A DISSERTATION ON PREVALENCE OF HYPOTHYROIDISM IN PREGNANCY AND PREGNANCY OUTCOME

Dissertation Submitted to

The Tamil Nadu Dr. M.G.R. Medical University Chennai

In partial fulfillment of the regulations for the

award of the degree of

M.S. OBSTETRICS AND GYNAECOLOGY

DEPARTMENT O F OBSTETRICS AND GYNAECOLOGY

CHENGALPATTU MEDICAL COLLEGE

CHENGALPATTU

TAMILNADU, INDIA

APRIL 2016

DECLARATION

I hereby declare that this dissertation entitled **"A DISSERTATION ON PREVALENCE OF HYPOTHYROIDISM IN PREGNANCY AND PREGNANCY OUTCOME"** was prepared by me under the direct guidance and supervision of **Prof. DR.NESAM SUSANNA MINNALKODI M.D(OG)** CHENGALPATTU MEDICAL COLLEGE. The dissertation is submitted to the Dr. M.G.R. Medical University in partial fulfillment of the University regulations for the award of MS degree in Obstetrics and Gynaecology Examination to be held in April 2016.

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CERTIFICATE

This is to certify that **Dr.R. MARY STELLA** postgraduate student (2013-2016) in the department of Obstetrics and Gynaecology, CHENGALPATTU MEDICAL COLLEGE has done this dissertation titled **"PREVALENCE OF HYPOTHYROIDISM IN PREGNANCY AND PREGNANCY OUTCOME"** under the direct guidance and supervision of guide Prof .DR.NESAM SUSANNA MINNALKODI in partial fulfillment of the regulations laid down by the **Tamilnadu Dr.M.G.R. Medical University**, Chennai, for M.S., Obstetrics and Gynaecology Degree Examination.

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Lastly, I thank the ethics committee for permitting me to do this study and more importantly I thank all my patients involved for their kind help and co operation.

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Mary Stella R,
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Chengalpattu Medical College,
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2. Patient information sheet and informed consent form in English and / or vernacular language.
3. Investigators Brochure, dated _____version
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Biological Scientist

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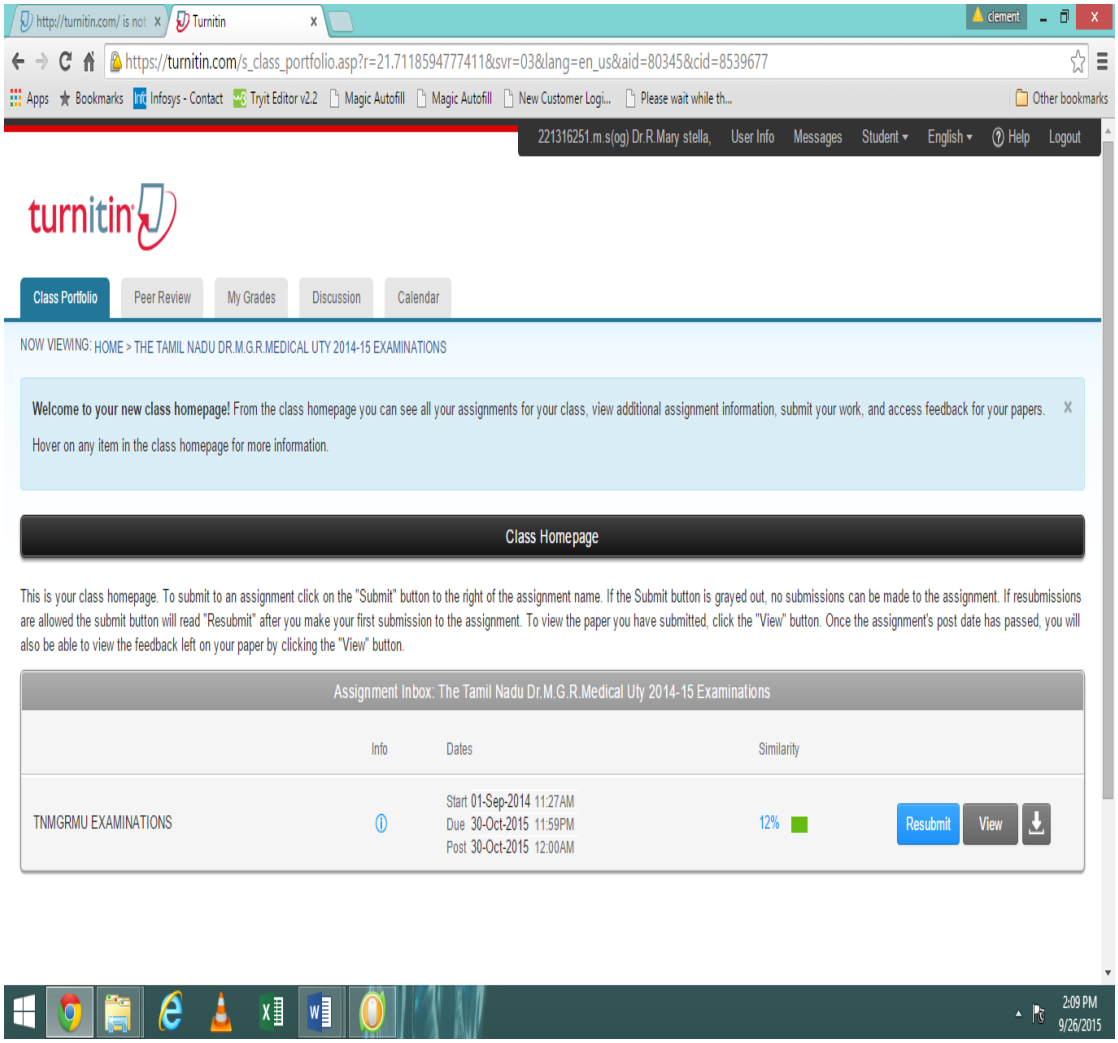
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LIST OF ABBREVATIONS

TSH	Thyroid Stimulating Hormone
T3	Tri iodo tyronine
T4	Tetra iodo tyronine
HCG	Human Chorionic Gonadotropin
Wks	Weeks
PIH	Pregnancy induced hypertension
IUGR	Intra uterine growth restriction
NVD	Normal vaginal delivery
LSCS	Lower segment caesarean section
PPROM	Preterm premature rupture of membranes
PROM	Premature rupture of membranes
LBW	Low birth weight
Rx	Treatment
GDM	Gestational diabetes mellitus
HTN	Hypertension
PPH	Post partumhaemorrage

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ABSTRACT

AIM: To study the prevalence of hypothyroidism in pregnancy and the pregnancy outcome in those pregnancies.

OBJECTIVES: To study the prevalence of hypothyroidism in pregnancy and pregnancy outcome.

DESIGN OF STUDY: A Prospective study.

PERIOD OFSTUDY: 1 Year.

MATERIALS AND METHODS: This study involves screening 1000 consenting eligible women during first trimester. The normal patients will serve as controls. The patients were classified as euthyroid, hypothyroid and hyperthyroid based on their TSH levels. Those with deranged TSH levels underwent T4 testing and they were further divided in to subclinical and overt hypothyroid patients these patients formed the study group. They were treated and followed up till the completion of their pregnancy. They underwent TSH testing at 16, 20 and 32 weeks their response to treatment and pregnancy outcome was noted and results analysed.

CONCLUSION:

Inadequately treated hypothyroid women in my study group had 3 fold higher risk of developing preeclampsia.There was a significant increase in the incidence of

abortion or fetal growth restriction in the inadequately treated group.

There was no case of placental abruption in my study group. Oligohydramnios was found to occur more commonly in the inadequately treated group.Adequate treatment of hypothyroidism in pregnancy significantly reduces certain complications like miscarriages, pre eclampsia, IUGR ,oligohydramnios, glucose intolerance, preterm labour, low birth weight babies, abruptio Placentae and stillbirth.

INTRODUCTION

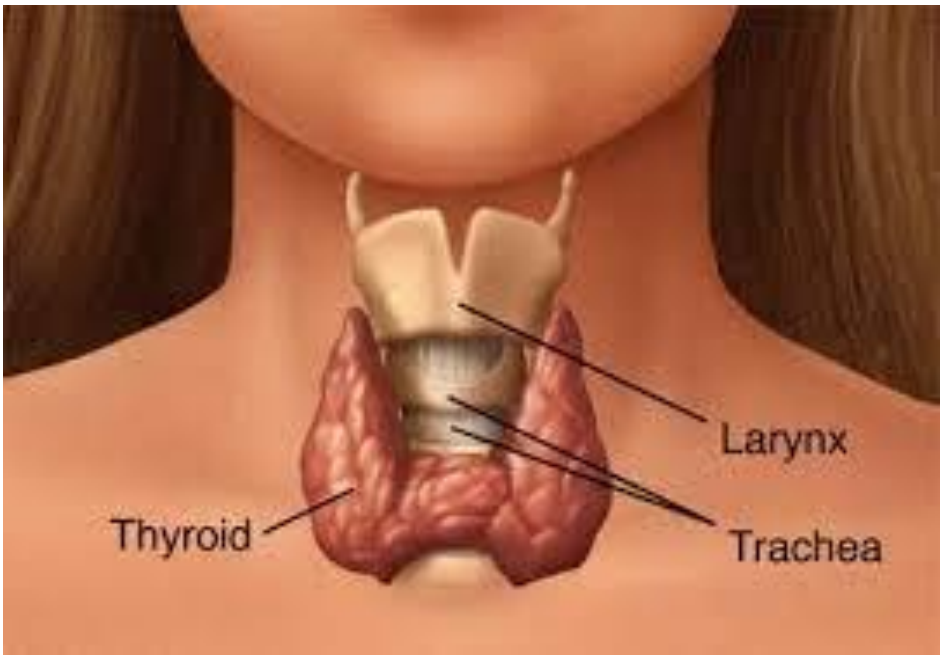

Figure 1.

The second most common endocrinological disorder in pregnancy is thyroid dysfunction. The most common cause of hypothyroidism is primary abnormality in thyroid. In some cases it is also caused by hypothalamic dysfunction. In antenatal women most common causes are hashimotos thyroiditis ,iodine deficiency, radio active iodine therapy and surgical removal of thyroid.

The commonest cause of hypothyroidism is iodine deficiency. Hashimotos thyroiditis is the commonest cause in the developed countries. The incidence of overt hypothyroidism is 0.3 to 0.5% and subclinical hypothyroidism 2-3%. Thyroid hormone is crucial for

normal development of placenta, neuronal Migration. Auto immune thyroiditis commonly occurs during the first postpartum yeDIar it can present with hypothyroidism or thyrotoxicosis following which patient may develop hypothyroidism.

Thyroid hormone is essential for the normal development of the placenta. There is evidence that preeclampsia, placental abruption and preterm labour are all causatively linked to faulty early placentation.

Thyroid hormone is important for normal neuronal migration, synaptic transmission and myelination during the early stages of neurodevelopment.

The only assumed physiological role of iodine is in thyroid hormone synthesis. Severe iodine deficiency which causes hypothyroidism is associated with increased incidence of decreased intelligence, congenital anomalies of the fetus and cretinism. Intra uterine growth restriction and fetal distress are more commonly seen in women with significant hypothyroidism.

Starting thyroxine treatment in the 1sttrimester(preferably prenatally) may decrease the incidence of complications. Starting treatment after completion of 1st trimester will not eliminate already established fetal neuro developmental delay, as during the first trimester

the fetus depends completely on maternal thyroid hormone for the normal brain development.

Many changes occur in thyroid physiology during pregnancy. The cutoff values are changed during pregnancy for the diagnosis of hypothyroidism. The symptoms and signs also common for both the conditions. Severe hypothyroidism pregnancy is not common because most of these women are infertile and they also have increased rates of abortions.

Not much studies available to see if early thyroxine supplementation and adequate treatment reduces the incidence of complications in pregnant woman with hypothyroidism.

My study is to see if diagnosed early and adequately treated hypothyroid women are able to reduce the complications like spontaneous miscarriages, preeclampsia, preterm labour, IUGR, still birth, low birth weight babies.

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REVIEW OF LITERATURE

Historical background:

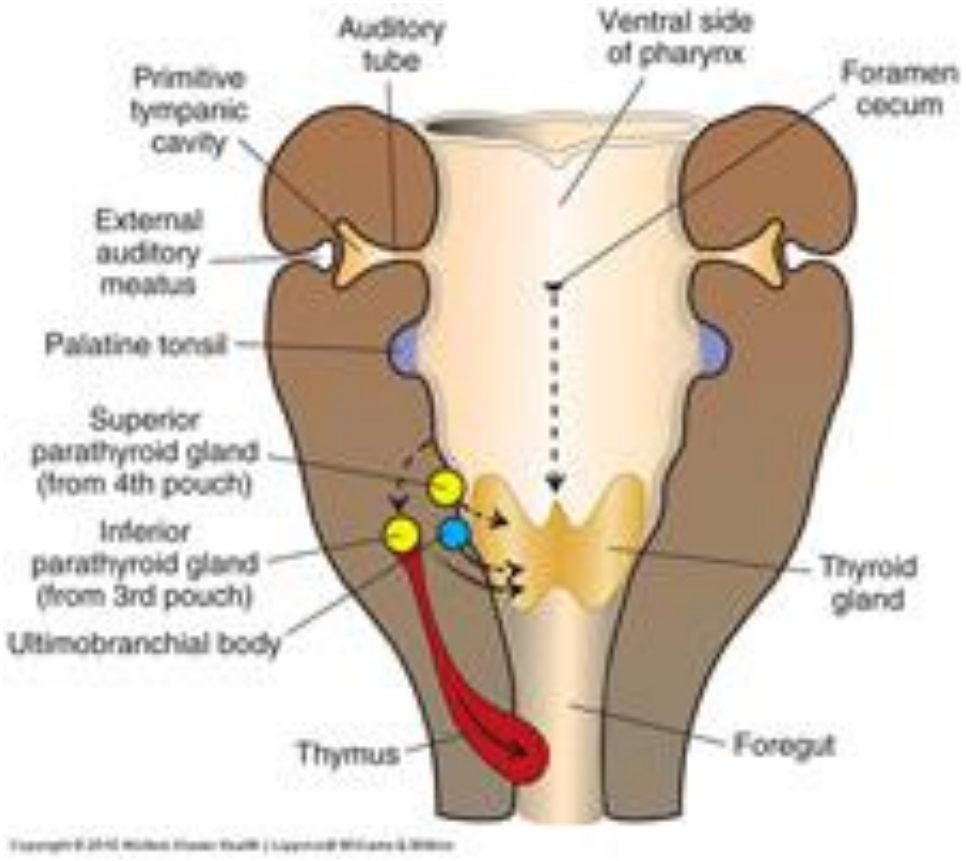
In 2700 BC, Goitres (Latin- guttur), defined as enlargement of the thyroid gland. The one who coined thyroid gland (Greek- thyroeides, shield shaped) is Thomas Wharton in the year 1656.

Thyroid gland has many functions ranging from acts as a reservoir of blood to supply the brain to decorating the women's neck. Once Seaweed was considered as a treatment for goitre. Kocher was awarded Nobel Prize in 1909, for his great work on the pathology, and surgery of the thyroid gland.

In 1874, William Gull, Governor of Guy's Hospital, described myxedema and he called it as "cretinous state in the adult"., Dr. Dawtrey Drewitt in 1883,presented a casein the clinical society of London,with the classical symptoms of hypothyroidism. In 1891 George redmayne described the treatment of hypothyroidism with thyroid extract.

Embryology

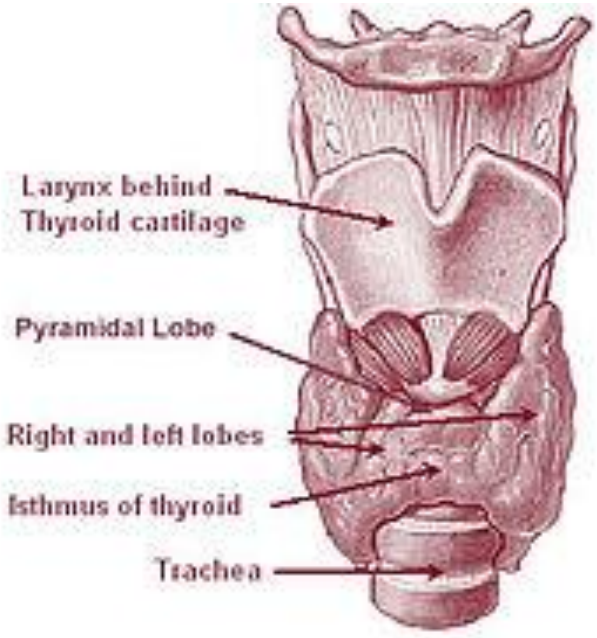
The thyroid gland arises as a primitive out pouching of primitive foregut around the third week of gestation. The thyroid gland originates at the base of tongue near the foramen caecum.



The pharyngeal anlage endodermal cells thicken to form the medial anlage of thyroid. It descends in the neck anterior to the hyoid bone the thyroglossal duct connects the median thyroid anlage to foramen caecum. From the epithelial cells of the thyroid anlage the thyroid follicle cells arises.

The paired lateral analages arises from the 4th brachial pouch and fuses with the medial thyroid anlage. They are neuroectodermal in origin and they secrete calcitonin. By 11th week of gestation colloid formation begins from the thyroid follicle.

Thyroid anatomy:



The thyroid gland is a butterfly-shaped organ and is composed of two cone-like lobes or wings, *lobusdexter* (right lobe) and *lobus sinister*(left lobe), connected via the isthmus. Each lobe is about 5 cm long, 3 cm wide and 2 cm thick. The organ is situated on the anterior side of the neck, lying against and around the larynx and trachea, reaching posteriorly the oesophagus and carotid sheath. It starts cranially at the oblique line on the thyroid cartilage (just below the laryngeal prominence, or 'Adam's Apple'), and extends inferiorly to approximately the fifth or sixth tracheal ring.[2]

It is difficult to demarcate the gland's upper and lower border with vertebral levels because it moves position in relation to these during

swallowing. There is occasionally (28%-55% of population, mean 44.3%)[3] a third lobe present called the **pyramidal lobe** of the thyroid gland. It is of conical shape and extends from the upper part of the isthmus, up across the thyroid cartilage to the hyoid bone. The pyramidal lobe is a remnant of the fetal thyroid stalk, or thyroglossal duct.[4] It is occasionally quite detached, or may be divided into two or more parts. The pyramidal lobe is also known as **Lalouette's pyramid**.[5]

The thyroid gland is covered by a thin fibrous sheath, capsulaglandulaethyreoideae, composed of an internal and external layer. The external layer is anteriorly continuous with the pretracheal fascia and posteriorolaterally continuous with the carotid sheath. The gland is covered anteriorly with infrahyoid muscles and laterally with the sternocleidomastoid muscle also known as sternomastoid muscle.

On the posterior side, the gland is fixed to the cricoid and tracheal cartilage and cricopharyngeus muscle by a thickening of the fascia to form the posterior suspensory ligament of thyroid gland also known as Berry's ligament. The thyroid gland's firm attachment to the underlying trachea is the reason behind its movement with swallowing.[8] In variable extent, the pyramidal lobe is present at the most anterior side of the lobe. In this region, the recurrent laryngeal nerve and the inferior thyroid artery pass next to or in the ligament and tubercle.

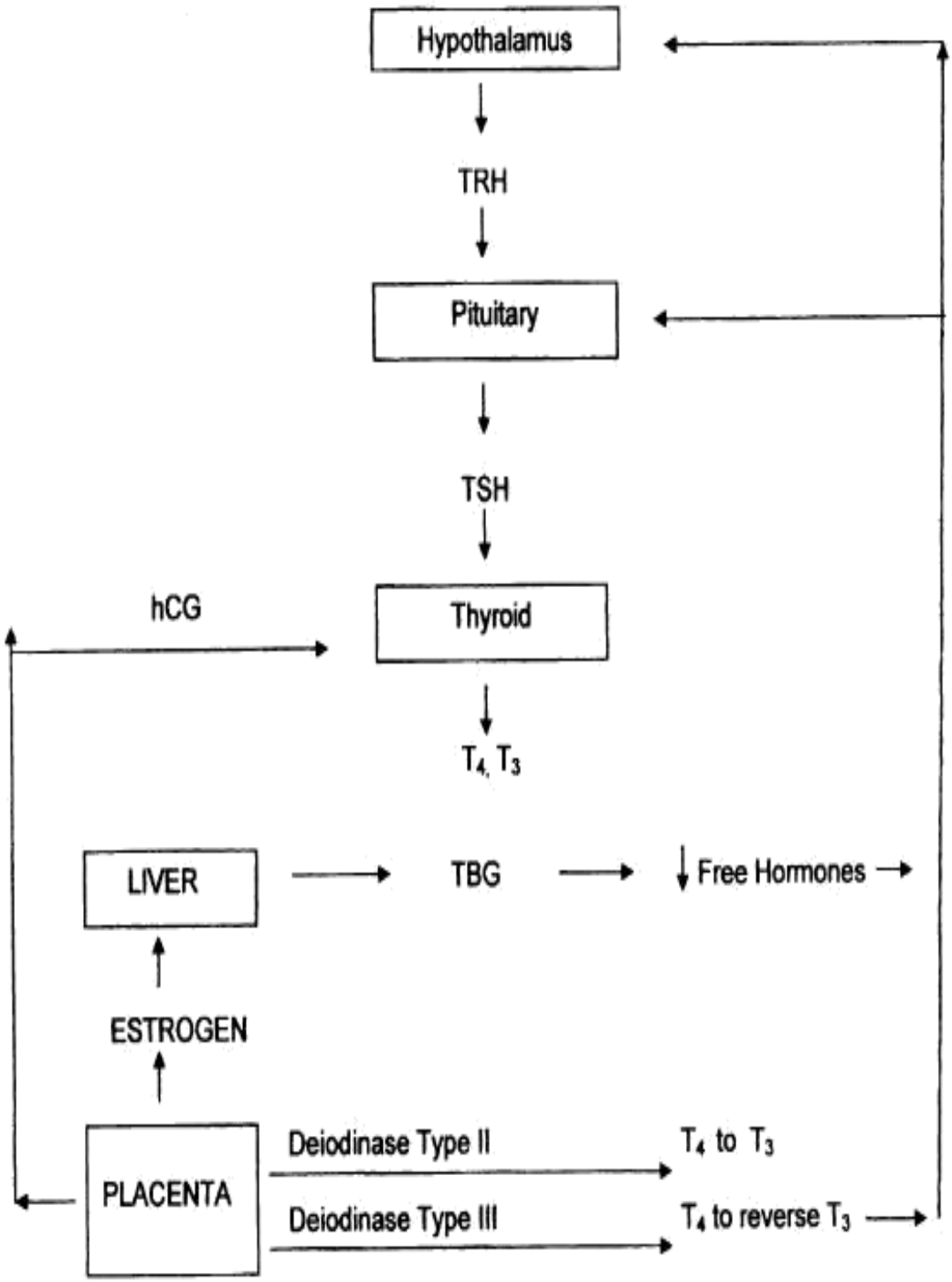
Between the two layers of the capsule and on the posterior side of the lobes, there are on each side two parathyroid glands.The thyroid isthmus is variable in presence and size, can change shape and size, and can encompass the pyramidal lobe (*lobus* or*processuspyramidalis*. The thyroid is one of the larger endocrine glands, weighing 2-3 grams in neonates and 18-60 grams in adults, and is increased in pregnancy.

In a healthy person the gland is not visible yet can be palpated as a soft mass. Examination of the thyroid gland includes the search for abnormal masses and the assessment of overall thyroid size.[9]

The thyroid is supplied with arterial blood from the superior thyroid artery, a branch of the external carotid artery, and the inferior thyroid artery, a branch of the thyrocervical trunk, and sometimes by the thyroid ima artery, branching directly from the subclavian artery. The venous blood is drained via superior thyroid veins, draining in theinternal jugular vein, and via inferior thyroid veins, draining via the *plexus thyreoideusimpar* in the left brachiocephalic vein.

Lymphatic drainage passes frequently the lateral deep cervical lymph nodes and the pre- and paratracheal lymph nodes. The gland is supplied by parasympathetic nerve input from the superior laryngeal nerve and the recurrent laryngeal nerve.

Thyroid physiology Iodine metabolism and increased Iodine requirement during pregnancy



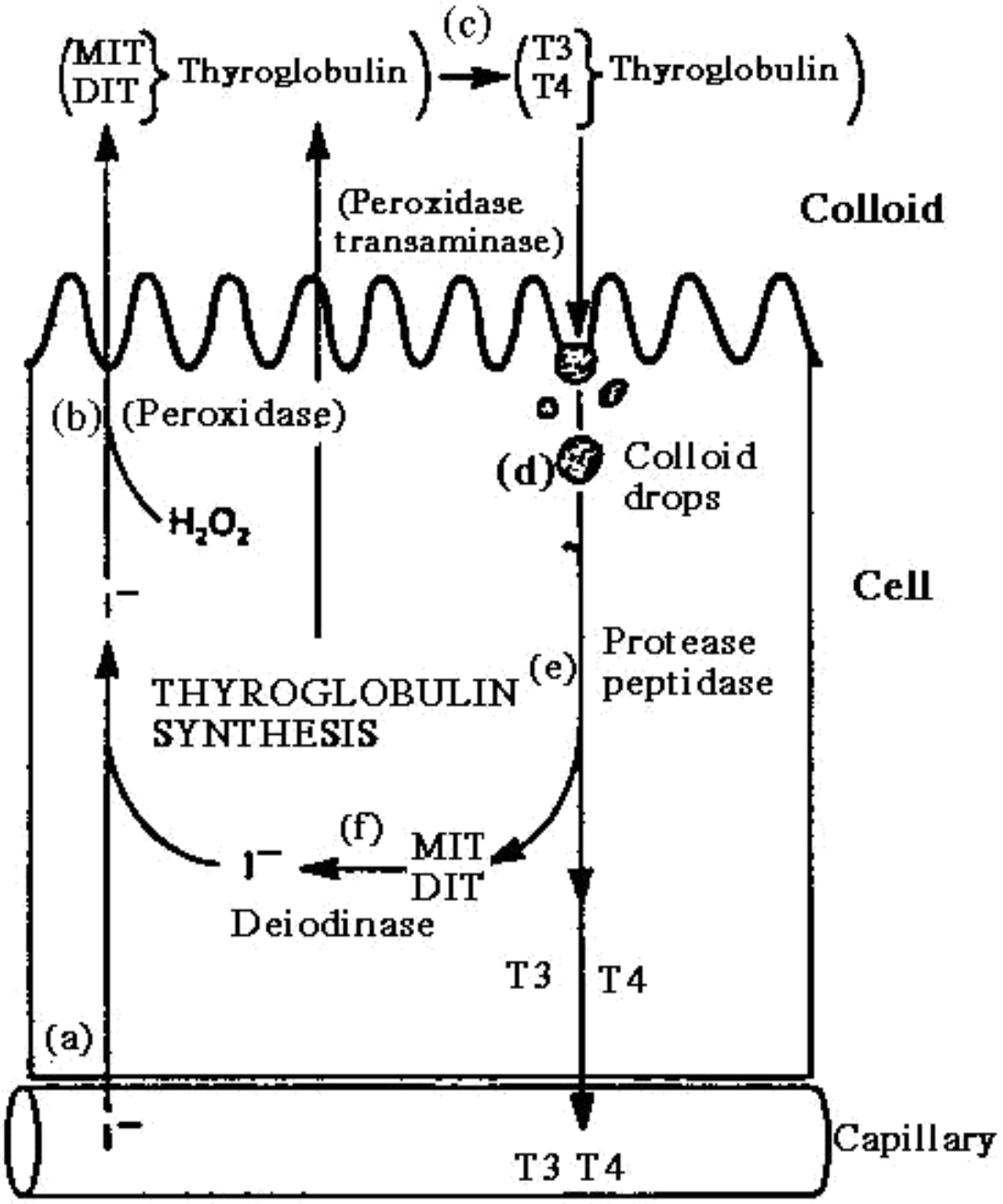
The recommended daily intake of iodine is 0.1mg. Milk, fish, eggs and salt fortified with iodine are rich sources of iodine. Iodine is converted rapidly to iodide in the stomach and jejunam. And absorbed into the blood . By an ATP dependent process iodide actively enters the thyroid follicular cells . Nearly 90% of body's iodine is stored in the thyroid. The excess iodine is excreted via the kidneys.

A daily intake of 250mcg of iodine for antenatal and lactating women is recommended by WHO because the raise in thyroid hormone production during pregnancy requires an equal increase in the availability of iodine.

Placental deiodinase (D3) removes iodine from T4 & T3 produces inactive iodothyronines and reverse T3.It also prevents much amounts of T4 from crossing the placenta .Raised GFR with raised urinary clearance of iodine accounts for increased demand for iodine during pregnancy. Though fetal thyroid starts developing by 12 wks of pregnancy, it cannot concentrate iodine till 20 wks of pregnancy

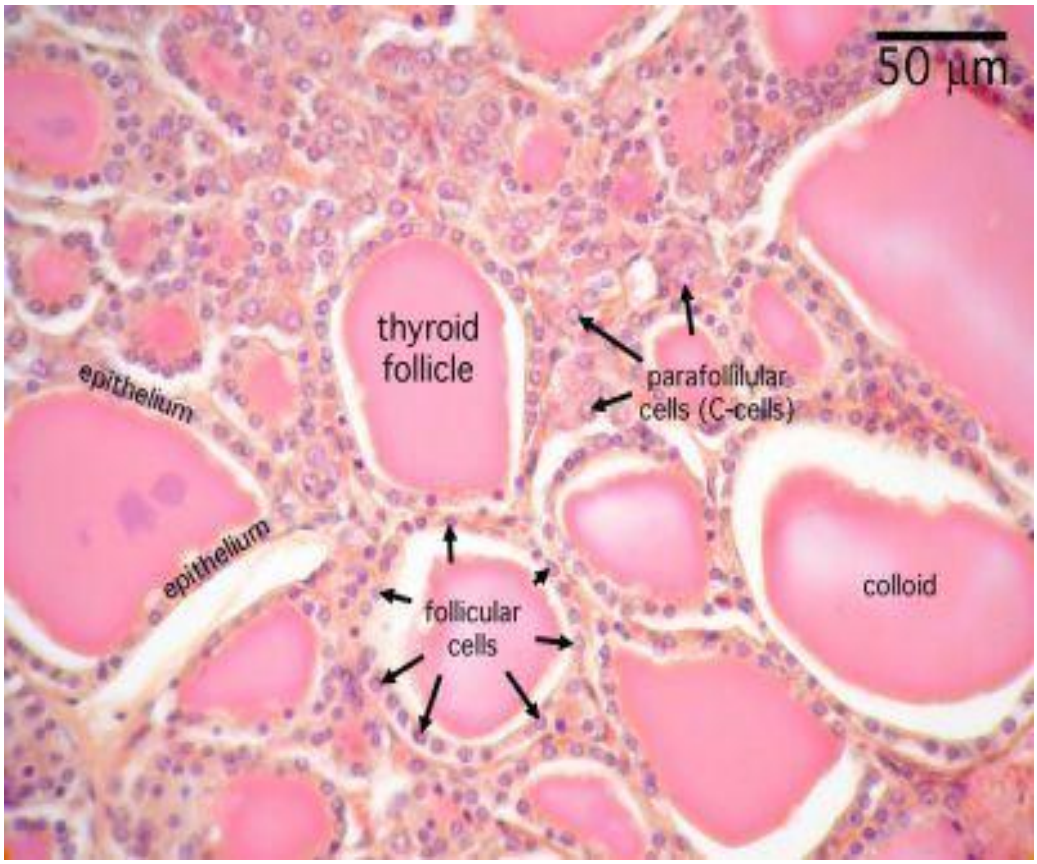
The maternal T4 is the only form of hormone that can cross the placenta till that period .In brain and other tissues D3 (Deiodinase) enzyme of the fetus converts maternal fT4 to T3. So the fetal iodine store is solely dependent on maternal iodine intake during this period.

Thyroid hormone synthesis, secretion and transport



Iodide trapping is the first step in the synthesis of thyroid hormones. By an ATP dependent active transport iodide trapping occurs. Iodide is oxidized to iodine then iodination of tyrosyl elements on the thyroglobulin occurs.

These steps are catalysed by thyroid peroxidase and the end products are mono and diiodotyrosine (MIT&DIT). Their coupling is the next step to form T4 (tetraiodothyronine) or one MIT(monoiodotyrosine) and one DIT(diiodotyrosine)molecule to form T3(triiodothyronine) or rT3(reverse triiodothyronine).



Hydrolysis of the thyroglobulin leads to release of free T3and T4 and MIT &DIT is the next step. Then the later are deiodinated to give raise to iodide and it is reused by the thyrocyte. Bound to thyroxine binding globulin (TBG), thyroxine binding pre albumin (TPBA) and albumin, thyroid hormones are transported in the serum .

Only a small amount of T3 is free, and it is the physiologically active hormone. T3 is 3 to 4 times more potent than T4. The T3 is less tightly bound to protiens, hence the circulating levels are much lower than T4. And it enters the tissues more easily. Half life of T3 is one day while half life of T4 is seven days. T4 is entirely released by thyroid gland while only 20% of T3 is released by thyroid gland, and the remaining 80% of T3 is produced by deiodination of T4 in liver, muscles and kidneys.

Metabolism and excretion of thyroid hormone:

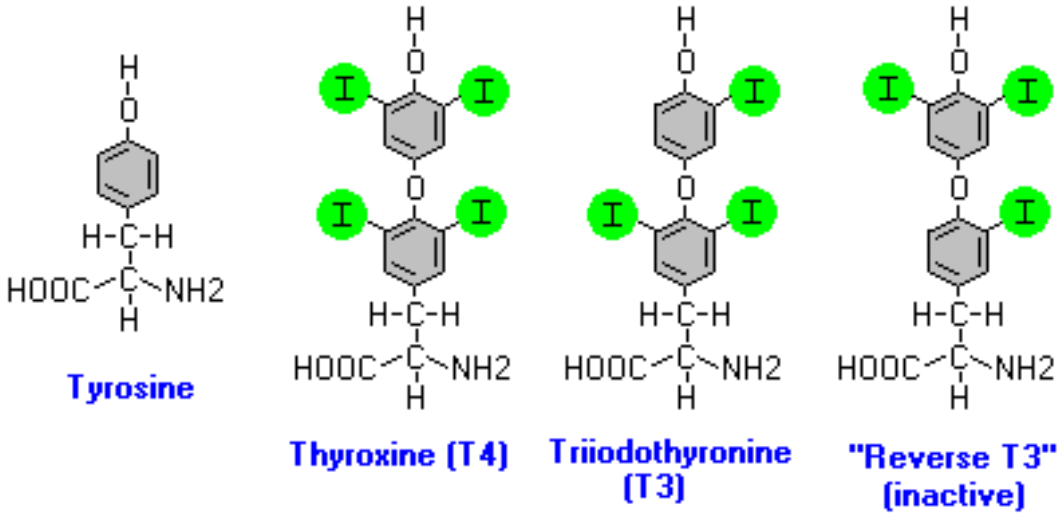
By glucuronide conjugation and de iodination, the metabolic inactivation of T3 occurs in the liver, kidneys and salivary glands and then they are excreted in bile. In the intestines a major fraction is deconjugated and re absorbed into entero hepatic circulation and finally excreted in urine.

Mechanism of action:

T3 penetrates the cells and combines with the specific DNA sequences over the nuclear receptor, leads to de repression or direct activation of gene transcription results in expression of predetermined pattern of protein synthesis.

Many of the clinical manifestations of thyroid hormone like By sensitization of adrenergic receptors to catecholamines the clinical manifestations of thyroid hormones like tachycardia, arrhythmias, hypertension, hyperglycaemia, tremor occurs.

Thyroid hormones functions



Thyroid hormones affect almost every system in the body.

Growth and development

Thyroid hormones exert a critical control over protein synthesis. Thyroid hormone deficiency affects mainly the nervous system in early fetal life. In cretinism there is mental retardation and neural deficit due to paucity of synaptic formation, dendritic and axonal ramification and reduced myelination. Overt hypothyroidism in the adult causes impairment of intelligence and slow movements.

Carbohydrate(CHO) Metabolism:

Thyroid hormones stimulate carbohydrate metabolism. Though the utilization of carbohydrates is raised due to an raised Basal Metabolic Rate (BMR), glycogenolysis& gluconeogenesis compensate for it. In hyper thyroidism there is a state of hyperglycaemia

Protein Metabolism:

The effect of T4 over the protiens is catabolic. Prolonged action results in negative nitrogen balance and tissue wasting. Hence there is loss of weight in hyperthyroidism and gain of weight in hypothyroidism. Mucoprotein synthesis is inhibited by thyroid hormones. Due to loss of inhibition they accumulate in myxedema.

Lipid Metabolism:

T3 and T4 enhance lipolysis though lipogenesis is also stimulated. Metabolism of Cholesterol is accelerated though its conversion to bile

acids dominate. Hence there is hypo cholesterolemia in hyperthyroidism and obesity & hypercholesterolemia in hypothyroidism.

Calorigenesis:

BMR is raised by stimulating cellular metabolism and resetting the energystat level. But BMR in gonads, uterus, spleen, brain and lymph nodes is not significantly affected. Uncoupling of oxidative phosphorylation results in releasing of excess energy as heat.

Cardio vascular system:

Contractility, heart rate, and cardiac output are all increased which results in fast & bounding pulse. Up regulation of beta adrenergic receptors by thyroid hormones results in positive chronotropic and inotropic effect. Effects of catecholamines are augmented, hence atrial fibrillation, arrhythmias, and angina are more common in hyperthyroidism. Systolic blood pressure is often raised.

Nervous system

Thyroid hormones maintain the normal hypoxic and hypercapnic drive of the respiratory centre in the brain. There is mental retardation in cretinism. Tremors, hyperreflexia, & anxiety are seen in hyperthyroidism whereas sluggishness is seen in hypothyroidism.

Skeletal muscle

T3&T4 increase the protein metabolism results in speed of muscle contraction andrelaxation. Muscle weakness is seen in myxedema and tremor, increased muscle tone is seen in thyrotoxicosis.

Gastro intestinal system

T3&T4 increase gastric motility. Constipation is seen in hypothyroidism while diarrhoea is seen in hyperthyroidism.

Haemopoiesis:

Anaemia occurs in hypothyroid patients hence it is proven that thyroid hormones play a role in haemopoiesis.

Reproduction:

Hypothyroid women have oligomenorrhea & infertility. Hence it is proven that thyroid hormones are essential for the maintenance of pregnancy and lactation.

Thyroid Physiology in Pregnancy

There is lot of changes in thyroid physiology occur during pregnancy. Iodination of tyrosine residues in thyroglobulin leads to form mono or di iodo tyrosine (MIT&DIT) which are then coupled to form T4 and T3.

Major portion of T4 is bound to circulating transport proteins like thyroxine binding pre albumin (TPBA), albumin & thyroxine binding globulin (TBG). Only 0.04% of total T4 is free and it is the physiologically active hormone. TSH which is secreted by anterior pituitary, increases the synthesis and release of thyroid hormone from thyroid gland.

TBG production is increased by estrogen during pregnancy. There is increased binding of T4,increased metabolism by the placenta& increased renal clearance leads to a greater demand for the production to maintain free T4 levels.

Total T4 level is greater than the normal non pregnant levels. There also increased placental transfer of iodine to the fetus results in increased demand for maternal iodine to maintain the normal thyroid hormone production.

HCG has common alpha subunit like TSH and unique beta subunit. Hence HCG has a weak TSH like activity and it stimulates thyroid gland results in decreased TSH level and increased T4 levels. Molar pregnancy, multiple pregnancy, hyperemesis gravidarum all these conditions are associated with increased HCG levels and leads to increased stimulation of the thyroid gland result in transient first-trimester thyrotoxicosis.

Once HCG returns to a steady state level TSH also rebound to normal non pregnant levels. Hence there is an increase in TSH & mild decline in free T4 after the first trimester. That is why TSH & FT4 levels should be interpreted with caution for each trimester.

Cut off values for TSH in pregnancy:

Because of the suppressive effect of increased thyroxin and increased TSH excretion, TSH is kept at its lowest minimal level in normal pregnancy.TSH level is 0.1-1.6 mIU/ml and thyroxin level is raised one and half times in euthyroid pregnancy state.

In 2005 Spencer ET al studied that S.TSH >2.5 mIU/ml in 1st trimester shows T4 deficiency.

In 2005 Green WL did a study which says normal range of TSH is 0.5 to 2.5mIU/ml(6)

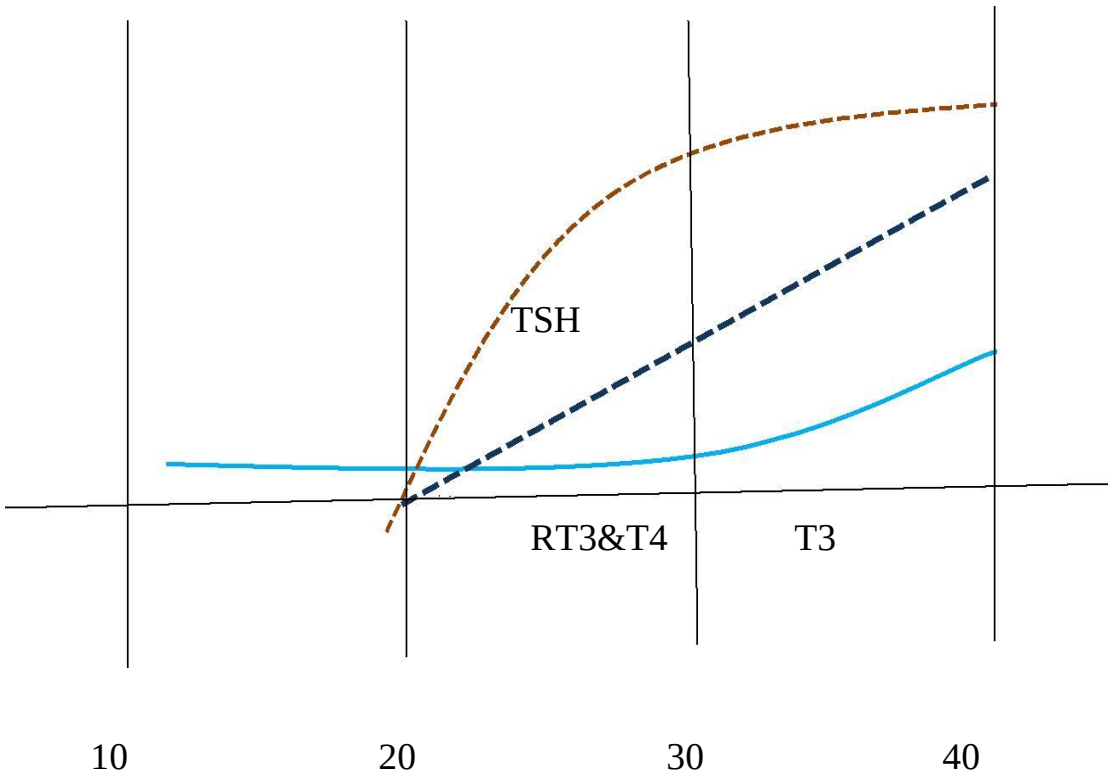
Prof. Ladenson said that adequate replacement should be given when TSH is > 2.5 mIU/ml and /or the lower T4 level in pregnancy.

Thyroid physiology in the fetus and neonate:

Between 8 and 10 weeks of gestation starts to concentrate iodine and to synthesis thyroid hormone along with the synthesis of TSH. Although around12 to 14 weeks of gestation pituitary thyroid axis is completely developed its function is minimal and only around 20 weeks

sudden surge in the fetal TSH occurs. And till 28 weeks TSH levels continue to increase till it reaches a plateau and remains at the same level till term gestation.

Fig: Fetal Thyroid Physiology



The major fetal thyroid hormone is T4and the level of T3 is quite low Throughout the pregnancyRT3 levels are parallelly elevates with the rise of T4.Thus the fetus goes from a state of relative T3 deficiency to T3 thyrotoxicosis during delivery.

By 48-72 hours the TSH values rise rapidly and then falls to baseline levels. The T3 and T4 levels increase in response and reach the peak levels by 24hrs and by 24-48 hrs of age respectively. The hyperactivity of thyroid takes about 3-4 weeks to completely disappear.

These changes mainly occur due to TRH surge and prolactin surge. These thyroid changes are protective mechanism against the rapid entry of neonate to the cold environment during delivery. During the first 72 hrs of life RT3 levels reach peak levels then it returns to the baseline level at 12 weeks.

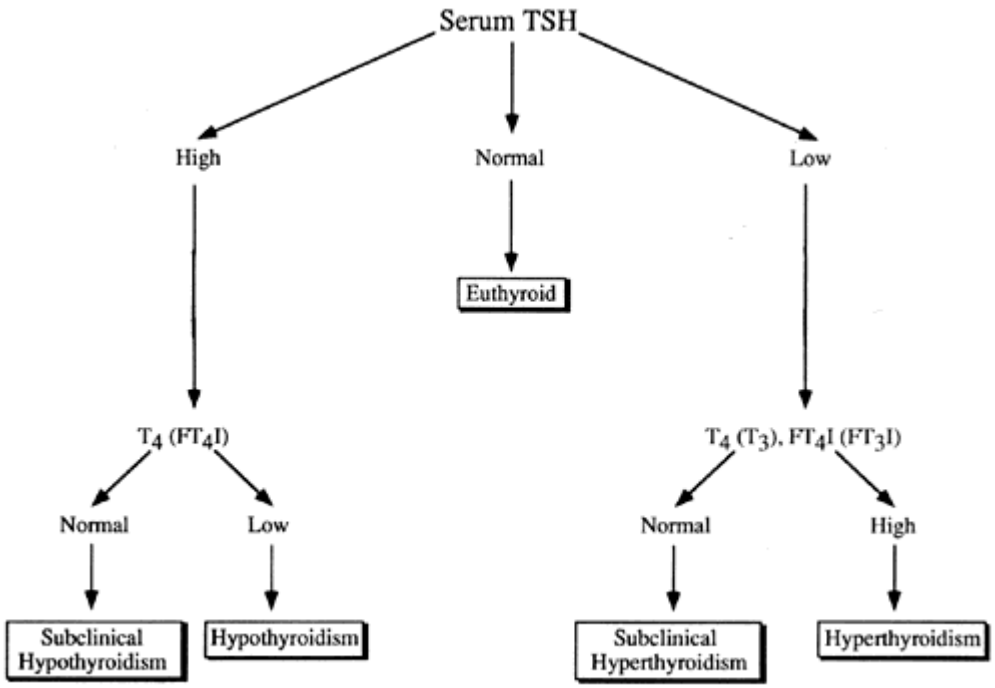
Summary of fetal and neonatal thyroid changes:

- By 10-13 wks of gestation TSH and T4 start appearing
- By 20 wks TSH &T4levels reach an abrupt rise
- At term T4 rapidly increases and exceeds maternal values
- T3 levels increase, but values are relatively low which is similar to hypothyroid adults
- RT3 levels exceed normal adult levels
- The fetal values of low T3 and high RT3 is similar to the values seen in calorie deprivation
- TSH peaks at 30mins, followed by a T3 peak at 24 hrs and T4 peak at 24- 48hrs after birth.

- Raised RT3 levels persist for 3-5 days then plateau down to normal levelsby2 Wks.

Causes of Hypothyroidism

Autoimmune	Hashimoto /chronic/subacute thyroiditis
	De Quervian's thyroiditis
Iatrogenic	Surgical removal of thyroid
	Radioactive iodine treatment
	Drug induced (eg. lithium, amio darone)
Congenital hypothyroidism	Thyroid gland agenesis
	Thyroid dyshormonogenesis
Substance deficiency	Iodine deficiency(most common cause)
Infiltrative disorders	Sarcoidosis



Overt hypothyroidism;

It is characterized by increased TSH and low T4 levels .the incidence is 0.3 -0.5%. overt hypothyroidism is associated with anaemia, miscarriage, preeclampsia, placental abruption, preterm labour, Postpartum haemorrhage, neonatal respiratory syndrome.

In 1969, Jones WS et al did a study in the American Journal of Obstetrics and Gynaecology which says that preterm deliveries were more Comman in pregnant women with low thyroxine levels.

Leung AS et al in 1993 did a study in 1993 and found that overt hypothyroidism associated with an increased incidence of preeclampsia and low birth weight babies. (14)

Allan WC et al in 2000 studied that fetal demises were increased in pregnant woman with TSH > 10mIU/ml. In 1988.

Davis et al followed 25 hypothyroid women in which 16 were overt hypothyroid and 12 had subclinical hypothyroidism and concluded that mothers with overt hypothyroidism are at increased risk for preeclampsia, preterm labour, abruption placentae, postpartum haemorrhage ,stillbirth and cardiac dysfunction . .

ACOG practice bulletin on thyroid disease in pregnancy in 2001 states that untreated hypothyroid women are more prone for pre eclampsia and inadequate treatment results in low birth weight babies.(26)

In 2010` Sahu MT et al published in Archives of gynaecology and obstetrics that gestational hypertension, IUGR, and Intra uterine fetal demise were more common in women with overt hypothyroidism.

A couple of studies have shown low thyroxine concentration in early pregnancy can be associated with low intelligent quotient of children at 7 years of age.

Ohara N et al in 2004 reviewed the literature on the role of thyroid hormone in trophoblast function and fetal neuro development. They concluded that close scrutiny of maternal thyroid hormones to ensure

adequate hormone levels in early pregnancy are of prime importance in preventing miscarriage and neuro developmental deficits in infants(15)

A study by Evelyn Man and colleagues in 1969 compared the outcomes of 1252 normothyroxinemic pregnancies with 168 hypothyroxinemic pregnancies.30 out of the 168 hypothyroid women ended up having preterm deliveries or fetal death(19.6%) compared only12.6 % in the euthyroid group.

Only few reports are available on the pregnancy outcome in hypothyroid pregnant women who are left untreated. These data show that adequate thyroxine replacement greatly improves but does not totally suppress the frequency of obstetric complications.(8)

Subclinical Hypothyroidism:

By definition, it is a condition in which TSH is elevated ,but FT4 is normal. Incidence of subclinical hypothyroidism is at least 2.5% .Usually it is asymptomatic, but there is evidence autoimmune thyroid disease (positive TPO Abs and or TG antibodies)in 50-60%(12)

Subclinical hypothyroidism was found to be more common in women delivering before 32 weeks.(12)Pregnancies complicated by subclinical hypothyroidism had a 3 fold increased risk of developing placental abruption and 2 fold increased risk of preterm labour compared to euthyroid women.(22) Gestational hypertension also

occurred more commonly in these women.(23) Even raised maternal TSH (high level of normal) is associated with neonatal respiratory distress, miscarriage and preterm delivery(12).

The likelihood of patients diagnosed as hypothyroids during pregnancy to continue to be hypothyroid even after pregnancy depends on the initial TSH value. The United States Preventive Services Task force reported that nearly almost all patients with an initial TSH >10 mIU/ml developed overt hypothyroidism within 5 years.(33)

ISOLATED HYPOTHYROXINAEMIA:

It is defined as a condition with normal TSH and low fT4.Cleary Goldman and colleagues in 2008 screened 10,990 patients for thyroid dysfunction. They noted that the presence of this isolated hypothyroxinemia in 1st trimester was associated with an increased occurrence of preterm delivery and macrosomia. Its occurrence in 2^{nd}trimester was associated with gestational diabetes.(28)

CLINICAL FEATURES OF HYPOTHYROIDISM:

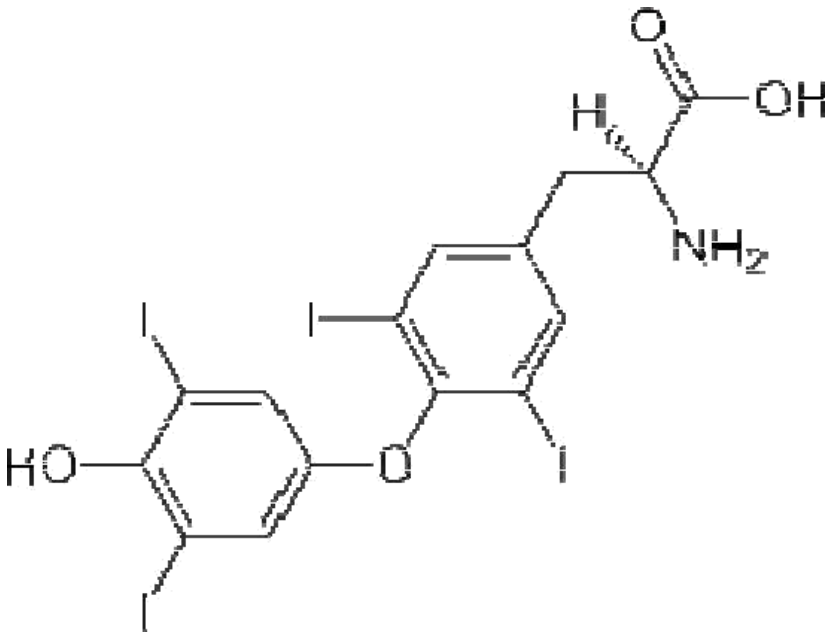
Hypothyroidism developing in childhood results in delayed development and may even cause abdominal distension, umbilical hernia and rectal prolapse. Mental performance is diminished but severe retardation is uncommon.

In adults mostly symptoms are non specific. They include weight gain, fatigue, intolerance to cold, constipation and menstrual irregularities like menorrhagia.

Patients with myxedema have typical facial features. Skin is yellowish due to reduced conversion of carotene to vitamin A. Hair becomes brittle and there is also a characteristic loss of the outer two third of eye brow. Untreated patients can develop dementia which is called myxedema madness. There is decreased libido and fertility in both sexes. Cardio vascular changes include bradycardia, pericardial or pulmonary effusions.

Treatment of Hypothyroidism:

Levothyroxine



Levothyroxine or T4, is a synthetic form of normally secreted by the thyroid chiral L-form. Edward Calvin Kendall its pure form from extracts of hog thyroid glands in 1914 synthesised by British chemist Absorption of L thyroxine is incomplete varying from 50-75%.

For therapeutic purposes L thyroxine is superior to lio thyronine because of its longer duration of action. The only accepted indication for the use of lio is myxedema coma where a quick response is essential.

Levothyroxine should be taken on an empty stomach approximately half an hour before meals. Patients should avoid taking thyroxine as these can interfere with the absorption of this drug.

According to the American Thyroid Association, pregnant women already being treated with thyroxine hormone often require a 30-50% increase in dose the need for dose increase starts as early as 5 weeks GA, The association urges physicians to be vigilant in identifying and treating women with subclinical thyroid dysfunction before conception.

Edward Calvin Kendall of the Mayo clinic first isolated thyroxine in its pure form from extracts of hog thyroid glands in 1914.

The hormone was synthesised by British chemist Charles Robert Harington in 1927. Absorption of L thyroxine is incomplete varying from 50 therapeutic purposes L thyroxine is superior to lio thyronine

because of its longer duration of action. The only accepted indication for the use of lio myxedema coma where a quick response is essential.

The Journal of Clinical Endocrinology and Metabolism published an executive Summary which stated that in patients with overt hypothyroidism the dose of thyroxine should be adjusted to reach a TSH not more than 2.8 IU/ml periconceptionally.

"When hypothyroidism is newly discovered during pregnancy, we suggest initiating the treatment with the following levothyroxine doses: 1.20 µg/kg/day for subclinical hypothyroidism with TSH less than 4.2 mIU/L, 1.42 µg/kg/day with TSH greater than 4.2 to 10, and 2.33 µg/kg/day for overt hypothyroidism," Dr. Abalovich and colleagues write.

The Thyroxine dosage usually needs to be increased by 4-6 wks of gestational age and may require a 30-50% increase. If a patient is diagnosed to have overt hypothyroidism during pregnancy, titrate the dose rapidly to keep the TSH at a level less than 2.5 IU/ml in the first trimester and less than 3 IU/ml in second and third trimesters.

The panel recommends also thyroxine replacement in women with subclinical hypothyroidism.

COMPLICATIONS OF HYPOTHYROIDISM IN PREGNANCY:

1. Spontaneous abortion

2. Pregnancy induced hypertension(pre eclampsia, eclampsia)

3. Placental abruption

4. IUGR

5. Oligohydramnios

6. Preterm delivery

7. Fetal distress

8. Low birth weight

Congenital Hypothyroidism:

Congenital Hypothyroidism (CH) is one of the most common preventable causes of mental retardation. The incidence is 1:4000 livebirths and the worldwide and the incidence in India is 1:2500-2800 live births.Thyroid dysgenesis is the commonest cause attributing for the majority of cases. CH can be permanent or transient. Maternal cytotoxic antibodies and genetic mutations causing inactivation of thyroid receptor can be a cause.

There is clinical and scientific evidence that hypothyroxinemia causes poor neurodevelopment outcome in the children of mothers with low thyroxine levels. In a study by Morreale de Escobar et al in2004, it

was noted that thyroid hormone accumulates in the cerebral cortex before 20 weeks.(30)

Primary evidence of the effect of the deficiency of thyroid hormone on cerebral cortex was studied by Lavado- Autric et al in 2003.(31) Defects in thyroid hormone synthesis account for 10% of all cases. These can be inherited as autosomal recessive disorders.

Pharoah et al did a landmark study in 1971 and came to a conclusion that iodine supplementation in pregnancy prevented subsequent cretinism.

Early and aggressive treatment with thyroxine is crucial for infants withcongenital hypothyroidism. Yet some infants with prompt replacement exhibit mild cognitive defects in adolescence.(47)

CLINICAL FEATURES OF CONGENITAL HYPOTHYROIDISM

Untreated severe congenital hypothyroidism leads to irreversible growth failure and mental retardation Early symptoms include feeding problems, constipation, growth failure and hoarse cry Later they develop dry skin and decreased growth of nails and hair; tooth eruption is delayed Closure of anterior and posterior fontanelles are delayed Cardiomegaly may be present .

The other clinical features are broad, flat nose, pseudohypertelorism, puffy, myxedematous facies, large, protruding

tongue, prolonged neonatal jaundice, protuberant abdomen, umbilical hernia.

Postpartum Thyroiditis:

Postpartum thyroiditis is a characterized by a lymphocytic infiltration of the thyroid gland .It's reported incidence is in about 5% of pregnancies(17).It usually occurs in the 1st month after delivery.It starts as a thyrotoxic phase followed by a phase of hypothyroidism lasting for months.

It is typically characterized by the presence of TPO antibodies although it's occurrence is women without these antibodies has also been reported. The risk is even greater when TPO antibodies are detected antenatally.Studies have shown that as many as 50% of women who developed postpartum thyroiditis continued to remain hypothyroid at the end of the 1st postpartum year. There is no compelling evidence to support the early treatment of this condition.

Thyroid antibodies:

These tests do not determine the thyroid function, instead they indicate the underlying disorder. Antithyroglobulin, antimicrosomal and thyroid stimulating immunoglobulin are the thyroid antibodies. Approximately 80% of patients with Hashimoto's thyroiditis have raised thyroid antibody levels.

Thyroid peroxidase(TPO)antibodies and AntiThyroglobulin(TG) antibodies are linked to pregnancy complications. There are studies to show that euthyroid women with recurrent miscarriages and preterm birth were found to have antibodies to either TPO or TG.TPO antibodies have also been implicated in the development of postpartum thyroiditis.

Association between auto immune thyroiditis and adverse obstetric outcome independent of thyroid function has also been proven in another prospective study where euthyroid TPO antibody positive women who received thyroxine supplementation in early pregnancy had a reduced rate of miscarriage and preterm delivery rate(12) .

Pregnant women with TPO antibodies were found to have a three times more chances of placental abruption when compared with antibody negative controls in a study by Abbassi-Ghanavati et al in 2010.

Pop et al revealed decrease in the intelligent quotient of children aged 5 years whose mothers were TPO antibody positive at 32 weeks of gestation even though they were actually euthyroid.(4)

Some thyroid autoantibodies cross the placenta causing fetal thyroid dysfunction. But maternal Hashimoto thyroiditis is not typically found to be associated with fetal thyroid abnormalities.

Brown and co-workers in 1996 did a study on over one million babies and found that only 1 in 180,000 neonates born to mothers with Hashimotos thyroiditis had thyroid dysfunction.(46)

Hypothyroidism and Infertility:

Infertility is defined as the inability to conceive after one year of intercourse without contraception (39). In mild degrees of hypothyroidism, ovulation and conception can occur, but the pregnancies that result are complicated by abortions, stillbirth or prematurity (13).

On the other hand, severe hypothyroidism is commonly associated with ovulatory dysfunction and, thus, infertility. Hypothyroid women can present with menstrual irregularities, especially oligomenorrhoea.

Thyroid underfunction can also act more indirectly, by altering the HPO axis, by reducing the binding activity of sex hormome-binding globulin (SHBG)causing an increase in serum free testosterone and estradiol, by decreasing the metabolic clearance of androstenedione and estrone.

Also, TRH is elevated in hypothyroidism which causes an increase in prolactin levels, and a delay in LH release to LH releasing hormone (LHRH). Treatment of thyroid underfunction with L-thyroxine (L-T4) usually restores a normal menstrual pattern and alleviates these pathological mechanisms (34)

It has been recently recognised that disturbances of cognition and mood develop in association with alteration in thyroid metabolism in the brain. There are even few small studies to show the connection between thyroid dysfunction and mood disorders like postpartum depression .

Thyroid Dysfunction and pregnancy loss:

Normal thyroid function is critical for normal functioning of the gonadal axis, thus important in maintaining normal reproduction. Gonadal steroid synthesis by oocytes depends on an adequate level of thyroid hormones. T3 modulates the regulating action of LH and FSH on steroid biosynthesis, thyroid hormones increase and enhance estrogenic responses(9).

Dysthyroidism is associated with anovulatory cycles, subfertility or infertility Abortion rate as high as 60% in inadequately treated overt hypothyroids and 70% in subclinical hypothyroids(10) Matsua et al showed that Free T3 and Free T4 values were significantly lower in women whose pregnancies terminated in abortions .(40)

Donmez M et al in 2005 did a case control study to investigate thyroid dysfunction as an causative factor for abortions. They performed thyroid function tests in 60 patients having spontaneous miscarriages and compared them with those of 40 pregnant women of same gestational age who were presumed to reach term.

They found that T3 and T4 values were significantly lower and TSH values were significantly higher among the abortion group suggesting that subclinical hypothyroidism may be responsible for the spontaneous abortions(16)

There are theories that consider autoimmune thyroiditis a consequence of increased lymphocytes T activation. Patients with antecedents of habitual abortions show an increased number of endometrial T lymphocytes.

Expression of the antithyroid antibodies may be an epiphenomenon that reflects an autoimmune imbalance, causing the rejection of the product of conception. This hypothesis is supported by the existence of an increased CD5/20 lymphocyte positivity in women with recurrent miscarriage(11)

In 1990 Stagnaro- Green et al showed that among 552 women who were screened for thyroid antibodies , abortion rate of 17% was observed in antibody positive group as compared to 8.4% in antibody negative group.(18)

Bussen Steck et al in 1995 screened 22 non pregnant women with bad obstretic history for thyroid antibodies and detected a higher prevalence of thyroid antibodies in 36% compared to 9% in multiparous controls and 5% in nulliparous controls.(19)

Matalon ST et al in 2001showed that elevated levels of thyroid auto antibodies areassociated with increased rate of abortions in euthyroid women.(20)

Vaquero et al in 2000 studied pregnancy outcomes in patients with mild thyroid abnormalities. Women mild thyroid abnormalities had an increased rate of miscarriage. Thyroid replacement therapy with intra-venous immunoglobulins (IVIG) was helpful in preventing a new miscarriage (37)

A study by Pratt et al found that the incidence of anti- thyroid antibodies in women who had repeated abortions were noticeably higher than other non-organ-specific auto-antibodies(38)

Screening for thyroid dysfunction during pregnancy:

For universal screening to be recommended for a disease,

1. The incidence of the disease should be high enough to warrant screening.
2. The screening needs to be as cost effective as possible.
3. There should be substantiative evidence that adverse outcomes are associated with the disease.
4. There should also be evidence that intervention improves outcomes.

The journal of clinical endocrinology and metabolism Adopted a clinical practice guideline in 2007 which recommended screening among the following high risk women(27)

a) Women with a previous history of hyper /hypo thyroid disease / thyroidectomy/goitre

b) Women with family history of thyroid dysfunction

c) Women with symptoms/signs suggestive of thyroid dysfunction

d) Women with autoimmune diseases like Type 1 DM

e) Women with a history of infertility

f) Women with history of head and neck irradiation

g) Women with history of recurrent miscarriages or preterm deliveries.

According to the ACOG Committee Opinion no.381(oct 2007) also thyroid screening in pregnancy should be carried out only on symptomatic women / those with a history of thyroid disease or other medical illnesses that may be associated with thyroid disease (eg:diabetes)

In a study by Bijay Vaidya et al published in JCEM in 2007,they found that thyroid function testing of only high risk women would miss about 1/3rd of women with overt/subclinical hypothyroidism.(21)

AIM OF THE STUDY

AIM: To study the prevalence of hypothyroidism in pregnancy and the pregnancy outcome in those pregnancies.

OBJECTIVES: To study the prevalence of hypothyroidism in pregnancy and pregnancy outcome.

DESIGN OF STUDY: A Prospective study .

PERIOD OFSTUDY: 1 Year..

MATERIALS AND METHODS: This study involves screening 1000 consenting eligible women during first trimester. The normal patients will serve as controls.

Blood should be collected in fasting state, because lipaemic content in blood interferes with serum TSH level if blood sample was collected in the fed state.

Blood was collected from the patients by venu puncture (2ml), allowed to clot, and serum was separated by centrifugation at room temperature. The serum was stored at 2 to 8°C till its usage. The TSH was estimated by using ELISA method.

If serum TSH is abnormal fT4 and fT3 were estimated. According to the biochemical values, those patients were divided into overt hypothyroidism, subclinical hypothyroidism, and euthyroid. overt hypothyroidism, subclinical hypothyroidism patients were treated with L Thyroxine in the dose of 1.20 µg/kg/day for subclinical hypothyroidism with TSH less than 4.2 mIU/L, 1.42 µg/kg/day with TSH greater than 4.2 to 10, and 2.33 µg/kg/day for overt hypothyroidism this dosing was based on a study by Dr. Abalovich and colleagues which was published in the journal of overt and subclinical hypothydism and which has been confirmed by numerous other studies according to the body weight to maintain serum TSH near normal. Serm TSH estimation was repeated at 4- 6weeks interval. TSH concentration is maintained less than 2.5MIU/L in the first trimester, less than 3MIU/L in the second and third trimester.

All the patients followed till the end of pregnancy. The normal patients serve as controls. Pregnancy outcome studied statistically.

INCLUSION CRITERIA:

1.less than 13 weeks of gestation.

2.Singleton pregnancy.

3.Primigravida or multigravida.

4.known hypothyroid patients.

EXCLUSION CRITERIA:

1. Multifoetal gestation.
2. Known chronic disorders like diabetes and hypertension, liver disorders, renal disorders
3. previous bad obstetric history with known cause.
4. Those who plan to deliver in other hospital.

METHODOLOGY:

Patients satisfying the inclusion criteria and who consent for the study are included.

Clinical history and relevant investigations are collected as mentioned in the proforma enclosed. All the eligible patients will be screened and their thyroid status defined. Patients who are hypothyroid and subclinical hypothyroid will be followed till termination of pregnancy.The clinical progression with the treatment given will be noted . The results from the study will be analyzed statistically.

RESULTS:

The data collected from the study will be analysed statistically and submitted

ESTIMATION OF FREE T_3

Method

RIA (Radio Immuno Assay) – IMMUNOTECH Prague, Cze ch republic

Principle

The radio immuno assay of the free tri-iodo thyronine (T_3) is a competitive assay done by using labeled antibody. Samples and calibrators are incubated with an ^{125}I- labelled antibody specific for T_3, as tracer, in tubes coated with an analog of T_3 (ligand). The free tri-iodo thyronine and the ligand compete for the binding to the labeled antibody. The content in the tubes is aspirated after incubation and bound radioactivity is measured. A calibration curve is designed and values are ascertained by interpolation from the curve.

Reagents

Ligand-coated tubes ^{125}I- labeled monoclonal antibody Calibrators Control serum

Specimen collection

Blood was collected in dry tubes or in tubes containing EDTA, in a fasting state. Serum/Plasma was separated from cells by centrifugation. Samples were stored at 2-8^{0}C.

Results

Normal range of Free T_3 was taken as 2.5 – 5.8 pM/L.

ESTIMATION OF FREE T_4

Method

RIA (Radio Immuno Assay) Principle, Reagents and procedure are similar to Free T_3 estimation.

Results

Normal range of Free T_4 was taken as 11.5 – 23 pM/L.

ESTIMATION OF TSH

Method

Solid Phase Two-Site ImmunoRadoMetric Assay (IRMA) with IRMAK-9 kit, BRIT, Mumbai.

Principle

In IRMA, two antibodies generated against different portions (epitopes) of the same antigen are used. One of the antibodies is bound to a solid phase, while the other is labeled with ^{125}I. Thus, the antigen binds both antibodies in a " sandwich" fashion. The radioactivity in the bound fraction is quantitated using a gamma counter.

Reagents

hTSH monoclonal antibody coated tubes ^{125}I- Anti hTSH Wash diluents .

Specimen collection

Serum or plasma can be used for assay. EDTA plasma is not used.

Results

The trimester specific Normal range of TSH are as follows:

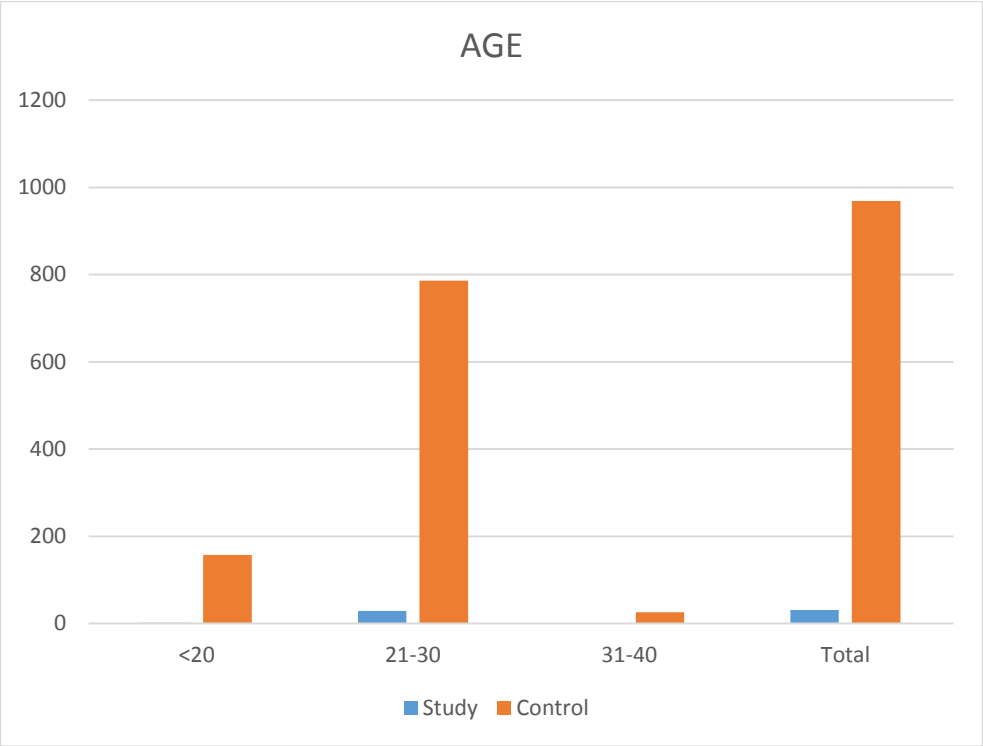
First trimester – 0.1 to 2.5mIU/ml

Second trimester - 0.2 to 3.0mIU/ml

Third trimester – 0.3 to 3.0mIU/ ml

OBSERVATIONS

AGE:



Age	Study	Control
≤20 yrs	2	157
21-30 yrs	29	786
31-40 yrs		26
Total	31	969

In my study most of the patients were in the age group of 21-30 years. There was no significant difference in distribution of cases between the groups based on age.

The incidence of hypothyroidism was more common in the 21-30 years age group but it might have been influenced by the fact that most of the study population was in the age group.

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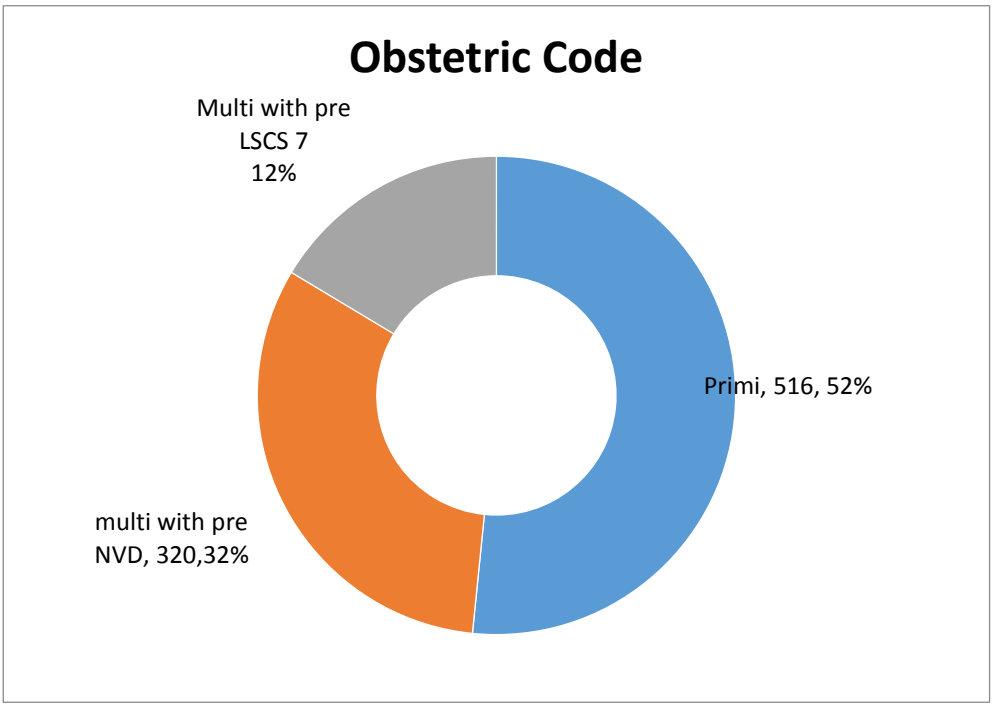
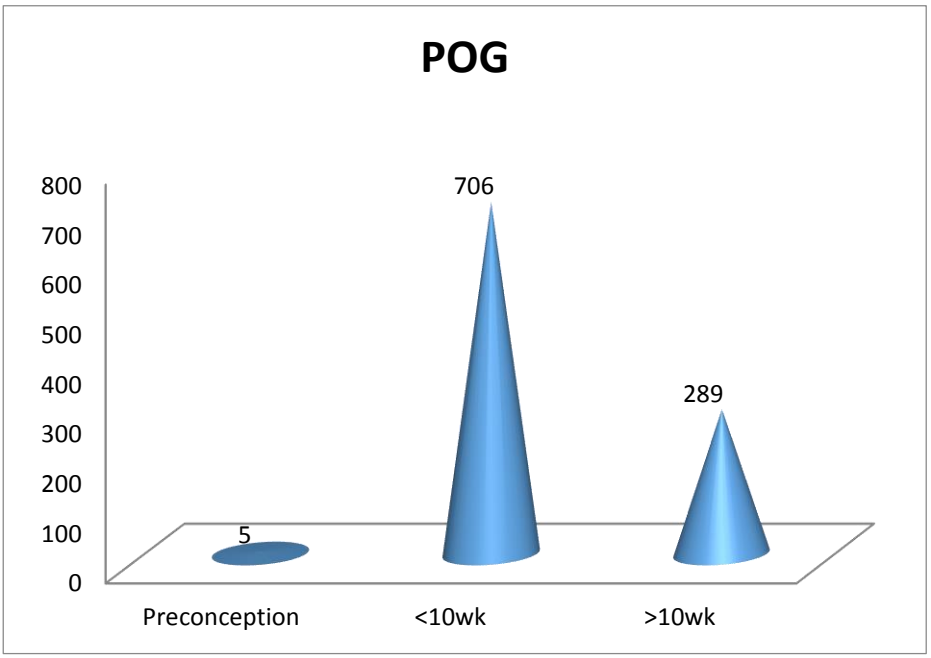


OBS.SCORE	Study	Control
Primi	15	501
Multi with prev normal delivery	9	311
Multi with pre LSCS	7	157
Total	31	969

in my study there was near equal distribution of cases based on obstetric score between the groups. There was equal number of primI gravida and multi gravida patients in the study.

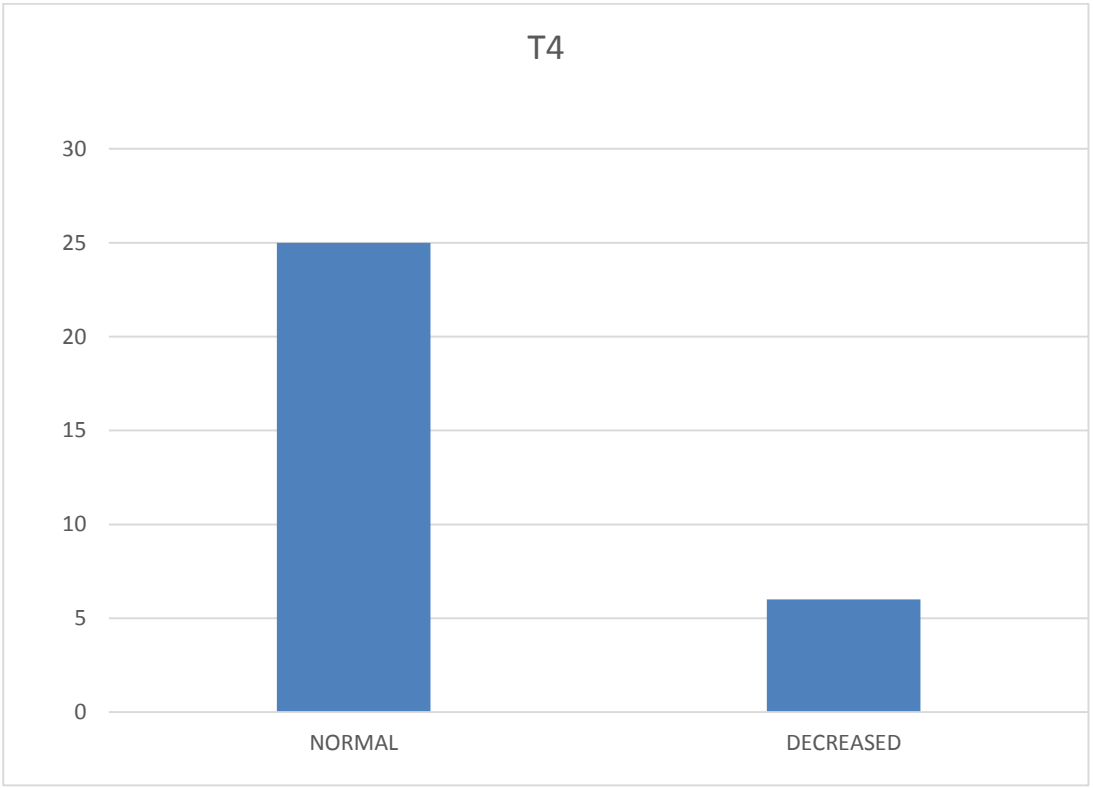
PERIOD OF GESTATION AT DIAGNOSIS:



POG	Study	Control
Preconceptional	5(16.12%)	
<10wk	13(41.9%)	693(71.51%)
>10wk	13(41.9%)	276(28.48%)
Total	31(100%)	969(100%)

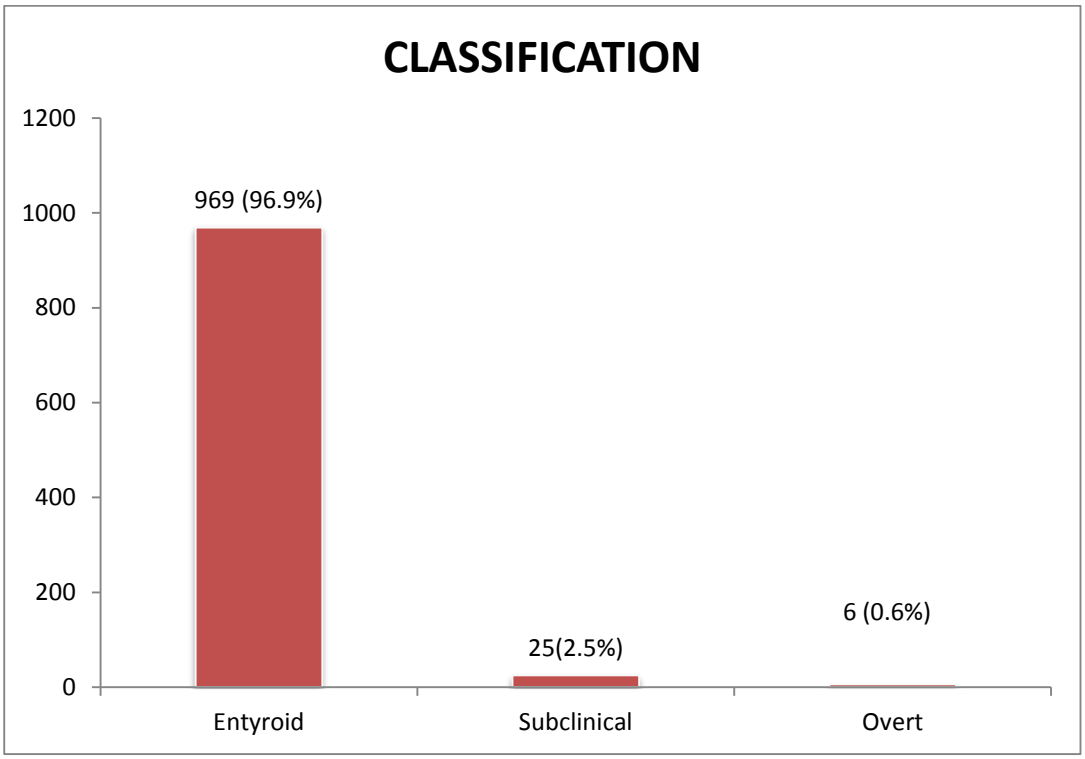
In my study most of the patients underwent screening at less than 10 weeks gestational age. There is no significant difference between the groups based on period of gestation between the groups.

T4 VALUES



In my study all the patients with deranged TSH values underwent fT4 testing based on the results it was found that most of them had normal T4 implying that the incidence of sub clinical hypothyroidism is more than overt hypothyroidism..

CLASSIFICATION



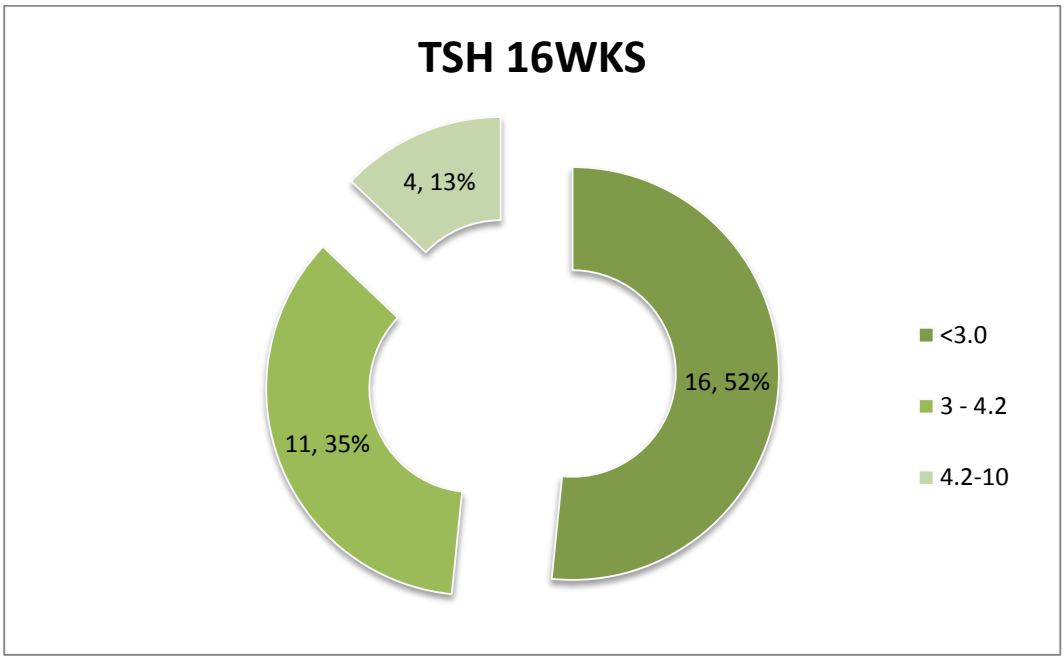
CLASSIFICATION	Study	Control	Total	Chi sq	P
Euthyroid	0	969	969 (96.9%)	1000	**0.0001**
Subclinical hypothyroid	25	0	25 (2.5%)		
Overt hypothyroid	6	0	6 (0.6%)		
Total	31	969	1000 (100%)		

PREVALENCE:

CLASSIFICATION	Frequency
Euthyroid	969 (96.9)
Subclinical hypothyroid	25 (2.5%)
Overt hypothyroid	6 (0.6%)
Total	1000

This table shows the prevalence of hypothyroidism in my study group that is 3.1% of the totally screened patients 2.5% of them are sub clinically hypothyroid, 0.6% of them are overt hypothyroid. Chi sq. & p value 0.0001 which is significant

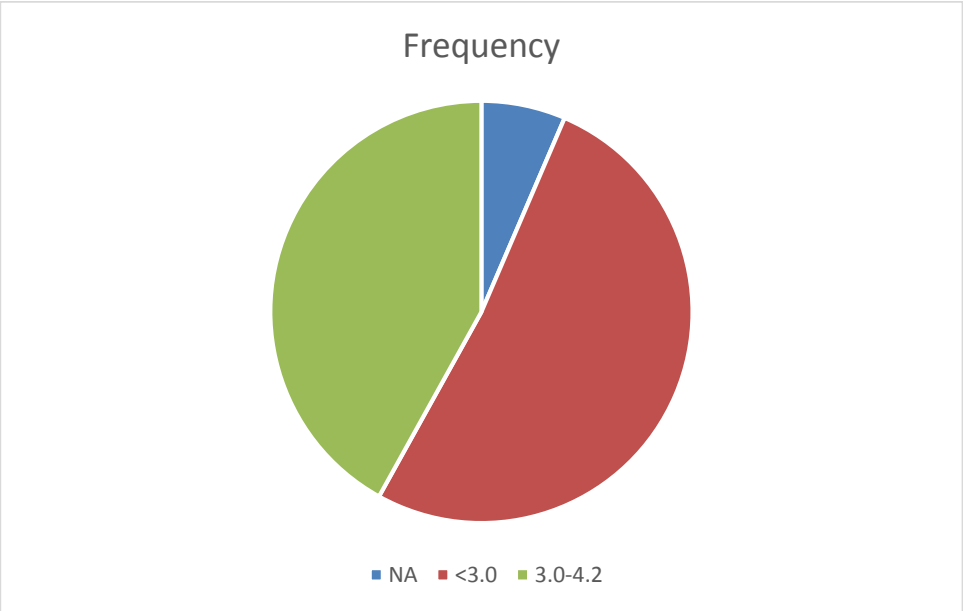
TSH AT 16 WEEKS:



TSH16	Frequency
<3	16
3-4.2	11
4.2-10	4
Total	31

In my study most of the patients who were started on treatment responded well to it so that by 16 weeks 52% of them had their TSH restored to normal range.

TSH AT 20 WEEKS:

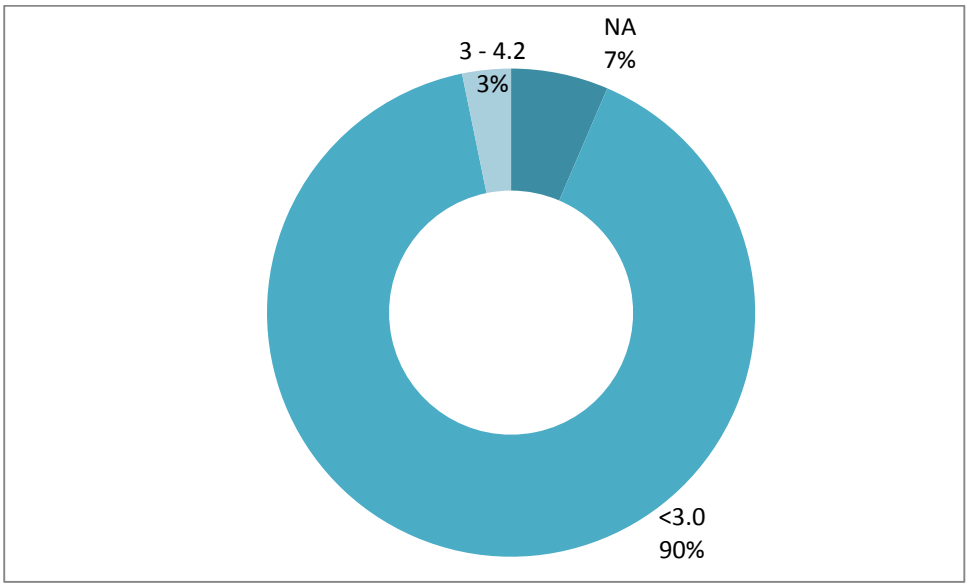


TSH at 20 wks	Frequency
Spontaneous abortion before 20 wks (NA)	2
<3.0	16
3-4.2	13
Total	31

In my study of 31 patients started on Levothyroxine 16 of them (52%) had normal TSH by 20 weeks but 13 of them 13 of them (35%) still had relatively higher levels of TSH which necessitated an increase in dose of Levothyroxine.

In this table NA denotes those who abort spontaneously before 20 wks of gestation.

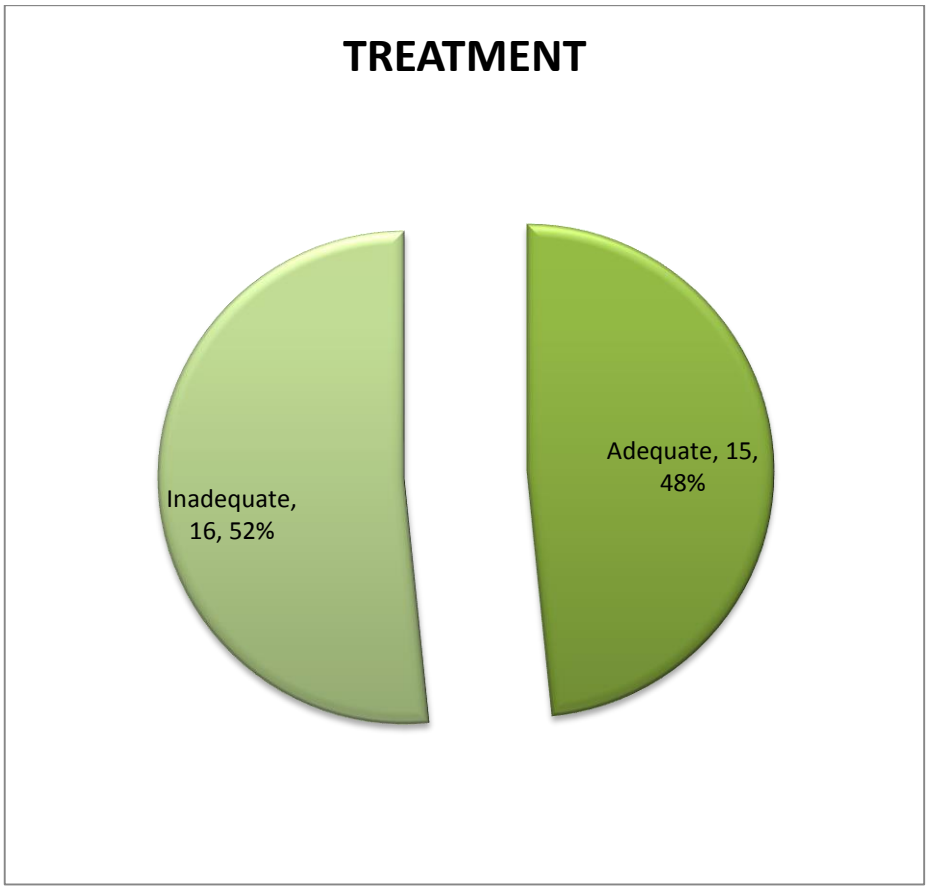
TSH AT 32 WEEKS:



TSH at 32 wks(miu/ml)	Frequency
Spontaneous abortion before 20 wks (NA)	2
<3	28
3-4.2	1
Total	31

In my study at 32 weeks period of gestation except for a single patient all the other patients attained normal TSH levels. one patient needed further increase in dose of Levothyroxine.

TREATMENT:



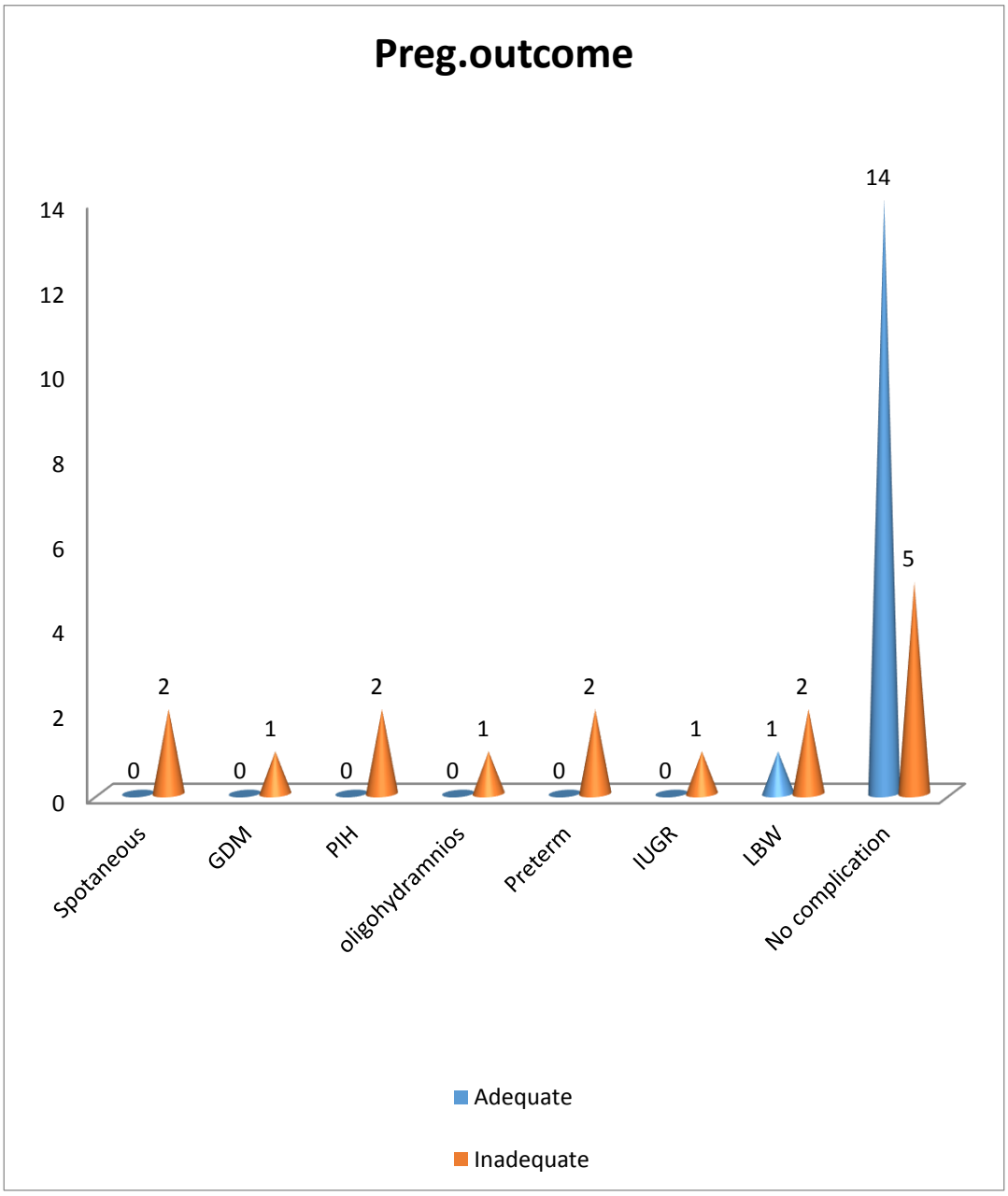
TREATMENT	Frequency
Adequately treated	15(48%)
Inadequately treated	16(52%)
Total	31(100%)

Those who have been diagnosed before 10 weeks and on treatment, if their repeat TSH values become normal they were grouped under adequately treated group.

Those who have been diagnosed after 10 weeks of gestation and treated of those who fail to reach normal levels of TSH despite aggressive treatment were classified as inadequately treated.

In my study group 48% patients are adequately treated and 52% of the patients are inadequately treated .

PREGNANCY OUTCOME:



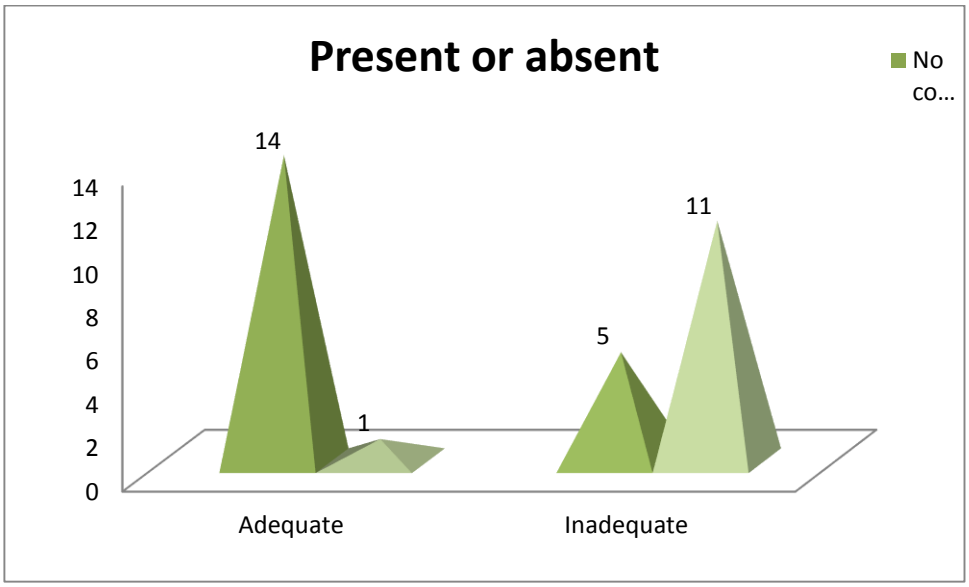
PREG.OUTCOME	Adequately treated	Inadequately treated	Total	Chi .Sq	P Value
Spontaneous abortion	0	2 (12.5%)	2	12.57	0.00039
GDM	0	1 (6.2%)	1		
PIH	0	2 (12.5%)	2		
oligohydramnios	0	1 (6.2%)	1		
Preterm	0	2 (12.5%)	2		
IUGR	0	1 (6.2%)	1		
LBW	1 (6.66%)	2 (12.5%)	3		
Total complications	1(6.6%)	11(68.75%)	12		
No complication	14(93.33%)	5 (31.25%)	19		
Total	15	16	31		

This table shows only 6.66% of the patients of adequately treated patients developed complication that is low birth weight, whereas 68.75% of the inadequately treated patients developed complications.

Overall Chi square value for complications: 12.57

P value for complications is:0.00039

COMPLICATIONS:



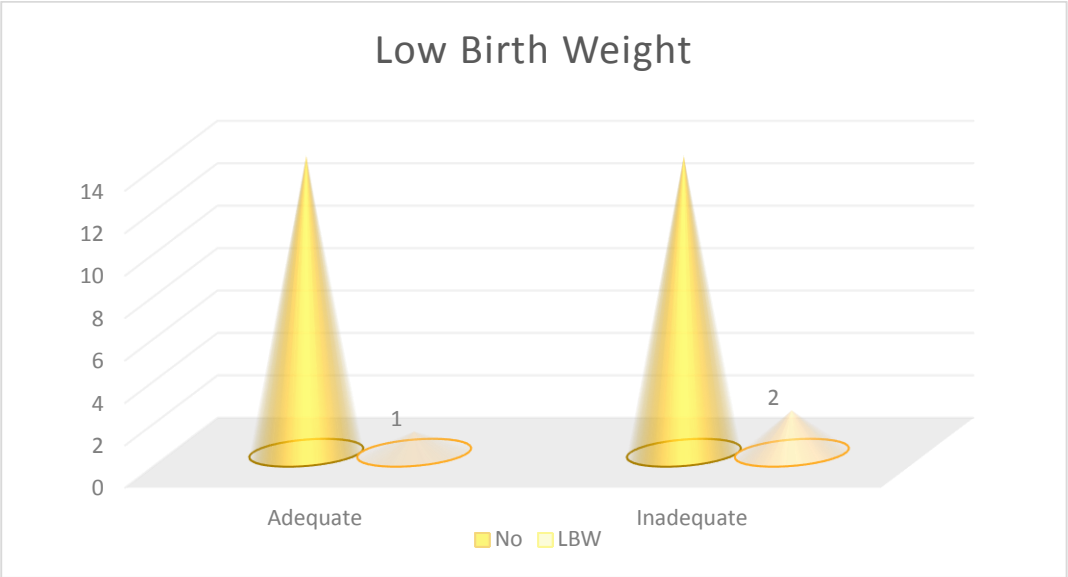
outcome	Adequately treated	Inadequately treated	Chi sq	p
No complications	14 (93.33%)	5(31.25%)	12.57	0.00039
With complications	1 6.66%)	11(68.75%)		
Total	15(100%)	16(100%)		

This table shows that 11 (68.75%) out of the16 inadequately treated hypothyroid mothers developed complications whereas only 1 (6.66%) out of 15 adequately treated patients developed complications.

Chi square value:12.57

p value: 0.00039which is significant

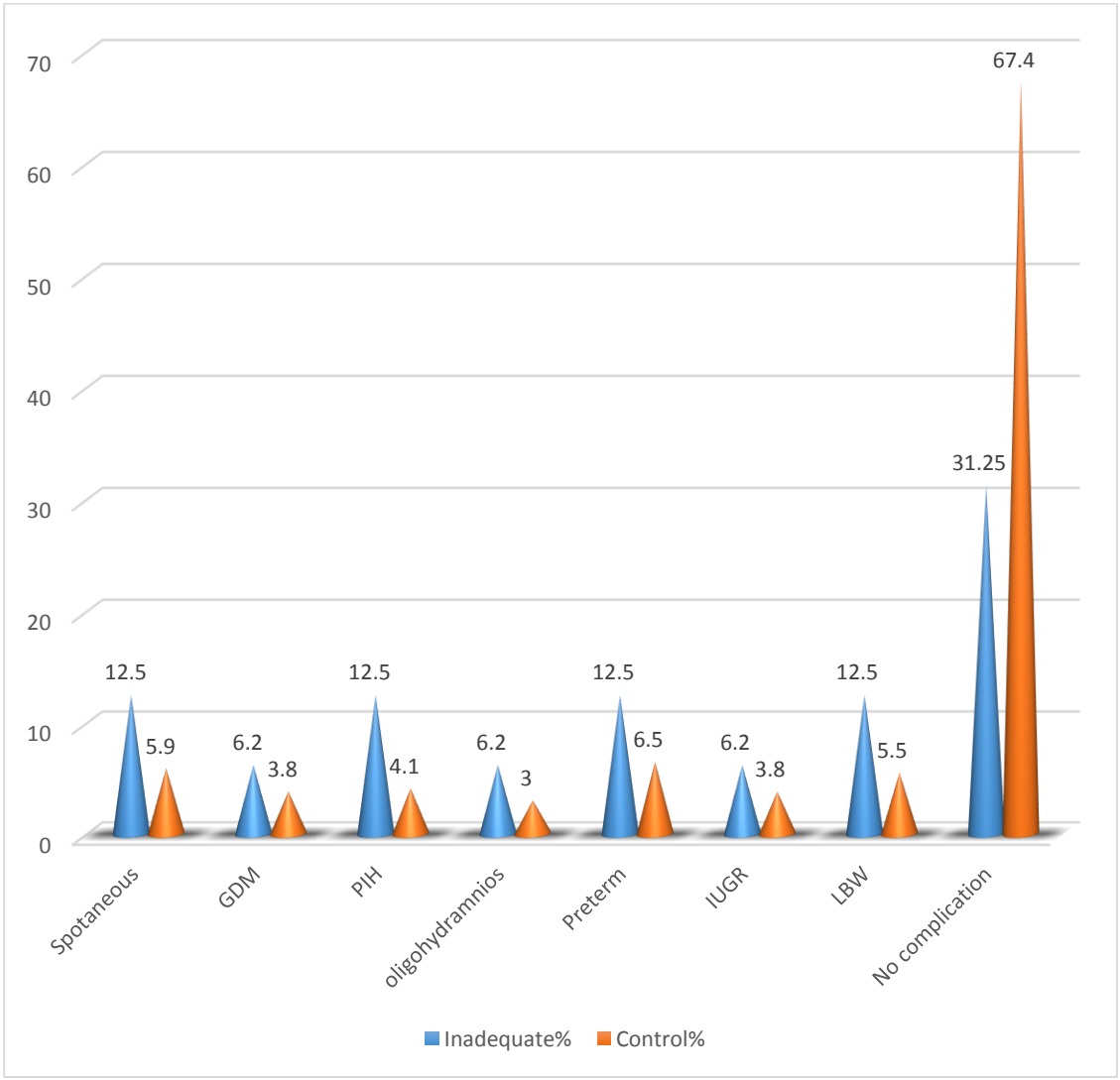
LOW BIRTH WEIGHT:



LBW	Adequately treated	Inadequately treated
No	14(93.33%)	14(87.5%)
YES	1(6.66%)	2(12.5%)

This table shows that 12.5% of the inadequately treated hypothyroid woman delivered low birth weight babies and only 6.66% of the adequately treated patients delivered low birth weight babies.

COMPARISON OF PREGNANCY OUTCOMES BETWEEN INADEQUATELY TREATED GROUP AND CONTROL:



PREG.OUTCOME	Inadequate	Inadequate%	Control	Contro l%	Chi sq	P
Spontaneous abortion	2	12.5%	57	5.9%	9.26	0.00233
GDM	1	6.25%	37	3.8%		
PIH	2	12.5%	40	4.1%		
Oligohydramnios	1	6.25%	29	3%		
Preterm	2	12.5%	63	6.5%		
IUGR	1	6.25%	37	3.8%		
LBW	2	12.5%	53	5.5%		
Total complications	11	68.75%	316	32.6%		
No complications	5	31.25%	653	67.4%		
Total	16	100%	969	100		

This table compares the outcome of inadequately treated hypothyroid pregnant mothers with normal control group. In my study group 12.5% the inadequately treated hypothyroid mothers had spontaneous miscarriages whereas only 5.9% of the control population had spontaneous miscarriages.

Again 12.5% of the inadequately treated hypothyroid mothers developed preeclampsia whereas only 4.1% of the control population developed preeclampsia.

In my study group 6.25% of the inadequately treated hypothyroid patients developed Oligohydramnios whereas only 3.5% of the control group developed Oligohydramnios.

Around 12.5% of the inadequately treated hypothyroid patients delivered preterm babies against the control group where only 6.5%. patients delivered preterm babies.

Around 6.25% of the inadequately treated patients delivered IUGR babies,whereas only 3.8% of the patients in the control group delivered IUGR babies.

In my study group 12.5% of the inadequately treated hypothyroid mothers delivered low birth weight babies , whereas in the control group only 5.5% patients delivered low birth weight babies.

From the above table we came to know that 68.75% of the inadequately treated patients developed complications like GDM, pre eclampsia, IUGR, oligohydramnios, preterm deliveries and low birth weight. Whereas only 32.6% of the control group developed these complications ,this implies a significant association between

inadequately treated hypothyroidism and poor pregnancy outcomes as evidenced by the p value of 0.002 which is very significant.

The overall chi sq. value: 9.26

P value: 0.00233

It is statistically significant.(<0.05%)

DISCUSSION

This study was conducted in Chengalpet medical college & hospital.

The purpose of the study was to follow the pregnancy outcomes in pregnant women with hypothyroidism to see whether they developed complications if left untreated and if adequate treatment altered the occurrence of complications.

The total number of pregnant women included in this study were 1000. All women who have been diagnosed as hypothyroid started on treatment over a period of 1 year were taken consecutively.

All antenatal women were screened using TSH at their first booking visit during first trimester.

Those who had an elevated TSH levels, were further tested with FT4 and started on treatment with levothyroxine irrespective of whether FT4 was elevated or not. The cut-off level for TSH was taken as 2.5 mIU/ml. Serum thyrotropin (TSH) level in early pregnancy is decreased because of thyroid stimulation from the weak TSH effects of HCG.

In a study by Green WL in 2005, truly normal range of TSH is defined as 0.5

2.5mIU/ml(6). So adequate replacement therapy should be given when TSH is above 2.5mIU/ml and/or with low T4, FT4 in pregnancy.

Overt hypothyroidism, subclinical hypothyroidism patients were treated with L Thyroxine in the dose of 1.20 µg/kg/day for subclinical hypothyroidism with TSH less than 4.2 mIU/L, 1.42 µg/kg/day with TSH greater than 4.2 to 10, and 2.33 µg/kg/day for overt hypothyroidism this dosing was based on a study by Dr. Abalovich and colleagues which was published in the journal of overt and subclinical hypothydism and which has been confirmed by numerous other studies according to the body weight to maintain serum TSH near normal

TSH levels were repeated for these patients after initiating the Treatment at 16wks, 20 wks,then at 32 wks and thyroxine dosage titrated accordingly.

Based on whether they were started on treatment before 10 weeks and given prompt dosage titration, or after 10 wks they were grouped as those receiving adequate treatment and inadequate treatment. A patient was considered to have received adequate treatment if the repeat TSH values were less than 3 mIU/ml Both the groups were followed till delivery and closely observed for the development of complications.

Out of 1000 pregnant woman screened in the first trimester 0.6% (6) patients were overt hypothyroid and 2.5% (.25) of the patients were subclinical hypothyroid.

Hence prevalence of hypothyroidism in my study group is 2.5% subclinical hypothyroidism and 0.6% overt hypothyroidism.

The prevalence of subclinical hypothyroidism in our study is 2.5% It is comparable with

Name	**Year**	**%**
Casey	2005	1.7
Casey[53]	2007	2.3
Canaris	2000	5
Janeclearygoldman	2008	2.2

Various studied showed when the cutoff value of serum TSH kept above 4mIU/L prevalence of thyroid disorder found to be less (2.2% - 2.5%).

Study	Prospective/ Retrospective	Place	Prevalence	Period ofscreening
Klein [54]1991	R	USA	2.5%, TSH >6	15 – 18 weeks
Glinoer[10] 1995	P	Belgium	2.2%, TSH >4	1st prenatal visit
Allan [55]2000	R	USA	2.2%, TSH >6	15 – 18weeks

When the cut off value of serum TSH kept >3mIU/L that incidence increased from 2.2% to 3.4%.

In our study prevalence of Hypothyroidism was 3.1%.

Casey 2007	R	USA	3.4%, TSH >3
Our study*	P	Chengalpet	3.1%, TSH >2.5

P-prospective study R- Retrospective study Out of the 1000 patients screened, 31 patients werefound to be hypothyroid out of them 15 adequately treated,while 16 patients received inadequate treatment. Out of the 15 adequately treated patients only 1 developed complications(6.7%).But 11 out of the 16 patients receiving inadequate treatment developed complications(68.75%).

Thyroid hormone is essential for normal development of the placenta. There is evidence that preeclampsia, placental abruption and preterm labour are causally linked to faulty early placentation. Hypothyroid mothers are also at an increased risk of developing fetal growth restriction and delivering low birth weight babies.(12)

The results of our study revealed that gestational diabetes .(GDM)was found in 1 out of the 16 inadequetely treated hypothyroid patients (6.2%). showing a possible relationship between hypothyroidism and glucose intolerance. on the other side 37 (3.8%)out of 969 patients in the control gestational diabetes .

Approximately 12.5% of inadequately treated patients end in spontaneous miscarriage (24) against 5.9% in the control group. It was also noted that in our study group , the women who had miscarriages had higher TSH values at diagnosis(>5mU/L).

Preeclampsia is identified in 2(12.5%) out of the 16 inadequately treated hypothyroid patients(48) against 40 out of 969that is 4.1% of control group patients.

Davis et al 1988 followed 25 hypothyroid women through 28 pregnancies who were divided into two groups, of which 16 were clinically hypothyroid and 12 had subclinical hypothyroidism. This

study showed that mothers with overt hypothyroidism are more at risk for preeclampsia.

Inadequately treated hypothyroid women in our study had 6.2% pregnancies complicated by Oligohydramnios which was higher than control group which is only 3% .

In our study population 12.5% of inadequately treated hypothyroid pregnancies ended up in preterm delivery (delivery before 37 weeks of gestation) which was higher than the control group which is 6.5%.

This is similar to the outcome of a study done by Jones WS et al in the American Journal of Obstetrics and Gynaecology in 1969 who concluded that premature deliveries were more frequent in pregnant women who had low thyroxine levels.

In our study 6.2% of the foetuses of inadequately treated mothers had intrauterine growth restriction which was higher than its occurrence in the control population which is only 3.8%.

Out of the 16 inadequately treated patients in our study, 2 women delivered babies with low birth weight (12.5%), whereas, only 1women in the adequately treated group had low birth weight babies (6.7%) and in the control population only 5.5% of the woman delivered low birth

weight babies. But, Low birth weight among these babies was mainly attributed to prematurity.

There was no case of placental abruption in the inadequately treated patients in my study although Casey Brian et al in 2005 in their study concluded that pregnancies complicated by subclinical hypothyroidism had a 3 fold increased risk of developing placental abruption and 2 fold increased risk of preterm labour compared to euthyroid women .

CONCLUSION

Thyroid hormone is essential for early placental development in pregnancy. Especially during the first twelve weeks of pregnancy the fetus entirely depends upon the maternal thyroid hormone for the normal neural and skeletal development.

Hence early diagnosis and adequate treatment of maternal hypothyroidism in pregnancy is essential in decreasing the incidence of complications like abortion, pre eclampsia, IUGR, placental abruption, oligohydramnios and low birth weight which are associated with hypothyroidism.

Inadequately treated hypothyroid women in my study group had 3 fold higher risk of developing preeclampsia.

There was a significant increase in the incidence of abortion or fetal growth restriction in the inadequately treated group.

There was no case of placental abruption in my study group.

Oligohydramnios was found to occur more commonly in the inadequately treated group.

Adequate treatment of hypothyroidism in pregnancy significantly reduces certain complications like miscarriages, pre eclampsia, IUGR ,oligohydramnios, glucose intolerance, preterm labour, low birth weight babies, abruptio Placentae and stillbirth.

RECOMMENDATION

Based on my study on prevalence of hypo thyroidism in pregnancy and pregnancy outcome I would like to recommend routine screening of at risk population followed by early and adequate treatment of all hypothyroid mother during pregnancy.

BIBLIOGRAPHY

1. Braverman LE.Adequate iodine intake-the good far outweighs the bad.Eur J Endocrinol.1998;139:14-15.

2. Glinoer D,De Nayer P,Bourdoux P,et al.Regulation of maternal thyroid during pregnancy.J Clin Endocrinol Metab.1990;71:276-287.

3. Haddow JE,Palomake GE,Allan WC,et al.Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child.NEJM.1999;341:549-555.

4. Pop VJ,Jl Kuijpens,van Baar AL,et al.Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy.Clin Endocrinol.1999;50:147-148.

5. Jones WS,Man EB.Thyroid function in human pregnancy.Premature deliveries and reproductive failures of pregnant women with low serum butanol-extractable iodines.Maternal serum TBG and TBPA capacities.Am J Obstet Gynecol.1969;104:909-914.

6. Green WL. New questions regarding bioequivalence of levothyroxine preparations: a clinician's response. AAPS J 2005;7:E54-E58.

7. Spencer et al. Thyroid function tests and pregnancy: what's normal? Endocrine Society Annual Meeting,May 2005

8. Montoro, M.M., Collea, J.V., Frasier, S.D. and Mestman, J.H. (1981) Successful outcome of pregnancy in women with hypothyroidism. Ann. Intern. Med., 94, 31±34

9. Cecconi S, Rucii N, Scadaferri ML, et al. Thyroid hormones effects on mouse oocyte maturation and granulose cell aromatase activity. Endocrinology 1999;140:1783-8.

10. Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle Oovert and subclinical hypothyroidism complicating pregnancy.2002 Jan;12(1):63-8

11. Roberts J, Jenkins C, Wilson R, et al. Recurrent miscarriage is associated with increased numbers of CD5/20 positive lymphocytes and an increased incidence of thyroid antibodies. Eur J Endocrinol 1996;134:84-6

12. Journal of thyroid research. Volume: 2011, article ID 397012, 4 pages. DOI: 10.4061/2011/397012. John .H.Lazaws

13. Davis, L.E., Leveno, K.J. and Cunningham, F.G. (1988) Hypothyroidism complicating pregnancy. Obstet. Gynecol., 72, 108±112.

14. Leung AS, Millar LK, Koonings PP. Perinatal outcome in hypothyroid pregnancies. Obstet Gynecol 1993; 81: 349-53.

15. Ohara N, Tsujino T, Mauro T. The role of thyroid hormone in trophoblast function, early pregnancy maintainence and fetal neurodevelopment. J Obstet Gynaecol Can, 2004; 26: 982-90.

16. Donmez M, Sisli T, Atis A, Aydin Y. Spontaneous Abortions and Thyroid Functions. Perinatal journal, 2005; 13: 110-4.

17. Prummel MF,Wiersinga WM.Thyroid peroxidase autoantibodies in euthyroid subjects.Best Pract Res Clin Endocrinol Metab.2005;19:1-15

18. Stagnaro-Green A,Roman SH,Cobin RH,et al.Detection of at risk pregnancy by means of highly sensitive assays for thyroid autoantibodies.JAMA.1990;264:1422-1425.

19. Bussen S,Steck T.Thyroid autoantibodies in euthyroid non-pregnant women with recurrent spontaneous abortions.Hum Reprod.1995;10:2938-2940.

20. Matalon ST,Blank M ,Ornoy A,et al.The association between anti-thyroid antibodies and pregnancy loss.Am J Reprod Immunol.2001;45:72-77.

21. Bijay Vaidya,Sony Anthony,Mary Bilous,Beverly Shields,John Druy,Stewart Hutchinson et al.Detection of thyroid dysfunction in pregnancy:Universal screening or targeted high risk case finding?JCEM 2007 92;203-207 doi:10,1210/jc:2006-1748

22. Casey,Brian.M;Dashe,Jodi.S;Wells,C.Edward;McIntire,Donald D;Byrd,William;Leveno Kenneth J. et al,Green Journal, Feb 2005 .105 (2):239-245.

23. D.K.James,P.J.Steer,C.P.Weiner,B.Gonik,High risk pregnancy management options,Third edition,Elsevier,Philadelphia,pg:1005

24. Leon Speroff M.D.Marc A.Fritz,Clinical Gynaecology and infertility,7th edition,Lippincott Williams &Wilkins,Philadelphia pg:815

25. Sejekan Prema,J.Obstet Gynecol India Vol60,No.3 May-June2010pg232-237

26. ACOG practice bulletin on thyroid disease in pregnancy. No :32 Nov 2001 issue. Am Fam Physicians 2001 May 15; 65(10) :2158 - 2162

27. The journal of clinical endocrinology and metabolism. J. Clin Endocrinol Metab : 92/8 (supplement) S1-S47, 2007. Management of thyroid dysfunction during pregnancy and post partum: An endocrine society clinical practise guideline

28. Cleary-Goldman J,Malone FD,Lambert-Messerlian G,Sullivan L,Canick J et al,Maternal thyroid hypofunction and pregnancy outcome.Obstet Gynecol.2008 Jul;112(1):85-92.

29. ACOG Committee Opinion Number:381,Oct 2007.

30. Morreale de Escobar G,Obregon MJ,Escobar del Rey F.Role of thyroid hormone during early brain development.Eur J Endocrinol.2004;151(suppl 3):U25-37.

31. Lavado-Autric R,Auso E,Garcia-Velasco JV et al.Early maternal hypothyroxinemia alters histogenesis and cerebral cortex cryoarchitecture of the progeny.J Clin Invest.2003;111:4037-4047.

32. Roberts CG,Ladenson PW. Hypothyroidism. Lancet .2004; 3:793-803.

33. Helfand M.Screening for subclinical thyroid dysfunction in nonpregnant adults:a summary of the evidence for The US Preventive Services Task Force.Ann Intern Med.2004;140:128-141.

34. Krassas, G.E. (2000) Thyroid disease and female reproduction. Fertil. Steril., 74, 1063±1070

35. Wang, C. and Crapo, L.M. (1997) The epidemiology of thyroid disease and implications for screening. Endocrinol. Metab. Clin. North Am., 26, 189± 218.

36. Brent GA. Maternal thyroid function: interpretation of thyroid function tests in pregnancy. Clin Obstet Gynecol 1997; 40: 3-15

37. Vaquero E, Lazzarin N, De Carolis H. Mild thyroid abnormalities and recurrent spontaneous abortion: diagnostic and therapeutic approach. Am J Reprod Immunol. 2000; 43: 204-8.

38. Pratt D, Novotny M, Kaberlein G. Antithyroid antibodies and the association with non-organ specific antibodies in recurrent pregnancy loss. Am J Obstet Gynecol, 1993; 168: 837-41.

39. Healy, D.L., Trounson, A.O. and Andersen, A.N. (1994) Female infertility: causes and treatment. Lancet, 18, 1539±1544.

40. Matsua K, Kaberlein G, Burrow G. Spontaneous pregnancy termination and thyroid abnormalities. Hum Reprod 2000; 15: 163-79

41. Thompson CC, Potter GB. Thyroid hormone action in neural development. Cereb Cortex 2000;10:939-45.

42. Sharma PP, Mukhopadhyay P. Mukhopadhyay A. et al. Hypothyroidism in pregnancy. J Obstet Gynecol India 2007;57:331-4.

43. AyalaAR,Wartofsky L. The case for more aggressive screening and treatment of mild thyroid failure. Cleve Clin J Med 2002;69:313-20

44. .McGregorAM, Hall R, Richards C.Autoimmune thyroid disease and pregnancy. Br Med J 1984;288:1780-1

45. Spong CY. Subclinical hypothyroidism: should all pregnant women be screened? Obstet Gynecol 2005;105:235-6.

46. Brown RS,Bellisario RL,Botero D et al; Incidence of transient congenital hypothyroidism due to maternal thyrotropin receptor-blocking antibodies in over one million babies..J Clin Endocrinol Metab81:1147,1996.

47. Song SI,Daneman D,Rovet J:The influence of etiology and treatment factors on intellectual outcome in congenital hypothyroidism.J Dev Behav Pediatr 22;376,2001.

48. .Martin J N Jr Thigpen B D, Moore RC,et al :stroke and severe preeclampsia and eclampsia:paradigm shift focusing on systolic blood pressure.Obstet Gynecol 105(2):246 2009

PROFORMA

Name :

Age :

Address :

Socioeconomic Class :

OP/IP No. :

Booked/Un booked:

Immunized:

Obstetric Formula :

LMP :

EDD :

Menstural History:

Marital History :

Past History:

Treatment History:

Risk Factors:

H/o Miscarriage,

H/oPreeclampsia,

FamilyH/oThyroid disorder

Symptoms ,signs of Thyroid disorder,

Thyroid nodule

O/E Conscious

Afebrile
Pallor
Pedaledema/nopedaledema,
Thyroid swelling
Breast
Spine
Pulse Rate
Blood Pressure
Cardiovascular system:
Respiratory system :
Abdomen :
Vaginal

Height
Weight
Body Mass Index

Investigation:

Urine: Albumin
Sugar
Deposit

Blood:

Haemoglobin
VDRL
HBSAg
HIV
Blood Sugar

Blood group Rh typing

Ultrasonogram

Specific Investigation:

Serum TSH

If TSH is abnormal,

Free T4

Treatment :

Endocrinologist Opinion :

Follow UP :

Maternal complication:

Fetal complication:

Mode of Delivery:

Baby details:

Birth weight-

APGAR-

KEY TO MASTER CHART:

OBSTERTRIC CODE:

1 – primigravida,

2- Multi gravida with previous normal delivery

3- Multi with previous LSCS

GESTATIONAL AGE AT DIAGNOSIS:

1- Preconceptionaly

2- Less than 10 weeks

3- More than 10 weeks

SCREENING TSH:

1. <2.5 mIU/ml

2. 2.5-4.2 mIU/ml

3. 4.2-10.0 mIU/ml

4. >10.0 mIU/ml

REPEAT TSH;

1. <3.0 mIU/ml
2. 3.0-4.2 mIU/ml
3. 4.2-10 mIU/ml
4. .10 mIU/ml

T4:

1. Normal
2. Decreased

TREATMENT ADEQUACY:

1. Adequate
2. Inadequate

MODE OF DELIVERY;

1. Normal Vaginal Delivery
2. LSCS
3. Vacuum Delivery
4. Forceps Delivery

PREGNANCY OUTCOME:

1. Spontaneous Miscarriage
2. Gestational Diabetes Mellitus
3. Preeclampsia
4. Oligohydramnios
5. Preterm Labour
6. IUGR
7. Low Birth weight
8. No Complications

MASTER CHART PREVALENCE OF HYPOTHYROIDISM AND PREGNANCY OUTCOME CONTROL GROUP

S.NO	OP NO	AGE	OBSTERTRIC CODE	GA AT SCREENING	SCREENING TEST	CLASSIFICATION	MODE OF DELIVERY	PREGNANCY OUTCOME
1	5012	23	1	2	1	1	1	8
2	5074	19	1	3	1	1	1	8
3	5089	24	2	2	1	1	1	8
4	5065	27	3	2	1	1	2	1
5	5118	28	2	2	1	1	1	8
6	5120	31	1	2	1	1	3	3
7	5121	27	1	3	1	1	1	8
8	5129	28	1	2	1	1	2	8
9	5134	25	2	2	1	1	1	8
10	5135	19	1	2	1	1	1	2
11	5156	24	2	3	1	1	1	8
12	5167	22	2	2	1	1	2	8
13	5163	26	1	2	1	1	2	6
14	5169	28	1	2	1	1	2	8
15	5170	26	2	2	1	1	2	5
16	5172	21	3	3	1	1	2	8
17	5178	18	1	2	1	1	2	4
18	5174	22	2	2	1	1	3	8
19	5235	26	3	2	1	1	3	8
20	5179	22	1	2	1	1	4	8
21	5184	29	2	2	1	1	NA	1
22	5187	30	3	3	1	1	2	8
23	5196	32	1	2	1	1	1	8
24	5212	19	1	2	1	1	1	2
25	5215	24	1	3	1	1	1	8
26	5217	23	1	2	1	1	3	8
27	5218	21	2	3	1	1	1	8
28	5230	27	3	2	1	1	2	8
29	5238	19	1	3	1	1	1	8
30	5242	20	1	2	1	1	2	8
31	5246	27	1	3	1	1	2	8
32	5254	22	3	2	1	1	2	6
33	5257	23	2	2	1	1	1	8
34	5259	27	1	2	1	1	3	8
35	5281	28	1	2	1	1	2	8
36	5287	25	3	3	1	1	2	8
37	5284	29	1	2	1	1	2	5
38	5291	21	1	2	1	1	NA	1
39	5296	20	2	2	1	1	1	8
40	5299	19	1	3	1	1	2	4
41	5304	29	3	2	1	1	2	2
42	5308	33	1	3	1	1	4	8
43	5318	26	2	3	1	1	1	8

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45	5317	28	1	2	1	1	2	8
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47	5329	22	3	2	1	1	2	8
48	5327	28	1	2	1	1	2	8
49	5331	29	1	3	1	1	1	8
50	5335	22	1	3	1	1	1	4
51	5338	21	2	3	1	1	1	8
52	5341	24	3	3	1	1	2	8
53	5347	30	2	2	1	1	NA	1
54	5349	27	1	2	1	1	1	8
55	5352	28	1	2	1	1	2	8
56	5356	26	1	2	1	1	1	8
57	5359	24	1	2	1	1	1	8
58	5362	26	2	3	1	1	2	8
59	5364	27	2	3	1	1	1	8
60	5367	21	1	2	1	1	1	2
61	5369	22	1	2	1	1	1	8
62	5371	26	2	2	1	1	1	8
63	5373	28	1	3	1	1	1	8
64	5376	22	1	3	1	1	2	5
65	5378	27	1	2	1	1	2	8
66	5382	29	1	2	1	1	2	6
67	5384	30	1	2	1	1	1	3
68	5389	32	3	2	1	1	2	8
69	5391	31	1	3	1	1	1	8
70	5396	25	2	2	1	1	1	8
71	5394	27	2	2	1	1	1	4
72	5395	28	3	2	1	1	NA	1
73	5405	25	1	3	1	1	3	8
74	5402	33	2	2	1	1	1	8
75	5409	31	2	2	1	1	1	8
76	5413	23	2	2	1	1	1	8
77	5417	18	1	3	1	1	2	2
78	5418	19	1	2	1	1	1	8
79	5427	22	2	2	1	1	1	6
80	5421	24	1	3	1	1	1	8
81	5424	25	1	2	1	1	2	8
82	5428	25	2	2	1	1	3	8
83	5431	26	3	3	1	1	1	8
84	5438	27	2	2	1	1	1	5
85	5437	29	3	2	1	1	1	4
86	5434	22	2	3	1	1	1	8

87	5443	25	2	2	1	1	1	8
88	5446	23	1	2	1	1	1	8
89	5448	24	2	2	1	1	3	8
90	5450	26	3	3	1	1	2	2
91	5452	28	1	2	1	1	1	8
92	5454	29	1	2	1	1	2	8
93	5458	21	2	2	1	1	1	6
94	5462	25	1	2	1	1	1	8
95	5464	22	1	2	1	1	1	8
96	5469	22	2	3	1	1	1	8
97	5472	26	3	2	1	1	2	8
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906	8537	26	1	2	1	1	1	8
907	8539	22	1	2	1	1	NA	1
908	8546	21	2	3	1	1	3	8
909	8549	24	3	2	1	1	1	8
910	8551	27	2	2	1	1	1	4
911	8563	28	3	2	1	1	1	8
912	8568	31	2	2	1	1	1	8
913	8571	27	2	2	1	1	1	8
914	8577	28	1	2	1	1	1	8
915	8584	25	2	3	1	1	2	2
916	8592	19	1	3	1	1	2	8
917	8597	24	1	2	1	1	1	8
918	8598	22	1	2	1	1	2	8
919	8604	26	2	2	1	1	2	8
920	8612	28	1	3	1	1	1	8
921	8617	26	1	2	1	1	1	8
922	8622	21	2	2	1	1	1	8
923	8634	18	1	2	1	1	2	8
924	8641	22	1	3	1	1	1	8
925	8645	26	2	2	1	1	1	5
926	8654	20	3	3	1	1	2	3
927	8658	21	3	2	1	1	2	8
928	8661	28	2	3	1	1	1	8
929	8669	22	3	3	1	1	2	8
930	8675	19	1	2	1	1	1	8
931	8677	26	1	2	1	1	1	8
932	8682	23	1	2	1	1	4	8
933	8685	20	2	3	1	1	1	2
934	8691	19	1	2	1	1	3	6
935	8695	20	3	2	1	1	2	8
936	8697	22	1	2	1	1	2	8
937	8702	23	3	2	1	1	2	4
938	8714	25	1	2	1	1	2	8
939	8719	27	1	2	1	1	1	8
940	8724	25	2	3	1	1	1	8
941	8728	21	1	2	1	1	2	8
942	8734	19	1	2	1	1	2	8
943	8743	20	1	2	1	1	4	8
944	8746	21	2	3	1	1	1	8
945	8753	28	1	2	1	1	3	8
946	8762	27	1	2	1	1	NA	1

947	8767	20	2	3	1	1	1	8
948	8771	22	3	2	1	1	2	8
949	8773	24	1	2	1	1	2	8
950	8784	26	1	3	1	1	1	8
951	8785	21	1	2	1	1	1	8
952	8792	25	2	2	1	1	1	3
953	8797	24	3	2	1	1	2	8
954	8804	21	2	3	1	1	1	8
955	8807	24	1	2	1	1	1	8
956	8812	27	1	2	1	1	2	8
957	8823	28	1	2	1	1	1	2
958	8832	31	1	2	1	1	1	8
959	8838	27	2	3	1	1	1	7
960	8842	28	2	2	1	1	1	8
961	8846	25	1	2	1	1	1	8
962	8857	19	1	3	1	1	1	8
963	8863	24	2	2	1	1	NA	1
964	8876	22	1	2	1	1	1	4
966	8884	28	1	2	1	1	2	8
967	8897	26	1	2	1	1	2	8
968	8906	21	1	3	1	1	1	8
969	8915	18	3	2	1	1	2	3

MASTER CHART PREVALENCE OF HYPOTHYROIDISM AND PREGNANCY OUTCOME STUDY GROUP

S.NO	AGE	AGE	Body wt wt(kg)	OBSTERTRIC CODE	POG AT DIAGNOSIS	SCREENING TEST	T4	CLASSIFICATION	REPEAT TSH			TREATMENT	MODE OF DELIVERY	PREGNANCY OUTCOME
									16 WEEKS	20 WEEKS	32 WEEKS			
1	5123	19	54	1	2	2	1	2	1	1	1	1	1	8
2	5234	21	52	1	1	3	1	2	2	NA	NA	2	NA	1
3	6123	21	58	1	2	2	1	2	1	1	1	1	2	8
4	7234	23	62	1	2	2	1	2	1	1	1	1	1	8
5	5345	22	53	2	3	4	2	3	3	2	2	2	1	3
6	6234	25	58	1	2	2	1	2	1	1	1	1	1	8
7	7456	28	57	3	3	4	2	3	3	2	1	2	2	2
8	5567	24	56	1	2	3	1	2	1	1	1	1	1	8
9	6345	22	50	2	3	3	1	2	2	2	1	2	2	4
10	5678	21	61	1	2	2	1	2	1	1	1	2	1	8
11	7345	26	58	2	3	2	1	2	2	2	1	2	1	7

12	5789	27	63	3	2	2	1	2	1	1	1	1	2	8
13	6456	20	62	1	3	4	2	3	2	NA	NA	2	NA	1
14	5890	24	56	2	2	3	1	2	1	1	1	1	1	8
15	7456	25	61	3	1	3	1	2	2	2	1	2	2	8
16	6567	24	59	2	3	4	2	3	2	2	1	2	1	7
17	7678	26	54	1	2	2	1	2	1	1	1	1	2	8
18	6789	22	58	3	3	3	1	2	2	2	1	2	2	6
19	8123	21	55	1	2	3	1	2	1	1	1	1	1	7
20	7789	23	61	2	3	2	1	2	2	2	1	2	3	8
21	8234	30	63	3	1	2	1	2	1	1	1	1	2	8
22	9123	21	56	1	3	4	2	3	3	2	1	2	1	5
23	6890	25	59	2	2	2	1	2	1	1	1	1	3	8
24	8345	27	62	3	2	3	1	2	1	1	1	1	2	8
25	7890	21	58	1	3	3	1	2	2	2	1	2	1	5
26	8456	27	59	3	1	3	1	2	1	1	1	1	2	8

27	8789	23	63	1	3	2	1	2	2	2	1	2	3	8
28	8567	26	59	1	1	3	1	2	1	1	1	1	4	8
29	8890	23	58	1	3	4	2	3	3	2	1	2	2	3
30	8678	24	60	2	3	3	1	2	2	2	1	2	3	8
31	5892	27	58	2	2	3	1	2	1	1	1	1	2	8

KEY WORDS

1. Sub Clinical Hypothyrodism,
2. TSH Screening,
3. Prevalence Of Hypothyroidism In Pregnancy,
4. fT4,
5. Complications Of Hypothyroidism In Pregnancy,
6. Pregnancy Outcome,
7. Levothyroxine,
8. Low Birth Weight,
9. Placental Abruption,
10. Spontaneous Abortion,
11. IUGR,
12. Overt Hypothyroidism,
13. Hyperthyroidism,