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EFFECT OF FIRST TRIMESTER PREGNANCY ON TRIIODOTHYRONINE, THYROXINE AND THYROID STIMULATING HORMONE AT VARIOUS AGE INTERVALS IN WOMEN OF PORT HARCOURT METROPOLIS, NIGERIA

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ABSTRACT

The effect of first trimester gestation on Triiodothyronine (T_3)**,** Thyroxine (T_4) and Thyroid stimulating hormone (TSH) were assessed in 90 female subjects between the ages of 18-45 years. The test subjects all in their first trimester pregnancy were 60 and the non-pregnant (control) subjects excluded by serum pregnancy test were 30. Age interval of 18-26, 27-35 and 36-45 years were considered for both the test and control subjects. Samples obtained from these subjects were analyzed using the enzyme immunoassay method and statistical analysis carried out using Graphpad prism 5.2. When control was compared to pregnant subject, T_4 and TSH showed significant increase and decrease respectively while T_3 indicated no significant difference. When age intervals were considered, pregnant women of 18 -26 years showed significant increases and decreases in T3, T4 and TSH respectively. In 27-35 years, significant increase and decrease were seen in T4 and TSH respectively while in 36-45 years, significant decrease was seen in TSH. These significant changes in the activities of the hormones in the early period of gestation indicate great demand fo r the hormones by the mother and for the sustenance of the growing child during pregnancy.

KEYWORDS: Pregnancy, T_3, T_4, TSH, First trimester.

1. INTRODUCTION

The thyroid gland is one of the largest endocrine glands which produces thyroid hormones: the principal ones being Triiodothyronine (T_3) and Thyroxine (T_4) that control the growth and rate of function of many other systems in the body as well as calcitonin which plays a role in calcium homeostasis.[1][2] T_3 and T_4 are synthesized from iodine and tyrosine.[2] The major function of the thyroid hormones is the regulation of the basal metabolic rate (BMR) and calorigenesis via increased oxygen consumption in tissues.[2][3] Hormonal output from the thyroid is regulated by thyroid stimulating hormone (TSH) from the anterior-pituitary and regulated by thyrotropin releasing hormone (TRH) of the hypothalamus.[2]

Pregnancy is the time during one or more offspring develop inside a woman. It is a period of vital hormonal changes (alterations in iodine metabolism, production of β-chorionic gonadotropin (β-HCC), increase in thyroid hormone-binding proteins and thyroid hormones) and metabolic demands that result in thyroid gland enlargement during normal pregnancy becoming distinct sometimes in pregnant women.[4][5] Gestation is divided into three trimesters and the first trimester being the most crucial to foetus development and it is at this period that the foetus undergoes major structural and functional changes.[4][5]

There is a great wealth of scientific evidence demonstrating the detrimental health effect in disorders of the thyroid in early stage of pregnancy, the first trimester.[5] Thyroid disorder is a disease that affects the thyroid gland, producing too much or too little thyroid hormones.[6] This is because; thyroid hormones play a vital role during pregnancy in neonatal development and maintenance of the health of the body. Thyroid maternal disorders can lead to obstetric complications and irreversible effects in foetus.[5][7]

Hypothyroidism and hyperthyroidism are the two main pathological condition attributed to the thyroid gland.[7][8] Hypothyroidism is common in pregnancy with an estimated prevalence of 2.3% and 0.3 – 0.5% for sub-clinical and overt hypothyroidism respectively.[9] Hyperthyroidism happens in about 0.2 – 0.4% of all pregnancies with most cases due to Grave's disease.[9]

The effects of thyroid disorders on the developing foetus are of interest with the most being decreased intelligence quotient (IQ) of offspring.[10][11] The foetus is totally dependent on maternal thyroid hormone supply during

the first trimester of pregnancy, the crucial time in organogenesis.[9][12] In the first trimester, exclusively the mother supplies thyroid hormones, whilst during and after the second trimester, thyroid hormones are supplied by both the mother and the foetus (though primarily by the mother.) Maternal thyroxine (T_4) is vital for foetal neural development throughout pregnancy but particularly during the first trimester when it is known to cross the placenta in substantial amounts.[8][13]

In developing countries like Nigeria, a great number of pregnant women develop thyroid diseases which might go unnoticed and these disorders may have harmful effects in foetal and maternal health. Therefore, the need to determine thyroid hormones in first trimester pregnancy among women attending antenatal clinic in Braithwaite Memorial Specialist Hospital, Port Harcourt since it is not part of routine antenatal check.

2. MATERIALS AND METHOD

2.1 Materials

Vortex mixer, micro-plate reader (Stat fax 2100 – Awareness Technology), T_3, T_4 and TSH reagents purchased from Bio-check, California, U.S.A. The Enzyme linked immunosorbent assay method was used and the procedure employed was in accordance with the manufacturer's instructions.

2.2 Study Area and subject description

The subjects were women recruited from the Braithwaite Memorial Specialist Hospital, Port Harcourt, attending antenatal clinic after obtaining ethical clearance and informed consent from all of the participants. A total of 90 women were used in this study between the ages of 18 -45 years. Of the ninety (90) subjects, sixty (60) were healthy pregnant women in their first trimester while thirty (30) were healthy non-pregnant women used as control subjects. Age interval of 18-26, 27-35 and 36-45 years were considered. Of the pregnancy subjects, 11, 35 and 14 women were within the age interval of 18-26, 27-35 and 36-45 years respectively while for the control subjects, 11, 13 and 6 women were within the age interval of 18-26, 27-35 and 36-45 years respectively. The selection criterion was based on serum pregnancy test. The sixty women used as test subjects were positive for pregnancy test with record of pregnancy within the first trimester while the other thirty (30) subjects used as control subjects showed negative pregnancy results.

2.3 Sample Collection and preparation

5ml of blood sample was collected by venupuncture into plain bottles from subjects. The samples were allowed to clot, retracted and centrifuged at 4000rpm for 5 minutes to obtain serum, which was separated into another plain bottle with a Pasteur pipette.

2.4 Statistical analysis

Data acquired were statistically analyzed using Graphpad Prism 5.2 version. Mean, standard deviation (SD) and inferential statistics using student's statistical t-test was used for the comparison with statistical significance seen at $p<0.05$.

3. RESULTS

The results obtained showed that first trimester pregnancy subjects had 1.48±0.48, 10.72 ± 3.32 and 1.33±0.80 for T_3, T_4 and TSH respectively while the control subjects had 1.54±2.20, 6.98±1.81 and 2.34±1.19 for T_3, T_4 and TSH respectively. The comparison showed significant increase in T_4 and significant decrease in TSH among pregnant subjects compared to the non-pregnant subjects (table 3.1). When age intervals were considered, pregnant subjects of 18-26 years had 1.30±0.53, 13.09±3.43 and 1.16±0.90 for T3, T4 and TSH respectively while the non-pregnant subjects (control) had 0.93±0.25, 5.85±0.76 and 2.26±1.31 for T3, T4 and TSH respectively (table 3.2). In 27-35 years age interval, pregnant women had 1.62±0.45, 10.88±2.88 and 1.28±0.78 while non-pregnant women (control) had 1.32±0.46, 7.45±2.20 and 2.23±1.25 for T3, T4 and TSH respectively (table 3.2). Finally, when pregnant women of 36-45 years age interval was considered, T3, T4 and TSH had 1.32±0.41, 9.19±3.15 and 1.41±0.82 respectively while control had 1.17±0.10, 8.02±1.20 and 2.78±0.93 for T3, T4 and TSH respectively (table 3.2). The comparison of pregnant and non-pregnant women of 18-26 years showed significant increases in T3 and T4 and decrease in TSH among pregnant women. In 27-35 years, significant increase and decrease was seen in T4 and TSH respectively among pregnant women compared to control women while in 36-45 years interval, significant decrease was seen TSH. T3 and T4 were not significant at $p<0.05$. The comparison of the various age intervals among one another using ANOVA showed no significant differences (table 3.3).

Table 3.1: Comparison of non-pregnant (control) and non-pregnant women (test subject)

Parameters	T_3(ng/ml)	T_4(ug/dl)	TSH (µlu/ml)
Non-pregnant women (Control)	1.54±2.20	6.98±1.81	2.34±1.19
Pregnant women (test subject)	1.48±0.48	10.72±3.32	1.33±0.80
pvalue	0.893	<0.0001	<0.0001
tvalue	0.2034	5.750	4.786
Remark	NS	S	S

TABLE 3.2: Comparison of non-pregnant and pregnant women at different age intervals

Parameters	T_3(ng/ml)	T_4(ug/dl)	TSH (µlu/ml)
Non-pregnant women (Control)	0.93±0.25	5.85±0.76	2.26±1.31

(18 -26 years)			
Pregnant women (test subject) (18-26 years)	1.30±0.53	13.09±3.43	1.16±0.90
pvalue	0.0468	<0.0001	0.0326
tvalue	2.119	6.831	2.297
Remark	S	S	S
Non-pregnant women (Control) (27 -35years)	1.32±0.46	7.45±2.20	2.23±1.25
Pregnant women (test subject) (27 -35years)	1.62±0.45	10.88±2.88	1.28±0.78
pvalue	0.0529	0.0004	0.0035
tvalue	1.990	3.845	3.095
Remark	NS	S	S
Non-pregnant women (Control) (36 -45years)	1.17±0.10	8.02±1.20	2.78±0.93
Pregnant women (test subject) (36 -45years)	1.32±0.41	9.19±3.15	1.41±0.82
pvalue	0.3712	0.3948	0.0054
tvalue	0.9139	0.8717	3.161
Remark	NS	NS	S

TABLE 3.3: Analysis of Variance (ANOVA) of non-pregnant and pregnant women at different age interval

Parameters	**T_3(ng/ml)**	**T_4(ug/dl)**	**TSH (µlu/ml)**
Non-pregnant women (Control)	1.54 ± 2.20^{a}	6.98 ± 1.81^{a}	2.34 ± 1.19^{a}
Pregnant women (test subject) (18 -26 years)	1.30 ± 0.53^{ac}	13.09 ± 3.43^{bc}	1.16 ± 0.90^{bc}
Pregnant women (test subject) (27 - 35years)	1.62 ± 0.45^{bcd}	10.88 ± 2.88^{bcd}	1.28 ± 0.78^{bcd}
Pregnant women (test subject) (36 -45 years)	1.32 ± 0.41^{acd}	9.19 ± 3.15^{acd}	1.41 ± 0.82^{bcd}
pvalue	0.893	<0.0001	<0.0001
Fvalue	0.2034	5.750	4.786
Remark	S	S	S

[a]not significantly different from control, [b]significantly different from control, [c]not significantly different from pregnant women (18-26 yrs), [d]not significantly different from pregnant women (27-35 years) at p<0.05; NS=Not significant; S=Significant.

DISCUSSION

The effect of first trimester pregnancy on thyroid stimulating hormone (TSH), triidothyronine (T_3) and thyroxine (T_4) was evaluated. Thyroid hormones are of utmost importance for maternal and neonatal health. And normal pregnancy results in a number of vital physiological and hormonal changes that alter thyroid function. Therefore, these changes imply that laboratory tests of thyroid function must be interpreted with caution during pregnancy. Changes occur due to the influence of two main hormones; human chorionic gonadotropin (HCG) and oestrogen and the level of circulating thyroid hormones biding globulin.[11] Increased HCG in circulation tends to induce increases in thyroid hormones and low TSH (subclinical hyperthyroidism) especially in the first trimester. TSH under the influence of placental HCG is decreased throughout pregnancy with lower normal TSH level in the first trimester.[12][13] Oestrogen increases the amount of thyroid hormone binding proteins in serum, which increases the total thyroid hormone levels in the blood since more than 99% of these hormones in the blood are bound to these proteins.[13]

The comparison of pregnant women and non-pregnant women showed significant increase and decrease in T4 and TSH respectively (table 1). The result obtained concurs with the reports of.[6][12][14] The increase and decrease in T4 and TSH respectively could be as a result of increased influence of placental hormones such HCG and placental lactogen on the thyroid glands reducing the effect of TSH on thyroid hormones. Physiologically, the increased thyroxine (T_4) might be due increased demand by the foetus since it cannot produce its own thyroid hormone. The increased T4 in turn reduces TSH as a result of negative feedback mechanism.

When the different age intervals were compared with their respective controls, age interval of 18-26years had significant increases in T3 and T4 while significant

decrease was seen in TSH. 27-35years had significant increase in T4 and significant decrease in TSH while 36 - 45 years had significant decrease in TSH only (table 2). The results obtained suggest that young women in their early reproductive ages (18-26 years) tend to have stronger influence of placental hormones on T3, T4 and TSH compared to reproductive women in their mid or late reproductive age (36-45 years). The increases seen in thyroid hormones especially T4 could also be as a result of increased thyroxine binding globulin (TBG) in the plasma which directly induces increase in circulating T4. The result obtained agrees with the finding of[11], who reported that T3, T4 and TSH tend to decrease in women during the fourth decade compared to first and second decade of life.

However, when the various age intervals were compared among themselves, no significant differences were observed between age interval of 18-26years, 27-35 years and 35 -45 years (table 3) when various age intervals were compared among one another. This also indicates that the influence of placental hormones on the hyper-activity of thyroid hormones and hypo-activity of TSH at different age interval in pregnant women do not differ significant when compared have increases seen at various age. This finding is in contrary to the report of.[11] They reported that T3, T4 and TSH are influenced by age differences.

CONCLUSION

The clinical evaluation of the thyroid hormones during pregnancy, particularly in the first trimester is of great importance as a result of extra requirement of thyroid hormones for the growth and metabolism of the growing foetus. The effects of thyroid disorders in pregnancy on developing foetus are of most devastating outcome with decreased intelligence quotient of the infant, insufficient or high production of these hormones, may present with miscarriages and delivery of preterm baby among other complications.

RECOMMENDATION

Thyroid function tests should form part of routine screening tests during the first trimester of pregnancy (antenatal) to avoid the unnecessary clinical outcomes especially in the early stage of foetus formation. Hyperthyroidism and hypothyroidism in pregnancy should be carefully evaluated to avoid adverse effect on both the mother and growing foetus.

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