Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 05, 2024

Original research article

A study of thyroid profile in pregnancy

[1]Dr. Abhishek Shukla, [2]Dr. Madhuri Singh, [3]Dr. Anwarul Kabir, [4]Dr. Shubhangi Pandey

[1, 2]Assistant Professor, Department of Physiology, Autonomous State Medical College Sultanpur, Uttar Pradesh, India

[3] Associate Professor, Department of Physiology, Shree Narayan Medical Institute and Hospital, Saharsa, Bihar, India

[4]Tutor, Department of Physiology, Autonomous State Medical College Sultanpur, Uttar Pradesh, India

Corresponding Author:
Dr. Shubhangi Pandey

Abstract

The expert panel recommends that all pregnant women undergo routine screening for thyroid function due to the possible negative consequences of maternal thyroid problems and the clear advantages of therapy. This study aimed to assess the thyroid profile and compare the perinatal outcomes between women with normal thyroid function and those with aberrant thyroid function.

Keywords: Thyroid profile, pregnancy, IUGR

Introduction

Thyroid problems are the most prevalent endocrine disorders that impact women in their reproductive years and can have negative consequences on pregnancy outcomes. The prevalence of thyroid impairment in pregnant women is estimated to be between 2.3% and 3.8% [1]. Maternal hypothyroidism is the prevailing thyroid condition during pregnancy. The prevalence of overt hypothyroidism in pregnancies is 0.2%, while the prevalence of subclinical manifestation of hypothyroidism is 2% [2]. Unregulated thyroid dysfunctions can be linked to negative pregnancy outcomes such as placental abruption, hypertension, preterm delivery, foetal death, impaired intellectual function in the offspring, and low birth weight [3]. The physiological changes during pregnancy result in a 40-100% increase in the synthesis of thyroid hormones to suit the needs of both the mother and the foetus [4-11]. During pregnancy, there are four significant changes that occur in the maternal thyroid: 1) the thyroid enlarges, 2) there is a change in how iodine is processed, 3) there is an increase in thyroid hormone The thyroid dysfunction in pregnant women is frequently disregarded due to the non-specific symptoms and the hypermetabolic condition of pregnancy. The expert panel recommends frequent monitoring of thyroid function in all pregnant women due to the possible negative consequences of maternal thyroid problems and the clear benefits of therapy. This study aimed to assess the thyroid profile and compare the perinatal outcomes between women with normal thyroid function and those with aberrant thyroid function [13-14].

Materials and Methods

This cross-sectional study was conducted in the Department of Physiology. Permission was obtained from the institutional ethical committee. A cohort of pregnant women without any health issues (group A) and an equivalent number of pregnant women with thyroid disorders (group B) were included in the study.

Each group consisted of 30 members. The A and B groups were matched based on their age, gravidity, parity, and geography. The selection of these women was conducted in a random manner from the antenatal outpatient department (ANOPD), antenatal ward, and the labour room of AMCH on their initial antenatal visit. The study excluded women who had multiple pregnancies, significant obstetrical difficulties (such as antepartum haemorrhage, malnutrition, and hydramnios), systemic diseases (including cardiac, renal, and hepatic conditions), and those who were using certain medications (such as steroids, amiodarone, methadone, and dopamine). Patients with thyroid-related diseases were permitted to receive treatment as needed. The pertinent data were gathered using a standardised proforma, following the acquisition of written consent from the women. Peripheral blood samples were taken from both the control and research groups. The RIAK-4/4A kit, RIAK-5/5A kit, and IRMAK-9 kit were utilised to quantitatively test T_3, T_4, and TSH, respectively. Hyperthyroidism is characterised by low levels of TSH and normal to high levels of T_3 and T_4. Hypothyroidism is characterised by elevated levels of TSH and normal-to-low levels of T_3 and T_4. Moreover, we categorised thyroid dysfunctions into the classes overt and Subclinical. Overt hypothyroidism was described as an elevated level of thyroid-stimulating hormone (TSH) along with low levels of thyroxine (T_4) and either low or normal levels of triiodothyronine (T_3). Overt hyperthyroidism is characterised by low levels of TSH in conjunction with high levels of T_4.Subclinical hypothyroidism is characterised by elevated levels of TSH along with

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 05, 2024

normal levels of T_4.Subclinical hyperthyroidism is characterised by low levels of TSH together with normal levels of T_4. The study population's normal thyroid levels were determined based on the data shown in table 1 [5, 6, 7]. Comparisons of findings were conducted using inferential statistical methods, namely $\chi 2$ tests and t-tests. Data are represented as numerical values, percentages, or the average value plus or minus the standard deviation. Significance was attributed to probability values less than 0.05.

Results

Table 1: Thyroid levels in control group range

Categories	Non pregnantadult	First trimester	Second trimester	Third trimester
TSH(µIU/ml)	0.35-4.26	0.18-4.44	0.44-5.18	0.26-4.46
T_4(µg/dl)	5.44-11.74	3.68-9.07	4.06-8.95	3.54-8.65
T_3(ng/dl)	77.65-135.46	71.66-175.85	84.34-195.85	97.69-182.47

*Thyroid Stimulating Hormone (TSH), Total Thyroxin (T_4), Total Triiodothyroxine (T_3)

Table 2: Thyroid levels in hypothyroid

Categories	Non pregnant adult	First trimester	Second trimester	Third trimester
TSH(µIU/ml)	1.35-5.26	3.18-4.44	4.44-5.18	4.26-5.46
T_4(µg/dl)	4.44-7.74	2.68-6.07	3.06-6.95	3.54-6.65
T_3(ng/dl)	33.65-66.46	38.66-100.85	43.34-104.85	66.69-123.47

*Thyroid Stimulating Hormone (TSH), Total Thyroxin (T_4), Total Triiodothyroxine (T_3)

Table 3: Thyroid levels in hyperthyroid

Categories	Non pregnant adult	First trimester	Second trimester	Third trimester
TSH(µIU/ml)	0.08-0.34	0.18-0.44	0.44-0.96	0.26-1.02
T_4(µg/dl)	7.74-11.44	9.07-13.68	8.95-14.06	3.54-15.65
T_3(ng/dl)	135.46-152.47	175.85-202.47	195.85-222.47	182.47-242.47

*Thyroid Stimulating Hormone (TSH), Total Thyroxin (T_4), Total Triiodothyroxine (T_3)

Table 4: Gestational age at delivery

Category	Group A (N=30)	Group B (N=30)	
	Number (%)	Hypothyroidism (150	Hyperthyroidism (15)
		Number (%)	Number (%)
Preterm	03	08	11
Term	27	07	04
Total	30	15	15

Discussion

The most significant reduction in serum TSH occurs in the initial trimester due to heightened levels of serum hCG, which directly stimulates the TSH receptor and consequently enhances the production of thyroid hormones. hCG levels rise after fertilisation and reach their highest point at 10~12 weeks of pregnancy. This causes an increase in the overall blood concentrations of T_4 and T_3, which in turn leads to a decrease in the levels of thyrotropin-releasing hormone (TRH) and TSH due to negative feedback. Thyroid-stimulating hormone (TSH) is the most accurate and responsive measure of thyroid activity. Interpreting free T_4 and T_3 levels during pregnancy is challenging due to elevated TBG and reduced albumin levels, which compromise the accuracy of immunoassays and result in artificially low levels in the third trimester [14]. Moreover, a significant proportion of pregnant women, specifically up to 18%, test positive for TPOAb or TgAb. Emerging evidence indicates that the presence of TPOAb has a negative effect on the influence of maternal thyroid state, particularly hypothyroidism, on both the pregnancy and the growing foetus. Thyroid antibody positive significantly raises the likelihood of developing thyroid dysfunction after giving birth and during the postpartum period. The levels of circulating thyroxine-binding globulin (TBG) and total thyroxine (TT_4) increase from the seventh week of pregnancy and reach their highest point during the sixteenth week of pregnancy. These levels remain elevated until birth [15]. Women with numerous pregnancies typically exhibit elevated serum hCG levels and decreased TSH levels. Therefore, it is advisable to exclude women with multiple pregnancies from reference populations when establishing TSH reference intervals. During the initial three months of pregnancy, the hormone hCG directly activates the TSH receptor, leading to an increase in the synthesis of thyroid hormones and a consequent decrease in the concentration of TSH in the blood [16]. Consequently, pregnant women have a decrease in serum TSH levels compared to their pre-pregnancy levels. It is worth noting that during the first trimester of pregnancy, up to 15% of healthy women have a TSH level below the lower limit of 0.4 mIU/L that is often found in non-pregnant women [17]. During the second and third trimesters of pregnancy, the levels of serum TSH and its reference range increase progressively. However, they still stay lower than in women who are not pregnant [18]. Due to larger levels of hCG in multiple pregnancies

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 05, 2024

compared to singleton pregnancies, the decrease in the TSH reference range is more significant in twin pregnancies [19]. The proportion of women with a suppressed thyroid-stimulating hormone (TSH) decreases to around 10% during the second trimester and 5% during the third trimester [20]. In women with normal somatotroph function, Persechini *et al*. (2015) found that there was a significant decrease in insulin-like growth factor 1 (IGF-1) levels during the first trimester of pregnancy. However, there were no significant changes in growth hormone (GH) or insulin-like growth factor binding protein 3 (IGF-BP3) concentrations. This suggests that the liver becomes resistant to the effects of GH due to the natural secretion of oestrogens during pregnancy [21]. Women might be categorised as having either normal or pathological TSH levels based only on their gestational age at the time of the thyroid test in the first trimester [22]. Human placenta expresses two kinds of iodothyronine deiodinase: type 2 (D2) and type 3 (D3). The amounts of these enzymes decrease as pregnancy progresses [23]. The D3 hormone is thought to have a protective function in preventing an excessive transfer of thyroid hormones from the mother to the growing foetus. Nevertheless, there was no observed disparity in the frequencies of clinical pregnancy, birth, or miscarriage when using a TSH cut-off of either 2.5 mIU/L or 4.5 mIU/L in women who underwent *in vitro* fertilisation (IVF) [24] or intrauterine insemination [25]. These findings support the concept that women with a generally normal reaction to hCG have a lower chance of poor pregnancy outcomes, as seen in successful assisted reproduction cycles [26]. Automated immunoassays used in the majority of clinical laboratories are made more complex in pregnant women due to the rise in TBG levels and the decrease in albumin concentrations. Alternative techniques for direct measurement, such as equilibrium dialysis (ED), ultrafiltration, or liquid chromatography/tandem mass spectrometry (LC/MS/MS), are less affected by the changes in serum proteins associated with pregnancy. However, these methods are considerably more costly and not as widely accessible. The international federation of clinical chemistry (IFCC) working group has suggested using isotope dilution-liquid chromatography/ tandem mass spectrometry (ID-LC/tandem MS) in combination with equilibrium dialysis (ED) as the reference measurement technique (RMP) for measuring serum FT_4 [27]. It is advisable for each laboratory to generate its own reference concentrations for TSH and FT_4, as there are various thyroid hormone tests that produce varying results during pregnancy [28]. Although reference ranges are commonly employed, they do not provide information on the likelihood of a specific concentration being linked to clinical illness [29]. The reference limits for Free T_4 during pregnancy weeks 9-12 may be slightly higher (about 5%) compared to the reference limits for non-pregnant individuals. Accurate measurements of free T_4 (and free T_3) can be achieved using procedures that include separating the free hormone using ultrafiltration or dialysis, and then directly measuring the hormone in the filtrate or dialysate using mass spectrometry or sensitive radioimmunoassay [30]. An undetectable level of TSH (<0.01 mIU/L) can nevertheless indicate a normal pregnancy. However, a low but detectable level of maternal TSH is unlikely to have any clinical significance [31]. Studies have demonstrated that the TSH, TT_4, total triiodothyronine (TT_3), FT_4, and FT_3 ranges may differ somewhat depending on the analytical methods used. However, these differences do not have any major impact on clinical interpretation [32-34]. Elevated levels of FT_4 in early pregnancy are linked to reduced birth weight and an elevated likelihood of having neonates that are tiny for their gestational age. This association holds true for pregnant women who do not have a history of thyroid problems. When determining the reference range for Serum TSH, it is important to include factors such as iodine intake, TPO (thyroid peroxidase) positivity, and, according to certain studies, body mass index (BMI). The maternal thyroid measures have a correlation with both the BMI before pregnancy and the weight gained during pregnancy [35]. Early research conducted on pregnant women in the United States and Europe resulted in the suggestion of a maximum TSH level of 2.5 mIU/L during the first trimester and 3.0 mIU/L during the second and third trimesters [36]. During pregnancy, Koreans have shown a slight decrease in the upper reference limit [37].

Conclusion

Present study concludes that there is significantly high association between thyroid disorders and preterm perinatal outcome.

References

1. Jackson I. The thyroid axis and depression. Thyroid. 1998;8(10):951-956.
2. 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.
3. 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.
4. Laurberg P, Andersen SL, Hindersson P, Nohr EA, Olsen J. Dynamics and predictors of serum TSH and fT_4 reference limits in early pregnancy: A study within the Danish National Birth Cohort. J Clin. Endocrinol. Metab. 2016;101(6):2484-2492.
5. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocr. Rev. 2010;31(5):702-705.
6. Lazarus JH, Smyth PPA. Iodine deficiency in pregnancy: iodine deficiency and supplementation in

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 05, 2024

pregnancy. Comprhensive Handbook of Iodine: Nutritional, Biochemical, Pathological and Therapeutic Aspects, Preedy Victor R, Burrow Gerard N, Watson Ronald. Oxford: Academic; c2009. p. 469-476.
7. Andersson M, De Benoist B, Delange F, Zupan J. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: Conclusions and recommendations of the Technical Consultation. Public Health Nutr. 2007;10(12A):1606-1611.
8. Brent GA. Maternal thyroid function: interpretation of thyroid function tests in pregnancy. Clin. Obstet. Gynecol. 1997;40(1):3-15.
9. Shields B, Hill A, Bilous M, Knight B, Hattersley AT, Bilous RW, *et al*. Cigarette smoking during pregnancy is associated with alterations in maternal and fetal thyroid function. J Clin. Endocrinol. Metab. 2009;94(2):570-574.
10. Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, *et al*. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Endocr. Pract. 2012;18(6):988-1028.
11. Tingi E, Syed AA, Kyriacou A, Mastorakos G, Kyriacou A. Benign thyroid disease in pregnancy: A state of the art review. J Clin. Transl. Endocrinol. 2016;23(6):37-49.
12. Velasco I, Taylor P. Identifying and treating subclinical thyroid dysfunction in pregnancy: emerging controversies. Eur. J Endocrinol. 2018;178(1):D1-D12. DOI: 10.1530/EJE-17-0598.
13. Stagnaro-Green A. Clinical guidelines: Thyroid and pregnancy–time for universal screening? Nat Rev. Endocrinol. 2017;13(4):192-194. DOI: 10.1038/nrendo.2017.17.
14. Lee RH, Spencer CA, Mestman JH, Miller EA, Petrovic I, Braverman LE, *et al*. Free T_4 immunoassays are flawed during pregnancy. Am J Obstet. Gynecol. 2009;200(3):260-e1-260-e6.
15. Weeke J, Dybkjaer L, Granlie K, Eskjaer Jensen S, Kjaerulff E, Laurberg P, *et al*. A longitudinal study of serum TSH, and total and free iodothyronines during normal pregnancy. Acta Endocrinologica. 1982;101(4):531-537.
16. Baloch Z, Carayon P, Conte-Devolx B, Demers LM, Feldt-Rasmussen U, Henry JF, *et al*. Laboratory medicine practice guidelines. Laboratory support for the diagnosis and monitoring of thyroid disease. Thyroid. 2003;13(1):3-126.
17. Orito Y, Oku H, Kubota S, Amino N, Shimogaki K, Hata M, *et al*. Thyroid function in early pregnancy in Japanese healthy women: relation to urinary iodine excretion, emesis, and fetal and child development. J Clin. Endocrinol. Metab. 2009;94(5):1683-1688.
18. Haddow JE, Knight GJ, Palomaki GE, McClain MR, Pulkkinen AJ. The reference range and within-person variability of thyroid stimulating hormone during the first and second trimesters of pregnancy. J Med. Screen. 2004;11(4):170-174.
19. Sapin R, D'Herbomez M, Schlienger JL. Free thyroxine measured with equilibrium dialysis and nine immunoassays decreases in late pregnancy. Clin. Lab. 2004;50 9-10:581-584.
20. Glinoer D. The regulation of thyroid function in pregnancy: Pathways of endocrine adaptation from physiology to pathology. Endocr. Rev. 1997;18(3):404-433.
21. Persechini ML, Gennero I, Grunenwald S, Vezzosi D, Bennet A, Caron P, *et al*. Decreased IGF-1 concentration during the first trimester of pregnancy in women with normal somatotroph function. Pituitary. 2015;18(4):461-464.
22. Murillo-Llorente M, Fajardo-Mont ñana C, Pérez-Bermejo M, Vila-Candel R, Gómez-Vela J, Velasco I, *et al*. Intra-individual variability in TSH levels of healthy women during the first half of pregnancy. Endocrinol. Diabetes Nutr. 2017;64(6):288-294.
23. Chan SY, Vasilopoulou E, Kilby MD. The role of the placenta in thyroid hormone delivery to the fetus. Nat Clin. Pract. Endocrinol. Metab. 2009;5(1):45-54.
24. Reh A, Grifo J, Danoff A. What is a normal thyroid-stimulating hormone (TSH) level? Effects of stricter TSH thresholds on pregnancy outcomes after *in vitro* fertilization. Fertil. Steril. 2010;94(7):2920-2922.
25. Karmon AE, Batsis M, Chavarro JE, Souter I. Preconceptional thyroid-stimulating hormone levels and outcomes of intrauterine insemination among euthyroid infertile women. Fertil. Steril. 2015;103(1):258-263.
26. Korevaar TI, Steegers EA, Pop VJ, Broeren MA, Chaker L, de Rijke YB, *et al*. Thyroid autoimmunity impairs the thyroidal response to human chorionic gonadotropin: Two population-based prospective cohort studies. J Clin. Endocrinol. Metab. 2017;102(1):69-77.
27. Thienpont LM, Beastall G, Christofides ND, Faix JD, Ieiri T, Miller WG, *et al*. Proposal of a candidate international conventional reference measurement procedure for free thyroxine in serum. Clin. Chem. Lab Med. 2007;45(7):934-936.
28. d'Herbomez M, Forzy G, Gasser F, Massart C, Beaudonnet A, Sapin R, *et al*. Clinical evaluation of nine free thyroxine assays: Persistent problems in particular populations. Clin. Chem. Lab Med. 2003;41(7):942-947.
29. Wald NJ. The triple test. Clin. Chem. 2014;60(1):269-270.
30. Laurberg P, Andersen SL. Endocrinology in pregnancy: Pregnancy and the incidence, diagnosing

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 05, 2024

and therapy of Graves'disease. Eur. J Endocrinol. 2016;175(5):R219-230.
31. Casey BM, Dashe JS, Wells CE, McIntire DD, Leveno KJ, Cunningham FG, *et al*. Subclinical hyperthyroidism and pregnancy outcomes. Obstet. Gynecol. 2006;107(2 Pt 1):337-341.
32. Thienpont LM, Van Uytfanghe K, Beastall G, Faix JD, Ieiri T, Miller WG, *et al*. Report of the IFCC working group for standardization of thyroid function tests;part 1: thyroid-stimulating hormone. Clin. Chem. 2010;56(6):902-911.
33. Thienpont LM, Van Uytfanghe K, Beastall G, Faix JD, Ieiri T, Miller WG, *et al*. Report of the IFCC working group for standardization of thyroid function tests; Part 2: Free thyroxine and free triiodothyronine. Clin. Chem. 2010;56(6):912-920.
34. Thienpont LM, Van Uytfanghe K, Beastall G, Faix JD, Ieiri T, Miller WG, *et al*. Report of the IFCC working group for standardization of thyroid function tests; Part 3: Total thyroxine and total triiodothyronine. Clin. Chem. 2010;56(6):921-929.