



THYROID PROFILE IN HYPOTHYROID PREGNANT WOMEN: A PROSPECTIVE CASE CONTROL STUDY

Priti Yadav¹, Jigar Katwala², Keyur Madhu³, Smita Rani Pradhan^{4*}

¹Assistant Professor, Department of Biochemistry, GS Medical College & Hospital, Pilkhuwa, Hapur, Uttar Pradesh, India

²Associate Professor, Department of Pharmacology, Swaminarayan Institute of Medical Sciences and Research, Kalol, Gandhinagar, Gujarat, India

³Assistant Professor, Department of Biochemistry, GMERS Medical College, Rajpipla, Gujarat, India

^{4*}Assistant Professor, Department of Physiology, Raipur Institute of Medical Sciences, Raipur, Chhattisgarh, India

***Corresponding author:** Smita Rani Pradhan

*Assistant Professor Department of Physiology Raipur Institute of Medical Sciences Raipur, Chhattisgarh, India Email-Smita06pradhan@gmail.com

ABSTRACT

Background: Thyroid dysfunction is the second most common endocrinological disorder seen during pregnancy. The main cause of hypothyroidism is a thyroid abnormality majorly with iodine deficiency. Thyroid hormones play a crucial role in the placental development. So, this study to assess thyroid levels in pregnant women who are hypothyroid.

Methods: The study included 70 hypothyroid pregnant and 70 non-pregnant women, with institutional ethical committee approval and informed written consent obtained. The student t test was used to compare thyroid hormones. Thyroid profile was done by fully auto COBAS 6000 system analyzer. all women with TSH level >2.5 mIU/l, considered to be hypothyroid

Results: A total of 140 women. Group 1 included all women with TSH levels greater than 2.5 mIU/l, who were considered hypothyroid (n=70); Group 2 included women with euthyroid status and TSH levels ranging from 0.1 to 2.5 mIU/l (n=70). Table 1 showed maternal characteristics. Graph-1 displayed the mean thyroid profile values, which included TSH, T3, and T4 levels.

Conclusion: The study's findings are useful for detecting thyroid dysfunction early in pregnancy and avoiding adverse maternal and fetal outcomes.

Keyword: Hypothyroidism; Pregnancy; Thyroid profile; non-pregnant women.

Introduction:

During early pregnancy, before the development of a functioning thyroid gland, thyroid stimulating hormone (TSH) is a very sensitive marker of thyroid dysfunction during pregnancy. Among maternal thyroid disorders, hypothyroidism (2.5%) is more prevalent than hyperthyroidism (1 to 0.4%). There is a significant change in thyroid hormone metabolism in pregnancy. In a woman with poor thyroid reserve, thyroid deficient state occurs due to increased urinary loss of thyroxine due to increase in glomerular filtration and placental transfer of thyroxine to growing foetus. ⁽¹⁾ Normal pregnancy is

associated with an increase in renal iodine excretion, an increase in thyroxine binding proteins, an increase in thyroid hormone production, and thyroid stimulatory effects of human chorionic gonadotrophin (hCG). There are significant changes in thyroid physiology and function during pregnancy. These are particularly important in the first trimester when the foetus relies on circulating maternal thyroxine (T4). Alteration in the hypothalamic–pituitary–thyroid (HPT) axis and the hypothalamic–pituitary–adrenal (HPA) axis is a main cause of depressive disorder. ⁽²⁾ In the HPT axis make change in thyroid function tests have been reported by various authors. The detection of anti-thyroid peroxidase (TPO-Ab), and anti-thyroglobulin (TG-Ab) antibodies an in the context of the clinical presentation of thyroid dysfunction, confirms the diagnosis of thyroid autoimmune disease. ⁽³⁾

The impairment of both HPA and HPT in our geriatric patients with psychiatric disorder support this good correlation between serum total cholesterol (TC) and TSH. Thyroid function within the euthyroid range was also associated with placental growth, independent from common confounders, such as maternal BMI and serum glucose and lipid concentrations. This dynamic change in thyroid physiology is more relevant in the early stages of gestation and, consequently, TSH reference limits differ widely within the first trimester of pregnancy ^(4,5)

Most prominently, human chorionic gonadotropin (h-CG) is structurally similar to TSH, and has a direct stimulating effect on the thyroid gland mediated through the TSH receptor. During pregnancy h-CG peaks towards the end of the first trimester followed by a decrease to a plateau in second and third trimesters. The thyrotrophic effect of h-CG causes increased thyroid hormone production resulting in a transient increase in free thyroxine (FT4) towards the end of the first trimester. This in turn leads to a concomitant lowering of TSH concentrations. With the decline in h-CG as pregnancy progresses there is a trend towards an increase in TSH. ^(6,7) Looking into above aspect, the present study was planned to evaluate thyroid levels in hypothyroid pregnant women.

Materials & Methods:

A prospective case control study was conducted in the department of Biochemistry, GS Medical college & hospital, Pilkhuwa, hapur, Uttar Pradesh, India. A total of 140 subjects were enrolled for this study in the extended period of January 2023 to January 2024. Study subjects were enrolled after getting an ethical approval from institutional ethical committee. Women with a singleton pregnancy who had first trimester thyroid function tests were the target population. The duration of pregnancy was calculated from the date of last menstrual period (LMP) and cross verified with their first-trimester Crown rump length (CRL) values. Women with multifoetal gestation threatened and missed abortion, preexisting known medical disorders such as chronic hypertension, thyroid disorders were excluded from the study. All individuals signed informed consent prior to their enrolment in the study. A total of 140 women were followed up till the delivery and their first trimester thyroid value were noted and based on that they were grouped into two i.e. group-1 all women with TSH level >2.5 mIU/l, considered to be hypothyroid (n=70), Group 2: women with euthyroid status with TSH levels 0.1 to 2.5 mIU/l (n=70). We used a cut-off value for TSH levels as 2.5 mIU/l to differentiate between hypo and euthyroid status according to the guidelines established by American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. ⁽⁸⁾

The participating woman's venous blood was drawn using aseptic techniques. The sample was centrifuged at 15,000 RPM for 15 minutes to extract serum. The serum was analyzed for thyroid parameters (TSH, T3, and T4) using the COBAS 6000 system.

Statistical analysis:

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) for Windows (Version 21.1. Chicago, SPSS Inc.). Descriptive statistics included estimation of mean, standard deviation. Histogram and normal curve feature of SPSS software is used to display data distribution graphically. Student T-test was used to test the statistical significance of different means and standard

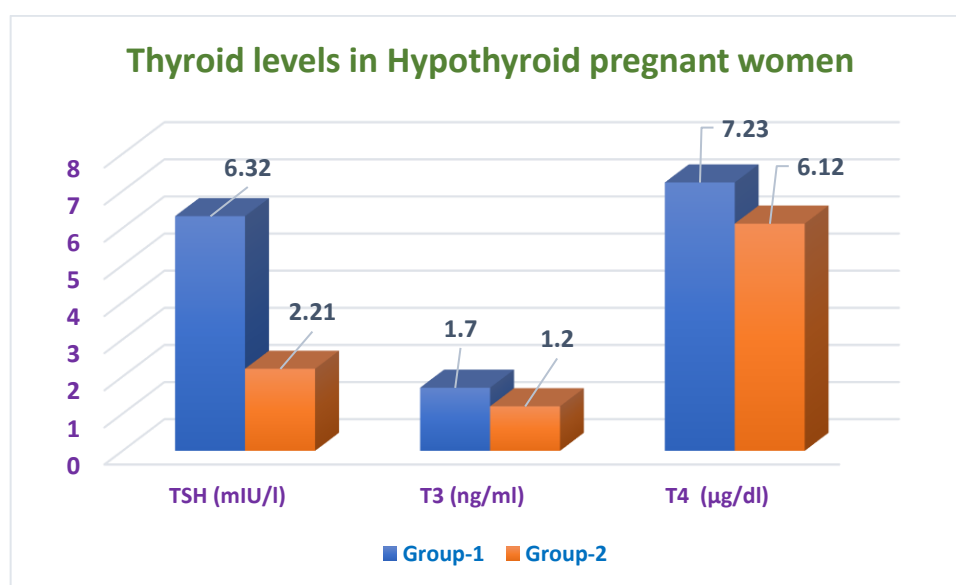
deviation of numerical data. Similarly, Chi square test was used for categorical data. A p value of <0.05 was considered as significant.

Results:

A total of 140 women. Group 1 included all women with TSH levels greater than 2.5 mIU/l, who were considered hypothyroid (n=70); Group 2 included women with euthyroid status and TSH levels ranging from 0.1 to 2.5 mIU/l (n=70). Table 1 showed maternal characteristics. Graph-1 displayed the mean thyroid profile values, which included TSH, T3, and T4 levels.

Table 1: Maternal characteristics for Demographic data

Demographic Data	Group-1 (N=70)	Group-2 (N=70)	P value
Age in Years (Mean \pm SD)	28.9 \pm 4.4	29.2 \pm 5.6	0.06 ^{NS}
Primigravida	38	49	NS
Multigravida	32	21	
Gestational age at delivery (weeks)	38.4 \pm 1.1	39.0 \pm 0.09	0.001**



Graph-1 Thyroid Profile in Pregnant Women

Discussion:

Thyroid dysfunctions are common during pregnancy and it can affect the outcome also. Our study revealed 15% prevalence of hypothyroidism in first trimester of pregnancy. Out of this 10%, 3.5% had overt hypothyroidism and 14.5% had sub-clinical hypothyroidism. There are only few reports on prevalence of hypothyroidism during pregnancy from India with prevalence rates ranging from 4.8% to 24%. Dhanwal et al⁽⁹⁾., reported 14.3% prevalence of hypothyroidism in the first trimester of pregnancy and majority of them had sub-clinical hypothyroidism. High prevalence of hypothyroidism is due to high intake of dietary iodine, goitrogens and minerals like iron, selenium deficiency⁽¹⁰⁾. Sailakshmi et al⁽¹¹⁾., showed a prevalence of 7.5%. Sahu et al.⁽¹²⁾, reported 6.4% prevalence of hypothyroidism.

Pregnancy is a crucial stage in the life of a woman. Untreated and undetected gestational thyroid disorders are known to cause many complications like anaemia, pregnancy-induced hypertension, haemorrhage, preterm delivery in mothers and low birth weight, prematurity, congenital malformation, intrauterine fetal death, and lower intelligence quotient in children.⁽¹³⁾

Estimation of TSH is the primary screening tool, but its levels are affected by HCG hormone (human Chorionic Gonadotrophin). Because of its alpha chain similarity with TSH, hCG has a weak stimulatory effect on the maternal thyroid gland, making it to enlarge physiologically and produce more thyroxine. The net effect is suppression of TSH levels and hence a different cut off is required to

make the diagnosis of hypothyroidism in pregnancy. ⁽¹⁴⁾ The reference ranges for thyroid hormone profile varies from laboratory to laboratory. If laboratory specific trimester ranges are not available, it is desirable to follow Regulation 14.2 of ATA (American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and Postpartum) guidelines. ⁽⁸⁾ In our 70 cases, first trimester TSH level was significantly higher ($P < 0.001$) than the recommended cut-off i.e. 2.5 mIU/l, thereby substantiating the diagnosis of maternal hypothyroidism stated in Graph-1 and T4 levels have had within limit. B. Chakrabarty et. al. derived RIs for T3, T4 and TSH in pregnant women were 1.21-1.51 ng/ml, 7.57-8.44 µg/dL and 2.26-2.85 mIU/L respectively ⁽¹³⁾ The results of this study pattern implies that all of our cases were belonging to the category of hypothyroidism. After a clinician consultation it was decided not to begin with any thyroxine replacement therapy.

Conclusion:

These data highlight the importance of estimating thyroid levels in pregnancy that an early detection of maternal hypothyroidism and appropriate thyroxine replacement can significantly improve obstetric and perinatal outcomes. It may be beneficial for the management of thyroid dysfunction during pregnancy, which is critical to avoiding adverse maternal and fetal outcomes.

References:

1. Renuka P, Akila S, Ebenezer W. Prevalence of metabolic syndrome and its components in women with subclinical hypothyroidism. *Asian J Pharm Clin Res* 2013; 6:82-4.
2. Jackson I. The thyroid axis and depression. *Thyroid*. 1998;8 10:951-956.
3. Pop V, Maartens L, Leusink G, van Son M, Knottnerus A, Ward A, et al. Are autoimmune thyroid dysfunction and depression related?. *J Clin Endocrinol Metab*. 1998;83 9:3194-3197.
4. Herrera E, Ortega-Senovilla H. Disturbances in lipid metabolism in diabetic pregnancy—are these the cause of the problem?. *Best Pract Res Clin Endocrinol Metab*. 2010;24 4:515-525.
5. Laurberg P, Andersen SL, Hindersson P, Nohr EA, Olsen J. Dynamics and predictors of serum TSH and fT4 reference limits in early pregnancy: a study within the Danish National Birth Cohort. *J Clin Endocrinol Metab*. 2016;101 6:2484-2492.
6. Hershman JM. The role of human chorionic gonadotropin as a thyroid stimulator in normal pregnancy. *J Clin Endocrinol Metab*. 2008; 93:3305–6.
7. Moleti M, Trimarchi F, Vermiglio F. Thyroid physiology in pregnancy. *Endocr Pract*. 2014;20:589–96.
8. Stagnaro-green A, Abalovich M, Alexander E. Guidelines of the American thyroid association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid* 2011;21:1081-125.
9. Dhanwal, D. K., Prasad, S., Agarwal, A. K., Dixit, V., & Banerjee, A. K. (2013). High prevalence of subclinical hypothyroidism during first trimester of pregnancy in North India. *Indian journal of endocrinology and metabolism*, 17(2), 281-284. 10.
10. Diyora V, Shah T, Mishra MK. Thyroid dysfunction in women during first trimester of pregnancy: Correlation with anti-thyroid peroxidase antibodies. *Scholarsh Int J Biochem* 2019;2:36-9
11. Sailakshmi, M. P. A., Pavan, G. A., Rekha, B. R., & Suhasini, S. A. (2014). Autoimmune thyroid disease in pregnancy. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 3, 321-324.
12. Sahu, M. T., Das, V., Mittal, S., Agarwal, A., & Sahu, M. (2010). Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. *Archives of gynecology and obstetrics*, 281(2), 215.
13. Rao VR, Lakshmi A, Sadhnani MD. Prevalence of hypothyroidism in recurrent pregnancy loss in first trimester. *Indian J Med Sci* 2008;62:357-61.
14. Shripad Hebbar, Sahan Kumar, Sapna Amin, Sneha Doizode. Subclinical hypothyroidism in pregnancy; is there a need for pharmacological intervention? *Int J Pharm Pharm Sci* 2017;9(3):186-191.