EVALUATION OF BETA HUMAN CHORIONIC GONADOTROPIN LEVELS IN PRE ECLAMPSIA-A CASE CONTROL STUDY

By

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DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA
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IN

OBSTETRICS AND GYNAECOLOGY

Under the Guidance of
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Dr. KOSINEPALLI CHARISHMA

LIST OF ABBREVATIONS USED

ACOG	American College of Obstetricians and Gynecologists
ALT	Alanine Transaminase
AST	Aspartate Transaminase
βhCG	Beta Human Chorionic Gonadotropin Hormone
BMI	Body Mass Index
BP	Blood Pressure
CRH	Corticotropin Releasing Hormone
DBP	Diastolic Blood Pressure
FSH	Follicular Stimulating Hormone
GnRH	Gonadotrophin Releasing Hormone
HLA	Human Leucocyte antigen
hPL	Human Placental Lactogen
LH	Leutinizing Hormone
LMP	Last Menstrual Period
MHC I&II	Major Histocompatibility Complex I & II
NO	Nitric Oxide
PGI2	Prostaglandin I_2
TSH	Thyroid Stimulating Hormone
TXA2	Thromboxane A_2
Th1 and Th_2 cells	T lymphocyte Helper cells
PE	Preeclampsia
PAPP-A	Pregnancy Associated Plasma Protein A
PIGF	Placental Growth Factor
SBP	Systolic Blood Pressure

sEng	Soluble Endoglin
sFlt	Soluble form of Tyrosine Kinase
TGF-β	Tumour Growth Factor - β

ABSTRACT

INTRODUCTION: Preeclampsia is a multisystem disorder characterised by hypertension, proteinuria and oedema after 20 weeks of gestation with proteinuria..It is major cause of maternal and foetal morbidity and mortality worldwide in up to 10 percent pregnancies. Approximately 800 women die due to pregnancy and childbirth related complications around the world every day.

The aim of the study is to quantify the serum β hCG level in normal pregnancy and Preeclampsia cases during 32-42 weeks of gestation and to estimate the level of significance between serum β hCG level in accordance to severity of Preeclampsia.

METHODS : It is A case control study with 84 study population between 32- 42 weeks of gestation with singleton pregnancy among which 42 were Normotensive pregnancies and 42 Preeclampsia cases. In all these patients β hCG levels are estimated by CLIA method. There are some inclusion and exclusion criteria mentioned in brief later. Various outcome results were recorded and tabulated. The results were statistically analyzed using parameters like mean, standard deviation and chi square test.

RESULTS: The mean β hCG level was higher in cases with Severe Preeclampsia (47915.82mIU/ml) when compared to Non severe Preeclampsia cases (24226.43mIU/ml) and Normotensive pregnancies (12799.11 mIU/ml) which is statistically significant showing that β hCG is a good diagnostic test for Preeclampsia with a sensitivity of 86.96% to diagnose Severity in preeclampsia cases.

CONCLUSION: Elevated levels of serum β hCG levels can be used as the Diagnostic marker for establishing Preeclampsia in third trimester of pregnancy and its levels are parallel to the severity in Preeclampsia.

KEYWORDS: Beta Human Chorionic Gonadotropin Hormone (β hCG), Eclampsia, Preeclampsia, Proteinuria.

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Introduction

INTRODUCTION

Preeclampsia is a multisystem disorder characterised by hypertension, proteinuria and oedema after 20 weeks of gestation compromising Placenta, Hepatic, Renal, Haematological, Neurological and Cardiovascular systems. Symptoms of preeclampsia include persistent headache, blurred vision, vomiting and abdominal pain.

It is a major cause of maternal and foetal morbidity and mortality worldwide in up to 10 percent pregnancies. Approximately 800 women die due to pregnancy and childbirth related complications around the world every day[1.]

In Asia and Africa nearly 1/10th of maternal death is related to hypertensive disorders of pregnancy.

The incidence of preeclampsia in India is about 8 to 10 percent associated with maternal mortality[2].

Human Chorionic Gonadoptropin (hCG) Hormone is a glycoprotein consisting of 2 sub units α and β subunits through covalent linkages which is produced by placental syncitiotrophoblastic cells. Its levels in maternal circulation reaches to peak during 8 to 10 weeks of gestation and then plateaus at 18 to 20 weeks of gestation. The release of free β hCG subunit from HCG is either from trophoblastic cells directly or due to dissociation of HCG itself.

The transformation of cytotrophoblastic cells which are dominant in early gestation period into later stage as syncitiotrophoblasts in pregnancy and placental vascular damage creates hypoxia which might be the reason for HCG production due to hyperplastic trophoblastic cells probably.

β hCG subunit levels in the circulation accounts less than 4% of the total hCG levels.

There is a need to know β hCG levels in the normotensive pregnancies and in preeclampsia in the local population where preeclampsia is more predominant.

Since the levels of β hCG considerably vary in third trimester in comparision between the normal and preeclamptic pregnancy measuring the levels of β hCG can be used as a yard stick in classifying preeclampsia according to severity in accordance to the levels of β hCG and to observe whether any correlation exists between the β hCG levels and various complications of preeclampsia.

Compared to β hCG levels in other obstetric complications , β hCG levels are well explained in preeclampsia due to hypertrophy of the placental trophoblasts .

Even though β hCG is a well established marker varying in concentration in other complications placental expression of β hCG is high in hypertensive disorders of pregnancy among which preeclampsia needs to be addressed.

Objectives

OBJECTIVES

This study aims to quantify the serum β Human Chorionic Gonadotropin levels in singleton normotensive pregnant women and Preeclamptic women and also to assess level of significance between the two groups. The study has the following objectives

1. To estimate the levels of serum β hCG in normotensive pregnant women and preeclampsia cases at 32-42 weeks of gestational age.

2. To assess the level of significance between β hCG levels in normal pregnancy and preeclampsia cases in accordance to severity of preeclampsia at 32-42 weeks of gestational age.

Review of Literature

REVIEW OF LITERATURE

HISTORY

Hypertensive disorders in pregnancy dates back to the ancient history. Several hypothesis have been made on pre eclampsia and eclampsia.

Bernhart(1939), stated that eclampsia have been mentioned in ancient Chinese, Indian, Egyptian and greek mythology. Even in writings of Atharva veda and Sushrutha there is a mention on hypertensive disorders in pregnancy.

In 4 th century BC , Hippocrates stated the significance of convulsions,head ache and drowsiness in the pregnant mother.

On this basis, several other concepts have emerged stating that pre eclampsia presents as various degrees of toxaemia in which hypertension, fluid retention, albuminuria with or without convulsions.[3]

Lever's (1843) discovered testing of urine for proteinuria, which is considered as a precursor for eclampsia. Cook and Briggs (1903) stated increase in blood pressure as the earliest sign of impending convulsions.

Zangemeister (1916), postulated that sudden increase in maternal weight is a warning sign for development of pre eclampsia and eclampsia.[3]

Many studies state that pathophysiology of preeclampsia is due to placental trophoblastic dysfunction and endothelial dysfunction of vasculature.[4]

Hence, proving that pathophysiological mechanisms of pregnancy induced hypertension points to early placentational abnormalities. Human placenta synthesizes steroid, protein and glycoprotein hormones throughout gestation. The production of hCG by the placenta in early pregnancy is critical for implantation and maintanence of the Blastocyst.

Hence preeclampsia is postulated as Trophoblastic disorder.[5]

A study done prospectively on 41 patients with serial monitoring of β hCG from the second trimester showed that out of 13 women with high values of serum β hCG ,7 of them developed preeclampsia, which showed that higher levels of β hCG are seen before the patient presents with clinical symptoms.[6]

In a case control study conducted on 30 women with singleton pregnancy during third trimester with severe preeclampsia and 21 normotensive women by matching the subjects for maternal age and gestational age. 28 patients in preeclampsia group showed higher β hCG levels when compared to the control group. Results concluded that the serum β hCG levels are significantly higher in patients with preeclampsia proving that pathogenesis of preeclampsia is due to the abnormal secretory function of placenta.[7]

According to a study conducted in 2001, 195 singleton pregnancies in second trimester are measured for the β hCG levels. Results showed that mean β hCG level is insignificantly higher in women with pregnancy induced hypertension when compared to normotensive women. It was also observed that no statistically significant correlation exists between the elevated β hCG levels and preeclampsia.[8]

A study conducted in second trimester on 784 women between 16 th to 20 th week of pregnancy showed that measuring beta hCG levels during second trimester of pregnancy are significant in predicting development of preeclampsia in later pregnancy.[9]

A study conducted by collecting blood samples during third trimester of pregnancy in 33,36 and 39 weeks followed by immediate postpartum in normotensive patients without hypertension or preeclampsia ,and the samples were analysed for β hCG and oestrodiol. Results showed that there was gradual decrease in the β hCG levels by the end of third trimester and significant decrease in levels of β hCG is seen 2 to 3 weeks before spontaneous onset of labour.[10]

A study conducted during second trimester of pregnancy on 164 singleton pregnant women by estimation of serum β hCG levels and lipid profile shows that both maternal dyslipidemia and elevated maternal serum β hCG levels at second trimester can be used as a good predictors for preeclampsia being the non invasive procedures.[11]

A study conducted in 2011 aimed to study the role of β hCG hormone and Adenosine Deaminase in pathogenesis of preeclampsia and effect of preeclampsia on the levels of these serum markers.this study was done on 90 women by dividing them into three groups as normal preganancy, mild preeclampsia and severe preeclampsia. Levels of serum β hCG are high in cases on severe preeclampsia when compared to other groups stating that maternal serum β hCG levels can be used as the marker for severity of preeclampsia.[12]

A study conducted on 100 women comprising of 50 preeclampsia cases and 50 normal singleton pregnancies in third trimester and the serum samples were estimated for serum β hCG levels. The maternal serum β hCG in preeclampsia group is 18,087mIU/ml in comparision with control group with serum β hCG level as 8,391 mIU/ml and the serum β hCG levels are parallel with the severity of the preeclampsia.[13]

An Indian study, conducted prospectively in 200 pregnant women by measuring β hCG serum levels in second trimester between 13 to 20 weeks of gestation .Results showed that 24 cases showed raised β hCG levels out of which 20 patients developed hypertensive disorders in the later pregnancy, against 2 cases with normal β hCG levels developing hypertension. Also, higher serum β hCG levels are directly proportional to the severity of the disease and the association between β hCG levels and pregnancy induced hypertension are statistically significant (p value <0.01).[14]

A prospective study conducted 500 pregnant women with singleton pregnancy during second trimester by classifying the patients under 3 groups as normotensive, mild preeclampsia and severe preeclampsia group respectively..Results showed that the levels of serum β hCG levels are significantly higher in cases who developed preeclampsia in the later pregnancy in comparison to the normotensive group and parallel with the severity of preeclampsia and states that serum β hCG levels play an major role in the pathogenesis of hypertensive disorders and the severity of disease occurrence.[15]

Preethi et al, conducted a prospective study on 400 antenatal women in second trimester .significant higher values of β hCG are see in cases who developed preeclampsia with mean serum β hCG level of 71,111mIU/ml and mean β hCG levels in normotensive groups is 25,365mIU/ml. Thus showing significant association between preeclampsia and higher levels of serum β hCG levels.[16]

A Case control study conducted on 74 pregnant women with preeclampsia and 76 normotensive women with similar demographic and obstetric characteristics, mean serum β hCG levels were high in cases with severe preeclampsia with mean of 45,439 mIU/ml and mean serum β hCG levels in control group is 4937mIU/ml. Thus serum β hCG levels exhibiting significant linear correlation with severity of preeclampsia.[17]

A study conducted on 100 singleton pregnancy women which included 50 preeclampsia cases and 50 normotensive patients in third trimester of pregnancy .Serum β hCG levels are Higher in preeclampsia case with mean value of 27,808 mIU/ml against mean value of 12,551 mIU/ml in normotensive patients.[18]

A study was conducted in London on 94989 patients to examine the distribution of serum β hCG and PAPP-A in maternal serum in 12, 22 and 32 weeks of gestation with singleton pregnancy. Prospective screening was done in all these cases .The results showed that serum β hCG levels are not significantly different in first trimester and levels are increased in second and third trimester with increase in the gestational age and with mean β hCG value more in preterm preeclampsia cases than in term preeclampsia cases .Hence,proving that β hCG can be used as a screening marker for predicting preeclampsia and diagnosing severity of Preeclampsia.[19]

A prospective study conducted in second trimester in 90 women with singleton pregnancy and were followed till term. Serum β hCG levels are higher in patients who developed hypertensive disorders in pregnancy with mean value of 69808.66 mIU/ml and mean serum β hCG levels in normotensive patients was 38126mIU/ml. Thus, indicating that patients with higher β hCG levels have increased risk of developing hypertensive disorders in pregnancy.[20]

HYPERTENSIVE DISORDERS IN PREGNANCY

Hypertensive disorders are the most common complications of pregnancy affecting 5 to 10% of all pregnancies.

American College of Obstetrician and Gynecologists (ACOG) committee on terminology in 2013, described Hypertensive diseases into four categories .[21]

1. Gestational hypertension
2. Preeclampsia and Eclampsia syndrome
3. Chronic Hypertension of any etiology –

   Hypertension is diagnosed in women with documented blood pressures more than 140/90 mm of Hg before pregnancy or before 20 weeks of gestation or both. These are the patients with chronic vascular diseases and other systemic abnormalities.
4. Preeclampsia superimposed on chronic hypertension.

This classification well differentiates the preeclampsia syndrome from other hypertensive disorders.

Diagnosis of Hypertensive disorders[22]

Hypertension is diagnosed when systolic Blood pressure exceeds 140 mm Hg or diastolic blood pressure exceeds 90 mm Hg in previously normotensive patients in two occassions atleast 6 hours apart, after 20 weeks of gestation.

To define diastolic pressure korotkoff phase V (i.e, disappearance of sounds) is used. Blood pressure is checked either in sitting position or in left lateral position with arm at the level of the heart with the appropriate sized cuff.

Gestational Hypertension

Elevation of the blood pressure to 140/90 mm of Hg or greater for the first time after the mid pregnancy with absent proteinuria and the blood pressure returns to normal after 12 weeks postpartum.

Preeclampsia superimposed with Chronic Hypertension

It is the sudden increase in proteinuria or BP or platelet count less than 1 lakh per ml in women with hypertension and proteinuria before 20 weeks of Gestation.[23]

Preeclampsia and Eclampsia syndrome

It is best described as the pregnancy specific disorder which causes multi organ dysfunction. It is characterised by increased blood pressure during pregnancy after 20 weeks of gestation associated with proteinuria (> 300 mg per 24 hours or Dip stick > +1).

Eclampsia

It is the presence of new onset Grand mal seizures in a woman with pre existing Preeclampsia excluding other causes of seizures. Eclampsia can occur before, during or after labour.

According to ACOG 2013-Diagnostic criteria for Preeclampsia (FIGURE -1)

Blood pressure	• Greater than or equal to 140 mm Hg systolic or greater than or equal to 90 mm Hg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure • Greater than or equal to 160 mm Hg systolic or greater than or equal to 110 mm Hg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy
and	
Proteinuria	• Greater than or equal to 300 mg per 24-hour urine collection (or this amount extrapolated from a timed collection) or • Protein/creatinine ratio greater than or equal to 0.3* • Dipstick reading of 1+ (used only if other quantitative methods not available)
Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:	
Thrombocytopenia	• Platelet count less than 100,000/microliter
Renal insufficiency	• Serum creatinine concentrations greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease
Impaired liver function	• Elevated blood concentrations of liver transaminases to twice normal concentration
Pulmonary edema	
Cerebral or visual symptoms	

* Each measured as mg/dL.

Preeclampsia is further classified into Non Severe and Severe Preeclampsia on the basis of following criteria.

Indicators of severity of Gestational Hypertensive disorders:

ABNORMALITY	NONSEVERE PE	SEVERE PE
Diastolic BP	<110 mm of Hg	>110 mm of Hg
Systolic BP	<160 mm of Hg	>160 mm of Hg
Proteinuria	None to positive	None to positive
Headache	Absent	Present
Visual disturbances	Absent	Present
Upper abdominal pain	Absent	Present
Oliguria	Absent	Present
Convulsions(Eclampsia)	Absent	Present
Serum Creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
Serum Transaminases elevation	Minimal	Marked
Fetal growth restriction	Absent	Present
Pulmonary oedema	Absent	Present
Gestational age	Late	Early

HELLP SYNDROME

This is the severe form of preeclampsia with the acronym of Hemolysis (H), Elevated Liver enzymes (EL)and low Platelet count(LP).

Diagnostic criteria for HELLP syndrome [24]

1. Hemolysis
    - Bilirubin levels >1.2mg/dl
    - Elevated LDH levels(>600 U/L)
    - Abnormal peripheral smear(with Burr cells ,schizonts)
2. Elevated Liver enzymes
    - Elevated LDH levels(>600 U/L)
    - Serum AST(Aspartate transaminase) >70 U/L
3. Low Platelet count-less than 1,00,000/mm^3

RISK FACTORS [25]

- Nulliparous women
- Young age
- Environmental factors
- Maternal age>35 years
- Multiple pregnancy
- Molar pregnancy
- Previous Preeclampsia
- Prior Abruption
- Prior still birth
- Diabetes

- High BMI
- Chronic Renal disease
- Chronic Hypertension
- Women with SLE or Anti Phospholipid Antibody Syndrome
- Family history of Preeclampsia
- Abnormal uterine Doppler at 18 -24 weeks of Gestation

ETIOPATHOGENESIS [21]

1. Normal and Abnormal Trophoblastic invasion

In normal pregnancy during implantation, uterine arteries undergo extensive remodelling due to the invasion of the Endovascular Trophoblasts. These trophoblasts replace the endothelial and muscular layers of the vessel wall to enlarge the diameter of the vessel thus, increasing its capacitance. This physiological change takes place in two phases.

PHASE I- This phase starts at the time of early implantation and ends by 12 to 14 weeks of gestation. In this phase the Trophoblastic tissue invades the Myometrial segment of the vasculature.

PHASE II- This phase begins at 12-14weeks of gestation and proceeds on till 20 to 24 weeks of gestation. During this phase there is further invasion of trophoblastic tissue into the Myometrial segment of the spiral arteries. This leads to dilataion of the arteries, by increasing their capacitance and there by converting high resistance system into low resistance system. This facilitates better exchange of gases and nutrients across the maternal-fetal circulation leading to enhanced intra uterine fetal growth.

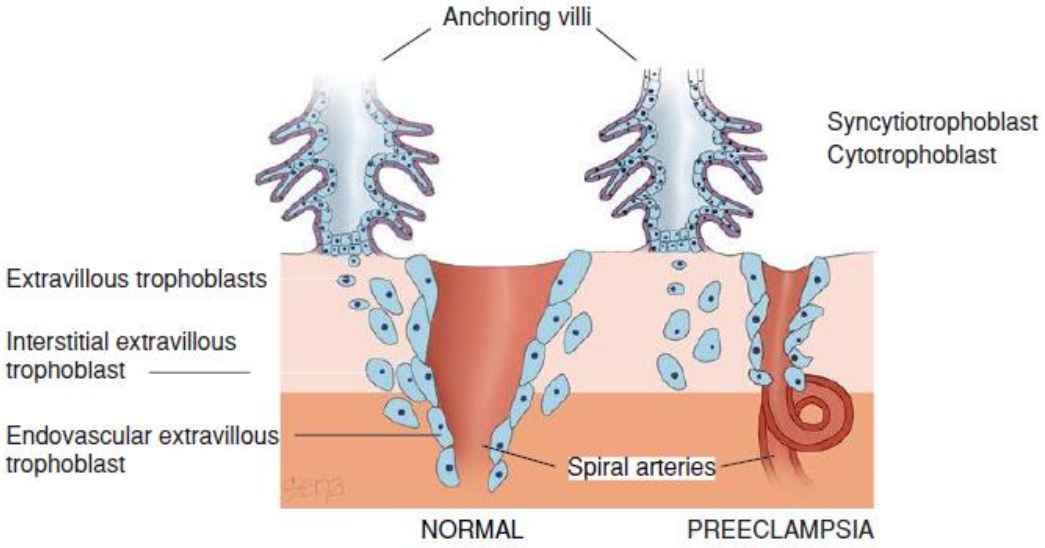


FIGURE -2 :Schematic representation of normal placental invasion and defective Trophoblastic invasion in Preeclampsia

Trophoblastic invasion of the maternal Decidua takes place by two different pathways [26]

1. Interstitial pathway-vessels are invaded by the interstistial trophoblastic cells and then these are further termed as the 'Endovascular Trophoblasts'.

2. Endovascular Pathway - The Endovascular trophoblastic cells migrate in retrograde direction i.e., in the direction opposite to the arterial flow.

Hence, the phenotypic expression of Preeclampsia syndrome is a "Two Stage Disorder"

All the above changes which occur physiologically in the spiral arteries replace the Musculo-Elastic Tunica media layer of the vessel wall by the "Mononuclear Trophoblasts embedded in the Fibrinoid". This converts the original Low capacitance- High resistance vessels into High capacitance –Low resistance vessels leading to increased blood flow to the inter villous space.

In normal pregnancy, this physiological conversion is seen in majority of the vessels at term, while only 1/3 rd of the arteries show myometrial invasion at 16-18 weeks of pregnancy. In hypertensive disorders, failure to complete late conversion i.e.,failure of invasion by trophoblasts is the pathological cause underlying in majority cases.

2. Immunological Factors [27]

Maternal immune system show physiological change in its immune tolerance to the Fetal and placental antigens by producing blocking Antibodies. Production of these Blocking Antibodies is impaired in patients with risk factors for Preeclampsia.MCH Class I and II play a important role in the immune activity.

3. Genetic Factors

Studies show that hereditary hypertension is a risk factor for Preeclampsia and thus tendency for Preeclampsia –Eclampsia is inherited.

Genes involved with Preeclampsia are

- HLA Antigen- involved in immune tolerance
- Factor V (Leiden)
- MTHFR gene-Methylene Tetra Hydrofolate reductase
- NOS3-helps in nitric oxide production in Endothelium
- AGT(M235 T)- Angiotensinogen
- F2-Prothrombin (Factor II)

4. Inflammatory and Angiogenic Factors [28, 29]

In response to the ischemic changes placental factors are released intiating a cascade of events.

- Preeclampsia is a state in which leucocytes are activated to their extremes in the maternal circulation.
- Reduced expression of HLA-G(immune suppressive Human Leucocute Antigen).
- Increase in cytokines Th1(Pro inflammatory cytokines) and Th2 (Anti-inflammatory cytokines).

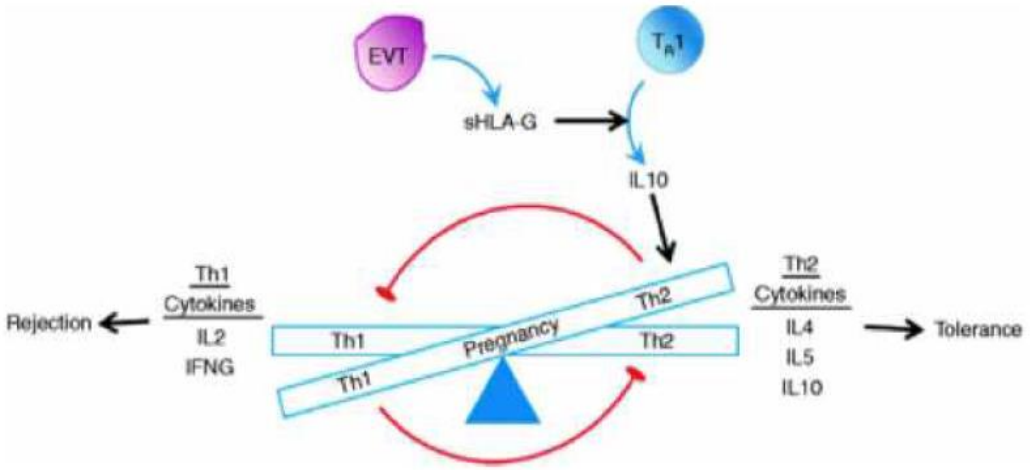


FIGURE -3: Schematic representation of immune factors in Preeclampsia

5. Endothelial Cell Activation

Due to the hypoxia leading to the ischemic changes various inflammatory changes takes place leading to the cascade of events releasing anti Angiogenic and metabolic factors and other leucocyte mediators which provoke systemic endothelial cell injury which ultimately causes Endothelial cell activation or dysfunction.

PATHOGENESIS:

1. **Vasospasm**

Vasoconstriction and increase in resistance to the flow is seen as a result of endothelial activation leading to Hypertension.

2. **Increased vasopressor response** [30,31,32]

In normal pregnancy, physiological development of resistance to the vasopressors is seen which is reduced in Preeclampsia cases as there is increase sensitivity to the Vasopressors due to various factors.

3. **Prostaglandins** [33]

In individuals predisposed to Preeclampsia, PGI2 (prostacyclin) levels decreases and TXA2 (Thromboxane) levels increases which ultimately leads to increased sensitivity to the vasopressors.

4. **Nitric Oxide**

Synthesis of Nitric oxide mimics the scenario of Preeclamsia by reducing Heart rate and increasing Mean arterial pressure.

5. **Angiogenic and Anti Angiogenic proteins** [34,35]

In normal pregnancy,increase in Endothelin -1(ET-1) levels are observed whose levels are more exaggerated in preeclampsia.

Increased levels of sFlt-1, sEng (Soluble Endoglin) begin to increase before the development of clinical features.

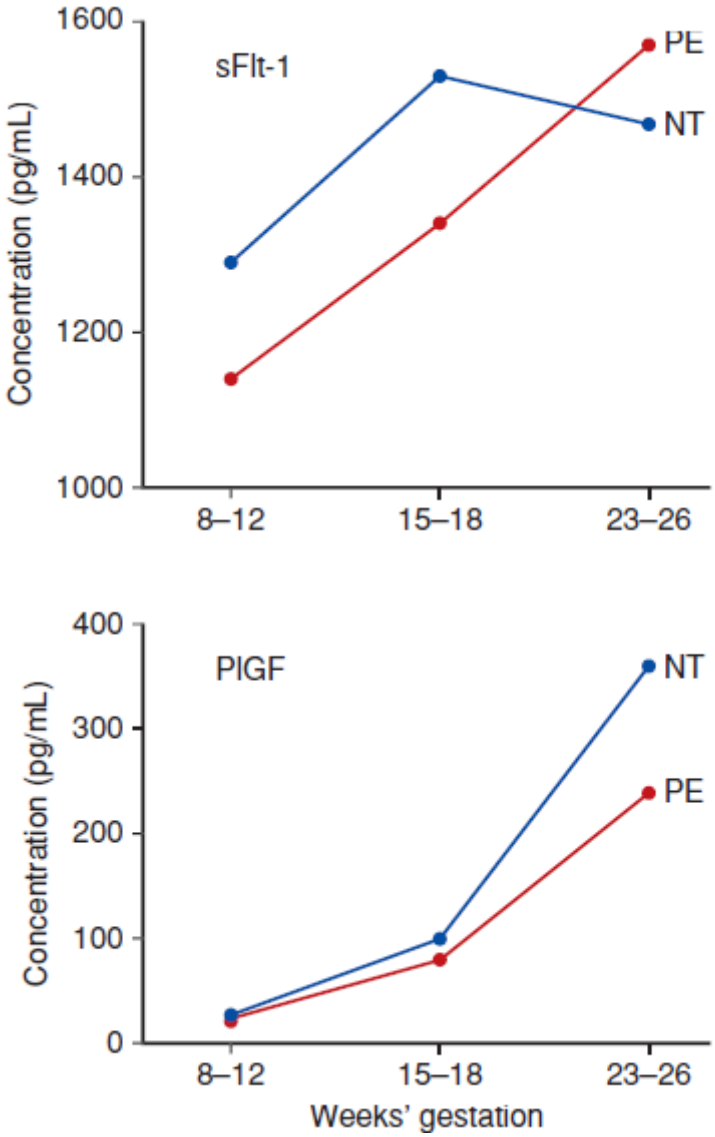


FIGURE-4 :Angiogenic and Anti Angiogenic factors in Normotensive and Preeclamptic women

SFlt-soluble fms-like tyrosine kinase

PIGF-placental growth factor

PATHOPHYSIOLOGY

Preeclampsia manifests as a muliorgan dysfunction affecting the cardiovascular system majorly.

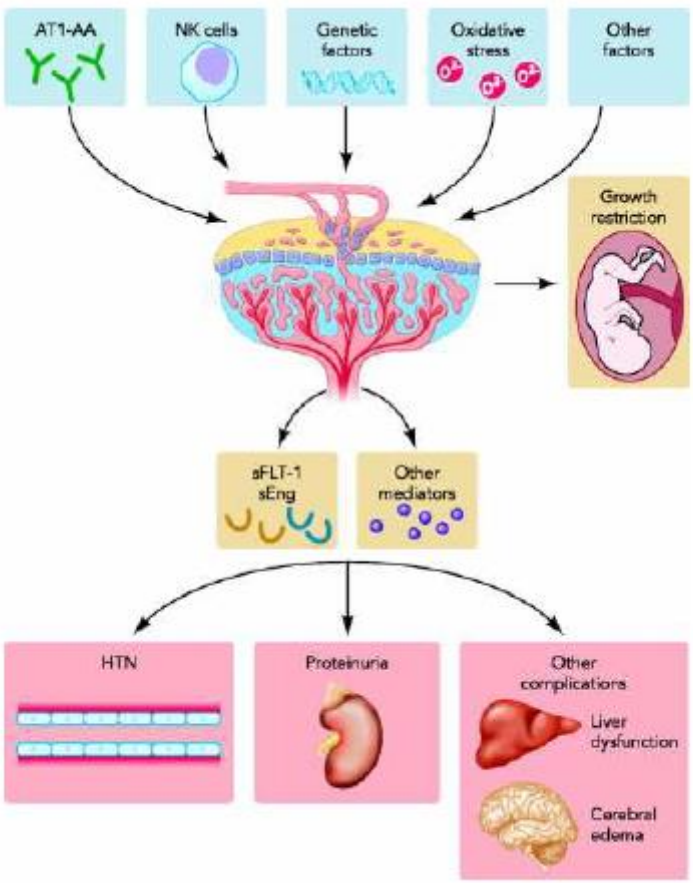


Figure -5 :SCHEMATIC REPRESENTATION OF PATHOPHYSIOLOGY IN PREECLAMPSIA.

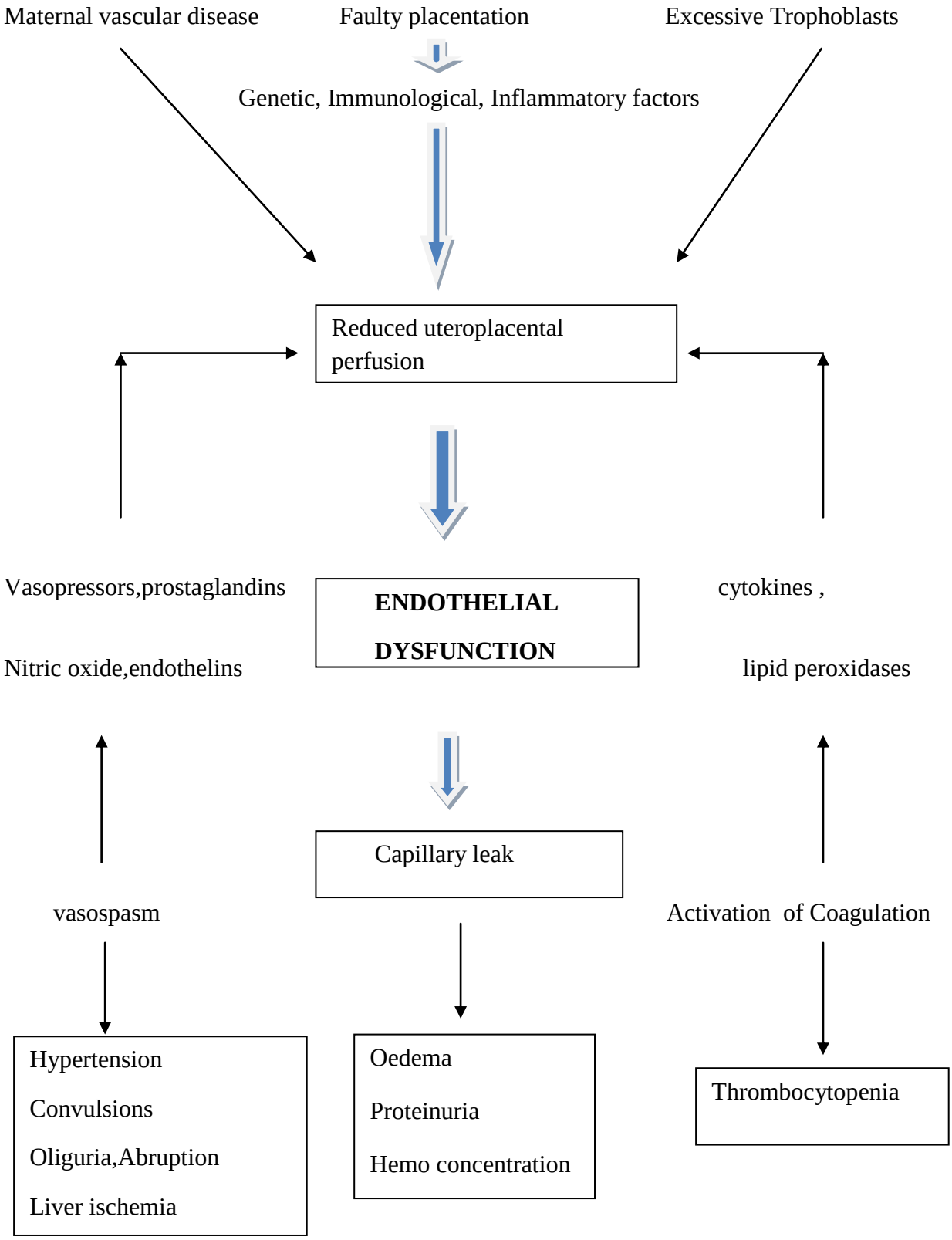


Figure 6:Schematic representation of Pathophysiology in the development of Hypertensive Disorders in Pregnancy

Cardiovascular system

- Increase in the cardiac afterload due to hypertension
- Reduced Cardiac preload, due to pathologically diminished volume expansion.
- Endothelial activation leading to the inter endothelial extravasation of intravacular fluid into extravascular space especially the lungs.

Hemodynamic changes and Cardiac function [36]

- Increase in the peripheral resistance due to decrease in the capacitance of the vessels.
- Decrease in the cardiac output.

Myocardial function

- Ventricular remodelling leading to Diastolic Dysfunction
- Diastolic dysfunction leads to cardiogenic pulmonary oedema

Hematological changes [37, 38]

- Hemoconcentration is the Hallmark of Eclampsia
- Fall in the Hematocrit level but shows false high hematocrit value.
- Maternal Thrombocytopenia- Platelet count < 1,00,000 cells/cu.mm
- Hemolysis of cells seen in HELLP syndrome

Hepatic changes [39]

- Elevated liver enzymes levels especially the serum Transaminases.
- Charectaristic Hepatic lesions are regions of Periportal hemorrhages in the periphery,ischemic lesions and fibrin depositions.
- Hepatic infarctions and subcapsular liver Hematomas are not uncommon.

Renal changes [40]

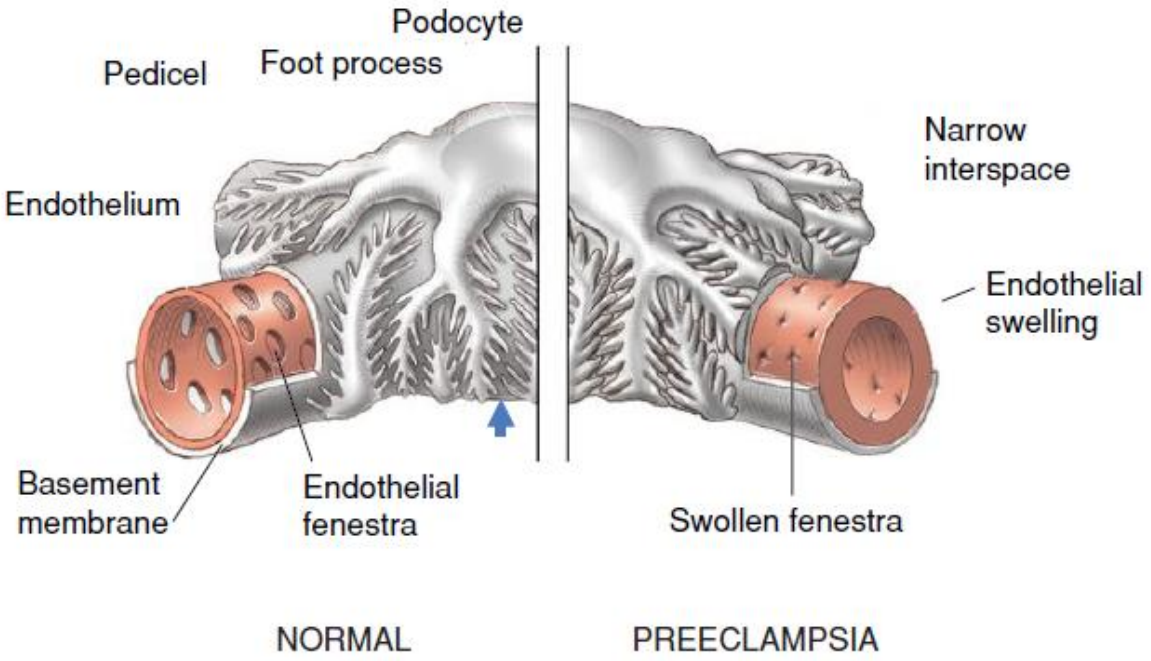


Figure 7:Schematic representation showing glomerular capillary Endotheliosis

- Decreased glomerular filtration rate is seen in Preeclampsia due to Vasospasm leading to decreased renal perfusion.
- Reduction in the GFR leads to decreased tubular reabsorption causing elevated plasma Uric acid levels.
- Morphology of kidney shows characteristic "Glomerular Endotheliosis"
- Increase in the urine osmolality is seen along with the Oliguria**.**

- **PROTEINURIA-** detection of proteinuria helps to establish preeclampsia

  24 hour urine excretion exceeding 300 mg

  urine protein: Creatinine ratio > 0.3

  >/= +1 dipstick

  - Acute tubular necrosis is seen in some of the cases

Central nervous system

- Headache and visual disturbances are the most common with Severe Preeclampsia.
- Associations with convulsions diagnose Eclampsia.
- Vasospasm in Preeclampsia attributes to Hypertensive Encephalopathy.
- Radiological studies show cerebral oedema, hemorrhagic lesions particularly in the posterior hemispheres.
- Some patients present with altered mentation.

Placenta

- Compromised Uteroplacental perfusion is seen attributed to the high resistance vessels.
- Chorionic villi congestion is seen with Proliferative Endarteritis and cytotrophoblastic celss proliferation
- Increased incidence of infarcts and hematomas.

MANAGEMENT OF PREECLAMPSIA

According to the ACOG criteria (2013), the first consideration in the management of Preeclampsia without severe features i.e., non severe Preeclampsia is safety of both mother and the fetus where as in case of severe Preeclampsia safety of the mother is considered more important.

Mild /Non severe Preeclampsia

- Once the diagnosis of mild Gestational hypertension has been established ,further management depends upon the maternal and Fetal investigations, Gestational age, presence of fetal membranes, stage of labour ,vaginal bleeding and other co morbidities.
- CRITERIA FOE HOME MANAGMENT OF MILD PREECLAMPSIA [41]

  -Ability to comply with the recommendations

  -DBP <100 mm of Hg

  -SBP <150 mm of Hg

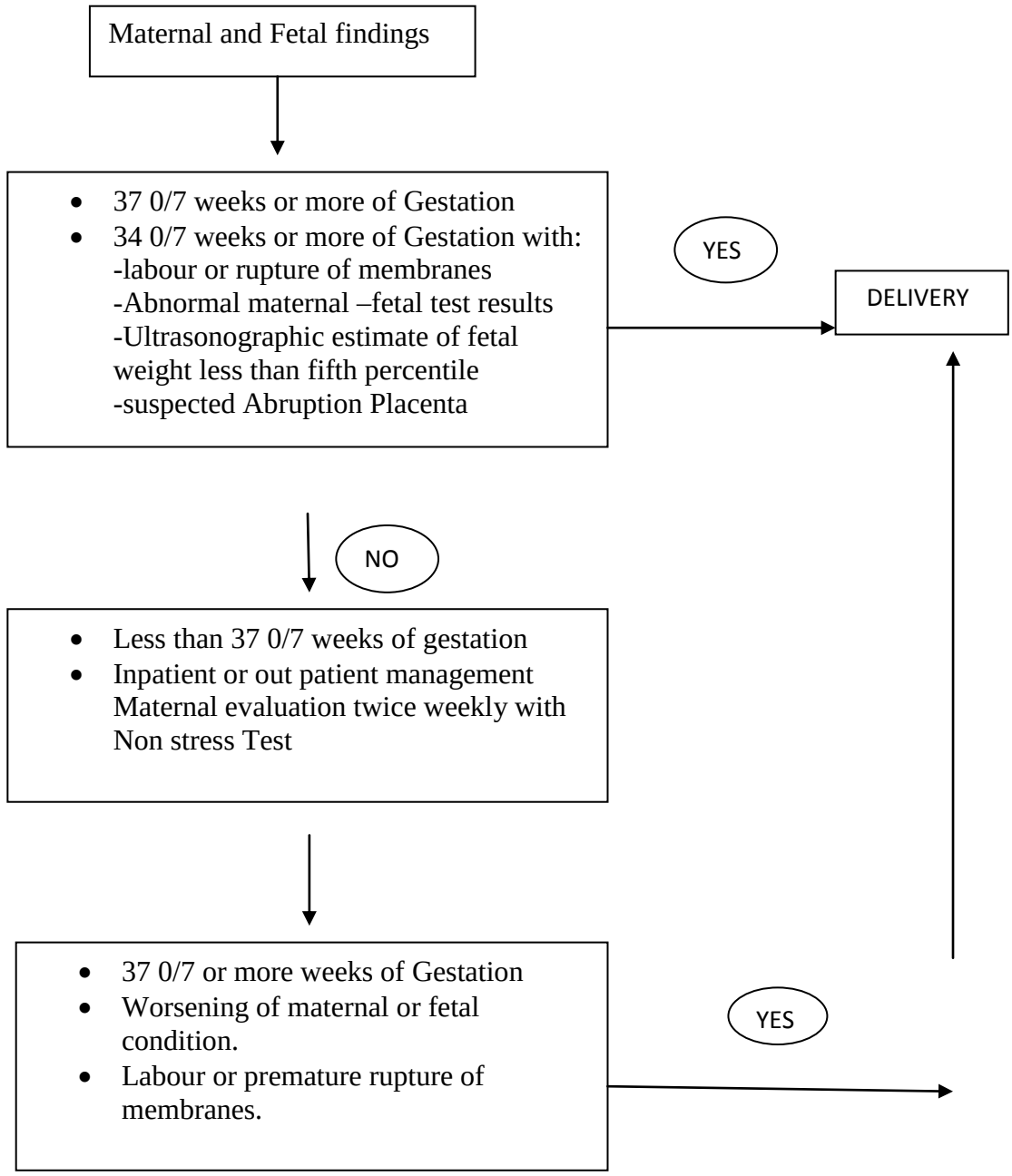
  -normal laboratory tests and no maternal symptoms

  -reassuring fetal status with appropriate growth

  - Urine protein 1 gm or less in 24 hours.

- If the patient doesnot fullfill the above mentioned criteria then the patient is managed by the hospital admission.

MANAGEMENT OF MILD PREECLAMPSIA



The preferred mode of delivery is vaginal. Caesarean section is considered only in the presence of other Obstetrical indications.

Figure 8:Schematic representation of management of Mild Preeclampsia

MANAGEMENT OF SEVERE PREECLAMPSIA [41]

- Severe Preeclampsia can result in both acute and long term complications in both mother and the newborn. Maternal complications of severe Preeclampsia include Pulmonary oedema, Myocardial Infarction, stroke, severe renal failure, acute Respuratory distress syndrome, coagulopathy and Retinal injury.These complications are more likely to occur in the presence of preexistent medical disorders and with acute maternal organ dysfunction related from exposure to uteroplacental insufficiency or from preterm birth or both.
- All women should undergo investigations for complete blood picture (CBC) with Hematocrit, assessment of serum Creatinine, Liver Function tests, 24 hour urine protein levels and detailed history is taken for any imminent signs or signs of severe Preeclampsia.
- Fetal evaluation is done for Estimated fetal weight and Amniotic fluid index by Ultrasonography, Non stress test (NST), Biophysical profile (BPP).

  - Consider deliver in women >34 weeks of gestation.

  - Patients at 32-34 weeks administer steroids and plan for delivery.

  - Patients at 23-32 weeks of gestation, expectant management is done

  - Women with non viable fetus should be presented with the option of pregnancy Termination.

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RECOMMEDED MANAGEMENT OF SEVERE PREECLAMPSIA

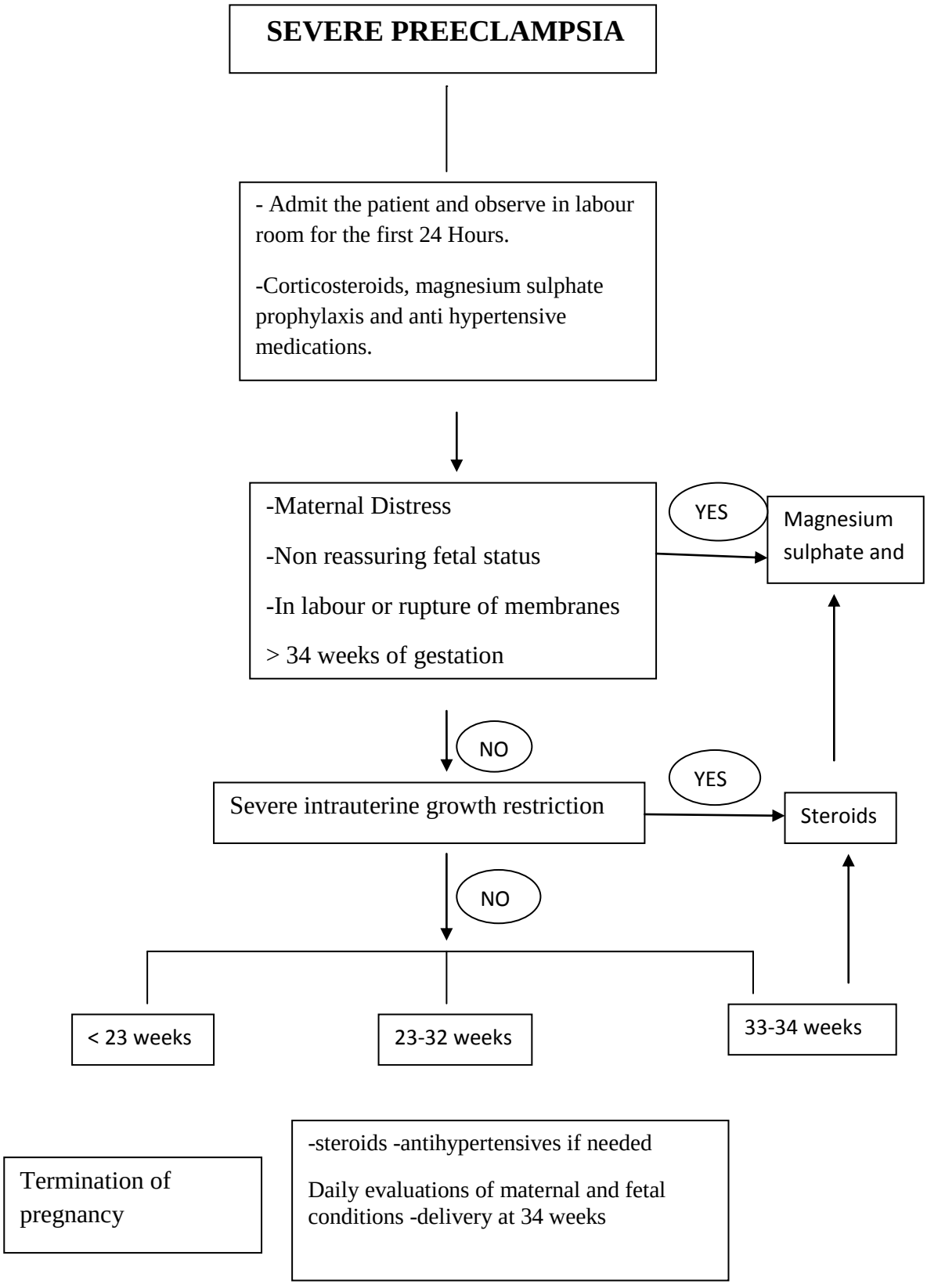


Figure 9: Schematic representation of management of severe Preeclampsia

Guidelines for expeditious delivery within 48-72 hours in severe Preeclampsia

Maternal

- Uncontrolled severe hypertension (SBP>160 mm of Hg ,DBP>/= 110 mm of Hg) despite maximum 2 doses of two anti Hypertensives.
- Eclampsia or persistent cerebral symptoms.
- Pulmonary oedema
- Placental Abruption
- Thrombocytopenia (platelet count less than 1 lakh per ml) or elevated liver enzymes(HELLP).
- Serum Creatinine of 1.5 mg/dl or more or oliguria(< 0.5 ml/kg/hr).

Fetal

- Severe fetal growth restriction (< 5 th percentile for gestational age).
- Persistent oligohydramnios amniotic fluid index of < 2 cm on atleast two occasions more than 24 hours apart.
- Umbilical artery Doppler studies with persistet reverse end diastolic flow.
- Biophysical profile < 4 on two occasions 4 hours apart.
- Repetitive Late declerations or prolonged variable decelerations or loss of beat to beat variability.

Anti Hypertensive Agents

Anti hypertensive agents used for Acute control of hypertension in pregnancy

DRUG	DOSE	COMMENTS
Labetolol	10-20 mg IV,then 20-80 mg every 20-30 min to a maximum dose of 300 mg or constant infusion of 1-2mg/Hr.	-First line of agent Tachycardia is less common contraindicated in patients with asthma, heart disease
Hydralazine	5 mg IV or IM,then 5-10 mg IV every 20-40 min or constant infusion 0.5-10 mg/Hr ,.	Higher dosage associated with maternal hypotension, fetal distress, head aches
Nifedepine	10-20 mg orally, repeat in 30min if needed, then 10-20 mg every 6 to 8 hours	Reflex tachycardia and head aches

Common oral anti Hypertensive agents in pregnancy

DRUG	**DOSAGE**	**COMMENTS**
Labetolol	200-2,400 mg/day orally in two to three divided doses	Well tolerated Potential bronchio constrictive effects
Nifedipine	30-120 mg/day orally of a slow release preparation	Donot use sublingual form
Methyl dopa	0.5 -3 gm/day orally in two to three divided doses.	May not be as effective in control of severe Hypertension
Thiazide Diuretics	Depends on agents	Second line agent
Angiotensin converting receptor blockers		Associated with fetal anomalies, hence contraindicated in pregnancy and preconceptional period.

HUMAN CHORIONIC GONADOTROPIN HORMONE (hCG)

Human Chorionic Gonadotropin hormone is discovered in 1930 by Zodek. It is a Glycoprotein with peptide frame work with side chains of carbohydrates attached to peptides.

MOLECULAR STRUCTURE

It is composed of 2 sub units

1. Alpha (α) –consists of 92 Amino acids

2. Beta (β) –consists of 145 Aminoacids

These two subunits are linked to each other by Disulphide bonds with the help of hydrophobic and electrostatic forces.

The Alpha(α) subunit sequences of Aminoacids is similar to the sequence of Thyroid stimulating hormone (TSH), Leutinising hormone and Follicle stimiulating hormone(FSH).All four glycoproteins share a common α subunit with distinct β subnit.

But the Beta (β) subunit is unique and specific in its structure and hence βhCG is used as the diagnostic tool specific for pregnancy and with unique terminal Carboxy tail piece it allows highly specific immunological assays.

Molecular weight of hCG_Hormone – 36000 Daltons

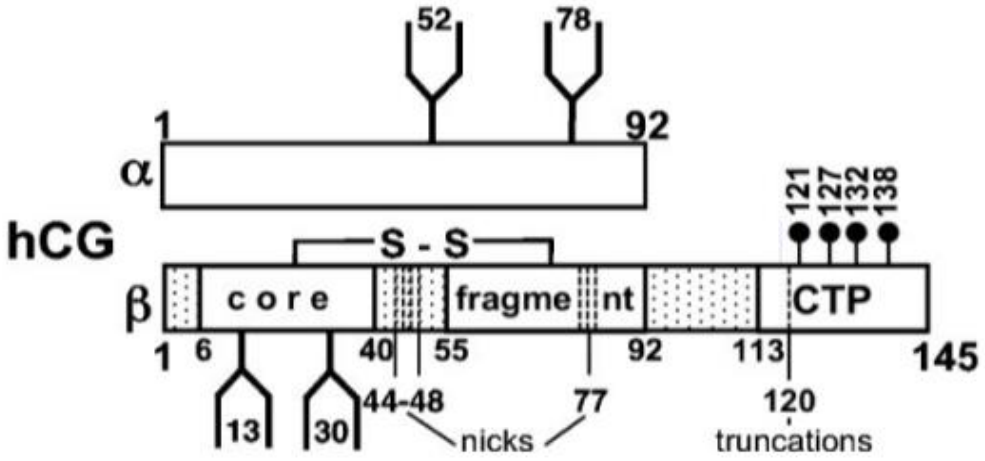


Figure 10: Schematic depiction of the molecular structures of Human Chorionic Gonadotropin Hormone (hCG)

BIOSYNTHESIS

Synthesis of α and β subunits of hCG are regulated separately.

Gene on chromosome 6 encodes for α subunit

Gene on chromosome 19 encodes for β subunit.

Both the subunits are synthesized separately as the precursors which are then cleacved by Endopeptidases. Intact hCG is later assembled and released by the exocytosis from secretory granules.

hCG is primarily secreted by the Trophoblasts i.e, before 5 weeks of gestation it is expressed in both cytotrophoblasts and syncitiotrophoblasts. Later hCG is expressed exclusively in the syncitiotrophoblasts.

hCG acts through LH- hCG receptors via plasma membrane.

Plasma half life – 36 hours.

Molecular forms of hCG:

1. Intact hCG

2. Hyper Glycosylated hCG

3. Nicked hCG

4. Free subunits (α, β)

Hyper Glycosylated hCG :

This is a sugar variant of hCG synthesized in the cytotrophoblasts and extra villous cells during pregnancy. It ia an autocrine Hormone which helps in cell proliferartion and implantation and invasion of the cells.

Regulation of hCG synthesis:

Exact mechanism is not known. But the most probable factors regulating are

- Placental GnRH (Gonadotrophin Releasing Hormone)
- CRH(Corticotropic Releasing Hormone)
- Interleukin 1, 6.
- Activin

All these above mentioned factors promote hCG secretion.

- Endorphin
- Inhibin .These act by inhibiting action of GnRH and CRH.

hCG Concentrations in Serum and Urine :

The combined hCG molecule is detectable in plasma of pregnant women from 7 to 9 days after the midcycle surge of LH (Leutinising Hormone) that precedes ovulation.

Thus, hCG likely enters maternal blood at the time of blastocyst implantation.

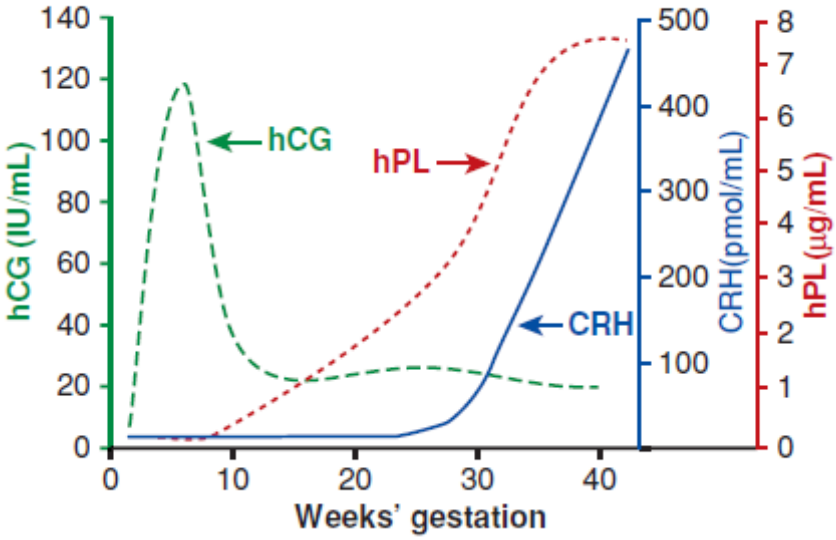


Figure 11:Distinct profiles for concentration of Human Chorionic Gonadotropin (hCG), human placental lactogen(hPL) and corticotrophin releasing hormone in serum through out normal pregnancy.

Various other Quantitative tests are developed for the analysis of hCGlevels which differ in methodology, sensitivity and specificity.(Fluorescent Immuno assay, Enzyme linked Assay, Radio ImmunoAssay).[42]

Peak maternal plasma levels reach approximately 50,000 to 1, 00,000 mIU/ml between 60 th to 80 th day of gestation.

At 10 to 12 weeks of gestation, plasma levels begin to decline and nadir is reached approximately by 16 weeks i.e, 10,000 to 20,000 mIU/ml and the plasma levels are maintained at this level throughout the pregnancy.

hCG doubling time is approximately 1.4-3.5 days and the doubling time prolongs with increase in gestational age.

Increased levels of hCG are seen in : Multiple Gestation

Gestational Trophoblastic disease

Fetus with Down's syndrome

Decreased levels of hCG are seen in: Impending Miscarriage

Ectopic Pregnancy

Serum hCG levels at various gestational ages throughout Normal Pregnancy [43]

Non Pregnant females : < 5.0 mIU/ml

At 3 weeks of LMP : 5-50 mIU/ml

At 4 weeks of LMP : 5- 426 mIU/ml

At 5 weeks of LMP : 8- 7,340 mIU/ml

At 6 weeks of LMP : 1,080- 56,500 mIU/ml

At 7-8 weeks of LMP : 7,650- 2, 29,000 mIU/ml

At 9-12 weeks of LMP : 25,700-2, 88,000 mIU/ml

At 13-16 weeks of LMP : 13,300- 2, 54,000 mIU/ml

At 17-24 weeks of LMP : 4,060- 1, 65,000 mIU/ml

At 25-40 weeks of LMP : 3,640- 1, 17,000 mIU/ml

The above mentioned values are obtained through ELISA method of analysis of maternal serum.

Metabolism and Clearance

30% of hCG clearance is taken up by Renal Clearance

Remaining is cleared by hepatic metabolism.

Biological functions of hCG

- The best known physiological function is - Rescue and Maintenance of Corpus Luteal function.
- Stimulation of fetal testosterone secretion by stimulating the Leydig cells.
- Promotion of secretion of Relaxin from Corpus Luteum.

- hCG promotes uterine vascular vasodilatation and myometrial smooth muscle relaxation.

hCG levels in preeclampsia [44]

Placenta being the main source of synthesis of hCG and the impaired placentation which plays a key role in the pathogenesis in the development of Preeclampsia is reflected by altered serum hCG levels. Hence, measurement of the maternal serum hCG levels acts as both screening tool and diagnostic tool for preeclampsia.

In Normal Pregnancy

During the first Trimester- Low Oxygen tension is developed (MEDIATED BY TGF-β)

Prevents Trophoblasts from differentiating into Invasive type

Between 10-12 weeks - physiological increase in oxygen tension(DECREAESE IN TGF-β)

Differentiation of Trophoblasts into invasive phenotype

In Preeclampsia

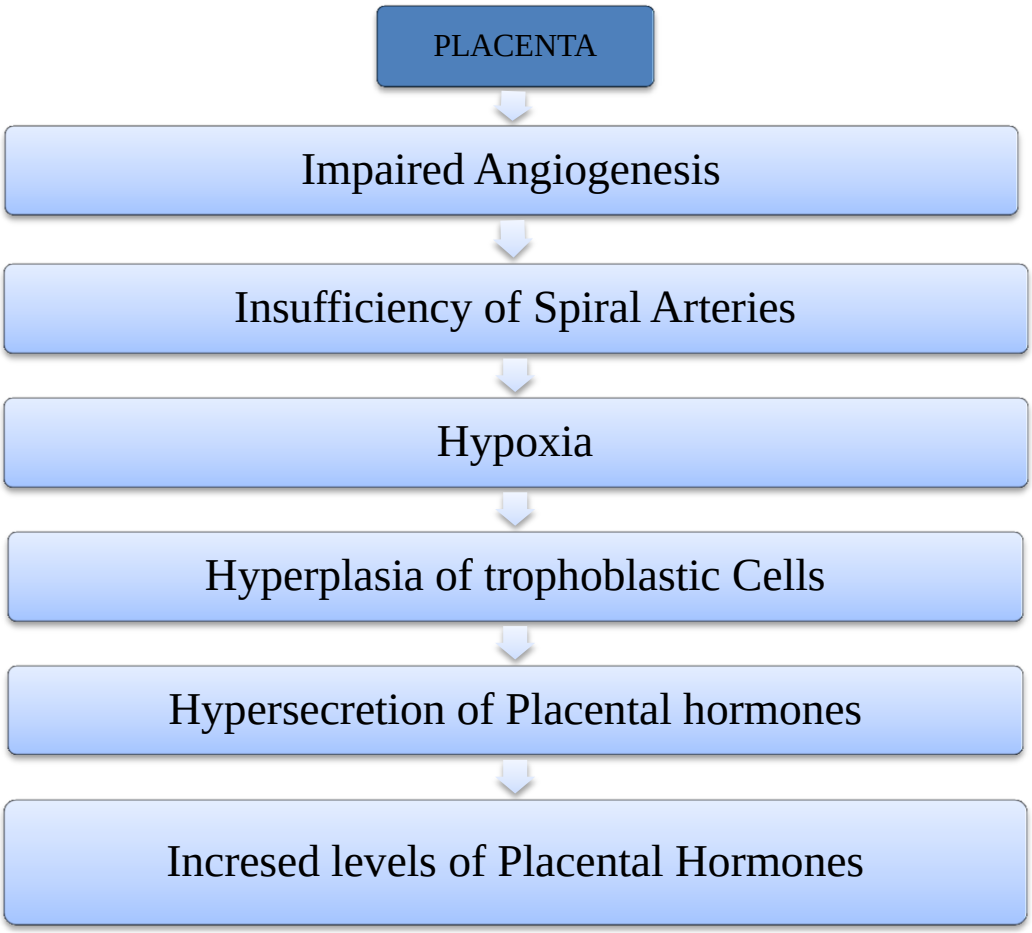
TGF-β levels remain high even after 10-12 weeks of gestation

Development of Immature Trophoblasts

In response to Hypoxia development of Hypersecretory state

Elevated levels of Placental Hormones prior to the development of Preeclampsia

Hypothesis for raised hCG levels in Preeclampsia



Prediction, Diagnosis and prevention of Preeclampsia

SCREENING AND DIGNOSTIC TESTS FOR PREECLAMPSIA

I. Alteration in the function of placental perfusion and resistance in vessels

Mean arterial blood pressure

Doppler ultrasound

Roll over test

Angiotensin infusion test

Isometric exercise test

Platelet angiotension II binding

Platelet calcium response to arginine vasopressin

Renin

24-hours Ambulatory blood pressure monitoring

II.Alteration in the function of Fetoplacental unit

Human chorionic gonadotrophin

Alpha fetoprotein

Inhibin A

Pregnancy-associated plasma protein A – decreased

Estriol

III. Alteration in the function of Renal parameters

Elevated Serum uric acid

Increased Microalbuminuria

Kallikrein in urine

Elevated Microtransferrinuria

IV.Alteration in the function of Endothelial & oxidant stress

Fibronectin-elevated

Endothelin-elevated

Thromboxane-elevated

Homocysteine-elevated,

The various predictors can be broadly classified as non-laboratory methods and

Laboratory methods.

LABORATORY TESTS :

Fetal placental unit – Endocrine dysfunction

HCG, Alpha Fetoprotein, Estriol, PAPP -A, inhibin A , activin A,

Placental protein 13, Corticotropin releasing hormone.

Markers of endothelial dysfunction

- Serum fibronectin
- Plasminogen activator inhibitors,cell adhesion molecules, serum
- thrombomodulin,endothelin-1
- coagulation factors and platelets
- serum uric acid
- Atrial natriuretic peptide, Haematocrit.

Urinary assays:

a. Microalbuminuria

b. Urinary calcium excretion56

c. Urinary calcium / creatinine ratio57

d. Urine kallikrien / creatinine ratio

e. Fasting urine albumin/ creatinine ratio

Proteinuria

Proteinuria means protein levels in urine of >150 mg/day.

In O.P settings, Dipstick method is used.

False positive results in,

1. Hematuria
2. Drugs like penicillin, sulphanamides
3. Pus,semen and vaginal secretions.

False negative reports in,

1. Diluted urine
2. Other nonalbumin or Low Molecular Weight protein

The results are graded as

- negative (less than 10 mg per dL),
- Trace (10 to 20 mg per dL),
- 1+ (30 mg per dL),
- 2+ (100 mg per dL),
- 3+ (300 mg per dL)
- 4+ (1,000 mg per dL).

This method preferentially detects albumin and it is less sensitive to globulins or parts of globulins (heavy or light chains or Bence Jones proteins).

Angiogenic factors

- Decrease in proangiogenic factors like vascular endothelial growth factors (VEGF) and placental growth factors (PlGF)
- Increase in antiangiogenic factors like sFlt -1 and sEng

Cell free fetal DNA:

Fetal maternal cell trafficking is increased in pregnancies complicated by preeclampsia. Its concluded that cell free fetal DNA quantification is not yet useful for prediction of preeclampsia.

Serum uric acid:

Serum uric acid concentration is raised in preeclampsia due to decreased clearance. Serum level correlates with disease severity and fetal outcome. [45]

The rise in serum levels occurs relatively late in the course of the disease. Hence not reliable as a predictor. Sensitivity ranges from 0-55% and specificity 77- 95%. Raised serum uric acid is probably better regarded not as a predictive, diagnostic or specific feature of preeclampsia, but as a sensitive indicator of impaired renal function.

SERUM FIBRONECTION:

Fibronectin is a glycoprotein that has a important role in cellular adhesions, migration, phagocytosis and homeostasis. It is a component of connective tissue and basement membrane. Following endothelial injury, it is released from endothelial cells and extracellular matrix into circulation.[46]

Cellular fibronectin levels of > 3.8 ug/mL within 22 to 26 weeks of gestation was proposed to be helpful in the early detection of preeclampsia in primigravida.

Sensitivity, specificity and positive & negative predictive values were inconsistent among different studies. Systemic review concluded that neither cellular nor total fibronectin was clinically useful to predict PIH.

Hyperhomocysteinemia:

Homocysteine causes oxidative stress and endothelial cell dysfunction and it is found to be elevated in preeclampsia. Although women with elevated serum homocysteine levels at 14-16 weeks of pregnancy had a 3 – 4 fold risk of developing preeclampsia, 80 it has not shown consistent results.

Serum inhibin A, Activin A:

Their role in etiology of preeclampsia is not clear. They are secreted by trophoblast cells of placenta, its levels peak at 8 weeks and then declines to rise again at term. They play a role in formation of placental bed in invasion of trophoblast.

Maternal serum levels are increased between 13-18 weeks in patients who later develop preeclampsia.[47]

Alpha-Fetoprotein (AFP):

Origin from,

i. Yolk sac

ii. Fetal liver

iii. Gastro intestinal tract

Maternal serum AFP increases until 30 weeks of gestation. The association between high maternal AFP levels and preeclampsia have been demonstrated in several studies. In fetal serum AFP reaches a peak value of 3mg/ml at 12 weeks of gestation and declines thereafter.[48]

Angiogenic and antiangiogenic factors:

Several proangiogenic and antiangiogenic substances are involved in placental vascular development. Factors like Vascular Endothelial Growth Factor (VEGF) placental growth factor (PLGF) are decreased in preeclampsia. This difference is consistently not seen in early pregnancy. Study demonstrated that placental growth factor is not a good marker for subsequent development of severe preeclampsia. Excessive amounts of antiangiogenic factors are stimulated by worsening hypoxia at the uteroplacental interface. Trophoblastic tissue of women destined to develop preeclampsia over produces at least 2 anti angiogenic peptides that enter the maternal circulation.

- Soluble Fms – like tyrosine kinase (sFlt-1) is a receptor for placental growth factor (PLGF) and Vascular Endothelial Growth Factor (VEGF).
- Soluble Endoglin (sEng) is a placental derived molecule that blocks
- Endoglin, a co-receptor for TGFB. It inhibits binding of TGFB to endothelial receptors and results in decreased endothelial nitric oxide dependent vasodilatation. The cause of placental overproduction of anti angiogenic proteins remains enigma.

- Soluble endoglin and soluble fms like tyrosine kinase 1 (SFlt-1) are increased prior to onset of clinical disease. Until better substantiated, their clinical usefulness is not recommended.

URINE TESTS

A number of investigators have evaluated the potential value of microalbuinuria as a predictive test. Microalbuminuric phase precedes clinical proteinuric phase. The development of a radioimmunoassay for albumin has made it possible to detect microalbuminuria in women who have not yet developed proteinuria as demonstrated by clinical methods.

Urinary calcium excretion:

Hypocalciuria occurs early and persists throughout the pregnancy affected with preeclampsia. Taufield et al measured 24 hours urinary calcium excretion and found lower total and fractional excretion in women with preeclampsia as compared to normotensive pregnant women.

Urinary Kallikerins excretion:

Kallikreins are proteases with indirect vasomotor effects mediated by kinins and by the renin-angiotensin system. Urinary Kallikreins excretion has been shown to increase in normotensive pregnancy, whereas in preeclampsia reduced levels as compared to non-pregnant subjects have been found.[49]

In Millar et al study, the ratio between inactive urinary Kallikreins and urinary creatinine concentrations at 16-20 weeks as predictor test to diagnose preeclampsia. This test does not have any significant sensitivity and specificity.[50]

But have some prognostic significance in development of PIH.

Difficulties with assay techniques have impeded assessment of Kallikrein-kinin system in PIH.

Microtransferrinuria :

Urinary microtransferrin levels in pregnant women who subsequently developed severe PE and eclampsia were significantly higher than those of the pregnant women who remained normotensive. It can be a potential predictor of preeclampsia.

Prevention

Various strategies have been proposed for the prevention of Hypertensive disorders in pregnancy.

NON PHARMACOLOGICAL INTERVENTIONS [51-53]

- Nutritional changes- Dietary changes like low salt diet, calcium and fish oil supplementations, as they contain cardio protective fatty acids. Control of obesity and Arginine supplementation

  Dietary protein and energy intake.
- Regular exercise with physical activity and stretching.
- Women with diabetes, chronic hypertension, chronic renal disease and other Auto immune diseases should have their primary condition under control before planning for pregnancy.

PHARMACOLOGICAL INTERVENTIONS

- Anti hypertensive drugs ,Diuretics
- Anti oxidants supplementation-vitamin C,D,E

  Lycopene, selenium, garlic intake
- Zinc supplementation
- Anti thrombotic agents

Low dose aspirin -50 -150 mg/day therapy during pregnancy selectively inhibits Thromboxane A2(TXA2).Overall the use of Aspirin is associated with 12% reduction in the incidence of Preeclampsia and reduction in the incidence of preterm delivery.

Low molecular weight Heparin- this is used in only patients with Anti Phospholipid Antibody Syndrome.

Materials and methods

METHODOLOGY

Materials: This is a case control study conducted in department of R L Jalappa hospital attached to Sri Devaraj urs medical college . The study population consists of clinically proven 42 preeclampsia cases between 32 -42 weeks of gestational age attending OBG department are recruited in the study after obtaining patient information consent. Similarly, the normotensive pregnant women at 32-42 weeks of gestational age visiting OBG department are also recruited in the study as the control group.

Ethical clearance is obtained from the Ethical Committee.

Study period - January 2017 to March 2018

Subjects:

A total number of 84 samples are collected with 42 normal pregnancy and 42 preeclampsia cases.

Sample collection:

Four milliliter of Venous blood samples is collected from Ante Cubital vein under aseptic condition from normotensive pregnancies and Preeclampsia group between the Gestation age of 32- 42 weeks of gestation..The samples are allowed to retract at room temperature for 10 minutes, and then samples are centrifuged at 3000 rpm for 10 minutes to obtain clear serum. Thus obtained clear serum samples were stored at – 20 ^{0}C and later analysed for βhCG levels.

Inclusion Criteria:

All Antenatal women of 32 to 42 weeks of gestational age of age group between 20 to 30 years admitted in labour room at Sri R L Jalappa Hospital and Research Centre during the study period.

Exclusion Criteria:

Pregnant women with-

1. Chronic hypertension
2. Multiple gestation
3. Molar pregnancy
4. Chromosomally abnormal fetus
5. Diabetes
6. Chronic renal diseases
7. Autoimmune disorders
8. Family history of diabetes mellitus and cardiovascular disorders

Pregnant women fulfilling the inclusion criteria are registered for the study.

Detailed history regarding age, parity, gestational age, menstrual history, obstetric history and any complications in present pregnancy is taken. General clinical examination, complete obstetric examination and necessary investigations are done.

Sample Size calculation: Estimated by using the Mean β–hCG (mIU/ml) between normal and preeclampsia subjects as 8091.44 ± 1493.68 and 15850.26 ± 1783.9.53 from the study by Vandana Yadav et. al., using these values at 95% Confidence limit and 80% power sample size of 42 was obtained in each group.

Formula used: $\frac{2SD^2 (Z_{\alpha/2}+Z_{\beta})^2}{d^2}$

SD-standard deviation =from previous studies

$Z_{\alpha}/2=Z_{0.05/2}=Z_{0.025}=1.96$ (From Z table)at type 1 error of 5%

$Z_{\beta}=Z_{0.20}=0.842$(From Z table) at 80% power

d=effect size=difference between mean values

now formula will be: $\frac{2SD^2(1.96+0.84)^2}{d^2}$

Methods:

Serum Beta Human Chorionic Gonadotropin (β hCG) levels are measured by Chemiluminescence immunoassay method (CLIA method).

Procedure

The serum β hCG concentration is verified by CLIA method as per the procedure supplied by ADVIA centaur kit from Seimens Asia Pacific, India. The principle of the method is based on using direct Chemiluminometric technology, which uses constant amounts of two antibodies. The first antibody, in the Lite Reagent, is a polyclonal goat anti-hCG antibody that has been affinity purified and labelled with Acridinium ester. The second antibody, in the solid phase, is a purified monoclonal mouse anti – hCG antibody, which is covalently coupled to paramagnetic particles. These two antibodies are specific for different epitopes that are present on both the free β subunit and the β subunit of intact hCG.

STATISTICAL ANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used.

Statistical tests were applied as follows -

1. Quantitative variables were compared using Independent T test/Mann-Whitney Test (as the data sets were not normally distributed) between the two groups and ANOVA test was used for comparison of serum B HCG between gestational age group.
2. Qualitative variables were correlated using Chi-Square test/Fisher's exact test.
3. Receiver operating characteristic curve was used to find out cut off point of serum B HCG for predicting preeclampsia and severity of preeclampsia.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results

RESULTS

The case control study was conducted in the Department of Obstetrics and Gynaecology of R L Jalappa hospital attached to Sri devaraj urs medical college from January 2017 to March 2018. Serum β human Chorionic Gonadotropin levels were estimated and compared between 42 cases of pre-eclampsia in the age group of 20-30 years at gestational age of 32-42 weeks and 42 age matched normotensive pregnant women (Controls).

Detailed history and clinical examination were done and the following results were obtained.

Study group	Frequency	Percentage
Cases (Preeclampsia)	42	50.00%
Control	42	50.00%

Eighty four total study subjects included in the study are grouped into normotensive pregnancy as control group (n=42) and clinically proven Preeclampsia cases (n=42). The results obtained are enclosed in the tabular format.

Table 1:- Distribution of study population depending on the age

Age Distribution	Group		Total	P value
	Cases(n=42)	Controls(n=42)		
20-25	23 (54.76%)	32 (76.19%)	55 (65.48%)	0.702
26-30	19 (45.24%)	10 (23.81%)	29 (34.52%)	
Mean ± Stdev	24.36 ± 2.87	24.05 ± 2.35	24.20 ± 2.61	

Note- p value <0.05 is considered statistically significant.

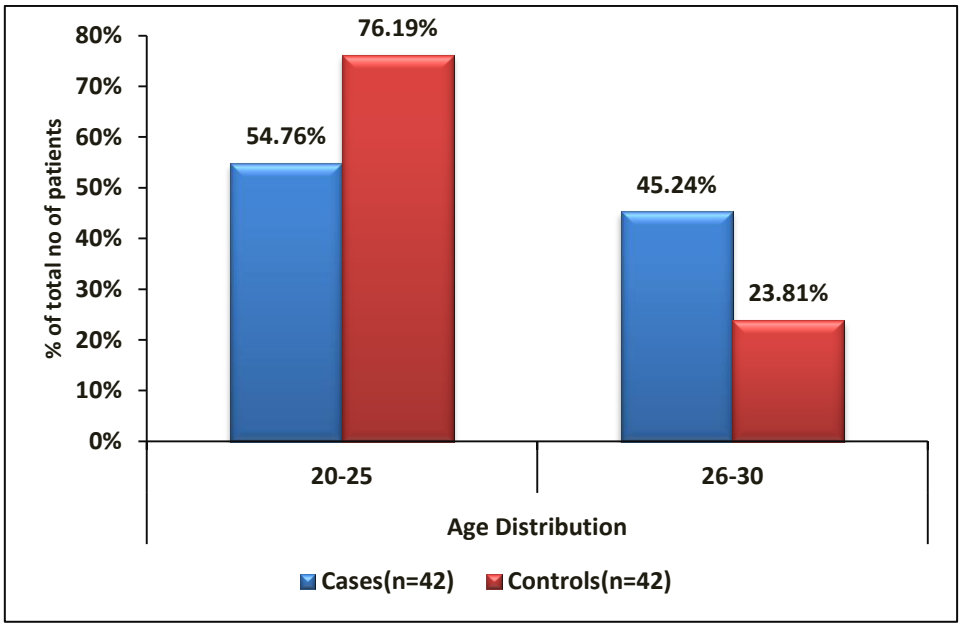


Figure 1:- Distribution of study population depending on the age

In this study, among the cases, the mean age of the patients is 24.36 ± 2.87 years and among the controls, it is 24.05 ± 2.35 years. The mean ages of the cases and controls are comparable. (P=0.702)

On categorisation, among the cases, 23 (54.76%) are in 20- 25 years of age and 19 (45.24%) are between 26-30 years of age; and among the controls 32 (76.19%) are in 20- 25 years of age and 10 (23.81%) are between 26-30 years of age as shown in table 1 and figure 1.

Table 2:- Distribution of study population based on the Gravida

Sl.No	Gravida	Group		Total	P value
		Cases(n=42)	Controls(n=42)		
1.	Gravida 1	20 (47.62%)	16 (38.10%)	36 (42.86%)	0.563
2.	Gravida 2	12 (28.57%)	18 (42.86%)	30 (35.71%)	
3.	Gravida 3	8 (19.05%)	7 (16.67%)	15 (17.86%)	
4.	Gravida 4	2 (4.76%)	1 (2.38%)	3 (3.57%)	

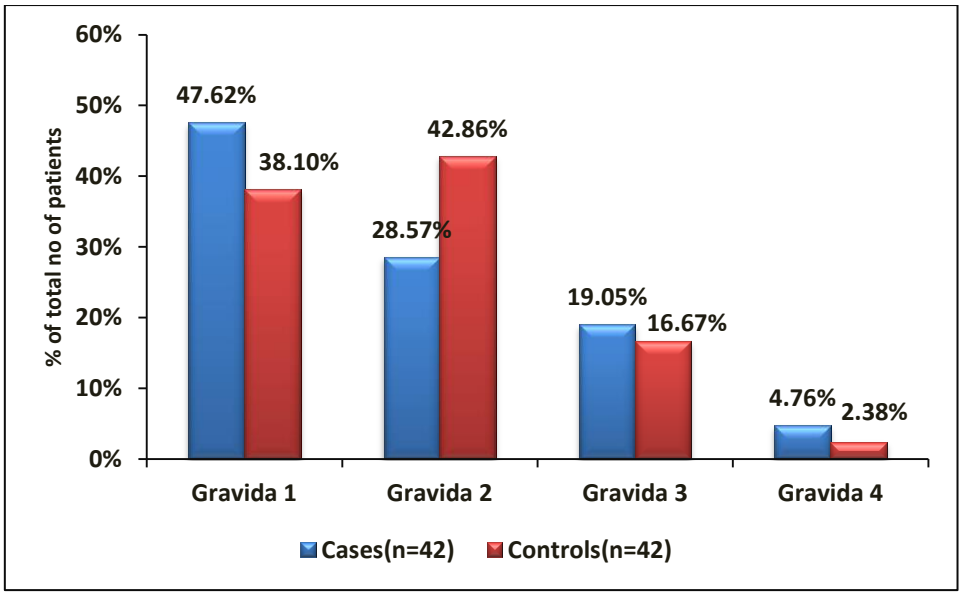


Figure 2:- Distribution of study population based on the Gravida

In this study, 36 (42.86%) patients are Gravida 1, 30 (35.71%) are Gravida 2, 15 (17.86%) are Gravida 3 and only 3 (3.57%) are Gravida 4. The distribution among the cases and controls is comparable. (P=.563) as shown in table 2 and figure 2.

Table 3:- Distribution of study population based on the Gestational age.(N=84)

Gestational Age in weeks	Group		Total	P value
	Cases(n=42)	Controls(n=42)		
32 + 1 to <34	5 (11.90%)	0 (0.00%)	5 (5.95%)	0.115
34+1 to 37	9 (21.43%)	8 (19.05%)	17 (20.24%)	
37+1 to 40	23 (54.76%)	26 (61.90%)	49 (58.33%)	
>40$_{+1\ weeks}$	5 (11.90%)	8 (19.05%)	13 (15.48%)	

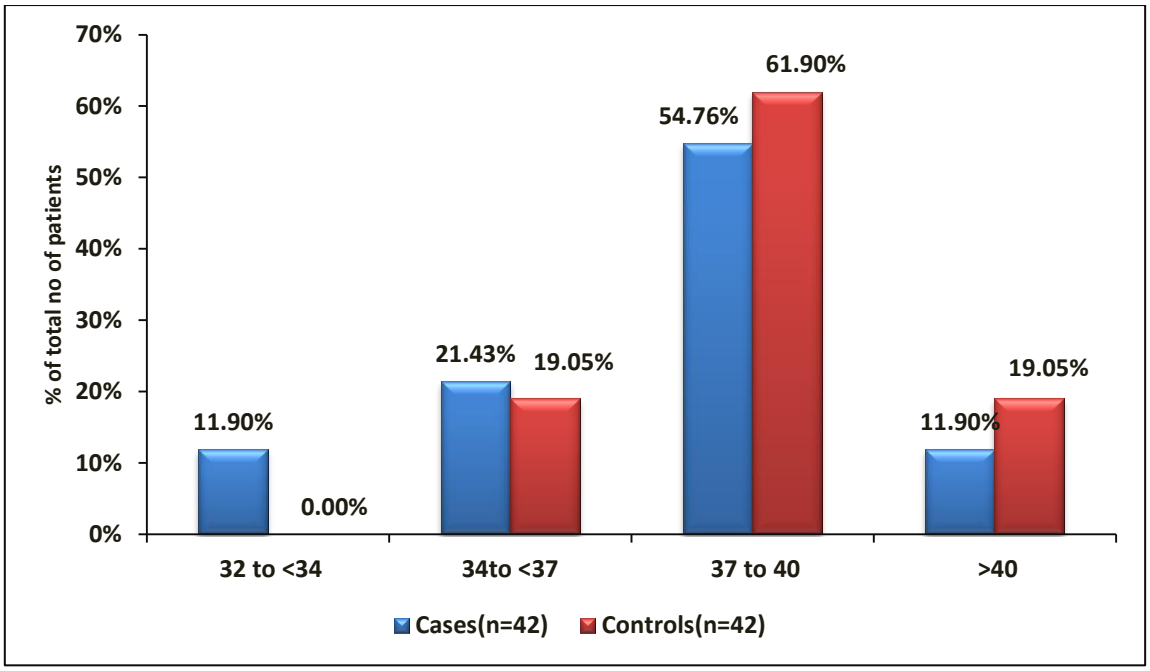


Figure 3:- Distribution of study population based on the Gestational age.

In this study, gestational age is 37-40 weeks in 49 (58.33%) patients, 32-34 weeks in 5 (5.95%) patients, 34-37 weeks in 17 (20.24%) patients, and more than 40 weeks in 13 (15.48%) patients. The distribution among the cases and controls is comparable.(P=.115) as shown in table 3 and figure 3.

Table 4:- Mode of delivery in the study population

Vaginal/Caesarean section	Group		Total	P value
	Cases(n=42)	Controls(n=42)		
Caesarean Section	28 (66.67%)	25 (59.52%)	53 (63.10%)	0.498
Vaginal	14 (33.33%)	16 (40.48%)	30 (36.90%)	

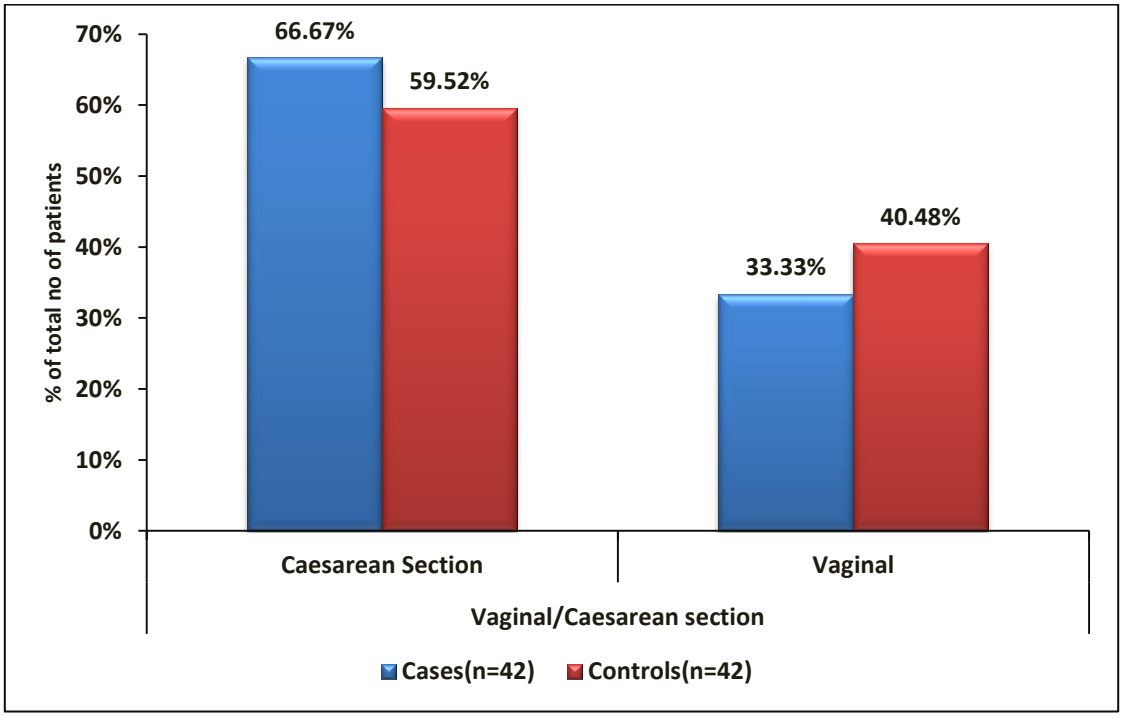


Figure 4:- Mode of delivery in the study population

In this study, 53 (63.10%) of the patients have caesarean section and 30 (36.90%) have normal vaginal delivery. (P=.498) as shown in table 4 and figure 4. The mode of delivery is insignificant in both the groups.

Table 5:- Fetal outcome in the study population

NPO/APO	Group		Total	P value
	Cases(n=42)	Controls(n=42)		
APO –Abnormal perinatal outcome	12 (28.57%)	1 (2.38%)	13 (15.48%)	0.002
NPO – normal perinatal outcome	30 (71.43%)	41 (97.62%)	70 (84.52%)	

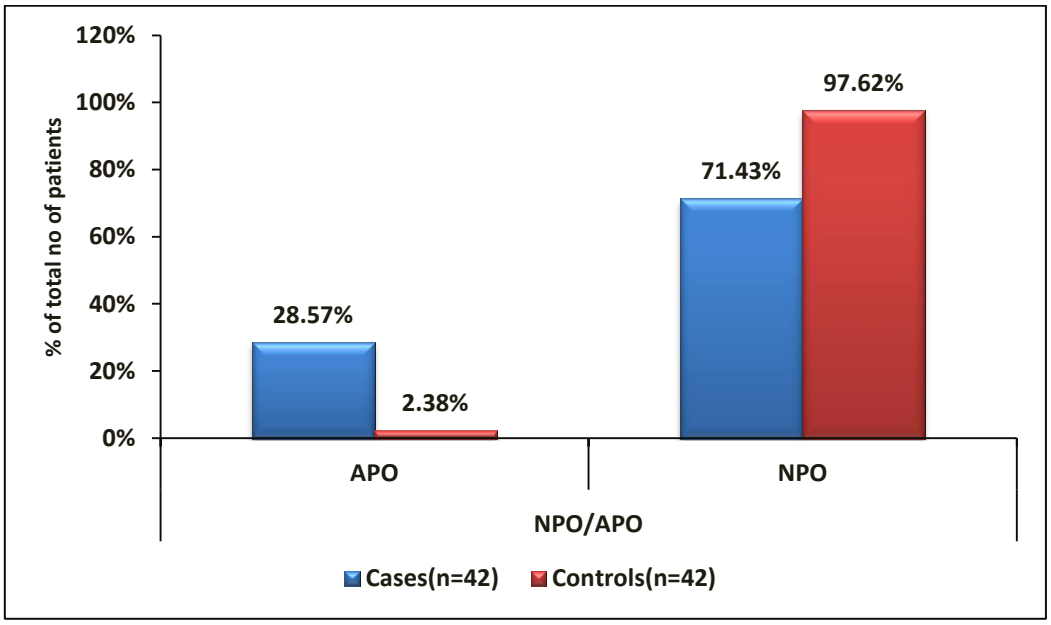


Figure 5:- Fetal outcome in the study population in terms of Abnormal perinatal outcome (APO) and Normal perinatal outcome(NPO)

In this study, 13 (15.48%) of the patients had abnormal perinataloutcome in terms of low APGAR score and NICU admission and perinatal morbidity and mortality. and 70 (84.52%) patients had normal perinatal outcome. Among the 13 patinets with abnormal perinatal outcome, 12 belong to the Preeclamptic group and 1 in control group. The distribution among the cases and controls is significantly different. (P=.002) as shown in table 5 and figure 5.

Table 6:- Comparison of blood pressure between cases and controls

Blood Pressure(mmHg)		Cases(n=42)	Controls(n=42)	P value
Systolic Blood Pressure(mmHg)	Mean ± Stdev	158.31 ± 15.46	117.95 ± 8.03	<.0001
	Median	160(140-200)	120(100-130)	
	Inter quartile Range	150.000 - 170.000	110.000 - 124.000	
Diastolic Blood Pressure(mmHg)	Mean ± Stdev	102.38 ± 8.78	74.14 ± 6.3	<.0001
	Median	(90-120)	(60-90)	
	Inter quartile Range	100.000 - 110.000	70.000 - 80.000	

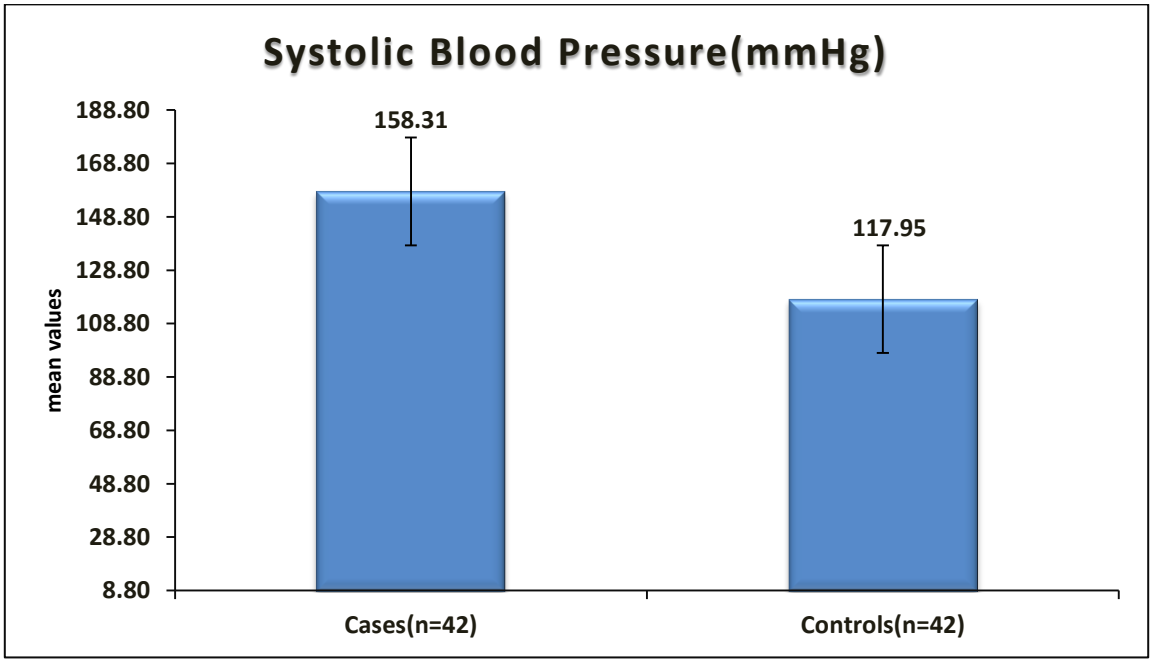


Figure 6.1:- Comparison of systolic blood pressure between cases and controls

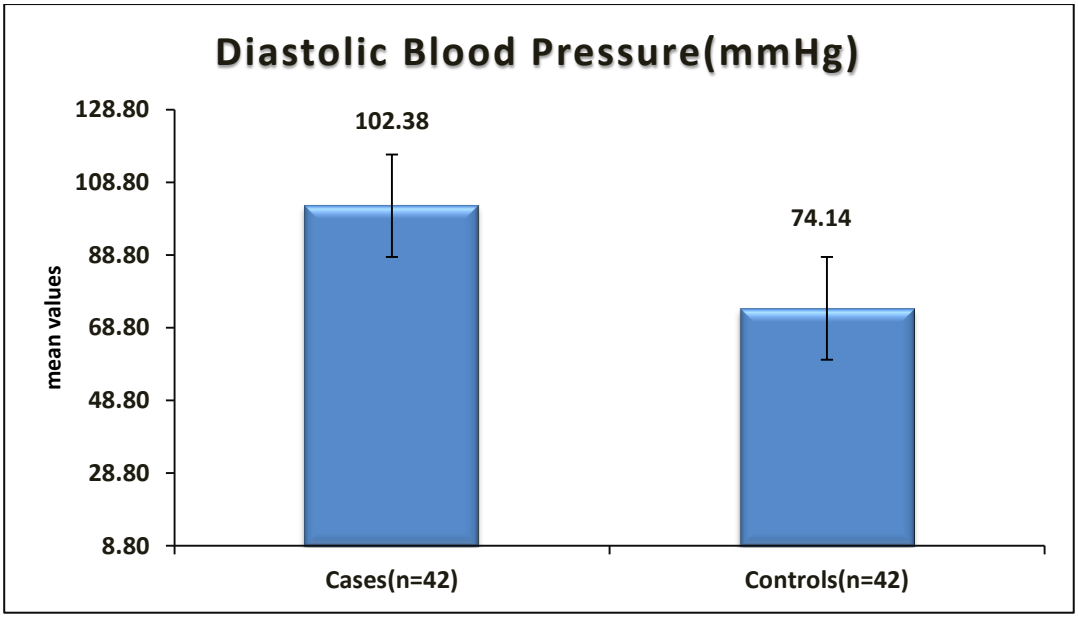


Figure 6.2:- Comparison of diastolic blood pressure between cases and controls

The mean SBP in cases is 158.31 ± 15.46 mm of Hg and in controls is 117.95 ± 8.03 mm of Hg; the difference is statistically significant.(P<0.0001) as shown in table 6, and figure 6.1

The mean DBP in cases is 102.38 ± 8.78 mm of Hg and in controls is 74.14 ± 6.3 mm of Hg; the difference is statistically significant.(P<0.0001) as shown in table 6, and figure 6.2

Table 7:- Comparison of urine albumin between cases and controls

Urine albumin	Group		Total	P value
	Cases(n=42)	Controls(n=42)		
NIL	3 (7.14%)	42 (100.00%)	45 (53.57%)	<.0001
1+	11 (26.19%)	0 (0.00%)	11 (13.10%)	
2+	7 (16.67%)	0 (0.00%)	7 (8.33%)	
3+	16 (38.10%)	0 (0.00%)	16 (19.05%)	
4+	5 (11.90%)	0 (0.00%)	5 (5.95%)	

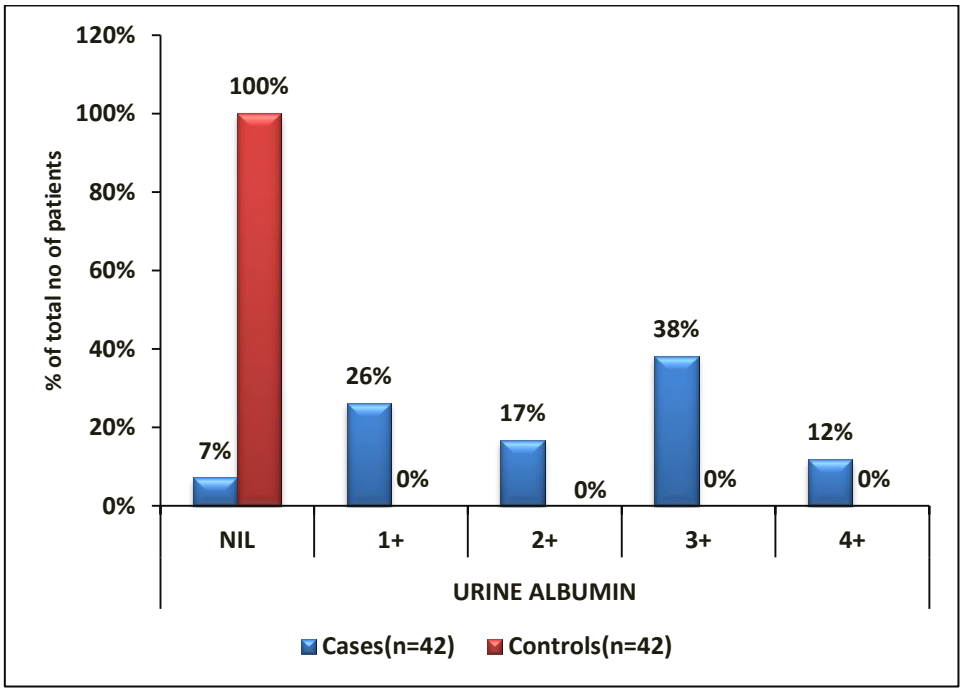


Figure 7:- Comparison of urine albumin between cases and controls

Urine albumin is nil in controls and predominantly 1+ (26.19%) and 3+ (38.10%) in cases. The difference is statistically significant.(P<0.0001) as shown in table 7 and figure 7.

Table 8:- Comparison of Serum β hCG levels between cases and controls

Serum β hCG(mIU/ml)	Cases(n=42)	Controls(n=42)	P value
Mean ± Stdev	37199.19 ± 16102.76	13366.77 ± 3149.74	<.0001
Median	34234.35(17688-74840.5)	13254.65(6575-19644.9)	
Inter quartile Range	22353 - 50179.900	10687.1 - 15553.7	

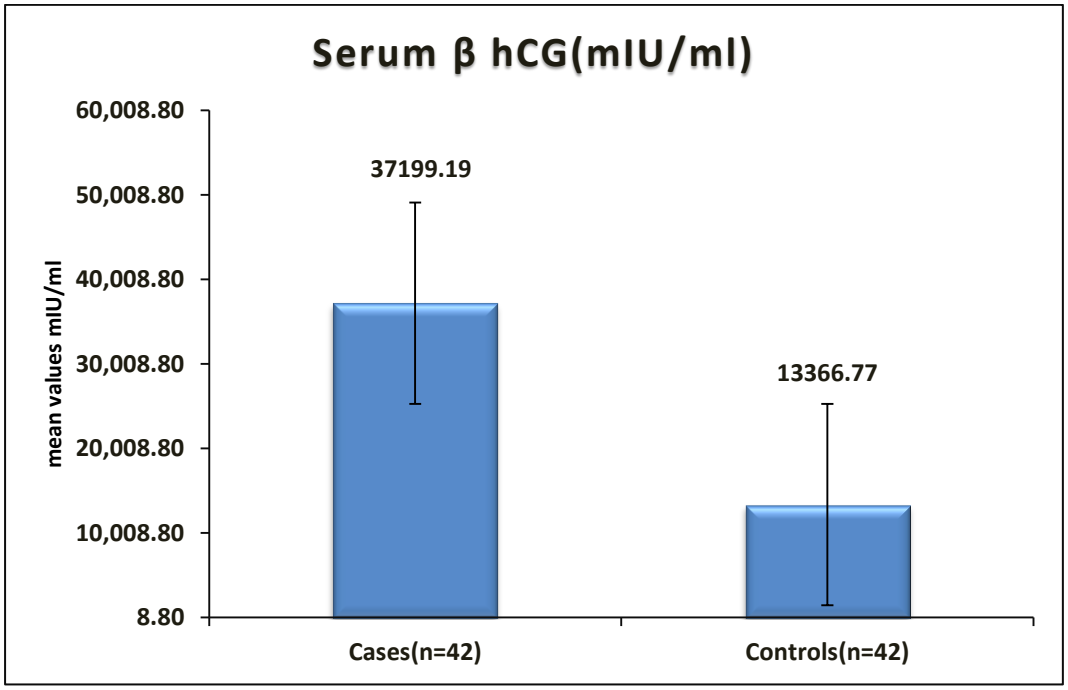


Figure 8:- Comparison of Serum β hCG levels between cases and controls

The mean β hCG in cases is 37199.19 ± 16102.76 mIU/ml and in controls is 13366.77 ± 3149.74 mIU/ml; the difference is statistically significant. (P<0.0001) as shown in table 8 and figure 8.

Table 9:- Receiver operating characteristic curve plotted for β hCG in diagnosing pre-eclampsia

For discriminating pre eclampsia	Area under the ROC curve (AUC)	Standard Error	95% CI	P value	Cut off
Serum β hCG(mIU/ml)	0.9932	0.00504	0.944199 to 0.999985	<0.0001	>18532.5

Sensitivity	95% CI	Specificity	95% CI	+PV	95% CI	-PV	95% CI
95.24	83.8 - 99.4	97.62	87.4 - 99.9	97.6	87.1 - 99.9	95.3	84.2 - 99.4

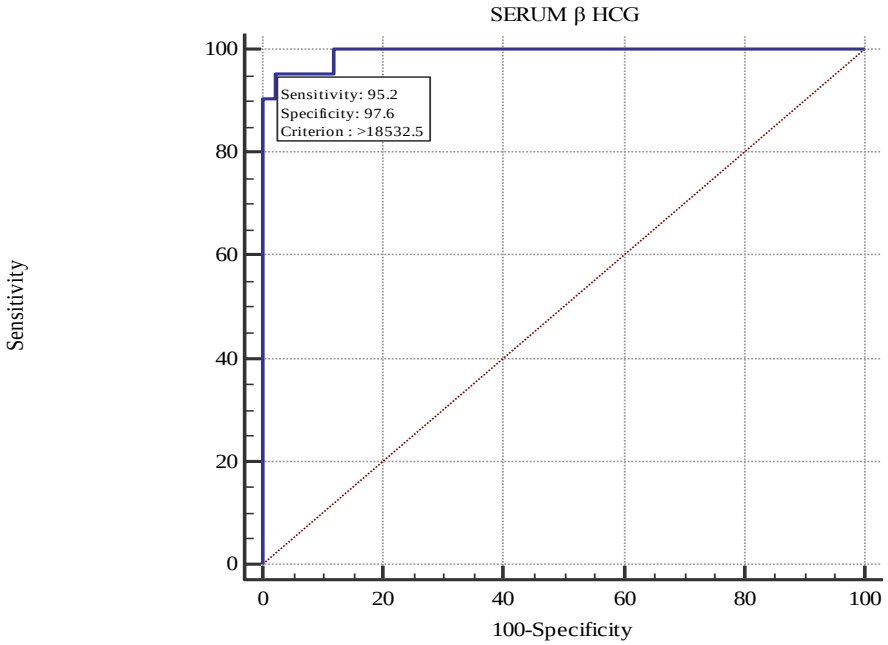


Figure 9:- Receiver operating characteristic curve plotted for β hCG for predicting pre eclampsia

After performing ROC, cut off point of serum β hCG level is 18532.5 with AUC of .993 and sensitivity and specificity of 95.24% and 97.62% respectively for predicting preeclampsia which is statistically significant with p value <.0001 as shown in table 9 and figure 9.

Table 10:- Receiver operating characteristic curve for predicting severity of pre eclampsia

For discriminating severe pre eclampsia	Area under the ROC curve (AUC)	Standard Error	95% CI	P value	Cut off
Serum β hCG(mIU/ml)	0.936	0.0357	0.815 to 0.988	<0.0001	>32344.4

Sensitivity	95% CI	Specificity	95% CI	+PV	95% CI	-PV	95% CI
86.96	66.4 - 97.2	94.74	74.0 - 99.9	95.2	76.2 - 99.9	85.7	63.7 - 97.0

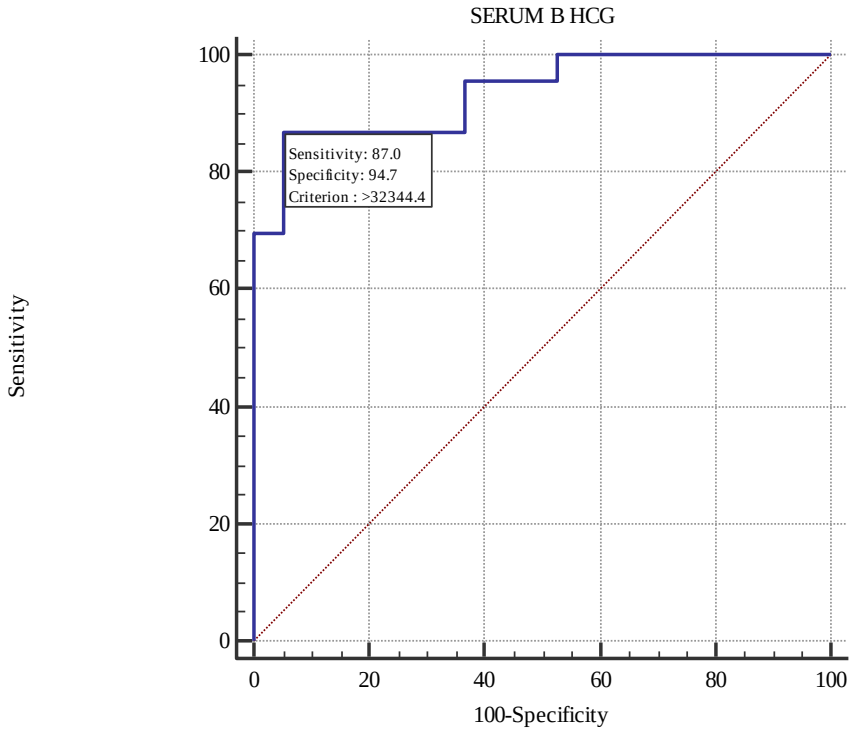


Figure 10:- Receiver operating characteristic curve for predicting severity of pre eclampsia.

After performing ROC, cut off point of serum β hCG level is 32344.4 with AUC of .936 and sensitivity and specificity of 86.96% and 94.74% respectively for predicting severity of pre eclampsia which is statistically significant with p value <.0001as shown in table 10 and figure 10.

Table 11:- Pre eclampsia distribution in cases

Pre Eclampsia(n=42)	Frequency	Percentage
Non severe Pre eclampsia	19	45.24%
Severe Pre eclampsia	23	54.76%

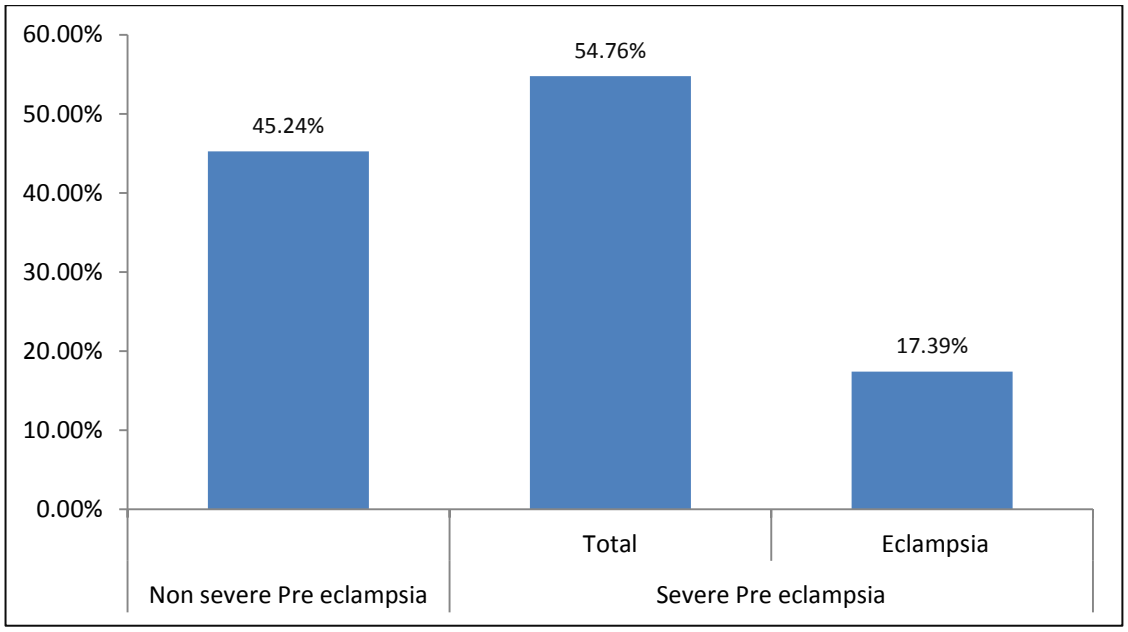


Figure 11:- Pre eclampsia distribution in cases

In this study, out of 42 cases of pre-eclampsia, 23 have severe pre-eclampsia; 19 have non-severe pre-eclampsia out of which 4 patients developed eclampsia after the admission as shown in table 11 and figure 11.

Table 12:- Comparison of Serum β hCG levels between gravida among cases

Serum β hCG (mIU/ml)	Gravida 1 (n=20)	Gravida 2 (n=12)	Gravida 3 (n=8)	Gravida 4 (n=2)	P value
Mean ± Stdev	38131.25 ± 18135.96	30951.32 ± 14951.49	43886.28 ± 11932.06	38617.4 ± 8871.36	0.221
Median	37955.65(17688-74840.5)	26045.7(17887-61256.2)	48663(27355.1-59841.3)	38617.4(32344.4-44890.4)	
Inter quartile Range	20267.450 - 50995.300	19309.050 - 38113.050	32209.450 - 51074.450	32344.400 - 44890.400	

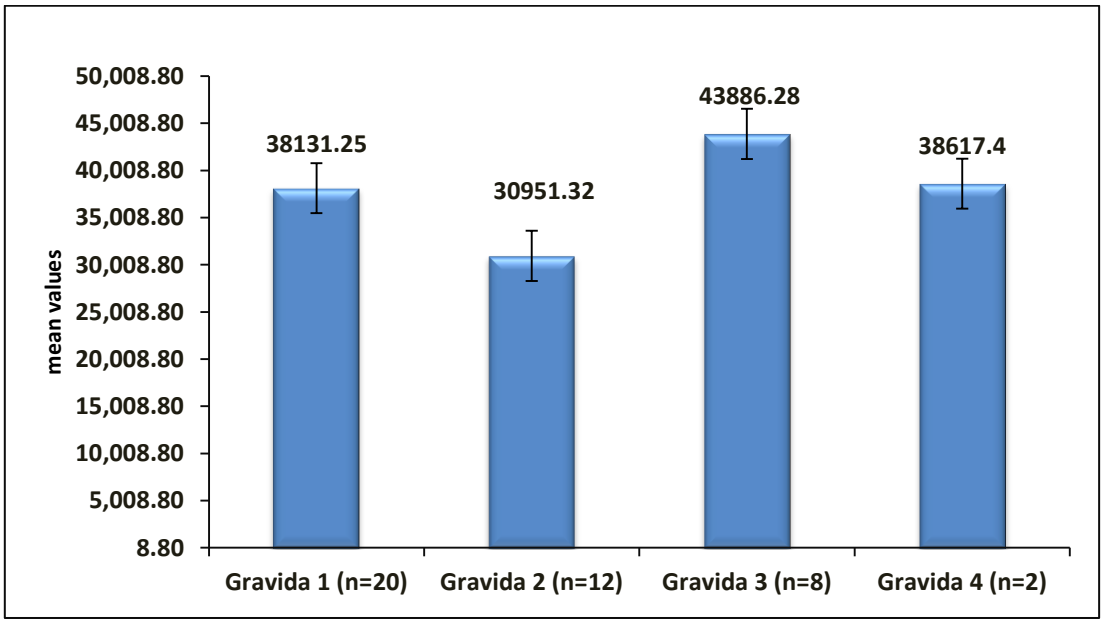


Figure 12:- Comparison of Serum β hCG levels between gravida among cases

Among cases, the mean β hCG in Gravida 1 is 38131.25 ± 18135.96 mIU/ml; in Gravida 2 is 30951.32 ± 14951.49 mIU/ml, in Gravida 3 is 43886.28 ± 11932.06 mIU/ml and in Gravida 4 is 38617.4 ± 8871.36 mIU/ml; the difference is statistically not significant.(P=.221) as shown in table 12 and figure 12.

Table 13:- Comparison of Serum β hCG levels between term/preterm among cases

Serum β hCG (mIU/ml)	Preterm(n=13)	Term(n=29)	P value
Mean ± Stdev	51539.48 ± 10434.01	30770.78 ± 13955.34	<.0001
Median	51625.3(32344.4-67894.1)	25676.9(17688-74840.5)	
Inter quartile Range	44468.475 - 60195.025	20115.400 - 40340.625	

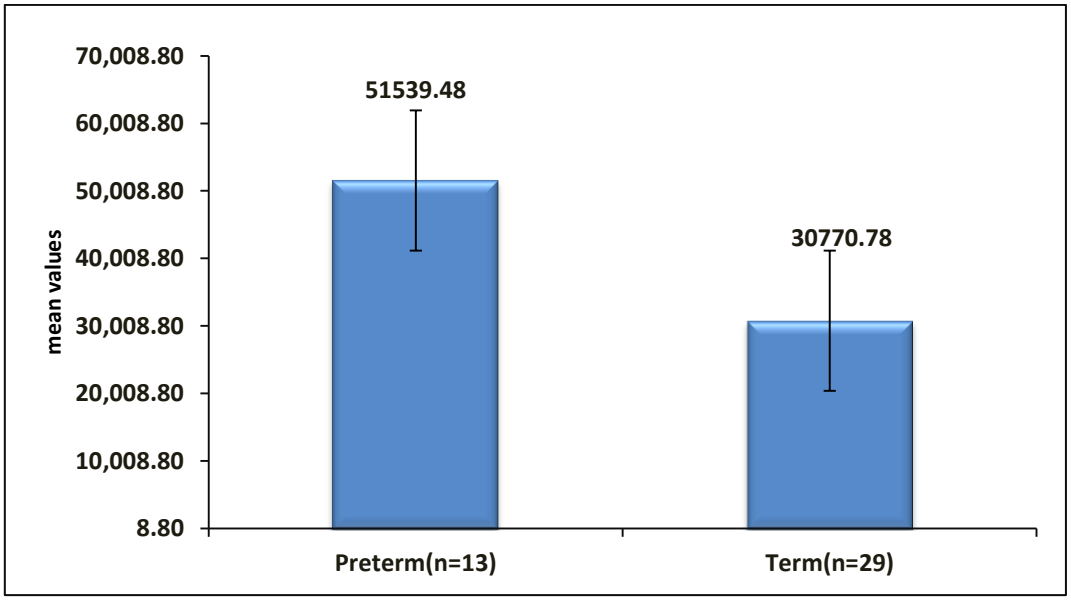


Figure 13:- Comparison of Serum β hCG levels between term/preterm among cases

Among cases, the mean β hCG in preterm is 51539.48 ± 10434.01 mIU/ml and in term is 30770.78 ± 13955.34 mIU/ml; the difference is statistically significant.(P<0.0001) as shown in table 13 and figure 13.

Table 14:- Comparison of Serum β hCG levels between gestational age among cases and controls

Serum β hCG(mI U/ml) in cases	**32_{+1} to <34 (n=5)**	**34+1 to <37 (n=9)**	**37+1 to 40 (n=23)**	**>40+1 weeks (n=5)**	**P value**
Mean ± Stdev	53645.82 ± 7626.34	47682.13 ± 13704.78	29977.43 ± 12032.52	35103.36 ± 23172.47	0.001
Median	51625.3(43635.9-62603)	47146.1(27355.1-67894.1)	25676.9(17688-56316.4)	24567.1(19793.8-74840.5)	
Inter quartile Range	48801.675 - 60531.725	35675.900 - 57870.325	19965.725 - 41447.875	20091.775 - 45803.350	
Serum β hCG(mI U/ml) in controls	**32 to <34(n=0)**	**34 to <37(n=8)**	**37 to 40(n=26)**	**>40(n=8)**	**P value**
Mean ± Stdev	-	13985.72 ± 2962.33	12667.91 ± 3548.06	12038.9 ± 2423.56	0.473
Median	-	14283.15(10580.4-18480.3)	13247.2(5799-19644.9)	11504.4(9724.8-16893.5)	
Inter quartile Range	-	10938.350 - 16191.050	10631.000 - 15526.900	10171.650 - 13170.400	

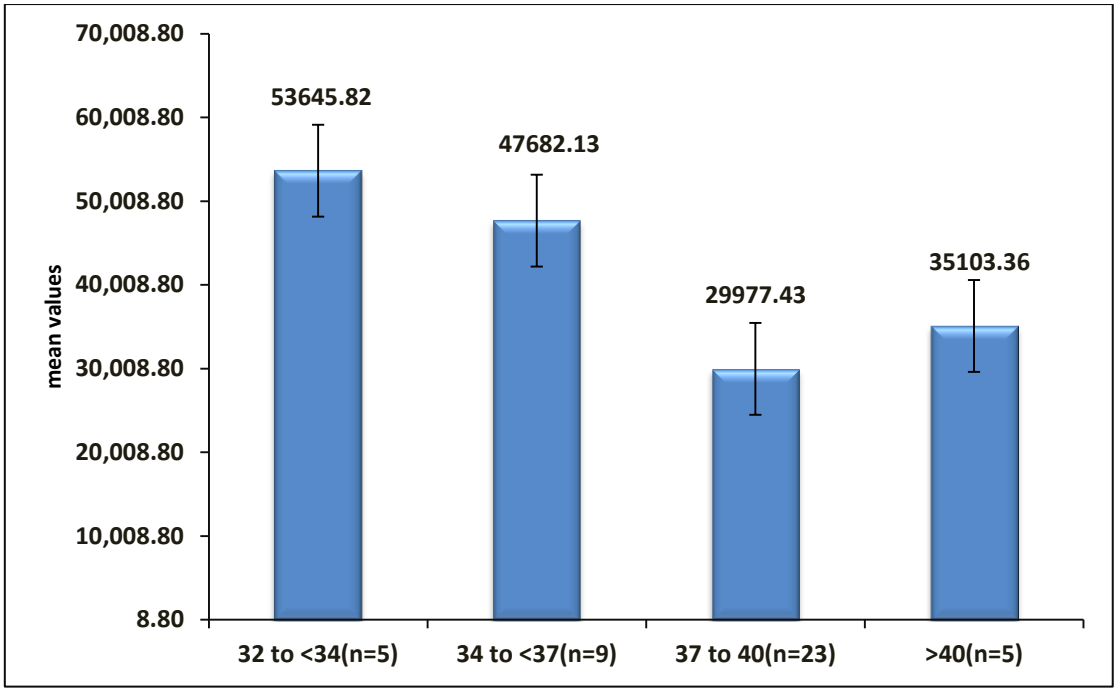


Figure 14.1:- Comparison of Serum β hCG between gestational age among cases

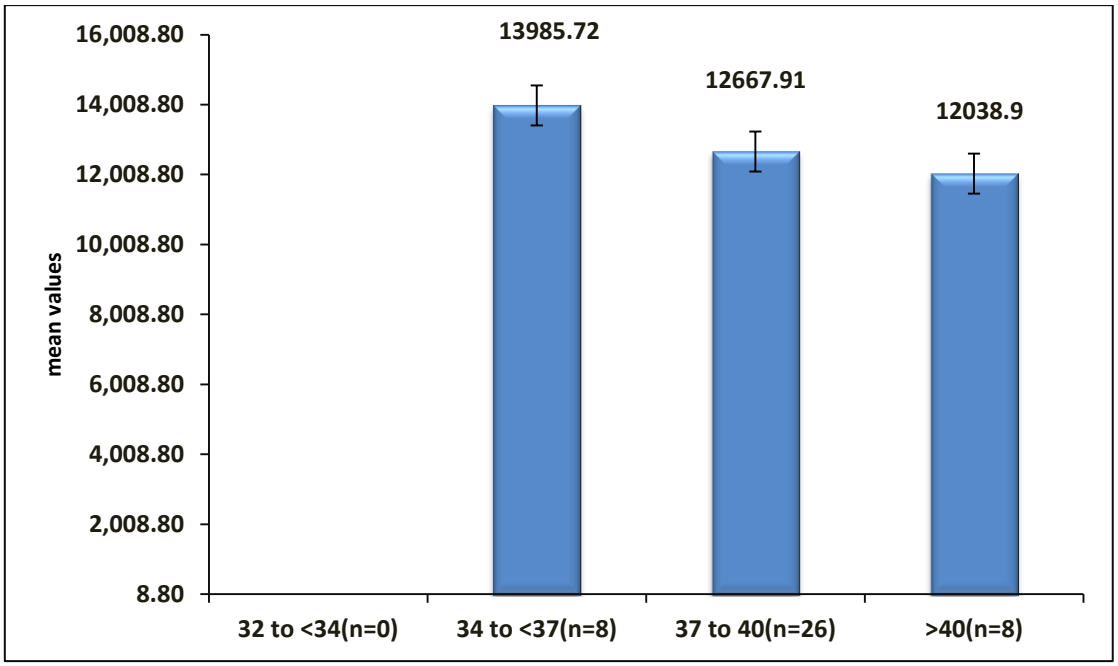


Figure 14.2:- Comparison of Serum β hCG between gestational age among controls

Among cases, the mean β hCG in gestational age 32-34 weeks is 53645.82 ± 7626.34 mIU/ml, in 34-37 weeks is 47682.13 ± 13704.78 mIU/ml, in 37-40 weeks is 29977.43 ± 12032.52 mIU/ml and in >40 weeks is 35103.36 ± 23172.47 mIU/ml; the difference is statistically significant.(P=.001) as shown in table 14 and figure 14.1.

Among controls, the mean β hCG in gestational age 34-37 weeks is 13985.72 ± 2962.33 mIU/ml, in 37-40 weeks is 12667.91 ± 3548.06 mIU/ml and in >40 weeks is 12038.9 ± 2423.56 mIU/ml; the difference is not statistically significant.(P=.473) as shown in table 14 and figure 14.2.

Table 15:- Correlation of age distribution with severity of pre-eclampsia

Age distribution	Pre eclampsia		Total	P value
	Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)		
20-25	12 (63.16%)	11 (47.83%)	23 (54.76%)	0.32
26-30	7 (36.84%)	12 (52.17%)	19 (45.24%)	

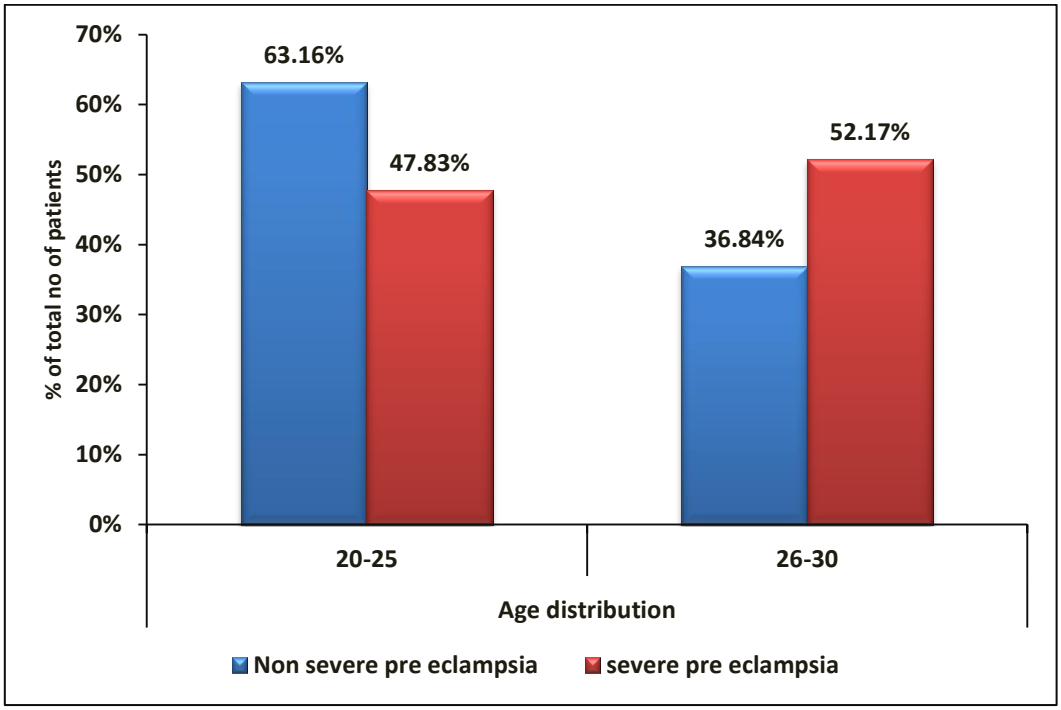


Figure 15:- Correlation of age distribution with severity of pre eclampsia

In this study, out of 19 cases of non-severe pre-eclampsia, 63.16% are in 20-25 years of age and 7 cases are in 26-30 years of age; and among 23 cases of severe pre-eclampsia, 47.83% are in 20-25 years of age and 52.17% are in 26-30 years of age. There is no statistically significant difference.(P=.32) as shown in table 15 and figure 15.

Table 16:- Correlation of gravida with severity of pre eclampsia

Gravida	Pre eclampsia		Total	P value
	Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)		
Gravida 1	8 (42.11%)	12 (52.17%)	20 (47.62%)	0.285
Gravida 2	8 (42.11%)	4 (17.39%)	12 (28.57%)	
Gravida 3	2 (10.53%)	6 (26.09%)	8 (19.05%)	
Gravida 4	1 (5.26%)	1 (4.35%)	2 (4.76%)	

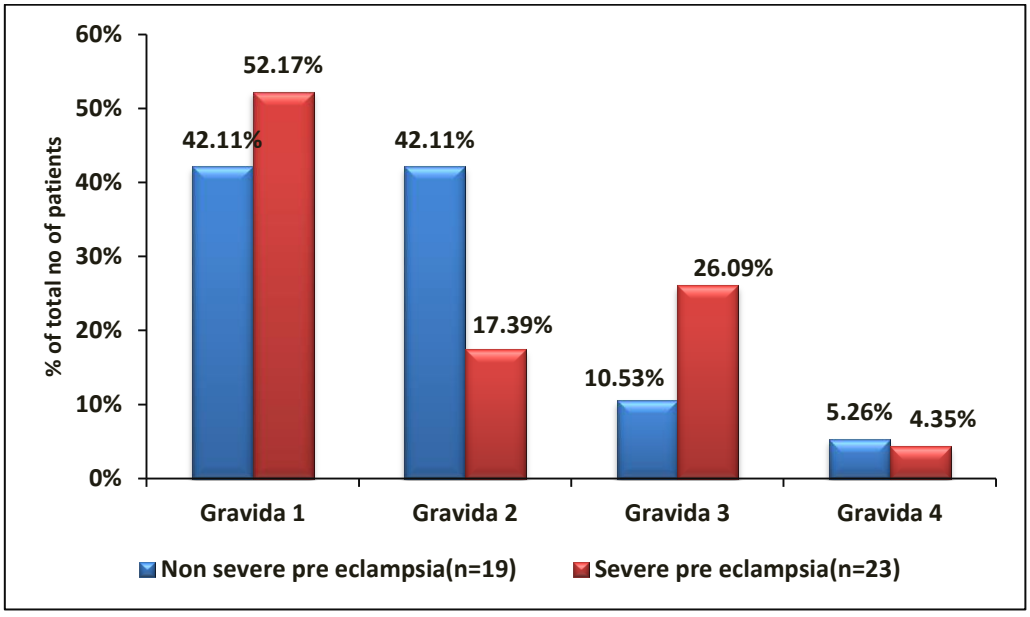


Figure 16:- Correlation of gravida with severity of pre eclampsia

In this study, out of 19 cases of non-severe pre-eclampsia, 57.89% are multigravida (42.1% Gravida 2, 10.53% Gravida 3 and 5.26% Gravida 4) and 42.1% cases are Gravida 1; and among 23 cases of severe pre-eclampsia, 47.83% are multigravida (17.39% Gravida 2, 26.09% Gravida 3 and 4.35% Gravida 4) and 52.17% are Gravida 1. There is no statistically significant difference.(P=.285) as shown in table 16 and figure 16.

Table 17:- Correlation of gestational age with severity of pre eclampsia

Gestational age in weeks	Pre eclampsia		Total	P value
	Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)		
32 to <34	1 (5.26%)	4 (17.39%)	5 (11.90%)	0.185
34to <37	2 (10.53%)	7 (30.43%)	9 (21.43%)	
37 to 40	13 (68.42%)	10 (43.48%)	23 (54.76%)	
>40	3 (15.79%)	2 (8.70%)	5 (11.90%)	

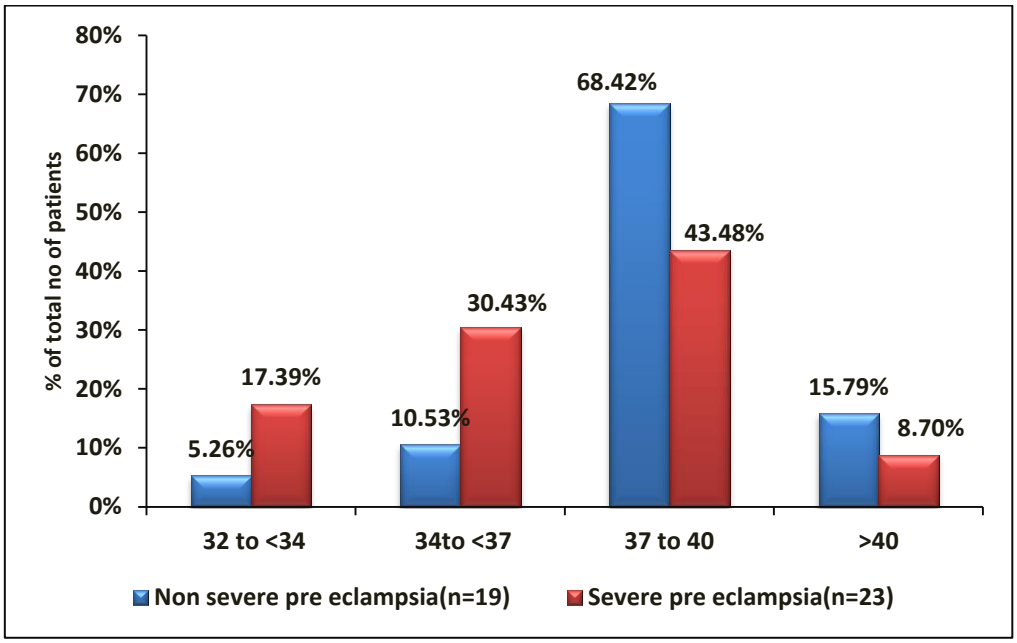


Figure 17:- Correlation of gestational age with severity of pre eclampsia

In this study, out of 19 cases of non-severe pre-eclampsia, 5.26% are at 32-34 weeks, 10.53% at 34-37 weeks, 68.42% at 37-40 weeks and 15.79% are at >40 weeks of gestational age; whereas among 23 cases of severe pre-eclampsia, 17.39% are at 32-34 weeks, 30.43 % at 34-37 weeks, 43.48% at 37-40 weeks and 8.7% are at >40 weeks of gestational age; the difference is statistically not significant.(P=.185) as shown in table 17 and figure 17.

Table 18:- Correlation of mode of delivery with severity of pre eclampsia

Vaginal/Caesarean section	Pre eclampsia		Total	P value
	Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)		
Caesarean Section	12 (63.16%)	16 (69.57%)	28 (66.67%)	0.661
Vaginal	7 (36.84%)	7 (30.43%)	14 (33.33%)	

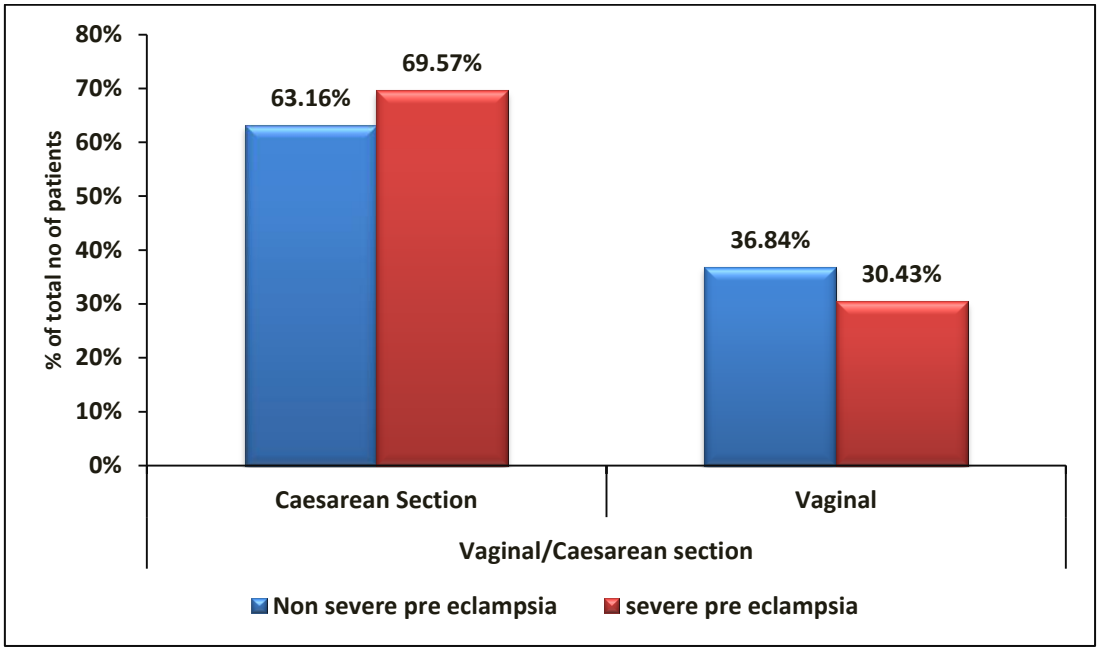


Figure 18:- Correlation of mode of delivery with severity of pre eclampsia

In this study, out of 19 cases of non-severe pre-eclampsia, 63.16% have caesarean delivery and 36.84% cases have normal vaginal delivery; and among 23 cases of severe pre-eclampsia, 69.57% have caesarean delivery and 30.43% cases have normal vaginal delivery. There is no statistically significant difference.(P=0.661) as shown in table 18 and figure 18.

Table 19:- Correlation of fetal outcome with severity of pre eclampsia

NPO/APO	Pre eclampsia		Total	P value
	Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)		
APO	1 (5.26%)	11 (47.83%)	12 (28.57%)	0.005
NPO	18 (94.74%)	12 (52.17%)	30 (71.43%)	

APO- Abnormal Perinatal outcome

NPO- Normal perinatal outcome

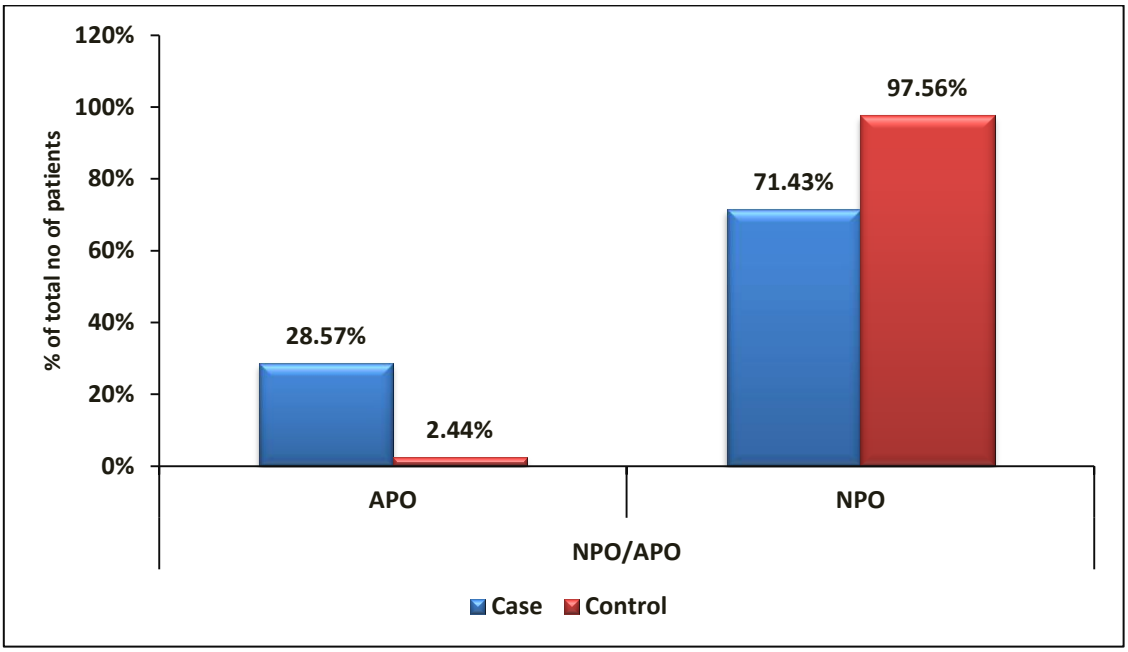


Figure 19:- Correlation of fetal outcome with severity of pre eclampsia

In this study, out of 19 cases of non-severe pre-eclampsia, only 1 case had abnormal perinata loutcome and 18 cases had Normal perinatal outcome; and among 23 cases of severe pre-eclampsia, 11 cases had abnormal perintal outcome in terms of Low APGAR,NICU admission, perinatal morbidity and mortality and 12 cases had Normal perinatal outcome; the difference is statistically significant.(P=0.005) as shown in table 19 and figure 19.

Table 20:- Correlation of blood pressure with severity of pre eclampsia

Blood Pressure(mmHg)		Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)	P value
Systolic Blood Pressure(mm Hg)	Mean ± Stdev	146.79 ± 6.69	167.83 ± 14.13	<.0001
	Median	150(140-160)	160(140-200)	
	Inter quartile Range	140.000 - 150.000	160.000 - 170.000	
Diastolic Blood Pressure(mm Hg)	Mean ± Stdev	95.79 ± 5.07	107.83 ± 7.36	<.0001
	Median	100(90-100)	110(90-120)	
	Inter quartile Range	90.000 - 100.000	100.000 - 110.000	

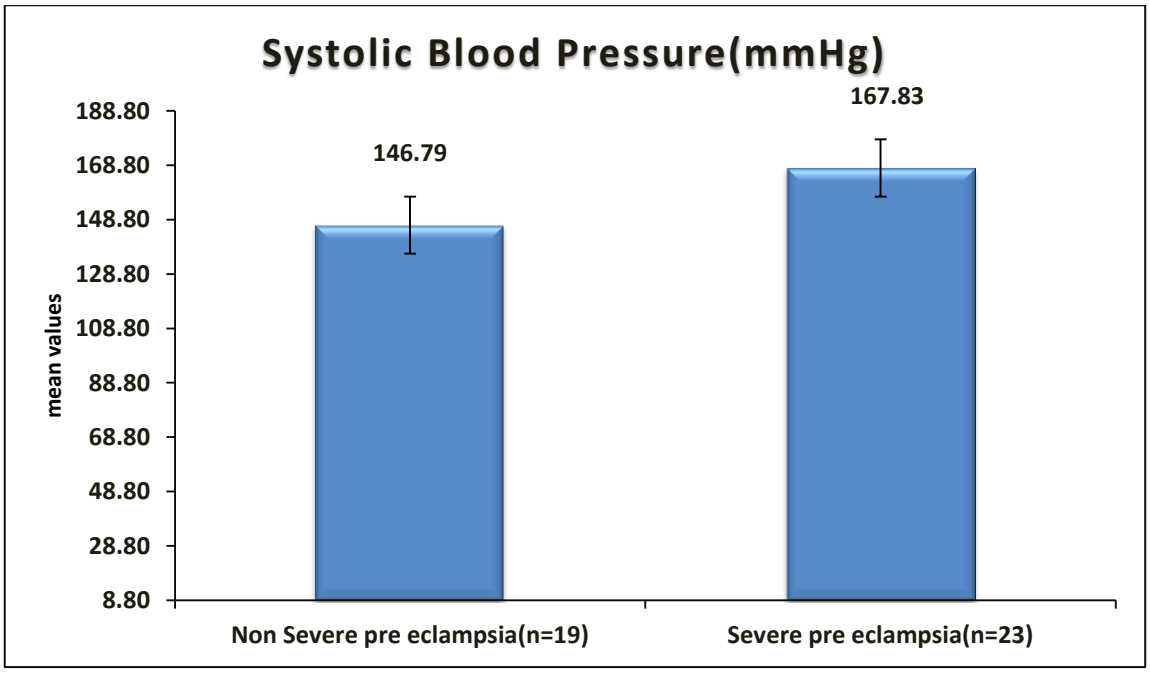


Figure 20.1:- Correlation of systolic blood pressure with severity of pre eclampsia

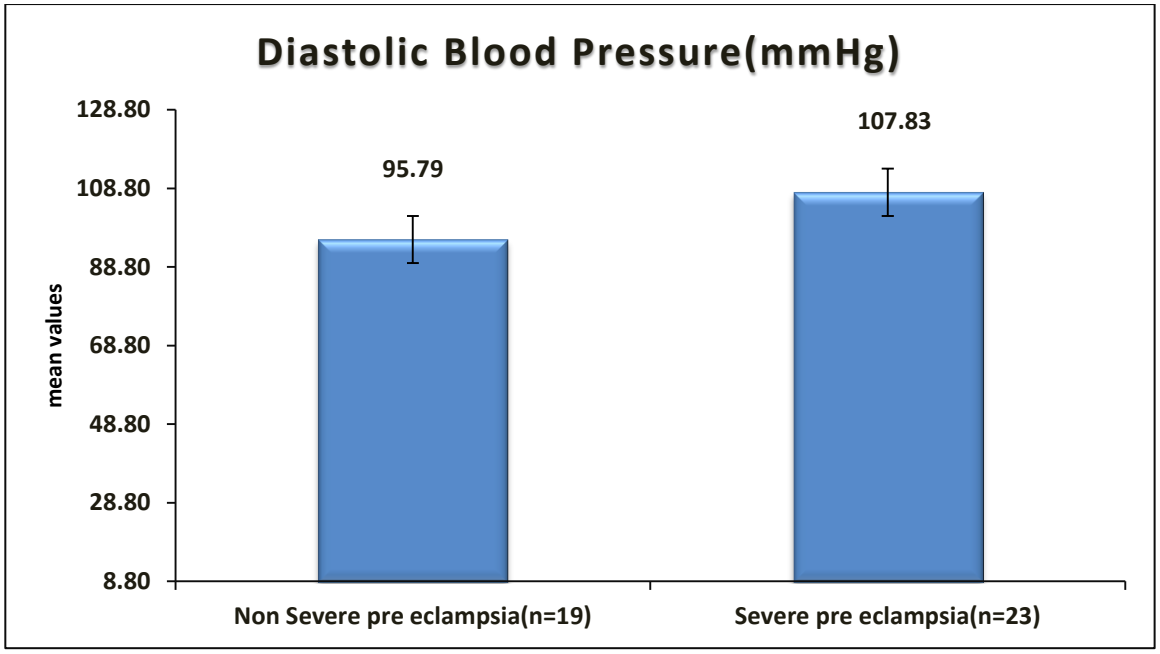


Figure 20.2:- Correlation of diastolic blood pressure with severity of pre eclampsia

In this study, the mean SBP and DBP in non-severe pre-eclampsia is 146.79 ± 6.69 and 95.79 ± 5.07 mm of Hg respectively; and among severe pre-eclampsia cases mean is 167.83 ± 14.13 and 107.83 ± 7.36 mm of Hg. There is a statistically significant difference between them.($P<0.0001$) as shown in table 20 and figure 20.1, 20.2.

Table 21:- Correlation of urine albumin with severity of pre eclampsia

Urine Albumin	Pre eclampsia		Total	P value
	Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)		
1+	11 (57.89%)	0 (0.00%)	11 (26.19%)	<.0001
2+	5 (26.32%)	2 (8.70%)	7 (16.67%)	
3+	0 (0.00%)	16 (69.57%)	16 (38.10%)	
4+	0 (0.00%)	5 (21.74%)	5 (11.90%)	
NIL	3 (15.79%)	0 (0.00%)	3 (7.14%)	

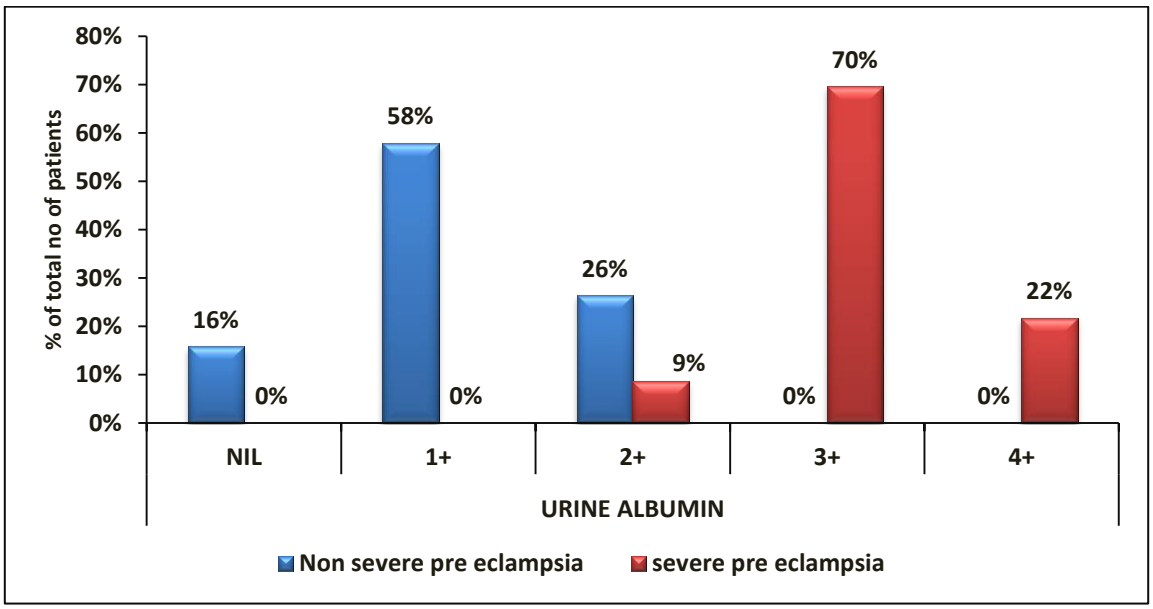


Figure 21:- Correlation of urine albumin with severity of pre eclampsia

In this study, out of 19 cases of non-severe pre-eclampsia, 11 cases have 1+ and 5 cases have 2+ urine albumin; and among 23 cases of severe pre-eclampsia, 16 cases have 3+ and 5 cases have 4+ urine albumin. A significant difference is seen between the amount of urine albumin with changing severity of pre-eclampsia.(P<0.0001) as shown in table 21 and figure 21.

Table 22:- Correlation of Serum β hCG levels with severity of pre eclampsia

Serum β hCG(mIU/ml)	Non severe pre eclampsia(n=19)	Severe pre eclampsia(n=23)	P value
Mean ± Stdev	24226.43 ± 6489.3	47915.82 ± 13541.57	<.0001
Median	22353(17688-43635.9)	47146.1(20336.9-74840.5)	
Inter quartile Range	19796.850 - 27563.150	40340.625 - 56635.375	

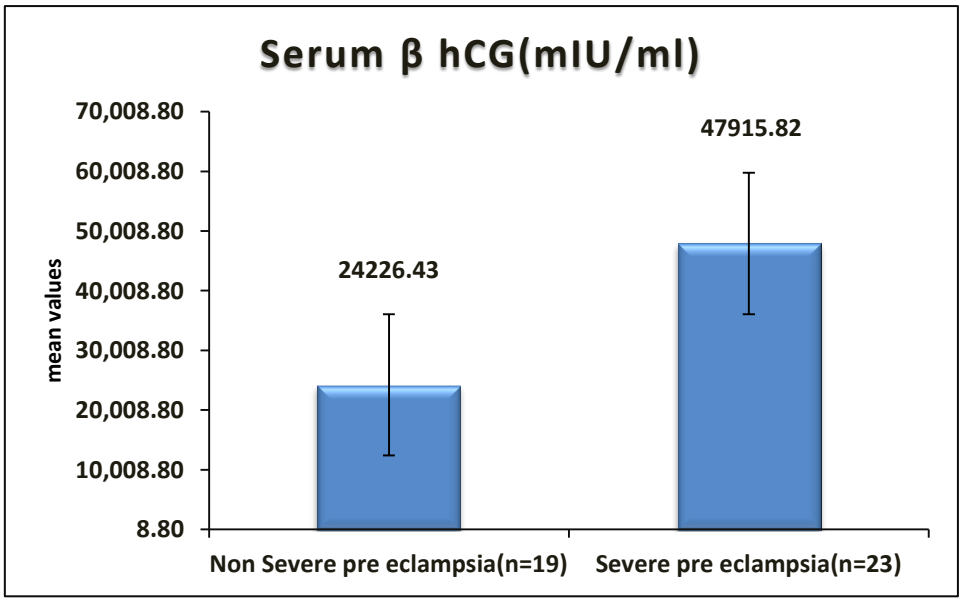


Figure 22:- Correlation of Serum β hCG levels with severity of pre eclampsia

In this study, among 19 cases of non-severe pre-eclampsia, the mean β hCG is 24226.43 ± 6489.3 mIU/ml and among 23 cases of severe pre-eclampsia, the mean β hCG is 47915.82 ± 13541.57 mIU/ml; the difference is statistically significant.(P<0.0001) as shown in table 22 and figure 22.

Table 23:- Comparison of Serum β hCG levels between eclampsia and preeclampsia

Serum β hCG(mIU/ml)	Eclampsia(n=4)	Pre eclampsia(n=38)	P value
Mean ± Stdev	58814.92 ± 15173.31	34923.85 ± 14588.84	0.003
Median	59208.85(42001.5-74840.5)	29381.9(17688-62603)	
Inter quartile Range	46262.550 - 71367.300	20336.900 - 46793.900	

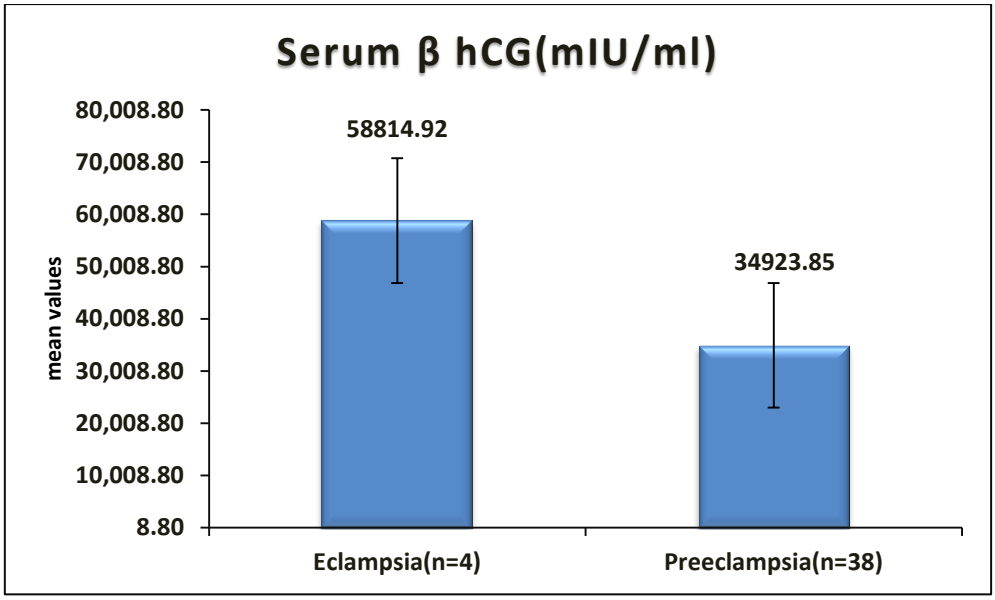


Figure 23:- Comparison of Serum β hCG between eclampsia and pre eclampsia

In this study, among 4 cases of eclampsia, the mean β hCG is 58814.92 ± 15173.31 mIU/ml and among 38 cases of pre-eclampsia, the mean β hCG is 34923.85 ± 14588.84 mIU/ml; the difference is statistically significant.(P=.003) as shown in table 23 and figure 23.

Discussion

DISCUSSION

The present study is a case control study conducted in R L Jalappa Hospital, Kolar with study population of 84 singleton pregnancies between 32- 42 weeks of gestation, 42 are normotensive pregnancies and 42 Preeclampsia cases out of which 19 are non severe Preeclampsia and 23 are Severe Preeclampsia. Among 42 Preeclampsia cases 4 of them developed Eclampsia later on admission.

In the study conducted by Kanika et al, 50 cases of Preeclampsia with singleton pregnancy and 50 normotensive singleton mothers during third trimester of gestation were analysed for β hCG serum levels, results showed that elevated maternal serum levels of β hCG plays a important role in the pathogenesis of Preeclampsia and its severity.[13]

In study done by Begum et al, 74 cases of Preeclampsia with singleton pregnancy and 76 normotensive controls were analysed for maternal serum β hCG levels during third trimester of pregnancy. The mean β hCG levels were higher in the women with Preeclampsia and further rise in β hCG serum levels in women with Severe Preeclampsia. [17]

In a study conducted by Mohammed et al, in 90 women , who are further divided into three groups as 30 normotensive women,30 women with mild Preeclampsia and 30 women with severe Preeclampsia. Analysis of serum β hCG levels show that levels of serum β hCG are higher in Severe Preeclampsia women when compared to mild Preeclampsia and normotensive women.[12]

AGE:

In this study, majority of study population(65.48%) belonged to the age group of 22-24 years .Mean age group among controls is 24.05 years and mean age group among cases is 24.36 years showing no statistical significance and these results are supported by study conducted by Choudary et al, Mean age was 22.36 years in normal pregnancy and 21.62 years among Pregnancy induced Hypertension group and mean age was 23.3 years in normotensive group and 24.3 years in Preeclampsia group in study conducted by Begum et al.

Blood Pressure at the time of admission :

In the present study there is statistically significance difference between systolic and diastolic blood pressure in both controls and cases. In this study, the mean systolic blood pressure in cases is 158.31 mm Hg and 117.95 in controls where as mean Diastolic Blood pressure in cases is 102.38 and 74.14 mm Hg in controls respectively.

Proteinuria:

Proteinuria is an important parameter to diagnose Preeclampsia. In the present study, urine albumin was moderate in 42.8% of preeclampsia cases and severe in 51 % cases where as it was negative in all the control groups (normotensive group) and positive correlation is seen between the amount of proteinuria and severity of Preeclamsia. This difference is statistically significant. In the study conducted by Begum et al, over half of Preeclampsia cases had moderate proteinuria (53.4%), severe proteinuria in about 45.2% cases and nil in normotensive group.

Serum **β hCG levels:**

The normal placenta differentiates during the pregnancy with the predominance of cytotrophoblasts in early gestation and sycitiotrophoblasts in the later gestation.the cytotrophoblasts are the undifferentiated stem cells and the syncitiotrophoblats are differentiated from the cytotrophoblasts and produce hCG.[54]

The marker β hCG is secreted by syncitiotrophoblasts and β hCG production is seen to be increased when normal placental villi in the organ culture were maintained under hypoxic conditions.

Remzi et al, showed that early placentation abnormality and vascular damage leading to hypoxia which inturn results in increased serum levels of β hCG which is produced by the hyperplastic cytotrophoblastic cells. [55]

Few studies have been conducted to determine the relation between the maternal serum levels of β hCG levels and subsequent development of Preeclampsia and the results showed significant relation between the elevated serum levels of β hCG and development of Preeclampsia.

In the study conducted by Begum et.al, in during third trimester mean serum β hCG levels in Preeclampsia cases is 45,439.6 mIU/ml and 4937 mIU/ml in normotensive group with mean of 47576.6 mIU/ml in Severe Preeclampsia women and 43334.9 in mild Preeclmapsia women which is statistically significant($p < 0.001$).

In Choudary et al, reported mean serum β hCG level in normotensive group is 8,391 mIU/ml and 18,087 mIU/ml in women with Preeclampsia.

In the study of Mohammad et.al., mean serum β hCG level in nornmotensive pregnancy is 16,708.67 mIU/ml , 22,504.67 mIU/ml in women with mild Preeclampsia and 29,306 in women with Severe Preeclampsia.

β hCG levels in mIU/ml

Authors	**Year**	Normotensive	Mild/Non severe Preeclampsia	Severe Preeclampsia
Mohammed et al,[12]	2011	16708.67	22504.67	29306
Begum et al,[17]	2014	4937	43334.9	47576.6
Present study	2018	13366.77	24226.43	47915.82

All the above studies showed predominant difference in β hCG levels between normotensive pregnant women and Preeclampsia cases was statistically significant.

In this present study mean serum β hCG levels in normotensive group(n=42) is 13366.77mIU/ml and Preeclampsia cases(n=42) is 37199.19mIU/ml. Among 19 cases of non Severe Preeclampsia(n=19) mean serum β hCG value in is 24,226.43mIU/ml and 47915.82mIU/ml among 23 Severe Preeclampsia cases. The difference is statistically significant ($p < 0.0001$).

The serum β hCG levels are higher in severe Preeclampsia group when compared to non severe Preeclampsia and normotensive group and β hCG levels more in Non severe Preeclmapsia cases than the control group.

Besides, it is also observed that serum β hCG levels are higher in Preterm Preeclampsia cases with mean value of 44468.4 mIU/ml in pre term cases and 20115.4 mIU/ml in Term Preeclampsia cases .This difference is statistically significant.

In this study out of 42 Preeclampsia cases 4 of the developed Eclampsia later after admission the mean value of β hCG levels in the Eclampsia cases is 58814.92mIU/ml.

In this study results show that the serum β hCG levels are increased in Preeclampsia cases and its levels indicate the severity of Preeclampsia. The serum β hCG levels are also high in Early onset Preeclampsia < 34 weeks of geastation (mean value 51651.7 mIU/ml) and Pre term Preeclampsia cases (44468.4 mIU/ml) and the difference is statistically significant.

The sensitivity of the study in detecting Severity of the Preeclamspia is 86.96%.

Thus serum β hCG level can be used as a indicator of Preecalmpsia and its Severity.

Limitations of the study

Sample size adopted for the study was found to be less and also β hCG levels are not measured in the first and second trimesters to understand the basal values of β hCG to diagnose Preeclampsia.

Summary

SUMMARY

This study is done to measure the of β hCG levels by Chemiluminiscent method (CLIA) in Normotensive pregnancies and Preeclmapsia cases.

84 pregnant women between 32 -42 weeks of gestation with singleton pregnancy irrespective of parity are selected randomly as the study population with 42 normal pregnancy and 42 cases with preeclampsia out of which 23 were Severe Preeclampsia cases and 19 were Non severe Preeclampsia .

- At the time of admission the blood pressure was measured and detailed history is taken for any maternal symptoms along with laboratory investigations are done for urine proteinuria levels, serum creatinine, Liver function tests.
- Age and BMI of the cases and control groups were similar.
- The mean age for cases i.e., preeclampsia group and control group were 24.36 years and 24.05 years respectively.
- Systolic and Diastolic Blood Pressure at the time of admission between the normotensive group, Non severe Preeclampsia and severe Preeclamsia group was statistically significant.
- Mode of delivery was not statistically significant between the cases and controls, as both the groups had significant number of vaginal and caesarean deliveries.
- Preeclampsia group had Abnormal perinatal outcome in 28.57% out of which 16% belong to Severe Preeclampsia cases where as only 1% cases had abnormal Perinatal outcome in normotensive cases.
- The mean serum β hCG levels in normotensive group was 12799.11mIU/ml where as mean value Preeclampsia group was 37199.19mIU/ml. The difference in the mean

β hCG levels was statically significant.

- The mean β hCG level among Preeclampsia cases in the primi gravida women was 38131.25mIUml where as mean value in Multigravida women was 36351.86mIUml which is not statistically significant.
- The maternal serum β hCG levels were higher in patients with Preeclampsia in Pre term gestation with mean β hCG level of 51539.48mIU/ml against mean value of 30770.78 mIU/ml in Preeclampsia during term gestation
- Out of 42 cases of Preeclampsia 4 women developed Eclampsia after admission and the mean value of β hCG in these patients is 58814.91mIU/ml.
- The mean β hCG level was higher in cases with Severe Preeclampsia (47915.82mIU/ml) when compared to Non severe Preeclampsia cases (24226.43mIU/ml) and Normotensive pregnancies (12799.11 mIU/ml) which is statistically significant showing that β hCG is a good diagnostic marker with a sensitivity of 86.96% to diagnose Severe preeclampsia cases.
- There were no maternal deaths in both cases and the control groups.

Conclusion

CONCLUSION

- Preeclampsia and its sequelae are the most common complications of pregnancy. Hence, establishment of a good marker for the diagnosis of Preeclampsia along with prediction of its severity is the need of the hour.
- The present study indicates, that the elevated levels of serum β hCG levels can be used as a diagnostic marker for Preeclampsia and to predict its severity during third trimester of pregnancy .However, combining serum β hCG levels with other serum markers and Ultrasound parameters like Doppler study, will further strengthen its role as a the diagnostic tool.

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Annexures

CASE PROFORMA

NAME: IP NO:

AGE: DOA:

OCCUPATION: DOD:

ADDRESS:

EDUCATION:

HUSBANDS OCCUPATION:

SOCIOECONOMIC STATUS:

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

OBSTETRIC HISTORY:

Marital life: Consanguinity:

Gravida: Para: living: Abortion: Dead:

Details of previous pregnancy:

Details of present pregnancy:

MENSTRUAL HISTORY:

Last menstrual period: Age of menarche:

Expected delivery date:

Period of gestation:

Period of gestation according to early scan:

Past menstrual cycles:

PAST HISTORY:

HTN/DM/BA/TB/BLOOD DYSCRASIAS/EPILEPSY/THYROID

DISORDER/CARDIAC DISEASE/ALLERGY

H/O blood transfusions:

H/O Surgeries or hospitalization:

PERSONAL HISTORY:

Sleep and appetite:

Diet:

Bowel and bladder:

FAMILY HISTORY:

DRUG HISTORY:

GENERAL EXAMINATION:

General condition: Fair/ moderate/ Poor

Built: Nourishment:

Ht: cms Wt: kgs BMI:

Pallor: Icterus:

Cyanosis: Clubbing:

Lymphadenopathy: Edema:

VITALS:

Pulse rate:

Respiratory rate:

Blood pressure

Temperature:

SYSTEMIC EXAMINATION:

Cardiovascular system:

Respiratory system:

Central nervous system:

Per abdomen: Uterus size:

Relaxed / Irritable / Acting

Presentation: cephalic/ Breech/ other

FHS:

LOCAL EXAMINATION:

Per vaginum: Effacement:

Dilatation:

Station:

Membranes:

Pelvis:

PROVISIONAL DIAGNOSIS:

INVESTIGATIONS:

Blood group and Rh typing:

CBC: HB: HIV:

PCV: HbsAG:

RBC: VDRL:

WBC:

PLT:

RBS:

Urine analysis: Albumin-

Sugar-

Microscopy-

Liver Function tests-

Renal function tests-

Uric acid-

OBSTETRICS SCAN:

DELIVERY DETAILS:

Mode of delivery: Vaginal delivery/ Caesarean section

CAESAREAN-

Indication:

DETAILS OF NEONATE:

Sex: Date: Time:

Birth weight:

APGAR : 1'- 5'-

Admission to NICU:

MATERNAL COMPLICATIONS:

Hypertension

Convulsions

Premature rupture of membranes

Ante partum hemorrhage

Postpartum hemorrhage

Uterine hyperstimulation

FETAL COMPLICATIONS:

Respiratory distress

Admission to NICU

CONDITION AT DISCHARGE:

Mother:

Baby:

PATIENT INFORMATION SHEET

Study title: EVALUATION OF HUMAN BETA CHORIONIC GONADOTROPIN LEVELS IN PREECLAMPSIA-A CASE CONTROLSTUDY

Study location: R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar.

Patients who are of clinically proven preeclampsia cases admitted to OBG department of R L Jalappa hospital attached to Sri Devaraj Urs medical college are recruited in the study after obtaining patient information consent.

Similarly, the normotensive pregnant women at third trimester visiting OBG department will also be included in the study after obtaining the patient information consent.

4 ml of venous blood is collected from the study subjects for serum Beta hCG levels estimation

Details-

Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or from a person

responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For further information contact

Dr. Kosinepalli Charishma

Post graduate, Department of obstetrics and Gynaecology

R L Jalappa hospital, Kolar .Phone no: 9740674052.

SRI DEVARAJ URS MEDICAL COLLEGE & RESEARCH CENTRE,

TAMAKA, KOLAR

PATIENT CONSENT FORM

Case no:

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I have understood that I have the right to refuse consent or withdraw it at any time during the study and this will not affect my treatment in any way. I consent voluntarily to participate in this study

"EVALUATION OF BETA HUMAN CHORIONIC GONADOTROPIN HORMONE LEVELS IN PRE ECCLAMPSIA- A CASE CONTROL STUDY."

Name of Participant_____

Signature/ thumb print of Participant _____
Date _____

Statement by the researcher/person taking consent:

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

4 ml venous blood sample taken for serum β hCG levels estimation.

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

Name of Researcher/person taking the consent_____

Signature of Researcher /person taking the consent_____

Date _____

Name and Address of Principal Investigator: Dr.kosinepalli charishma.
R.L Jalappa Hospital
Tamaka, Kolar.

ತಿಳುವಳಿಕೆಯ ಒಪ್ಪಿಗೆ ಪತ್ರ

ಅಧ್ಯಯನ ಶೀರ್ಷಿಕೆ:– **“EVALUATION OF BETA HUMAN CHORIO GONADOTROPIN LEVELS IN PRE ECCLAMPSIA- A CASE CONTROL STUDY”**

ಶ್ರೀ/ಶ್ರೀಮತಿ ಆದ ನಾನು ಈ ಮೇಲಿನ ಸಂಶೋಧನ ವಿಷಯದ ಬಗ್ಗೆ ನನಗೆ ಅರ್ಥವಾಗುವ ರೀತಿಯಲ್ಲಿ ನನ್ನದೇ ಭಾಷೆಯಲ್ಲಿ ತಿಳಿಸಿರುತ್ತಾರೆ. ಈ ಸಂಶೋಧನಾ ವಿಷಯದಲ್ಲಿ ನಾನು ಒಬ್ಬ ವಿಷಯಿಯಾಗಿ ಭಾಗವಹಿಸಲು ನನ್ನ ಸಂಪೂರ್ಣವಾಗಿ ಒಪ್ಪಿಗೆ ಇರುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ಉದ್ದೇಶವನ್ನು ಪೂರ್ಣವಾಗಿ ಅರಿತಿರುತ್ತೇನೆ. ಈ ಸಂಶೋಧನೆಗೆ ನನ್ನಿಂದ ಯಾವುದೇ ಆರ್ಥಿಕತೆಯ ಅವಶ್ಯಕತೆ ಇರುವುದಿಲ್ಲ. ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನನ್ನ ಸಹಕಾರವನ್ನು ಹಿಂಪಡೆದು ಈ ಸಂಶೋಧನೆಯಿಂದ ಹೊರಹೋಗುವ ಹಕ್ಕನ್ನು ಹೊಂದಿರುತ್ತೇನೆ. ಇದರಿಂದ ನನ್ನ ಚಿಕಿತ್ಸೆಗೆ ಯಾವುದೇ ರೀತಿಯ ತೊಂದರೆಯಾಗುವುದಿಲ್ಲ. ಮುಖ್ಯವಾಗಿ ನನ್ನಿಂದ ಪಡೆದ ಈ ಮಾಹಿತಿಯು ಸಂಶೋಧನೆಗೆ ಮಾತ್ರ ಸೀಮಿತವಾಗಿರುತ್ತದೆ. ಮತ್ತು ಈ ಮಾಹಿತಿಯು ಎಲ್ಲೂ ಸೋರಿಕೆಯಾಗದಂತೆ ಎಚ್ಚರಿಕೆ ವಹಿಸುವುದಾಗಿ ತಿಳಿವಳಿಕೆ ನೀಡಿರುತ್ತಾರೆಂದು ನಾನು ದೃಢಪಡಿಸಿಕೊಂಡು ಒಪ್ಪಿಗೆ ನೀಡಿರುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ/ ಸಾಕ್ಷಿ ಸಹಿ. ಸಂಶೋದಕನ ಸಹಿ

ಬೆರಳಚ್ಚು.

KEY TO MASTER CHART

- **AGE**

  1.20-25 years

  2.26-30 years

- Socio economic status (Modified B G Prasad Classification)

  1. Class-I

  2. Class –II

  3. class-III

  4. class-IV

  5. class-V

- Gravida

  1. Primigravida

  2. G2

  3. G3

  4. G4

- Parity

  1. P1

  2. P2

  3. P3

- Gestation in weeks

  1. Early preterm (32-34 weeks)

  2. Late preterm (34+1 to 37 weeks)

  3.37-40 weeks

  4.40-42 weeks

- Systolic Blood pressure

- Diastolic Blood Pressure

- Urine Albumin

  0-Nil

  1-+

  2-++

  3-+++

  4-++++

- Serum β hCG levels

- Mode of delivery

  C-caesarean delivery

  V-vaginal delivery

- Time of delivery

  T-Term

  PT-Pre term

- Peri natal outcome

  NPO –Normal perinatal outcome

  APO – Abnormal perinatal outcome

- Ecclampsia

  0-No

  1-yes

S.NO	NAME	AGE	H.NO	SOCIOECONOMIC STATUS	GRAVIDA	PARITY	GESTATION	SBP(mm Hg)	DBP (mm Hg)	URINE ALBUMIN	SERUM B HCG mIU/ML	MODE OF DELIVERY	TIME OF DELIVERY	PERINATAL OUTCOME	ECLAMPSIA
1	Veena	1	562778	4	2	1	3	120	70	0	15526.9	C	T	NPO	0
2	ANJUM	1	573205	5	3	2	3	120	80	0	17417.4	C	T	NPO	0
3	DHARINI	1	567221	3	1	0	4	106	70	0	10687.1	C	T	NPO	0
4	RUMAIZA	1	570720	4	1	0	2	110	70	0	18480.3	C	PT	NPO	0
5	KAVERI	1	572370	5	1	0	2	130	90	0	10580.4	C	PT	NPO	0
6	VEDAVATHI	1	572485	4	2	1	4	126	80	0	9805.3	V	T	NPO	0
7	RUKSAR	1	564864	3	3	1	3	110	70	0	13611.9	C	T	NPO	0
8	CHAITHRA	1	572378	4	2	1	3	130	80	0	10675.5	C	T	NPO	0
9	ASHWINI	1	573197	5	1	0	4	126	70	0	13662.2	V	T	NPO	0
10	UMRAJ	2	574126	4	3	2	3	124	70	0	18480.3	V	T	NPO	0
11	MAHALAKSHMI	2	574707	4	3	1	2	108	60	0	18532.5	C	T	NPO	0
12	NEELOFUR	2	542095	4	1	0	4	116	70	0	9724.8	V	T	NPO	0
13	ASHWINI	1	575680	5	1	0	3	110	80	0	6575	C	T	NPO	0
14	KANAKA	2	576127	5	2	0	4	112	70	0	12678.6	V	T	NPO	0
15	YAMUNA	2	565819	3	2	1	3	120	80	0	9646.2	C	T	NPO	0
16	SAHANA	2	560783	4	2	1	3	130	80	0	13248.3	C	T	NPO	0
17	NAJMA TAJ	1	565313	5	2	1	3	126	84	0	16241.8	C	T	NPO	0
18	MAMATHA	1	579772	4	2	1	3	112	76	0	11287.4	C	T	NPO	0
19	SUSHMA	1	562543	3	1	0	3	120	70	0	13246.1	C	T	NPO	0
20	JYOTHI	2	577999	4	4	3	2	116	70	0	15553.7	C	T	NPO	0
21	SULTHANA	1	587345	4	2	1	3	110	70	0	10631	V	T	NPO	0
22	NIRUPAMA	1	513633	4	3	1	4	120	80	0	12321.7	C	T	NPO	0
23	MADHAVI	1	587721	5	1	0	3	106	70	0	13261	V	T	NPO	0
24	ASHWINI	1	587242	4	2	0	3	124	70	0	9456.3	V	T	NPO	0
25	VANITHA	1	533755	3	3	2	4	130	80	0	16893.5	V	T	NPO	0
26	LAVANYA	1	588167	3	2	0	4	124	80	0	10538	V	T	NPO	0

27	ARCHANA	2	513104	4	1	0	3	120	70	0	11742.9	V	T	NPO	0
28	MOUNIKA	1	589244	5	2	1	3	116	80	0	16529.1	V	T	NPO	0
29	MUHEERA	1	590581	4	1	0	2	110	70	0	15487.9	C	PT	NPO	0
30	RANJITHA	1	525857	5	2	1	3	120	70	0	18532.5	V	T	NPO	0
31	NETHRAVATHI	2	573935	3	1	0	3	110	74	0	13562	V	T	NPO	0
32	VEENA	1	567821	4	2	1	3	110	80	0	19644.9	C	T	NPO	0
33	SAMEENA	1	596739	4	2	1	2	110	80	0	16894.2	C	PT	NPO	0
34	ANJALI	1	596650	4	1	0	2	130	80	0	14567.3	C	PT	NPO	0
35	LAKSHMI	1	598499	4	1	0	2	120	70	0	13999	V	PT	NPO	0
36	SRIMATHI	1	598929	5	2	1	2	126	70	0	10898.4	C	PT	**APO**	0
37	PADMAVATHI	1	596867	3	1	0	3	100	60	0	8789.9	C	T	NPO	0
38	AMARAVATHI	1	576541	4	3	1	2	120	70	0	10978.3	V	PT	NPO	0
39	MEENA	2	598742	5	1	0	3	116	70	0	11231	C	T	NPO	0
40	SINDHU	1	566110	4	2	1	3	110	80	0	13891.8	C	T	NPO	0
41	SUSHMA	1	594614	3	1	0	3	120	80	0	13562.1	C	T	NPO	0
42	SWAPNA	1	600116	4	2	1	3	130	70	0	12329.9	V	T	NPO	0

S.NO	NAME	AGE	H.NO	socio economic status	GRAVIDA	PARITY	GESTATION	SBP(mm Hg)	DBP(mm Hg)	URINE ALBUMIN	pre eclampsia	SERUM B hCG mIU/ml	Mode of delivery	TIME OF DELIBVERY	PERINATAL OUTCOME	Ecclampsia
1	RAMYA	2	571156	4	1	0	1	160	110	3	2	62603	V	PT	APO	0
2	HASEENA KHANUM	2	571882	4	1	0	2	170	110	3	2	44746	V	PT	APO	0
3	ASHA	1	533629	5	1	0	4	140	100	2	1	19793.8	C	T	NPO	0
4	SOWMYA	2	571997	4	4	0	3	160	100	3	2	44890.4	C	T	NPO	0
5	JYOTHI	1	573911	3	1	0	4	190	120	4	2	74840.5	C	T	APO	1
6	GOWRAMMA	2	573113	4	1	0	3	160	90	2	2	25409	C	T	APO	0
7	RADHA	2	574603	3	2	1	2	160	110	3	2	54869.2	C	PT	NPO	0
8	BHARGAVI	1	574962	5	2	0	3	150	110	3	2	46793.9	C	T	NPO	0
9	ANUPREMA	2	575749	4	3	0	3	170	100	2	2	50179.9	V	T	NPO	0
10	SUSHMITHA	1	567457	4	1	0	3	140	110	3	2	56316.4	C	T	NPO	0
11	SHILPA	2	576776	3	3	2	2	190	120	4	2	47146.1	C	PT	APO	0
12	SUJATHA	2	577328	3	3	2	3	140	90	2	1	27632.5	V	T	NPO	0
13	SOORA SULTHANA	2	571005	5	1	0	3	170	110	3	2	20336.9	V	T	APO	0
14	RAMYA	2	571156	4	1	0	1	150	100	1	1	43635.9	V	PT	NPO	0
15	NAGAVENI	1	579789	5	1	0	3	140	100	2	1	24188.2	V	T	NPO	0
16	CHAITHRA	1	522585	3	4	1	2	150	90	1	1	32344.4	V	PT	APO	0
17	KANAKA	2	565773	4	3	1	1	170	110	4	2	50523.6	V	PT	APO	1
18	SUMAVATHI	2	566552	4	2	1	3	150	90	0	1	22353	C	T	NPO	0
19	NAJMA	1	567637	4	1	0	4	160	100	3	2	36124.3	C	T	NPO	0
20	TABASUM	2	588202	5	2	0	3	150	90	1	1	29331.6	C	T	NPO	0
21	SHALINI	1	588657	4	3	2	1	160	110	3	2	51625.3	C	PT	APO	0
22	RAMYA	2	585252	5	2	1	2	170	100	3	2	61256.2	V	PT	APO	0
23	NAGMA KOUSER	1	589128	4	3	2	1	200	120	4	2	59841.3	V	PT	APO	0
24	BIBI FATHIMA	1	590218	3	2	0	3	140	100	1	1	26414.5	C	T	NPO	0
25	RUKMANI	2	561678	4	1	0	2	160	100	3	2	56741.7	C	PT	NPO	0
26	SHWETA	1	592579	5	1	0	3	170	110	3	2	42001.5	C	T	NPO	1
27	SABIHA	2	593100	4	3	2	2	140	100	2	1	27355.1	C	T	NPO	0
28	MUNI RATHNA	1	594102	4	1	0	3	160	110	3	2	39787	C	T	NPO	0
29	MOUNIKA	1	595324	4	2	1	3	140	100	1	1	29432.2	V	T	NPO	0
30	ASMA	1	596201	3	1	0	2	180	110	4	2	67894.1	C	PT	APO	1
31	SHABANA TAJ	2	600108	5	2	1	3	160	100	3	2	25676.9	C	T	NPO	0
32	LAKSHMI	1	465692	4	3	2	2	190	110	3	2	36786.4	C	PT	NPO	0
33	POORNIMA	1	595628	5	1	0	4	150	90	1	1	24567.1	C	T	NPO	0
34	CHANDRAKALA	1	596232	4	2	1	3	149	100	0	1	19806	C	T	NPO	0
35	AMRUTHA	1	598483	4	1	0	3	140	100	1	1	20198	V	T	NPO	0
36	SHILPA	1	598154	4	1	0	3	160	110	3	2	45674.2	C	T	NPO	0

37	VISHNUPRIYA	1	598069	5	1	0	3	150	90	1	1	17688	C	T	NPO	0
38	SWAPNA	1	600116	4	2	1	3	140	100	1	1	18812.1	V	T	NPO	0
39	SUPRIYA	1	599864	4	1	0	4	160	90	0	1	20191.1	C	T	NPO	0
40	SUSHMA	2	599605	5	1	0	3	150	100	1	1	19888.3	C	T	NPO	0
41	VINODHA	2	521358	4	2	1	3	160	90	2	1	18783.3	C	T	NPO	0
42	SHYAMALA	1	601391	5	2	1	3	150	100	1	1	17887	C	T	NPO	0