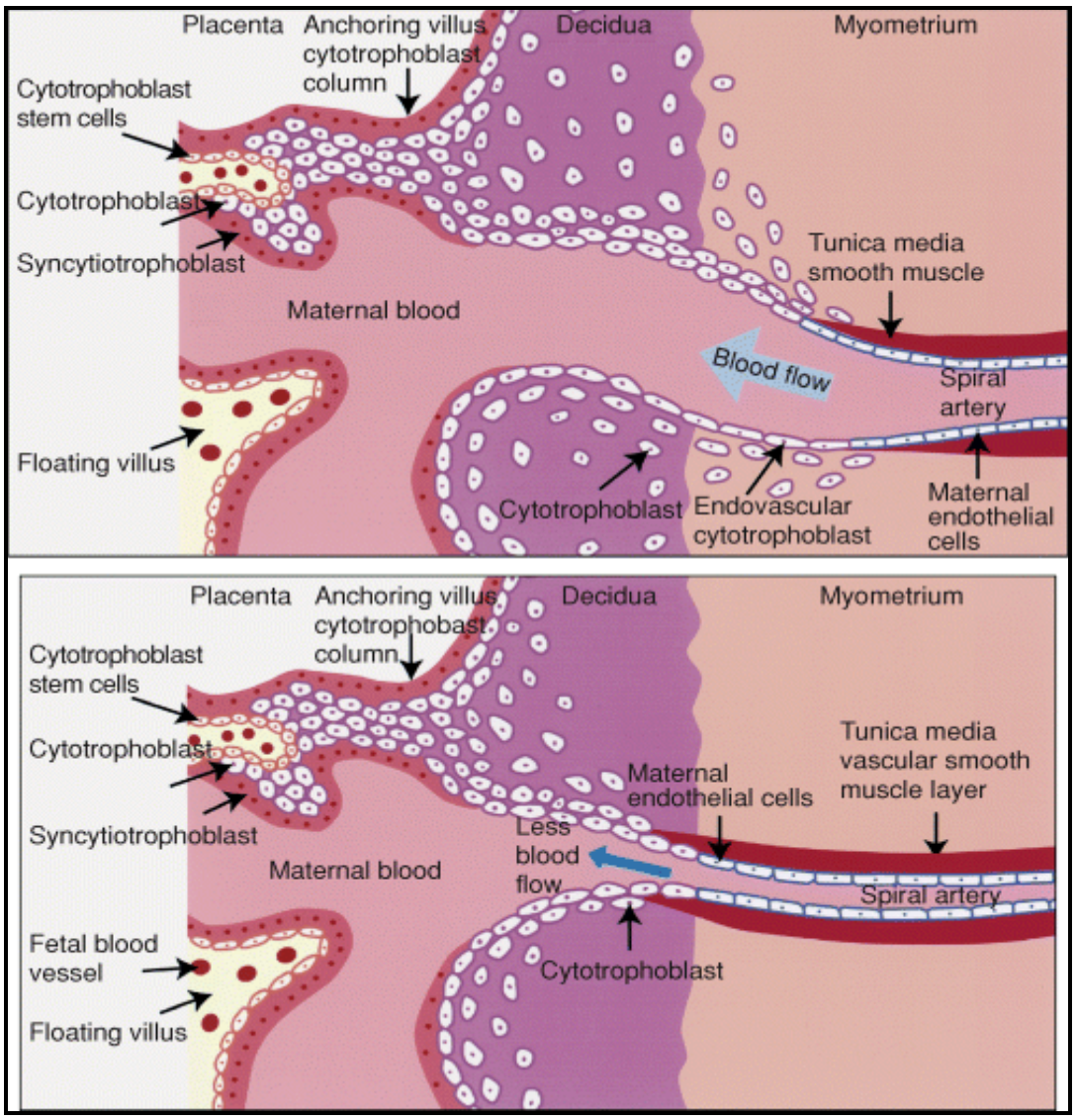
Secondary prevention of a disease is possible only

When the accurate knowledge of pathogenesis and genetics available,

Availability of method for early identification and means of intervention and modification of the pathophysiology of disease process.

Hence screening methods with criteria including proper history taking , examination and laboratory values have been used as the methods of secondary prevention of the preeclampsia.

Abnormal placentaion with the impaired trophoblastic invasion is the initiating factor for preeclampsia. During mid trimester of pregnancy the immunological changes in the trophoblasts and secretory response leads to a rise in beta HCG levels.



In the second trimester of pregnancy serum beta HCG levels helps to predict pregnancy induced hypertension and hence prevention will follow routinely. Serum Beta HCG levels are measured from gestational age 13 to 20 weeks and they are followed till term and postnatal for prediction of pregnancy induced hypertension and its complications.

AIM AND OBJECTIVE

1) To predict the pregnancy induced hypertension by elevated Beta HCG levels in the second trimester of pregnancy.

2) To assess the severity of PIH correlated with the elevated levels of Beta HCG.

3) Secondary outcome to study the prediction of PIH based on the parameters like Age, Parity, Gestational Age ,Body Mass Index and the Past History of PIH.

REVIEW OF LITERATURE

HYPERTENSIVE DISORDERS IN PREGNANCY

1) Chronic hypertension

2) Gestational hypertension

3) Preeclampsia

4) Preeclampsia superimposed on chronic hypertension

CHRONIC HYPERTENSION

It affects 3–5% of pregnancies, incidence being higher in 30-40yrs of age. It is diagnosed by with the past history of hypertension in pre pregnancy period or an increased blood pressure > 140/90 mm Hg before 20 weeks gestation and the occurrence of hypertension before pregnancy.

GESTATIONAL HYPERTENSION

Hypertension occurring after 20 weeks of gestational period in the previously normal woman without significant proteinuria or other features of preeclampsia is known as gestational or pregnancy induced hypertension. It occurs in

6–7% of pregnancies and disappears by 6 weeks of postpartum period. The risk of superimposed preeclampsia is 15–25% but this risk is depends upon the gestational period at which the hypertension develops. But the risk falls to10% when gestational hypertension is diagnosed in the third trimester of pregnancy.

PREECLAMPSIA

Preeclampsia usually occurs after 20 weeks gestation and it is a multi organ involvement disorder. It consists of triad of hypertension, oedema, and proteinuria, also it includes an gestational elevation of blood pressure together with 0.3 g/dl proteinuria per 24 hours. Nowadays oedema is not included in the criteria for the diagnosis

PATHOGENESIS

Abnormal placentation

In the first trimester of healthy pregnancy the trophoblast normally invades the uterine decidua layer the inner layer of the myometrium. The interstitial trophoblast surrounds the arteries and endovascular trophoblast penetrates the spiral artery lumen[19].This migration will

convert the small calibre muscular arteries into large capacitance low resistance vessels in the intervillous space[23].

Development of uteroplacental vessels proceeds in two stages :

1) Before 12 weeks post fertilisation upto the interface between decidua and myometrium

2) Between 12-16 weeks and involves invasion of intra myometrial segments of spiral arteries

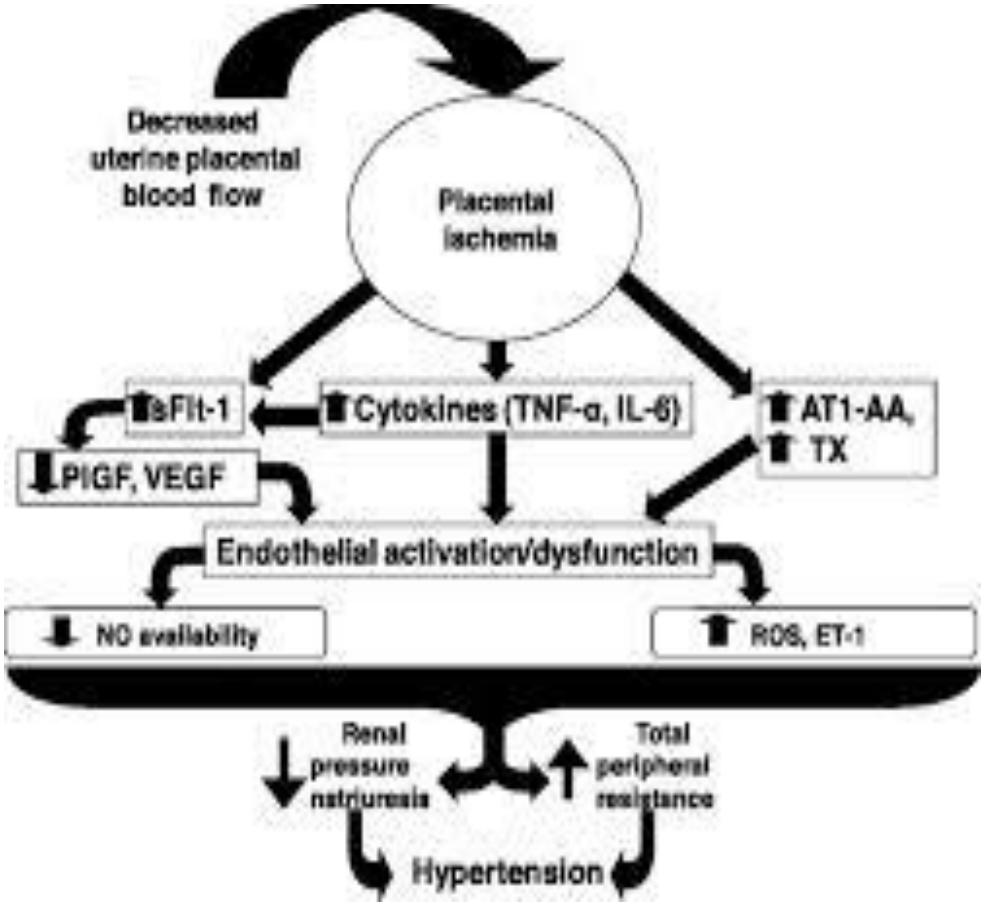
These changes starts occurring in the first trimester and completed in the second trimester of pregnancy when another wave of trophoblast migration alters the myometrial segments of the arteries.

In preeclampsia these vascular alterations do not occur or they are limited to vessels in the decidua. In addition trophoblastic invasion is incomplete, shallow and it's deeper myometrial arterioles do not lose their endometrial lining and musculo elastic tissue .

The secondary stage of preeclampsia involves the endothelial dysfunction and vasospasm .Endothelial

dysfunction is a central feature in preeclampsia resulting in vascular reactivity ,activation of coagulation cascade and loss of vascular integrity.Biochemical markers of endothelial dysfunction such as plasma fibronectin and thrombomodulin are elevated in preeclamptic patients.

Several angiogenenic and anti angiogenenic substances are involved in the placental vascular development ,imbalance in circulating proangiogenic (VEGF,PGF) and antiangiogeneic factors contribute to pathogenesis.



RISK FACTORS FOR PREECLAMPSIA[21]

- Parity
- Age>35 years
- History of preeclampsia in previous pregnancy
- Pre-existing medical disorders
    - Hypertension
    - Diabetes mellitus
    - Obesity
    - Renal disease
    - Vascular disease
    - Autoimmune disease
- Low socioeconomic status
    - Obstetric factors
    - Multiple gestation
    - Hydatidiform mole
    - Hydrops foetalis

- Abnormal uterine artery Doppler at 18-24 weeks

❖ Interval from last pregnancy >10 years

SIGNS AND SYMPTOMS

❖ Headache ,visual disturbances

❖ Epigastric or right upper quadrant pain

❖ Oliguria <500ml urine in 24 hours

❖ Thrombocytopenia

❖ Significant protenuria >5g/24 hour

❖ Convulsions (cerebral oedema)

LABORATORY TESTS IN PREECLAMPSIA

❖ Urinalysis >1+on dipstick,

24 hours urinary protein for quantification of proteinuria

❖ Complete blood count – Thrombocytopenia <1,00,000cells /mm^3

- Renal parameters: elevated serum creatinine >1.2mg/dl associated with reduced creatinine clearance and ‘‘normal’’ values indicate renal impairment.

- Liver function tests - Increase transaminase concentrations and increase LDH >800IU/L

- Serum Uric acid - Like blood urea this value is also lower in normal pregnancy due to increased clearance ,it is raised in preeclampsia resulting in hyperuricaemia

- Coagulation studies -platelet count, prothrombin time, partial thromboplastin time, fibrin degradation products and fibrinogen levels to exclude disseminated intravascular coagulation

- Plasma and urinary metanephrines , serum renin and aldosterone levels to exclude other causes of hypertension

COUNSELLING

Nearly half of pregnancies are unplanned and hence pre pregnancy counselling is not possible for all patients. Women with chronic hypertension should be assessed before

pregnancy. Hence exclusion of the secondary causes of hypertension like vascular ,renal and endocrine causes and the control of hypertension before pregnancy explain the patients regarding the risk of preeclampsia superimposed and alteration of drugs taken before and their need to change during first trimester, continuing till term and to continue in the postpartum.

General maternal care, blood pressure measurement and the search for proteinuria forms the basis of antenatal screening of all pregnant women for preeclampsia. If ‘‘white coat’’ hypertension is suspected, ambulatory monitoring will be helpful as in the non-pregnant population. Women who have been defined as at increased risk of preeclampsia are monitor more closely, often in a specialised obstetric clinic. Early risk assessment involves Doppler ultrasound evaluation of the uterine arteries around the time of the foetal anomaly scan at 20–22 weeks.

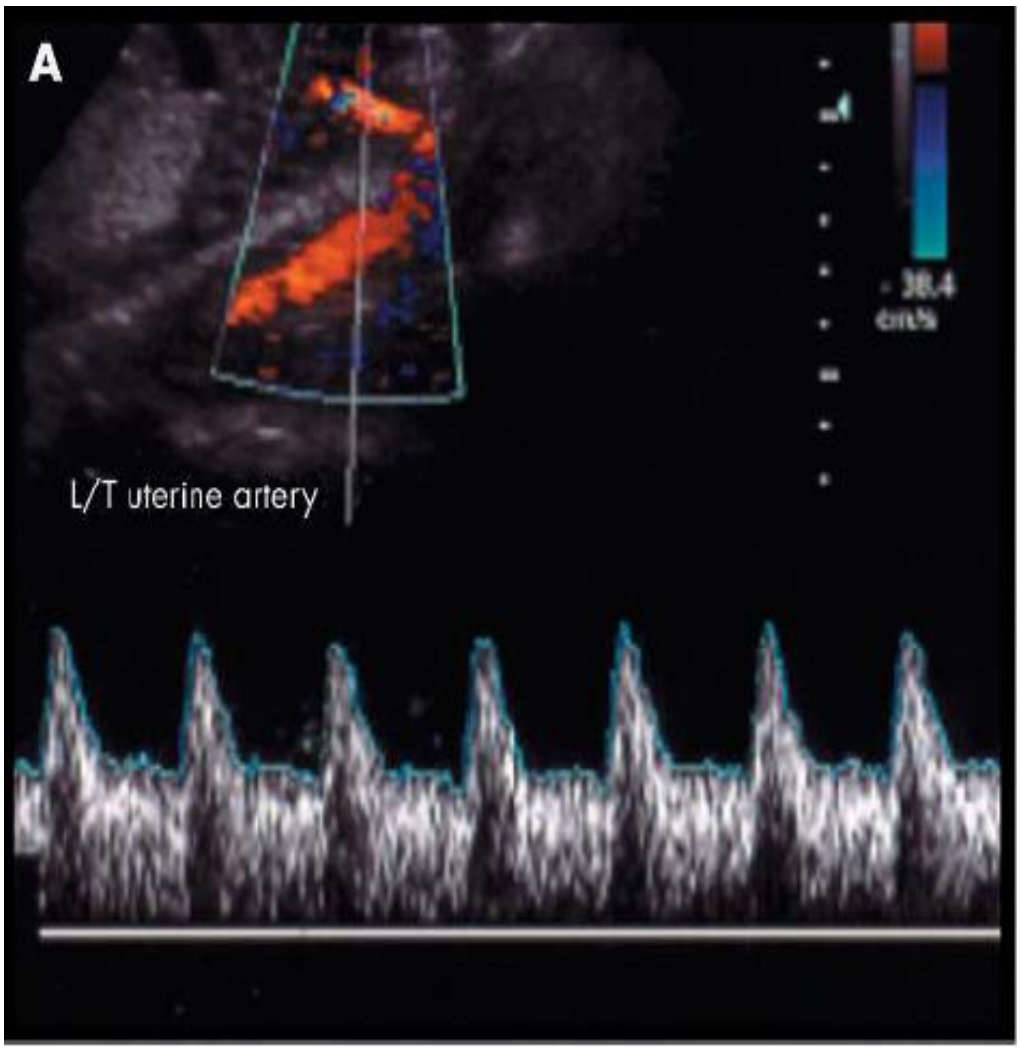
Increasing blood pressure, deranged blood results, and the development of significant proteinuria require enhanced surveillance. Greater than 1+ proteinuria on dip stick needs to be quantify with a 24 hour urine collection or

protein:creatinine ratio. The onset of significant proteinuria in the presence of renal disease is among the best indicators of superimposed preeclampsia. According to the maternal symptoms and clinical result and the growth nature of foetus a woman can be referred to a day appraisal unit for the routine outpatient assessment.

Doppler evaluation of uterine arteries, Pulsed wave analysis and colour flow Doppler ultrasound assessment of the uterine arteries can divulge the augmented placental vascular resistance which result from complete or partial failure of trophoblast invasion of the spiral arteries.

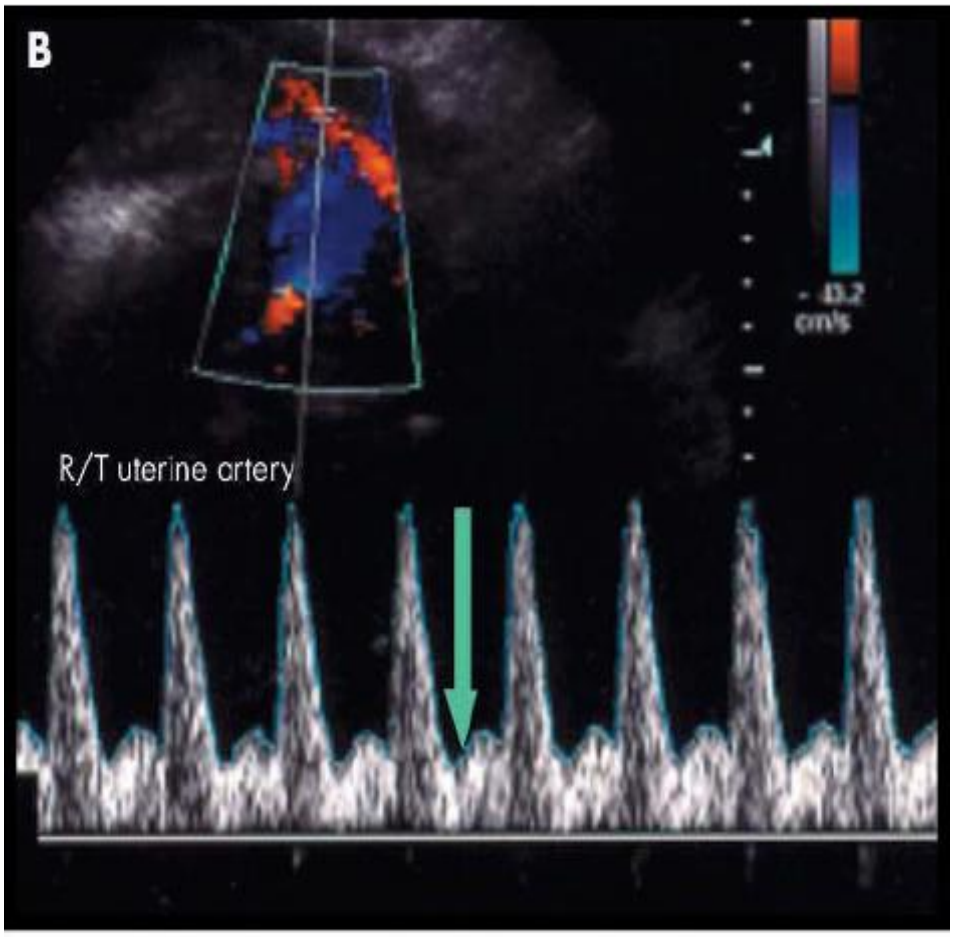
Besides to the amount of the resistance index, the presence of an abnormal uterine artery waveform also identified. Uterine artery Doppler is presented to high risk women at between 20–24 weeks of pregnancy and has useful prognostic control. For the woman with normal uterine Doppler evaluation at 20–24 weeks consider as low risk, whereas those with abnormal Doppler have about a 20% risk of developing preeclampsia and needs more attention.

DOPPLER STUDY OF UTERINE ARTERY



Normal Uterine Artery Doppler flow form showing low resistance, high velocity wave form indicating low risk pregnancy. It is usually done at 16-20 weeks of pregnancy.

DOPPLER STUDY OF UTERINE ARTERY



Abnormal flow velocity wave form with early diastolic notch indicates superimposed preeclampsia devel oping in women with chronic hypertension. It has high resistance and low velocity wave form.

- Foetal surveillance

- Women with both chronic hypertension and preeclampsia are at danger of IUGR. Such women are monitored by regular foetal ultrasound scans to measure the foetal growth, liquor volume, and umbilical artery blood flow. When preeclampsia is severe and there is important risk of delivery before 34 weeks gestation, intramuscular steroids like dexamethasone or betamethasone are given to the mother to improve foetal outcome.

Over many years different laboratory tests that has been used for the prediction of preeclampsia .These tests are used as predictors when preeclampsia occurs in a full fledged form. Thus this explains the fact why screening in the first trimester is unlikely to make results as in the second trimester. The present use of several markers in the screening process reflects that various aspects of the disease processes thus increasing sensitivity and specificity of the disease .Finally the screening tests used to predict needs to be simple, fast and cost effective. Several angiogenic factors ,antiangiogeneic factors and proteomics studies are used as

promising predictors that can be used in the future .Hence these promising tests are not used routinely since due to its high cost.

- Preeclampsia is one of types of hypertension in pregnancy that occurs in 4-8% of all pregnancies.

- Preeclampsia/eclampsia complex is responsible for nearly half of the maternal deaths in India. Infants born to women of preeclampsia have an increased risk of complications compared to other pregnant women. Most dreaded and avoidable complication of infants of preeclampsia is prematurity due to premature termination of pregnancy. About 15% of preeclampsia occurs in early pregnancy before foetal maturity and hence preterm births occur only in about 15% of all pregnancies .

- Clinical history, examination findings ,laboratory tests and other tests

have been used to predict preeclampsia .In order to predict the disease early in first trimester and early second trimester seems sensible related to the impaired

uteroplacental tissue adaptation that is responsible for established manifestation of the disease process.

Numerous clinical,biochemical and biophysical tests in early or mid pregnancy have been proposed for the prediction of preeclampsia

These predictive tests related to placental perfusion and vascular resistance.

Mean second trimester BP, intravenous infusion of Angiotensin 2, roll over test , 24 hour ambulatory BP monitoring.

Foetoplacental Endocrinology

Alpha fetoprotein, Human Chorionic Gonadotrophin

Renal function

Serum Uric Acid or Microalbuminuria

Endothelial function and endothelial platelet interaction

Platelet Count, Anti Phospholipid Antibodies, or Homocysteine.

Placental Hormones

Activin, Inhibin A, Corticotrophin Releasing Hormone (CRH)

Angiogenic factors

Vascular endothelial growth factor (VEGF), Placental growth factor (PGF) and Antiangiogeneic factors like soluble fms like tyrosine kinase 1 and soluble endoglin levels.

- At present the link between angiogenic factors (placental growth factor vascular endothelial growth factor) and antiangiogenic factors found be promising. However endoglin (sEng) acting in concert with sFlt-1 could improve the prognostic performance. Alterations in placental proteins were considered using MALDI-TOF MS/MS proteomics study and revealed that there was over demonstration of chaperones 60 , ERp29, Cathepsin C, VDAC, and Cathepsin D in preeclampsia.

Angiotensin Sensitivity Test

Normally a pregnant woman displays reduced responsiveness to effects of angiotensin 2 , in patients with

preeclampsia plasma renin activity and angiotensin 2 levels are lower than normal throughout pregnancy .Only in the third trimester does the aldosterone level increase in hypertensive pregnancy.

In addition the refractoriness to Angiotensin 2 is lost as early as the early second trimester , several weeks before the onset of hypertension ,in women who are destined to develop preeclampsia later in gestation. A greater presser response to infused angiotensin 2 has been demonstrated as early as 18-22 weeks of gestation in normotensive who subsequently develop hypertension.

This increased sensitivity to angiotensin 2 is the result of loss of vessel refractoriness is because of the down regulation of angiotensin receptors in the presence of persistently its elevated level.

Over past two decades, various studies reported that preeclamptic women showed an elevated presser response to vasopressin. The low sensitivity of these tests have raised the doubt of using angiotensin sensitivity as a predictor of preeclampsia.

Renal Laboratory Tests

Establishing abnormal levels of urine protein and urine albumin as sole predictor has not been established. The 24 hours urinary quantitative specimen >300mg /24 hours have been established and determination of urinary protein or albumin :creatinine ratio may supplant the 24 hour urinary protein.

Random urine protein:creatinine ratio below 130 to 150 mg/g -0.13 to 0.15 –indicate the likelihood of proteinuria exceeding 300mg/day is low and mid ranges that is 300mg /g -0.3-have poor sensitivity and specificity.

Uric acid, Creatinine and Urine Microprotein, Calcium levels

Renal blood flow and glomerular filtration are reduced in preeclampsia. Since renal blood flow and glomerular filtration are normally increased during pregnancy , levels usually reach the normal non pregnant values and very low levels are the consequence of reduction in GFR and the plasma uric acid concentration is typically elevated.

High serum uric acid levels > 6.5 g/dl were associated with severity of preeclampsia. Hyperuricaemia an early sign

of renal involvement in preeclampsia, is due to enhanced tubular reabsorption and increased placental urate production compensatory to increased oxidative stress. Urine sodium concentration is elevated in most preeclamptic patients and urine osmolality ,urine :plasma creatinine ratio and fractional excretion of sodium is indicative of pre renal involvement of the disease process.

Urinary proteomics

Proteomic fingerprint associated with serpina and albumin fragments predicts preeclampsia with the accuracy and it also differentiates preeclampsia with other types of hypertensive disorders.

Urinary Inhibin A

Urinary Inhibin value is greatly increased in patients with preeclampsia,values more than 90pg/mg is associated with greater risk of developing preeclampsia. Cut off value for development of preeclampsia is 45pg/mg and values above this have a predisposition for development of preeclampsia.

Urinary Kallilrein Creatinine Ratio(Uk:Cr)

Urinary kallikrein to creatinine ratio is measured and is a useful test for the predicting preeclampsia later in pregnancy and it is usually done between 16-20 weeks of gestation. This test has a better sensitivity and specificity compared to other renal parameters.

Clinical value of Microtransferrunia and Microalbuminuria

A number of investigators have evaluvated the potential value of micro albuminuria as a predictive test for preeclampsia.

As reviewed by Conde Agudelo sensitivity was ranging between 7 to 90 percent,and specificity 29 and 97 percent and a recent study has shown that unacceptable sensitivity and specificity for urine albumin:creatinine ratio.

Urinary microalbuminuria and micro transferrinuria both has a better sensitivity and specificity than other parameters. Microtranferrinuria is potentially used as a better predictor of preeclampsia than micro albuminuria level.

Urinary excretion of N-acetyl-beta-glucosaminidine

Urinary excretion of N acetyl beta glucosaminidase is increased in patients with preeclampsia and in normal pregnant woman than non pregnant woman. N-acetyl –beta – glucosaminidine is an enzyme present in the lysosome of the renal tubules .The rise of N acetyl glucosaminidase is gestational age related and increases with increase in the gestational age.

SERUM MARKERS

Serum Inhibin A

Serum Inhibin A measured in the first trimester is used as a predictor of preeclampsia, Serum hCG level added to serum inhibin did not give a better screening tool for preeclampsia. Serum Inhibin A and serum beta HCG are markers of the underlying impaired trophoblastic invasion .Serum Inhibin level measured alone have a very low sensitivity and specificity.

Maternal Serum Alpha Fetoprotein (MSAFP)

In many studies conducted using multivariate analysis using maternal serum alpha fetoprotein along with elevated mean arterial pressure,previous history of pre eclampsia,family history of preeclampsia,low serum oestriol levels and with the measurement of serum beta HCG levels has a predictive value with low sensitivity and specificity.

Serum Oestriol

Serum oestriol is not used as a single predictive factor for the preeclampsia ,with the addition of several markers like HCG evaluation and alpha fetoprotein along with strong risk factors such as nulliparity, obesity(BMI>35), history of PIH in previous pregnancy, family histoy of preeclampsia contribute to the prediction of preeclampsia.

Tumour necrosis factor of plasma was measured in patients with preeclampsia, TNF alpha levels were elevated in all the three trimesters of the pregnancy. Hence due to its universal elevation throughout pregnancy it cannot be used as a predictor that can used in first trimester and early second trimester to predict preeclampsia.

Coagulation Factors and Platelets

Thrombocytopenia , reduced levels of clotting factors ,evidence of platelet activation ,intravascular coagulation and haemolysis are present.

In general lower the platelet count cause greater the maternal morbidity and mortality. Increased platelet consumption is evidenced by reduced platelet count, increased beta thromboglobulin levels and elevated platelet volume. Preeclamptic patients have increased antigen expression on their surface during the first and second trimester of pregnancy and no tests can be used reliably for the prediction of preeclampsia based on platelet activation.

Plasma fibronectin

These high molecular weight glycoproteins serve a variety of functions such as adhesion, morphology , migration , phagocytosis and haemostasis .Fibronectins are released from endothelial cells and extracellular matrix following endothelial injury. Stubbs and colleagues have demonstrated that plasma fibronectin levels were elevated in patients with preeclampsia.

Serum androgen markers and Sex Hormone Binding Globulin (SHBG) markers

Low levels of sex hormone binding globulin in early pregnancy was associated with later development of preeclampsia. When preeclamptic patients were compared with normal pregnant women sex hormone binding globulin, serum testosterone, dehydroepiandrosterone sulphate showed no difference which is of statistically significant.

It has a better sensitivity than specificity for it to be a specific marker for preeclampsia but its negative predictive value is too low for as a predictor of preeclampsia.

Serum Thrombomodulin

Serum thrombomodulin antigen levels were higher in patients with preeclampsia, chronic hypertension superimposed by preeclampsia, gestational hypertension and chronic hypertension. Serum thrombomodulin levels were higher in preeclampsia patients than patients with gestational hypertension or chronic hypertension. Serum thrombomodulin helps to differentiate preeclampsia from other hypertensive disorders of pregnancy. It is a better clinical marker compared to other biochemical markers.

Angiogenic factors in preeclampsia

Several angiogeneic and anti angiogeneic factors are involved in the placental vascular development .An imbalance is in circulating proangiogeneic(VEGF and PGF) and anti angiogeneic (soluble fms like tyrosine , soluble endoglin levels) factors.

Elevated levels of soluble endoglin levels and soluble fms like tyrosine levels in second trimester have been associated with an increased risk of preeclampsia .These two anti angiogeneic factors are produced by the trophoblastic tissue of women destined to develop preeclampsia.

Soluble fms like tyrosine levels

Soluble fms like tyrosine levels are variant of placental growth factor and vascular endothelial growth factor and its increased levels decrease the PGF and VEGF levels leading to angiogeneic imbalance.

Soluble Endoglin levels

Soluble endoglin levels is a placenta derived molecule which causes decrease in the endothelium nitric oxide

dependent vasodilatation. The levels of both soluble fms like tyrosine levels and soluble endoglin levels in maternal circulation begin to raise months before the clinical syndrome of preeclampsia develops and dissipate after delivery.

Since due to an excess of circulating anti angiogenic growth factors, most particularly soluble fms like tyrosine kinase 1 (sFlt1) and soluble endoglin (sEng) hypertension and proteinuria develops.sFlt1 is an endogen which is able to bind to the vascular endothelial growth factor and placental growth factor(angiogeneic factors)and therefore abolish their

actions. Soluble endoglin was found to help with the soluble form of vascular endothelial growth factor receptor 1 in the pathogenesis of preeclampsia by inducing endothelial cell dysfunction.

High serum concentrations of sFlt1 and low concentrations of free vascular endothelial growth factor and free placental growth factor were obvious clinically prior to clinical expression of preeclampsia. The disproportionate production of these two anti angiogenic proteins induce

endothelial dysfunction by preventing circulating proangiogenic factors for example the placental growth factor, the vascular endothelial growth factor but also the transforming growth factor beta.

Oxidative stress factors

Increased levels of lipid peroxides along with decreased anti oxidant activity have raised the possibility that markers of oxidative stress might predict preeclampsia. A variety of pro-oxidants or potentiators of pro-oxidants including iron, transferrin, ferritin, blood lipids including triglycerides and free fatty acids are used as predictors of pre-eclampsia.

Hyper homocystenemia is associated with oxidative stress and endothelial dysfunction and hyper homocystenemia is associated with three to four fold increased risk of preeclampsia.

Hence over many years, the methods and tests to predict preeclampsia prior to the appearance of the clinical disease has increased marginally not up to a remarkable level.

None of the clinical laboratory, biochemical tests can be used for the prediction of the preeclampsia.

The preventive measures being used for the prevention of preeclampsia, various serum tests and urinary tests has been evaluated earlier has failed to establish itself as an predictor for patients with preeclampsia earlier than the clinical signs and symptoms has established.

However in the future newer markers like s-Flt1, s-Eng,VEGF and PIGF to predict the changes in the maternal cardiovascular system preeclampsia before the clinical manifestation sets in .Hence now there is a absolute need in this decade to find a predictor and ideal screening test due to the increased incidence of preeclampsia nowadays.

Prevention of pre eclampsia

It includes,

Dietary manipulation- low salt diet, calcium supplementation, fish oil supplementation

Cardiovascular drugs- diuretics, antihypertensive drugs,

Antioxidants **-** absorbic acid (vitamin c),alpha tocopherol,

Antithrombotic drugs- low dose aspirin, aspirin/dipyridamole, aspirin with heparin, aspirin with ketanserin.

DIETARY MANIPULATION

Low Salt Diet

One of the earliest research to prevent preeclampsia was salt restriction, studies conducted by knuist and colleagues showed that a sodium restricted diet was ineffective in preventing preeclampsia.

Calcium supplementation

Studies performed in United States showed that women with low calcium intake were at significant risk of gestational hypertension in aggregate various trials show that unless women are calcium deficient supplementation has no salutary effects.

Fish oil supplementation

Cardioprotective fatty acids are found in some fatty fishes. The most common dietary sources are EPA-eicosapentanoic acid and ALA –alpha linoleic acid. These

oils are helpful in preventing inflammatory mediated atherogenesis. Several randomised trials show that there were no benefits to support this fish oil supplementation.

Antihypertensives

Because of the putative effects of sodium restriction it was not surprising that diuretics had a decreased incidence of oedema and hypertension but not preeclampsia.

Anti oxidants

Two naturally occurring antioxidants vitamin C and E may decrease such oxidation[24] moreover women who develop preeclampsia were found to have reduced levels of these two vitamin. Thus dietary supplementation was proposed as a method to improve the oxidative capability of women at risk for preeclampsia.[27]

Anti thrombotic drugs

As discussed the syndrome is characterised by vasospasm, endothelial dysfunction and the activation of platelets and antithrombotic drugs can reduce the incidence of preeclampsia.

Low dose aspirin

In oral doses of 50 to 150mg daily aspirin effectively inhibits platelet thromboxane biosynthesis with minimal effects on vascular prostacyclin synthesis[26]. For women destined to receive anti platelet drug aspirin has 10% decreased risk of preeclampsia , superimposed preeclampsia, preterm delivery, or any pregnancy with an adverse outcome. The number needed to treat was high, hence it seems reasonable to individualise use of low dose aspirin to prevent preeclampsia.

A large randomised controlled trial ,the collaborative low dose aspirin study in pregnancy (CLASP) investigating the role of low dose aspirin used for the prevention of preeclampsia showed a non significant reduction of preeclampsia. Moreover the study showed that low dose aspirin was generally safe for the foetus and the neonates.

Cochrane review showed 17% reduction in the risk of preeclampsia in high risk women and no benefit has been demonstrated for administrating low dose aspirin in low risk women.

Based on the clinical evidence National institute of clinical excellence UK recommends 75mg of aspirin for all women at high risk of preeclampsia from 12 weeks until the birth of the baby.

Low dose aspirin and heparin

Because of the high prevalence of placental thrombotic lesions with severe preeclampsia there were many observational studies to evaluvate the effect of heparin. Many studies reviewed that low molecular heparin with low dose aspirin have a beneficial effect in women with a history of severe early onset preeclampsia and low birth weight infants.

Rest and Reduce Physical Activity

Cochrane review included trials which investigated the effect of rest or reduced physical activity in normal pregnant women who are risk of preeclampsia from 28 to 32 weeks and it showed that rest couldn’t be recommended as a prophylactic intervention to prevent the preeclampsia.

THE PERFECT SCREENING TEST

- Simple
- Non invasive
- Rapid
- Inexpensive
- Easy to perform early in pregnancy
- Highly sensitivity & predictive

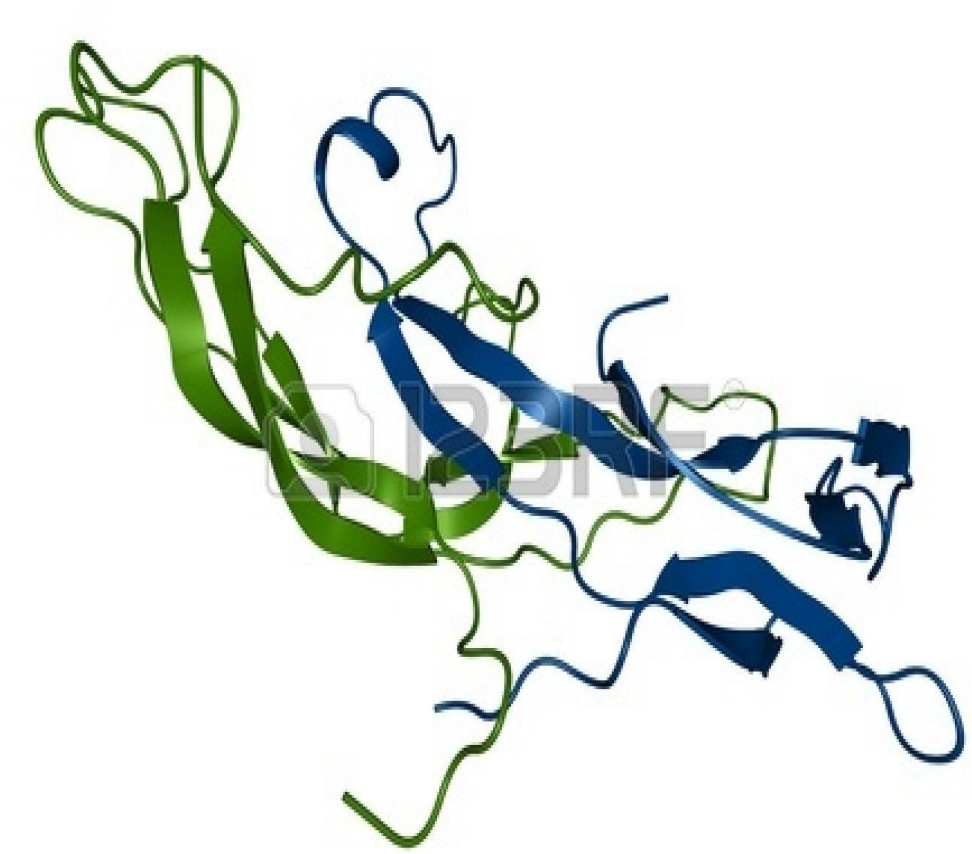
HUMAN CHORIONIC GONADOTROPIN

Human chorionic gonadotropin (HCG) is a pregnancy hormone with biological similar to luteinizing hormone. Both act via through plasma membrane LH, HCG receptor. Hormone is produced by the syncytiotrophoblast cells after implantation in myometrium. Most cancer cells produce this hormone, increased levels may be used as a diagnostic and prognostic factor in diagnosis. The HCG component of pituitary is analogous to luteinizing hormone (LH) and it is present in the pituitary gland of all human beings at all ages.

STRUCTURE

Chorionic gonadotrophins is a glycoprotein with molecular weight of 36,000 to 40,000 Da. It has the highest carbohydrate content of any hormone about 30 percent .The carbohydrate component and especially the terminal sialic acid , protects the molecule from catabolism. The 36 hour plasma half life of intact HCG is much longer than the 2 hours for LH

The HCG molecule has two dissimilar subunits, one is designated alpha and is composed of 92 amino acids ,whereas beta subunit contains 145 aminoacids .These are non covalently linked and are held together by electrostatic and hydrophobic forces .Isolated subunits are unable to bind the LH receptor and lack biological activity.



Structure of Beta HCG molecule

FUNCTION

Both HCG subunits are required for binding to the LH-HCG receptor in the corpus luteum and the foetal testis .Best known biological function of HCG is maintenance of the corpus luteum.HCG stimulates foetal testicular testosterone secretion which is maximum when the peak levels of HCG levels are obtained.

It is well established that HCG act as a placental link for the maternal immunological process .For example HCG treated cells of the endometrium have been used in the treatment of cancer cells.

HCG is linked with the development of peritrophoblastic immune tolerance, and for the trophoblast invasion and it is also raised in patients with hyperemesis gravidaram. HCG levels correlate well with of morning sickness in early pregnancy.

HCG since it has a resemblance with the LH level in the pituitary it is used to detect ovulation process as well as testosterone production in the testes. Since the source of HCG is pregnant women urine ,marketing companies prefer to obtain urine to use them in the treatment of infertility. HCG trigger apoptosis and play a role in cell proliferation and differentiation, helps to promote apoptosis.

BIOSYNTHESIS

Both alpha and beta chain synthesis of HCG are regulated separately. A single gene located on chromosome 6 encodes the alpha subunit for HCG,LH, FSH and TSH. Both

subunits are synthesised as large precursors, which are cleaved by endopeptidase and intact HCG is then assembled and rapidly released by exocytosis of secretary granules.

SITE OF HCG SYNTHESIS

Before 5 weeks HCG is expressed in both syncytiotrophoblast and cytotrophoblast and later when serum beta HCG level is peak , it is almost solely produced by syncytiotrophoblast. At this time HCG mRNA for both alpha and beta subunits are greater than at term .This may be important consideration when HCG is used as a screening procedure to identify abnormal foetus.

REGULATION OF HCG SYNTHESIS

Placental GnRH is involved in the regulation of HCG formation, both GnRH and its receptor are expressed on cytotrophoblast and syncytiotrophoblast .Also GnRH administration elevates the circulating HCG levels and cultured trophoblastic cells respond to GnRH treatment with increased HCG secretion.Pituitary GnRH production also is regulated by inhibin and activin. In cultured Placental cells activin stimulates and inhibin will inhibits GnRH and HCG production.

METABOLIC CLEARANCE OF HCG

Renal clearance of HCG accounts for 30% of its clearance ,the reminder is likely cleared by metabolism in the liver.Clearances of beta and alpha subunit are about 10-fold and 30-fold respectively greater than that of intact HCG. By contrast renal clearance of these subunits is considerably lower than that of dimeric HCG.

METHODOLOGY

Tests used to identify the HCG levels in serum mostly use monoclonal antibody. This procedure usually is used since these do not give false positive results by its resemblance with LH & FSH. HCG assays are used on the principle of sandwich method which detects HCG using antibodies linked to enzyme or luminescent dye. It can also be detected by chemiluminescent method , lateral flow technique also detects HCG linked on a dipstick.

Early morning urine samples are taken to detect the beta HCG levels since early morning urine sample have the highest levels of beta HCG when the specific gravity of the urine sample is low due to diluted urine , HCG could not be detected in the urine sample.

Chemiluminescent assay and fluorometric assays detect beta HCG levels when the serum sample size of 2 to 4 ml is drawn , and hence quantification of serum beta HCG levels according to the gestational age can be done.

MOLECULAR FORMS OF HCG IN PLASMA AND URINE

Free subunits

Circulating free beta subunits are too low to become undetectable throughout pregnancy .This is the result of its rate limiting synthesis .Free alpha subunit are found in placental tissue and maternal plasma .These levels increase gradually and steadily until they plateau at about 36 weeks. At this time they account for from 30 to 50 %of hormone .Thus alpha HCG secretion roughly corresponds to placental mass ,whereas secretion of complete HCG molecules is maximal at 8 to 10 weeks.

Concentration of HCG in serum and urine

The intact HCG molecule is detected in the plasma of pregnant women 7 to 9 days after the mid cycle surge of LH precedes ovulation. Thus it is likely that HCG enters maternal blood at the time of blastocyst implantation .Plasma levels

increase rapidly and doubling every 2 days with maximal levels being attained at 8 to 10 weeks.

The pattern of HCG appearance in foetal blood is similar to that in the mother. Foetal plasma levels however are only about 3% of those in maternal plasma level. As pregnancy progresses HCG concentration in amniotic fluid declines and near term the levels are about 20% of those in maternal plasma.

Reference values in normal pregnant woman

The HCG levels increase after conception and peak plasma levels about 1,00,000 m IU/ ml between the 60^{th} and 80^{th} days after LMP. At 10 to 12 weeks plasma levels begin to decline and a nadir is reached by about 16 weeks. Plasma levels are maintained at this lower level for the reminder of the pregnancy.

Weeks of gestation	***HCG levels (mIU/ml)***
4	45
6	350
15	7230

1,500	55,000
75,560	232,000
11,35,725	299,000
17,12,200	224,000
255,080	155,425
404,720	1,24,000

Serum beta HCG levels estimation done by CLIA method.

The Multiples of median was calculated from the median of the diagnostic study. Beta HCG levels are said to be elevated if levels raised more than 2MOM. Follow up of AN mothers done till third trimester by monitoring blood pressure and proteinuria .Prediction of PIH done according to the elevated beta HCG level. Severity of the PIH is classified according to the elevated beta HCG levels.

MANAGEMENT OF PREECLAMPSIA

Ideally all patients with mild preeclampsia is hospitalised once diagnosis is made. All patients receive a regular diet with no salt restriction and no activity limits. The

blood pressure should be measured for every 4hours and the patients should be assessed for their weight and oedema. Also 24 hour urine collection for protein excretion, haematocrit, platelet count and liver function test should be done.

For the less than 37 weeks but the presence of persistent hypertension, protenuria, abnormal lab values, abnormal foetal growth and unreliable patient admit the patient for further management.When the above mentioned factors were absent, they were managed in home with frequent evaluations of BP and urine.

For the patients with more than 37weeks, favourable cervix, foetal jeopardy, visual disturbances and persistent headache treatment with MgSO4 and delivery should be done.

MATERNAL MONITORING[43]

1) Blood pressure every 4 hours during the day
2) Presence of facial or abdominal oedema.
3) Measure the weight daily
4) Haematocrit and platelet count twice a week
5) LFT 1-2 times a week
6) Symptoms of impending eclampsia

FOETAL MONITORING[43]

1) Daily foetal movements

2) NST 3 times a week

3) Biophysical profile if NST – ve

4) USG evaluation of foetal growth every 3-4 weeks

INDICATIONS FOR TERMINATION IN PREECLAMPSIA[29]

Maternal Indications

1) Persistent increase in BP to severe level(>160 systolic and >110 diastolic)

2) Development of persistent cerebral symptoms (imminent symptoms)

3) HELLP syndrome

4) Onset of labour,Rupture of membrane or bleeding

FOETAL INDICATIONS

1) Severe IUGR by USG

2) Non reactive NST with abnormal biophysical profile

3) Development of oligohydramnios

4) Gestational age 38-40 weeks

INTRAPARTUM MANGEMENT[44]

- Maternal Analgesia-Intermittent use of small doses-25 to 50mg IV Meperidine or segmental epidural analgesia.
- Empiric Antihypertensive therapy recommended for more than 160/110mmHg.
- Diuretics are not needed except in the presence of pulmonary edema and this may exacerbrate the maternal cerebral ischaemia ,decrease the renal function and jeopardise the foetal well being.

POSTPARTUM MANAGEMENT

After delivery the patient should continue to be monitored and the patient should be seen at weekly intervals until blood pressure is in normal range without medication.

REMOTE FROM TERM

- Uncontrolled severe hypertension
- Eclampsia
- Platelet count <1,00,000mm^3
- Pulmonary oedema
- Compensatory renal function
- Abruptio placentae

Consider Expectant Management

- ❖ Controlled Hypertension
- ❖ Urinary protein of any amount
- ❖ Oliguria(<0.5ml/kg/hr) which resolves with routine fluid and food intake
- ❖ AST or ALT >2 x upper limits of normal without epigastric or right upper quadrant tenderness

Foetal Indication

- ❖ Expeditious delivery within 72 hours
- ❖ One or more of the following
- ❖ Repetitive or severe variable deceleration
- ❖ Biophysical profile <4 on two occasions 4 hrs apart
- ❖ AFI<2
- ❖ USG estimation of foetal weight <5th percentile
- ❖ Reduced umbilical artery diastolic flow.

TREATMENT

Anti Hypertensives in Preeclampsia

The guidelines to start anti hypertensives in non severe hypertension is to maintain systolic BP at 130-155mmHg and diastolic BP at 80 -105mmHg in women without comorbid

factors.In those without comorbidities,systolic BP should be kept at 130-139mmHg and diastolic BP at 80-89mmHg.

The most common first line oral drugs used to treat non evere hypertension are labetalol42 and methyldopa.If adequate control is not attained by first line drugs,then second line drugs such as calcium channel blockers ,beta blockers like metaprolol, acebutol and propanolol are used.

ALPHA METHYL DOPA

The commonest first choice of drug used to control hypertension due to its long safety record.This drug is a centrally acting drug an alpha adrenergic agonist .It decreases the sympathetic tone and blood pressure.It is started at a initial dose of 250 to 500mg 2-3 times a day upto a maximum dose of 2gm/day.

The maximum drug effect occurs at 4 to6 hours and it persists for 12 hours.

MATERNAL SIDE EFFECTS

Postural hypotension,lethargy,dry mouth,drug induced hepatitis and very rarely haemolytic jaundice.

FOETAL SIDE EFFECTS

Although methyl dopa crosses the placenta and almost 100% secreted in the milk secretion but has no teratogenecity.

LABETOTOL

Labetolol43 has both alpha and beta blocking actions.

Its is started at a dose of 100mg to 400mg upto a maximum of 1200 mg/day.Labetolol has replaced nowadays alpha methyl dopa as a first line therapy. Due to its beta blocking property it usually masks the signs of hypoglycaemia in patients treated with insulin therapy.

MATERNAL SIDE EFFECTS

Dizziness, drowsiness, fatigue, bradycardia, insomnia, shortness of breath, nausea, vomiting.

FOETAL SIDE EFFECTS

Hypoglycaemia, neonatal hyperbilirubinemia, IUGR

NIFEDIPINE

It is a calcium channel blocker and it is used in patients who do not attain adequate control with first line drugs.

Dose;10-20mg tds, Maximum dose 180mg per day. Side effects include headache, dizziness, palpitation, nasal congestion.

INDICATION OF DIURETICS

It is not routinely used in preeclampsia due to depletion of intravascular volume. It is used only special situations like congestive cardiac failure,actue pulmonary oedema,increased cerebral vascular tension.

$MGSO_4$ FOR ECLAMPSIA

1) Pitchard Regimen;

   a. 10gm loading dose followed by 5gm every 4hours

2) Continuous intravenous infusion-Zuspan,4 gm loading dose followed by 1gm/hr

3) Sibai: 6 gm loading dose followed by 2gm/hr

Approximate serum levels of Mg; 3.5-7mg/L or 4.2-8.4 mEq/dl

Effects of $MgSO_4$ Therapy[42]

Beneficial effects

- ❖ Vasodilatation in vascular beds
- ❖ Increased uterine blood flow
- ❖ Increased renal blood flow
- ❖ Increased prostacyclin release by endothelial cells

- ❖ Decreased plasma rennin activity
- ❖ Decreased Angiotensin converting enzyme levels
- ❖ Attenuation of vascular response to pressor substances
- ❖ Bronchodilatation
- ❖ Decreased platelet aggregation

DETRIMENTAL EFFECTS

- ❖ Decrease the uterine activity and causes prolonged labour
- ❖ Decrease the foetal heart rate variability
- ❖ Increase the blood loss after delivery
- ❖ Neonatal neuromuscular and respiratory depression
- ❖ Low APGAR score.

Mg Level(mg/dl)	Findings
1.5 - 2.5	Normal level
5 - 8	Therapeutic range for severe prophylaxis
9 – 12	Loss of patellar reflex
14 – 17	Muscular paralysis & Respiratory arrest
28 – 35	Cardiac arrest.

MATERIALS AND METHODS

Duration of the Study : January 2014 —October 2014

Type: Prospective Randomized Control trial

Place: Department of Obstetrics & Gynaecology, Institute Of Obstetrics And Gynecology,Egmore,Chennai.

INCLUSION CRITERIA

All normotensive non proteinuric pregnant women selected randomly between gestational age 13 to 20 weeks attending AN clinics irrespective of parity.

EXCLUSION CRITERIA

- Women with Multiple pregnancy
- Essential hypertension
- Diabetes mellitus
- Molar pregnancy

Institutional Ethics Committee approval was obtained with EC NO:15022014.

Informed consent was taken from all patients who underwent the study.All the patients details were recorded as per the Proforma(Appendix A). All Antenatal patients attending antenatal clinics in the inclusion criteria has been selected between the gestational age13 to 20 weeks and serum Beta HCG levels were taken for them.Complete history of the patient was taken and through clinical examination was done for all patients.

Gestational age of the patient was confirmed by the crown rump length measurement in the first trimester by dating scan at 7 week. All patients were advised congenital anomaly USG at 20-22 weeks. All the basic investigation including blood grouping were taken.

All these patients were followed upto their third trimester by the blood pressure evaluation,proteinuria and allocated into three groups with no PIH,mild PIH and severe PIH.

- Serum beta HCG levels estimation done by CLIA method.
- The Multiples of median was calculated from the median of the diagnostic study.

- Beta HCG levels are said to be elevated if levels raised more than 2MOM.

- Prediction of PIH done according to the elevated beta HCG levels.

- Severity of the PIH was classified according to the elevated beta HCG levels.

- Prediction of PIH based on parameters like Age,Parity,Gestational Age,Body Mass Index and the Past History of PIH.

STATISTICAL ANALYSIS

Descriptive statistics were used to illustrate the study population. The statistical significance of these correlations was assessed using a two sided p-value. A p-value of <0.05 was considered as statistically significant. The Chi Square test and ANOVA test were used to assess the statistical significance. Multiple comparision test and paired T test are also used for the comparision of various descriptive within the groups. A commercially available computer software package (Statistical Package for the Social Sciences (SPSS) version 17) was used for statistical analysis.

RESULTS

AGE GROUP ;NO PIH-0,MILD PIH-1,SEVERE PIH-2

			PIH			
			0	**1**	**2**	**Total**
Age Group	1	Count	60	25	12	97
		% within Age Group	61.9%	25.8%	12.4%	100.0%
		% within PIH	44.8%	55.6%	57.1%	48.5%
		% of Total	30.0%	12.5%	6.0%	48.5%
	2	Count	74	20	9	103
		% within Age Group	71.8%	19.4%	8.7%	100.0%
		% within PIH	55.2%	44.4%	42.9%	51.5%
		% of Total	37.0%	10.0%	4.5%	51.5%
	Total	Count	134	45	21	200
		% within Age Group	67.0%	22.5%	10.5%	100.0%
		% within PIH	100.0%	100.0%	100.0%	100.0%
		% of Total	67.0%	22.5%	10.5%	100.0%

Chi squre= 2.269 P=0.322 not significant.

Out of 200 patients, 97 patients belong to age group below 25,60 patients(61.9%) had no PIH ,25 patients(25.8%) had mild PIH,12 patients (12.4%) had severe PIH.

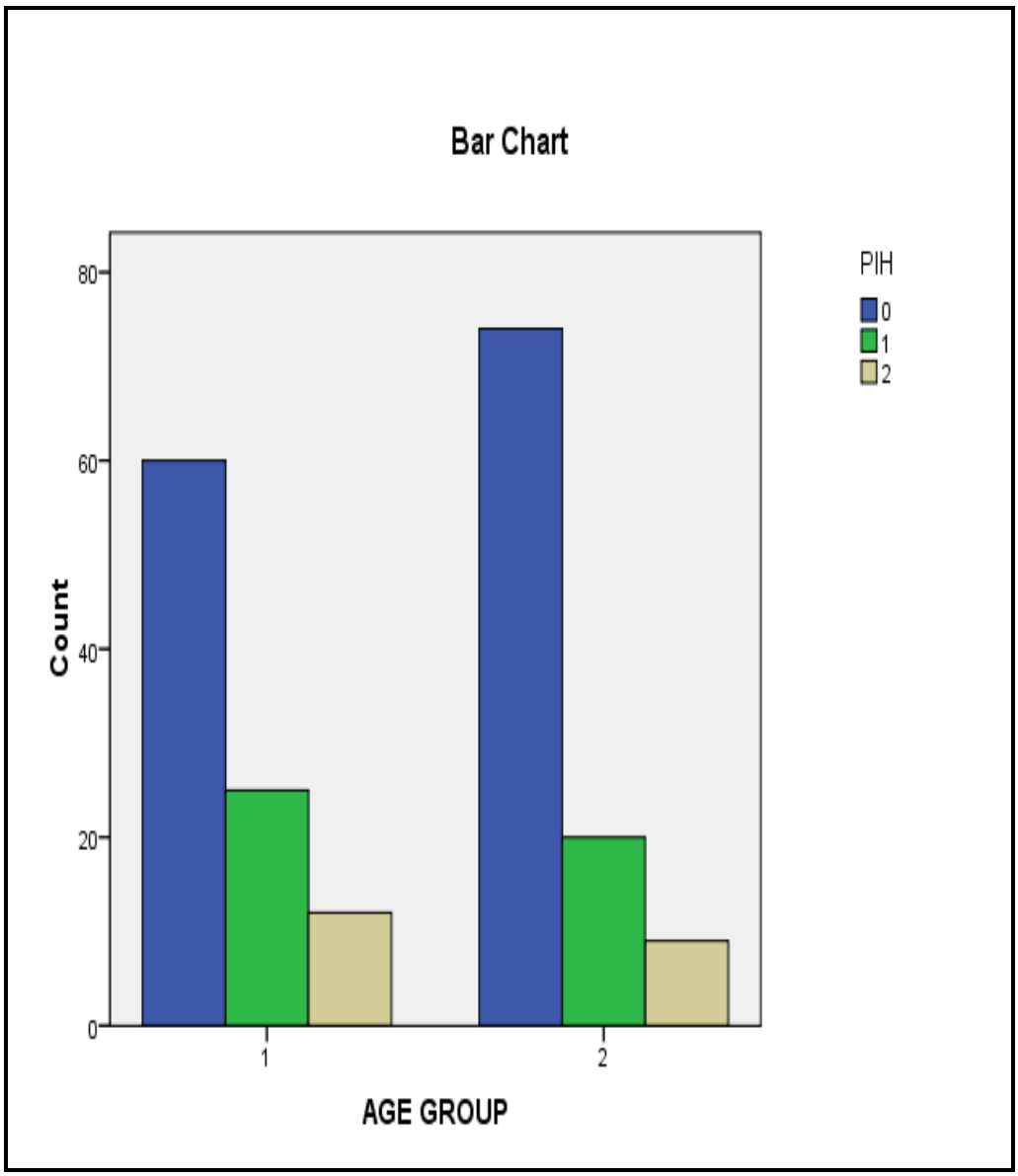
103 patients belong to age group above 25 and 74 patients(71.8%)had no PIH,20 patients (19.4%)had mild PIH and 9 patients (8.7%) had severe PIH.

CHI-SQUARE TESTS

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.269a	2	.322
Likelihood Ratio	2.272	2	.321
Linear-by-Linear Association	2.024	1	.155
N of Valid Cases	200		

0 cells (.0%) have expected count less than 5. The minimum expected count is 10.19.

According to chi square tests correlation between age and occurrence of preeclampsia have no significance since expected count is less than 5 .Age groups do not have significant correlation with the development of preeclampsia.



Group 1-Age <25 years, Group 2-Age >25 years.

AGE GROUP <25 YEARS - GROUP 1, >25 YEARS - GROUP 2

PIH GROUP 0-NO, 1-MILD, 2-SEVERE

Crosstab

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
0	134	25.61	2.138	.185	25.25	25.98
1	45	24.60	3.306	.493	23.61	25.59
2	21	25.14	3.021	.659	23.77	26.52
Total	200	25.34	2.562	.181	24.98	25.69

AGE

	Minimum	Maximum
0	21	31
1	19	31
2	19	32
Total	19	32

Age groups without PIH are between 21 and 31years , age groups with mild PIH are between 19 and 31 years,age groups with severe PIH are between 19 and 32 years.

Age doesn't have any significance for the occurrence of PIH.

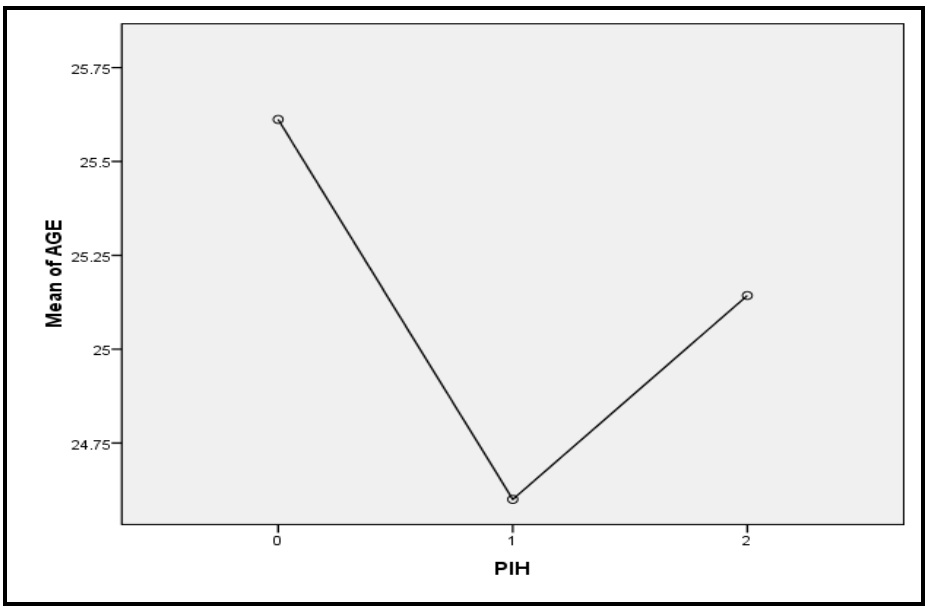
MULTIPLE COMPARISIONS

AGE; 0-NO PIH, 1-MILD PIH, 2-SEVERE PIH

(I) PIH	(J) PIH				95% Confidence Interval	
		Mean Difference (I-J)	Std. Error	Sig.	Lower Bound	Upper Bound
0	1	1.012*	.438	.022	.15	1.88
	2	.469	.596	.432	-.71	1.64
1	0	-1.012*	.438	.022	-1.88	-.15
	2	-.543	.671	.420	-1.87	.78
2	0	-.469	.596	.432	-1.64	.71
	1	.543	.671	.420	-.78	1.87

The mean difference is significant at the 0.05 level.There is no significant difference when the age is compared between the groups.

MEANS PLOTS



Mean age for patients without PIH group (0) - 25.61 . Mean age for patients with mild PIH group (1) - 24.60 . Mean age for patients with severe PIH group (2)- 25.14

GESTATIONAL AGE

No PIH – 0, Mild PIH – 1, Severe PIH - 2

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
0	134	15.75	1.629	.141	15.48	16.03
1	45	15.20	1.618	.241	14.71	15.69
2	21	15.24	1.411	.308	14.60	15.88
Total	200	15.58	1.618	.114	15.35	15.80

Mean gestational age for no PIH, mild PIH, severe PIH is 15.75,15.20 and 15.24 respectively. Mean gestational age for the study is 15.58.

GEST. AGE (WKS)

	Minimum	Maximum
0	13	19
1	12	19
2	13	19
Total	12	19

Age group between the ages 13 and 19 with no PIH. Age group between the ages 12 and 19 with mild PIH. Age group between the ages 13 and 19 with severe PIH.

GESTATIONAL AGE(WKS)-ANOVA

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	12.992	3	6.496	2.520	.083
Within Groups	507.883	197	2.578		
Total	520.875	200			

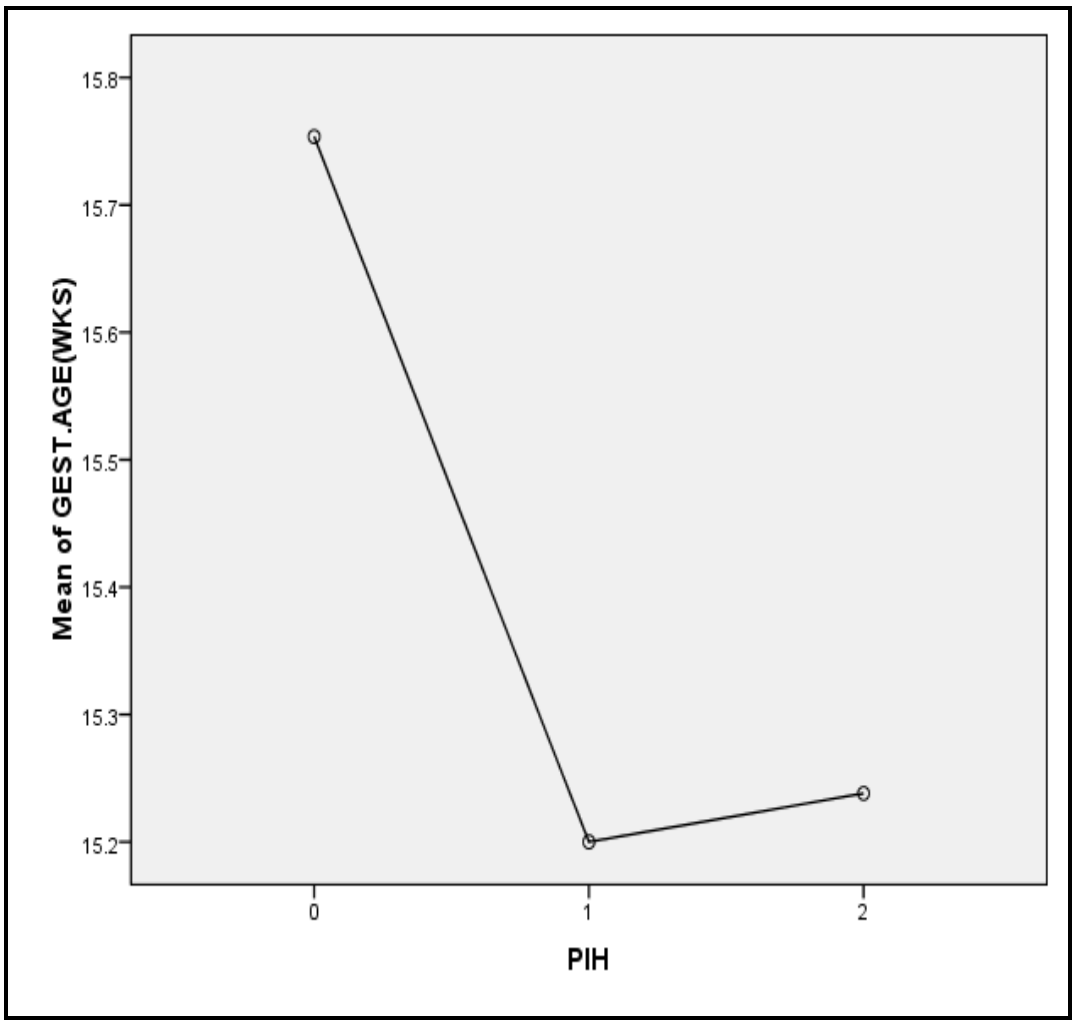
According to anova analysis correlation between the gestational age and occurrence of PIH is insignificant with a P value of 0.083.

GEST.AGE(WKS)-MULTIPLE COMPARISIONS

(I) PIH	(J) PIH				95% Confidence Interval	
		Mean Difference (I-J)	Std. Error	Sig.	Lower Bound	Upper Bound
0	1	.554*	.277	.047	.01	1.10
	2	.516	.377	.173	-.23	1.26
1	0	-.554*	.277	.047	-1.10	.00
	2	-.038	.424	.929	-.87	.80
2	0	-.516	.377	.173	-1.26	.23
	1	.038	.424	.929	-.80	.87

The mean difference is significant at the 0.05 level.

When the gestational age is compared between the groups, there is no significant p value.



Mean age for patients without PIH -15.75

Mean age for patients with mild PIH-15.24

Mean age for patients with severe PIH-15.58

SERUM BETA HCG LEVELS

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
0	134	71205.60	12483.383	1078.400	69072.57	73338.64
1	45	101178.49	37804.364	5635.542	89820.80	112536.18
2	21	154560.05	27929.414	6094.698	141846.73	167273.36
Total	200	86701.72	34547.956	2442.909	81884.41	91519.03

Out of 200 patients,134 patients had no PIH had mean beta hcg levels of 71205, 45 patients had mild PIH with the beta hcg level of 101178 and 21 patients had severe PIH with the mean beta hcg levels of 154560.

SERUM BETA HCG

	Beta Hcg Level	
Group	**Minimum**	**Maximum**
0	36092	142000
1	51906	186214
2	96999	197650
Total	36092	197650

Patients without PIH have a serum beta hcg levels ranging between 36,092 and 1,42,000. Patients with mild PIH have serum beta hcg levels ranging between 51,906 and 1,86,214. Patients with severe PIH have a serum beta hcg levels ranging between 96,999 and1,97,650.

SERUM BETA HCG-ANOVA

	Sum of Squares	**Df**	**Mean Square**	**F**	**Sig.**
Between Groups	1.383E11	3	6.915E10	137.318	.000
Within Groups	9.921E10	197	5.036E8		
Total	2.375E11	199			

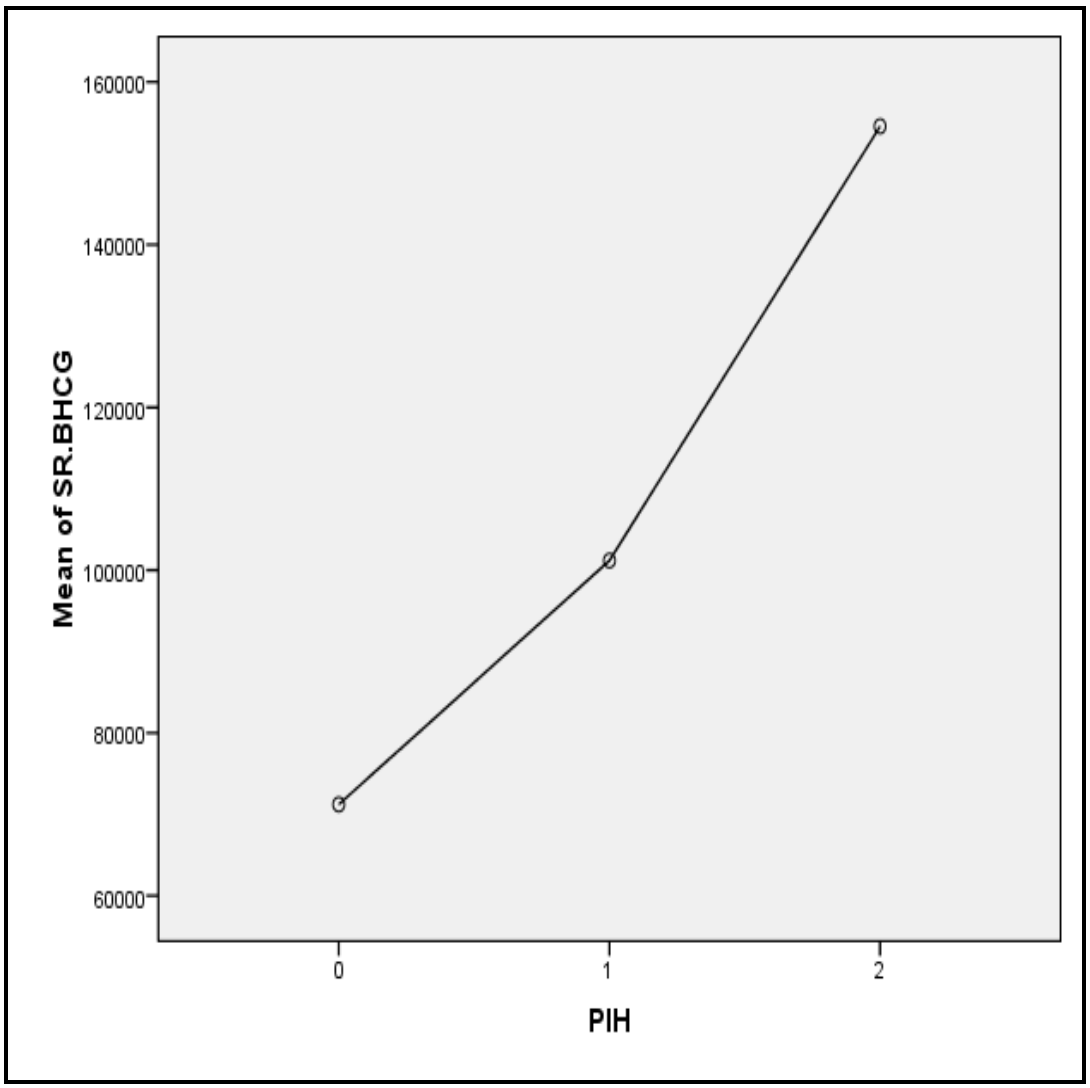
Anova analysis of serum beta hcg values of patients between the groups and within the groups have a significant p value of 0.000.

MULTIPLE COMPARISONS
SERUM BETA HCG BETWEEN THE GROUPS

(I) PIH	(J) PIH				95% Confidence Interval	
		Mean Difference (I-J)	Std. Error	Sig.	Lower Bound	Upper Bound
0	1	-29972.884*	3866.461	.000	-37597.85	-22347.92
	2	-83354.443*	5266.834	.000	-93741.06	-72967.83
1	0	29972.884*	3866.461	.000	22347.92	37597.85
	2	-53381.559*	5930.645	.000	-65077.26	-41685.86
2	0	83354.443*	5266.834	.000	72967.83	93741.06
	1	53381.559*	5930.645	.000	41685.86	65077.26
*. The mean difference is significant at the 0.05 level.						

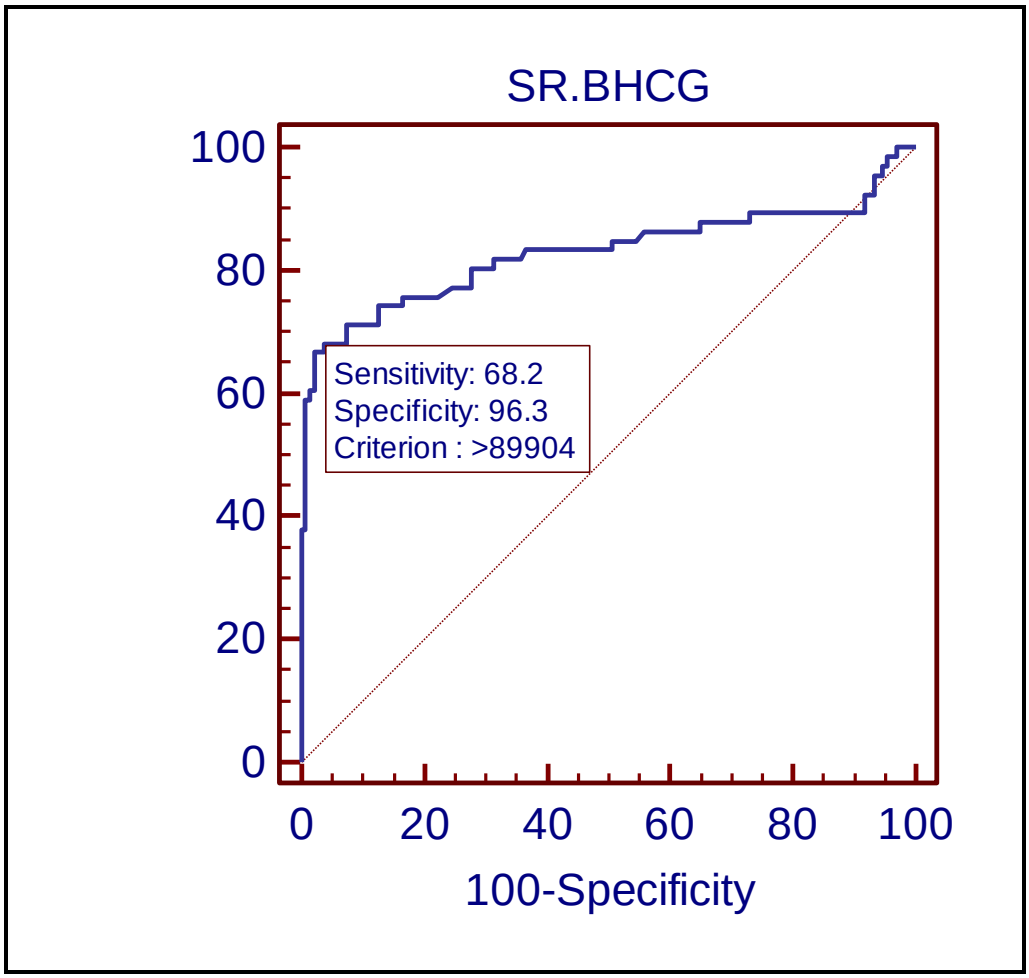
Comparisons of patients without PIH and patients with mild and severe PIH have a p value 0.0 in correlation of Beta HCG levels which is very significant.

MEANS PLOTS



Mean value of serum beta hcg level in patients without PIH –71,205.60 mIU/ml. Mean value of serum beta hcg level in patients with mild PIH –1,01,178.49 mIU/ml. Mean value of serum beta hcg level in patients with severe PIH – 1,54,560.05 mIU/ml.

ROC CURVE



Variable	SR.BHCG
Classification variable	PIH

Sample size		200
Positive group :	PIH = 1	66
Negative group :	PIH = 0	134

Disease prevalence (%)	unknown

Area under the ROC curve (AUC)

Area under the ROC curve (AUC)	0.828924
Standard Error	0.0390
95% Confidence intervalb	0.769440 to 0.878374
z statistic	8.430
Significance level P (Area=0.5)	<0.0001

YOUDEN INDEX

Youden index J	0.6445
Associated criterion	>89904

CRITERION VALUES AND COORDINATES OF THE ROC CURVE

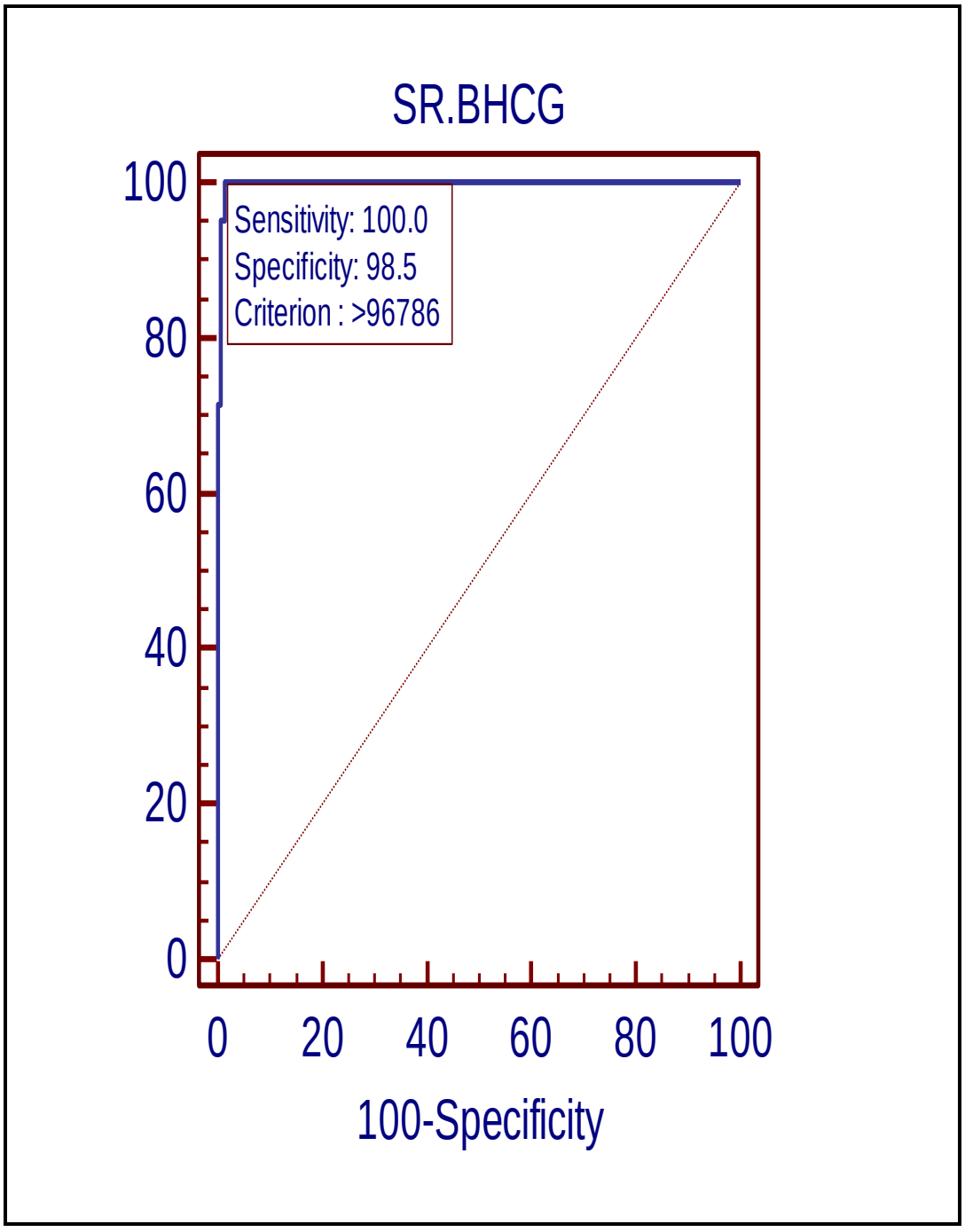
Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
≥36092	100.00	94.6 - 100.0	0.00	0.0 - 2.7	1.00	
>50108	100.00	94.6 - 100.0	2.99	0.8 - 7.5	1.03	0.00
>51906	98.48	91.8 - 100.0	2.99	0.8 - 7.5	1.02	0.51
>52608	98.48	91.8 - 100.0	4.48	1.7 - 9.5	1.03	0.34
>52806	96.97	89.5 - 99.6	4.48	1.7 - 9.5	1.02	0.68
>52908	96.97	89.5 - 99.6	5.22	2.1 - 10.5	1.02	0.58
>54108	95.45	87.3 - 99.1	5.22	2.1 - 10.5	1.01	0.87
>55606	95.45	87.3 - 99.1	6.72	3.1 - 12.4	1.02	0.68
>56124	92.42	83.2 - 97.5	6.72	3.1 - 12.4	0.99	1.13
>56786	92.42	83.2 - 97.5	8.21	4.2 - 14.2	1.01	0.92
>56980	89.39	79.4 - 95.6	8.21	4.2 - 14.2	0.97	1.29
>64567	89.39	79.4 - 95.6	26.87	19.6 - 35.2	1.22	0.39
>64623	87.88	77.5 - 94.6	26.87	19.6 - 35.2	1.20	0.45
>67706	87.88	77.5 - 94.6	35.07	27.0 - 43.8	1.35	0.35
>67802	86.36	75.7 - 93.6	35.07	27.0 - 43.8	1.33	0.39

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
>68806	86.36	75.7 - 93.6	44.03	35.5 - 52.9	1.54	0.31
>68902	84.85	73.9 - 92.5	45.52	36.9 - 54.3	1.56	0.33
>71704	84.85	73.9 - 92.5	49.25	40.5 - 58.0	1.67	0.31
>71924	83.33	72.1 - 91.4	49.25	40.5 - 58.0	1.64	0.34
>74804	83.33	72.1 - 91.4	63.43	54.7 - 71.6	2.28	0.26
>74806	81.82	70.4 - 90.2	64.18	55.4 - 72.3	2.28	0.28
>76000	81.82	70.4 - 90.2	68.66	60.1 - 76.4	2.61	0.26
>76101	80.30	68.7 - 89.1	68.66	60.1 - 76.4	2.56	0.29
>77404	80.30	68.7 - 89.1	72.39	64.0 - 79.8	2.91	0.27
>78124	77.27	65.3 - 86.7	72.39	64.0 - 79.8	2.80	0.31
>78802	77.27	65.3 - 86.7	75.37	67.2 - 82.4	3.14	0.30
>78804	75.76	63.6 - 85.5	77.61	69.6 - 84.4	3.38	0.31
>78965	75.76	63.6 - 85.5	83.58	76.2 - 89.4	4.61	0.29
>79102	74.24	62.0 - 84.2	83.58	76.2 - 89.4	4.52	0.31
>80608	74.24	62.0 - 84.2	87.31	80.5 - 92.4	5.85	0.30
>81806	71.21	58.7 - 81.7	87.31	80.5 - 92.4	5.61	0.33

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
>85503	71.21	58.7 - 81.7	92.54	86.7 - 96.4	9.54	0.31
>86704	68.18	55.6 - 79.1	92.54	86.7 - 96.4	9.14	0.34
>89904	68.18	55.6 - 79.1	96.27	91.5 - 98.8	18.27	0.33
>90961	66.67	54.0 - 77.8	96.27	91.5 - 98.8	17.87	0.35
>95904	66.67	54.0 - 77.8	97.76	93.6 - 99.5	29.78	0.34
>96708	60.61	47.8 - 72.4	97.76	93.6 - 99.5	27.07	0.40
>96786	60.61	47.8 - 72.4	98.51	94.7 - 99.8	40.61	0.40
>96999	59.09	46.3 - 71.0	98.51	94.7 - 99.8	39.59	0.42
>98750	59.09	46.3 - 71.0	99.25	95.9 - 100.0	79.18	0.41
>135906	37.88	26.2 - 50.7	99.25	95.9 - 100.0	50.76	0.63
>142000	37.88	26.2 - 50.7	100.00	97.3 - 100.0		0.62
>197650	0.00	0.0 - 5.4	100.00	97.3 - 100.0		1.00

In this study out of 200 patients 66 patients were with PIH and 134 patients were without PIH ,which had sensitivity of 68.2 and specificity of 96.3 and significant p value of <0.0001.

ROC CURVE


SR.BHCG
Sensitivity: 100.0
Specificity: 98.5
Criterion : >96786
100
80
60
40
20
0
0
20
40
60
80
100
100-Specificity

Variable	SR.BHCG
Classification variable	PIH

Sample size		155
Positive group :	PIH = 1	21
Negative group :	PIH = 0	134

Disease prevalence (%)	Unknown

Area under the ROC curve (AUC)	0.997512
Standard Errora	0.00235
95% Confidence intervalb	0.971611 to 1.000000
z statistic	211.275
Significance level P (Area=0.5)	<0.0001

YOUDEN INDEX

Youden index J	0.9851
Associated criterion	>96786

CRITERION VALUES AND COORDINATES OF THE ROC CURVE

Criterion values and coordinates of the ROC curve

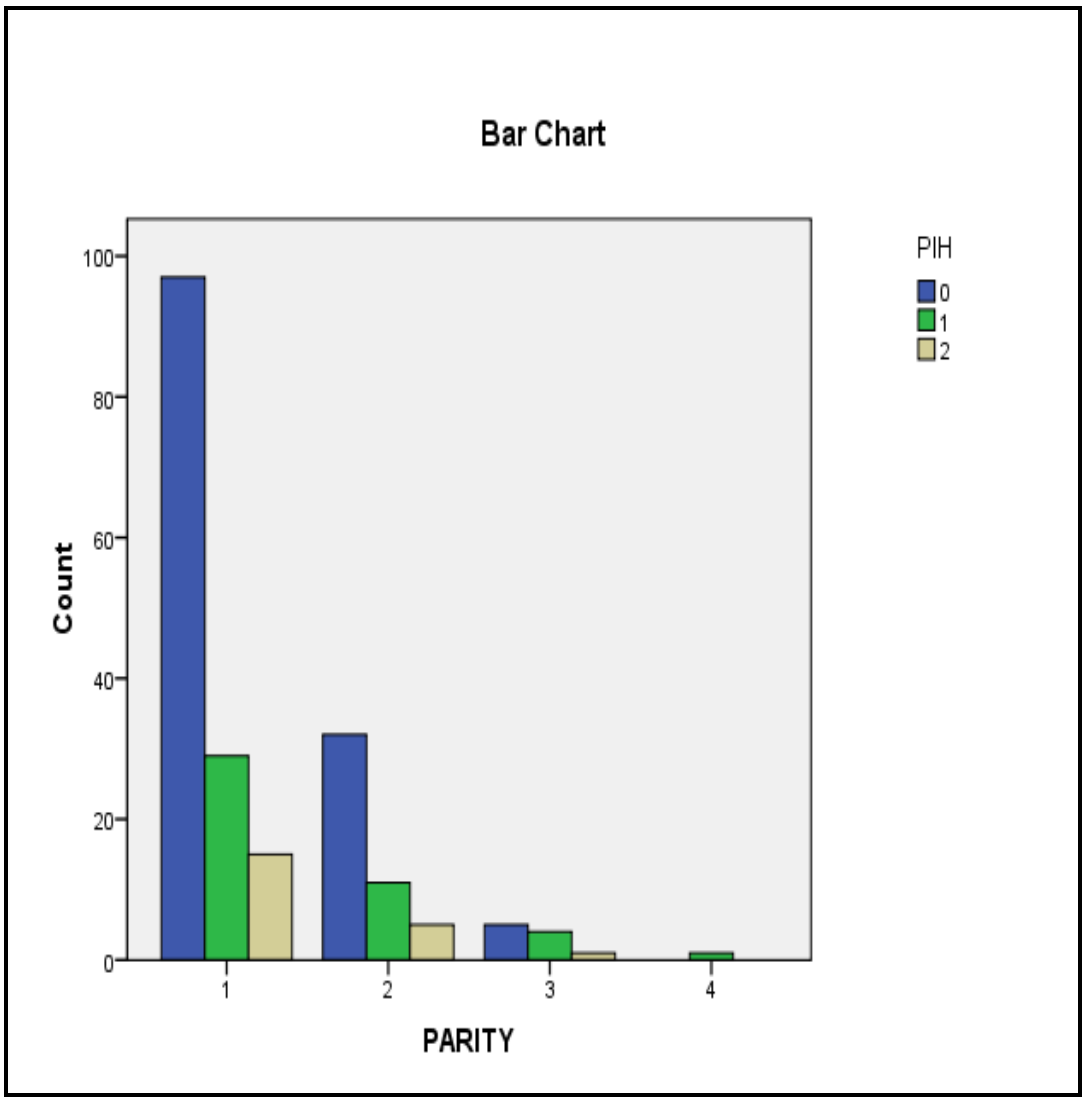
Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
≥36092	100.00	83.9 - 100.0	0.00	0.0 - 2.7	1.00	
>96786	100.00	83.9 - 100.0	98.51	94.7 - 99.8	67.00	0.00
>96999	95.24	76.2 - 99.9	98.51	94.7 - 99.8	63.81	0.048
>98750	95.24	76.2 - 99.9	99.25	95.9 - 100.0	127.62	0.048
>135906	71.43	47.8 - 88.7	99.25	95.9 - 100.0	95.71	0.29
>142000	71.43	47.8 - 88.7	100.00	97.3 - 100.0		0.29
>197650	0.00	0.0 - 16.1	100.00	97.3 - 100.0		1.00

When the prediction of severe PIH based on maternal serum Beta HCG had 100% sensitivity and 98.5%specificity with significant p value.

PARITY * PIH

			PIH			Total
			0	**1**	**2**	
Parity	1	Count	97	29	15	141
		% within PARITY	68.8%	20.6%	10.6%	100.0%
		% within PIH	72.4%	64.4%	71.4%	70.5%
		% of Total	48.5%	14.5%	7.5%	70.5%
	2	Count	32	11	5	48
		% within PARITY	66.7%	22.9%	10.4%	100.0%
		% within PIH	23.9%	24.4%	23.8%	24.0%
		% of Total	16.0%	5.5%	2.5%	24.0%
	3	Count	5	4	1	10
		% within PARITY	50.0%	40.0%	10.0%	100.0%
		% within PIH	3.7%	8.9%	4.8%	5.0%
		% of Total	2.5%	2.0%	.5%	5.0%

			PIH			Total
			0	**1**	**2**	
	4	Count	0	1	0	1
		% within PARITY	.0%	100.0%	.0%	100.0%
		% within PIH	.0%	2.2%	.0%	.5%
		% of Total	.0%	.5%	.0%	.5%
	Total	Count	134	45	21	200
		% within PARITY	67.0%	22.5%	10.5%	100.0%
		% within PIH	100.0%	100.0%	100.0%	100.0%
		% of Total	67.0%	22.5%	10.5%	100.0%


Bar Chart
PIH
0
1
2
Count
100
80
60
40
20
0
1
2
3
4
PARITY

BODY MASS INDEX

					95% Confidence Interval for Mean	
	N	Mean	Std. Deviation	Std. Error	Lower Bound	Upper Bound
0	134	25.15	3.486	.302	24.55	25.75
1	45	25.18	3.540	.534	24.10	26.26
2	21	25.86	3.787	.847	24.09	27.64
Total	200	25.23	3.517	.251	24.73	25.72

Out of 200 patients 134 patients who had no pih had a mean BMI 25.15 45 patientswho had mild pih had a BMI of 25.18 21patients who had severe pih had a BMI of 25.86.

BMI

	Minimum	Maximum
0	19	32
1	19	32
2	20	33
Total	19	33

Of patients without PIH and with mild PIH had BMI between 19 and 32, patients with severe PIH had range between 20 and 33.

BMI-ANOVA

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	9.015	4	4.507	.362	.697
Within Groups	2415.663	196	12.452		
Total	2424.678	200			

In anova analysis within the group and between the groups BMI had no significance.

MULTIPLE COMPARISONS- BODY MASS INDEX

(I) PIH	(J) PIH				95% Confidence Interval	
		Mean Difference (I-J)	Std. Error	Sig.	Lower Bound	Upper Bound
0	1	-.032	.614	.959	-1.24	1.18
	2	-.715	.846	.399	-2.38	.95
1	0	.032	.614	.959	-1.18	1.24
	2	-.683	.952	.474	-2.56	1.19
2	0	.715	.846	.399	-.95	2.38
	1	.683	.952	.474	-1.19	2.56

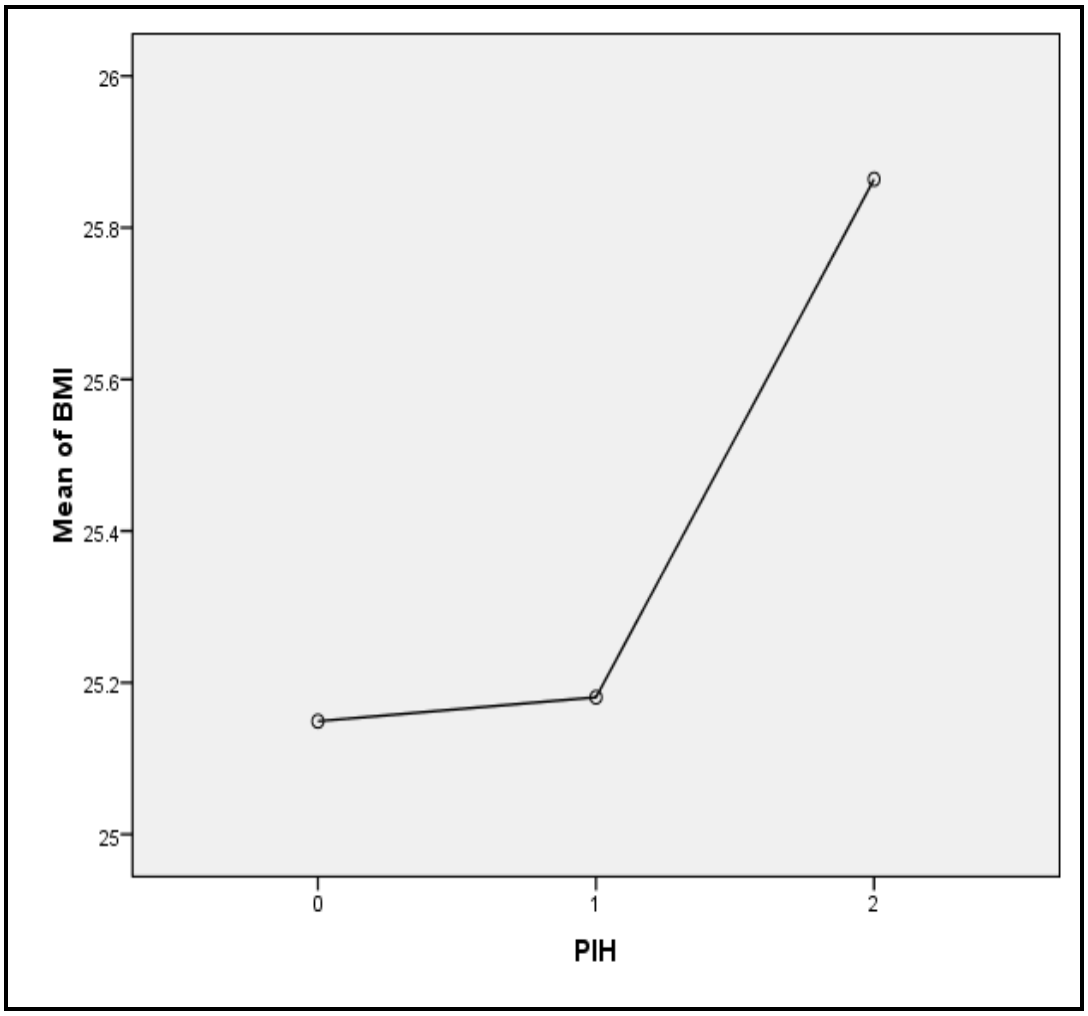
Comparison of BMI of patients without PIH with the BMI of patients with mild PIH and severe PIH have a p value of insignificant level 0.959 and 0.399.

Comparison of BMI of patients with mild PIH with BMI of patients without PIH and severe PIH have a p value of insignificant level 0.959 and 0.474.

Comparison of BMI of patients with severe PIH with BMI of patients without PIH and mild PIH have a p value of insignificant level 0.399and 0.474.

So,body mass index does not have significant correlation with the development of PIH.

MEANS PLOTS



Mean BMI value of patients without PIH -25.15

Mean BMI value of patients with mild PIH -25.18

Mean BMI value of patients with severe PIH -25.86

PREVIOUS LSCS

Crosstab

			PIH			
			0	**1**	**2**	**Total**
PRE. LSCS	N	Count	122	38	17	177
		% within PRE.LSCS	68.9%	21.5%	9.6%	100.0%
		% within PIH	91.0%	84.4%	81.0%	88.5%
		% of Total	61.0%	19.0%	8.5%	88.5%
	Y	Count	12	7	4	23
		% within PRE.LSCS	52.2%	30.4%	17.4%	100.0%
		% within PIH	9.0%	15.6%	19.0%	11.5%
		% of Total	6.0%	3.5%	2.0%	11.5%
	Total	Count	134	45	21	200
		% within PRE.LSCS	67.0%	22.5%	10.5%	100.0%
		% within PIH	100.0%	100.0%	100.0%	100.0%
		% of Total	67.0%	22.5%	10.5%	100.0%

Out of 200 patients with the previous LSCS were 23 patients, of which 12 patients(52.2%) had no PIH ,7 patients (30.4%)had mild PIH ,4 patients(17.4%)had severe PIH.

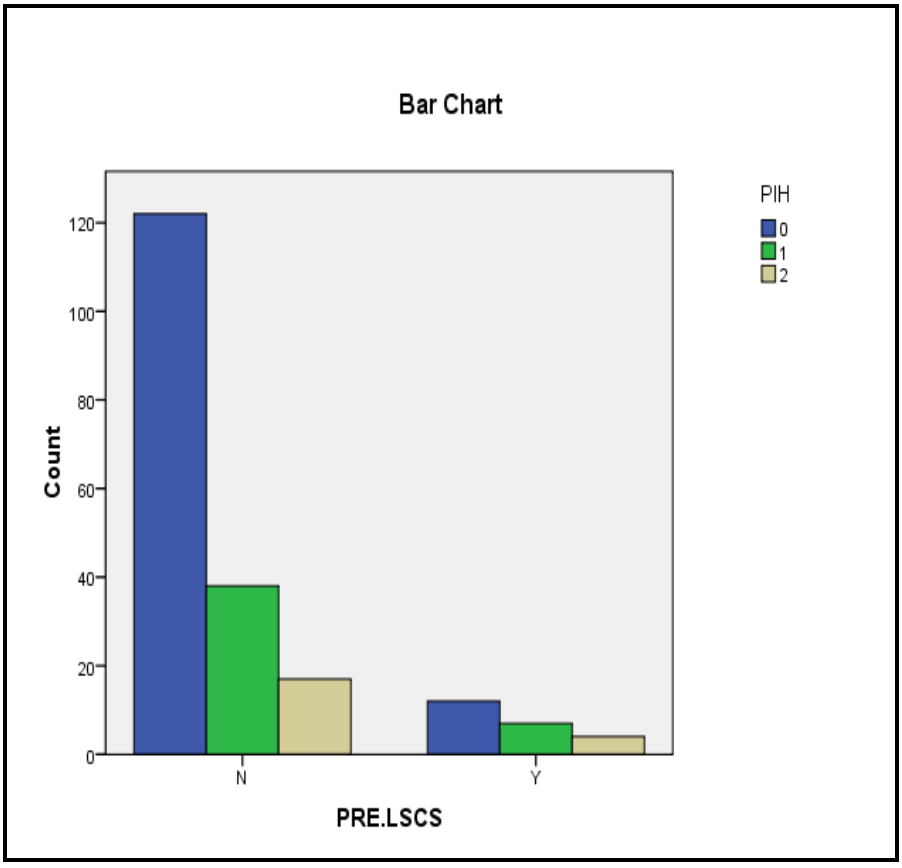
Without previous LSCS were 177 patients,of which 122 patients(68.9%)had no PIH ,38 patients(21.5%)had mild PIH and 17 patients(9.6%) had severe PIH.

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.755a	2	.252
Likelihood Ratio	2.584	2	.275
N of Valid Cases	200		

a. 1 cells (16.7%) have expected count less than

5. The minimum expected count is 2.42.Chi-Square test showed that there was no significant difference by the previous history of LSCS on the development of PIH.



Patients with previous scar and patients without previous scar have same values on the development of PIH and the P value is not significant.

ECLAMPSIA * PIH

Crosstab

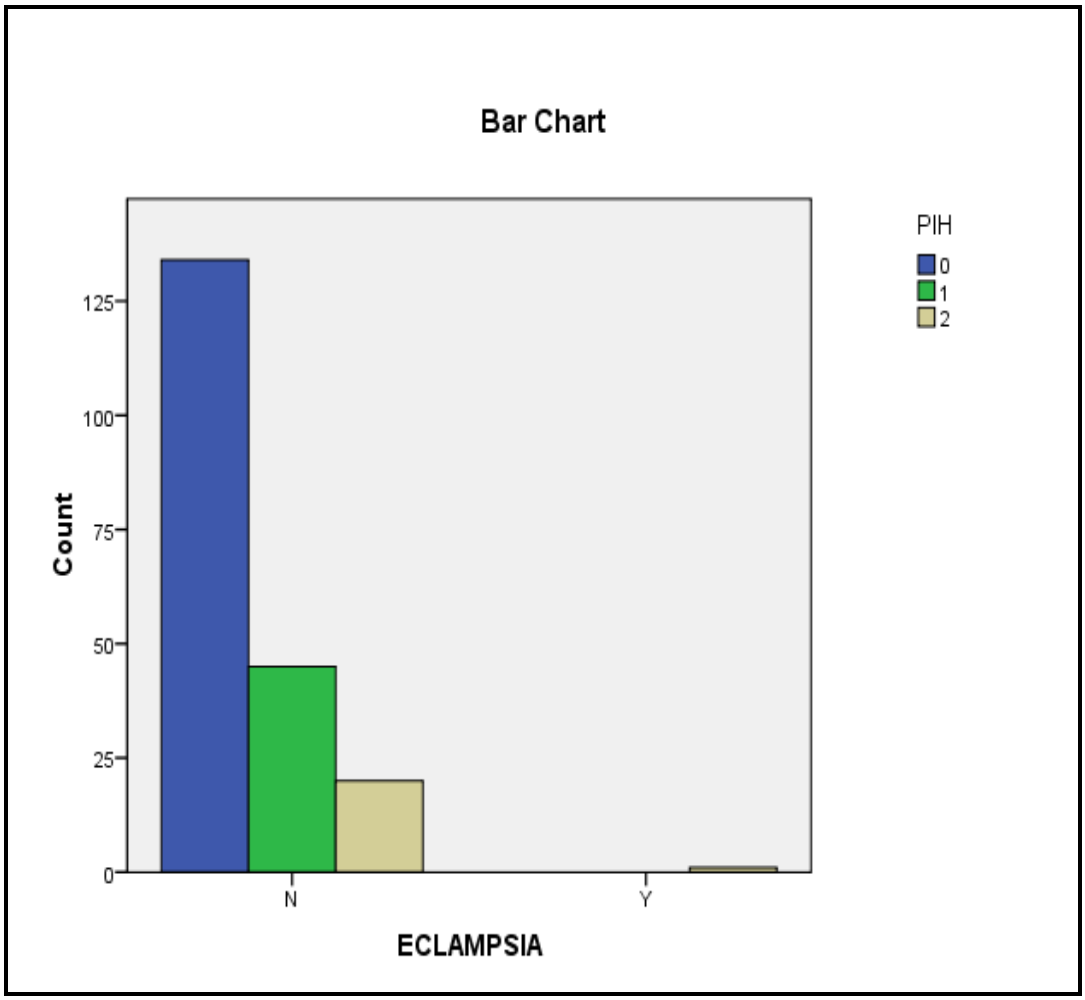
			PIH			
			0	**1**	**2**	**Total**
Eclampsia	N	Count	134	45	20	199
		% within ECLAMPSIA	67.3%	22.6%	10.1%	100.0%
		% within PIH	100.0%	100.0%	95.2%	99.5%
		% of Total	67.0%	22.5%	10.0%	99.5%
	Y	Count	0	0	1	1
		% within ECLAMPSIA	.0%	.0%	100.0%	100.0%
		% within PIH	.0%	.0%	4.8%	.5%
		% of Total	.0%	.0%	.5%	.5%
	Total	Count	134	45	21	200
		% within ECLAMPSIA	67.0%	22.5%	10.5%	100.0%
		% within PIH	100.0%	100.0%	100.0%	100.0%
		% of Total	67.0%	22.5%	10.5%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.567a	2	.014
Likelihood Ratio	4.551	2	.103
N of Valid Cases	200		

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is 11.

Eclampsia is present with only severe PIH patients ,and the P value in significant



PAST H/O PIH

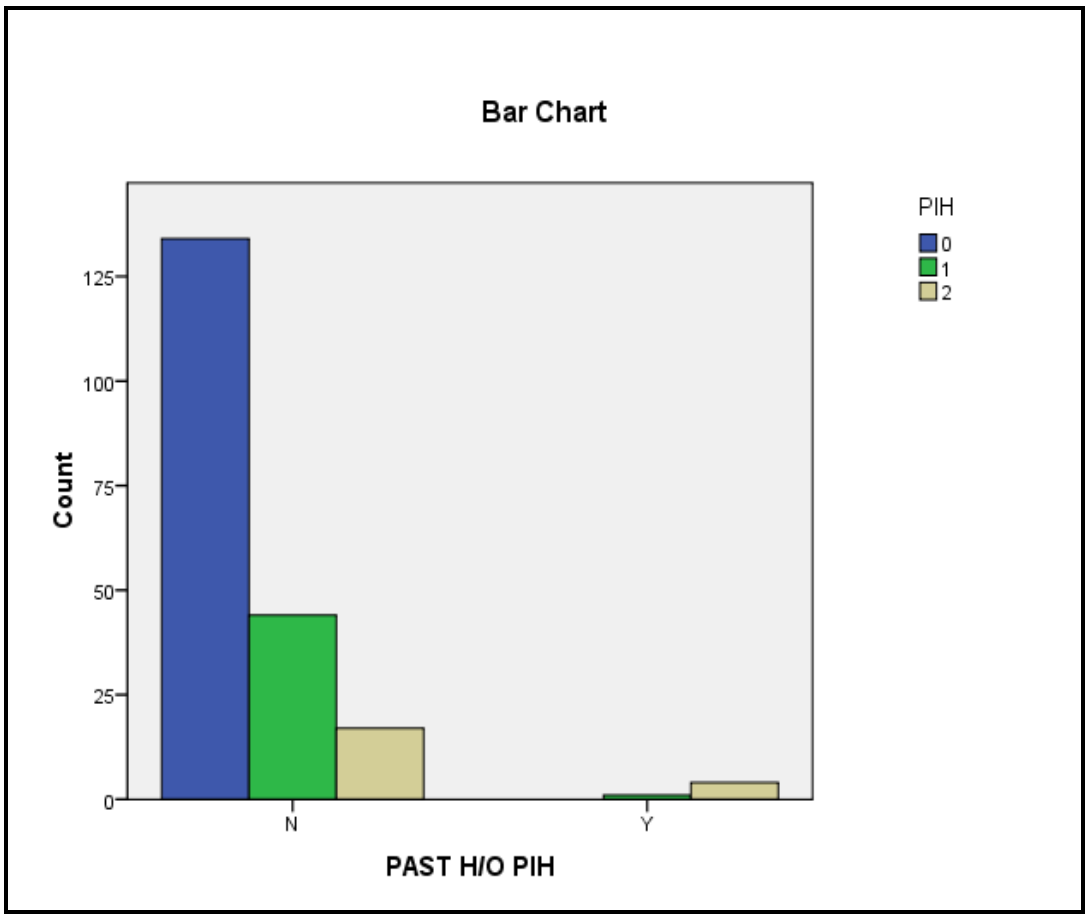
			PIH			
			0	**1**	**2**	**Total**
Past H/O PIH	N	Count	134	44	17	195
		% within PAST H/O PIH	68.7%	22.6%	8.7%	100.0%
		% within PIH	100.0%	97.8%	81.0%	97.5%
		% of Total	67.0%	22.0%	8.5%	97.5%
	Y	Count	0	1	4	5
		% within PAST H/O PIH	.0%	20.0%	80.0%	100.0%
		% within PIH	.0%	2.2%	19.0%	2.5%
		% of Total	.0%	.5%	2.0%	2.5%
	Total	Count	134	45	21	200
		% within PAST H/O PIH	67.0%	22.5%	10.5%	100.0%
		% within PIH	100.0%	100.0%	100.0%	100.0%
		% of Total	67.0%	22.5%	10.5%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	27.041a	2	.000
Likelihood Ratio	16.721	2	.000
N of Valid Cases	200		

a. 3 cells (50.0%) have expected count less than 5. The minimum expected count is 53.

Patients with previous history of PIH have significant correlation, So patients with past history of PIH have more chance for development of PIH in the future pregnancy.

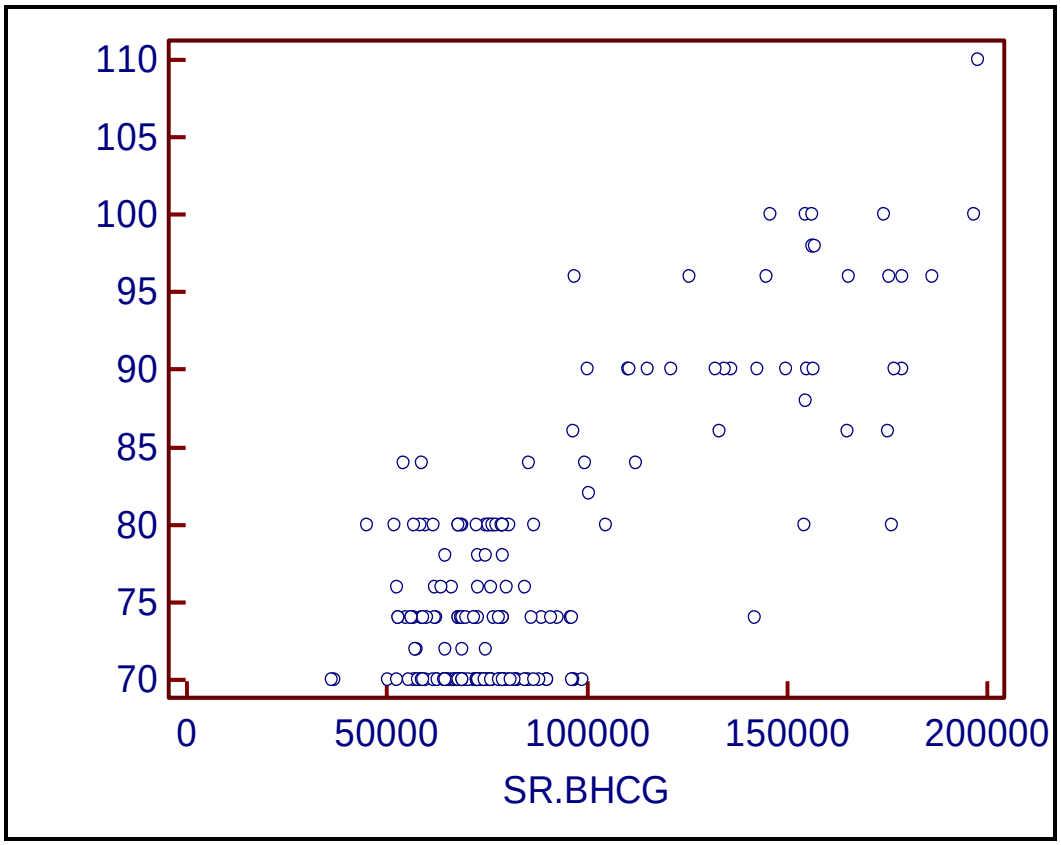


Correlation of Diastolic Blood Pressure with Serum BHCG

Variable Y	BP DIASTOLIC
Variable X	SR.BHCG

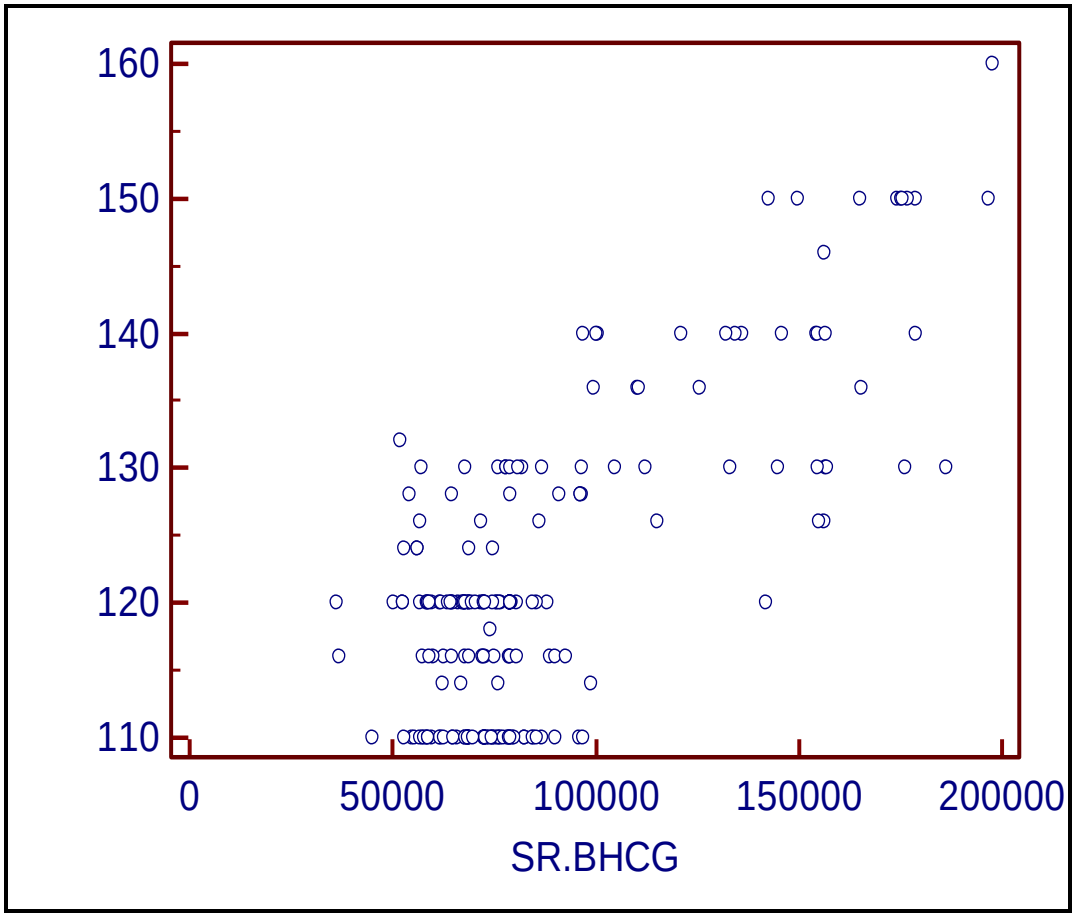
Sample size	200
Correlation coefficient r	0.7891
Significance level	P<0.0001
95% Confidence interval for r	0.7303 to 0.8363

Correlation of Diastolic Blood Pressure with Serum Beta HCG



When the diastolic blood pressure is correlated with serum beta HCG,there is a significant p value is present.

Correlation of Systolic Blood Pressure with Serum Beta HCG



Correlation

Variable Y	BP SYSTOLIC
Variable X	SR.BHCG

Sample size	200
Correlation coefficient r	0.7462
Significance level	P<0.0001
95% Confidence interval for r	0.6776 to 0.8019

When the systolic BP is correlated with the maternal serum beta HCG,significant correlation is present in between them.

DISCUSSION

The primary objective of this study was to predict the pregnancy induced hypertension and its severity by elevated serum beta HCG levels in early second trimester of pregnancy gestational age between 13 and 20weeks.There were many predictors of PIH described but none of them known to be with more sensitivity and specificity.

A similar study was conducted in obstetrics and gynaecology department of SMS medical college, Jaipur which showed the association of serum beta HCG levels with PIH and its severity. In this study Out of 200 patients 141 patients were primigravida,of which 97 patients(68.8%) had no PIH,29 patients (20.8%)had mild PIH ,15 patients (10.6%) had severe PIH. 48 patients were G2 of which 32 patients (66.7%)had no PIH ,11patients (22.9%)had mild PIH and 5 patients(10.4%)had severe PIH.10 patients were G3 of which 5 patients (50%) had no PIH ,4 patients (40%.) had mild PIH and 1 patient(10%) had severe PIH.

In the Jaipur study ,Out of 178 patients studied ,94 patients were primiparous (52.80%),women with PIH was

16(17.02%),without PIH was 78(82.98%) ,84 patients were multiparous(47.20%),women with PIH was 6(7.14%) and without PIH was 78(92.86%).Hence , parity with association of PIH has no significance with the occurrence of PIH ,Hence parity association with PIH is insignificant.

For the Serum beta HCG levels in correlation with PIH, Jaipur study showed out of 13 patients who developed severe PIH, 12 patients had beta HCG values more than 80,000miu/ml which had chi square value of 7.167 and p value <0.01.

In this study out of 200 patients 66 patients were with PIH and 134 patients were without PIH which had a sensitivity of 68.2% and specificity of 96.3% and p value significant <0.0001.And out of 155 patients, comparison of 134 patients without PIH and 21 patients with PIH had a sensitivity of 100% and specificity of 98.5% and p value < 0.0001. In Correlation of diastolic blood pressure of all 200 patients with their diastolic blood pressure have a significant correlation 0.7891 and p value of < 0.000.

Out of 200 patients studied the correlation of diastolic blood pressure with serum beta HCG levels showed a

correlation of 0.7462 and p value of <0.0001 which is statistically very significant .Out of 200 patients studied,134 patients with no PIH had mean beta HCG levels of 71205 mIU/ml ,45 patients with mild PIH had beta HCG level of 101178 mIU/ml,and 21 patients with severe PIH had mean beta HCG levels of 1,54, 560 mIU/ml.Thus patients without PIH had beta HCG levels <80,000 mIU/ml. Both patients with mild PIH and severe PIH had beta HCG values >1,00,000mIU/ml.Particularly 21 patients with severe PIH had mean beta HCG values of 1,54,560 mIU/ml.

In general recurrent risk of preeclmpsia[43] in a women whose previous pregnancy was complicated by preeclampsia near term is approximately 10%.If a woman has previously suffered from severe preeclampsia,she has 20% risk of developing preeclampsia. If a woman had HELLP syndrome or eclampsia, the risk of recurrence is 2%.

The earlier the disease manifesting the levels of serum beta HCG levels was higher in patients with preeclampsia than in normotensive women.Wheras preeclampsia is a syndrome with multisystem involvement[44], so the ideal predictive test for it should utilise a combination of many prediction.

The identification of reliable parameter indicates is a clinically relevant issue that could result in early therapeutic intervention and the better maternal and fetal outcome.

Although there is no proven effective method for prevention of preeclampsia,identification of affected pregnancies in first trimester opens up a live window, that is potentially very valuable and can ultimately lead to improved pregnancy outcome. Identification at the end of first trimester allows increased surveillance[42] of high risk pregnancies, earlier diagnosis of the clinical signs of disease, earlier identification of associated IUGR, wider ranging intervention possibilities.

By identifying pregnant women at risk for preeclampsia and starting them on low dose Aspirin before 16 weeks of gestation, physician can reduce half the risk of preeclampsia, pre term birth and IUGR. For the better prediction of early onset preeclampsia, detection is possible only

Hence elevated beta HCG level >1,00,000 mIU/ml associated with pregnancy induced hypertension and the severe PIH is associated with elevated beta HCG values >1,54,560 mIU/ml.

CONCLUSION

1) The present study shows elevated maternal serum BETA HCG levels in early second trimester was associated with development of pregnancy induced hypertension later in the pregnancy.

2) Elevated levels of serum BETA HCG values more than 1,00,000 m IU/ml was associated with increased severity of PIH with significant p value.

3) Other parameters like age of the patient, parity, gestational age, BMI of the patient which was included in the study did not correlate with both with development of PIH and its severity.

4) Compared with other biochemical parameters which was used in the prediction of PIH, serum Beta HCG levels is associated with more sensitivity and specificity.

5) Still, it needs further large randomised trials to validate the serum Beta HCG levels as better predictor of pregnancy induced hypertension and its severity.

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. G. Preetha,
PG in MS Obstetrics & Gynaecology,
Institute of Obstetrics & Gynaecology,
Madras Medical College, Chennai-8.

Dear Dr. G. Preetha,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Prediction of Pregnancy Induced Hypertension and its severity by elevated Serum B-HCG level in second trimester of pregnancy"** No.15022014

The following members of Ethics Committee were present in the meeting held on 04.02.2014 conducted at Madras Medical College, Chennai-3.

1. Dr. G. Sivakumar, MS FICS FAIS -- Chairperson
2. Dr. Kalai Selvi, MD -- Member Secretary
   Prof. of Pharmacology, MMC, Ch-3
3. Prof. Dr. K.Ramadevi, MD -- Member
   Director i/c, Instt. of Biochemistry, Chennai.
4. Dr. Geetha Devadoss, -- Member
   Associate Professor of Pathology, MMC,Ch-3.
5. Prof. Dr. Sivasubramanian, -- Member
   I/c Director, Institute of Internal Medicine, MMC, Ch-3.
6. Thiru. S. Govindasamy, BABL -- Lawyer
7. Tmt. Arnold Saulina, MA MSW -- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

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

24/2/14

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE

INFORMATION SHEET

Title of the Project

PREDICTION OF PIH AND ITS SEVERITY BY MATERNAL SRRUM BETA HCG LEVEL IN SECNOD TRIMESTER OF PREGNANCY

- We are conducting a study on "PREDICTION OF PIH AND ITS SEVERITY BY MATERNAL SERUM BETA HCG LEVEL IN SECOND TRIMESTER OF PREGNANCY" among patients attending antenatal clinic at IOG,EGMORE,CHENNAI and for that your co-operation may be valuable to us.
- The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.
- During pregnancy the occurrence of PIH is very high and it is harmful to both mother and the fetus.Hence measuring the serum Beta HCG level during the second trimester helps to predict PIH and prevent its adverse effects on maternal and the fetus.

Signature of Investigator

Date :

Signature of Participant

Date :

PATIENT CONSENT FORM

Title of the Project

PREDICTION OF PIH AND ITS SEVERITY BY MATERNAL SERUM BETA HCG LEVEL IN SECOND TRIMESTER OF PREGNANCY.

Institution : Institute of Obstetrics& Gynaecology

Egmore,Chennai-08.

Name : Date :

Age : IP No :

Sex : Project Patient No :

The details of the study have been provided to me in writing and explained to me in my own language.

I confirm that I have understood the above study and had the opportunity to ask questions.

I understood that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected.

I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

I have been given an information sheet giving details of the study.

I fully consent to participate in the above study and regarding Serum Beta HCG level in second trimester of pregnancy.

Name of the Subject	Signature	Date
Name of the Investigator	Signature	Date

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு

பிரசவ இரத்தக் கொதிப்பு மற்றும் அதன் பக்கவிளைவுகள் பற்றி பிரசவத்தின் 2வது பகுதியில் இரத்தத்தில் அதிகரிக்கும் பீட்டா எச்.சி.ஜி அளவை வைத்து ஆராய்ச்சி செய்தல்

ஆராய்ச்சி நிலையம் : **மகப்பேறு மற்றும் மகளிர் மருத்துவமனை மற்றும் ஆராய்ச்சி நிலையம்,**
இராஜீவ் காந்தி அரசு பொது மருத்துவமனை,
எழும்பூர், சென்னை-8.

பெயர் : வயது :

ஆராய்ச்சி சேர்க்கை எண் : தேதி:

பங்கு பெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் 'இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிகிறேன். எனது உடல்நலம் பாதிக்கப்பட்டாலோ அல்லது வழக்கத்திற்கு மாறான நோய்க்குறி தென்பட்டாலோ உடனை அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என்று உறுதி அளிக்கிறேன். ☐

எனக்கு ஆராய்ச்சிக்காக இரத்தத்தில் பீட்டா எச்.சி.ஜி எனும் ஹார்மோன் அளவை பார்ப்பதற்கு சம்மதிக்கிறேன். ☐

.....	.....	.....
பங்கேற்பாளர் பெயர்	கையொப்பம்/ கைரேகை	தேதி

.....	.....	.....
ஆராய்ச்சியாளரின் பெயர்	கையொப்பம்	தேதி

ஆராய்ச்சி தகவல் தாள்

தலைப்பு

பிரசவ இரத்தக் கொதிப்பு மற்றும் அதன் பக்கவிளைவுகள் பற்றி பிரசவத்தின் 2வது பகுதியில் இரத்தத்தில் அதிகரிக்கும் பீட்டா எச்.சி.ஜி அளவை வைத்து ஆராய்ச்சி செய்தல்

தங்களுக்கு பிரசவத்தின் போது இரத்தக்கொதிப்பு வருவதால், அது பிரவசத்தின் சிகிச்சை முறையிலும், தங்களது வயிற்றில் வளரும் சிசுவிற்கும் தங்களுடைய உயிருக்கும் ஆபத்து ஏற்படலாம். தங்களுடைய 2வது பகுதி பிரசவத்தின்போது இரத்ததில் பீட்டா எச்.சி.ஜி அளவை பார்த்து தங்களுக்கு பிரசவ இரத்தக்கொதிப்பு மற்றும் அதனால் ஏற்படும் விளைவுகளை அறிந்துகொண்டு நாம் சிகிச்சை செய்யலாம். இதனால் தங்களது வயிற்றில் வளரும் சிசுவையும், தங்களையும் பிரசவ இரத்தக்கொதிப்பு பாதிப்பிலிருந்து காப்பாற்றலாம். எனவே தங்களுடைய பிரசவத்தின்போது இரத்தத்தில் பீட்டா எச்.சி.ஜி எனும் ஹார்மோன் அளவைப் பார்த்து பிரசவ இரத்தக்கொதிப்பு பற்றி ஆராய்ச்சி செய்யலாம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்பு சிகிச்சையின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

.....	.....	.....
பங்கேற்பாளர் பெயர்	கையொப்பம்/ கைரேகை	தேதி

.....	.....	.....
ஆராய்ச்சியாளரின் பெயர்	கையொப்பம்	தேதி

PROFORMA

INTRODUCTION

Name of patient

Age of patient

Occupation

Obstetric score

Socio economic status-

Gestational .age

LMP: & EDD

Booked & immunized

PRESENTING COMPLAINTS;

H/O: fever

H/O bleeding per vaginum

MENSTRUAL HISTORY

Regular cycles

Reliability of LM.P

MARITALHISTIORY

Obstetric history

Previous mode of-deliveries

Booked

Immunized

Last child birth

Previous live child

Miscarriages

Bad obstetric history

H/O GDM, gestational hypertension in previous pregnancies

H/O recurrent urinary tract infection

H/O anemia

PAST HISTORY

H/O chronic illnesses

H/O- HT&DM

H/O hypothyroidism

H/O Surgeries

GENERAL EXAMINATION

Height

Weight

BMI

Pallor

Pedal edema

Hydration

VITALS

Temperature

Pulse rate

Respiratory rate

Blood pressure

SYSTEM EXAMINATION

CVS

RS

ABDOMINAL EXAMINATION

Fundal height

INVESTIGATIONS

Urine analysis

Blood- grouping

CBC

High vaginal swab

Sr.Beta HCG

ULTRA SOUND

Gestational age

viability

MONITORING

INTERVENTION

OUTCOME MEASURES

MASTER CHART

S. No	NAME	AGE	PARITY	GEST.AGE(WKS)	PRE.LSCS	PAST H/O PIH	BMI	BP SYSTOLIC	BP DIASTOLIC	SR.BHCG	PROTENURIA	PIH	ECLAMPSIA
1	HARIPRIYA	25	1	16	N	N	21.99	120	70	36092	0	0	N
2	KANNAMMAL	24	1	16	N	N	20.92	116	70	36980	0	0	N
3	PREMA	26	1	15	N	N	24.89	110	80	45096	0	0	N
4	BINDU	23	2	17	N	N	30.79	120	70	50108	0	0	N
5	PONMALAR	26	2	17	N	N	28.99	132	80	51906	0	1	N
6	PRIYA	28	1	13	N	N	30.4	120	76	52606	0	0	N
7	MANGAI	26	1	17	N	N	19.09	120	70	52608	0	0	N
8	SARASWATHI	26	1	16	N	N	24.65	124	74	52806	0	1	N
9	KAVITHA	29	2	18	N	N	24.78	110	74	52908	0	0	N
10	SENTHAMARAI	24	1	16	N	N	31.63	128	84	54108	0	1	N
11	FLORET	24	3	17	Y	N	24.98	110	74	54808	0	0	N
12	PONNAMMAL	26	2	18	N	N	31.09	110	70	55606	0	0	N
13	MAHESWARI	29	3	19	Y	N	23.9	124	74	56102	0	1	N
14	VENNILA	19	1	14	N	N	19	124	74	56124	0	1	N
15	KARUNYA	23	1	15	N	N	22.79	120	70	56708	0	0	N
16	AYUSHA	26	1	17	N	N	27.98	110	74	56786	0	0	N
17	MARAGATHAM	28	1	15	N	N	30.71	126	80	56806	0	1	N
18	SASIKALA	30	2	18	N	N	27.82	130	72	56980	0	1	N
19	SRIDEVI	24	1	16	N	N	30.65	116	72	57302	0	0	N
20	ARUNA	22	1	15	N	N	24.77	110	70	57506	0	0	N
21	INDUJA	27	1	13	N	N	23.76	110	70	57704	0	0	N
22	LOGESWARI	26	1	17	N	N	27.99	110	80	58404	0	0	N
23	VASANTHA	26	1	16	N	N	19.87	120	70	58404	0	0	N
24	RUBINI	26	1	16	N	N	24.76	120	70	58604	0	0	N
25	KAVYA	26	1	17	N	N	19.8	120	74	58604	0	0	N
26	MARYAMMAL	28	1	16	N	N	23.09	110	70	58804	0	0	N
27	SARANYA	28	1	15	N	N	26.88	110	84	58805	0	0	N
28	DEVAKI	29	2	17	N	N	18.98	116	74	58904	0	0	N
29	ANUSHA	28	1	15	N	N	26.59	120	70	58906	0	0	N
30	SAVITHRI	23	1	13	N	N	22.09	110	80	59702	0	0	N
31	AROKIYAMARY	25	1	17	N	N	29.06	120	70	59802	0	0	N
32	SARANYA	27	1	16	N	N	19.89	116	74	59906	0	0	N

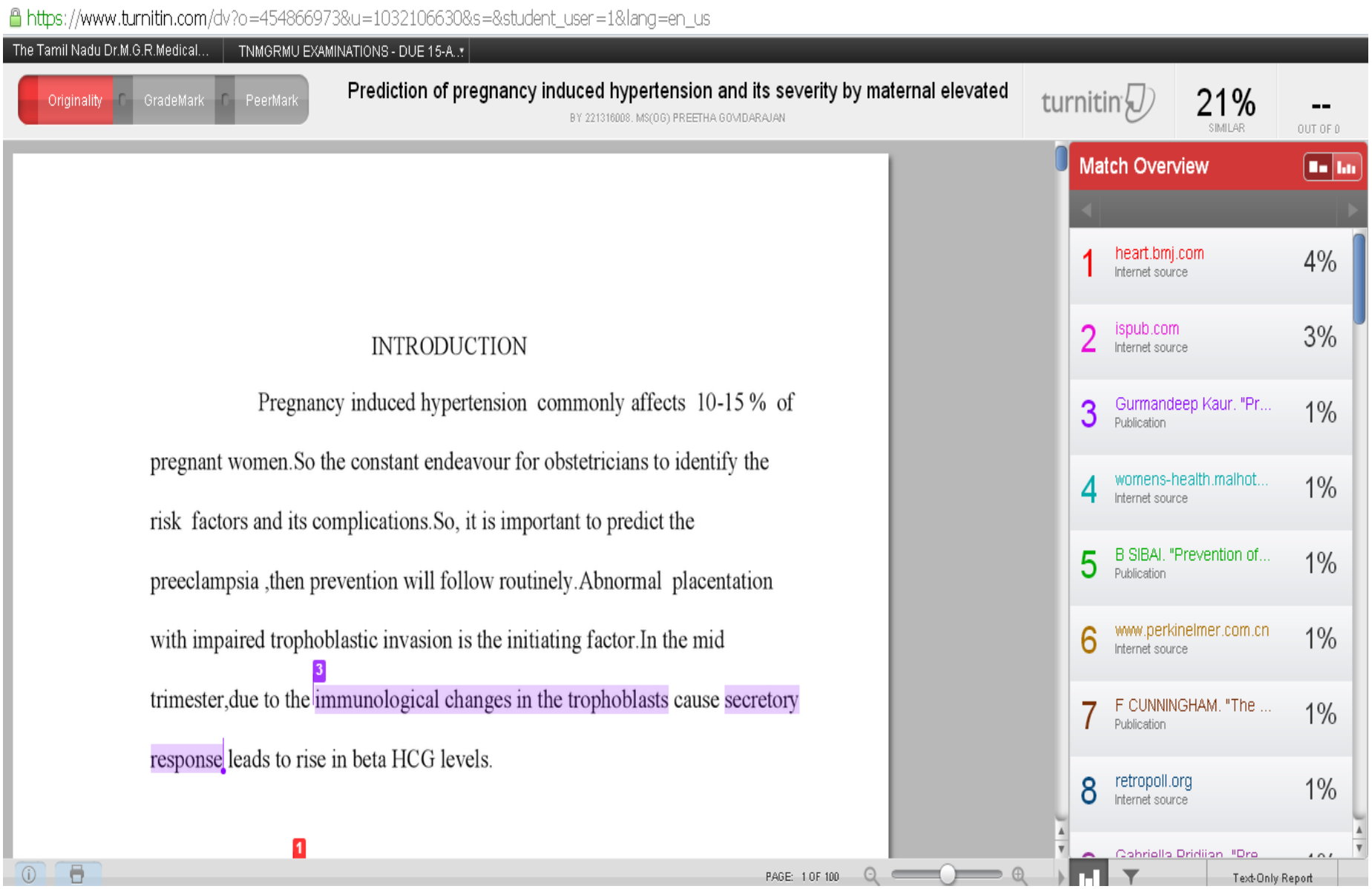
S. No	NAME	AGE	PARITY	GEST.AGE(WKS)	PRE.LSCS	PAST H/O PIH	BMI	BP SYSTOLIC	BP DIASTOLIC	SR.BHCG	PROTENURIA	PIH	ECLAMPSIA
33	BAGYAM	24	1	13	N	N	19.85	110	80	61806	0	0	N
34	PAVAI	25	1	13	N	N	25.05	120	70	61806	0	0	N
35	SUMATHI	22	1	13	N	N	24.87	110	76	61906	0	0	N
36	ROJA	26	1	14	N	N	24.59	120	74	61908	0	0	N
37	BABYAMMAL	25	1	17	N	N	26.98	114	74	62404	0	0	N
38	VANITHA	25	1	17	N	N	28.62	110	70	62508	0	0	N
39	GANGA	23	1	14	N	N	28.99	116	70	62606	0	0	N
40	JOSPIN	27	2	19	Y	N	22.67	120	76	63504	0	0	N
41	DEVI	30	2	15	N	N	24.9	120	70	64362	0	0	N
42	SAROJA	24	1	18	N	N	26.99	120	70	64506	0	0	N
43	KALAI	23	2	18	N	N	29.59	120	72	64567	0	0	N
44	SEETHA	22	2	16	N	N	19.8	128	70	64623	0	1	N
45	GOVINDAMMAL	26	2	15	N	N	26.87	116	78	64706	0	0	N
46	MONISHA	24	1	16	N	N	23.75	110	70	64806	0	0	N
47	VARALAKSHMI	24	2	15	N	N	24.87	120	70	64806	0	0	N
48	SHOPIA	26	1	14	N	N	24.97	110	70	64906	0	0	N
49	KARUNYA	24	1	14	N	N	30.83	110	70	65906	0	0	N
50	SRIDEVI	23	1	17	N	N	23.6	120	76	66123	0	0	N
51	SEETHALAKSHMI	25	1	18	N	N	21.89	114	70	66808	0	0	N
52	KAVITHA	24	1	17	N	N	22.55	120	70	67097	0	0	N
53	BANUMATHI	26	1	14	N	N	27.66	120	70	67508	0	0	N
54	SIVASAKTHI	25	2	13	N	N	27.98	116	70	67704	0	0	N
55	HEMA	22	1	15	N	N	22.09	120	70	67706	0	0	N
56	SOWMYA	24	3	13	Y	N	24.87	130	80	67802	0	1	N
57	KANNATHAL	22	1	14	N	N	26.9	120	74	67806	0	0	N
58	KANTHA	23	1	17	N	N	26.04	110	74	67808	0	0	N
59	VASANTHI	28	2	13	Y	N	21.87	120	70	67895	0	0	N
60	CHELLAMMAL	27	1	14	N	N	26.96	110	80	67902	0	0	N
61	CHANDRA	24	1	17	N	N	22.51	120	70	67908	0	0	N
62	GOVINDAMMAL	26	1	15	N	N	20.67	110	74	68408	0	0	N
63	SELVI	29	1	13	N	N	26.97	110	80	68504	0	0	N
64	BABY	23	1	16	N	N	25.78	110	74	68508	0	0	N
65	PAPATHI	26	2	17	N	N	21.99	110	74	68702	0	0	N
66	PRIYA	25	1	15	N	N	22.87	110	72	68802	0	0	N

S. No	NAME	AGE	PARITY	GEST.AGE(WKS)	PRE.LSCS	PAST H/O PIH	BMI	BP SYSTOLIC	BP DIASTOLIC	SR.BHCG	PROTENURIA	PIH	ECLAMPSIA
67	VERAMMAL	23	1	14	N	N	24.9	110	70	68804	0	0	N
68	MONISHA	26	1	16	N	N	26.87	120	70	68806	0	0	N
69	MANGAI	23	2	16	N	N	31.87	120	74	68902	0	0	N
70	YOGALAKSHMI	24	1	17	Y	N	19.88	120	80	68902	0	0	N
71	KANNATHAL	23	1	16	N	N	23.78	124	70	68902	0	1	N
72	HARINI	29	1	15	N	N	27.9	116	70	68904	0	0	N
73	KANTHA	28	1	16	N	N	25.8	120	70	69406	0	0	N
74	NITHYA	29	2	13	Y	N	28.7	110	74	69807	0	0	N
75	STELLAMARY	28	1	16	N	N	21.77	120	70	70608	0	0	N
76	SINDU	26	1	14	N	N	21.85	120	70	71704	0	0	N
77	MALA	21	1	14	N	N	22.8	126	74	71924	0	1	N
78	RAJESHWARI	22	2	16	N	N	19.7	116	74	72106	0	0	N
79	GEETHA	27	1	18	N	N	19.32	110	80	72404	0	0	N
80	MANJULA	27	2	16	N	N	23.4	120	70	72410	0	0	N
81	MARY	28	1	15	N	N	24.78	120	70	72503	0	0	N
82	KANIMOZHI	28	2	18	N	N	30.88	116	70	72508	0	0	N
83	GIRIJA	24	1	16	N	N	26.09	116	70	72606	0	0	N
84	AMUTHA	27	1	16	N	N	19.44	120	78	72606	0	0	N
85	GAJALAKSHMI	26	3	14	Y	N	27.34	110	76	72608	0	0	N
86	PREMA	29	1	15	N	N	23.77	120	70	72608	0	0	N
87	JEYANTHI	28	1	14	N	N	23.93	110	70	72802	0	0	N
88	KANTHA	24	1	17	N	N	25.09	110	74	72804	0	0	N
89	GOVINDAMMAL	28	2	17	N	N	26.56	110	70	72806	0	0	N
90	KANTHA	24	1	16	N	N	21.77	110	70	72904	0	0	N
91	ANUSHA	25	1	16	N	N	29.78	110	70	73306	0	0	N
92	RAJATHI	23	1	18	N	N	26.99	110	70	73806	0	0	N
93	RESHMI	23	2	14	N	N	28.62	118	70	74204	0	0	N
94	SINDHU	29	1	17	N	N	28.7	110	70	74403	0	0	N
95	VETRISELVI	23	1	13	N	N	26.84	110	80	74602	0	0	N
96	ANANTHI	24	1	16	N	N	23.89	110	72	74804	0	0	N
97	KASTHURI	28	1	18	N	N	28.99	120	70	74806	0	0	N
98	KALAISELVI	26	2	16	Y	N	29.64	124	78	74806	0	1	N
99	SUMATHI	26	1	15	N	N	21.09	116	70	74902	0	0	N
100	ROJA	27	1	16	N	N	19.5	110	80	75506	0	0	N

S. No	NAME	AGE	PARITY	GEST.AGE(WKS)	PRE.LSCS	PAST H/O PIH	BMI	BP SYSTOLIC	BP DIASTOLIC	SR.BHCG	PROTENURIA	PIH	ECLAMPSIA
101	PONMALAR	23	1	18	N	N	31.55	120	80	75604	0	0	N
102	GAYATHRI	26	1	14	N	N	26.99	120	70	75706	0	0	N
103	MUNEERA	24	3	15	N	N	24.66	110	70	76000	0	0	N
104	INDUJA	26	2	19	Y	N	29.7	114	76	76000	0	0	N
105	AMMU	19	1	16	N	N	27	130	70	76101	0	1	N
106	INDUMATHI	26	1	14	N	N	24.66	120	70	76404	0	0	N
107	STELLA	27	2	16	N	N	18.77	110	80	76508	0	0	N
108	KANNAKINAGHY	24	1	18	N	N	26.54	120	80	76802	0	0	N
109	SARANYA	26	1	18	N	N	22.09	110	74	76804	0	0	N
110	NITHYAGANESAN	27	1	19	N	N	20.56	110	80	77404	0	0	N
111	RENUKADEVI	21	1	18	N	N	26.8	130	70	78107	0	1	N
112	VANISHREE	22	1	16	N	N	19.9	130	74	78124	0	1	N
113	DEEPIKA	24	1	17	N	N	22.87	110	70	78302	0	0	N
114	ARULAMMAL	29	1	18	N	N	28.97	110	80	78502	0	0	N
115	SAROJA	25	1	17	N	N	29.65	116	70	78506	0	0	N
116	DEVI	26	2	16	N	N	25.98	120	70	78802	0	0	N
117	ELLAMMAL	27	1	15	N	N	23.79	120	70	78804	0	0	N
118	NIRUBAMA	28	2	17	N	N	21.87	120	74	78804	0	0	N
119	ROSEMARY	23	1	16	N	N	21.58	120	74	78804	0	0	N
120	PONVASUKI	24	2	14	N	N	23.11	130	78	78804	0	1	N
121	SNEHA	26	1	18	N	N	28.09	110	80	78806	0	0	N
122	PARASAKTHI	26	1	14	N	N	23.98	116	70	78806	0	0	N
123	DEVI	22	1	18	N	N	24.87	120	74	78806	0	0	N
124	SAKTHIPRIYA	25	1	15	N	N	23.01	120	80	78806	0	0	N
125	MAHESWARI	24	2	16	N	N	29.31	110	70	78905	0	0	N
126	ANUSIYA	29	1	14	N	N	24.83	110	80	78906	0	0	N
127	NANTHINI	26	1	13	N	N	24.79	116	70	78906	0	0	N
128	AMUTHA	28	1	15	N	N	20.66	120	70	78965	0	0	N
129	NITHYA	25	1	13	N	N	21.99	128	70	79102	0	1	N
130	CHRISTINA	24	1	14	N	N	23.8	120	70	79124	0	0	N
131	DEEPTHI	26	1	16	N	N	29.04	110	70	79508	0	0	N
132	SUGANTHA	28	1	15	N	N	30.98	110	76	79902	0	0	N
133	SAGUNTHALA	28	2	15	Y	N	31.9	116	70	80508	0	0	N
134	PONNAMMAL	23	1	14	N	N	30.78	120	80	80608	0	0	N

S. No	NAME	AGE	PARITY	GEST.AGE(WKS)	PRE.LSCS	PAST H/O PIH	BMI	BP SYSTOLIC	BP DIASTOLIC	SR.BHCG	PROTENURIA	PIH	ECLAMPSIA
135	MALAR	29	3	13	N	N	24.09	130	70	80987	0	1	N
136	VINITHA	20	1	16	N	N	30.2	130	70	81806	0	1	N
137	SUGANTHA	26	2	14	N	N	32.09	110	70	82604	0	0	N
138	GOVINDAMMAL	24	1	16	N	N	27.99	110	70	82608	0	0	N
139	SUMATHY	31	3	17	Y	N	21.5	120	70	84506	0	0	N
140	MALLIKA	26	1	18	N	N	19.76	110	76	84602	0	0	N
141	PARVATHY	21	2	19	N	N	22.6	110	70	84827	0	0	N
142	KANNAMAL	30	3	15	Y	N	22.8	120	70	85403	0	0	N
143	SUNITHA	27	2	17	N	N	22.8	110	84	85503	0	0	N
144	PRAVITHA	21	1	15	N	N	21.7	126	74	86124	0	1	N
145	BAGYAM	24	1	15	N	N	20.32	130	70	86704	0	1	N
146	ANNAMMAL	26	1	17	N	N	29.77	110	80	86804	0	0	N
147	SUNITHA	27	1	15	N	N	29.07	120	70	88000	0	0	N
148	MALLI	22	2	13	N	N	24	116	74	88806	0	0	N
149	HEMA	24	1	14	N	N	21.08	110	70	89904	0	0	N
150	KAVITHA	23	1	13	N	N	21.98	116	70	89904	0	0	N
151	BHARATHI	22	1	16	N	N	21.5	128	74	90961	0	1	N
152	JOTHI	27	2	18	Y	N	29.04	116	74	92606	0	0	N
153	MARY	23	1	15	N	N	28.9	110	74	95904	0	0	N
154	RANI	22	2	13	Y	N	24.7	128	70	96107	0	1	N
155	MALLIGA	21	1	15	N	N	24.9	128	74	96162	0	1	N
156	RATHIDEVI	19	1	14	N	N	26.9	128	70	96427	0	1	N
157	KANNATHAL	25	1	16	N	N	21.99	130	86	96708	0	1	N
158	SRIDEVI	25	1	16	N	N	31..09	110	70	96786	0	0	N
159	HEMAMALINI	29	2	16	Y	Y	26.99	140	96	96999	1	2	N
160	KANATHA	29	2	17	Y	N	21.6	114	70	98750	0	0	N
161	PANIMALAR	27	1	15	N	N	27.66	136	84	99609	0	1	N
162	RAJI	24	1	15	N	N	28.9	140	90	100124	0	2	N
163	VALLIARASI	22	1	14	N	N	24.83	140	82	100567	0	1	N
164	GOVINDAMMAL	26	1	13	N	N	23.19	130	80	104608	0	1	N
165	KAVITHA	26	1	14	N	N	23.45	136	90	110307	1	1	N
166	MUTHAMMA	31	1	18	N	N	23.75	136	90	110450	0	1	N
167	SONIA	29	4	15	Y	Y	26..98	130	84	112306	0	1	N
168	MONISHA	30	1	16	N	N	24.87	126	90	115308	0	1	N

S. No	NAME	AGE	PARITY	GEST.AGE(WKS)	PRE.LSCS	PAST H/O PIH	BMI	BP SYSTOLIC	BP DIASTOLIC	SR.BHCG	PROTENURIA	PIH	ECLAMPSIA
169	RAMYA	21	1	16	N	N	21.8	140	90	121006	1	2	N
170	VAISNAVI	22	1	14	N	N	27.8	136	96	125508	0	1	N
171	FATHIMA	26	1	15	N	N	26.88	140	90	132000	1	2	N
172	SARITHA	28	3	16	N	N	22.09	130	86	132987	0	1	N
173	SUMANGALI	24	1	14	N	N	24..98	140	90	134508	0	2	N
174	MANJULA	19	2	15	N	N	26.7	140	90	135906	0	2	N
175	vaisnavi	28	2	17	N	N	26.98	120	74	142000	0	0	N
176	VANITHA	25	2	14	Y	N	29.71	150	90	142604	0	2	N
177	GEETHA	22	1	12	N	N	31.99	130	96	144802	0	1	N
178	VANITHA	32	1	14	N	N	29.9	140	100	145762	2	2	N
179	KANNAKI	26	2	16	Y	N	30.54	140	80	154378	1	1	N
180	ABI	29	2	14	Y	N	25.9	140	88	154606	1	1	N
181	REVATHY	25	1	15	N	N	24.09	130	100	154734	0	2	N
182	SHALINI	26	1	14	N	N	30.45	126	90	154906	0	1	N
183	SEETHA	24	1	18	N	N	26.88	126	98	156406	0	1	N
184	DEEPTHI	26	1	14	N	N	21.78	140	90	156704	1	2	N
185	ARUNA	22	1	14	N	N	21.56	130	98	156706	1	1	N
186	BARANI	28	2	15	N	N	31.67	130	98	156804	1	1	N
187	VIMALA	29	2	13	Y	Y	20.76	150	86	165000	2	2	N
188	SHEEPA	27	2	16	N	N	21.93	136	96	165345	2	1	N
189	MAHESWARI	20	1	15	N	N	29.9	150	100	174230	1	2	N
190	DEVAKI	26	3	18	Y	N	25.75	150	86	175302	1	2	N
191	GOWRI	28	2	16	N	N	19.59	150	96	175602	1	2	N
192	VIJI	22	1	17	N	N	23.9	130	80	176102	0	1	N
193	SANTHAYI	27	1	16	N	N	28.09	150	90	176987	1	2	N
194	DHANAM	26	1	16	N	N	29.7	150	96	178760	1	2	N
195	SELVI	24	1	16	N	Y	21.43	140	90	178908	2	2	N
196	SUMATHI	24	1	19	N	N	21.87	150	100	196768	2	2	N
197	TAMILSELVI	25	1	14	N	Y	32.85	160	110	197650	1	2	Y
198	SENTHAMIL	23	1	15	N	N	27.09	150	90	149802	0	2	N
199	NAGESHWARI	28	2	13	N	N	22.8	130	96	186214	1	1	N
200	MURUGAMMAL	25	1	14	N	N	23.5	146	100	156405	1	2	N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Pregnancy induced hypertension commonly affects 10-15 % of pregnant women.So the constant endeavour for obstetricians to identify the risk factors and its complications.So, it is important to predict the preeclampsia ,then prevention will follow routinely.Abnormal placentation with impaired trophoblastic invasion is the initiating factor.In the mid trimester,due to the immunological changes in the trophoblasts cause secretory response leads to rise in beta HCG levels.
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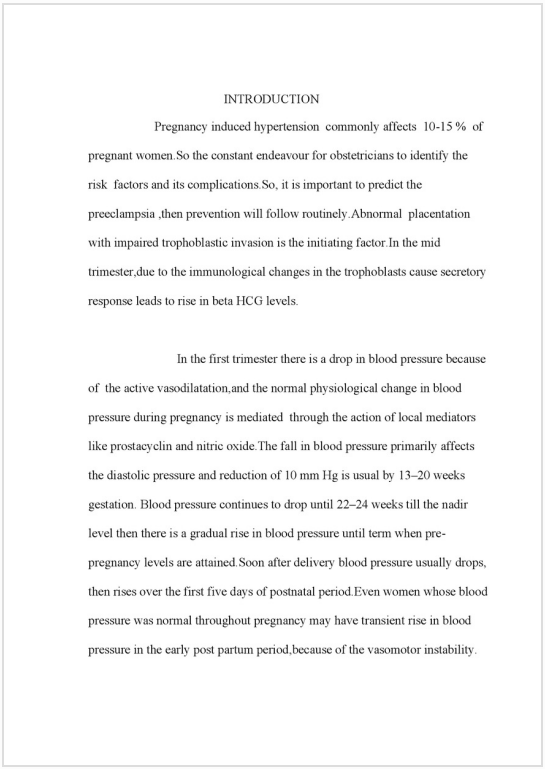

INTRODUCTION

Pregnancy induced hypertension commonly affects 10-15 % of pregnant women.So the constant endeavour for obstetricians to identify the risk factors and its complications.So, it is important to predict the preeclampsia ,then prevention will follow routinely.Abnormal placentation with impaired trophoblastic invasion is the initiating factor.In the mid trimester,due to the immunological changes in the trophoblasts cause secretory response leads to rise in beta HCG levels.

In the first trimester there is a drop in blood pressure because of the active vasodilatation,and the normal physiological change in blood pressure during pregnancy is mediated through the action of local mediators like prostacyclin and nitric oxide.The fall in blood pressure primarily affects the diastolic pressure and reduction of 10 mm Hg is usual by 13–20 weeks gestation. Blood pressure continues to drop until 22–24 weeks till the nadir level then there is a gradual rise in blood pressure until term when pre-pregnancy levels are attained.Soon after delivery blood pressure usually drops, then rises over the first five days of postnatal period.Even women whose blood pressure was normal throughout pregnancy may have transient rise in blood pressure in the early post partum period,because of the vasomotor instability.