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Original Article

Physiology Section

Correlation of Body Mass Index (BMI) with Thyroid Function in Euthyroid Pregnant Women in Manipur, India

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ABSTRACT

Introduction: Body Mass Index (BMI) is significantly increased during pregnancy due to gain of weight with normal progression of pregnancy. The exact influence of thyroid function on BMI are ill defined in euthyroid pregnant women.

Aim: To correlate serum levels of Free Triiodothyronine (FT3), Free Thyroxine (FT4) and Thyroid Stimulating Hormone (TSH) level with BMI of participant normal pregnant women in all the three trimesters.

Materials and Methods: In this cross-sectional comparative study, total of 210 healthy pregnant women comprising of 70 participants in each trimester, attending Obstetrics Outpatient Department (OPD) for antenatal check-up were consecutively selected. Estimation of serum FT3, FT4 and TSH level was done by ELISA based methods. The correlation of BMI with serum levels of FT3, FT4 and TSH was done using Pearson correlation test (r) by SPSS version 21.0 software.

Results: TSH level of participant normal pregnant women showed significant positive correlation with BMI during first (r=0.254 and p=0.034) and second trimester (r=0.263 and p=0.028) of pregnancy. FT4 level showed significant negative correlation in second (r= -0.454 and p<0.001) and third trimester (r= -0.351 and p=0.003) of pregnancy. Correlation between BMI and FT3 level showed no significant association in any of the trimesters.

Conclusion: BMI correlates positively with TSH level in first and second trimesters while it correlates negatively with FT4 level in second and third trimesters, but, failed to demonstrate significant association with FT3 level in any of trimesters in euthyroid pregnant women. Serum TSH along with FT4 level appears more useful modality compared to serum TSH alone for targeted thyroid screening particularly in obese pregnant women.

Keywords: Free thyroxine, Thyroid gland, Thyrotropin

INTRODUCTION

Euthyroid women experience dramatic changes in the demand for thyroid hormone production as early as first trimester of pregnancy. Pregnancy induces specific complex changes in thyroid economy such as increase in level of Thyroid Binding Globulin (TBG) concentration and direct stimulation of the maternal thyroid gland by elevated level of human Chorionic Gonadotropin (hCG) [1]. During first trimester, changes in the serum hCG and serum TSH are mirror image of each other, and there is a significant negative correlation [2]. The metabolic adjustment cannot be reached easily when functional capacity of thyroid gland is impaired as in autoimmune thyroid disease, hyperthyroidism, hypothyroidism or iodine deficiency [3]. The progression of pregnancy and foetal outcome are dependent on adequate hormonal output from maternal thyroid gland throughout pregnancy. The concentration of FT4 in the coelomic fluid in the first trimester is approximately 50% of that found in the maternal circulation, although, transfer is small quantitatively, such concentrations qualitatively represented an extremely important source of thyroid hormone to ensure adequate development of the foetomaternal unit and neuropsycho-intellectual well-being of the offspring [4]. Gestation related reference intervals for Thyroid Function Tests (TFT) are significantly different from non pregnant normal reference intervals. Comparison of thyroid function in pregnant women using non pregnant reference intervals could potentially result in misinterpretation of thyroid function in pregnancy.

Some change in weight is common in patients with thyroidal dysfunction and Nyrnes A et al., reported that in women and men who are non smokers, serum TSH levels are positively associated with BMI [5]. During pregnancy, BMI is significantly increased due to normal weight gain with progression of pregnancy and exact relationship between thyroid function and BMI is ill-defined in euthyroid pregnant women.

MATERIALS AND METHODS

The cross-sectional comparative study was conducted between January 2015 to September 2016 in the Department of Physiology in collaboration with Department of Obstetrics and Gynaecology, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India. Sample size for each trimester was calculated based on mean TSH levels during different trimesters from the previous study of Kumar A et al., [6]. The statistical sample size formulae for comparing k means was used with confidence interval and power of the study set at 95% and 80% respectively. Out of total 237 apparently normal healthy pregnant women recruited for the study after obtaining written informed consent, 210 normal healthy pregnant women (70 in each trimester) showed normal laboratory thyroid profile study.

Institutional Research Ethics Board and Manipur University approved the research protocol of study. “Written informed consent” was taken from the participant and their participation was completely voluntary and their right to refuse to participate in the study was respected.

Criteria for recruitment for the study were; uncomplicated intrauterine singleton pregnancies without any history of thyroid disease or any chronic illness in the age group of 18-40 years. Total of 27 participants with abnormal thyroid function were excluded from the study as per laboratory reference range guidelines USPSTF [7]. After enrollment, participants were subjected to detailed history and general physical examination including height and weight measurement (BMI calculated as weight in kilogram/height in meter^2) and findings were recorded in a predesigned proforma. Normal weight gain during pregnancy was considered as per revised Institute of Medicine (IOM) guidelines [8].

A 2 ml syringe was used for drawing venous blood from the antecubital vein under aseptic precautions and blood transferred to a plain sterile vial after removing the needle hub. After centrifugation of the blood samples at 2000 x g for 10 minutes in a centrifuge, the serum were prepared and stored in freezer compartment of refrigerator at -2°C to -10°C. Prior to use, all the samples were

brought to room temperature and analyzed for thyroid profile studies, which included FT3, FT4 and TSH estimation using ELISA automated microplate reader (ERBA LisascanTM EM SR 120710, Germany) with adsorbance at 450 nm and commercially available ELISA thyro-kit (BeneSphera Avantor Inc, India) with the analytical sensitivity for serum FT3, serum FT4 and serum TSH assays as 0.05 picogram per decilitre (pg/dl), 0.05 nanogram per decilitre (ng/dl) and 0.027 micro international unit per milliliter (μIU/ml) respectively. The intra-assay Coefficients of Variation (CV) for the assays were 5.5%, 4.5% and 5% respectively. The inter-assay CV for the assays was 5.2%, 5.2% and 6% respectively. Trimester specific cut off values for TSH were in range of 0.1–2.5 μIU/L, 0.2–3.0 μIU/l and 0.3–3.0 μIU/L, respectively, in first, second and third trimesters while cut off laboratory reference range used for FT3 and FT4 levels were 2.3-4.2 pg/dl and 0.76-2.24 ng/dl respectively during pregnancy.

STATISTICAL ANALYSIS

Statistical analysis of the data was done at the end of the study using Statistical Package for the Social Sciences software, IBM SPSS (Statistics for Windows) Version 21.0. Armonk, NY: IBM Corp; 2014. Continue variables were checked for normality and results were expressed as mean ± standard deviation. Standard parametric tests as one-way Analysis of variance (ANOVA) was used for comparison of data in different trimester groups. Correlation studies between weight, BMI and thyroid parameters were done by Pearson correlation (r) test. The p-value < 0.05 was taken as significant (S).

RESULTS

Out of 210 participants across all trimesters, the mean age in pregnant normal women were 25.5±4.2, 27.6±4.8 and 28.2±4.5 years in the first, second and third trimester respectively (p = 0.159). Maximum numbers of participants were in the age group of 24-30 years [Table/Fig-1].

The mean duration of pregnancy were 9.6±1.9, 19.6±2.37 and 30.6±2.66 weeks in first, second and third trimesters respectively. Maximum numbers of participants were in 8-10 weeks, 19-23 week and 28-30 weeks of pregnancy in first, second and third trimesters respectively [Table/Fig-2].

Age group	First trimester	Second trimester	Third trimester	p*-value
18 – 23 years	22	17	17	0.159 (NS)
24 – 30 years	37	34	37	
31 – 40 years	11	19	16	
Total	70	70	70	
Mean±SD	25.5±4.2 years	27.6±4.8 years	28.2±4.49 years	

[Table/Fig-1]: Age wise comparison of participant normal pregnant women between the three trimester groups.
*One-way ANOVA test.

The mean heights were 153.1±4.9, 151.3±4.6 and 152.8±3.0 cm. in first, second and third trimesters respectively (p=0.106) [Table/Fig-3]. There was significant difference in weight among the three groups (p<0.001) as expected due to normal gain in the weight during pregnancy [Table/Fig-4].

BMI of participant pregnant women in the first, second and third trimester were 21.28±1.11, 23.27±1.89 and 25.04±1.63 Kg/m^2 respectively. There was significant increase in BMI in women in second and third trimester when compared with first trimester (p< 0.001) [Table/Fig-4].

Serum FT4 level showed significant negative correlation with weight in second trimester pregnant participant group (r=0.284 and p=0.017) [Table/Fig-5]. Serum TSH level of the women showed significant positive correlation with BMI during first trimester (r=0.254 and p=0.034) and second trimester (r=0.263 and p= 0.028 [Table/Fig-6]. Serum FT4 level showed significant negative correlation with BMI of the participants in second trimester (r= -0.454 and p<0.001) and third trimester (r= -0.351 and p = 0.003) [Table/Fig-6].

First trimester				
Duration of pregnancy	< 7 weeks	8-10 weeks	11-13 weeks	Total
Number of participant	09	36	25	70
Mean±SD	9.6 ± 1.9 weeks			
Second trimester				
Duration of pregnancy	14-18 weeks	19-23 weeks	24-27 weeks	Total
Number of participant	29	31	10	70
Mean±SD	19.6 ± 2.37 weeks			
Third trimester				
Duration of pregnancy	28-30 weeks	31-33 weeks	34-37 weeks	Total
Number of participant	41	19	10	70
Mean±SD	30.6 ± 2.66 weeks			

[Table/Fig-2]: Duration of completed weeks of pregnancy of participants across different trimesters in normal pregnant women.

Height (cm)	First trimester	Second trimester	Third trimester	p*-value
140 – 147	21	16	17	0.106 (NS)
148 – 156	37	35	37	
157 – 164	12	19	16	
Total	70	70	70	
Mean±SD	153.1±4.9 cm	151.3±4.6 cm	152.8±3.0 cm	

[Table/Fig-3]: Comparison of height of participant normal pregnant women between the three trimester groups.
*One-way ANOVA test.
NS-Not Significant

Parameter		First trimester	Second trimester	Third trimester	p*-value
Weight (Kg)	Mean±SD	49.01±2.95	54.68±4.96	58.48±4.2	<0.001 (S)
	Range	43-59 Kg	45-69 Kg	49-69Kg	
BMI(Kg/m^2)	Mean±SD	21.28±1.11	23.27±1.89	25.04±1.63	<0.001 (S)
	Range	19.1–24.2	18.9-27.9	21.6-28.6	

[Table/Fig-4]: Comparison of weight and Body Mass Index (BMI) of participant normal pregnant women between the three trimester groups.
*One-way ANOVA test.
p>0.05: Not Significant (NS); p< 0.05: Significant (S)

DISCUSSION

In the present study, BMI showed significant positive correlation with TSH level during first and second trimesters of normal pregnancy while, there was significant negative correlation of Serum FT4 level with BMI during second and third trimesters of pregnancy. Serum FT3 level failed

Correlation between weight of pregnant women in First trimester and thyroid function						
Parameter	Serum FT3 level		Serum FT4 level		Serum TSH level	
	r	p	r	p	r	p
Weight of first trimester pregnant women	0.065	0.591	- 0.113	0.351	0.061	0.619
Correlation between weight of pregnant women in Second trimester and thyroid function						
Parameter	Serum FT3 level		Serum FT4 level		Serum TSH level	
	r	p	r	p	r	p
Weight of second trimester pregnant women	- 0.129	0.286	- 0.284*	0.017(S)	- 0.044	0.717
Correlation between weight of pregnant women in Third trimester and thyroid function						
Parameter	Serum FT3 level		Serum FT4 level		Serum TSH level	
	r	p	r	p	r	p
Weight of third trimester pregnant women	- 0.044	0.715	- 0.192	0.111	- 0.217	0.071

[Table/Fig-5]: Correlation of weight with serum FT3, FT4 and TSH level in each of first, second and third trimester groups of participant normal pregnant women.
* Correlation is Significant at 0.05 level (2-tailed);
Pearson correlation (r) test

Pearson correlation between BMI in first trimester and thyroid function						
Parameter	Serum FT3 level of First trimester pregnant women		Serum FT4 level of First trimester pregnant women		Serum TSH level of First trimester pregnant women	
	r	p	r	p	r	p
BMI of first trimester pregnant women	0.010	0.932	0.110	0.364	0.254*	0.034(S)
Pearson correlation between BMI in second trimester and thyroid function						
Parameter	Serum FT3 level of Second trimester pregnant women		Serum FT4 level of Second trimester pregnant women		Serum TSH level of Second trimester pregnant women	
	r	p	r	p	r	p
BMI of second Trimester pregnant women	- 0.182	0.132	-0.454**	<0.001(S)	0.263*	0.028(S)
Pearson correlation between BMI in third trimester and thyroid function						
Parameter	Serum FT3 level of Third Trimester pregnant women		Serum FT4 level of Third Trimester pregnant women		Serum TSH level of Third Trimester pregnant women	
	r	p	r	p	r	p
BMI of third trimester pregnant women	0.070	0.566	-0.351**	0.003(S)	- 0.110	0.367

[Table/Fig-6]: Correlation of BMI with serum FT3, FT4 and TSH level in each of the first, second and third trimester group of participant normal pregnant women.
* Pearson correlation is Significant at 0.05 level (2-tailed)
** Pearson correlation is Significant at 0.01 level (2-tailed)

to show any significant correlation during any trimesters of pregnancy. It has been reported that TSH values were distributed at higher normal range while FT4 at lower normal range in obese pregnant women compared to normal weight pregnant women but exact influences of FT3 and FT4 on BMI are ill-defined in euthyroid pregnant women [9].

Haddow JE et al., in a cross-sectional observational study among pregnant women during early pregnancy reported that FT4 values decreased steadily as weight increased but TSH level had no relationship with maternal weight, thereby they concluded a continuous reciprocal relationship between weight and FT4 level but they did not report any correlation with serum FT3 level during any of trimesters [10]. Pop VJ et al., reported that gestational weight gain and maternal thyroid parameters were related to both pre-pregnancy BMI and weight gained throughout gestation [11]. Han C et al., reported from China that during early pregnancy, high BMI strongly correlated with hypothyroidism, hypothyroxinemia, and Thyroid Peroxidase Antibody (TPOAb) positivity but not with TPOAb positivity during early pregnancy in iodine sufficient region [12].

Mosso L et al., Haddow JE et al., and Pop VJ et al., reported findings similar to the present study but they reported that BMI was not related with serum TSH levels in any of trimesters which contradicts the findings of the present study [9-11]. Han C et al., reported that serum TSH level was significantly higher in the overweight group [12]. According to Ashoor G et al., FT4 decreased while FT3 increased with higher BMI scores but reported paradoxical effects of FT3 and FT4 on maternal weight [13]. Mannisto T et al., reported positive correlation of BMI with serum TSH level similar to the present study [14]. BMI positively correlated with serum FT3 level and showed no correlation with serum FT4 level. Gowachirapant S et al., reported that FT4 values were lower in obese patients compared with normal weight patients [15]. These findings suggest that variations of normal thyroid function in euthyroid pregnant women are associated with changes in body weight and BMI. The reasons may be simple or multifactorial, but the biological mechanism is still not completely known.

LIMITATION

Firstly, the FT3, FT4 and TSH levels could not be measured serially in each participant but age-matched comparison was done. Second, we did not evaluate the iodine status by urine iodine estimation although history of iodized salt intake was mandatory inclusion criteria for participation in the study.

CONCLUSION

Serum TSH and FT4 levels showed correlation with BMI during pregnancy. Serum FT4 level also showed significant negative correlation with weight in second trimester. Hence, weight and BMI can be used for screening pregnant women with suspected abnormal thyroid function. Serum TSH along with FT4 level screening will be more useful modality compared to serum TSH alone for targeted screening.

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