

Original Article

## Correlation of Thyroid Hormones With Gestational Age in Normal Pregnancy

Shyamal Chandra Banik<sup>1</sup>, Farjana Ahmed<sup>2</sup>, Md. Ziaur Rahman Mamun<sup>3</sup>, Ferdous Towhid<sup>4</sup>, Khushruha Rahman Khan<sup>5</sup>, Mahaboba Rahman<sup>6</sup>

<sup>1</sup>Assistant Professor, Department of Physiology, Dhaka National Medical College, <sup>2</sup>Assistant Professor, Department of Physiology, Dhaka National Medical College, <sup>3</sup>Assistant Professor (cc), Department of Community Medicine, Dhaka National Medical College, <sup>4</sup>Lecturer, Department of Biochemistry, Dhaka National medical College, <sup>5</sup>Associate Professor (cc), Department of Anatomy, Dhaka National Medical College, <sup>6</sup>Assistant Professor, Department of Physiology, University Dental College

### Abstract

**Background:** Pregnancy has a profound impact on the thyroid gland & its function.

**Objective:** To correlate TSH, FT<sub>4</sub> & FT<sub>3</sub> levels with gestational age to observe their relationship.

**Method:** This cross sectional study was conducted in the Department of Physiology, Sir Salimullah Medical College, Dhaka from July 2016 to June 2017. Total 90 apparently healthy pregnant women of different trimesters, age ranged from 20 to 35 years were selected as study group (Group I). Again according to gestational age, study group was subdivided into 1st trimester of gestation (Group Ia, n=30), 2nd trimester of gestation (Group Ib, n=30) and 3rd trimester of gestation (Group Ic, n=30) respectively for comparison. For correlation, serum TSH, FT<sub>4</sub> and FT<sub>3</sub> levels were measured. The statistical analysis was done by Unpaired t test and Pearson's correlation coefficient test.

**Results:** In this study, mean serum TSH level was positively correlated with gestational age and both mean serum FT<sub>4</sub> & FT<sub>3</sub> levels were negatively correlated with gestational age and these relationships were statistically highly significant.

**Conclusion:** There is a negative association of thyroid hormone (FT<sub>4</sub> & FT<sub>3</sub>) levels with gestational age.

**Key words:** Thyroid hormones, Gestational age, Pregnancy.

### Introduction

Pregnancy is followed by a series of hormonal and metabolic changes that involve most maternal endocrine systems.<sup>1</sup> Pregnancy is a state of stress which influences thyroid gland and its function in multiple ways.<sup>2</sup> Not only the maternal hypothalamo-pituitary thyroid (HPT) axis undergoes a series of adjustment but also the fetus develops its own HPT axis and the placenta also plays an active role in iodine and thyroxine transport and metabolism.<sup>3</sup> Thyroid function in pregnant women is modified by various factors such as 50% increase in plasma volume, increased levels of protein binding thyroid hormones including TBG, hCG, increase in estrogen concentration.<sup>4</sup> Thyroid hormones have most profound effects on the terminal stages of fetal brain development including synaptogenesis, dendrites growth & axons myelination and neuronal migration.<sup>5</sup> The average duration of pregnancy is about 280 days or 40 weeks when calculated from the first day of the last menstrual period. 1st trimester considered as 1st 12 weeks, 2nd trimester considered as 13-28 weeks & 3rd trimester considered as 29-40 weeks.<sup>6,7</sup>

### Methods

This cross sectional study was conducted in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from July 2016 to June 2017. The study was approved by the Institutional Ethics Committee of SSMC. For this, 90 apparently healthy pregnant women aged 20-35 years of different trimesters were selected as study group (group I). On the basis of gestational period, group I was further subdivided into three groups such as 1st trimester of gestation (Ia), 2nd trimester of gestation (Ib) & 3rd trimester of gestation (Ic) and each group was consisted of 30 different pregnant women of different trimesters. They were selected from Out Patient Department (OPD) of Obstetrics & Gynaecology of SSMC and Mitford Hospital by consecutive purposive sampling. All the subjects were belonged to middle socioeconomic status. Subjects having history of any chronic or systemic diseases, known thyroid abnormalities, goitre, twin pregnancy, psychiatric illness etc. were excluded from the study.

After selection the aim, benefits, risks and the procedure of the study were explained to each subjects and a written consent was taken. Detailed personal, family, medical and occupational histories were taken and thorough physical examination of all subjects were done and recorded.

With all aseptic precautions, seven (7) ml of venous blood was drawn from antecubital vein. Serum TSH, FT4 and FT3 levels were measured by chemiluminescent microparticle immunoassay (CMIA) method in the laboratory of Department of Biochemistry, BSMMU, Dhaka. Data were expressed as mean  $\pm$  SD. The statistical analysis was done by using SPSS version 22. Unpaired t test and Pearson's correlation coefficient test were used to compare the data as applicable. p value  $<0.05$  was considered as level of significance.

### Results

Table I shows the mean ( $\pm$ SD) serum TSH level was significantly & gradually higher in 3rd trimester and the mean ( $\pm$ SD) serum FT4 & FT3 levels were significantly & gradually lower in 3rd trimester in comparison to that of 1st trimester.

**Table-I: Serum thyroid stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3) levels of the subjects in different groups (N=90)**

Parameters	Groups		
	Ia (n=30)	Ib (n=30)	Ic (n=30)
TSH (mIU/L)	1.42 $\pm$ 1.47	2.16 $\pm$ 1.13	2.82 $\pm$ 0.71
FT4 (pmol/L)	16.14 $\pm$ 1.45	13.12 $\pm$ 2.02	11.75 $\pm$ 1.48
FT3 (pmol/L)	4.66 $\pm$ 0.58	3.66 $\pm$ 0.49	3.33 $\pm$ 0.40

### Statistical analysis

Groups	p-value		
	TSH	FT4	FT3
Ia vs Ib	0.034*	$<0.001$ ***	$<0.001$ ***
Ia vs Ic	$<0.001$ ***	$<0.001$ ***	$<0.001$ ***
Ib vs Ic	0.008**	0.004**	0.006**

Data are expressed as mean  $\pm$  SD. For statistical analysis, Unpaired t test was performed for comparison between the groups. Group I: Study group, Group Ia: 1st trimester of gestation, Group Ib: 2nd trimester of gestation, Group Ic: 3rd trimester of gestation, n= number of subjects. \*\*\*= Significant at  $p<0.001$ , \*\*= Significant at  $p<0.01$ , \*= Significant at  $p<0.05$ , N= Total number of subjects.

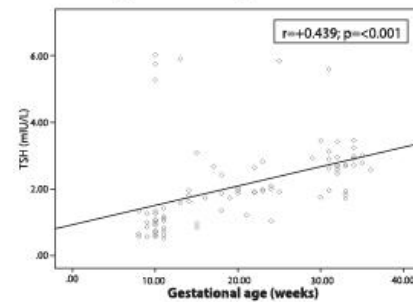
In this study, serum thyroid stimulating hormone (TSH) level was positively correlated ( $r = +0.439$ ), serum free thyroxine (FT4) level was negatively correlated ( $r = -0.679$ ) and serum free triiodothyronine (FT3) level was negatively correlated ( $r = -0.693$ ) with gestational age and these relationships were statistically ( $p<0.001$ ,  $p<0.001$ ) highly significant (Table-II).

**Table-II: Correlation of serum TSH, FT4, FT3 levels with gestational age in study subjects (N=90)**

Parameters	r-value	p-value
Serum TSH	+0.439	$<0.001$ ***
Serum FT4	-0.679	$<0.001$ ***
Serum FT3	-0.693	$<0.001$ ***

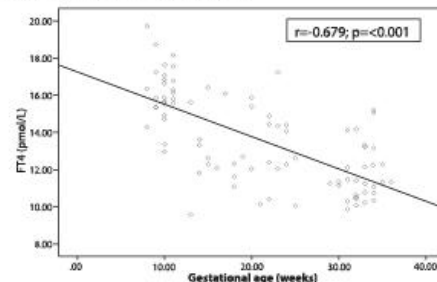
Pearson's correlation coefficient (r) test was performed to compare relationship between parameters of study group, N = Total number of subjects, \*\*\*= Significant at  $p<0.001$ .

Again, figure-I: shows that, there is a positive association of TSH level with gestational age.



**Figure-I: Correlation of serum TSH level with gestational age in the study subjects (N=90)**

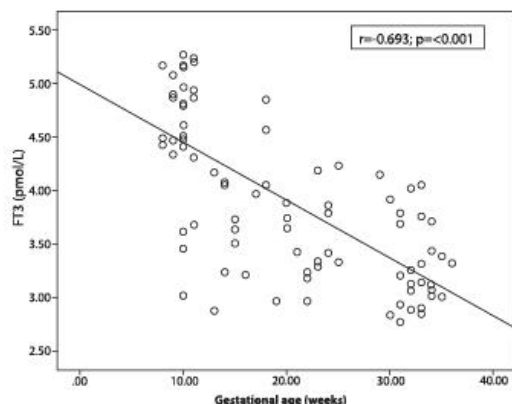
Figure-II: shows that, there is a negative association of FT4 level with gestational age.



**Figure-II: Correlation of serum FT4 level with gestational age in the study subjects (N=90)**



Figure-III: shows that, there is a negative association of FT<sub>3</sub> level with gestational age.



**Figure-III: Correlation of serum FT<sub>3</sub> level with gestational age in the study subjects (N=90)**

#### Discussion

In this study, serum TSH, FT<sub>4</sub> & FT<sub>3</sub> showed significant variation during different trimesters of gestation which is supported by other studies.<sup>8,9</sup>

In this study, serum TSH level showed significant ( $p<0.001$ ) positive correlation with gestational age. This findings are in consistent with those of other researchers.<sup>10,11</sup> On the other hand, Patal et al.<sup>12</sup> found that there was no correlation between serum TSH and gestational age.

Serum FT<sub>4</sub> level was negatively correlated with gestational age and it was statistically significant ( $p<0.001$ ). Similar relationships were also observed by others.<sup>13</sup> On the contrary, Bautista et al.<sup>14</sup> found that FT<sub>4</sub> level was significantly and positively correlated with gestational age.

Serum level of FT<sub>3</sub> showed significant ( $p<0.001$ ) negative correlation with gestational age. This finding is in agreement with that of other investigator.<sup>12</sup> On the other hand, Bautista et al.<sup>14</sup> found no correlation between serum FT<sub>3</sub> and gestational age.

#### Conclusion

In this study it was observed that serum TSH level was positively correlated and FT<sub>4</sub> & FT<sub>3</sub> levels were negatively correlated with gestational age. So, interpretation of thyroid function tests needs trimester specific reference interval.

#### Acknowledgement

Authors of this study acknowledge the tremendous support from Biochemistry departments of BSMMU for conducting thyroid function testing. The authors are also thankful to the study subjects for their active & enthusiastic participation.

#### References

1. Burrow GN, Fisher DA, Larsen PR. Maternal and fetal thyroid function. *The New England Journal of Medicine* 1994; 331(16): 1072-1078.
2. Rajput R, Singh B, Goel V, Verma A, Seth S, Nanda, S. Trimester-specific reference interval for thyroid hormones during pregnancy at a tertiary care hospital in Haryana, India. *Indian Journal of Endocrinology and Metabolism* 2016; 20(6): 810-815.
3. Smallridge RC, Ladenson PW. Hypothyroidism in pregnancy: Consequences to neonatal health. *The Journal of Clinical Endocrinology & Metabolism* 2001; 86(6): 2349-2353.
4. Glinoe D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. *Endocrine Reviews* 1997; 18(3): 404-433.
5. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. 1999, Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *The New England Journal of Medicine* 1999; 341(8): 549-555.
6. Keele CA, Neil E, Joels N. Samson Wright's Applied Physiology. 13th ed. New Delhi: Oxford University Press; 1982. 581-584.
7. Cunningham FG, Gant NF, Leveno KJ, Gilstrap LC, Hauth JC, Wenstrom KD. *Williams Obstetrics*, 21st ed. USA: Mcgraw-Hill Company; 2001. 130.
8. Elahi S, Hussain Z. A longitudinal study of changes in thyroid related hormones among pregnant women residing in an iodine deficient urban area. *ISRN Endocrinology* 2013; 2: 1-6.
9. Panesar NS, Li CY, Rogers MS. Reference intervals for thyroid hormones in pregnant Chinese women. *Annals in Clinical Biochemistry* 2001; 38: 329-332.

10. Ekinci EI, Lu ZX, Sikaris K, Bittar I, Cheong KY, Lam Q, et al. Longitudinal assessment of thyroid function in pregnancy. *Annals of Clinical Biochemistry* 2013; 50(6): 595-602.
11. Matyja MK, Fedorowicz A, Andziak EB, Bednarczuk T, Bereza MB, Dumnicka P, et al. Reference values for TSH and free thyroid hormones in healthy pregnant women in Poland: A prospective, multicenter study. *European thyroid Journal* 2017; 6: 82-88.
12. Patal P, Hamin J, Bautista A, Jimeno C, Acampado L, Hipolito M, et al. Trimester specific reference interval for thyroid function tests in pregnant Filipino women. *JAFES* 2016; 31(1): 18-22.
13. Vieira JGH, Kanashiro I, Tachibana TT, Ghiringhello MT, Hauache OM, Maciel RMB. Free thyroxine values during pregnancy. *Brazilian Archives of Endocrinology & Metabolism* 2004; 48(2): 305-309.
14. Bautista AA, Antonio MQ, Jimeno C, Acampado L, Abrahan MAL, Domingo E. Reference intervals in thyroid function tests in the third trimester in pregnant Filipino women. *Philippine Journal of Internal Medicine* 2014; 52(3): 1-5.