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ORIGINAL ARTICLE

Analysis of thyroid stimulating hormone (thyrotrophin) level as a gold standard marker for assessing frequency of subclinical hypothyroidism in the first fifteen weeks of gestation.

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ABSTRACT… Objective: To find out the frequency of subclinical hypothyroidism in the first trimester of pregnancy. **Study Design:** Cross-Sectional study. **Setting:** Bacha Khan Medical Complex Swabi. **Period:** May 2019 to October 2019. **Material & Methods:** Total ninety (90) subjects visiting antenatal unit were taken for the study by using non-probability sampling technique. The sample size was calculated by Andrew Fisher's formula. After the informed consent 5ml of blood was collected in EDTA tube from the enrolled patient. The blood was centrifuged and their serum was preserved in cuvets for forthcoming TSH analysis. The cut-off value for TSH was 4.0 mIU/L as per new American guidelines 2017. **Results:** The cases were described according to their thyroid function tests. There were eleven (11) cases in which TSH value was more than 4.0 mIU/L. To rule out hypothyroid state we also do Ft4 for these cases whose results were normal. This interpretation identifies subclinical hypothyroid state in these cases. We did not perform ft4 for cases whose TSH was in normal range. The p-value < 0.5 was considered significant. Pearson correlation values were given in the Table-III. **Conclusion:** it has been concluded from the results that pregnant women are associated with subclinical hypothyroidism (TSH $>$ 4.0 mIU/L and Free T4 within normal range) which requires proper assessment during pregnancy to avoid from any further risk.

Key words: Free Thyroxin, Pregnancy, Prevalence, TSH.

INTRODUCTION

Thyroid stimulating hormone (TSH) is released from the pituitary gland. It controls the function of thyroid gland to release the thyroid hormone. Pregnancy is associated with multiple physiological variations in the body and hormonal function. It affects thyroid hormone concentration as well as deteriorates thyroid function. In pregnancy human chorionic gonadotrophin gradually increases and reaches to its peak at the end of the 1st trimester.[1] After that it decreases in 2nd and 3rd trimester. As HCG is structurally similar to TSH so it has direct stimulating effect on the thyroid gland facilitated through TSH receptors. Measuring of thyroid functions tests (TFT'S) in pregnancy is an area of concern because some women are known to have thyroid disease before pregnancy and it needs proper monitoring to ensure no harmful affect on their baby.[2,3]

It is estimated that thyroid gland is enlarged during pregnancy in 10% countries where iodine provision is deficient. Iodine requirement and production of thyroid hormone increases approximated 50% during pregnancy. During pregnancy daily need of iodine is enhanced which leads to 10-40% increase in thyroid volume.[4] Pregnancy puts stress on thyroid gland leads to production of hypothyroid state in women with less thyroid hormone reserve or deficiency of iodine supplement. Hypothyroidism produces deleterious effects in both mother and child during pregnancy.[5]

It is well known that hypothyroidism have very harmful effects on pregnancy at childbearing

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age but the impact of subclinical hypothyroidism (SCH) characterized by an increased level of thyroid stimulating hormone (TSH) with normal thyroixe (fT4) have not been studied a lot yet.[3] SCH is associated with several obstetric complications like pre- eclampsia, pre-term delivery and placental abruption. According to 2017 "Guidelines of the American Thyroid Association (ATA) for the diagnosis and treatment of thyroid diseases during pregnancy and postpartum" recommends the upper limit of TSH at 4.0 mIU/L in healthy pregnant women.[6,7]

In untreated or under treatment mother can give born children which have serious effects on brain development in future.[8] Hyperactivity syndrome and concentration deficit have been reported in children born to hypothyroid mother. SCH during pregnancy can cause poor development of neurological functions like attention deficit disorders, lower IQ and motor scores, decrement in general cognitive index and visual disorders. According to western literature prevalence of hypothyroidism is around 25% in pregnancy where from India its rate ranges from 4.8 to 11%.[8,9]

Except of the deterioration of thyroid function and enlargement of thyroid gland during pregnancy other thyroid related illnesses like nodular diseases, hyperplasia, goiter formation, adenoma and cancer are occasionally seen in pregnancy and this may require treatment. Jointly the burden of thyroid disease affecting women before, during and after pregnancy is substantial. Due to these reasons TFTs are regularly assessed during gestational period but accurate assessment of maternal and fetal TFT's during gestation is difficult. Its interpretation is different from non-pregnant women.[10]

The aim of this study was to check status of thyroid function parameter (TSH) in our population with 1st trimester of pregnancy in order to note its association with thyroid disorder.

MATERIAL & METHODS

It was a cross-sectional descriptive study. Total ninety subjects visiting antenatal unit were taken for the study by using non-probability sampling technique. The sample size was calculated by Andrew Fisher's formula with 95% confidence level and 5% margin of error (confidence interval).
Sample size = (Z- score) □ 2 X Std-Dev X (1- Std-Dev)
(Confidence interval) □ 2

The duration of study was six months from May 2019 to October 2019. The study was carried out at Pathology Department Bacha Medical Complex Swabi after approval from the institutional ethical review committee (No. GKMCs/EC/00398).

Inclusion Criteria

Only the patients up to fifteen weeks of gestation were enrolled for the study.

Exclusion Criteria

Those patients with known thyroid illnesses and after fifteen weeks of gestation were excluded from the study. After the informed consent 5ml of blood was collected in EDTA tube from the enrolled patient. The blood was centrifuged and their serum was preserved in cuvets for forthcoming TSH analysis. TSH analysis was performed by Architect hormonal analyzer by using abbot reagent kit. The cut-off value for TSH was 4.0 mIU/L as per new American guidelines 2017.[10]

RESULTS

In this study we take total ninety cases whose tests were positive for pregnancy. For the statistical analysis the data was entered in the SPSS version 24. The results obtained were shown in the form of tables. The cases were distributed according to their age of gestation as shown in Table-I. There were 34 cases in age of 3-7 weeks of gestation, 38 cases in 8-10 weeks and 18 cases were in 11-15 weeks of gestation.

In Table-II we calculate the mean age of the cases. The maximum age was 43 and minimum age was 18 with mean ± standard deviation was 28.32 ± 4.35. Similarly the gestational age mean ± standard deviation was 8.34 ± 2.7 and TSH value was maximum 4.0 mIU/L and minimum 0.6 mIU/L with 1.94± 1.47.

In the Table-III the cases were described according to their thyroid function tests. There were eleven (11) cases in which TSH value was more than 4.0 mIU/L. To rule out hypothyroid state we also do Ft4 for these cases whose results were normal. This interpretation identifies subclinical hypothyroid state in these cases. We did not perform ft4 for cases whose TSH was in normal range. The p-value < 0.5 was considered significant. Pearson correlation values were given in table.

Age in Weeks	Cases
	N (%)
3-7	34 (37.7%)
8-10	38 (42.2%)
11-15	18 (20.0%)
Total	90 (100%)

Table-I. Gestational age wise distribution of patients

Age (Year)	Max	Min	Mean ± Std
	43	18	28.32 ± 4.35
Gest. age in wks	15	6	8.34 ± 2.7
Parity status	4	0	Median parity 1
TSH (mIU/L)	4	0.6	1.94± 1.47

Table-II. Mean age, Gestational age, Parity status and TSH level

TSH (mIU/L) 0.6-4.0	No. of Cases	fT4 (ng/dl) 0.8-1.8	P-Value	P-Correlation
0.6- 2.5	39 (43.3%)		0.7	-0.05
2.6- < 4	40 (44.4%)		0.3	-0.04
>4.0	11 (12.2%)	Mean 1.1± 0.1	0.4	0.06

Table-III. TSH level in the first fifteen weeks of gestation

DISCUSSION

The present study was performed to notice the impact of TSH level on pregnancy and its effect on thyroid gland performance status. We founded that TSH level more than 4.0 mIU/L is associated with increased risk of subclinical hypothyroidism. It requires further analysis to find out other risky complications like miscarriage, postpartum hemorrhage and fetal growth restriction correlated with thyroid dysfunction during pregnancy.[11,12]

Inter-study variation may exist in the form of demographic profile; sample size and study design. In china many pregnant women visit prenatal care centers between 6-8 weeks of gestation. Therefore we select the gestational age up to 15 weeks for our study to check the TSH level.

Indian study reported subclinical hypothyroidism in 8.1% by using upper limit 5mIU/L and a Chinese study reported 4% prevalence of SCH by taking cut off value 5.08 mIU/L. similarly in our study we founded 12.1% cases having subclinical hypothyroidism. According to geographic and ethnic origin TSH level may shows variation.[13,14,15]

American thyroid association and European endocrine society 2011 and 2012 recommends trimester specific thyroid function test range should be formed on locality base because there is great variation in the frequency of thyroid dysfunction according to geographic region and ethnic group.[16,17]

There is still insufficient evidence regarding SCH diagnosed at different cutoff points in early pregnancy and adverse pregnancy outcomes, especially for changes in thyroid function with TSH levels of 2.5–4.0 mIU/l.[18,19,20] in the present study we also take almost the same cut value for the assessment of thyroid function in pregnancy.

LIMITATIONS

There are several limitations in carrying this study. First it lacks data on confounding variables like irregular menstruation, family history of miscarriage, environmental toxins and antiphopholid antibodies. Secondly HCG values and chromosomal abnormalities are not evaluated. Third matched case control study waste some data and minimizes the amount of statistical information. Fouth this study may lead to measurement omission or bias.

CONCLUSION

We found that pregnant women in their first trimester have thyroid dysfunction in the form of raised TSH level from their upper limit but fT4 level was within normal range. This manifests subclinical hypothyroidism state. It needs proper

assessment in pregnancy and follows up after pregnancy.

Pregnant women in SCH state are on increase risk of miscarriage and development of other fetal abnormalities which requires further studies.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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2	Masood-uz-Zaman	References + Objective.	
3	Tufail Ahmad Soomro	Introduction, Material & Methods.	