IJSAR, 6(12), 2019; 01-13

International Journal of Sciences & Applied Research

www.ijsar.in

Hypothyroidism in pregnancy and it's maternal outcome

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Abstract

Introduction: Hypothyroidism in pregnancy is one of the most common endocrine disorder in pregnancy. It is associated with increased risk of maternal complications.

Objective: To study the impact of hypothyroidism in pregnancy on maternal outcome

Material and Methods: Prospective study conducted on the women who fulfil inclusion and exclusion criteria attending antenatal clinic at a tertiary care centre in North India.

Conclusion: Hypothyroidism in pregnancy is associated with increased maternal complications.

Keywords: Hypothyroidism, pregnancy, euthyroid

Introduction

A variety of endocrine disorders can complicate pregnancy and vice versa. Thyroid disorder is one of the commonest among them. Numerous hormonal changes as well as alterations in metabolic demands occur during pregnancy, resulting in profound and complex effects on thyroid function. Because thyroid disorders are much more prevalent in women of childbearing age than in men of the same age group, it is not surprising that common thyroid disorders, such as chronic autoimmune thyroiditis, hypothyroidism, Graves' disease (GD), etc, are relatively frequently observed in pregnant women. Hypothyroidism during pregnancy is deleterious to both mother and child. Children born to untreated or undertreated mothers have profound effect on future intellectual development.[1]The main change in thyroid function associated with the pregnant state is the requirement for an increased production of thyroid hormone which depends directly upon adequate availability of dietary iodine and a normal and functional thyroid gland. During pregnancy, the thyroid gland may enlarge by 10% in countries where iodine sources are sufficient and to a greater extent in iodine poor countries.[2]Production of thyroid hormones and iodine requirement each increases by approximately 50% during pregnancy. [3] The physiological adaptation to the pregnant state can only take place when the iodine intake is appropriate. When iodine intake is deficient, however, pregnancy can reveal an underlying iodine deficiency. Iodine deficiency (ID) during pregnancy and infancy may impair growth and neurodevelopment of the offspring and increase infant mortality. It is noteworthy

that assessment of iodine status in pregnancy is difficult. Meanwhile, it remains unclear whether iodine intakes are sufficient in this group, leading to calls for iodine supplementation during pregnancy in several industrialized countries.[2] The economy of the thyroid is modified by several complex physiological changes such as the marked increase in both serum thyroid binding globulin (TBG) concentrations and extra thyroidal thyroxine (T_4) distribution space that take place during the first half of gestation. To maintain the homeostasis of T_4concentrations, the thyroid machinery must produce more T_4 until a new steady state is reached around mid-gestation. Thus, the main change in thyroid function associated with the pregnant state is the requirement of an increased production of thyroid hormone which, in turn, depends directly upon the adequate availability of dietary iodine and integrity of the thyroid gland. Therefore, any functional perturbation of normal thyroid function may have consequences for pregnancy outcome, and conversely, pregnancy by itself may affect the presentation and course of most thyroid disorders.

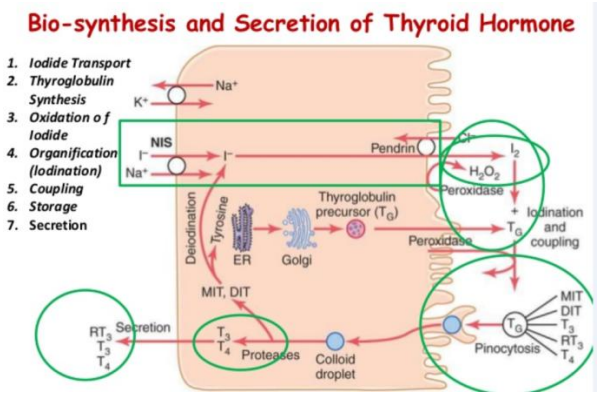
In addition to changes in thyroid function tests occurring in pregnancy, hyper metabolic syndromes of normal pregnancy mimic clinical picture of some thyroid disorders So diagnosis or exclusion of abnormal thyroid function are critically important. Pregnancy constitutes a unique experimental model in human, where in plethora of hormonal changes contribute to the physiological changes in pregnancy and that of in thyroid gland. An understanding of normal physiological variation of thyroid function is required for appropriate interpretation of results.

THYROID HORMONESYNTHESIS AND METABOLISM[4]

Thyroid gland is located in front of trachea in neck where synthesis and release of thyroid hormones occur. Triiodothyronine (T3), Tetraiodothyronine (T4) are the thyroid hormones released into circulation. T3 is 3 times more potent than T4. T3 & T4 are mostly protein bound. Unbound portion have biological activity. Binding proteins are TBG, Albumin. T3 is available as free & activate compound in higher proportion. These are 3 deiodinases which regulate metabolism of T3 & T4[4]. Most circulatingT3 is found by peripheral deiodination of T4. TSH is glycoprotein released from anterior pituitary consisting of alpha sub unit shared with other anterior pituitary hormones and unique B subunit. TSH increases synthesis and release of thyroid hormones.

Biosynthesis of thyroid Hormones

The majority (90%) of hormone produced by the follicular cells is T4. T4 can only be made in the thyroid gland. It can then be converted by other tissues into T3.

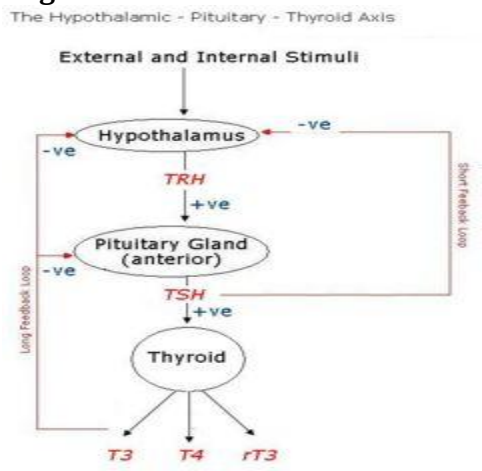


Transport: Thyroid hormones are lipid soluble, thus need a transporting protein in order to travel in the blood. 99% of thyroid hormones in circulation are bound. The primary transport protein for thyroid hormones is TBG. The remainder are carried by **thyroxin-binding prealbumin** or **albumin**.

Degradation: Only free T3 and free T4 can enter cells to exert their actions. T4 is

deiodinated to T3 in many cells of the body, particularly the liver and kidneys. The thyroid secretes 90% T4, with 50% of this being deiodinated to T3. The remainder is converted to **rT3**. This is an inactive form of T3, and so creation of it is a regulatory mechanism. More rT3 is created when the body needs to reduce the action of T3 and T4.The hormones are further deiodinated to diiodothyronine and monoiodothyronine in the liver and kidneys. Iodine is recycled or excreted in the urine.

Regulation



CHANGES IN THYROID PHYSIOLOGY DURING PREGNANCY[4]

Size of thyroid gland - increased by 10-20%

Altered thyroid binding globulin production

- There is increased estrogen synthesis ----> greater sialylation of carbohydrate moieties on TGB, so half-life is increased from 15min to 3 days.
- Increased TBG synthesis.

Iodine Deficiency:

- In early pregnancy increased GFR causes increase renal loss of iodine . Iodine deficiency enlargement of thyroid occurs.
- In early second trimester transport of iodine to fetus occurs[4].

Production of hCG

- TSH and hCG share a common alpha subunit and their beta subunit also have considerable similarity.
- In 1st trimester increase in hCG ------ > stimulates TSH receptor in thyroid gland causing increased hormone production.
- Certain fractions of hCG have TSH like activity than others. Partially desialated hCG has greater TSH like activity[4].

Deiodination of thyroid hormone

- Type 1 deiodinase is not altered during pregnancy.
- Type 2 deiodinase activity increases as gestation increases which causes conversion of T3 to T4
- Type 3 deiodinase activity increases as pregnancy advances which causes increase in conversion of T4 to reverse T3, thus increasing placental availability for fetal transfer.

BIOCHEMICAL ASSESMENT OF THYROID FUNCTION IN PREGNANCY[4]

TBG increases, total T3, total T4 increases, circulating FT3, FT4 levels are largely unchanged.

1st trimester: TSH decreases, FT4 increases

2nd trimester: TSH, T4 remain in normal limits

3rd trimester:

1. TSH increases , FT4 decreases ---> this biochemical hypothyroidism is well tolerated with no clinical features of hypothyroidism as euthyroidism is maintained by an increase sensitivity of tissue to thyroid hormones.
2. It could be physiological adaptation to try to conserve energy in preparation of parturition.
3. May be due to increase fetal demand.

In pregnancy FT4 and TSH should be monitored rather than total T4 and total T3

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HYPOTHYROIDISM IN PREGNANCY

Overt hypothyroidism complicates from 2-3 pregnancies per 1000[6,7]

Prevalence of hypothyroidism in pregnancy in India is 6.3%[8]

Causes of hypothyroidism

1) Iodine defeciency Commonest cause
2) Auto immune
   i. Hashimotos thyroiditis(chronic) next common
   ii. Dequervains thyroiditis (sub acute, transient)
3) Iatrogenic
   i. Thyroidectomy
   ii. previous RAI treatment
   iii. Drug therapy (lithium , amiodarone)
4) Congenital hypothyroidism
   i. thyroid dysgenesis
   ii. genetic mutation of thyroid receptors
   iii. hyroiddys hormonogenes
5) Infiltrative disorders.Eg: Sarcoidosis

EFFECT OF PREGNANCY ON HYPOTHYROIDISM

There is aneed for increase in dose of thyroxine during pregnancy

Pregnancy outcome in hypothyroidism

There is increased incidence of PIH, anemia, FGR, placental abruption, PPH, Cardiac dysfunction, increased risk of miscarriage.

FETAL:

Congenital abnormality

Still birth

Prematurity

Increased risk of fetal distress in labour, neonatal encephalopathy, reduced intellect, ovarian hyperstimulation(rare).

Increase rate of 16 alpha hydroxylation of estradiol resulting in increase formation of estriol instead of (N) 2 alpha hydroxylation cause inadequate feedback mechanism at pitutary levels , cause increased gonadotropin release ---> cystic reaction in ovaries.

DIAGNOSIS OF HYPOTHYROIDISM IN PREGNANCY

Symptoms of hypothyroidism such as tiredness, constipation, weight gain, anemia, carpel tunnel syndrome , thinning of hair are seen during pregnancy even in absence of thyroid disorder. So we need to rely on biochemical measurement for diagnosisof hypothyroidism in pregnancy[9].

The diagnosis of hypothyroidism based on maternal signs and symptoms is particularly difficult because of non specific nature and considerable overlap with the changesthat occur in normal pregnancy.

Guidelines by American Thyroid Association Taskforce on Thyroid Disease in Pregnancy and Postpartum[10]

Screening for Thyroid Dysfunction during Pregnancy[10,11]

Although the benefits of universal screening for thyroid dysfunction (primarily hypothyroidism) may not be justified by current evidence , it is recommended in following women at high risk for thyroid disease by measurement of TSH.

1.Women with history of hyperthyroid or hypothyroid disease , PPT (postpartum thyroid dysfunction) or thyroid lobectomy.

2. Women with a family history of thyroid disease

3. Women with a goiter

4. Women with thyroid antibodies (when known)

5. Women with symptoms or clinical signs suggestive of thyroid underfunction or over function , including anemia , elevated cholesterol, and hyponatremia.

6. Women with type 1 diabetes

7. Women with other autoimmune disorders.

8. Women with infertility who should have screening with TSH as part of their infertility work up.

9. Women with previous therapeutic head or neck irradiation

10. Women with a history of miscarriage or preterm delivery.

Hypothyroidism and Pregnancy: **Maternal and Fetal Aspects**[11]

Both maternal and foetal hypothyroidism are known to have serious adverse effects on the foetus. Therefore maternal hypothyroidism should be avoided.

lf hypothyroidism has been diagnosed before pregnancy, it is recommended to adjust the preconception thyroxine dose to reach a TSH level not higher than 2.5 mIU/L prior to pregnancy.

The T4 dose usually needs to be incremented by 4-6 wks.Gestation and may require a 30-50% increase in dosage.

If overt hypothyroidism is diagnosed during pregnancy, thyroid function tests (TFTs) should be normalized as rapidly as possible. The dosage should be titrated to rapidly reach and thereafter maintain serum TSH concentrations of less than 2.5 mIU/L in the first trimester (or 3 mIU/L in the second and third trimester) or to trimester-specific normal TSH ranges Thyroid function tests should be repeated within 30 to 40 days. Subclinical hypothyroidism (serum TSH concentration above the upper limit of the reference range with a normal free T4) has been shown to be associated with an adverse outcome for both the mother and offspring. T4 treatment has been shown to improve obstetrical outcome but has not been proved to modify long-term neurological development in the offspring. However, given that the potential benefits outweigh the potential risks, it is recommended to replace T4 in women with subclinical hypothyroidism. After delivery, most hypothyroid women need a decrease in the thyroxine dosage they received during pregnancy.

MANAGEMENT OF HYPOTHYROIDISM

Thyroxine therapy is mainstay of medical treatment of hypothyroidism in pregnancy. Thyroxine is considered to be safe in pregnancy and lactation.

According to clinical practice guidelines by American endocrine society[11]

1. Both maternal and foetal hypothyroidism are known to have serious adverse effects on the fetus. Therefore maternal hypothyroidism should be avoided.
2. If Hypothyroidism has been diagnosed before pregnancy, adjust the preconception thyroxine dose to reach before pregnancy a TSH level not higher than 2.5mIU/l
3. The thyroxine dose often needs to be incremented by 4-6wk gestation and may require a 30-50% increment in dosage.
4. If overt hypothyroidism is diagnosed during pregnancy, thyroid function tests should be normalized as rapidly as possible. Thyroxine dosage should be titrated to rapidly reach and thereafter maintain serum TSH concentrations of less than 2.5mIU/L in first trimester (or 3 mIU/L in second and third trimester) or to trimester specific normal TSH ranges. Thyroid function tests should be measured within 30-40days.
5. Subclinical Hypothyroidism (serumTSH concentration above the upper limit of the reference range with a normal free T4) has been shown to be associated with adverse outcome for both mother and fetus. Thyroxine treatment has been shown to improve obstetrical outcome, but has not been proved to modify long term neurological development in the offspring. However, given that the potential benefits outweigh the potential risks, it is recommended replace thyroxine in women with subclinical hypothyroidism
6. After delivery, most hypothyroid women need to decrease thyroxine dosage they received during pregnancy.

FETAL & NEONATAL OUTCOME

Hypothyroidism in 1st trimester has adverse effect on developing fetal brain. Antiperoxidase and antithyroglobulin antibodies cross the placenta and they

appear to have no effect on fetal thyroid development. So Hashimotos thyroiditis does not cause fetal or neonatal thyroid dysfunction. TSH receptor blocking antibodies may rarely cause fetal or transient neonatal hypothyroidism.

AIMS AND OBJECTIVES

1. To study antenatal problems in women with thyroid disorders.
2. To test hypothyroid pregnant women for TPO antibody status and study the associated complications and perinatal outcome.
3. To achieve optimal euthyroid status by serial TSH estimation and Replacement

Materials and methods

TYPE OF STUDY: Prospective Study

SOURCE OF DATA: Pregnant women attending antenatal clinic ina tertiary care hospital , Jodhpur ,who fulfil the inclusion criteria and are diagnosed with hypothyroidism.

STUDY PERIOD: Period of study is from January 2018 to December 2018.

METHOD OF COLLECTION OF DATA

Inclusion criteria:

- Pregnant women attending antenatal clinic of our hospital and with known correct gestational age.
- Women with known thyroid disorder.
- Women with singleton pregnancy.
- Pregnant women who understands, agrees, and signs consent form.

Exclusion criteria:

- Pregnant women whose dates were not known.
- Pregnant women with already known medical disorder.
- Multifetal gestation

Women with TSH > 2.5mIU/L who satisfied inclusion criteria were allotted to study population.

Method of study: Women who fulfil the inclusion criteria will be taken into study group after taking informed consent. Serum TSH and TPO antibodies will be done irrespective of gestational age. Trimester specific ranges for TSH levels are as follow:

First trimester : 0.1 to 2.5mIU/L
Second trimester: 0.2 to 3.0mIU/L
Third trimester : 0.3 to 3.0mIU/L

Reference range for TPO antibody < 35IU/mL

Below this level is considered as TPO Negative and above this is considered as TPO positive

Women will be treated accordingly. These women will be followed up throughout their antenatal period till delivery by serial measurement of TSH and thyroxin dose adjusted according to the changes in TSH level.The parameters evaluated during study

Maternal:

1. Gest.HTN
2. Pre-eclampsia
3. GDM
4. Preterm
5. IUGR

RESULTS

Table.No.1. DISTRIBUTION OF CASES ACCORDING TO TPO ANTIBODY STATUS

Patient	TPO Negative	TPO Positive	Total
Number	63	34	97
%	64.9	35.1	100

In the studied 97 hypothyroid pregnant women, 34 women were TPO positive and 63 women were TPO negative.

Table.2. AGE WISE DISTRIBUTION OF CASES ACCORDING TO TPO ANTIBODY STATUS

Age	**TPO Negative**	**%**	**TPO Positive**	**%**
< or = 20	6	9.53	2	5.88
21 – 25	22	34.9	18	52.94
26 – 30	21	33.34	9	26.47
31-35	12	19.05	4	11.76
>35	2	3.18	1	2.94
Total	**63**	**100%**	**34**	**100%**

In TPO negative hypothyroid women, maximum women (34.9%) belonged to the age group of 21-25 years. Among TPO positive hypothyroid women, majority women belonged to the age group of 21-25 years. Minimum age was 19 years and maximum age was 39 years.

Table.3: DISTRIBUTION OF CASES ACCORDING TO TIME OF DIAGNOSIS

Diagnosis	TPO Negative group	%	TPO Positive Group	%
Pre Pregnancy	27	42.86	10	29.4
Pregnancy	36	57.14	24	70.6
Total	63	100%	34	100%

Out of 63 TPO negative hypothyroid women, 27 women were diagnosed before pregnancy and 36 women were diagnosed during pregnancy. Out of 34 TPO positive hypothyroid women, 10 women were diagnosed before pregnancy and 24 women were diagnosed during pregnancy.

Table.No.4. DISTRIBUTION OF CASES ACCORDING TO ACHIEVEMENT OF EUTHYROIDSTATUS

Euthyroid status	TPO negative	TPO positive
Achieved	63	34
Not Achieved	Nil	Nil

In TPO negative group all 63 pregnant women achieved euthyroid status by serial TSH monitoring and adequate replacement.
In TPO positive group all 34 pregnant women achieved euthyroid status by serial TSH monitoring and adequate replacement.

Table.No.5.DISTRIBUTIONS OF CASES ACCORDING TO PRESENCE OF COMPLICATIONS

Complications	TPO Negative	%	TPO Positive	%	P value

Yes	21	33.34	25	73.53	p< 0.00015
No	42	66.66	9	26.47	
Total	63	100%	34	100	

Out of 63 TPO negative hypothyroid women, 21(33.34%) women had complications. Out of 34 TPO positive hypothyroid women, 25 (73.53%) women had complications which is statistically significant **(p< 0.00015)** and 9 members had more than one complication.

Table.No.6.DISTRIBUTION OF CASES ACCORDING TO COMPLICATIONS

Complications	TPO Negative group	Percentage	TPO positive Group	Percentage
Pre Term	3	4.76	16	47
GDM	7	11.1	7	20.58
Gest HTN	10	15.87	1	2.94
Pre-Eclampsia	1	1.59	7	20.58
IUGR	2	3.17	3	8.8

Out of 63 TPO negative hypothyroid women, 21(33.34%) women had complications and the commonest complication was gestational hypertension. Out of 34 TPO positive hypothyroid women, 25 (73.53%) women had complications and the commonest complication was preterm labour, followed by gestational diabetes mellitus and pre eclampsia which is statistically significant **(p< 0.00015)**.

Table.No.7.DISTRIBUTION OF CASES ACCORDING TO GESTATIONAL AGE AT DELIVERY

Gestational Age	TPO Negative group	%	TPO Positive group	%	P value
< 32 Wks (Early Preterm)	0	0	0	0	
32-33.6 Wks (Moderate Preterm)	0	0	1	2.94	
34-36.6Wks (Late Preterm)	3	4.76	15	44.18	
37-38.6Wks (Early Term)	34	53.97	11	32.3	P<0.000036
39-40.6Wks (Full Term)	24	38.1	7	20.58	
41-41.6Wks (Late Term)	2	3.17	0	0	
42 Wks (Post Term)	0	0	0	0	
Total	63	100	34	100	

In TPO Negative group 34 (53.97%) were delivered at early term, 24(38.1%) were delivered at full term, 3 (4.76%) delivered at late preterm, 2 (3.17%) delivered at late term.

While in TPO Positive group 15 (44.18%) were delivered at late preterm, 11(32.3%) were delivered at early term, 7 (20.58%) delivered at full term , 1(2.94%) delivered at moderate preterm.

Table.No.8. DISTRIBUTION OF CASES ACCORDING TO MODE OF DELIVERY

Mode of delivery	TPO Negative Group	%	TPO positive Group	%
Vaginal	36	57.14	17	50%
LSCS	27	42.86	17	50%
Total	63	100	34	100

Out of 63 TPO negative hypothyroid women, 36 (57.14%) women had vaginal deliveries and 27 (42.86%) women underwent caesarean section. Out of 34 TPO positive hypothyroid women, 17 (50%) women had vaginal deliveries and 17 (50%) women underwent caesarean section.

Table.No.9: DISTRIBUTION OF VAGINAL DELIVERY CASES (INDUCED OR SPONTANEOUS)

Vaginal	TPO Negative	%	TPO Positive	%
Spontaneous	26	72.22	12	70.58
Induced	10	27.78	5	29.42
Total	36	100	17	100

In TPO negative group, out of 36 vaginal deliveries, 26 (72.22%) were spontaneous and 10 (27.78%) were induced. In TPO positive group, out of 17 vaginal deliveries, 12 (70.58%) were spontaneous and 5 (29.42%) were induced.

Table.No.10: DISTRIBUTION OF INDUCED VAGINAL DELIVERIES ACCORDING TO INDICATION

Indication for Induction	TPO Negative	%	TPO Positive	%
Gest HTN	5	50	0	0
Pre-eclampsia	1	10	3	60
Oligohydraminos	3	30	1	20
IUGR	1	10	1	20
Total	10	100	5	100

Out of 36 TPO negative hypothyroid women who had vaginal delivery, 10(27.78%) women had induction and the most common indication for induction was gestational hypertension. Out of 17 TPO positive hypothyroid women who had vaginal delivery, 5(29.42%) women had induction and the most common indication for induction was pre-eclampsia.

During the period of study (January 2018 to December 2018), 97women who were diagnosed to be hypothyroid before and during pregnancy, who fulfilled the inclusion criteria were included in the study. The cases were studied in detail by noting the history (symptoms), physical examination and with relevant investigations. TSH and TPO antibodies were estimated by highly sensitive ECLIA (electro chemiluminiscence immune assay).
97 women who were diagnosed to be hypothyroid before and during pregnancy were divided into two groups based on TPO

antibody status. Group 1 included women who were TPO negative and Group 2 included women who were TPO positive, containing 63 and 34 women respectively.

These women were followed up throughout their antenatal period till delivery and thyroxin dose adjusted according to the changes in serum TSH level. Maternal complications like PIH, GDM, preterm etc. were noted

Statistical Analysis was done with SPSS-19 Programme. Variables are described first, then compared with using ANOVA and Chi-square Test. P value < 0.05 was considered significant.

Discussion

DISTRIBUTION OF CASES ACCORDING TO TPO ANTIBODY STATUS

From the observational table 1, out of 97 hypothyroid women, 63 (64.9%) women were TPO negative included in Group 1 and 34 (35.1%) women were TPO positive included in Group 2.

AGE WISE DISTRIBUTION OF CASES ACCORDING TO TPO ANTIBODY STATUS

From the observational table 2, out of 97 hypothyroid women, majority of women in Group 1, belonged to the age group of 21-25 years (34.9%), followed by age group 26-30 years (33.34%)

In Group 2, majority of women belonged to the age group of 21-25 years. (52.94%)

The age group in our study ranged from 19 to 39 years

Majority of population in 21 - 25 years age is due to early marriage before 20 years. This also decreases thyroid disorder in population due to increased age, as age is also an independent factor for increased thyroid disorder

DISTRIBUTION OF CASES ACCORDING TO THE TIME OF DIAGNOSIS

Diagnosis of thyroid disorder was made using following guidelines.

Guidelines by American Thyroid Association Taskforce on Thyroid Disease in pregnancy and Postpartum[10] for normal TSH range is

First trimester	0.1 – 2.5 mIU/L
Second Trimester	0.2 – 3.0 mIU/L
Third Trimester	0.3 – 3.0 mIU/L

From observational Table.3.In group 1, 27 (42.86%)women were diagnosed before pregnancy and 36 (57.14%)women were diagnosed during pregnancy. In group 2,10(29.4%) women were diagnosed before pregnancy and 24 (70.6%)women were diagnosed during pregnancy

Pre pregnancy patient were diagnosed while undergoing evaluation for infertility or menstrual irregularity. Few were diagnosed with hypothyroidism during previous Pregnancy. TPO antibodies were done in women diagnosed with hypothyroidism.

ACHIEVEMENT OF EUTHYROID STATUS.

From observational table .No.4. it is evident that all women in both groups had achieved euthyroid status by serial estimation of TSH and adequate replacement.

DISTRIBUTION OF CASES ACCORDING TO NUMBER OF COMPLICATIONS

From observational table No 5in group 1, 21(33.34%) women had complications out of 63 women and two women had more than one complication.. In group 2, 25 (73.53%) women had complications which is statistically significant **(p< 0.00015)** and 9 members had more than one complication.

SHARMEEN M, SHAMSUNNAHAR PA et al., (2014)[12]conducted a study. They found that Over thypothyroidism were prone to have pregnancy-induced hypertension 42.9%, intrauterine growth restriction (P = 0.001) and gestational diabetes (38.1%) as compared to subclinical cases. Neonatal complications were significantly more in overt hypothyroidism group.Majority of the patient underwent caesarean section in both groups due to associated medical and obstetrical complications. None of the babies showed hypothyroidism by cord blood tests. In this analysis they concluded that overt hypothyroidism was associated with more maternal complication & adverse perinatal outcome. The adequate treatment of hypothyroidism during gestation minimizes risks and generally, makes it possible for pregnancies to be carried to term without complications. Significant adverse effects on maternal and foetal outcome were seen emphasizing the importance of routine antenatal thyroid screening.

DISTRIBUTION OF CASES ACCORDING TO COMPLICATIONS

From observational Table No.6 in group 1, 33.34% women had complications and the commonest complication was gestational hypertension (15.87%) followed by GDM (11.1%), preterm (4.76%), IUGR (3.17%), Pre-eclampsia(1.59%)

In group- 2, 73.53% women had complications and the commonest complication was preterm labour (47%) which is statistically significant (p< 0.00015).followed by GDM (20.58%), Pre-eclampsia (20.58%) IUGR (8.8%), Gest HTN (2.94%)

In comparison to group 1, group 2 had more number of complications. The mechanism by which thyroid autoimmunity leads to complications is not known. It may be due to more generalized activation of the immune system or subtle changes in maternal and foetal thyroid metabolism.[16]

Pradhan M , Anand B, Singh N, Mehrotra M (2013)[13]Conducted similar study on well-controlled hypothyroid pregnant patients attending the antenatal clinic at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India . The study showed similar results. They divided study population into two groups depending on presence or absence of TPO antibody. Amongst the women with hypothyroidism, 40% were TPO positive. Complications like threatened abortion, spontaneous abortion, preterm delivery, fetal malformations, intrauterine growth restriction, and adverse fetal outcomes like poor apgar scores and prolonged nursery admissions were more in patients with positive TPO antibodies. They concluded that TPO positivity is considered as high risk for pregnancy complications and hence those patients should be monitored more carefully

Another study conducted by Kumru P, Erdoqdu E, Arisoy R et al (2015)[14]showed similar results conducted Prospective study. Cases were classified into four groups according to thyroid function and anti-TPO results. The pregnancy outcomes included gestational diabetes mellitus, preeclampsia, preterm delivery, caesarean rate, small for gestational age, low birthweight .They concluded that pregnant women with anti-TPO antibody positivity alone or with subclinical hypothyroidism were more likely to experience a spontaneous preterm delivery.

DISTRIBUTION OF CASES ACCORDING TO GESTATIONAL AGE AT DELIVERY

From observational Table. No 7, in group 1 (TPO Negative group) 34 (53.97%) were delivered at early term, 24(38.1%) were delivered at full term , 3 (4.76%) delivered at late preterm , 2 (3.17%) delivered at late term.

While in group 2 (TPO Positive group) 15 (44.18%) were delivered at late preterm, 11(32.3%) were delivered at early term, 7 (20.58%) delivered at full term, 1(2.94%) delivered at moderate preterm.

In hypothyroid women when compared to group 1(TPO negative group), group 2 (TPO positive group) had more number deliveries at late preterm which is significant (p value < 0.00015)

A similar study was conducted **by Korevaar et al(2013)**[15].They investigated the relation between maternal serum thyroid parameters and the risk of premature delivery in a large prospective population-based study. They found that antiTPOAb positivity was associated with a 1.7-fold increased risk of premature delivery (<37 weeks) (P = .01). They concluded that Hypothyroxinemia and antiTPOAb positivity are associated with an increased risk of premature delivery. The increased risk in antiTPOAb-positive women seems to be independent of thyroid function.

Mode of delivery

From observational Table No.8., In group 1, 36 (57.14%) women had vaginal deliveries and 27 (42.86%) women underwent caesarean section.In group 2, 17 (50%) women had vaginal deliveries and 17 (50%) women underwent caesarean section

From observational Table No.9. In group 1(TPO negative), 26(72.22%) women had spontaneous vaginal deliveries and 10(27.78%) women had induction. In group 2(TPO positive), 12 (70.58%) women had spontaneous vaginal deliveries and 5 (29.42%) women had induction.

The commonest indication for induction in group 1 was gestational hypertension and in group 2 the most common indication was pre-eclampsia.

Conclusion

The present study indicates the value of testing TPO antibodies in diagnosed hypothyroid pregnant women as TPO positive pregnant women are associated with more complications and preterm delivery compared to TPO negative pregnant women. To conclude the above statement further studies with larger sample size is required.Increase in thyroxine dose is required in women who were diagnosed with hypothyroidism before pregnancy**.** Serum TSH should be a part of antenatal profile and all pregnant women should be tested at the first antenatal visit**.** Effort should be made to achieve euthyroid status to decrease antenatal complications. Complications occur in spite of achieving the euthyroid level.

TPO Positivity is significantly associated with preterm deliveries. To recommend TPO antibody screening in hypothyroid women further studies with larger sample size is required. In view of associated complications in hypothyroid pregnant women delivery should be conducted at a centre where facilities for caesarean section and NICU are present.

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