



HYPERTHYROIDISM DURING PREGNANCY LEADS TO THE PREMATURE DELIVERY

Uhood abbas obed¹, ZAINAB SABEEH ABD UL RAZZA²

¹*Alhindia general hospital, Iraq; Uhood.abbas81@gmail.com*

²*Ministry of Health, Karbala Health Department, Hindi General Hospital, Iraq; drzainabsabeeh760@gmail.com*

Article history:

Received: January 20th 2023
Accepted: February 11th 2023
Published: March 26th 2023

Abstract:

Thyroid hormones are very essential for fetal development and brain growth. A pituitary gland secretes thyroid stimulating hormone (TSH) which in turn regulates Secretion of thyroid hormones. These hormones are T4 (thyroxine) and T3 (triiodothyronoinine). In the current study, effect of hyperthyroidism during pregnancy on prenatal outcome was evaluated. A pregnant woman (n=50) with unusual serum thyroid hormone levels was considered for disease group. The age match women (n=50), without unusual serum thyroid hormone levels, were enrolled in the healthy group. Their serum thyroid hormones and thyroid stimulating hormone (TSH) were evaluated and correlated with the pregnancy outcome.

American Thyroid Association guidelines were followed for consideration of reference range. In the disease group, about 36 (60%) and 24 (40%) women were in 25-30 and 30-35 years age group, respectively. The serum T3 levels were found to be 5.871 ± 0.39 mIU/ml and 2.714 ± 0.92 mIU/ml in disease and normal groups, respectively. The serum T4 levels were 174.367 ± 8.36 and 86.256 ± 3.51 nmol/ml. In the disease group, serum TSH levels were 6.926 ± 1.93 mIU/ml which was found to be significantly high as compared to normal group (3.781 ± 0.72 mIU/ml). About 83.25% women showed a caesarean delivery while about 16.75% women showed normal delivery. The delivery time was about 38.61 ± 0.14 weeks for normal group and 36.70 ± 0.93 weeks for disease groups.

Keywords: Hyperthyroidism, Thyroid hormones, Thyroid stimulating hormone

INTRODUCTION

Thyroid hormones (THs), T4 (thyroxine) and T3 (triiodothyronoinine), are vital for the growth of fetal and development of fetal brain (De-Escobar et al., 2004). The release of THs is controlled by thyroid stimulating hormone (TSH) which is secreted by pituitary gland. TSH secretion, in turn, is controlled through negative response by THs. During pregnancy several physiological changes occur that affect maternal thyroid function and thyroid hormone levels. Normal pregnancy is related with increased renal iodine excretion, increased thyroid hormone secretion and stimulatory effects of human chorionic gonadotrophin (hCG) (Stagnaro-Green and Pearce, 2012).

THs have extreme effects on later phases of embryonic brain development, such as synaptogenesis and dendritic formation, neuronal cells myelination and migration (Bernal, 2007). Thyroid gland disorders, such as hypothyroidism, hyperthyroidism, and thyrotoxicosis, can have an impact on the health of the mother and the fetus including mental retardation.

Hypothyroidism is conditions in which thyroid gland does not produce enough TH. Its slowed metabolism

can lead to weight gain, menstrual cycle irregularities, and dry skin, fatigue and other conditions. According to estimates, subclinical hypothyroidism affects 2-3% of pregnant women and evident hypothyroidism affects 0.3-0.5% (Bose et al., 2015). While Hashimoto's illness (an autoimmune ailment) is mostly to blame for hypothyroidism in women with adequate Iodine level (Alemu et al., 2016), and endemic iodine shortage is a key cause of hypothyroidism in pregnancy. Various complications on the foetus can be occur due hypothyroidism which include neonatal respiratory distress, decreased brain development, preterm birth, low birth weight, and intrauterine death, are commonly observed.

Thyrotoxicosis denotes to elevated TH levels in the blood, whereas hyperthyroidism is often the illness process. This is due to too much TH is created. The prominent cause of hyperthyroidism is Graves' disease. According to a study by Marvisi et al. (2002), hyperthyroidism is closely linked to less TSH levels and high pulmonary arterial pressure. The coexistence of this contributes to severe pulmonary hypertension. During the first pregnancy trimester, natural increase in



total T4 and total T3 were observed. This is due to estrogen-induced increases in TBG concentration and HCG thyroid stimulation with simultaneous TSH suppression. Together all this delays in the identification of maternal hyperthyroidism.

Preeclampsia, preterm labour, low birth weight, fetal death and other pregnancy problems have all been associated to substantial maternal thyroid insufficiency during the first half of the pregnancy (Marvisi et al., 2002). To check the thyroid gland is functioning properly or not, blood thyroid hormones are generally evaluated by thyroid blood tests including TSH, thyroid hormones and antithyroid antibodies concentrations in serum (Saadi et al., 2019). These blood tests facilitate to diagnose thyroid diseases. Analysis of TSH is generally firstly done to check for thyroid hormone imbalance. Thyroid hormone excess (hyperthyroidism) is normally associated with a low TSH level, whereas thyroid hormone shortage (T4 and T3) is typically associated with a high TSH level. Thyroid hormone imbalance is associated with a higher risk of a number of negative consequences for both the mother and the child, such as intrauterine development retardation, a lower child IQ, miscarriage, premature birth, hypertensive diseases, etc. Therefore, it is vital to observe for pre-existing thyroid disease and/or any suspected thyroid abnormalities, during pregnancy. The present study aimed to evaluate the effect of hyperthyroidism during pregnancy on prenatal outcome.

2. MATERIAL AND METHODS

2.1 Patient enrollment

A pregnant woman (n=50) with unusual serum thyroid hormone levels was considered for disease group. The age match women (n=50), without unusual serum thyroid hormone levels, were enrolled in the healthy group. The enrolled patients are between the age group between 25-35years.

2.2 Study parameters

Their serum thyroid hormones and thyroid stimulating hormone (TSH) were evaluated and correlated with the pregnancy outcome. The exclusion criterion was high blood pressure women and presence of gestational diabetes.

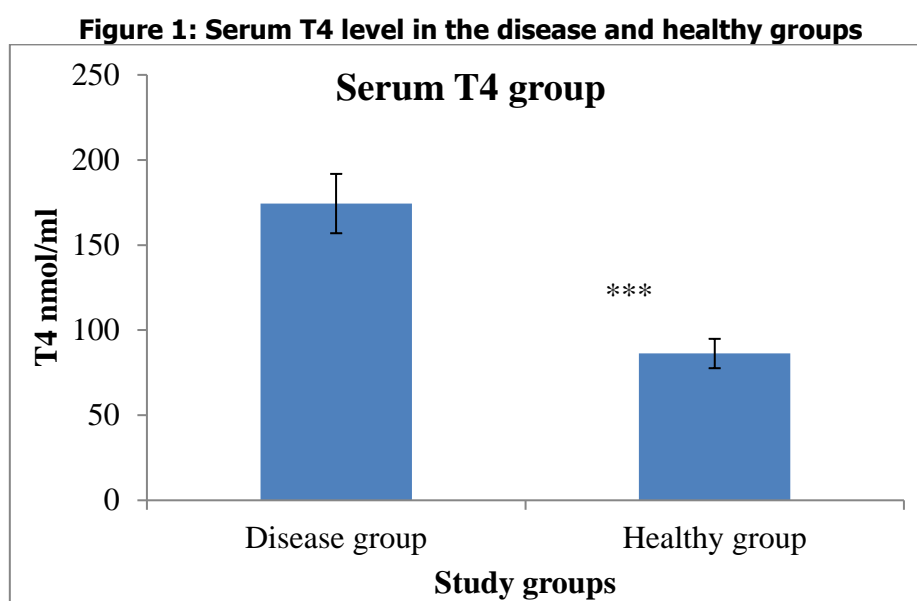
2.3 Statistical analysis

Results were given as Mean \pm Standard Error (SE). For statistical significance calculation, One way Analysis of Variance (ANOVA) along with Dunnett Multiple Comparison Test was performed.

3. RESULTS AND DISCUSSION

The response rate and respondent age were 94.25 % and 26.15 ± 4.21 years, respectively. In the disease group, around 60 % (n = 36) were included in the age of 30-35 years and 40 % (n = 24) in the 25-30years age.

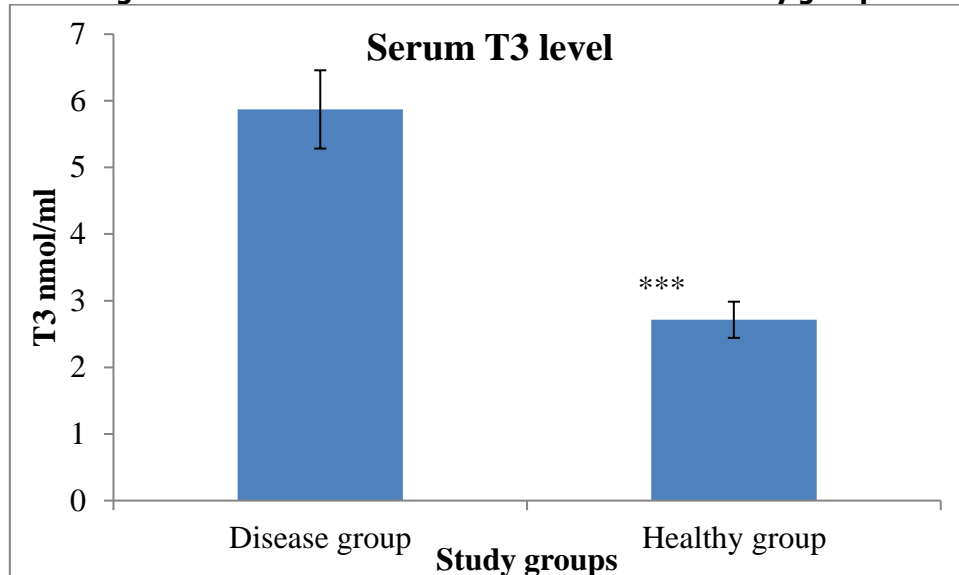
About 87.32% women increased TSH levels as compared to the healthy control. The serum T4 levels were 174.367 ± 8.36 and 86.256 ± 3.51 nmol/ml (Figure 1).



The results are represented as mean \pm SD.

The serum T3 levels were found to be 5.871 ± 0.39 mIU/ml and 2.714 ± 0.92 mIU/ml in disease and normal groups, respectively (Figure 2).

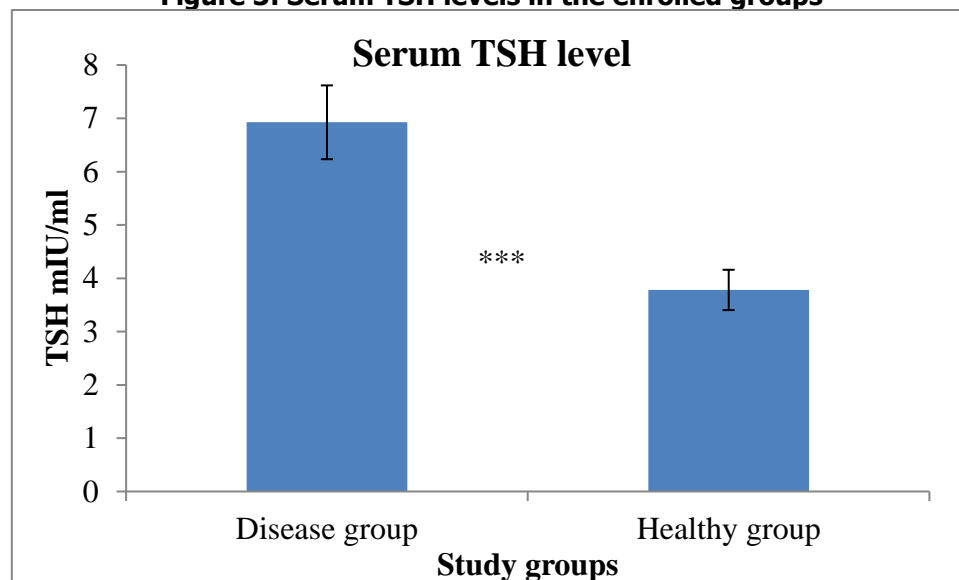
Figure 2: Serum T3 levels in the disease and healthy groups



The results are represented as mean ± SD.

The serum TSH levels were found to be 6.926 ± 1.93 mIU/ml and 3.781 ± 0.72 mIU/ml in disease and normal groups, respectively (Figure 3).

Figure 3: Serum TSH levels in the enrolled groups



The results are represented as mean ± SD.

In the disease groups, maximum women underwent caesarean delivery (83.25%). The delivery time was about 38.61 ± 0.14 weeks for normal group and 36.70 ± 0.93 weeks for disease groups.

4. DISCUSSION

Approximately 82.32% of the 60 pregnant women in the study (Saadi et al., 2019) exhibited elevated TSH

levels (overt hypothyroidism), which is higher than the percentage of pregnant women who were healthy. The reported blood TSH values for thyroid hormone shortage were 7.0762.01mIU/ml and for normal groups they were 4.1460.37mIU/ml. About 80.32% of the women in the thyroid hormone insufficiency groups had caesarean deliveries. Whereas thyroid hormone deficiency groups showed early delivery at about



36.641.93 weeks, normal delivery takes about 39.220.34 weeks. This means that caesarean birth may occur as a result of abnormal thyroid hormone levels (Saadi et al., 2019). This report agrees with our report. In the recent prospective study (Juneja et al., 2020) of 200 antenatal cases, TSH was reported to be less than the conventional cutoff of 2.5 IU/l, at 1.6 IU/l. In 61% of cases, TSH levels decreased as gestational age increased. An abnormal thyroid function has been recorded in instances 8.5% of the time. TSH, T3, and T4 standardization remain a problem since they differ greatly among cross-sectional research. In another prospective observational study by Mukherjee et al. (2022) showed maternal incidences such as pregnancy loss (4%) and preterm birth (8%) due to hypothyroidism among pregnant women. Manousou et al. (2021) carried out one randomized, pilot, and double-blind trial on 200 thyroid deficient and healthy pregnant women. According to the study, a daily supplement of 150 g of iodine helped a group of pregnant women who had mild iodine insufficiency transition to having enough iodine. The maternal thyroglobulin had been positively impacted by this development. The purpose of this study's extension is to look at the cognitive growth of the kids.

A study conducted in Iran, reported that the serum TSH, T3 and T4 and levels were 1.84 ± 1.32 mIU/L, 4.50 ± 0.64 pmol/L, and 1.01 ± 0.15 ng/dL, respectively in the first trimester. While in nonpregnant women, these levels were 4.49 ± 0.57 pmol/L, 1.10 ± 0.21 ng/dL and 2.58 ± 1.77 mIU/L, respectively (Kianpour et al., 2018). Different cross sectional reports have shown that thyroid dysfunction is during pregnancy basics significant changes in the thyroid function markers. Women of reproductive age are typically affected by thyroid disease, and caring for these women during pregnancy necessitates close observation of mother and the foetus. To reduce the risk of difficulties, thyroid dysfunction must be properly diagnosed, treated, and managed during the pre-pregnancy, pregnancy, and post-partum periods.

Mehran et al. (2013) has reported that in Iranian women reference intervals of T3, T4 and TSH were first (137.8–278.3ng/dl; 8.2–18.5 μ g/dl; 0.2–3.9mIU/l), second (154.8–327.6ng/dl; 10.1– 20.6 μ g/dl; 0.5–4.1mIU/l) and third (137–323.6ng/dl; 9–19.4 μ g/dl; 0.6–4.1mIU/l) trimesters respectively (Mehran et al., 2013). Yan et al. (2011) and Soldin et al. (2011) both report on related reports (2004). T3 and T4 levels peaked in the first trimester and began to decline by the third. The first, second, and third specific ranges of the trimester were examined by Soldin et al. in 2004. He discovered that the values for T4 in the first, second, and third trimesters vary from 6.3-14.6, 6.4-14.8, and 6.3-16.7 g/dL, respectively, and for T3, from 92-218, 112-278, and 111-265 ng/dL. Similar reports were

published by various authors (Brent, 1997; Abbassi-Ghanavati et al., 2009; Stagnaro-Green et al., 2011; Medici et al., 2015; Nazarpour et al., 2016; Tehrani, 2018).

Human chronic gonadotropin stimulates thyroid function during pregnancy (hCG). Hence, any aberration of thyroid function causes abnormalities in the development of the mother and the foetus (Kianpour et al., 2018). Unfortunately, data on the levels of the thyroid hormones in pregnant women is sparse and varies based on the research population's ethnicity. Some writers observed lower serum free T3 and T4 levels, although earlier reports indicated unchanged or even higher levels. Hence, there is debate concerning the thyroid hormone change during pregnancy. Nonetheless, many of the authors noted that the levels of free hormones were lower in pregnant women than in non-pregnant ones. Thus, it is crucial to find out the hormone levels of T3 and T4 in pregnant people of a certain age.

5. CONCLUSIONS

The study can be concluded as the disease groups showed maximum women (83.25%) underwent caesarean delivery. The delivery time was about 38.61 ± 0.14 weeks for normal group and 36.70 ± 0.93 weeks for disease groups. Evident hypothyroidism was observed in the Iraqi women. These abnormal levels of the thyroid hormones can be lead to miscarriage caesarean delivery with high weight infants.

6. Ethical clearance: The blood was collected from **Hindi General Hospital** after their investigation. Oral consent was taken before enrolled the patients in the study.

REFERENCES

1. De-Escobar GM, Obregón MJ, del Rey FE. Maternal thyroid hormones early in pregnancy and fetal brain development. *Best Pract Res Clin Endocrinol Metab.* 2004;18:225–248
2. Stagnaro-Green A, Pearce E. Thyroid disorders in pregnancy. *Nature Reviews Endocrinology.* 2012 Nov;8(11):650-8.
3. Bernal J. Thyroid hormone receptors in brain development and function. *Nature clinical practice Endocrinology & metabolism.* 2007 Mar;3(3):249-59.
4. Bose A, Soni N, Dashore N, Gajria K, Jhamad S, Hemvani N, Chitnis DS. An enumeration of the prevalence of hypothyroidism during pregnancy in central India. *Clinical Epidemiology and Global Health.* 2015; 3:S34-S37.
5. Alemu A, Terefe B, Abebe M, Biadgo B. Thyroid hormone dysfunction during pregnancy: A



- review. *International journal of reproductive biomedicine*. 2016 Nov;14(11):677.
6. Marvisi M, Brianti M, Marani G, Del Borello R, Bortesi ML, Guariglia A. Hypothyroidism and pulmonary hypertension. *Respire Med*. 2002;96:215–220.
 7. Saadi RK, Habash MM. Evaluation of Serum Thyroid Hormones and its Effect/Complications During Pregnancy. *Indian Journal of Public Health Research & Development*. 2019 Nov 1;10(11).
 8. Carvalho GA, Perez CL, Ward LS. The clinical use of thyroid function tests. *Arquivos Brasileiros de Endocrinologia & Metabologia*. 2013;57:193-204.
 9. Juneja M et al. Study of thyroid hormones in pregnancy. *Int J Reprod Contracept Obstet Gynecol*. 2020 Oct;9(10):4086-4090
 10. Mukherjee et al. Study of hypothyroidism among pregnant women in the first trimester of pregnancy in a tertiary care hospital. *IJMCCR*. 2022;5: 764-769
 11. Manousou S, Eggertsen R, Hulthén L, Filipsson Nyström H. A randomized, double-blind study of iodine supplementation during pregnancy in Sweden: pilot evaluation of maternal iodine status and thyroid function. *European Journal of Nutrition*. 2021 Sep;60(6):3411-22.
 12. Kadhim M. Total Oxidants, Lipid Peroxidation and Antioxidant Capacity in the Serum of Rheumatoid Arthritis Patients. *Journal of Pharmaceutical Negative Results*; Volume. 2022;13(3).
 13. Kianpour, M., Aminorroaya, A., Amini, M., Feizi, A., Janghorbani, M. Thyroid function test reference ranges in the first trimester of gestation and pregnancy outcomes: Protocol and preliminary results for cohort population-based study Isfahan, Iran. *J Res Med Sci*, 2018; 23: 99
 14. Mehran L., Amouzegar A., Delshad H., Askari S., Hedayati M., Amirshkari G., Azizi F. Trimester-specific reference ranges for thyroid hormones in Iranian pregnant women. *Journal of thyroid research*, 2013, Article ID 651517, 1-6.
 15. Yan Y. Q., Dong Z. L., Dong L., Wang F. R., Yang X. M., Jin X. Y., Lin LX, Sun YN, Chen ZP. Trimester-and method-specific reference intervals for thyroid tests in pregnant Chinese women: methodology, euthyroid definition and iodine status can influence the setting of reference intervals. *Clin endocrinol*, 2011; 74(2): 262-269.
 16. Soldin, O. P., Hilakivi-Clarke, L., Weiderpass, E., & Soldin, S. J. Trimester-specific reference intervals for thyroxine and triiodothyronine in pregnancy in iodine-sufficient women using isotope dilution tandem mass spectrometry and immunoassays. *Clinica Chimica Acta*, 2004; 349(1-2): 181-189.
 17. Tehrani F. R., Behboudi-Gandevani S. Hypothyroidism in pregnancy. *Ann. Thyroid*, 2018;3.
 18. Medici M., Korevaar T. I., Visser W. E., Visser T. J., Peeters R. P. (2015). Thyroid function in pregnancy: what is normal? *Clinical chemistry*, 61(5):704-713.
 19. Nazarpour S., Tehrani F. R., Simbar M., Tohidi M., Azizi F. Thyroid and pregnancy in Tehran, Iran: objectives and study protocol. *International journal of endocrinology and metabolism*, 2016; 14(1): e33477.
 20. Brent GA. Maternal thyroid function: interpretation of thyroid function tests in pregnancy. *Clin Obstet Gynecol*. 1997;40(1):3-15.
 21. Abbassi-Ghanavati M, Greer LG, Cunningham FG. Pregnancy and laboratory studies: a reference table for clinicians. *Obstet Gynecol*. 2009;114(6):1326-1331
 22. Mohammed AK, Al-Shaheeb S, Fawzi OF, Almashhadani HA, Kadhim MM. Evaluation of Interleukin-6 and Vitamin D in Patients with COVID-19. *Research Journal of Biotechnology Vol*. 2022 Oct;17(10).
 23. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, Nixon A, Pearce EN, Soldin OP, Sullivan S, Wiersinga W; American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid*. 2011;21(10):1081-125.