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THYROID HORMONES AND SOME HAEMATOLOGICAL INDICES AT DIFFERENT TRIMESTERS OF PREGNANCY IN YENAGOA NIGERIA

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ABSTRACT

There are profound physiological changes in the pregnant woman that have been insinuated to have significant effects on maternal thyroid function and haematological indices. These changes are capable of complicating the interpretation of maternal thyroid function tests (TFTs) results as well as the haematological indices. This study evaluates the thyroid function and some haematological indices at different trimesters of pregnancy carried out at Federal Medical Centre Yenagoa. A total of 120 subjects within the age range of twenty and thirty-five years were recruited for this study. Ninety (90) subjects were pregnant women (30 each in 1st, 2nd and 3rd trimester) and thirty (30) were non-pregnant women which serve as control. 7ml of blood sample was collected from each subject; 5ml was dispensed into a plain bottle allowed to clot, centrifuged and serum stored at -20°c for hormonal analysis; 2ml of whole blood was dispensed into tri-potassium EDTA (K_3EDTA) bottle for haematological analysis using Enzyme Linked Immunosorbent Assay (ELISA) and SYSMEX pocH-100i automated analyzer. The result showed a statistically significant ($p<0.05$) low Thyroid Stimulating Hormone (TSH) from the first trimester (1.05 ± 1.34 uIU/ml) and a significantly higher TSH at the third trimester (1.42±6.01 uIU/ml) when compared with the control (5.00 ± 0.22uIU/ml). There was a negative correlation (r= -0.812) with low haemoglobin concentration. The thyroid hormones T4 and T3 showed a statistically significant ($p<0.05$) elevation in the first trimester (1.21±4.11nmol/L and 2.81±2.44nmol/L) and second trimester (1.29±6.21nmol/L and 3.42±6.00nmol/L) respectively. Haemoglobin (Hb) (10.23±0.76g/dl) and Packed Cell Volume (PCV) (33.23±4.00%) levels decreased significantly ($p<0.05$) during the first trimester when compared with the control (12.99±0.69g/dl and 36±5.00%) respectively. Platelets ($244\pm34x10^9$/L) levels increased significantly ($p<0.05$) in the first trimester and decreased significantly in the second and third trimesters ($233\pm44x10^9$/L and $217\pm29x10^9$/L) respectively when compared with the control ($214\pm41x10^9$/L). In conclusion, pregnancy alters the concentration of thyroid hormones and some haematological parameters in women.

KEYWORDS: Heamatological indices; Pregnancy; Thyroid hormone.

INTRODUCTION

During pregnancy, hormonal changes are not only limited to oestrogen and progesterone levels, but include other hormones like thyroid hormones, as the endocrine glands play very important role in reproductive physiology.[1] The factors precipitating these changes owes the need for an adjustment in the internal environment of the developing foetus to meet the additional requirements imposed by the metabolic, physiological and biochemical changes during pregnancy,[2] which to an extent borders on the hematological parameters like Heamoglobin (Hb), Packed cell volume (PCV), and platelets.

The heamatological indices of an individual to a large extent reflects the general health.[3] It is influenced by several factors like sex, seasonal variation, lactation, pregnancy, and nutritional status.[4] During pregnancy, there are several physiological alterations of various endocrine glands such as the pituitary, thyroid, parathyroid, adrenal, and pancreatic glands, which show distinct physiological changes accompanied by an increase in the output of corresponding hormones.[2]

Pregnancy induces a given amount of changes in the normal physiology of women, either directly or indirectly, most importantly the haematological indices. Plasma expansion and haemodilution during pregnancy contribute to majority of these changes. Haematological profile can reflect nutritional, immunological, haemostatic status of the pregnant women.[5] It is also an important predictor of pregnancy outcomes.[6] In normal physiology, activation of renin-angiotensin-aldosterone system during pregnancy increases extracellular fluid

and consequently plasma volume.[7,8] The haematological system in the body adapts to make provision for foetal haematopoiesis, ensuring proper blood supply to the enlarged uterus and its content thereby protecting both mother and foetus against the effects of impaired venous return in both the supine and erect positions in addition to safeguarding against bleeding at deliver.[9] Maternal erythropoiesis, neutrophil apoptosis, platelets activation, and clearance are enhanced during pregnancy.[10,11] The hematocrit (HCT), plateletcrit (PCT), counts of red blood corpuscles (RBC), white blood corpuscles (WBC) and platelets (PLT) are expected to change according to the degree of plasma volume expansion and the amount of blood formed elements being added or removed from the circulation.[11] Release of reticulocytes and activation of platelets affect the readings of some haematological indices like mean corpuscular volume (MCV), red cell distribution width (RDW), mean platelets volume (MPV) and platelets distribution width (PDW).[5]

Pregnancy produces a series of profound physiological changes in the mother that has a significant effect on maternal thyroid function. During pregnancy, physiological maternal thyroid function is important for both the mother and child.[12] This is especially true during the first trimester, when the developing foetus is completely dependent on the mother for thyroid hormones that are critical for optimal development.[13] Human chorionic gonadotropin (hCG) values are high in early trimester, α component of which has similarity to thyroid stimulating hormone (TSH), causing partial TSH suppression.[14] Thyroid stimulating hormone produced by the pituitary gland released into the blood circulation. The target tissue for TSH is thyroid gland. The TSH is synthesized in the pituitary in response to the Thyrotropin Releasing Hormone (CRH) produced in the hypothalamus. At the time TSH reached the thyroid gland, it binds to its receptor on the thyroid membrane, activating the receptor, finally an enzyme called Adenylate Cyclase activated on the thyroid gland and cyclic AMP (cAMP) is produced cAMP, subsequently activate the enzymes which are required for thyroid hormone synthesis and process, such as Iodine entry into thyroid gland by active transport through activation of sodium-potassium pump which are required for the production of thyroxin(T4) and triiodo-thyronine (T3).[4]

Maternal thyroid dysfunction during pregnancy has been shown to be associated with a number of adverse outcomes. Casey et al.[15] and Allan et al.[16] reported that elevated maternal thyroid-stimulating hormone (TSH) has been associated with an increased risk of pre-term births, placental abruption, foetal deaths, and impaired neurological development in children. Similarly, the presence of antibodies to thyroid peroxidase (TPO-Ab) has been associated with increased risk of miscarriage, preterm birth, and maternal post-partum thyroid disease.[17] A study by Gyamfi *et al.*[18] revealed that production of thyroid hormones and iodine requirement each increases by approximately fifty percent (50%) during pregnancy, and various other changes in thyroid function tests (TFT) during pregnancy include increased serum free thyroxine (FT4) associated with reciprocal decrease in thyrotropin (TSH) due to thyrotropic activity of human chorionic gonadotropin during the first trimester, increased sialylation of thyroid hormone mediated by oestrogens and reduced clearance of thyroxine-binding globulin which results in increased levels of total T4 and T3. Krassas et al.[19] also reported the prevalence of thyroid disorders in women of child-bearing age, adding that uncorrected thyroid dysfunction in pregnancy may have adverse effects on foetal and maternal well-being with possible neuro-developmental disorders in the child. There are profound physiological changes in the pregnant woman that have been insinuated to have a significant adverse effect on maternal thyroid function and haematological indices. Therefore, this present study is aimed to evaluate thyroid hormone levels and some haematological indices at different trimesters of pregnancy in women attending antenatal clinic at Federal Medical Centre Yenagoa.

METHODS

Study area

The study was carried out on pregnant women at different trimesters of pregnancy attending antenatal clinic at Federal Medical Centre, Yenagoa. Bayelsa is a state in the Southern Nigeria in the core Niger Delta region, between Delta State and Rivers State. Yenagoa is the capital of Bayelsa State, Nigeria. It lies in $4^{o}55'29"$ N $6^{o}15'51$ "E. Coordinates: $5^{o}02'$N $6^{o}20'$E/ 5.033^{o}N 6.333^{o}E. The State has an area of $706km^2$ and a population of 352,285 by the 2006 census (NPC, 2006). The Ijaw form the majority of the indigenes. Occupational practices in the area include fishing, poultry farming and harvesting of crayfish, shrimps, periwinkle and other sea foods. English is the official language, but Epie- Atissa language is one of the local languages spoken in Yenagoa. The inhabitants are predominantly Christians.

Subjects

The study was carried out on pregnant women at different trimesters of pregnancy attending antenatal clinic at Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria. A total of one hundred and twenty (120) subjects were recruited for this study, ninety (90) were at different their trimesters of pregnancy attending antenatal Clinic at Federal Medical Centre, Yenagoa, while thirty (30) were non-pregnant women which served as control. The subjects were between the age range of twenty (20) and thirty-five (35) years. Subjects who consented to the study and without a medical history of any known metabolic disorders were included for the study. Subjects who do not consent to the study and have a known metabolic disorder were excluded. The ethical clearance was approved by the ethical committee of Federal Medical Centre Yenagoa, Bayelsa State.

Sample Collection

Blood samples were collected from each of the one hundred and twenty (120) subjects. Seven (7) millilitres of blood sample was collected by venopuncture technique from each subject, 5ml was dispensed into a plain bottle, allowed to clot, centrifuged at 1,500rpm for 5mins and serum stored at -20^{o}c prior to analysis. Two (2) millitres was dispensed into tripotassium EDTA for haematological estimation. All analysis was carried out in Chemical pathology and Haematology Laboratory in Federal Medical Centre Yenagoa. Serum TSH, T4 and T3 was analysed using Enzyme Linked Immunosorbent Assay (ELISA). Haematological indices PCV, HB and Platelet were determined by SYSMEX pocH-100i automated analyzer.

Analysis of Parameters

Haematological parameters PCV, Hb and platelets were determined by SYSMEX pocH-100i automated haematology analyzer as described by Soldin et al.[20]

Analysis Biochemical Parameters

Total Triiodothyronine (tT3), Total thyroxine (T4) and Thyrotropin (TSH) were analysed using microplate immunoenzymatic assay method as described by Hepburn.[21] The principle: Total Triiodothyronine (tT3): The essential reagents required for a solid phase enzyme immunoassay include immobilized antibody, enzyme antigen conjugate and native antigen. Upon mixing immobilized antibody, enzyme antigen conjugate and a serum containing the native antigen a competition reaction results between the native antigen and the enzyme antigen conjugate for a limited number of insolubilized binding sites. After equilibrium is attained, the antibody bound fraction is separated from unbound antigen by decantation or aspiration. The enzyme activity in the antibody bound fraction is inversely proportional to the native antigen concentration.[21]

Data analysis

The data from this study were analysed and expressed as mean $\pm$ standard deviation. The Student T- test was calculated using SPSS version 15.0 and it was used to compare the parameters (at levels of significance 0.05). P< 0.05 was considered as statistically significant.

RESULT

Table 4.1 shows the Mean ± SD values of studied thyroid parameters at the different trimesters of pregnancy. There were statistically significant differences (p<0.05) in the levels of all the studied parameters with particular increases in TSH at the third trimester of pregnancy. However, there was a decrease in the concentrations of TSH across the different trimesters (1.05 ± 1.34, 1.29 ± 0.01, 1.42 ± 0.12) uIU/ml and significant increase (P<005) in the concentrations of T_4, T_3 when compared with the control (1.01 ±0.12, 2.14 ±0.11) nmol/L. **Table 4.2** show the mean ± SD values of studied haematological parameters at the different trimesters of pregnancy. There were statistically significant differences (P <0.05) in the levels of all the studied parameters with particular increase in PCV and Hb at the third trimester of pregnancy (35± 9.01%, 12.60±0.99 **g/dl**). However, there was a decrease in the concentrations of PCV and Hb across the different trimesters and significant increase (P<0.05) in the concentrations of platelets across the trimesters when compared with the control (214±41 x 10^9). **Table 4.3:** Test of significance of the observed group induced differences between control and different trimesters of pregnancy was presented in table 4.3. The post hoc test following ANOVA among the control group and the three trimesters of pregnancy showed non-significant differences in comparison of control to the first trimester for T_4(p=0.156), first trimester to second for T_3 (p=0.117), and in second to third trimesters for Hb concentration (p=0.050). While comparison of control to the second and third trimesters as well as the first and third trimesters were statistically significant for all the studied parameters as shown in the table. **Table 4.4:** Shows the Pearson correlation between measured thyroid hormones and some hematological indices in pregnant women. A significantly strong and negative correlation was observed between TSH and Hb (r=-0.812, p=0.000), T_4 and Hb (r=-0.746, p=0.001), T_3 and Hb (r=-0.748, p=0.000), TSH and PCV (r=-0.719, p=0.000), T_4 and PCV (r=-0.707, p=0.000), T_3 and PCV (r=-0.800, p=0.002); and a moderately negative correlation between platelets and the thyroid parameters (TSH, T_4, and T_3) thus: (r = -0.599, -0.698, -0.672) respectively. All observed correlations were statistically significant (p<0.05). **Table 4.5:** Shows Mean ± SD values of studied parameters among different Age Intervals. Highest Mean and SD of (1.40 ± 0.11uIU/ml) for TSH, (1.25 ± 0.00nmol/L) forT_4, (2.61 ± 0.12nmol/L) for T_3, (11.91± 0.22g/dL) for Hb, (35 ± 0.87%) for PCV, and (231 ± 89 x10^9/L) for platelets were all recorded within the 20-25 years interval. ANOVA showed statistically non-significant difference (p>0.05) in inter Age interval and Test of significance of the observed Age interval induced differences post hoc test following ANOVA also showed a non-significant difference in all comparison.

Table 4.1: Mean ± SD Values of Studied Thyroid Parameters at different Trimesters of Pregnancy.

Parameters	TSH (uIU/ml)	T_4 nmol/L)	T_3 (nmol/L)
Control	5.00±0.22	1.01±5.01	2.14±3.22
1st Trimester	1.05±1.34	1.21±4.11	2.81±2.44
2nd Trimester	1.29±0.01	1.29±6.21	3.42±6.00
3rd Trimester	1.42±6.01	1.23±0.93	3.21±3.24
F Value	3.976	5.628	8.317
P Value	0.026*	0.039*	0.042*

* = mean difference is significant at the 0.05 level.

Table 4.2 Mean ± SD values of studied Haematological Parameters at different Trimesters of Pregnancy,

Parameters	Hb (g/dl)	PCV(%)	Platelets ($\times10^9$/L)
Control	12.99±0.69	36±5.00	214±41
1st Trimester	10.23±0.76	33±4.00	244±34
2nd Trimester	11.59±0.46	34±6.00	233±44
3rd Trimester	12.60±0.99	35±9.01	217±29
F Value	8.746	12.107	3.979
P Value	0.014*	0.020*	0.048*

* = mean difference is significant at the 0.05 level.

Table 4.3: Comparison of the studied parameters between the control (C) and different Trimesters of Pregnancy.

Parameters	TSH	T_4	T_3	Hb	PCV	Platelets
C Vs. 1st	0.029[a]	0.156[b]	0.007[a]	0.048[a]	0.036[a]	0.019[a]
C Vs. 2nd	0.000[a]	0.007[a]	0.036[a]	0.005[a]	0.001[a]	0.024[a]
C Vs. 3rd	0.001[a]	0.004[a]	0.000[a]	0.038[a]	0.028[a]	0.034[a]
1st Vs. 2nd	0.004[a]	0.000[a]	0.117[b]	0.046[a]	0.050[b]	0.039[a]
1st Vs. 3rd	0.000[a]	0.017[a]	0.000[a]	0.004[a]	0.001[a]	0.004[a]
2nd Vs. 3rd	0.001[a]	0.010[a]	0.046[a]	0.050[b]	0.044[a]	0.048[a]

[a]mean difference is significant at the 0.05 level.
[b]mean difference is not significant at the 0.05 level.

Table 4.4: Relationship between the studied thyroid parameters and the Hematological indices in Pregnancy by Pearson's Correlation.

Parameters	TSH		T_4		T_3	
	r-Value	p-value	r-Value	p-value	r-Value	p-value
Hb	-0.812**	0.000	-0.746**	0.001	-0.748**	0.000
PCV	-0.719**	0.000	-0.707**	0.000	-0.800**	0.002
Platelets	-0.599**	0.026	-0.698**	0.034	-0.672**	0.030

** Correlation is significant at the 0.01 Level (2-tailed).
Mean difference is significant at the $p<0.05$ level.

Table 4.5: Mean ± SD Values of Studied Parameters in Relation to Age.

Age (Years)	TSH (uIU/ml)	T_4 (nmol/L)	T_3 (nmol/L)	Hb (g/dl)	PCV (%)	Platelets ($\times10^9$/L)
20-25	1.40±0.11	1.25±0.00	2.61±0.12	11.91±0.22	35±0.87	231±89
26-30	1.38±0.99	1.24±1.01	2.59±1.54	11.89±0.49	34±1.10	229±94
31-35	1.40±0.00	1.24±0.92	2.61±0.00	11.76±1.90	35±0.11	230±02
F Value	0.285	1.718	0.084	0.790	0.102	0.314
P Value	0.651	0.156	0.890	0.454	0.698	0.061

Statistical significance is set at $P<0.05$.

DISCUSSION

There are profound physiological changes in the pregnant woman that have been insinuated to have adverse effects on maternal thyroid function and haematological parameters. These changes are capable of complicating the interpretation of maternal thyroid function tests (TFTs) results as well as the haematological indices.[12] The present study revealed that thyroid stimulating hormone (TSH) was significantly reduced ($P<0.05$) in the various trimesters of pregnancy especially during the first trimester when compared with the control. This observation may be linked to the partial suppressive effect of high hCG levels during the first trimester as earlier published by

Ballabio et al.[14] This finding is in agreement with Mansourian et al.[22] who reported a significant decrease in TSH during the first trimester. However, this observation was independent of the age of the patients and contrary to previous finding which revealed that the decrease was according to the age of the mother. The TSH significantly increased ($p<0.05$) at the third trimester and correlated negatively ($r=-0.812$) with low haemoglobin concentration.

There was statistically significant increase ($P<0.05$) in the concentrations of the thyroid hormones (T_3 and T_4) during the first and second trimesters which slightly reduced in the third trimester as observed in this study. This is in agreement with the findings of Kumar et al.[23] and Kurioka *et* al.[24] who reported a steady increase in TSH with each trimester, and T_4, T_3 values increased in the first and second trimester. This increase is probably due to elevated serum levels of Thyroxin binding globulin (TBG) which is always seen during normal pregnancy as also reported by Glinoer et al.[25] The study also revealed a decrease in the concentration of haemoglobin (Hb) and packed cell volume (PCV) during the first trimester which may be due to the increase in plasma volume with dilutional anaemia experienced during pregnancy.

Initially, the platelets in this present study increased (probably due to increase platelet activation) and then dropped towards the end of pregnancy. Shehlata et al.[26] had earlier reported that platelet count does decrease during pregnancy, particularly in the third trimester (gestational thrombocytopenia) partly due to hemodilution and accelerated clearance. Platelets and TSH levels varied throughout the three trimesters of pregnancy when compared with the control subjects.

Significant variations ($P<0.05$) were observed in the concentration of the assayed thyroid parameters (TSH, T4 and T3) when compared with the haematological parameters (Hb, PCV and Platelets). This variation could probably be attributed to the difference in their mechanisms of action. The Pearson's correlation Coefficient revealed a strong and negative correlation between the assayed thyroid hormones and the haematological indices. And all the changes were independent on the age of the subjects.

CONCLUSION

The findings of this study revealed significant changes in the studied parameters throughout pregnancy. TSH levels increased gradually with each trimester, increased T_3 and T_4 values eventually decreased in the last trimester, and the platelets dropped as pregnancy progressed. This study therefore concludes that there are observable changes in the Thyroid hormone levels and Platelets of pregnant women attending Federal Medical Centre Yenagoa.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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