Original Research Paper

Volume - 7 | Issue - 5 | May - 2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Biochemistry

Tt_3, TT_4 and TSH levels during pregnancy in a known Iodine deficient region of upper Assam

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ABSTRACT Body adapts to the increased demands of Thyroid hormones by increasing activity of the thyroid gland. The present study is carried out in subjects visiting Jorhat Medical College Hospital from three upper Assam districts of Jorhat, Golaghat and Sivsagar in their first trimester of pregnancy with an aim to compare their thyroid hormone status with similar age/sex matched controls hailing from the same districts. Serum total T3 (TT3), total T4 (TT4) and thyroid stimulating hormone (TSH) levels evaluated in 301 first trimester pregnant women and 300 non- pregnant controls using Access Immunoassay Systems (Beckman Coulter) at the clinical biochemistry wing of Central Clinical Laboratory, Jorhat Medical College & Hospital, Jorhat , Assam. Statistical analysis done using SPSS 16.0 version. Highly significant increased results were obtained in pregnancy for TT3 (1.5212 µgm/dl ± .27952 µgm/dl) and TT4 (11.5142 ngm/ml ± 2.60105 ngm/ml) when compared with the controls – TT3 (1.0926 µgm/dl ± 0.2678 µgm/dl) and TT4 (8.4423 ngm/ml ± 2.03523 ngm/ml). Thus, the study reaffirms the physiological hyperactive state of the thyroid gland in first trimester of pregnancy.

KEYWORDS : Total triiodothyronine (TT3), total thyroxin (TT4), thyroid stimulating hormone (TSH).

Introduction:

Pregnancy is a physiological state associated with significant but reversible changes in thyroid function. [1] The requirement of thyroid hormones increase during pregnancy. Since fetal thyroid is not fully functional until about sixteen weeks of gestation, the fetus is dependant on transplacental passage of maternal thyroxin. [1] Maternal thyroid hormones play the vital role in early fetal brain development and their deficiencies may impair future neuropsychological development of the fetus. [2]

Both hypo and hyperthyroidism can occur during pregnancy. Two pregnancy related conditions associated with abnormal thyroid activity are hyperemesis gravidarum and trophoblastic disease. Hyperthyroidism in pregnancy is estimated at 0.2 % and Graves disease accounts for 85% - 90 % of these cases. [3]

Planned laboratory testings are very important in pregnancy considering that untreated hyperthyroidism can lead to adverse obstetrical outcomes including first trimester spontaneous abortions, high rates of still births, neonatal deaths , two to three fold increase in the frequency of low birth weight infants, pre-term delivery, fetal or neonatal hypothyroidism and intrauterine growth retardation. [3]

The incidence of hypothyroidism in pregnant women is estimated to be 0.3 % to 0.7 %. [2] Association between hypothyroidism and decreased fertility is known. [4]

Increased glomerular filtration rate increases substantially the renal iodide clearance. [2] In areas of the world where iodine intake is sufficient, this iodide loss in urine during pregnancy is not important. However, in iodine deficient regions, iodine deficiencies during pregnancy can lead to hypothyroidism and goiter. Untreated hypothyroidism in pregnancy may cause significant decrease in the IQ of the children. [5] This is in fact a serious public

health problem. Hypothyroidism in pregnancy is also associated with pregnancy induced hypertension, placenta abruptio, post partum hemorrhage and low birth weights. [3]

The present study is undertaken among apparently healthy euthyroid pregnant women in their first trimester of pregnancy visiting antenatal OPD of Jorhat Medical College & Hospital from Jorhat, Golaghat and Sivsagar districts of upper Assam – A known iodine deficient region of the sub Himalayan iodine deficient belt with the aim to evaluate their TT3, TT4 and TSH levels and statistically analyze the results by comparing with an age / sex matched non pregnant control group of the same region in light of the findings of similar studies done elsewhere.

Materials and methods:

Cases:

A total number of 301 women in their first trimester of pregnancy visiting antenatal OPD of Jorhat Medical College Hospital were estimated for total T3, total T4 and TSH. Age of the cases were between 20 years and 40 years.

Selection criteria of cases:

1. The cases were apparently healthy and euthyroid.
2. Cases did not have any history of taking any drugs apart from pregnancy related supports.
3. All cases belonged to 1st trimester of pregnancy.

Controls:

A total number of 300 non pregnant women between the age of 20 to 40 years visiting Eye, ENT, Orthopaedics and Surgery OPDs of Jorhat Medical College Hospital were included.

Selection criteria:

The study subjects were apparently not suffering from thyroid related problems and diabetes mellitus.

Time of study:

Between March 2014 and September 2015.

Specimen collection for tests:
Collected 2cc of venous blood in sterile empty vial from each of the study subjects maintaining all routine precautions.
Allowed the samples to clot and serum was separated.
Then serum was shifted to storage tubes and was tested within four hours of collection at room temperature.
Haemolysed samples were discarded.

Estimation:
It was carried out in Access Immuno Assay Systems (Beckman Coulter) at the clinical Biochemistry wing of Central Clinical Laboratory, Jorhat Medical College Hospital.

Assays:
The Access Total T3 and total T4 assays are competitive binding immunoenzymatic assay.

The Access TSH assay is a two site immunoenzymatic ("Sandwich") assay.

Calibration:
Regular calibrations were done as per following schedule-
T3: every 14 days
T4: every 21 days
TSH: every 28 days

Quality control:
QC material simulate the characteristics of patient samples are commercially available and supplied by the manufacturers-Beckman Coulter, were used.

Quality control materials were run in every 24 hours time for authenticity of the reports.

These QC materials cover at least two levels of the analyte. The test results were accepted only when quality control results were found to be within acceptable ranges.

Results :
Results of the tests were determined automatically by the system's software. The amount of analyte in the sample was determined from the measured light production by means of calibration data.

Statistical analysis:
Statistical analysis of the datas were done using SPSS 16.0 version according to the following sequence:
1. Mean and Standerd deviation were calculated
2. Normality of the data were examined
3. Homogenity of variances between control and test groups for TT3, TT4 and TSH levels performed.
4. Finally two tailed independent t test was undertaken

Results:
Table I: Seum TT_3, TT_4 and TSH levels

Source of variation (subject)	No.	Total T4 (ngm/ml)		Total T3 (µgm/dl)		TSH (µIU/ml)	
		Mean±SD	P value	Mean±SD	P value	Mean ±SD	P value
Pregnant(cases)	301	11.5142± 2.60105	0.000	1.5212± 0.27952	0.000	2.2124± 1.05245	0.112
Non pregnant (control)	300	8.4423± 2.03523		1.0926± 0.26782		2.4947± 1.75256	

Table I shows the detailed statistical analysis for TT4, TT3 and TSH level in and between cases(pregnant) and controls. This includes total numbers, means ± standard deviation and the sig 2-tailed (P value) results.

1. Total T_4 levels were found to be 11.5142±2.60105 (ngm/ml) in pregnant women (cases) and 8.4423±2.03523 (ngm/ml)in the non pregnant women (control). On examination by two tailed independent t test higher levels in pregnant women were found to be statistically highly significant (P<0.001) with 95% confidence interval when compared with controls (non pregnant).
2. Total T_3 levels were found to be 1.5212± 0.27952(µgm/dl) in pregnant women (cases) and 1.0926± 0.26782(µgm/dl) in the non pregnant control group. On examination by two tailed independent t test, higher levels in pregnant women for TT_3 levels were found to be statistically highly significant(P<0.001) with a confidence interval of 95% when compared with controls(non pregnant)
3. Total TSH levels were found to be 2.2124±1.05245 (µIU/ml) in pregnant women (cases) and 2.4947±1.75256 (µIU/ml) in non pregnant women (controls). On statistical analysis, the findings revealed not to be statistically significant (P>0.05). The results being almost same in both groups.

Discussion:
There is a highly significant increased value obtained for total T_3 and total T_4 levels in first trimester of pregnancy compared to the normal non pregnant controls with 95 % confidence interval. Similar significantly higher results were also reported by Mujawar et al [6], Wohll K N et al [7] and Jugare S et al [8], Manjunatha S et al [9] and Kumar et al [10] also reported higher values for TT_3 and TT_4 in pregnancy. Although the increases were not statistically significant in 1st trimester when compared with non pregnant.

Serum concentrations of Total T_4 and Total T_3 are increased in pregnancy, often outside the health related reference interval. TT3 andTT_4 concentrations increase sharply in early pregnancy and plateau early in second trimester at concentrations 30-100% greater than pre pregnancy values.[11,12] This increase is attributed to mainly three reasons. Firstly, it is the estrogen induced increase in concentration and scialisation of plasma thyroxin binding globulin (TBG).[2,11,12]

Secondly, production of type III deiodinase by the placenta [2,14] and thirdly due to the mild thyrotropic activity of human chorionic gonadotropin (HCG).[15,16]

The mean TSH level in the study was found to be lower among the first trimester pregnant when compared with the control non pregnant which is not statistically significant. Similar non significant lower values were also reported by Jugare S et al [8], Mujawar et al [6] and Zarghami et al [1]. This observation of reduced TSH value in pregnancy is due to feedback inhibition of TSH secretion by increased thyroxin levels. TSH excretion is also increased in pregnancy. [17] The present study found TSH values to be 2.2124±1.05245 (µIU/ml) in 1st trimester of pregnancy and2.4947±1.75256 (µIU/ml) among the non pregnant control group of women. Both these values are towards the upper limit or about to cross the upper limit of euthyroid TSH levels.

Many authors had suggested upper limit of TSH level to be 2µIU/ml in pregnancy and others had even slightly extended the upper limit of TSH to <2.5µIU/ml.[17,19,20] Non pregnant TSH levels are unreliable in pregnancy [17] and also there has not been a consensus on a fixed maximum permissible limit for TSH levels for safe pregnancy considering the widespread demographic and geographical variation around the globe.

Moreover, the physiological adjustments in stimulation, activity and regulation of the thyroid demands the need for a separate extended study to correlate increased thyroxin levels and the proportionate suppression of TSH levels in pregnancy.

Conclusion
The study shows increased thyroid gland activity during pregnancy and emphasizes the need for pregnancy specific separate region/ laboratory based reference values of TT_3, TT_4 and TSH.

References:

1. Zarghami N, Noubar M R and Khosrawbeygi A, Thyroid hormone status during pregnancy in normal Iranian women. Indian Journal of Clinical Biochemistry.2005, 20(2):182-185.
2. Glinoer D: The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocrine Reviews, 1997; 18(3): 404–433.cross ref Medline order article via infotrieve web of sciences
3. Mestman J, Goodwin TM, Montoro MM.Thyroid disorders of pregnancy. Endocrinol Metab Clin N Am.1995;24:41-71.cross ref Medline order article via infotrieve web of sciences
4. . Gronstein F, Goldman MB, Ryan L et al. Self reported use of pharmaceuticale and primary ovulatory infertility. Epidemiology.1993; 4:151-156. cross ref Medline order article via infotrieve web of sciences
5. Haddow J E, Palomaki G E, Allan W C et al. Maternal thyroid deficiency during pregnancy and subsequent neurophysiological development of the child. N Engl J Med.1999; 341:549-555.cross ref Medline order article via infotrieve web of sciences
6. Mujawar S A, Patil V W, Daver R G. Human chorionic Gonadotropin and Thyroid Hormones status during normotensive pregnancy. Journal of Pharmaceutical and Biomedical Sciences.2010:2(01)
7. Wohll K N, Osorio M, Aguayo J et al. Thyroid profile in normal pregnancy. Rev Med Chil.1993:121(6); 652-9
8. Jugare S, Sonual S. Study of Thyroid Profile in First Trimester of Pregnancy. International Journal of Recent trends in Science and Technology.2013:9(2); 171-173
9. Manjunatha S, Basavraja G N, Veena H C et al. Thyroid Status in Non-Pregnant & Pregnant Women. Scholars Journal of Applied Medical Sciences.2014:2(6G); 3349-3352
10. . Kumar A, Gupta N, Nath T et al. Thyroid function test in pregnancy. Indian Journal of Medical Sciences.2003: 57(6); 252-258.
11. Skjoldebrand L, Brudin J, Carlstrom A et al. Thyroid associated components in serum during normal pregnancy. Acta Endocrinol.1982:100; 504-511
12. Guillaume J, Schussler G C, Goldman J et al. Components of the total serum thyroid hormone concentrations during pregnancy: high free thyroxine and blunted thyrotropin (TSH) response to TSH-releasing hormone in the first trimester. J Clin Endocrinol Metab.1985; 60: 678-684.
13. Burrow G N, Fisher D A, Larsen P R. Maternal and fetal thyroid function. N Engl J Med.1994; 331: 1072-1078.
14. . Fischer D A, Polk D H, Wn SY. Fetal Thyroid metabolism: a pluralistic system. Thyroid.1994; 4:367-371.
15. . Fantz C R, Jack S D, Ladenson J H et al. Thyroid function during pregnancy. Clinical Chemistry.1999; 45(12): 2250-2258
16. Yoshimura M, Hershmans J M. Thyrotropic action of human chorionic gonadotropin. Thyroid.1995; 5:425-434.
17. Pema S. Thyroid screening in pregnancy – A study of 82 women. J Obstet Gynecol India.2010; 60(3): 232-237.
18. Idris I, Srinivasan R, Simm A et al .Maternal Hypothyroidism in early and late gestation: effects on neonatal and obstetric outcome. Clin Endocrinol.2005; 63:560-565
19. . McGregor A M, Hall R, Richards C. Autoimmune thyroid disease and pregnancy. Br Med J.1984; 288:1780-1
20. . Green WL, New questions regarding bioequivalence of levothyroxine preparations: a clinician's response. AAPSJ.2005;7:E54-E58