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Studying Effect of Pregnancy on Levels of TT4 and FT4 Indicators in Serum Pregnant Women in Diyala Province

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Abstract **Background:** Thyroxine is crucial for fetal development, especially brain growth. During pregnancy, physiological changes affect thyroid function, causing increased TT4 levels and variable FT4 levels, influenced by TBG, hCG and iodine availability. Detecting effect of pregnancy on levels of TT4 and FT4 in pregnant women in Diyala province. **Methods:** The research was conducted at Al-Batool Teaching Hospital in Diyala province from November 2024 to January 2025, involving 60 blood samples from pregnant patients and 30 healthy individuals as a control. Serum levels of FT4 and TT4 indicators were quantified using a Biorex machine. **Results:** The study found that pregnant women have higher levels of TT4 indicator compared to non-pregnant women, with a significant difference ($p<0.05$). However, no significant difference was found between FT4 and study groups. The ROC curve showed TT4 having the highest sensitivity and specificity (94 and 90%) for diagnosing thyroid disorders in pregnant women, while FT4 had the lowest sensitivity and specificity (55 and 54%). A significant positive correlation was found between FT4 and TT4 indicators in pregnant women. **Conclusion:** Pregnancy significantly impacts thyroid gland function, leading to significant changes in TT4 levels but not FT4 due to physiological and hormonal disorders. The TT4 is preferred for thyroid disorder screening.

Key Words Pregnancy, Thyroid, FT4, TT4, Hyperthyroidism

INTRODUCTION

Elevated metabolic demands during a normal pregnancy have a major effect on the thyroid physiology of the mother. A minor expansion of the thyroid gland caused by hyperplasia and enhanced vascularity is one of the main alterations in thyroid functioning; nevertheless, such an expansion does not represent a real goiter or severe thyromegaly. Both straightforward pregnancies and pregnancies in people with problems with the thyroid result in different thyroid function test findings, which vary each trimester [1]. Detecting thyroid abnormalities in pregnant women is crucial as both hypothyroidism and hyperthyroidism can lead to complications for the mother and baby. Hypothyroidism increases the risk of miscarriage, preeclampsia and developmental issues in the fetus, while hyperthyroidism can cause preterm birth and fetal growth restriction [2]. Thyroxine (T4) and triiodothyronine (T3) amounts rise during a normal pregnancy; human chorionic gonadotropin (hCG) cross-reacts with TSH receptors to cause a small reduction in thyroid-stimulating hormone (TSH), although this decrease is typically within the normal range; total T4 (TT4) levels rise while free T4 (FT4) levels stay constant [3]. Hypothyroidism, hyperthyroidism, postpartum thyroiditis and goiter are among the most prevalent perinatal thyroid conditions in the world [4]. Pregnancy-related goiter is uncommon in the United States, because the general population consumes enough iodine. Nonetheless, goiter during gestation is more prevalent in areas with low iodine levels [5]. Decreased FT4 and elevated TSH values during pregnancy are considered overt hypothyroidism [3]. According to Urgatz and Poppe [5]. Elevated TSH and adequate FT4 readings during the pregnancy are indicative of subclinical thyroid disease. Due to the many criteria of explicit and subclinical hypothyroidism that possess been used over the years in a

number of studies with varying findings, the epidemiology and prevalence of these conditions during pregnancy varies widely around the world [4]. Geographical location, socioeconomic level, race and ethnicity have all been linked to the wildly disparate diagnosis and management of subclinical hypothyroidism in pregnancy in the United States [6]. The majority of women who were pregnant with subclinical hypothyroidism received no treatment, according to a study by Maraka *et al.* [6]. Both healthcare providers and patients' factors, such as absence of established treatment procedures, an absence of awareness of evolving guidelines, confusion brought on by conflicting evidence and competent society suggested changes and patients' refusal of treatments, were linked to this are lacking of treatment starting [7]. About 0.1 to 0.4% of pregnancies are complicated by the rare illness known as hyperthyroidism [8].

The disorder is characterized by a reduction in Thyroid-stimulating Hormone (TSH), commonly referred to as thyrotropin and a rise in the circulation thyroid hormones T4 and T3. Directly hyperthyroidism is generally uncommon, but it should be recognized and treated to prevent difficulties for both the mother and the fetus [9]. In order to attain euthyroid state, hyperthyroidism should ideally be identified prior to pregnancy and treated. An early identification of thyroid disease is crucial, though, as up to half of births in the US are unplanned [10].

Due to a little study about effect pregnancy on thyroid function in Diyala province, our study aims to detecting effect of pregnancy on levels of TT4 and FT4 in pregnant women in this province.

Material and Methods Samples Collection

The conducted research was applied in Al-Batool Teaching Hospital/Diyala province within time (November 2024 to January 2025). About 60 blood samples were taken it randomly from pregnant who visiting Al- Batool Hospital and after diagnosis them by the physician in advisory units within hospital. Additionally, 30 samples were collected from randomly healthy individuals and considered them as a control category.

METHODS

To obtain serum, 5 mL of blood human was centrifuged at 4000 rpm for 5 minutes. Serum levels of FT4 and TT4 indicators were quantified in all participants samples by Biorex machine (United Kindom).

Statistical Analysis

The normality of FT4 and TT4 indicators were first assessment (Kolmogorov-Smirnov and Shapiro-Wilk test). Indicators pass normality tests (non-significant different) were described like Mean±SD, with use student t-test to calculate differences significance between indicators levels and study groups. The type of association between indicators was tested by Pearson correlation. Receiver Operating Characteristic (ROC) curve was done to calculate Area under the Curve (AUC), sensitivity and specificity of FT4 and TT4. The $p \leq 0.05$ was done for detect significant differences. All data were done by SPSS v. 22.0 and Graph pad prism v.6 programs.

RESULTS

Levels of FT4 and TT4 Indicators Within Study Groups

Present outcomes showed increased levels of TT4 indicator in pregnant women (163.35±30.95) compared to non-pregnant (104.13±33.63) with significant different ($p<0.05$). In contrast, our findings showed no significant difference ($p>0.05$) between levels of FT4 indicators and study groups (Table 1 and Figure 1).

ROC Curve of FT4 and TT4 Indicators

ROC curve results showed the TT4 indicator scored highest sensitivity and specificity (94 and 90%) at cut off (121.5) in diagnosis pregnant women have thyroid disorders with significant difference ($p<0.05$), compared to FT4 indicator which showed lowest sensitivity and specificity (55 and 54%) at cut off (15.5) (Table 2 and Figure 2).

Correlation Relationship Between FT4 and TT4 Indicators

Pearson correlation showed there is significant positive correlation between FT4 and TT4 indicators in pregnant women ($r = 0.561^{**}$ and significant = $p<0.01^{**}$) (Table 3 and Figure 3).

Table 1: Comparative concentration of FT4 and TT4 indicators between pregnant versus non-pregnant women

Groups	N	Mean	Std. deviation	p-value
FT4				
Pregnant	60	15.75	2.53	p>0.05
Non-pregnant	30	15.13	3.27	
TT4				
Pregnant	60	163.35	30.95	p<0.05*
Non-pregnant	30	104.13	33.63	

Table 2: ROC curve, sensitivity and specificity of FT4 and TT4 indicators in screening women with thyroid disorders

Variables	AUC*	St. Error	p-value	Cut off	Sensitivity %	Specificity %
FT4	0.551	0.064	p>0.05	15.5	55	54
TT4	0.894	0.046	p<0.01**	121.5	94	90

AUC*: Area under curve

Table 3: Correlation relationship between FT4 and TT4 indicators in pregnant women with thyroid disorders

TT4	FT4
Pearson correlation coefficient (r)	0.561**
Significant	p<0.01**

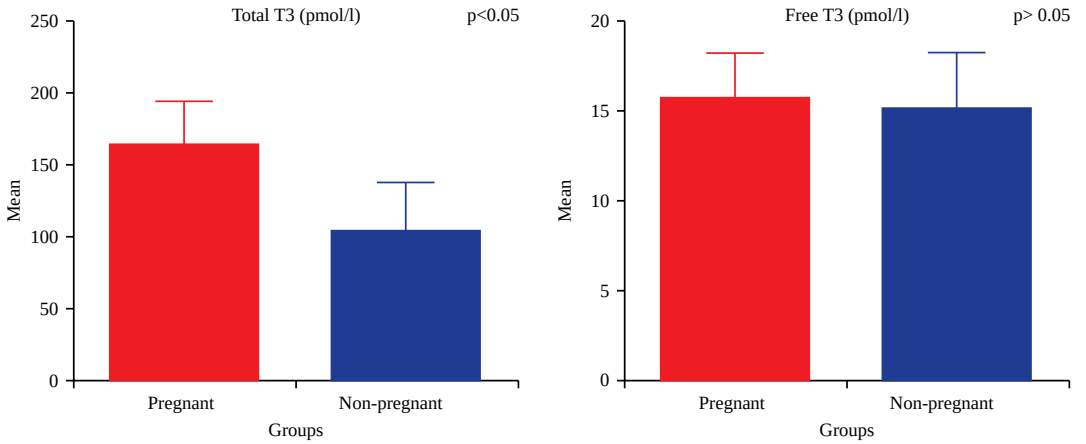

Figure 1: Comparative concentration of FT4 and TT4 indicators between study groups

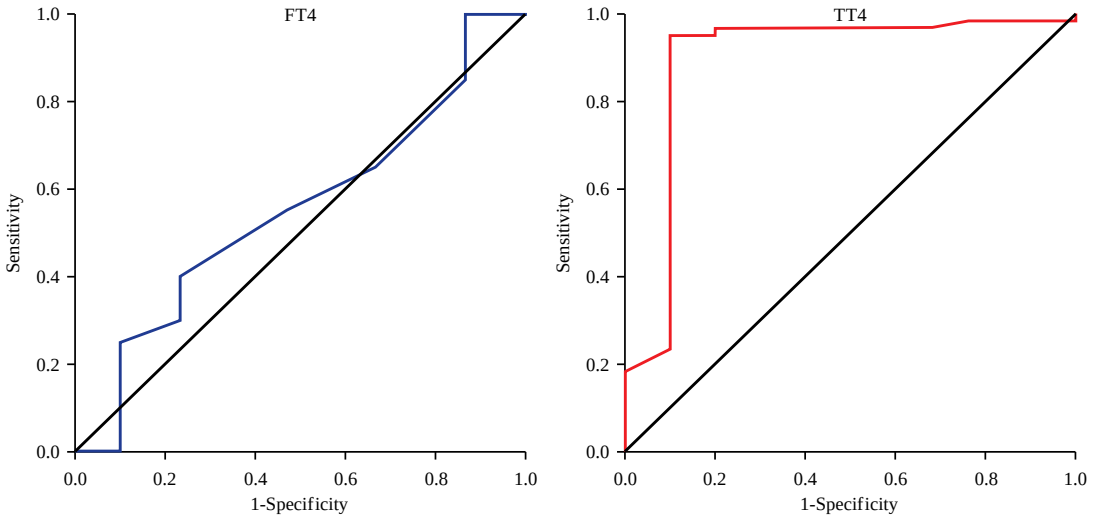

Figure 2: ROC curve of FT4 and TT4 indicators

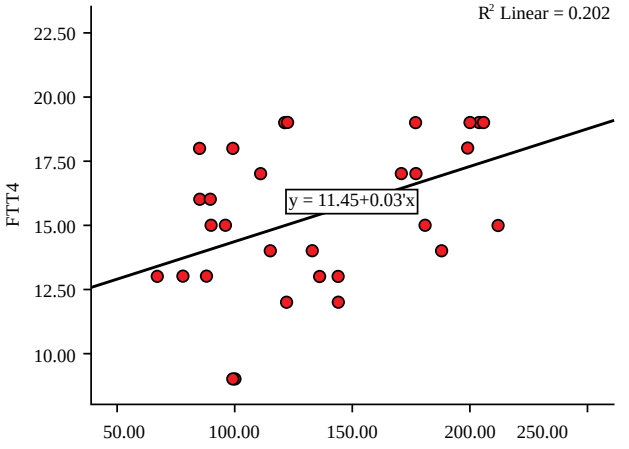

Figure 3: Correlation relationship between FT4 and TT4 indicators in pregnant women with thyroid disorders

DISCUSSION

The goal of the current study was to determine how pregnancy affected the levels of TT4 and FT4 in expectant mothers. However, due to the numerous physiological shifts that impact the amounts of thyroid-related analytes, assessing thyroid function during pregnancy is difficult. Due to FT4 remains stable during pregnancy due to thyroid adaptation, including increased TBG (thyroxine-binding globulin), placental hormone regulation and feedback mechanisms that maintain hormonal balance. The authors found that pregnant women had higher levels of total thyroxine (TT4) (hyperthyroidism) than non-pregnant women [11]. These results aligned with the research we conducted. Similarly, pregnant women have elevated levels of TT4 [12]. However, prior research revealed that pregnant women have a higher frequency of thyroid conditions, particularly hypothyroidism (25%) than non-pregnant women [13]. The variations among investigations are linked to variations in gestational age plus hormonal and physiological controls. According to Mizher *et al.* [12] FT4 quantities progressively drop as gestational age increases. To prevent incorrect thyroid status categorization, it is crucial to include trimester-specific reference periods when interpreting thyroid condition test outcomes.

Although their primary purpose is to control the initial metabolic rate, thyroid gland hormones also play a significant role in the growth of babies and the functioning of reproduction. Preeclampsia, low birth weight and other problems have been linked to both hyperthyroidism and hypothyroidism during pregnancy [13]. Additionally, neurodevelopmental delay is caused by a thyroid hormone deficit in the growing fetus. Identification of maternal thyroid insufficiency is crucial since the fetus depends solely on the mother's thyroid hormone for the majority of the first trimester and needs the mother's supply until delivery [14].

Women are four to five times more likely than males to have thyroid issues, particularly during periods of pregnancy. Therefore, biochemical anomalies in thyroid functioning during a "routine" lab examination in pregnant women is not uncommon. Additionally, pregnancy is linked to significant changes in thyroidal economy because of three different variables: the significant rise in serum binding abilities brought on by a boost in Thyroxine-binding Globulin (TBG) levels; the placental aspects, specifically human chorionic gonadotropin (hCG), which stimulate the mother's thyroid; and a reduced amount of iodine, that is primarily brought about by a faster kidney's elimination of iodide [13].

Directly hyperthyroidism is characterized by elevated FT4 and low TSH and its occurrence during pregnancy is 0.2% [15]. Gestational trophoblastic illness, nodular goiter, single toxic adenoma, viral thyroiditis and pituitary or ovarian tumors are some of the less frequent triggers for hyperthyroidism. According to Jiao *et al.* [16] hyperthyroidism may have been linked to a higher risk of a number of pregnancy issues, such as spontaneous abortion, early labor, low birth weight at delivery, stillbirth, preeclampsia and maternal cardiac disease.

Gestational Transitory Thyrotoxicosis (GTT), often referred to as transient gestational hyperthyroidism, can result from early increases in hCG throughout pregnancy that boost thyroid hormone production. The symptoms and warning signs of Graves' disease and GTT are similar to those of hyperthyroidism. Consequently, for a proper diagnosis, a comprehensive patient history, a physical examination and the recommended laboratory tests are essential [17]. TSH-secreting pituitary adenomas, trophoblastic tumors, hyperemesis gravidarum, multinodular goiter, familial nonautoimmune hyperthyroidism, autoimmune thyroiditis and de Quervain thyroiditis are among the possible differential diagnoses for hyperthyroidism [4]. Because poorly managed thyrotoxicosis significantly increases the risk of unfavorable fetomaternal effects, it is imperative that thyroid problems in pregnant women be identified early and treated appropriately. Furthermore, antithyroid drugs or maternal thyroid-stimulating antibodies can cross the placenta and may disrupt fetal thyroid function, which could have an impact on the fetus's prognosis [17].

Prior studies have shown that thyroid problems are more common in younger ages. Demographic changes including postponed marriages, postponed pregnancies and longer intervals between pregnancies may be the cause of these discrepancies. Moreover, patients with hypothyroidism exhibit more marked differences between urban and rural locations. Furthermore, a sizable portion of expectant mothers with thyroid problems had less education. Pregnancy problems and incorrect healthcare-seeking behaviors may result from this factor's contribution to an abundance of awareness and neglect for early signs [18].

Numerous hyperthyroid women were shown to have a tendency to become pregnant more than once. Thyroid problems in multigravida women may result from the depletion of vitamins and other vital components caused by more than one pregnancy. Additionally, hypothyroid women are more likely to have a caesarean section and have a lower likelihood of unplanned delivery [19]. Abortion is more prevalent in people with hyperthyroidism. On the other side, considering hypothyroidism is linked to diseases like preeclampsia, it is linked to low birth weight (LBW). The functioning of the newborn's pituitary-thyroid axis, the production of growth hormone in the prenatal pituitary gland, blood vessel responsiveness and maturing and cardiac balance throughout the fetal period can all be affected by low fetal thyroxine concentration [20]. Furthermore, babies delivered to mothers with thyroid disorders may experience a variety of issues, including birth asphyxia, meconium aspiration syndrome, neonatal sepsis, respiratory distress syndrome, preterm delivery and jaundice [21] (Table 1).

Our findings were consistent with those of Mizher *et al.* [12], who demonstrated that the TT4 had a higher sensitivity score of 90% than the FT4 50%.

Concentrations of thyroid hormones (FT4 and FT3) were shown to differ significantly between pregnant women at various phases and non- pregnant women in a newest study. The study discovered that FT3 and FT4 were greater in both the beginning and the end of pregnancy. Furthermore, in ROC analysis, TSH, FT3 and FT4 showed a greater area under the curve (AUC) for detecting hyperthyroidism than hypothyroidism and their combination increased diagnostic confidence ($p<0.05$). Lastly, the amount of thyroid hormone differs between pregnant and non-pregnant women as well as over the course of the pregnancy. Thyroid issues during pregnancy can be identified and consequences can be prevented by setting local reference intervals [22] (Table 2).

Finally, the positive correlation between FT4 and TT4 indicators in pregnant women related to hormonal and physiological disorders in pregnant (Table 3).

CONCLUSIONS

Pregnancy is playing important role in effect on thyroid gland function, where it is found the pregnancy led to large changes in levels of TT4 but not FT4 in pregnant women due to physiological and hormonal disorders. TT4 indicator is more preferred in screening pregnant with thyroid disorders than FT4 due to TT4 has high sensitivity and specificity. Finally, FT4 is positive correlate with TT4. Further studies were required for detect levels of thyroid hormones at different stages in pregnancy. Diyala province's environmental iodine deficiencies may have increased thyroid dysfunction, impacting study results, especially in vulnerable groups like pregnant women. In future Should Investigating TT4 and FT4 changes across different pregnancy trimesters, exploring the impact of dietary iodine supplementation on TT4 and FT4 levels and conducting longitudinal studies to monitor hormonal fluctuations over the full gestational period.

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