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Assessment of Thyroid Function Parameters among Sudanese Pregnant Women in Different Trimesters

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Authors' contributions

This work was carried out in collaboration between all authors. Author OIAH designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors GAM and AMA managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: The thyroid gland plays an important role in pregnancy outcome as well as in fetal development. The changes caused by pregnancy in the mother establish a new homeostatic equilibrium. Thyroid disorders are common during pregnancy, and adequate treatment is essential to prevent adverse maternal and fetal outcomes.
Objectives: To assess FT3, FT4 and TSH levels in pregnant Sudanese women, and to correlate their levels with the gestation age.
Materials and Methods: This analytical cross-section study was performed at Teanbool hospital obstetrics and gynaecology department in Aljazeera state- Sudan, during the period from January to October 2017. 150 samples were collected from pregnant women (50 in first, 50 in second and 50 in third trimester) as a study group. In addition to other 50 non-pregnant healthy women and

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age-matched as a control group. The thyroid hormones TSH, FT3 and FT4 levels in both test and control groups, were estimated by automated Cobas e 411 analyzer using electrochemiluminescence immunoassay "ECLIA".

Results: FT3 and FT4 is significantly decreased (3.9±0.84 verses 4.54±0.65 pmol/L, p ≤ 0.05.12.77±2.54 verses 14.80±1.95 pmol/L, P ≤ 0.001 respectively), where as TSH is slightly increased (1.86±1.01 verses 1.99±0.95 uIU/ml, P ≥ 0.05) in the study group when compared with the reference group, FT3 is significantly correlated with FT4 (r = 0.47, p=0.001) in pregnant women. According to gestational age FT3 is significantly decreased in the three trimesters (4.1 ±0.18 verses 4.54±0.65, pmol/L, P ≤ 0.05, 3.8±0.59 verses 4.54±0.65, pmol/L, P ≤ 0.052, 3.7±0.42 verses 4.54±0.65, pmol/L, p=0.02), where as FT4 is significantly decreased in the second and third trimesters (3.8±0.59 verses 14.80±1.95 pmol/L, P ≤ 0.045, 11.28±1.68 verses 14.80±1.95 pmol/L, p=0.000). In contrast TSH is significantly increased in the third trimester (2.08±0.58 verses 1.99±0.95 uIU/ml, P = 0.05) in the test group when compared with reference one. The study illustrated significant inverse correlation of both FT3 and FT4 with gestation age (r =-0.21, p=0.05, r =-0.39, p 0.02 respectively), whereas TSH is insignificantly correlated with gestation age in the test group (r= 0.14, p = 0.34).

Conclusion: The study revealed a significant decrease in both FT3 and FT4 levels in the pregnant women, with significant negative correlation with gestation age.

Keywords: Thyroid hormone; pregnancy; trimester; Sudanese; gestation age.

1. INTRODUCTION

Pregnancy is a natural physiological change that is accompanied with numerous hormonal changes as well as alterations in metabolic demands [1], that results in many path physiologic processes, some of which have potentially dangerous outcomes if left untreated [1-3]. Many physiological alterations of various endocrine glands occurred during pregnancy [2, 3], namely the pituitary, thyroid, parathyroid, adrenals and pancreas, domain distinct physiological difference resulting in alteration in the output of respective hormones [3-6]. Pregnancy causes complex changes in circulating maternal steroid hormones and in thyroid binding globulin (TBG) concentrations [1, 2,5,6].

Thyroid disorders is a medical condition when the thyroid gland secreted too much thyroid hormone from an overactive thyroid gland is called hyperthyroidism [7], it speeds up the body's metabolism. One of the most common forms of hyperthyroidism is known as Graves' disease [7,2]. When too little thyroid hormones are secreted from an underactive thyroid gland is called hypothyroidism. In hypothyroidism, the body's metabolism is slowed [7-9].

Thyroid function parameters are mostly comprised of free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH), is primarily performed for the diagnoses of the thyroid dysfunctions [10]. Numerous studies have illustrated that maternal thyroid hormones are cornerstone for fetal development during pregnancy, and their alteration may affect the pregnancy outcome and developing fetus [11,12]. The thyroid disorders during pregnancy are a risk factor to both the mother and the fetus [13-15]. A research study [16], recorded that increased TSH with decreased FT4 is correlated with more operative vaginal deliveries and caesarean sections. Other study [17], revealed that elevated maternal FT4 levels during the first half of pregnancy were correlated with decreased birth weight and raised the risk of small gestational age newborns. Thyroid disorders can cause potential damage to fetal brain development, and increased the numbers of miscarriage, preterm delivery or fetal mortality [18,19]. Some studies documented relation of neurological changes in children of women with subclinical hypothyroidism during pregnancy [3, 13,14]. The prevalence of high rate of thyroid disorders in pregnant women has led to increase the attention of the importance of thyroid function parameters in all pregnant women [13,14]. Accurate assessment of thyroid function parameters during pregnancy is essential for both initiation of thyroid hormone treatment and management of thyroid hormone dose already receiving therapy [1,10,11]. Hence this study targets to highlight the possible relationship between thyroid function parameters and pregnancy in Sudanese pregnant women.

2. MATERIALS AND METHODS

This is an analytical cross-sectional hospital based study was done at Teanbool hospital department of obstetrics and gynecology in Algazera state during the period from January to October 2017. 150 pregnant women (50 in first, 50 in second and 50 in third trimester) as study group. In addition to other 50 non pregnant healthy women and age matched as control group.

2.1 Inclusion Criteria

Pregnant woman without thyroid diseases agree to participate in this study.

2.2 Exclusion Criteria

Pregnant woman with diagnosed thyroid diseases or with sign or symptoms of thyroid diseases. Pregnant women that refused to participate in the study.

2.3 Data Collection and Clinical Examination

Each site used a standardized questionnaire which collected the demographic and symptom information assessed in this study. Clinical examinations done by clinicians in above mentioned hospital.

2.4 Sample Collection

Subjects who met the criteria were then included in the study and their serum FT3, FT4 and TSH levels were estimated.

2.5 ml venous blood sample was obtained from each participant using standard vein puncture technique, blood specimens were collected in plain container, allowed to clot at room temperature for 30 minute, centrifuged at 3000 rpm for 5 minutes to obtain the serum. Then the serum was separated in penal and preserved at-20C until analysis.

2.5 Ethical Considerations

The procedure described here was approved by Alneelain University research committee and is consistent with the Declaration of Helsinki. Informed consent was obtained from all participants.

2.6 Estimation of Thyroid Function Parameters

The thyroid hormones FT3, FT4 and TSH levels in both test and control group were estimated by automated Cobas e 411 analyzer using electrochemiluminescence immunoassay “ECLIA”(Ruch company - Germany) in laboratory of National Cancer Institute - Gezira University.

2.7 Estimation of Growth Hormone, IGF, Leptin, Adiponectin, Resistin and TNF-α

Growth hormone, adiponectin,leptin and resistin hormone levels in the serum was determined by using ELISA kits produced by Komabiotech, Korea.

2.8 TNF-alpha

Enzyme-linked immunosorbent assay was used for quantitative detection of human TNF-alpha, Bender Medsystems GmbH (BMS223HS), and Austria.

IGF level was determined in Siemens Immulite 2000 analyzer (Siemens Healthcare Diagnostics, Deerfield, IL, USA) by solid phase enzyme marked chemiluminescence method.

2.9 Quality Control of Cobas E411

Preci Control Universal was used in addition to other three control levels (low, normal, and high) of control sera of FT3, FT4 and TSH values were used to verify the performance of measurement procedure, and results of +/- 2SD of target values of the control sera were accepted.

2.10 Data Management and Analysis

The demographic characteristics of the study and control groups were compared using SPSS program version 21. Statistical mean and SD of FT3, FT4 and TSH was obtained .T- test and anova were used for the comparison of FT3, FT4 and TSH levels between the test and control group, between different pregnancy trimesters, and the difference is significant at $p \leq 0.05$, Correlation(r) between Ft3, FT4 and TSH levels with gestational age is considered significant at $P \leq 0.05$.

3. RESULTS

In this analytical cross sectional hospital base study the population is comprised of 150 pregnant women (50 in first , 50 in second and

50 in the third trimester) as test group , with age range (19- 32 years), in addition to 50 non pregnant healthy volunteer and age matched as control group.

Table 1. shows baseline clinical characteristic of study group between patients and control group, which presented the mean of total FT3, FT4 and TSH in the study group and control group. Ft3 and FT4 is significantly decreased (3.9±0.84 verses 4.54±0.65 pmol/L, p ≤ 0.05.12.77±2.54 verses 14.80±1.95 pmol/L, P ≤ 0.001 respectively), where as TSH is slightly decreased (1.86±1.01 verses 1.99±0.95 uIU/ml, P ≥ 0.05) in the study group when compared with the reference group. In Table 2 FT3 is significantly correlated with FT4(r = 0.47, p=0.001) in pregnant women.

According to gestational age FT3 is significantly decreased in the three trimesters (4.1 ±0.18 verses 4.54±0.65, pmol/L, P ≤ 0.05, 3.8±0.59 verses 4.54±0.65, pmol/L, P ≤ 0.052, 3.7±0.42 verses 4.54±0.65, pmol/L, p=0.02), FT4 is significantly decreased in the second and third trimesters (3.8±0.59 verses 14.80±1.95 pmol/L, P ≤ 0.045, 11.28±1.68 verses 14.80±1.95 pmol/L, p=0.000), and TSH is significantly increased in the third trimester (2.08±0.58 verses 1.99±0.95 uIU/ml, P = 0.05) in the test group when compared with reference one in Table 3.

As shown in Table 4 FT3 and FT4 were inversely correlated with gestation age (r =-0.21, p=0.05, r =-0.39, p 0.02 respectively), TSH is insignificantly correlated with gestation age in the test group (r= 0.14, p = 0.34).

As illustrated in Table 5. Comparison of interquartile ranges of thyroid hormones levels in our study with a previous Sudanese studies, FT3, T4 levels was decreased in the three studies. Whereas TSH level was increased in the present study and decreased in the previous Sudanese studies.

Table 1. Comparison of the mean concentrations of total thyroid hormones of the three trimesters in the case with their control

Parameter	Case (Mean±SD) N=150	Control (Mean±SD) N=50	*P-value*
Free T3 (pmol/L)	3.9±0.84	4.54±0.65	0.05
Free T4 (pmol/L)	12.77±2.54	14.80±1.95	0.000
TSH (uIU/ml)	1.86±1.01	1.99±0.95	0.481

Table 2. Correlation between FT3, FT4 and TSH levels in pregnant women

Parameter	Statistic	FT4	TSH
FT3	Person correlation	0.47***	0.29*
	Significance (tow tail)	0.001	0.04
FT4	Person correlation	1	-0.199
	Significance (tow tail)		0.17

. Correlation is significant at the p ≤ 0.05, **. Correlation is significant at the p ≤ 0.01, *. Correlation is significant at the p ≤ 0.001.*

Table 3. Comparison of the mean concentrations of the thyroid hormones level according to trimester in the case with their control

Triimester	Parameters	Control(Mean±SD)	Case(Mean±SD)	*P-value*
First	FT3 (pmol/L)	4.54±0.65	4.1 ±0.18	0.052*.
Trimester	FT4(pmol/L)	14.80±1.95	15.58±1.84	0.154
	TSH(Uiu/L)	1.99±0.95	1.88±1.54	0.699
Second	FT3(pmol/L)	4.54±0.65	3.8±0.59	0.045*.
Trimester	FT4 (pmol/L)	14.80±1.95	11.76±1.65	0.000***.
	TSH (uIU/ml	1.99±0.95	1.60±0.70	0.157
Third	FT3(pmol/L)	4.54±0.65	3.7±0.42	0.02*.
Trimester	FT4 (pmol/L)	14.80±1.95	11.28±1.68	0.000***.
	TSH (uIU/ml)	1.99±0.95	2.08±0.58	0.05*

**. Correlation is significant at the p ≤ 0.05*
***. Correlation is significant at the p ≤ 0.01*
****. Correlation is significant at the p ≤ 0.001*

Table 4. Correlation of FT3, FT4, TSH levels with the gestational age in pregnant women

Parameter	Statistic	FT3	FT4	TSH
Gestational age	Person correlation	-0.21*	-0.39*	0.14
	Significance (tow tail)	0.05	0.02	0.34

Table 5. Comparison of interquartile ranges of thyroid hormones between our study and a previous Sudanese studies

Study	Parameter	First Trimester	Second Trimester	Third Trimester
Present study	FT3 nmol/L	3.9-4.9	3.7- 4.2	3.5- 3.9
	FT4 pmol/L	12.3-15.6	11.4-13.1	9.7-11.3
	TSH IU/ml	0.8-1.6	0.9-1.88	1.1-2.08
Elhaj et al. [20]	FT3 nmol/L	4.4–5.3	3.9–4.7	3.7–4.5
	FT4 pmol/L	15.1–21.4	12.3–17.8	11.5–16.4
	TSH IU/ml	0.5–1.5	0.9–1.7	1.0–1.8
Eltom et al. [21]	FT3 nmol/L	2.1–3.2 2	2-3.5	2.2–2.9
	FT4 pmol/L	9.6–13.4	8.6–10.8	9.4–12.6
	FTSH IU/ml	0.5–1.5	0.7–1.8	0.6–1.6

Table 6. Correlation of thyroid function parameters with growth hormone, insulin growth factor, leptin, adiponectin, resistin and TNF-α in the study group

Parameter	Statistic	Growth hormone	IGF	Leptin	Adiponectin	Resistn	TNF-a
TSH	Person correlation	-0.13	-0.46*.	0.15	0.17	0.091	0.06
	Significance (tow tail)	0.45	0.04	0.23	0.14	0.7	0.53
FT4	Person correlation	0.18	0.08	0.14	0.17	0.15	0.09
	Significance (tow tail)	0.24	0.65	0.31	0.22	0.19	0.73
FT3	Person correlation	0.12	0.18	0.10	0.16	0.07	0.11
	Significance (tow tail)	0.47	0.13	0.41	0.21	0.58	0.52

**. Correlation is significant at the p ≤ 0.05*
***. Correlation is significant at the p ≤ 0.01*
****. Correlation is significant at the p ≤ 0.001*

Thyroid function parameters was insignificantly correlated with growth hormone, insulin growth factor, leptin, adiponectin, resistin and TNF-α($p \geq 0.05$), only IGF was significantly negatively correlated with TSH ($r=0.46$, $p= 0.03$) in the study group Table 6.

4. DISCUSSION

The thyroid gland plays a vital role in body metabolism, through the production of thyroid hormones, which are known to have important actions in controlling many of the human reproductive functions [22]. Thyroid dysfunctions are most prevalent in women during their most reproductive age [23], and the thyroid disorders have been related to poor reproductive health and pregnancy outcomes [24]. Numerous authors related the presence of thyroid dysfunction with higher rate of pre-eclampsia, spontaneous abortion, premature delivery, intra-uterine fetal death and disturbed fetal psychomotor development [25].

The current study demonstrated significant decreases in both FT3 and FT4 with slight increases in TSH level in pregnant women when compared with nonpregnant women.Which disagree with Yeasmin et al. [26], who concluded that there is no change of serum FT3, FT4 and TSH levels in pregnancy. But is consistent in FT3 and FT4 level with previous Sudanese studies; Elhaj et al. [20] and Eltom et al. [25]. Whom stated that pregnancy is likely to suppress T3,

and T4 levels in healthy pregnant Sudanese women, and inconsistent with them in TSH level, which is increased in this study.

Across pregnancy trimester our study illustrated significant decrease of FT3 level in the three trimester, and FT4 is significantly decreased in the second and third trimester, where as TSH is slightly fluctuation in the first and second trimester, but is significantly increased in the third trimester in pregnant women when compared with no pregnant. These results agree with numerous previous studies. Ren et al. [27], in china deduced that pregnant women are likely to have lower thyroid hormone levels throughout pregnancy [27]. The possible cause of decreased of FT3 and FT4 is increase the estrogen level that lead to increase production of TBG causing an increased binding form and decrease the free form of thyroxin(T4) [28,29]. Hypothyroidism is common in pregnant with an estimated prevalence 2-3% and 0.3-0.5% for subclinical and overt hypothyroidism respectively [30]. In addition to increased demand of iodine supply during pregnancy for synthesis of FT3 and FT4 that might cause hypothyroidism in pregnant women [31,32].

The present study recorded inverse correlation of FT3 and FT4 levels with gestation age, TSH is insignificantly correlated with gestation age in the test group. Which is congruent with *Perpetua* Patal et al. [33], whom concluded that FT4 and FT3 are strongly and negatively correlated with age of gestation.

The possible explanation for decrease of FT3 and FT4 is due to salivation, mediated by estrogens, reduces the hepatic clearance of thyroxin binding globulin, which causes elevation of both TT4 and TT3 levels [34]. Alteration in albumin and free fatty acid levels facilitate the binding of T4 and T3 to carrier proteins; which induce decreased FT4 and FT3 levels in the blood as pregnancy progresses [34,35].

5. CONCLUSION

The study demonstrated that pregnant women are at risk for developing primary hypothyroidism complication. Thyroxin therapy is beneficial for all pregnant women with low FT3 and FT4.

Further research that also considers iodine homeostasis in pregnant women may provide further support for the conclusions of the study.

Further study that determine the proportion of pregnant women in each trimester had thyroid disorders is needed, and with specific prevalence values.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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