“A STUDY OF MATERNAL THYROID HORMONE STATUS AND LIPID PROFILE IN PRE ECLAMPSIA”

BY

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APRIL- 2014

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Dr. Aparna A. Patil

LIST OF ABBREVIATIONS

S.NO	Abbreviation	Full form
1.	TSH	Thyroid Stimulating Hormone
2.	LDL	Low Density Lipoprotein
3.	HDL	High Density Lipoprotein
4.	VEGF	Vascular Endothelial Growth Factor
5.	LPL	Lipoprotein Lipase
6.	TG	Triglyceride
7.	VLDL	Very Low Density Lipoprotein
8.	VCAM-1	Vascular Cell Adhesion Molecule-1
9.	TC	Total Cholesterol
10.	GH	Gestational Hypertension
11.	BP	Blood Pressure
12.	SBP	Systolic Blood Pressure
13	DBP	Diastolic Blood Pressure
14	HLA-G	Human Leukocyte Antigen G
15	TNF	Tumour Necrosis Factor

S.NO	Abbreviation	Full form
16.	IL	Interleukins
17.	TXA2	Thromboxane A2
18.	PGI2	Prostaglandin I2
19.	PGF	Placental Growth Factor
20.	TGF	Transforming Growth Factor
21.	TPO	Thyro-peroxidase
22	MIT	Monoiodotyrosine
23	DIT	Diiodotyrosine
24	TBPA	thyroxin binding pre albumin
25	BMR	Basal Metabolic Rate
26	HPTA	Hypothalamic-Pituitary-Thyroid Axis
27	TRH	Thyrotropin releasing hormone
28	DBP	Diastolic Blood Pressure
29	TBG	Thyroxine binding globulin
30	hCG	Human chorionic Gonodotropin

S.NO	Abbreviation	Full form
31	IQ	Intelligent Quotient
32	FFA	Free Fatty Acids
33	HSL	Hormone-sensitive Lipase
34	CLIA	Chemi-luminescence Immunoassay
35	BMI	Body Mass Index
36	SGA	Small for Gestation age

ABSTRACT

Objective

To evaluate the thyroid hormone levels and lipid profile in normotensive pregnant women and in women with preeclampsia and to compare and correlate the thyroid hormone levels and lipid profile between the two groups.

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Study design

A prospective study conducted in the Department of Obstetrics and Gynecology at R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar, from January 2012 to June 2013.

Materials and methods

The present study was carried out in 100 pregnant women of whom 50 were Preeclampsia Cases and 50 were Normotensive pregnant women (control).The subjects in the two groups were age and gestation matched. Informed consent was obtained from all the subjects and the study was approved by the ethical committee of the institute. A standard Proforma was used to collect the data. 10 ml of fasting sample was obtained and T3, T4 and TSH was estimated by CLIA and lipid profile was estimated by dry chemistry using VITROS 250 Analyser.

Results

Majority of the patients selected were between the age group of 21-25 years in both the groups. Pre eclampsia was more common among primigravida. Most of the patients were in the gestational age group of 38-40 wks in the study population. The mean SBP in the normotensive group was 115.20±7.62 and in pre eclampsia group was 156.20±16.02. The mean DBP in the normotensive group was 73.80±4.90 and in Pre-eclampsia Group was 103.00±11.47. Among the pre-eclampsia group 52% were severely pre eclamptic while 48% were mild pre eclamptic. The mean BMI was significantly higher in Pre-eclampsia group with ($p<0.005$).

The mean TSH value was significantly higher and the mean T3 and T4 values were significantly lower in the pre eclampsia group as compared to normotensive group. (p

value <0.001) however there was no significant difference between mild and severe pre eclampsia group. The mean Total cholesterol and Triglyceride levels were significantly elevated in the pre eclampsia group as compared to the normotensive group.(P value <0.001) while the mean HDL and LDL values were comparable in the two groups.

Conclusion

The conclusion of the present study is that pre eclampsia patients have a significantly higher levels of TSH and low levels of T3 and T4 in comparison to normotensive pregnant women. However, the changes in the thyroid hormones did not correlate with the severity of pre eclampsia, since there was no statistical significance observed between mild and severe pre eclampsia groups. Dyslipidemia is more pronounced and found statistically significant in pre eclampsia group than in the normotensive group. The serum levels of lipid parameters between these groups evincing possible atherogenic potential.

Key words: thyroid profile, lipid profile, pre eclampsia

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INTRODUCTION

Hypertensive disorders of pregnancy continue to be one of the major causes of maternal and fetal morbidity and mortality. It occurs in 5-7 % of the pregnancies worldwide.[1]The incidence is still higher in India of around 8-10%.[2]As per the World Health Report (WHO 2005) the maternal mortality during pregnancy and puerperium is around 12 %. In developing countries, 17% of direct obstetric deaths are as a result of hypertension.

Preeclampsia is a clinical condition characterized by hypertension and proteinuria. It is a multisystem disorder affecting nearly every organ and system in the human body. Different studies clearly show that the utero-placental blood flow, vascular resistance, endothelial integrity, endothelial damage, the platelets, coagulation system and neutrophils all interact in preeclampsia.

It is likely that unless more is known about the dynamics of utero-placental blood flow and its influence on the vascular endothelium, confusion and inconsistency will continue. It is therefore, understandable why this condition is sometimes referred to as "the disease of theories"

Preeclampsia more commonly occurs in first pregnancies than subsequent pregnancies with the mother's blood pressure returning to normal after delivery. Potential causes and mechanisms behind preeclampsia remain unknown, but maternal immune, genetic factors and placenta have been implicated.

Pregnancy is associated with significant, but reversible changes in thyroid function. Sufficient provision of thyroid hormone during pregnancy is essential for normal fetal brain development.[3] There is enhanced transplacental uptake of iodine and increased maternal renal clearance during pregnancy. This relative iodine

deficiency is compensated by increasing iodine uptake and synthesis of thyroid hormones.[4]

Pre-eclamptic women have high incidence of hypothyroidism that might correlate with severity of preeclampsia. Elevated TSH values are associated with increased rate of fetal death – adds another reason that routine TSH screening should be offered as a way to improve pregnancy outcome and maternal wellbeing.[5]

Women with preeclampsia also have an increased risk of dyslipidemia, cardiovascular and renal disease.[6] There is alteration in the lipid metabolism with increased concentration of Triglycerides, Total Cholesterol, LDL-cholesterol and decreased concentration of HDL-cholesterol, which in turn results in atherogenesis.[7] Wakatsuki et al. suggested that oxidized LDL-cholesterol particles might be involved in vascular endothelial damage in preeclampsia.[8]

The present study is taken up to assess whether thyroid function and lipid profile are impaired in women with Pre eclampsia.

AIMS AND OBJECTIVES

1. To evaluate the thyroid hormone levels in normotensive pregnant women and in women with preeclampsia.

2. To assess the lipid profile in normotensive pregnant women and in women with preeclampsia.

3. To compare and correlate the thyroid hormone levels and lipid profile between the normotensive pregnant women and in preeclampsia cases.

REVIEW OF LITERATURE

HISTORY

The occurrence of fits in pregnant women has been documented as early as 4th Century B.C. by Hippocrates, hence the condition termed ECLAMPSIA, a Greek word which literally means "shine forth'' due to the visual phenomenon accompanying the condition.[9] It was also recognized that hypertension and proteinuria herald the onset of fits in these pregnant women and as such the term PRE-ECLAMPSIA was devised.

Utero-placental ischemia and infarction leading to reduction in maternal utero-placental blood flow leading to hypertension and proteinuria through utero-renal reflex all have been implicated in preeclampsia. Later, with the advancement of science, the importance was laid more on genetic, hematological, biochemical, hormonal and immunological factors.

Recently, some studies have related vitamin and calcium dysregulation with preeclampsia.[10]Hypo-proteinemia and vitamin deficiency have also been implicated in the etiology of this condition.

Wilson *et al* (1992) suggested that activation of the coagulation system and the hematological changes are secondary effect consequent to the primary vascular or endothelial damage.[11]Others have revealed a decrease in spontaneous lymphocytic transformation. Endothelin-1 gene expression is increased in placental villous tissue of pre-eclamptics that contributes to placental vasoconstriction and vascular insufficiency.

THYROID FUNCTION IN PRE ECLAMPSIA

Although physiological changes in the thyroid function during pregnancy are well documented, not many studies address the thyroid function disturbances in pre eclampsia and their effects on the fetus supporting the view that pre-eclamptic women have increased incidence of hypothyroidism that might correlate with the severity of pre-eclampsia.[12, 13]

Clinical identification of hypothyroidism is difficult during pregnancy because many of the signs and symptoms are common to pregnancy itself. Overt hypothyroidism complicates from 2 to 3 pregnancies per thousand.[14]

The incidence of subclinical hypothyroidism in women between 18 and 45 years of age is about five percent. Subclinical hypothyroidism is associated with the occurrence of pre eclampsia. There is also significant risk of perinatal mortality in women with subclinical hypothyroidism.[15]

There are controversies about the mechanism and the clinical significance of low concentration of thyroid hormones in pre-eclampsia, which are attributed to decreased plasma protein concentration.[16]

The levels of T_3 and T_4 are more during pregnancy when compared to non-pregnant women.[17,18] The etiology of increase in circulating thyroid hormones primarily involves increased concentrations of plasma thyroxine binding globulin during pregnancy. Increased sialylation, mediated by estrogens, reduces the hepatic clearance of thyroxine binding globulin, resulting in increased levels of thyroid hormones.[19]

Women with low serum free-T4(fT4) values but a normal range of TSH level are considered to have isolated maternal hypothyroxinemia. It has no apparent serious adverse effects on pregnancy outcome and may simply be a biochemical finding. Because of this, routine screening for isolated hypothyroxinemia is not recommended.[20]

In a study, comprising of 82 pregnant women including both normal pregnant women and those with thyroid disease, showed that potential and inadequately treated hypothyroid patients presented with problems in pregnancy, while adequately treated hypothyroid and euthyroid women had normal ongoing pregnancy.[21]

Overt hypothyroids are prone to have pre eclampsia, intrauterine growth restriction and intra uterine fetal demise .[22] In 1998, A study was done by Leung et al and reported that, pregnancy induced hypertension was significantly more in overt and subclinical hypothyroidism patients than in the general population with rates of 22.15 and 7.6% respectively.[23]

In an animal model it was reported that nitric oxide - a vasodilator released from vascular endothelium regulates secretion of thyroid hormones by modulating regional blood flow or activating follicular cells in the gland, and its release is impaired in rats with hypothyroidism.[24]

Vascular Endothelial Growth Factor [VEGF] a potent mitogen for in vitro endothelial cells was shown to increase the permeability of vascular endothelium. In vivo, it is reported to stimulate neo-angiogenesis. Immunohistochemical studies showed that progression of goiter was accompanied by increased capillary endothelial

cell growth.[25]

Women who develop preeclampsia early in their pregnancies had thyroid function identical to that of the normal pregnant women. But, women with preeclampsia towards the end of their pregnancies had much higher levels of TSH than women with no history of preeclampsia. Moreover, the increase in TSH was strongly associated with an increase in blood levels of sFLT-1.

The rise in TSH level in women who had preeclampsia in their first pregnancy was 1.7 times higher compared to the women who did not have preeclampsia. Similarly, Women who had preeclampsia in both their first and second pregnancies had nearly six times higher levels of TSH.

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LIPID METABOLISM IN PRE-ECLAMPSIA

In Pre eclampsia, the hyperlipidemia of normal pregnancy is exaggerated further through greater synthesis and lower peripheral catabolism. Although, direct evidence for impairment of peripheral catabolism is lacking, there is a suggestion of common mutations in the Lipoprotein Lipase [LPL] gene in women with pre eclampsia. These mutations are associated with a reduction in LPL activity and dyslipidemia in the non-pregnant state.[26]

It has long been recognized that maternal hypertriglyceridaemia is significantly higher among pre-eclamptic women than normal controls. [27, 28]There are some important qualitative changes in lipid composition as a consequence of high plasma TG levels. There is an almost three fold higher VLDL1 and two fold higher VLDL2 concentration in preeclampsia than in healthy pregnant women. Total LDL concentrations are also elevated three times in preeclampsia women than the normal pregnancy.[29, 30]

It has been established in Preeclampsia that the atherogenecity occurred due to dyslipidemia resulting in endothelial damage through oxidative stress and further to cardiovascular disease. LDL particles under the condition of prevailing oxidative stress undergo oxidation in to oxidized LDL particles that are known to be highly atherogenic in nature and promote endothelial dysfunction and cardio vascular risk in preeclampsia. Soluble Vascular Cell Adhesion Molecule-1 (VCAM-1) a marker of vascular dysfunction is elevated in pre eclampsia that also correlates with LDL cholesterol.[31]

Oxidized LDL but not native LDL inhibits trophoblastic cell invasion in a concentration dependent manner and this may be a further mechanism by which

dyslipidemia leads to impaired placentation and Pre eclampsia.[32] furthermore, there is a reduction in endothelial protective HDL cholesterol level.

In a recent study in 2010 serum lipid profile was measured between 14 and 20 weeks of gestation. Lipid profile was significantly impaired in those who developed pre eclampsia. This Study suggested that lipid profile are effective predictors of preeclampsia.[33]

Another study measured serum Triglycerides at 18 weeks of gestation and followed up, which showed Hypertriglyceridemia before 20 weeks of gestation is associated with risk of developing preeclampsia.[34]

It is showed that there was significant elevation of total cholesterol, triglycerides, LDL, VLDL and risk ratios TC/HDL and TGL/HDL and decrease in HDL in Pre-eclamptic group compared to normotensives. The dyslipidemic pattern of elevated TG and reduced HDL which was also reflected in highly elevated TGL/HDL seen in preeclamptic patients is definitely atherogenic and may lead to future maternal cardiovascular disease.[35]

HYPERTENSIVE DISORDERS IN PREGNANCY

The Working Group classification of hypertensive disorders in pregnancy describes four types of hypertensive diseases:

GESTATIONAL HYPERTENSION

Gestational Hypertension (GH) is defined as onset of hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) after 20 weeks of gestation in the absence of significant proteinuria and is generally characterized by good maternal and fetal outcomes. BP returns to normal before 12 weeks postpartum. If preeclampsia does not develop and hypertension resolves by 12 weeks postpartum, it is re-designated as transient hypertension.

PRE-ECLAMPSIA-ECLAMPSIA SYNDROME

Preeclampsia is an intriguing disease, whose etiology has remained obscure for centuries. Preeclampsia can be life-threatening for both mother and fetus, additionally it accounts for induction of labour and caesarean sections performed in many hospitals.

Preeclampsia is a multisystem disorder characterized by blood pressure of ≥140/90 mm of Hg noted for the first time during pregnancy on ≥2 occasions at least 6 hours apart, after 20 weeks of gestation with proteinuria of ≥300 mg/24 hours or ≥ 1+ by dipstick method in a random urine sample.

MINIMUM CRITERIA

1. BP ≥ 140/90 mmHg after 20 wks of gestation
2. Proteinuria ≥ 300mg/24 hrs or ≥ 1+ dipstick

INCREASED CERTAINTY OF PRE-ECLAMPSIA

- BP ≥ 160/110mmHg
- Proteinuria 2.0g/24hrs or ≥ 2+ dipstick
- Serum creatinine > 1.2mg/dl unless known to be previously elevated
- Platelets < 100,000/µL
- Micro- Angiopathic Hemolysis- increased LDH
- Elevated Serum Transaminase levels- ALT or AST
- Persistent headache or other cerebral or visual disturbances
- Persistent epigastric pain

ECLAMPSIA

Eclampsia is defined as seizures that cannot be attributed to other causes in a woman with pre-eclampsia. Eclamptic seizures are relatively rare and occur in less than 1 % of women with preeclampsia. Beck and Menezes established that 7% of deaths due to eclampsia were attributable to haemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome) a modification of severe hypertension that results in multi organ failure.

SUPERIMPOSED PRE-ECLAMPSIA ON CHRONIC HYPERTENSION

- New onset proteinuria ≥ 300mg /24 hrs in hypertensive woman but no proteinuria before 20 weeks gestation
- A sudden increase in proteinuria or blood pressure or platelet count < 100,000/µL in woman with hypertension and proteinuria before 20 weeks gestation

The incidence of superimposed preeclampsia in chronic hypertension ranges from 4.7 to 18.4% for mild hypertension (DBP >90 mmHg) up to 54% to 100% for severe hypertension (DBP >100 mmHg). Superimposed preeclampsia on chronic hypertension is associated with significantly increased risk of maternal and fetal death, fetal growth restriction, and placental abruption.

CHRONIC HYPERTENSION

- BP ≥ 140/90 mmHg before pregnancy or diagnosed before 20 weeks gestation not attributable to Gestational Trophoblastic Disease OR
- Hypertension first diagnosed after 20 weeks gestation and persistent after 12 weeks postpartum.

Chronic hypertension affects about 1-5 % of pregnant women. It is associated with increased risks of preeclampsia and abruption placentae, as well as increased neonatal mortality and morbidity. Most of them usually have a positive family history of hypertension as well as its complications, including congestive heart failure, coronary artery disease, stroke, and renal dysfunction.

RISK FACTORS FOR PRE-ECLAMPSIA

- Primigravida
- Extremes of reproductive age (young and elderly)
- Ethnicity: African –Americans
- Previous pre-eclampsia: is a strong predictor of recurrence. Risk is increased by 6 times.
- Family history: hypertension, pre-eclampsia, eclampsia
- Placental abnormalities: molar pregnancy, multiple gestation, placental ischemia
- Associated medical conditions
- New paternity: Man previously fathered pregnancy complicated by pre-eclampsia
- Thromboplilias: Anti-Phospholipid Antibody Syndrome, protein C,S deficiency, factor V Leiden mutation
- Genetic
- Immunological.

ETIOLOGY FOR DEVELOPMENT OF PRE ECLAMPSIA

I. Placental implantation with abnormal trophoblastic invasion of uterine vessels

II. Endothelial dysfunction

III. Immunological maladaptive tolerance between maternal, placental, and fetal tissues

IV. Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy

V. Genetic factors including inherited predisposing genes as well as epigenetic influences.

PATHOPHYSIOLOGY OF PRE ECLAMPSIA

a) ABNORMAL TROPHOBLASTIC INVASION

In the normal pregnancy the uterine spiral arterioles are invaded by endovascular trophoblasts. These cells replace the vascular endothelial and muscular lining to enlarge the vessel diameter. Virtually every spiral artery in the decidua basalis will have undergone these physiological changes by the end of first trimester.

Early in the second trimester, a second wave of cytotrophoblast invasion occurs and transforms the myometrial segments of the spiral arteries and occasionally the distal segment of radial arteries. This transforms the utero-placental arterial bed from a high pressure- low flow system into a low resistance- low pressure- high flow system. Loss of the endothelial and muscular layers renders these vessels unable to respond to vascular stimuli.

In pre-eclampsia, endovascular invasion is observed only in the decidual segments of the utero-placental arteries. Myometrial segment of the spiral arteries are left with their musculo-elastic wall thereby rendering them high resistance, low flow system. The second lesion in the spiral arteries is “acute atherosis” aggregates of fibrin , platelets and lipid laden macrophages which partially or completely block the arteries.

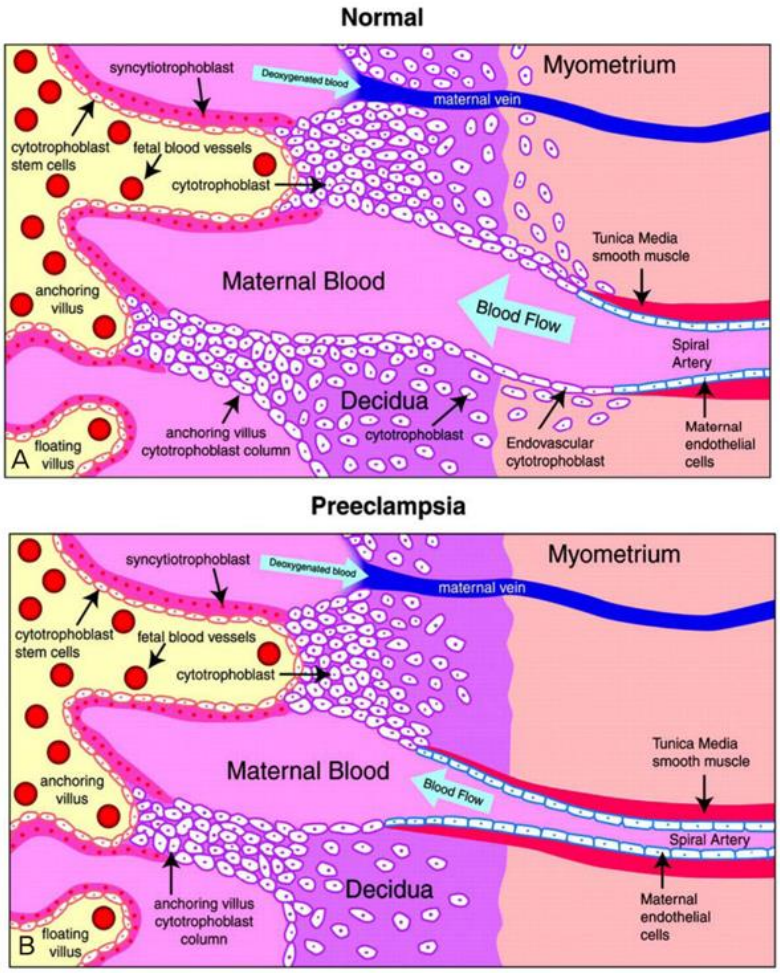


Fig 1: Depicting the Trobhoblastic invasion in normal pregnancy and Pre eclampsia

Source: *Obstet Gynecol Sci*. 2013 Jan; 56(1):2-7

b) IMMUNOLOGICAL FACTOR

Normally, there is maternal immune tolerance to paternally derived placental and fetal antigens. Loss of this tolerance, is another theory cited to account for pre-eclampsia. The histological changes at the maternal- placental interface are suggestive of 'acute graft rejection'.

Tolerance dysregulation might also explain an increased risk when the paternal antigenic load is increased, i.e. with 2 sets of paternal chromosomes- "double dose". Eg: women with molar pregnancies. Also woman with a trisomy 13 fetus have a 30- 40% incidence of pre-eclampsia.

Redman and colleagues (2009) reviewed the possible role of *immune maladaptation* in the pathophysiology of preeclampsia. Early in a pregnancy destined to be preeclamptic, extravillous trophoblast express reduced amounts of immunosuppressive human leukocyte antigen G (HLA-G). This may contribute to defective placental vascularization in early stages of pre eclampsia

c) ENDOTHELIAL CELL ACTIVATION

Endothelial cell dysfunction is due to an extremely activated state of leukocytes in the maternal circulation. The cytokines such as tumor necrosis factor (TNF) and the interleukins (IL) may contribute to the oxidative stress associated with pre eclampsia.

These in turn generate highly toxic radicals that injure endothelial cells, modify their nitric oxide production and interfere with prostaglandin balance. Other consequences of oxidative stress include production of the lipid-laden macrophage foam cells seen in atherosis. Activation of microvascular coagulation manifested by thrombocytopenia; and increased capillary permeability manifested by edema and proteinuria.

d) **GENETIC FACTORS**

Pre-eclampsia is a multifactorial, polygenic disorder. Ward and Lindheimer cited an incident risk for pre-eclampsia of 20-40% for daughters of pre-eclamptic mothers; 11-37% for sisters of pre-eclamptic women; 22-47% in twin studies.

There is an extensive list of other variables that affect genotypic and phenotypic expression of the preeclampsia syndrome. Some of them are as follows

1. Multiple genotypes: maternal and paternal (fetal and placental)
2. Associated disorders such as diabetes and characteristics such as parity
3. Genomic ethnicity: frequency of polymorphisms, genetic drift, founder effect, and selection
4. Gene-gene interaction: specific alleles or products of two or more genes affect one another and thus the phenotype
5. Epigenetic phenomena: variations in expression of a functional stable gene for example, monozygotic twin differences
6. Gene-environmental interactions: these are infinite.

Table 1: Genes frequently studied for their association with pre eclampsia syndrome

Gene(polymorphisms)	Function affected	chromosome	Biological association
MTHFR (C6771)	Methylene tetra hydrofolate reductase	1p36.3	Vasular diseases
F5(Leiden)	Factor v Leiden	1q23	Thrombophilia
AGT(M235T)	Angiotensinigen	1q42-q43	Blood pressure regulation, linked to essential HTN
HLA(Various)	Human Leukocyte Antigens	6p21.3	Immunity
NO53(glu 298 Asp)	Endothelial Nitric Oxide	7q36	Vascular endothelial function
F2(G20210A)	Prothrombin (factor II)	11p11-q12	Coagulation
ACE	Angiotensin converting Enzyme	17q23	Blood pressure regulation

Source: *Williams Obstetrics*. 23rdEdition. McGraw Hill Medical Publishing Division 2010; section VII, 34: 713

PATHOGENESIS

VASOSPASM

The Vascular constriction causes increased resistance and subsequent hypertension. At the same time, endothelial cell damage causes interstitial leakage through which the blood constituents, including platelets and fibrinogen, are deposited sub endothelially.

ENDOTHELIAL CELL ACTIVATION

Intact endothelium has anticoagulant properties and endothelial cells blunt the response of vascular smooth muscle to agonists by releasing nitric oxide. Damaged or activated endothelial cells may produce less nitric oxide and secrete substances that promote coagulation and increase the sensitivity to vasopressors.

ROLE OF ENDOTHELIUM DERIVED FACTORS

- Vasopressors: In pre-eclampsia the vascular system is increasingly sensitive to different vasopressors like angiotensin II, norepinephrine, endothelin.
- Endothelial production of PGI2 is decreased and there is enhanced production of TXA2 by the platelets. The ratio of PGI2: TXA2 is decreased that leads to increased sensitivity of angiotensin II to the vascular system and ultimately vasoconstriction.
- Nitric oxide and endothelins: Pre-eclampsia is associated with decreased endothelial nitric oxide synthase expression. Its production is increased in severe pre-eclampsia as a compensatory mechanism for the increased synthesis and release of vasoconstrictors and platelet aggregators. It is also produced as a result of reduced placental perfusion causing oxidative stress resulting in widespread endothelial damage.

- Angiogenic factors: Role of vascular endothelial growth factor (VEGF) and placental growth factor (PGF) are important. They promote angiogenesis, production of nitric oxide and vasodilatory prostaglandins. Serum level of VEGF and its soluble receptor-I (SFlt-I) are elevated in pre-eclampsia. VEGF is known to induce functional change in the myometrial resistance arteries to the vasodilator bradykinin. Therefore it is suggested that raised levels of VEGF in pre-eclampsia is involved in the pathogenesis of endothelial damage.
- Tumor necrosis factor (TNF): Plasma levels of TNF-α are high in pre-eclampsia. The microvascular permeability is significantly increased in pre-eclampsia, this is correlated with plasma levels of TNF-α.
- Soluble Fms-like tyrosine kinase 1 (sFlt-1): is a variant of the Flt-1 receptor for placental growth factor (PGF) and vascular endothelial growth factor (VEGF). Increased maternal sFlt-1 levels inactivate and decrease circulating free PGF and VEGF concentrations leading to endothelial dysfunction .sFlt-1 levels begin to increase in maternal serum months before preeclampsia is evident.
- Soluble endoglin (sEng): is a placenta-derived 65-kDa molecule that blocks endoglin—also called CD105 which is a co-receptor for the TGF family. This soluble form of endoglin inhibits various TGF isotopes from binding to endothelial receptors and results in decreased endothelial nitric oxide-dependent vasodilatation.

THYROID GLAND

Thyroid is one the largest endocrine glands present in the body. The function of the thyroid is production and secretion of thyroid hormones. These hormones have multiple metabolic actions in the body. Synthesis and release of thyroid hormones are under the control of thyroid stimulating hormone (TSH) produced by the pituitary gland. Thyroid hormones in turn inhibit the secretion of TSH.

ANATOMY

The thyroid gland is located in front of the neck. It comprises of two small lobes joined by an isthmus at the midline. With adequate iodine intake, the weight of the gland is about 10 to 20gm, whereas in iodine deficiency the gland may be much larger.

MICROSCOPIC STRUCTURE OF THYROID GLAND

Thyroid gland is composed of follicles, lined by a single layer of epithelial cells. These are of variable size and resemble a spheroidal sac lined by follicular cells. They are filled with an amorphous colloidal material. There are two cell types in thyroid gland:

1) Follicular cells 2) Para follicular cells

FOLLICULAR CELLS

The follicular cells vary in shape depending on the level of their activity. Normally they are cuboidal. These cells secrete two hormones that influence the rate of metabolism. Iodine is an essential constituent of these hormones. One hormone containing three atoms of iodine in each molecule is called triiodothyronine (T_3). The

second hormone containing four atoms of iodine in each molecule is called tetraiodothyronine, thyroxine (T_4). T_3 is much more active than T_4.

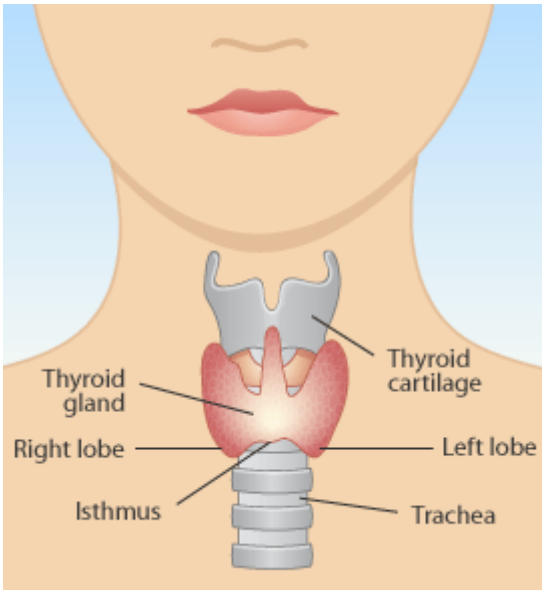


FIGURE.2 THYROID GLAND

Source: www.natural-supplements-guide.com/thyroid-gland

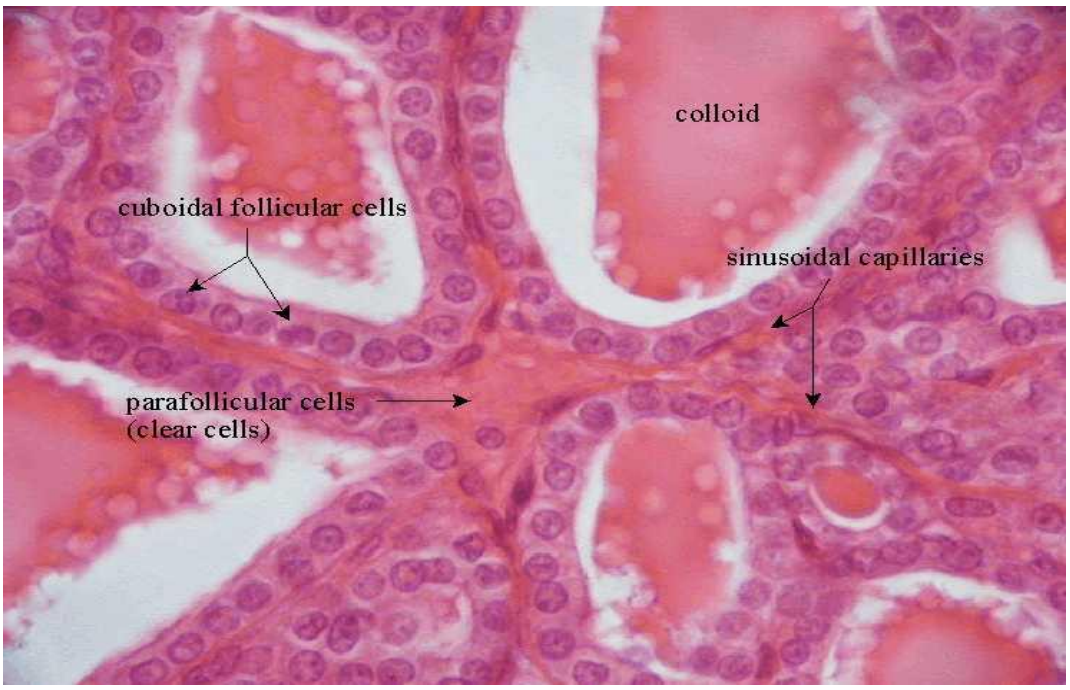


FIGURE.3 MICROSCOPIC STRUCTURE OF THYROID GLAND

Source**:** biology.clc.uc.edu

PARAFOLLICULAR CELLS

They are also called clear cells or light cells or C-cells. They are polyhedral, with oval eccentric nuclei. C-cells secrete the hormone Thyro-calcitonin. This hormone has an action opposite to that of parathyroid hormone on calcium metabolism. It comes into play when serum calcium levels are high.

PHYSIOLOGY

Three important and interrelated functions involved in the synthesis and secretion of thyroid hormones include synthesis of the thyroglobulin, iodine uptake and incorporation into thyroglobulin and thyroid hormone secretion.

a) SYNTHESIS AND STORAGE OF THYROGLOBULIN

Thyroglobulin is a glycoprotein with a molecular weight of about 660 KD is synthesized by the follicular cells. Intracellular thyroglobulin serves as a preformed matrix, containing 123 tyrosine residues to which reactive iodine is attached to form monoiodotyrosine and diiodotyrosine. After their formation, enzymatic coupling of mono and diiodotyrosine takes place to form T_3 and T_4

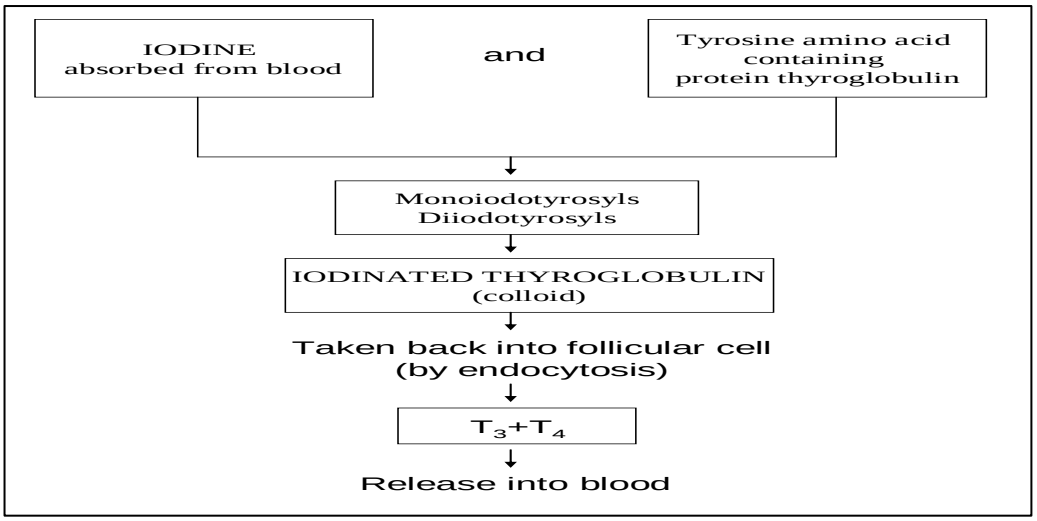
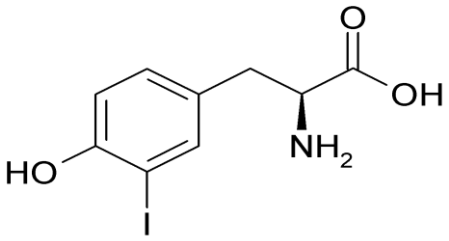
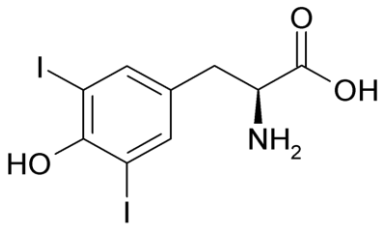


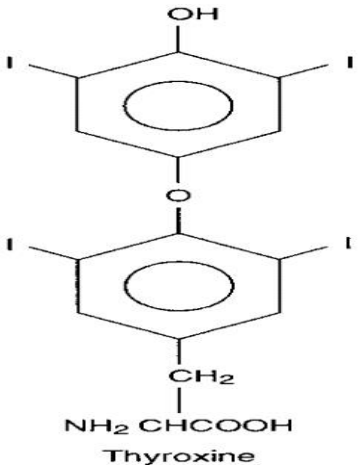
Fig 4: Synthesis of thyroid hormone



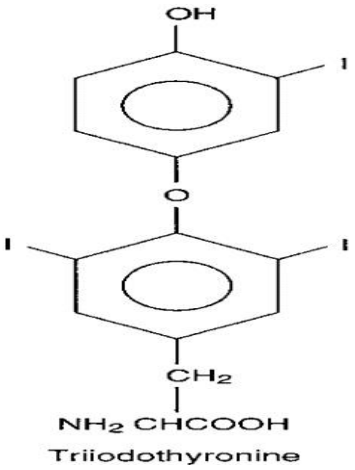
Monoiodotyrosine[MIT]



Diiodotyrosine [DIT]



T4



T3

Fig 5: showing the Structure of Thyroid Hormones[MIT,DIT,T3 and T4]

b) BIOSYNTHESIS OF THYROID HORMONES

Ingested iodine is absorbed by the small intestine and distributed throughout the extra cellular water. Within the thyroid follicular cell, iodide (I-) is oxidized to active Iodine (I+) while it is bound to tyrosine residues within the thyroglobulin molecule by the action of the enzyme Thyro peroxidase[TPO] forming Monoiodotyrosine, Diiodotyrosine further on coupling of two DIT in to T4 and one DIT and one MIT in to T3.

c) THYROID HORMONE SECRETION

TSH from the pituitary gland binds to the TSH receptor on the basal membrane of the follicular cell and via a cyclic adenosine mono phosphate (cAMP) dependent mechanism which stimulates the uptake of thyroglobulin from stored colloid into cellular lysosomes, where the thyroglobulin is hydrolyzed and T_4, T_3, monoiodotyrosine and diiodotyrosine are released.

d) TRANSPORT AND METABOLISM OF THYROID HORMONES

After release from thyroid gland both T_4 and T_3 circulate within the blood, primarily bound to one of three binding proteins with the thyroid hormones being distributed in equilibrium among all binding proteins. The most important of the thyroid hormone binding protein is the 54KD thyroxine- binding globulin (TBG), which has a higher binding affinity for T_4 than for T_3. Transthyretin (prealbumin, thyroxin binding prealbumin [TBPA]) a 55KD protein has a lower affinity for T_4 than does TBG. Albumin has low affinity but high capacity for thyroid hormones.

T_3 has more biological activity than does T_4. Indeed, T_4 can be considered more as a prohormone to T_3. Peripheral tissue deiodination of T_4 to T_3 leads to increased amounts of biologically active T_3. This peripheral conversion can vary from tissue to tissue. T_3 and T_4 probably enter cells through a combination of diffusion and active transport

Thyroid hormones are metabolized predominantly by deiodination, although small amounts of T_3, T_4 and reverse T_3 (rT_3) are conjugated with glucoronide or sulfate in the liver and excreted in the bile or are metabolized to the acetic acid analogues. There are three deiodinases called D_1, D_2, and D_3.

⇒ D_1 is present in high concentrations in liver and kidney and it converts T_4 to T_3 and rT_3 in equimolar concentration.

⇒ D_2 is present in high concentrations in muscle, brain, skin, and placenta and it converts T_4 to T_3.

⇒ D_3 is present in brain and placenta and it inactivates T_4 by converting it into rT_3 and inactivates T_3 by converting it to 3,3'- diiodotyrosine (DIT)

FUNCTIONS OF THYROID GLAND

The thyroid gland is a major endocrine gland which regulates metabolism, growth, development and puberty. It controls metabolism by secreting thyroid hormones that regulates the metabolic rate.

The functions of thyroid hormones may be classified as

- General metabolic effects
- Growth and maturation effects
- Organ specific effects.

GENERAL METABOLIC EFFECTS

- Specific metabolic pathways are stimulated by triiodothyronine, resulting in increased oxygen consumption and calorigenesis (generation of body heat).
- Regulates Basal Metabolic Rate [BMR], body temperature, appetite and cholesterol levels.
- Promotes expulsion of glucose for energy, stimulates protein synthesis and increases lipolysis.

GROWTH AND MATURATION EFFECTS

- Thyroid hormone has important action as a promoter of cell differentiation, growth and maturation.
- Promotes body and skeletal growth and development of muscle and muscle fractions.

ORGAN SPECIFIC EFFECTS

- **On cardio vascular system**
  - Increases adrenergic activity and sensitivity
  - Increases heart rate
  - Increases myocardial contractility, cardiac output, blood volume
  - Decrease in peripheral resistance
- **On bone**
  - T_3 stimulates production of cytokines, growth factors and angiogenic factors that influence bone development and growth. Excess serum thyroid hormone is associated with osteoporosis and bone fractures.
- **On brain**
  - The developing fetus requires thyroid hormone for normal brain development. Insufficient first – trimester levels of maternal thyroid hormone have been demonstrated to increase the risks of mental and psychomotor deficits in the new born
  - In the adult brain, most T_3 is produced locally from T_4 through the action of D_2 deiodinase. Although the mechanisms are not well

understood, cerebral blood flow to regions that mediate attention, memory and visuospatial processing is decreased in hypothyroid patients.

- **On gastro intestinal tract**
    - Thyroid hormones increase the gastro intestinal motility.

REGULATION OF THYROID HORMONES

The hypothalamic-pituitary-thyroid axis (HPTA) consists of a group of physiologically inter related neuroendocrine and endocrine organs that regulate and control the secretion of thyroid hormone through a highly integrated feedback system. Thyrotropin releasing hormone [TRH] is a biologically important tripeptide produced in the para ventricular nucleus of the hypothalamus and secreted into portal venous system, which then drains to the pituitary. Thyrotropin releasing hormone binds to receptors in the pituitary causing increased production and secretion of TSH. At the thyroid, TSH binds to specific cell membrane receptors, thereby activating adenylate cyclase and increasing intracellular levels of cAMP.

The increased levels of cAMP have two main functions:

- Tropic action involves the stimulation of cell reproduction and growth (hypertrophy)
- The stimulation and secretion of thyroid hormones by follicular cells.

These hormones in turn feedback to the hypothalamus and pituitary to reduce the secretion of thyrotropin releasing hormone and TSH depicted in the following Fig 6.

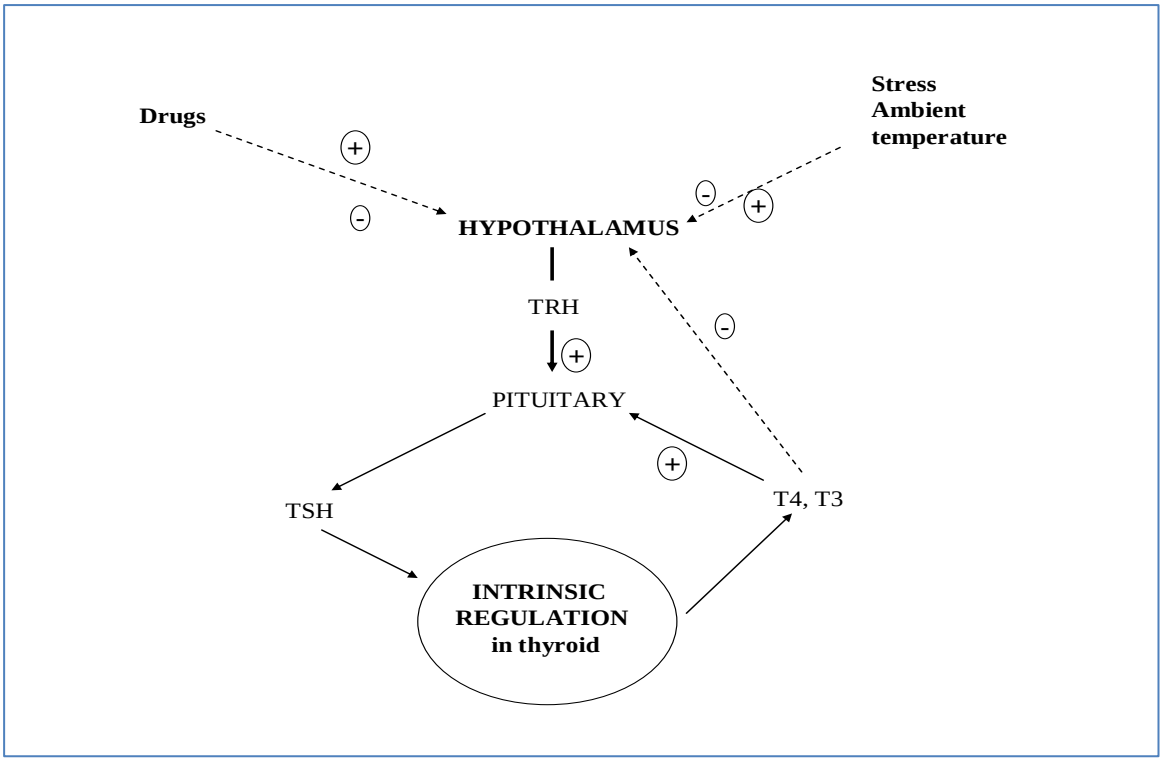


FIGURE 6: REGULATION OF THYROID HORMONE SYNTHESIS

THYROID FUNCTION TESTS

Thyroid function testing is an important element in assessing the patients with possible thyroid disease.

1. **Nuclear imaging of the thyroid** with the use of isotopes of iodine or Technetium 99 (^{99}TC), is an important part of clinical investigation of thyroid disease.

2. **Static tests of thyroid function**

   a) **TSH**

   TSH is regulated by negative feedback by free thyroid hormone concentration. Thyroid disease is almost always primary, as it is usually caused by a disorder of the thyroid gland rather than occurring as a result of disorders of the pituitary, and therefore changes in TSH are invariably a reliable indicator of thyroid status.

   b) **Total thyroid hormones**

   Changes in total thyroid hormone concentration are far less sensitive indices of thyroid function than TSH.

   c) **Free thyroid hormone**

   The free T_4 index (FT_4I) indirectly estimates the levels of free T_4 in blood and adjusts for most interference caused by binding protein abnormalities. The FT_4I is determined from total T_4.

d) **Thyroid antibodies**

-Anti thyroid peroxidase antibodies (anti – TPO)

-Anti thyroglobulin antibodies (Anti – TG Ab)

-Thyroglobulin (TG)

-Thyroid receptors antibodies (TR Ab)

3. Dynamic tests of thyroid function

a) TRH stimulation test

This was important until the early 1980's when TSH assays did not have the capacity to measure the lower end of the euthyroid reference interval.

b) Recombinant TSH stimulation test for identifying residual malignant thyroid cancer tissue

Thyroid cancer usually is treated by total thyroidectomy coupled with high dose radioiodine, followed by replacement with thyroxine to suppress TSH secretion, so that any remaining ectopic/metastatic thyroid tissue is not stimulated. Follow up for the presence of any residual thyroid tissue is accomplished by measurements of thyroglobulin, which is produced only by thyroid tissue. This is an unpleasant procedure for patients and there is a place to use recombinant TSH (rTSH) to stimulate ectopic tissue and eliminate the need for the patient to become hypothyroid.

THYROID HORMONE LEVELS DURING NORMAL PREGNANCY

It is known that the fetus is totally dependent on maternal thyroid hormone supply during the first trimester of pregnancy, which is the crucial time in organogenesis.[36] Thyroid dysfunction has a relatively high prevalence during pregnancy, affecting up to 5% of all pregnant women. The effects of thyroid dysfunction on pregnancy outcome and on the developing fetus are currently of interest, with the most devastating observation in the literature being decreased intelligence quotient of the offspring.

The various physiological changes in thyroid function during pregnancy are:

INCREASE IN THYROID-BINDING GLOBULIN

Thyroid hormones are transported in serum bound to three proteins: Thyroxine binding globulin (TBG), transthyretin, and albumin. Although TBG is present in low abundance in serum, it has a high affinity for thyroid hormones and is responsible for the transport of the majority of T4 (68%) and T3(80%) During pregnancy, the affinities of the three binding proteins for T4 and T3 are not significantly altered, but the circulating concentration of TBG increases two- to threefold, whereas the concentrations of albumin and transthyretin remain unchanged.[37]

Serum TBG increases a few weeks after conception and reaches a plateau during mid gestation. The mechanism for this increase in TBG involves both an increase in hepatic synthesis of TBG and an estrogen-induced increase in sialylation, which increases the half-life of TBG [from 15 min to 3 days for fully sialylated TBG.

INCREASE IN TOTAL T4 AND T3

Plasma concentrations of total T4 and T3 are also increased during pregnancy, often outside the health-related reference interval. Total T4 and T3 concentrations increase sharply in early pregnancy and plateau early in the second trimester at

concentrations 30–100% greater than pre pregnancy values. The etiology of this increase in total circulating thyroid hormones involves, primarily, increased concentrations of plasma TBG.

Another proposed mechanism for this increase in total thyroid hormone concentrations is production of type III deiodinase from the placenta. This enzyme, which converts T4 to reverse T3, and T3 to diiodotyrosine (T2), has extremely high activity during fetal life.[38] Increased demand for T4 and T3 has been suggested to increase production of these hormones with ultimately, increased concentrations in the circulation. The increase in T4 and T3 concentrations is less than would be expected by the increase in TBG. Glinoer refers to this as a "relative hypothyroxinemia". This is reflected by a decrease in free T4 concentrations as well as a progressively decreasing T4/TBG ratio during pregnancy.

Changes in free T4 and T3 concentrations during pregnancy have been controversial. Some authors have reported a decrease in free hormones whereas others have reported no change or even an increase. These discrepancies may have been attributable to the techniques used for free hormone measurement.

Roti et al. demonstrated variability in serum free thyroid hormones in pregnant women at term among ten commercially available methods. Regardless of the method, however, pregnant women, on average, had lower free hormone concentrations at term than non-pregnant women. Other studies have confirmed that serum free T4 and T3 are 25% lower in women at delivery than non-pregnant subjects. However, most pregnant women (78%) remain within the same reference interval as non-pregnant women.

THYROID STIMULATION BY HCG

Human chorionic Gonodotropin [hCG] has mild thyrotropic activity. During the first trimester of pregnancy, when hCG is at its greatest concentration, serum TSH concentrations drop, creating the inverse image of hCG. In most pregnancies, this decrease in TSH remains within the health-related reference interval. Under pathological conditions in which hCG concentrations are markedly increased for extended periods, significant hCG-induced thyroid stimulation can occur, decreasing TSH and increasing free hormone concentrations.

Members of the glycoprotein hormone family of luteinizing hormone, follicle-stimulating hormone, TSH, and hCG contain a common α subunit and a hormone-specific β subunit. Because the hCG and TSH β subunits share 85% sequence homology in the first 114 amino acids and contain 12 cysteine residues at highly conserved positions, it is likely that their tertiary structures are very similar.[39]

Purified hCG, like TSH, has been shown to:

(*a*) increase iodide uptake and cAMP production in FRTL-5 rat thyroid cells;

(*b*) increase cAMP production dose dependently and displace binding of 125I-labeled TSH in Chinese hamster ovary cells stably transfected with human TSH receptor; and

(*c*) stimulate iodide uptake, organification, and T3 secretion in cultured human thyroid follicles

Glinoer has estimated that a 10 000 IU/L increment in circulating hCG corresponds to a mean free T4 increment in serum of 0.6 pmol/L (0.1 ng/dL) and in turn, to a lowering of serum TSH of 0.1 mIU/L. Hence, he predicts that an increase in serum free T4 during the first trimester will be observed only when hCG concentrations of 50 000–75 000 IU/L are maintained for 1 week.

Rodien et al. described two patients, a mother and her daughter, with recurrent gestational hyperthyroidism and severe nausea, despite serum hCG concentrations within the health-related reference interval.[40] Both women were heterozygous for a mis sense mutation in the extracellular domain of the thyrotropin receptor. The mutation, a substitution of guanine for adenine at codon 183, led to the replacement of a lysine residue with an arginine (K183R). When expressed in COS-7 cells, the mutant receptor was 30-fold more sensitive than the wild-type receptor to hCG. The mutation thereby could account for the occurrence of hyperthyroidism in these two women despite the presence of hCG concentrations within the reference interval. Further studies are needed to determine the incidence of this mutation in the general population.

INCREASE IN RENAL IODIDE CLEARANCE

In pregnancy, the renal clearance of iodide increases substantially because of an increased glomerular filtration rate. The iodide loss lowers the circulating concentrations of iodide and produces a compensatory increase in thyroidal iodide clearance. In areas of the world where iodine intake is sufficient, the iodide losses in the urine are not clinically important. In other areas of the world, however, iodine deficiency during pregnancy can lead to hypothyroidism and goiter and poses a serious public health issue.

Approximately 500 million people live in areas of overt iodine deficiency. In the non-pregnant condition, adequate iodine intake is estimated to be 100–150 mg/day. The World Health Organization recommends that during pregnancy, iodine intake be increased to at least 200 mg/day.

INCREASE IN SERUM THYROGLOBULIN

Although, Thyroglobulin lacks specific hormonal activity, it can indicate the activity of or injury to the thyroid gland. Thyroglobulin frequently is increased during pregnancy, reflecting the increased activity of the thyroid gland during pregnancy. The increase in thyroglobulin can be seen as early as the first trimester, but it is more pronounced in the latter part of pregnancy. Increased serum thyroglobulin concentrations are also associated with an increase in thyroid volume. Despite this, goiter occurs in only 5–15% of women at term. This low incidence is attributable to adequate intake of dietary iodine.

HYPOTHYROIDISM DURING PREGNANCY

There is a known association between hypothyroidism and decreased fertility. For this reason, the frequency of hypothyroidism in pregnancy is actually lower than the frequency in the general population. Autoimmune thyroid disease (Hashimoto Thyroiditis) and post thyroid ablation therapy are the most common causes of hypothyroidism. Hypothyroidism during pregnancy has been associated with pregnancy-induced hypertension, placental abruption, postpartum hemorrhage, and an increase in the frequency of low birth-weight infants.

Recently, Haddow et al. reported that untreated hypothyroidism during pregnancy may cause a significant decrease in the intelligent Quotient [IQ] of children. The IQ scores of children born to these women were, on average, seven points lower than those of children born to women with thyroid values within the appropriate reference intervals. Approximately 20% of these children had IQ levels of 85 or lower. This study suggests that TSH should be measured before or early in pregnancy to allow adequate treatment of the mother.

DIAGNOSIS OF HYPOTHYROIDISM

Laboratory evaluation of hypothyroidism should be made using TSH and an assessment of free hormone values, either directly or via a calculated index. Total T4 and T3 measurements should be considered unreliable because of the increase in TBG concentrations. Anti-TPO antibodies and anti-thyroglobulin antibodies are increased in most patients with Hashimoto thyroiditis and therefore may be useful in establishing this diagnosis.

It is important to note that the natural course of Hashimoto thyroiditis is altered in pregnancy, with amelioration in the second half of pregnancy and aggravation in the postpartum period. In addition, pregnant women who are on thyroid replacement therapy require larger doses compared with non-pregnant patients because of increases in the TBG concentration and increased type III deiodinases from the placenta. TSH should be monitored closely, and the dose of thyroid replacement should be adjusted to maintain TSH in the reference interval. Doses of thyroid replacement therapy can be lowered to pre pregnancy levels at parturition. The diagnostic interpretation of hypothyroidism is presented below in Fig 7

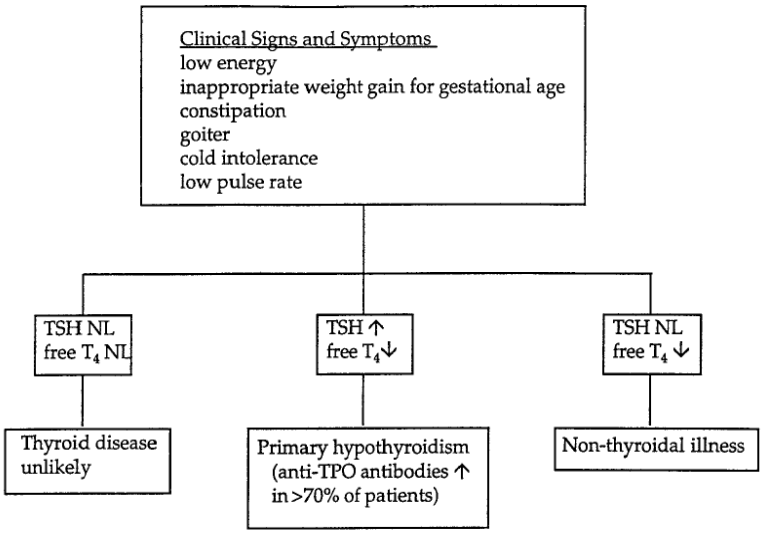


Fig 7: The diagnostic interpretation of hypothyroidism

PREGNANCY COMPLICATIONS ASSOCIATED WITH THYROID DYSFUNCTION

Mothers with untreated hypothyroidism more often have complications such as preeclampsia, placental abruption, postpartum hemorrhage and cardiac dysfunction. A recent study showed that those with late-onset preeclampsia more often had subclinical hypothyroidism in early pregnancy.[41]

Mothers treated for hypothyroidism are more often seem to have preexisting hypertension and preeclampsia compared with healthy women. Cesarean section and induction of labour are also more prevalent among those with treated hypothyroidism.[42] In large cohort studies, mothers with antibodies have been found to have a higher risk of preterm premature rupture of membranes.

Placental abruption has been found to be three times more common in women with subclinical hypothyroidism but this association has not been confirmed in other studies. However, mothers with TPO-Ab positivity have shown a 3-fold increase in placental abruption.[43] and a slightly smaller association with autoimmune thyroiditis and placental abruption was observed in another large study.[44]

LIPID METABOLISM IN PREGNANCY

EARLY PREGNANCY

Maternal metabolism during pregnancy adapts to benefit the growth and development of the fetus and during the initial two thirds of gestation, when fetal energy demands are limited, maternal fat stores increase. This is attributable in part to maternal behavioral change including hyperphagia and to increased lipogenesis.

In early pregnancy, insulin sensitivity is normal or even slightly improved with normal peripheral sensitivity to insulin and hepatic basal glucose production. This metabolic environment together with pregnancy related endocrine changes including increasing levels of oestrogen, progesterone and cortisol favours lipogenesis and fat accumulation.

LATE PREGNANCY

During the later stages of pregnancy the anabolic state switches to a state of catabolism with a marked increase in lipolysis and a corresponding rise in maternal free fatty acids (FFA) and glycerol. This change is enhanced by an increase in hormone-sensitive lipase (HSL) activity and mRNA expression and a decrease in lipoprotein lipase (LPL) activity.

Effects on lipolysis (adipose tissue) and fat oxidation (in liver and muscle) are significantly impaired during the 3rd trimester compared to earlier in pregnancy and also post-partum period. Reduced expression of *PPARγ* may also contribute to accelerated fat metabolism in late pregnancy. This catabolic state corresponds to the time of maximum fetal growth and by increasing free Fatty Acids [FFA] use in the mother , increases availability of glucose and amino acids for the fetus.

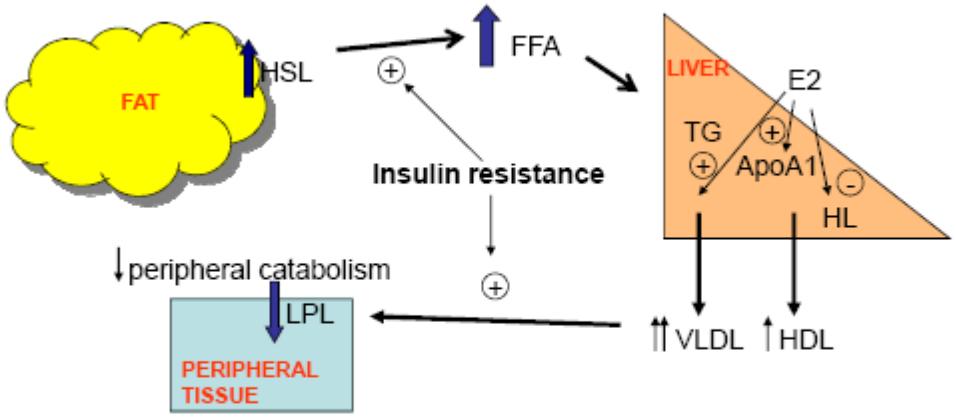


Fig 8: Lipoprotein Metabolism in late pregnancy

This above Fig 8 summarizes the important changes in lipoprotein metabolism which occur in advancing gestation. Due to increasing insulin resistance there is an increase in hormone sensitive lipase (HPL) activity and a decrease in lipoprotein lipase (LPL) activity. This results in a marked increase in lipolysis rates and corresponding increase in free fatty acids (FFA), delivered to the liver. These are channeled into hepatic triglyceride synthesis and increased secretion of VLDL. Oestrogen (E2) is the primary determinant of increased hepatic VLDL production. E2 also acts to promote Apo A1 production and reduce hepatic lipase (HL) activity with a resultant increase in HDL production. The reduced LPL activity contributes to the increase in plasma VLDL levels by reducing the peripheral catabolism of this lipoprotein**.**

CHANGES IN LIPOPROTEIN PROFILE DURING PREGNANCY

Pregnancy is characterized by marked increase in plasma lipid concentrations as gestation advances. Plasma cholesterol and triglyceride concentrations rise by 25-50%. The increase in triglyceride is mainly due to VLDL-C which shows a three-fold increase from 14 weeks' gestation to late pregnancy.

VLDL comprises of two fractions, VLDL1 which is secreted by the liver to supply tissues with triglyceride fatty acids in the post-absorptive state and VLDL2 which is the major precursor of the cholesterol transporting particles IDL and LDL. VLDL1 and VLDL2 increase in parallel by an average of 4-fold as plasma triglyceride increases with advancing gestation.

There is increased lipolysis resulting in increased delivery of FFA and glycerol to the liver where they are re-esterified for the synthesis of triglycerides and incorporated into VLDL. The insulin resistant condition of pregnancy may contribute to the increased VLDL production but the effect of oestrogen is more likely the primary determinant of increased VLDL production by the liver. In addition to increased VLDL production there appears to be a decrease in maternal VLDL catabolism which may be due to a reduction in LPL activity in the third trimester.

Oestradiol concentration rises steadily throughout pregnancy which suppresses hepatic lipase activity which in turn results in reduced triglyceride hydrolysis in IDL and LDL particles. Moreover there is an increase in cholesteryl ester transfer protein activity in mid trimester of pregnancy which would contribute to enrichment of lipoprotein fractions with triglyceride.

Despite a rise in TG in normal pregnancy, HDL-cholesterol levels are elevated by the 14th week and rise by a maximum of around 40% at 28 weeks' gestation mainly due to an increase in the HDL2 Sub fraction with a proportionate fall in HDL3a and HDL3b. The mean concentration of HDL-cholesterol is around 2 mmol/L compared to around 1.5 mmol/L in the non-pregnant.

This increase in HDL is driven by rising oestrogen concentration which acts on the liver to promote apo AI production and a simultaneous fall in hepatic lipase activity (which is responsible for hydrolysis of HDL2 to smaller HDL3 which is more rapidly removed from the circulation).

During normal pregnancy there is a rise in LDL of around 70%. Although this increase is less marked than TG there are some important qualitative changes in the LDL composition favoring a more "atherogenic" profile with a proportional increase in small dense LDL (LDLIII) in late pregnancy.

MATERIALS AND METHODS

SOURCE OF DATA

In the present study, a total number of 100 pregnant women were included out of which 50 were Preeclampsia (cases) and 50 were normotensive pregnant women (control) who attended Department of Obstetrics and Gynecology at R L Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Academy Of Higher Education, Tamaka, Kolar between January 2012 to June2013.

INCLUSION CRITERIA

1) All pregnant women beyond 28 weeks of gestation with preeclampsia diagnosed as per (National High Blood Pressure Education Programme working group (NHBPEP) Classification admitted at R L Jalappa Hospital and Research Centre were included in the study group.
2) Age and gestation matched normotensive pregnant women were included in the control group.

EXCLUSION CRITERIA

1) Patients with pre-existing thyroid disease.
2) History of renal disease.
3) History of any metabolic disorder before or during the pregnancy.
4) History of chronic hypertension.
5) History of medication known to affect the thyroid function.

METHODOLOGY

The present study was carried out in 100 pregnant women of which 50 were preeclampsia cases and 50 were normotensive pregnant women (control).The subjects in the two groups were age and gestation matched. Informed consent was obtained from all the subjects and the study was approved by the ethical committee of the institute. A standard proforma was used to collect the data.

Pre-eclampsia was diagnosed as blood pressure of ≥140/90 mm of Hg noted for the first time during pregnancy on ≥2 occasions at least 6 hours apart, after 20 weeks of gestation with proteinuria of ≥300 mg/24 hours or ≥ 1+ by dipstick method in a random urine sample (NHBPEP and ACOG criteria)

Pre eclampsia patients were further subdivided into 2 groups based on severity of pre eclampsia:

Mild pre eclampsia: pregnant women who showed the following criteria

- Systolic blood pressure (SBP) less than 160mmHg or diastolic blood pressure (DBP) less than 110mmHg on 2 occasions 6 hours apart.
- Proteinuria <2gm/24H or up to +2 by dipstick method.

Severe pre eclampsia: pregnant women with any of the following criteria

- Systolic blood pressure >160 mmHg or diastolic blood pressure >110 mmHg
- Proteinuria ≥ 2.0g/24hrs or ≥ 2+ dipstick
- Serum creatinine > 1.2mg/dl unless known to be previously elevated
- Platelets < 100,000/µL
- Micro- Angiopathic Hemolysis- increased LDH
- Elevated liver enzymes - Serum Transaminase levels- ALT or AST

- Urine output less than 400ml/ 24H
- Persistent headache or other cerebral or visual disturbances
- Persistent epigastric pain

All the selected women were then subjected to:

1) **Detailed history taking**
2) **Complete Clinical Examination**
3) **Investigations:**

- Routine investigations:

a) Complete Blood Count

b) Blood grouping and Rh typing

c) Complete urine analysis: special concern was given to proteinuria and presence of pus cells or casts in urine

- Special investigations: 10 ml of fasting sample was drawn and tested for the following:
- **THYROID PROFILE:** T3, T4 and TSH were analysed by chemi-luminescence assay (CLIA)using Vitros immunodiagnostic kits employing the Vitros 250 analyser (Johnson and Johnson) The Revised Endocrine Society Clinical Practice Guidelines of 2012 were followed for cut‑off values for TSH, T3 and T4 (based on pregnancy‑specific and trimester‑specific) reference ranges.
- The normal values for T3,T4 and TSH are as follows :
- T3 : 1.2-1.6ng/ml
- T4 : 6.3-9.7 mcg/dl
- TSH: 0.38 to 4.04mcIU/ml.

- Women with serum T3, T4 and TSH values within the normal range were considered to be euthyroid. Those with an abnormally low TSH but normal T4 levels were classified as having subclinical hyperthyroidism. Conversely, women with abnormally high TSH but normal T4 levels were classified as having subclinical hypothyroidism. And those with abnormally high TSH and low levels of T4 and T3 were classified as having overt hypothyroidism.
- **LIPID PROFILE:** Serum Lipid profile estimation was done by dry chemistry using Vitros 250 analyser. (Johnson &Johnson manufacturer). Serum LDL cholesterol (LDL-C) was calculated by Frederickson-Friedwald's formula according to which LDL cholesterol = Total cholesterol - (HDL cholesterol +VLDL cholesterol). Lipid profile concentration was measured in milligram per deciliter.
- **LIVER FUNCTION TESTS**
- **RENAL FUNCTION TESTS**
- **COAGULATION PROFILE**

STATISTICAL ANALYSIS:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous variables are presented as Mean ± SD and results on categorical variables are presented as Numbers and Percentage (%). Student‘t’ test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures

+ Suggestive of significance (P value: $0.05<P<0.10$)

* Moderately significant (P value:$0.01<P \leq 0.05$)

** Strongly significant (P value: $P \leq 0.01$)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

RESULTS

Table 2: Age distribution of the subjects under the study groups

Age in years	Normotensive Group		Pre-eclampsia Group	
	No	%	No	%
18-20	12	24.0	16	32.0
21-25	28	56.0	20	40.0
26-30	8	16.0	9	18.0
>30	2	4.0	5	10.0
Total	50	100.0	50	100.0
Mean ± SD	23.70±3.37		24.08±4.69	

There is no statistical significance in the age distribution of the patients studied. The mean age among the normotensive group was 23.70±3.37 and the mean age among the pre eclampsia group was 24.08±4.69

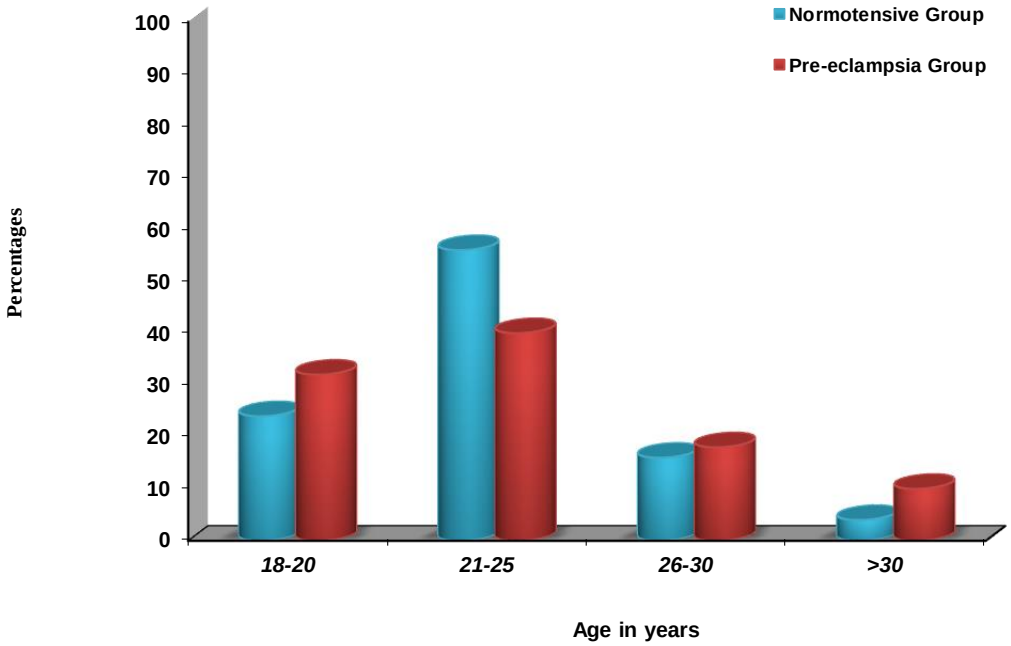


Chart 1: Showing the details of age distribution of the subjects under the study groups

Table 3: Parity distribution among the two groups studied.

Parity	Normotensive Group		Pre-eclampsia Group	
	No	%	No	%
Primi	26	52	35	70
Multi	24	48	15	30
Total	50	100.0	50	100.0

Among the Normotensive group 52 % were primigravida and 48% were multigravida where as in the Preeclampsia group 70% were primigravida and 30% were multigravida.

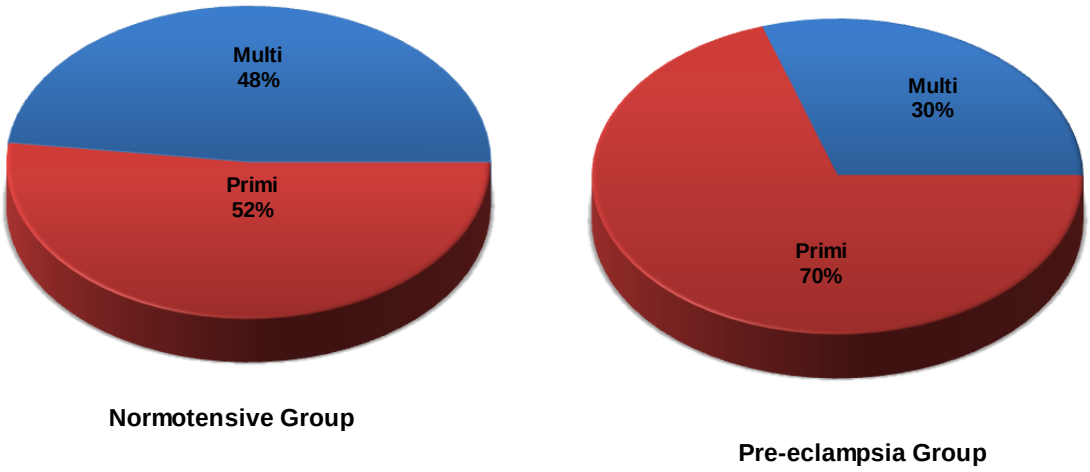


Chart 2: Pie diagram depicting parity distribution pattern amongst normotensive and preeclampsia groups

Table 4: Gestational age distribution of the subjects under the study groups

Gestational age(wks)	Normotensive Group		Pre-eclampsia Group	
	No	%	No	%
28-33	4	8	4	8
34-37	4	8	11	22
38-40	40	80	32	64
>40	2	4	3	6
Total	50	100.0	50	100.0

Majority of the patients were in the gestational age group of 38-40 wks in the study population ie 80% in the normotensive group and 64% in the pre eclampsia group. While 8% in the normotensive group were between 28-33 wks, 8% between 34-37 and 4% were beyond 40 weeks. In the pre eclampsia group 8% were between 28-33 wks, 22% between 34-37 weeks and 6% had crossed 40 wks of gestation.

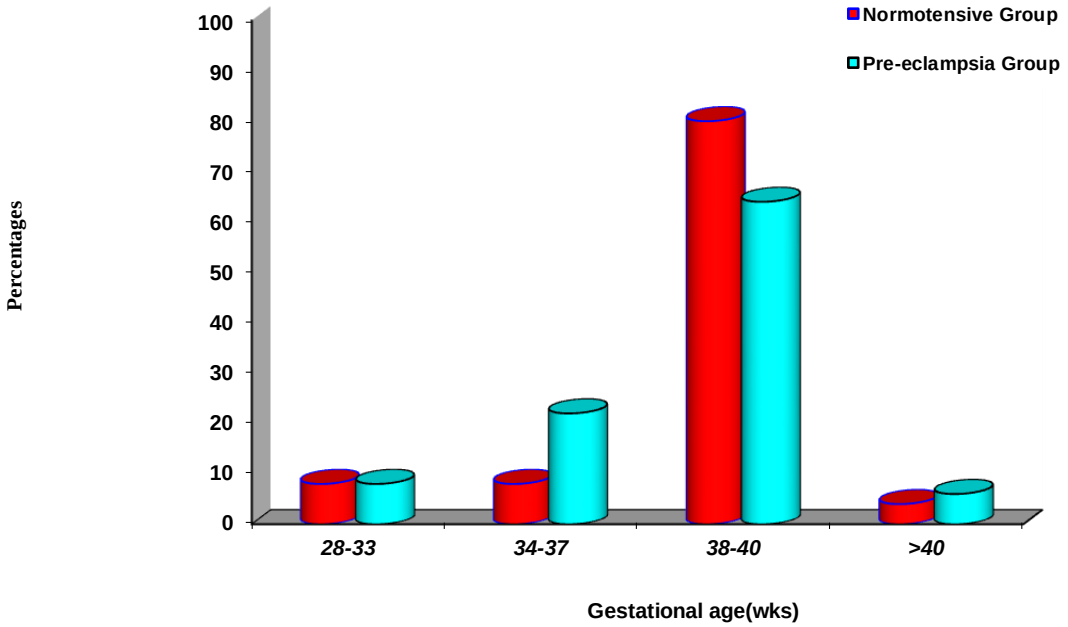


Chart 3: showing Gestational age distribution of the subjects under the study groups

Table 5: Mean SBP and DBP in the two groups studied

	Normotensive Group (Mean±SD)	Pre-eclampsia Group (Mean±SD)	p value
SBP(mm Hg)	115.20±7.62	156.20±16.02	<0.001**
DBP(mm Hg)	73.80±4.90	103.00±11.47	<0.001**

The mean SBP in the normotensive group was 115.20±7.62 and in pre eclampsia group was156.20±16.02. The mean DBP in the normotensive group was 73.80±4.90 and in Pre-eclampsia Group was 103.00±11.47.

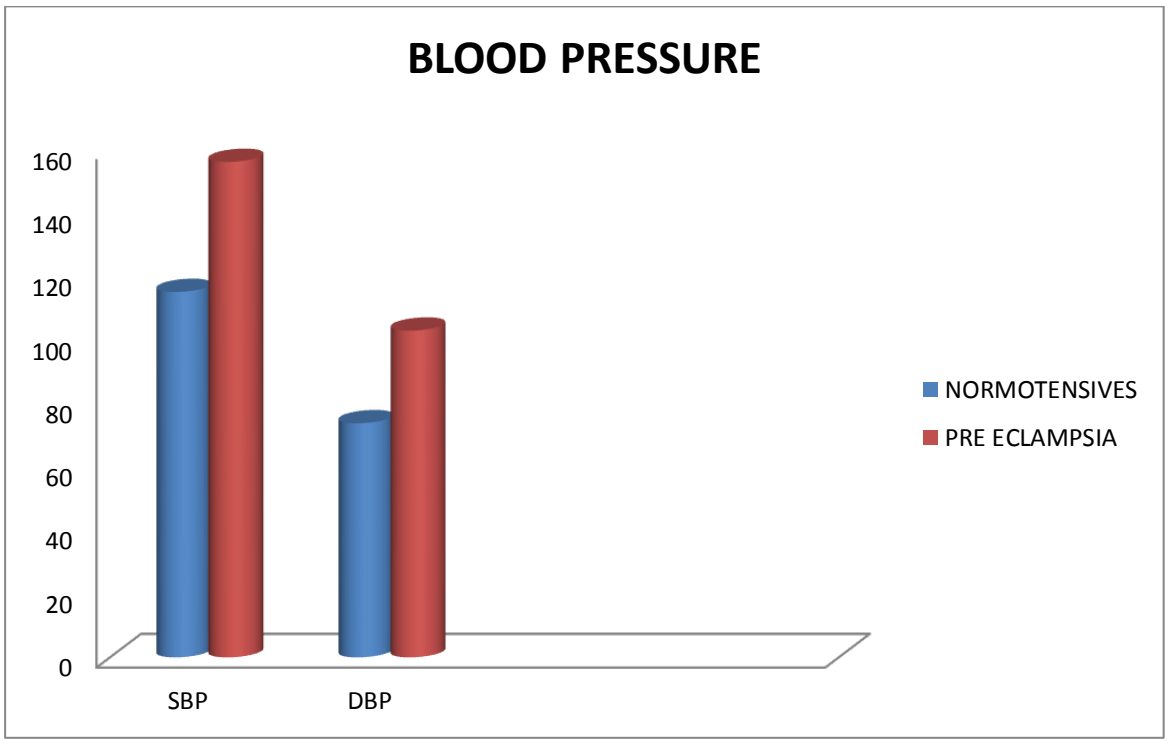


Chart 4: Indicating the Mean SBP and DBP in the two groups studied

Table 6: Distribution of Mild and Severe pre-eclampsia cases in the study groups

	Number of patients	%
Mild pre-eclampsia	24	48.0
Severe pre-eclampsia	26	52.0
Total	50	100.0

Among the pre-eclampsia group 52% were severely pre eclamptic while 48% were mild pre eclamptic.

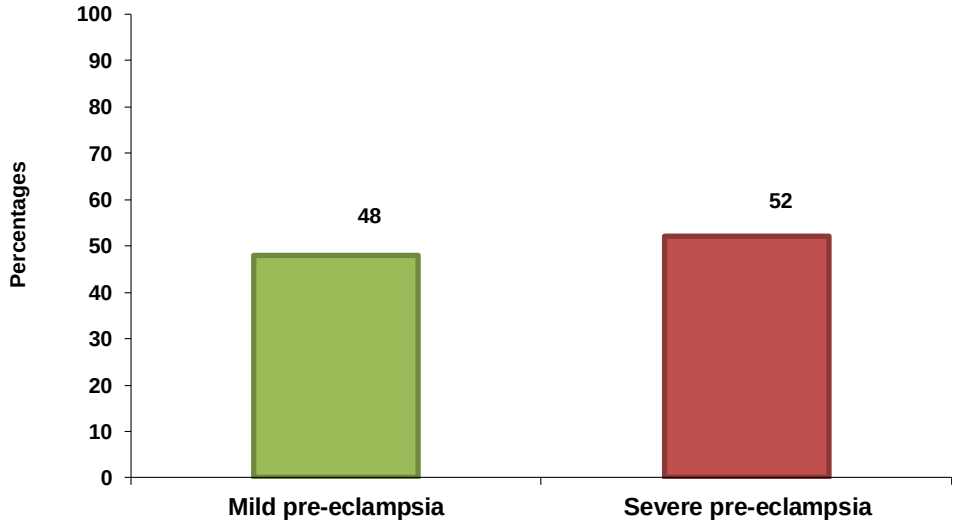


Chart 5: Distribution of Mild and Severe pre-eclampsia cases in the study groups

Table 7: Distribution of BMI (kg/m^2) among the groups studied

BMI (kg/m^2)	Normotensive Group		Pre-eclampsia Group	
	No	%	No	%
<18.5	0	0.0	0	0.0
18.5-25.0	50	100.0	48	96.0
25-30	0	0.0	2	4.0
>30	0	0.0	0	0.0
Total	50	100.0	50	100.0
Mean ± SD	21.74±1.07		22.52±1.63	

The mean BMI is significantly higher in Pre-eclampsia group with p=0.006. Majority of the patients had BMI in the range of 18.5-25.0. (100%) in the Normotensive group and (96%) in the pre eclampsia group

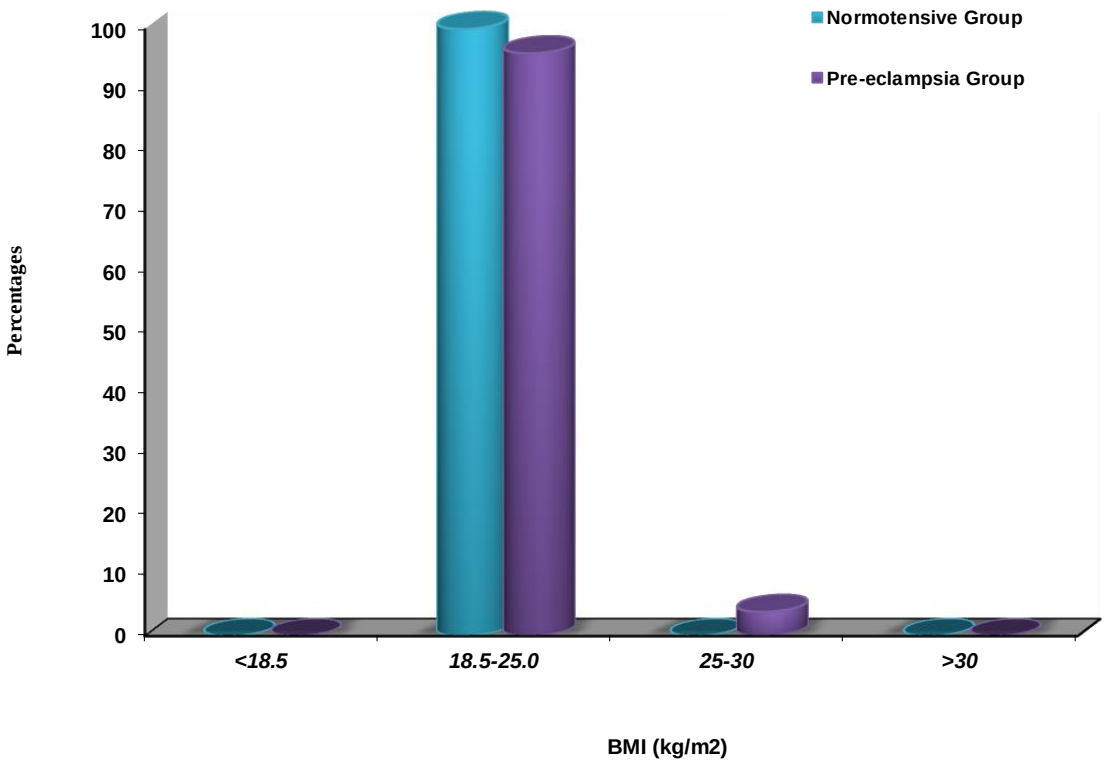


Chart 6: Represents the distribution of BMI (kg/m^2) among the groups studied

Table 8: Comparison of Thyroid hormone levels in two groups studied:

Thyroid	Normotensive Group (Mean±SD)	Pre-eclampsia Group (Mean±SD)	p value
T3(ng/ml)	1.56±0.38	1.37±0.36	0.011*
T4(mcg/dl)	11.61±3.64	9.87±2.83	0.009**
TSH (mcIU/ml)	2.45±1.23	6.15±5.51	<0.001**

The mean TSH value is significantly higher and the mean T3 and T4 values are significantly lower in the pre eclampsia group as compared to normotensive group. (p value <0.001)

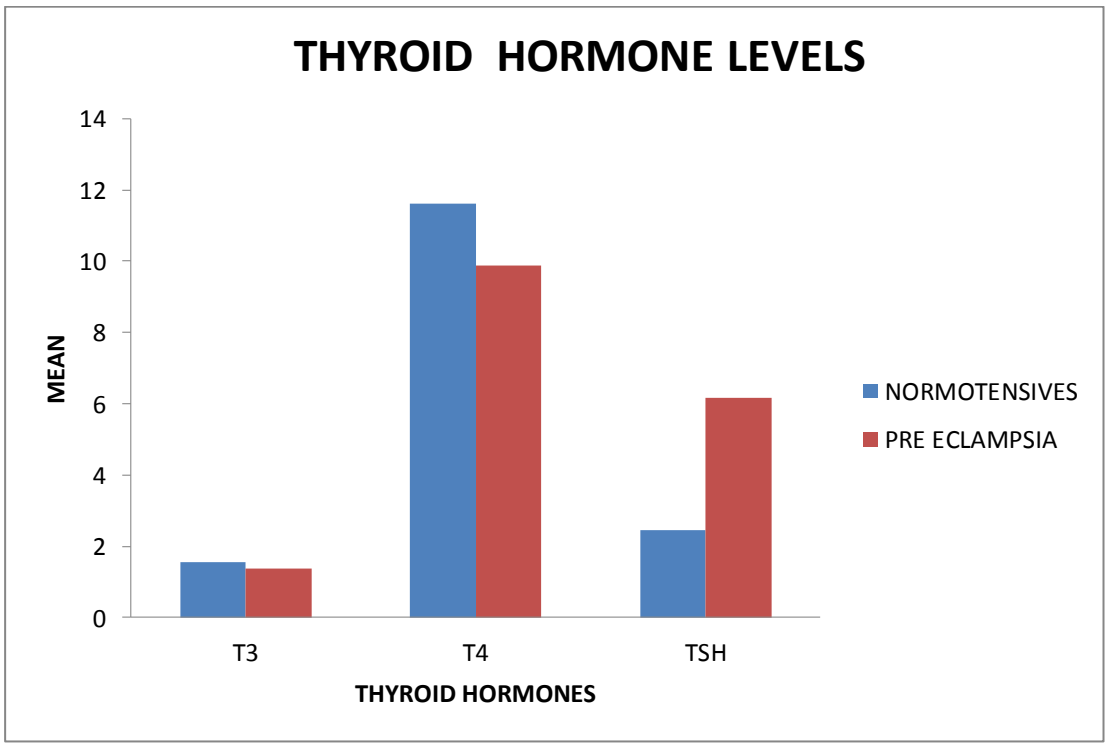


Chart 7: showing the comparison of Thyroid hormone levels in two groups studied

Table 9: Comparison of Thyroid hormone levels in Mild and severe pre-eclamsia patients

Thyroid parameters	Mild pre-eclampsia (Mean±SD)	Severe pre-eclampsia (Mean±SD)	p value
T3(ng/ml)	1.47±0.39	1.28±0.3	0.057+
T4(mcg/dl)	9.61±2.23	10.11±3.33	0.540
TSH (mcIU/ml)	5.07±4.94	7.15±5.91	0.165

The mean T3, T4 and TSH levels are not statistically significant in the mild and severe pre eclampsia groups

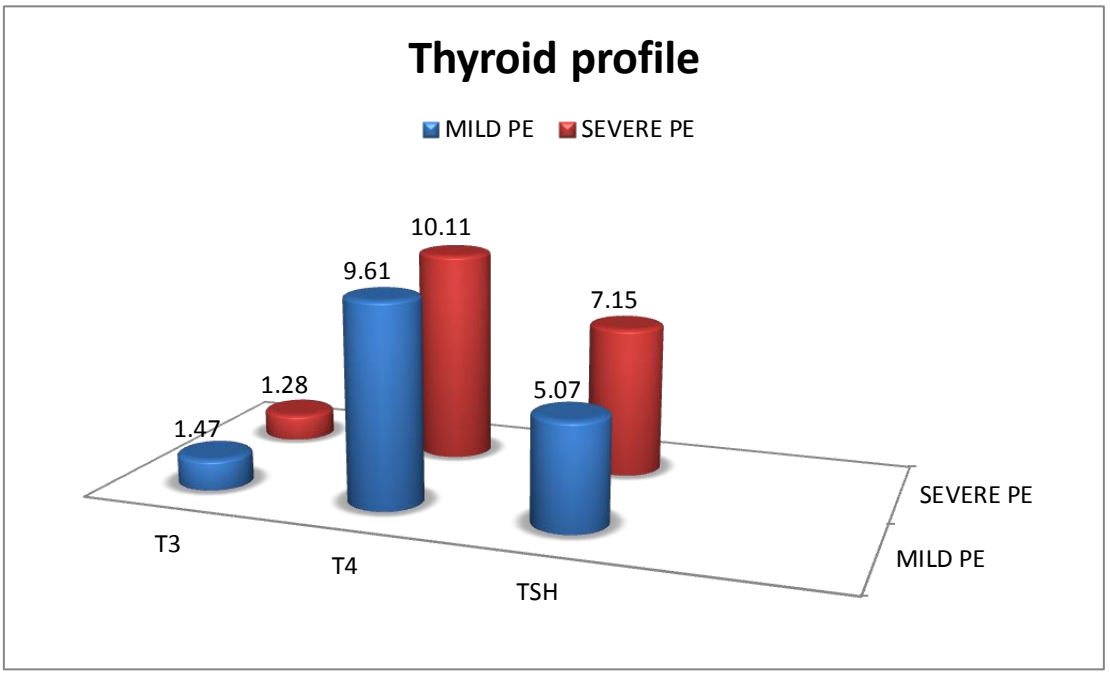


Chart 8: Comparison of Thyroid hormone levels in Mild and severe pre-eclamsia patients

Table 10: Comparison of Lipid profile in two groups studied

Lipid parameters	Normotensive Group (Mean±SD)	Pre-eclampsia Group (Mean±SD)	p value
Total cholesterol (mg/dl)	181.62±44.33	222.60±70.07	0.001**
TGL (mg/dl)	198.10±49.84	278.66±93.46	<0.001**
HDL (mg/dl)	49.44±11.54	45.92±11.81	0.135
LDL (mg/dl)	104.90±29.58	116.52±49.26	0.161

The mean Total cholesterol and Triglyceride levels are significantly elevated in the study group as compared to the control group. ($p<0.001$) where as the mean HDL and LDL values are comparable in the two groups.

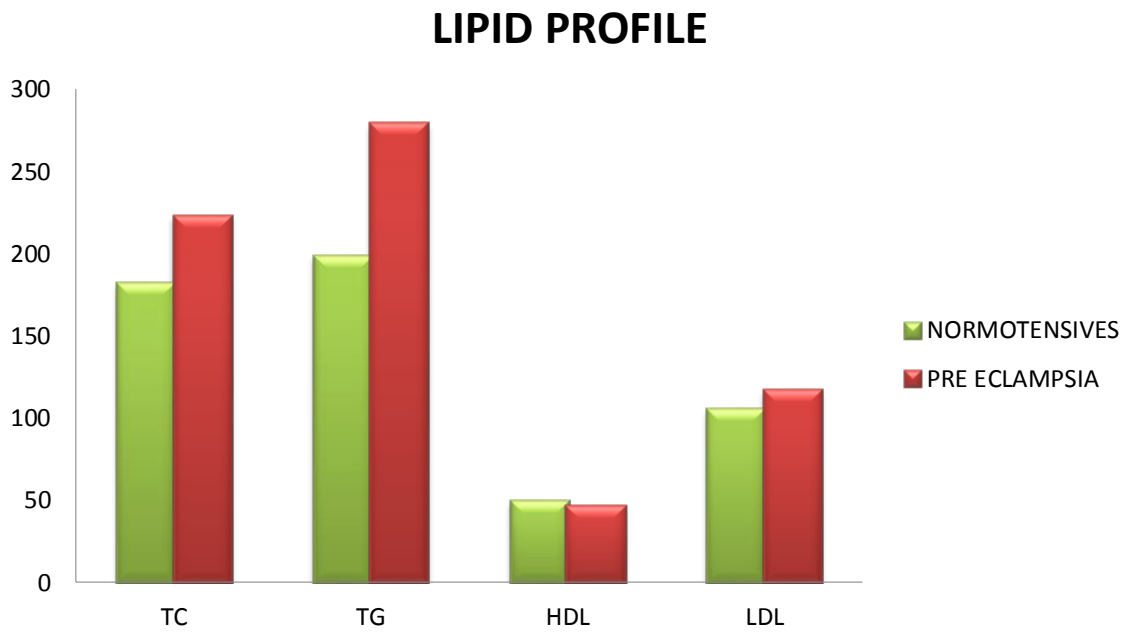


Chart 9: Depicting comparison of Lipid profile in two groups studied

Table 11: Comparison of Lipid profile in mild and severe pre eclampsia groups

Lipid parameters	Mild pre-eclampsia (Mean±SD)	Severe pre-eclampsia (Mean±SD)	p value
Total cholesterol (mg/dl)	213.13±61.02	231.35±77.67	0.364
TGL(mg/dl)	263.04±93.77	293.08±92.63	0.264
HDL(mg/dl)	48.29±12.48	43.73±10.93	0.175
LDL(mg/dl)	110.7±51.65	122.35±47.17	0.429

The lipid profile is statistically similar in both the groups. (p >0.05)

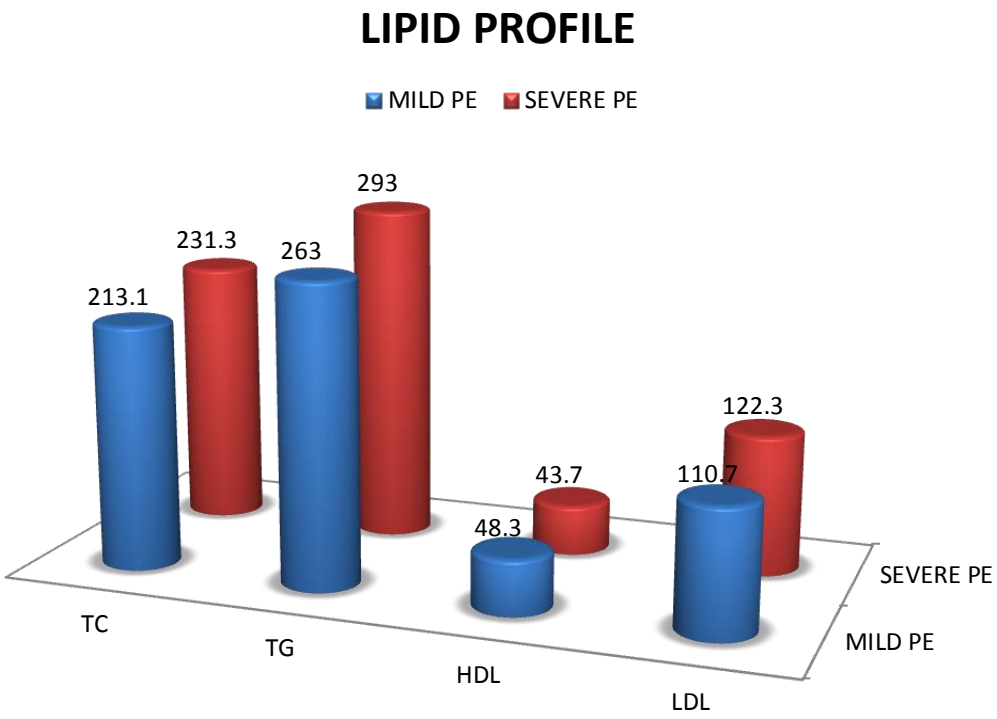


Chart 10: showing comparison of Lipid profile in mild and severe pre eclampsia groups

Table 12: Mode of delivery among the two groups studied

Mode of delivery	Normotensive Group		Pre-eclampsia Group	
	No	%	No	%
Spontaneous Vaginal	24	48	11	22
Misoprostol Induced	17	34	08	16
Forceps	00	00	01	02
Elective LSCS	02	04	00	00
Emergency LSCS	07	14	29	58
Assisted Breech	00	00	01	02
Total	50	100.0	50	100.0

The commonest mode of delivery among the normotensive group was spontaneous vaginal delivery (48%) followed by Misoprostol induced vaginal delivery (34%) and emergency LSCS (14%) In the pre eclampsia group commonest mode of delivery was Emergency LSCS (58%) followed by spontaneous vaginal delivery and Misoprostol induced vaginal delivery respectively. (22% and 16%)

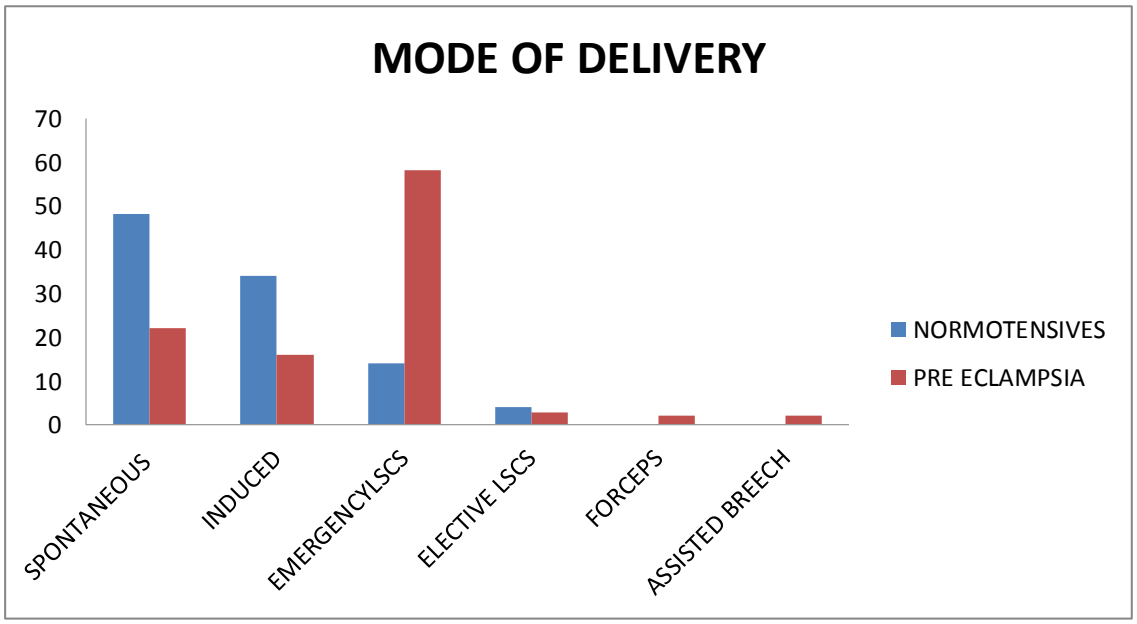


Chart 11: showing the mode of delivery among the two groups studied.

Table 13: Indication for LSCS

Indication for LSCS	Normotensive Group (n=9)		Pre-eclampsia Group (n=29)	
	No	%	No	%
APH	0	0.0	1	3.4
CPD	3	33.3	4	13.8
Failed Induction	1	11.1	0	0.0
Fetal distress	3	33.3	14	48.3
FP insufficiency	0	0.0	1	3.4
Non progression	0	0.0	1	3.4
placenta previa	1	11.1	0	0.0
Previous 2 LSCS	1	11.1	5	17.2
primary Infertility	0	0.0	1	3.4
Severe oligoamnios	0	0.0	2	6.9
Total	9	100.0	29	100.0

The commonest indication for LSCS among the normotensive group was Cephalo-pelvic disproportion and Fetal Distress (33% each) while the commonest indication among the pre eclampsia group the groups is Fetal distress (48.3%)

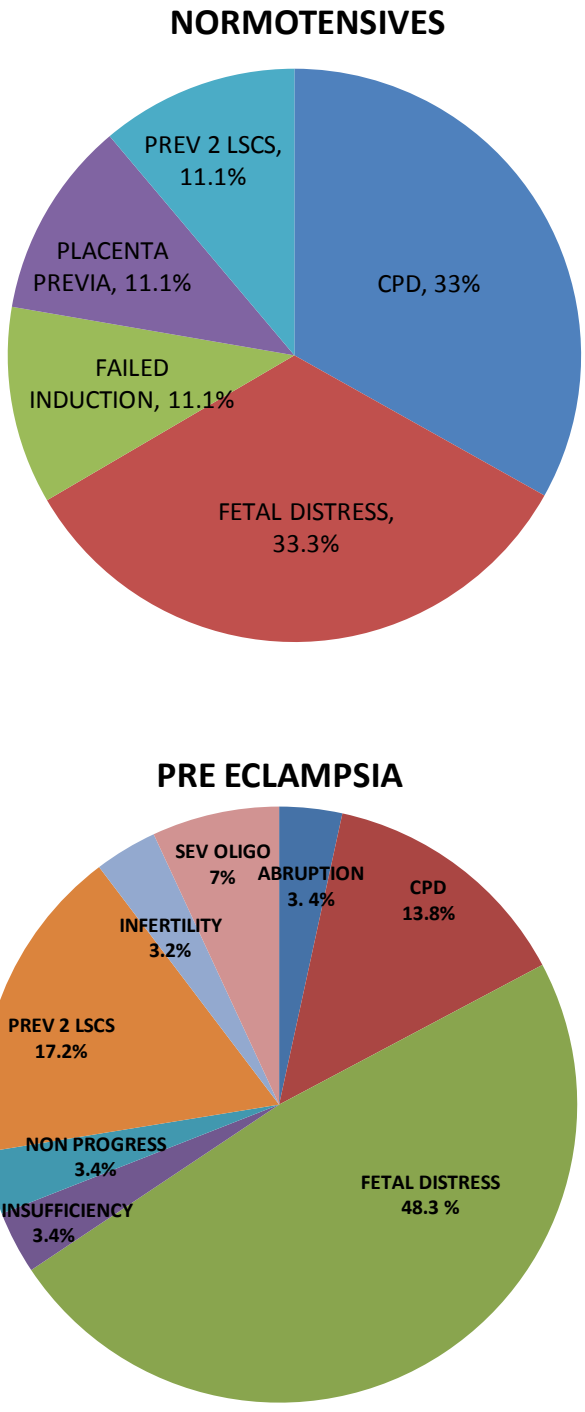


Chart 12: Pie Diagram depicting the indications for LSCS in the two groups studied.

Table 14: Fetal outcome in the groups studied

Fetal outcome	Normotensive Group		Pre-eclampsia Group	
	No	%	No	%
IUGR	4	8.0	11	22.0
Preterm	5	10.0	7	14.0
Term	41	82.0	32	64.0
Total	50	100.0	50	100.0

Majority of the babies were term in both the groups (82% and 64%) however the incidence of IUGR/Preterm is significantly associated with pre-eclmpsia (p=0.003)

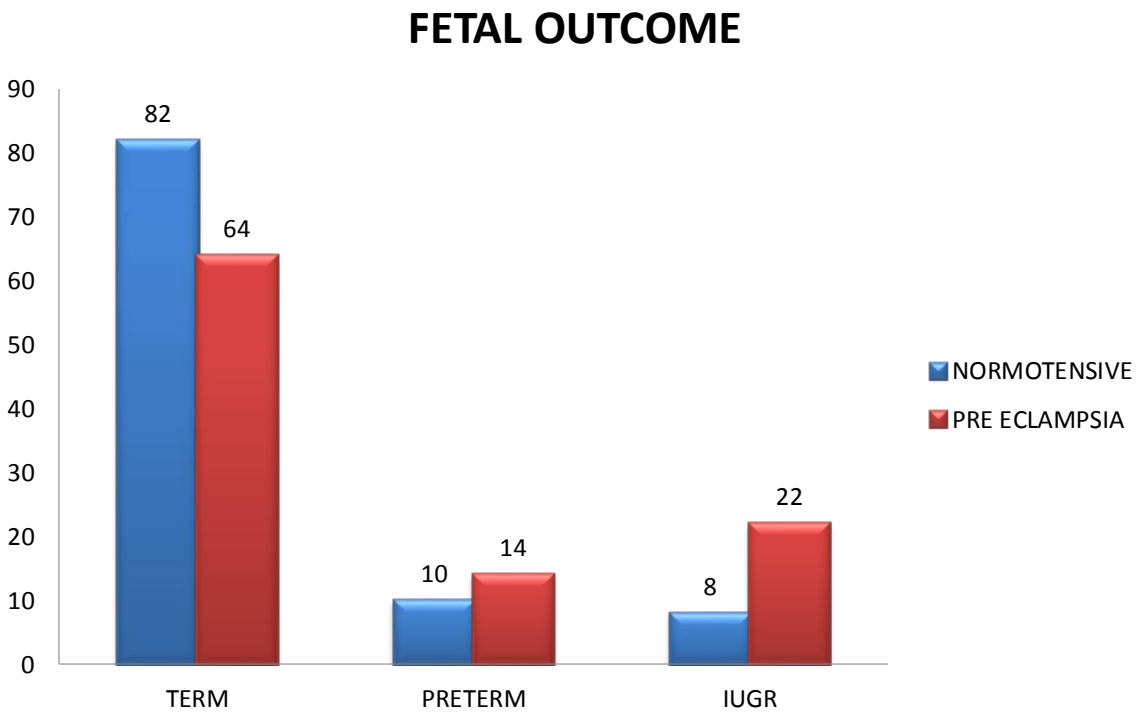


Chart 13: Bar chart showing fetal outcome among the groups studied.

Table 15: Birth weight (kg) of the neonates in the two groups studied

Weight (kg)	Normotensive Group		Pre-eclampsia Group	
	No	%	No	%
< 2.5	13	26.0	22	44.0
2.6-3.0	25	50.0	19	38.0
>3.0	12	24.0	9	18.0
Total	50	100.0	50	100.0
Mean ± SD	2.66±0.53		2.42±0.66	

Majority of the babies had birth weight between 2.6-3.0 kg in normotensive group (50%) while majority of the babies in pre eclampsia group had birth weight less than 2.5 kg. (44%)

The mean Birth weight (kg) is modestly decreased in Pre-eclampsia group (2.42±0.66) as compared to normotensive group (2.66±0.53) with p=0.048

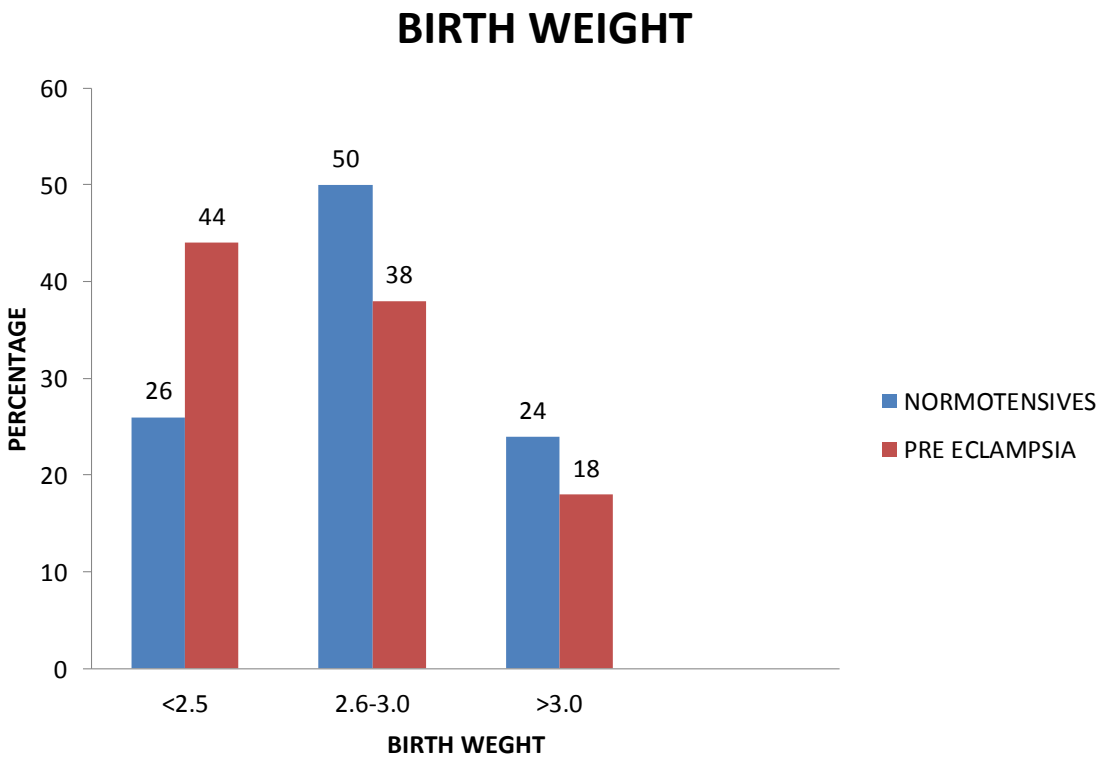


Chart 14: Birth weight (kg) of the neonate among the two groups studied

Table 16: Maternal complications among pre eclampsia patients

Maternal complications	Pre-eclampsia Group (n=50)	
	No	%
Abruption placenta	4	8.0
Eclampsia	1	2.0
Preterm labour	1	2.0
Severe Anaemia	1	2.0
Thrombocytopenia	1	2.0

The commonest Maternal complication associated with pre eclampsia was Abruptio placentae (8%) followed by eclampsia, preterm labour,, severe Anemia and thrombocytopenia.(2% each)

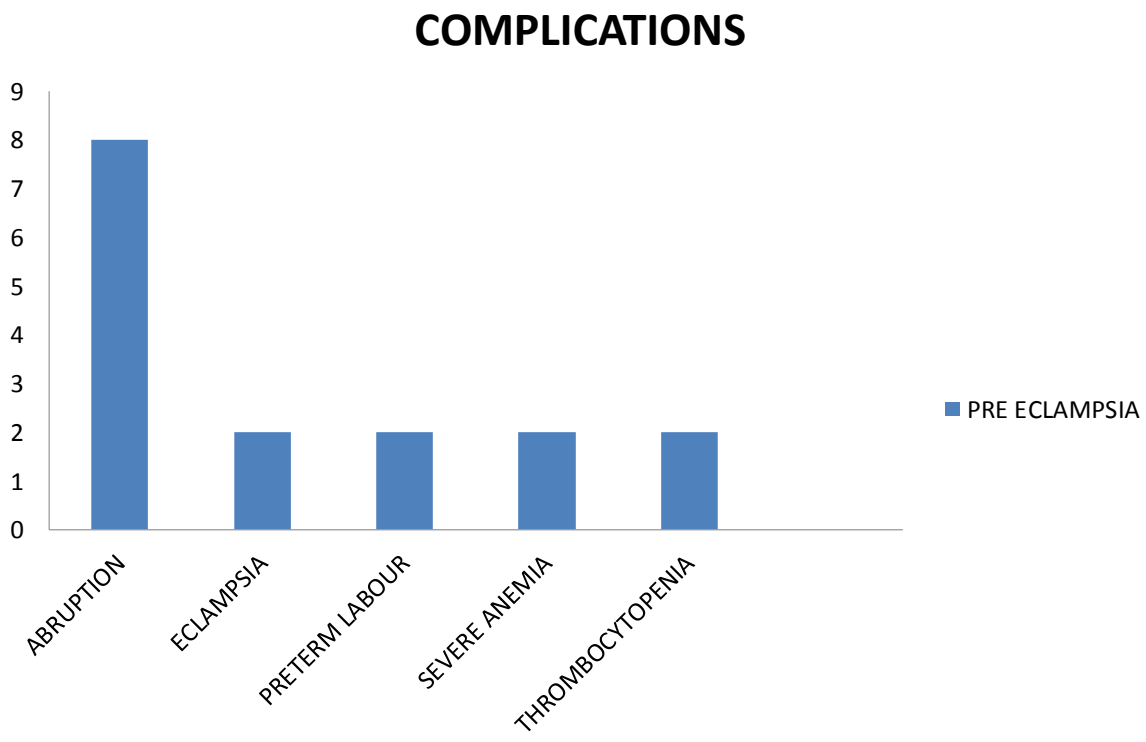


Chart 15: showing the maternal complications in pre eclampsia group.

DISCUSSION

Pre eclampsia is a syndrome of hypertension, with proteinuria and/or edema. In majority of the patients, the clinical presentation is mild, only with slight increase in blood pressure or proteins in the urine. Severe maternal and fetal complications such as the HELLP syndrome, eclampsia, preterm delivery, abruptio placenta, intra-uterine fetal death or fetal growth restriction are seen in a minority of patients.

Maternal age is one of the essential risk factors in women with Pre eclampsia. The risk of pre-eclampsia is higher when the age of pregnant women is less than 25 years. [45] In present study, majority of the patients selected were in the age group of 21-25years in both the groups comprising 56% in the control group and 40% in pre eclampsia group. However, this study did not show any statistical significance with respect to age distribution among patients. The calculated mean age among the normotensive group was 23.70±3.37 and the mean age among the pre eclampsia group was 24.08±4.69. This observation holds good in a study conducted by Procopciuc et al[46] and Basbug et al[47] where there was no statistically significant difference in the age of the patients reported.

Different case-control studies proposed that women with Pre eclampsia are two times expected to be Primiparous as women without PIH. [48, 49-53] similarly, a study from Canada reported that women with hypertensive disorders were more expected to be nulliparous in the range of 42.2% - 78.2% when matched with normotensive (41.9%) pregnant women.[54] Duckitt and Harrington (2005) found that nulliparous women are at increased risk of preeclampsia, and It is believed that this high risk is related to the maternal first exposure to chorionic villi, specifically the trophoblast, which is of fetal origin.[55] In the similar way, our study indicated about

70% were primigravida among the preeclampsia group where as 52 % were Primigravida among the controls.

As per the observation of the study, majority of the patients were in the gestational age group of 38-40 weeks belongs to 80% in the normotensive group and 64% in the pre eclampsia group. This was comparable to the study carried out by Basbug et al and Ashoor et al.[41] where they found no statistical significance between the studied groups.

The mean BMI was significantly higher in Pre-eclampsia group (P<0.005) as compared to normotensive pregnant women. This was comparable to Pasupati et al[17] where Indices of obesity such as weight and BMI were significantly increased in the pre eclampsia group as compared to the normotensive controls.

Increased BMI found in the present study could probably be due to significant increase in triglycerides because increase in weight and body mass index is associated with increase in body fats. The major modulator of this hypertriglyceridemia is hyperoestrogenaemia seen during pregnancy. Oestrogen induces hepatic biosynthesis of endogenous triglycerides, by rising the hepatic VLDL-TG synthesis and impaired LPL activity.

In the current study, the mean TSH value is significantly higher and the mean T3 and T4 values are significantly lower in the pre eclampsia group as compared to normotensive group. (p value<0.001). However the mean T3, T4 and TSH levels were similar in the mild and severe pre eclampsia groups. These findings supported the reports that pre eclamptic women had higher incidence of hypothyroidism compared to normotensive pregnant women.[16, 47, 56-59]

The decrease in the thyroid hormones with a concomitant increase in the TSH levels has been found to correlate with the severity of pre eclampsia. It has also been observed that pre eclamptic women with higher TSH and lower thyroid hormones are likely to have Small for Gestation age infants(SGA).[16 , 56] These results supported by a study conducted by Pasupati et al [17] where they concluded that higher levels of mean TSH values in pre eclampsia in comparison with control group.

In the study of Procopciuc et al (2011) preeclamptic patients were genotyped for TSH receptors and serum TSH levels and they found that TSH levels were significantly higher in preeclamptic women than in the normal pregnant women, and concluded that high TSH represent a risk factor for preeclampsia and could be correlated with its severity.

Bankowska *et al* reported that thyroid dysfunction was seen in 78.2% of pregnant women with preeclampsia. They concluded that the thyroid function tests should be performed in all pregnant women with preeclampsia[60]

In the present study, the mean total cholesterol and Triglyceride levels are significantly elevated in the pre eclampsia group as compared to the normotensive group.(P value <0.001) whereas the mean HDL and LDL values were found to be statistically non- significant. This observation differs from the study reported by Phalak et al where he showed that there was a significant rise in Serum Triglycerides, Total cholesterol and LDL-C levels and a significant decrease in HDL-C levels in cases as compared to controls.[61,62]

Earlier studies reported that the striking changes in the lipid profile in normal pregnancy is Serum hypertriglyceridemia, which may be as high as two to three folds in the third trimester over the levels in non pregnant women.[63] In our study also this observation holds true and the rise in serum triglycerides was statistically significant

(P<0.001) in pregnancy induced hypertensive patients when compared to women with normal pregnancy. The change in LDL-C cholesterol was not significant in the two groups. Our study results are similar to the study carried out by Lima et al where the preeclamptic patients had significantly higher concentrations of triglycerides than healthy women. It was also suggested that triglyceride assessment between 28 and 32 weeks could be predictive of preeclampsia.[64-67]

Several other investigators have reported that hypertriglyceridemia could be involved in the pathogenesis of hypertensive disorders during pregnancy. They also found a significant and positive association between proteinuria and triglyceride levels. These findings suggest that these lipids may be involved in the endothelial damage observed in preeclampsia patients.[68, 69]

CONCLUSION

The conclusion of the present study is that pre eclampsia patients have a significantly higher levels of TSH and low levels of T3 and T4 in comparison to normotensive pregnant women. However, the changes in the thyroid hormones did not correlate with the severity of preeclampsia, since there was no statistical significance observed between mild and severe pre eclampsia groups.

Dyslipidemia is more pronounced and found statistically significant in pre eclampsia group than in the normotensive group. The lipid parameters between these groups evincing possible atherogenic potential. This association may be useful in understanding the pathologic processes of preeclampsia. Thus, estimation of lipid profile may have a predictive role in the assessment of the extent of endothelial damage in preeclampsia and may help by preventing or foreseeing the complications of pre-eclampsia.

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SUMMARY

The present study entitled "***A study of maternal thyroid hormone status and lipid profile in pre eclampsia"*** was conducted at R.L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar from January 2012 to June 2013. This study consists of 100 cases, of which fifty were pre-eclampsia cases and another fifty were normotensive pregnant women.

Based on the results of the study it can be summarized that:

- Majority of the patients selected were in the age group of 21-25years in both the groups and the incidence of pre eclampsia was more among the Primigravida. (70% were Primigravida among the preeclampsia group as compared to 52% in the normotensive pregnant women)
- The mean BMI was significantly higher in Pre-eclampsia group ($p<0.005$) as compared to normotensive pregnant women.
- The Thyroid hormone levels were compared between the preeclampsia and normotensive group. Pre eclamptic patients have higher incidence of hypothyroidism compared to normotensive pregnant women. However, it does not correlate with the severity of pre eclampsia.
- The findings of the current study suggest an abnormal lipid metabolism, particularly high triglycerides and cholesterol in the pre eclampsia group which may contribute to promotion of oxidative stress and vascular dysfunction seen in preeclampsia. It is, therefore, imperative that blood lipid concentrations be evaluated in pregnant women during antenatal care since it could be helpful in the early detection and prevention of pre eclampsia.

- Prematurity and IUGR was significantly associated with pre eclampsia group when compared to normotensive pregnant women and the Mean Birth weight was significantly lower among the pre eclampsia group.
- Complications like abruption placenta, eclampsia, severe anemia and thrombocytopenia were noted among the pre eclampsia group.

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ANNEXURE-1

PROFORMA

- Name: I.P. No:
- Age: D.O.A:
- Occupation: D.O.D:
- Address:
- Husband's Occupation:
- Socio-economic Status:
- History of presenting illness:
  - Menstrual history: LMP- EDD-

    POG-

    Age of menarche:

    Past menstrual history:
- Obstetric history:

    ML: Consanguinity:

    Details of previous pregnancy:

    Details of Present pregnancy:
- Past history: Any Medical illness/ Previous Surgeries/renal disease/thyroid disease
- Drug History:
- Family History:
- Personal History:
-

Sleep: Appetite:

Diet: Bowel & Bladder:

- G.P.E:
- Build: Nourishment:
- Pallor: Icterus: Cyanosis: Clubbing: Lymphadenopathy: Pedal edema:

- Pulse: B.P.: Temp: RR:
- Breast: Thyroid: Spine:
- Systemic examination:

  CVS:

  RS:

  CNS:

  Abdominal Examination:

- Local Examination:

  External Genitalia:

  P/S: P/V:

- Investigations:

  Hb%: TC: Bl. GRP & Rh TYPING:

  PCV : RBC : PLT COUNT :

  HIV/HBSAG/VDRL : BT: CT:

Urine Examination

Random blood sugar:

- Blood urea: Serum creatinine: S.Uric acid:
- LFT :

PT : APTT : INR : Ratio :

- Obstetric Ultrasound :

- T3:
- T4:
- TSH:
- Serum lipid profile:
- Diagnosis:

KEY TO MASTER CHART

BMI Body Mass Index

TC Total Cholesterol

TG Triglycerides

HDL High Density Lipoprotein

LDL Low Density Lipoprotein

Del Delivery

Indn Indication

BW Birth Weight

Em LSCS - Emergency lower segment caesarean section

SVD – Spontaneous vaginal delivery

IUGR - Intra uterine growth restriction.

KG – Kilograms

LSCS - Lower segment caesarean section

Primi – Primigravida

Wks – weeks

Yrs – Years

BP- Blood Pressure

Admn- Admission

MIVD- Misoprostol Induced Vaginal Delivery

Elect LSCS - Elective LSCS

Sl.No	Hosp No	Name	Age	Parity	Gest age	Bld pressure	BMI	T3 ng/ml	T4 mcg/dl	TSH mcIU/ml	TC mg/dl	TG mg/dl	HDL mg/dl	LDL mg/dl	mode of del	Ind for CS	fetal outcome	weight(KG)	maternal complications
1	823864	Bharati	32yrs	G2P1L1	term	110/70	23	1.24	11.6	1.47	170	291	40	72	SVD		TERM	3.2	
2	788064	Mubasheera	28yrs	G3A2	term	120/80	22	0.8	5.53	4.49	249	200	35	174	MIVD		TERM	3.1	
3	788160	Vidyashree	21yrs	primi	term	110/70	21	1.68	13.3	1.43	252	199	63	149	MIVD		TERM	2.8	
4	790476	Zaiba	18yrs	primi	30wks	120/80	22	1.55	13.7	2.32	244	237	66	131	SVD		preterm	1.2	
5	788415	Shabana taj	22yrs	primi	32wks	110/70	21	1.3	6.98	4.68	186	160	56	98	MIVD		IUGR	1.4	
6	773886	Lakshmi	20yrs	primi	term	120/80	23	1.09	16.2	0.899	198	203	40	117	Em LSCS	Fetal distress	TERM	2.61	
7	779253	Kalavathi	25yrs	G3P2L1D1	term	110/70	21	1.68	11.2	2.46	221	222	38	138	Em LSCS	Prev 2 Lscs	TERM	2.9	
8	793099	Haseena	22yrs	G4P3L3	term	120/70	23	1.13	8.81	1.41	167	189	43	86	SVD		TERM	2.1	
9	817823	Sabiha	32yrs	G4P2L2A1	term	110/80	21	1.66	15.3	2.58	243	189	49	157	SVD		TERM	2.6	
10	795030	Meena	21yrs	primi	term	120/70	22	1.71	9.66	1.9	278	303	58	159	SVD		TERM	3	
11	832274	Deepa k j	20yrs	primi	term	130/80	21	1.77	9.15	0.779	185	165	61	91	SVD		TERM	2.75	
12	823569	Jayanthi	20yrs	primi	term	120/70	22	1.76	13.6	3.6	181	132	50	105	SVD		TERM	2.8	
13	866203	Pavithra	28yrs	G2P1L1	term	110/80	21	1.51	9.4	1.66	189	206	32	114	Elect LSCS	CPD	TERM	2.71	
14	860803	Salma	28yrs	G3P1L1A1	term	120/70	22	1.81	15.1	3.36	192	152	64	97	Em LSCS	CPD	TERM	3	
15	890363	Radha	25yrs	primi	term	110/80	21	1.29	14.3	1.16	261	290	60	143	SVD		TERM	2.9	
16	890362	Shwetha	23yrs	G2P1L1	term	120/80	24	1.76	7.82	3.65	152	147	38	85	SVD		TERM	2.6	
17	895320	Akshatha	25yrs	primi	term	120/70	21	1.8	9.82	2.71	221	289	37	126	MIVD		IUGR	1.5	
18	880703	Veena	23yrs	primi	term	120/80	23	2.34	15.4	2.12	219	192	56	124	SVD		TERM	3.03	
19	895309	Geetha	20yrs	G2A1	term	100/70	21	1.34	13.4	2.7	145	159	53	60	MIVD		TERM	2.8	
20	866270	Poorna	22yrs	primi	term	120/70	20	1.6	15.2	2.18	215	228	45	124	Elect LSCS	placenta previa	TERM	2.7	
21	897587	Heena kousar	25yrs	G3P2L2	term	120/80	21	1.09	11.4	2.22	132	145	46	91	SVD		TERM	2.8	
22	898311	Bhavya	23yrs	primi	term	110/80	24	2.39	9.86	2.56	114	216	39	31	Em LSCS	Failed Indctn	TERM	3.2	
23	898619	Rajani	25yrs	G3P1L1D1	term	110/70	21	1.33	9.27	0.79	220	134	78	115	SVD		IUGR	1.27	
24	880875	Shilpa	20yrs	G3P2L2	term	120/70	20	1.74	13	2.54	232	173	83	115	SVD		TERM	2.75	
25	900199	Shanti	24yrs	primi	36wks	120/70	21	1.74	16.2	6.39	181	160	54	96	MIVD		TERM	2.3	
26	900977	Sunanda	28yrs	primi	term	100/70	23	2.04	16	2.28	232	184	61	134	MIVD		TERM	2.63	
27	858756	Hemavati	29yrs	G2P1L1	36wks	120/70	21	1.39	12.2	1.67	208	257	31	125	MIVD		preterm	2.6	
28	857877	Anitha	23yrs	primi	PDP	120/80	23	1.53	9.11	1.38	210	189	50	122	MIVD		TERM	2.6	
29	856059	Aruna	25yrs	G2P1L1	term	110/70	22	1	9.07	1.68	168	209	35	92	Em LSCS	Fetal distress	IUGR	2.1	
30	825511	Sunitha	25yrs	primi	term	130/80	21	1.26	11.1	2.88	170	291	40	72	MIVD		TERM	3.5	
31	793089	Shobha	20yrs	primi	term	110/70	23	0.94	6.32	0.84	202	225	49	108	MIVD		TERM	3.1	
32	874169	Ayesha Banu	20yrs	primi	35wks	120/80	21	1.67	19.4	4.9	155	198	56	109	SVD		TERM	2.5	
33	905231	Pavithra	22yrs	primi	term	120/70	23	1.49	7.26	4.96	116	209	54	112	SVD		TERM	2.4	
34	877718	Usha	25yrs	primi	term	110/70	21	2.09	11.4	1.85	178	150	46	87	SVD		TERM	2.8	
35	844386	Shwetha	21yrs	G2P1L1	term	120/80	23	2.19	10.7	1.83	114	198	43	132	MIVD		TERM	3.1	
36	899515	Nethra	23yrs	primi	term	110/70	22	1.77	13.4	3.27	154	178	48	94	MIVD		TERM	2.6	
37	899760	Lakshmi	23yrs	G2P1D1	term	100/70	20	1.73	12.1	2.57	178	153	54	87	MIVD		TERM	2.75	
38	899928	Bhagyamma	28yrs	G2P1L1	PDP	130/80	22	1.1	9.07	0.72	150	178	65	112	SVD		TERM	3.2	
39	859863	shylaja	27yrs	G2P1L1	term	120/70	21	1.59	9.72	2.88	119	167	56	123	SVD		TERM	3.3	
40	905022	Shyamala	25yrs	primi	term	120/70	23	2	16.9	2.83	145	258	42	52	MIVD		TERM	2.49	
41	908094	Bhavani	20yrs	G2A1	32wks	110/70	21	1.22	13.1	1.67	115	84	40	58	SVD		preterm	1.8	
42	917865	Saraswati	30yrs	G3P1D1A1	33wks	100/70	23	1.28	8.32	3.05	143	243	26	69	Em LSCS	Fetal distress	preterm	2.1	
43	911860	Kamala	20yrs	primi	term	110/70	21	1.44	1.36	4.26	239	215	45	151	MIVD		TERM	3.5	
44	898234	Varalakshmi	25yrs	G3A2	36wks	100/70	20	1.45	14.3	2.45	162	247	40	74	SVD		preterm	2.2	
45	907739	Chandrakala	23yrs	primi	term	120/80	21	2.64	21	3.69	203	292	58	87	SVD		TERM	2.8	
46	916653	Gousiya Begum	20yrs	G2P1L1	term	120/80	22	1.44	10.5	2.69	123	154	46	94	Em LSCS	CPD	TERM	3	
47	918819	Prabhavathi	21yrs	primi	term	110/70	23	1.43	7.19	1.61	154	201	56	87	SVD		TERM	2.9	
48	902016	Aruna	25yrs	G2P1L1	term	120/70	21	1.03	11.1	1.22	132	165	43	84	MIVD		TERM	2.4	
49	907427	Kalpana	20yrs	primi	term	120/80	23	1.71	10.9	1.15	112	132	54	98	SVD		TERM	3.3	
50	907388	Susheela	25yrs	G2P1L1	term	110/70	21	1.53	13.8	1.98	152	147	50	84	SVD		TERM	3.1	