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Evaluation of Trimester specific Thyroid Function Hormone Assay in Pregnant Females

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ABSTRACT

Introduction: Pregnancy is a physiological phenomenon in which there is the maternal adjustment of multiple organ systems, including metabolic and hormonal adjustments, to supply adequate nutrition to the fetus. Thyroid hormones are necessary to ensure the healthy development of the fetus, especially during the first trimester, during which the fetus is entirely dependent on the maternal thyroid supply delivered through the placenta. during pregnancy, there is increased maternal renal iodine loss, increased levels of serum total thyroxine binding globulin (TBGs), and increased degradation of thyroid hormone by placental enzymes. Human chorionic gonadotropin (HCG) has a striking structural resemblance with thyroid-stimulating hormone (TSH), leading to an increase in thyroid hormone production during pregnancy followed by a plateau phase around 16 weeks of gestation. In pregnancy, overt hypothyroidism is seen in 0.2% cases and sub clinical hypothyroidism in 2.3% cases. Fetal loss, fetal growth restriction, pre-eclampsia and preterm delivery are the usual complications of overt hyperthyroidism (low TSH and high T3, T4) seen in 2 of 1000 pregnancies whereas mild or sub clinical hyperthyroidism (suppressed TSH alone) is seen in 1.7% of pregnancies and not associated with adverse outcomes.

Aim:Evaluation of trimester specific thyroid function hormone assay in pregnant females.

.**Materials and Methods:**100 pregnant females be selected to ANC based on the inclusion and exclusion criteria during pregnancy was recruited from Gynae OPD of Sarojini Naidu medical college & hospital.

Result: The number, percentage and mean and Standard deviation (SD) levels of both the parameters as well as the clinical characteristics of the study subjects are mentioned in Table-1 out of 100 pregnant women across all trimesters, the mean age of pregnant women was 22.44 ± 3.60 in first trimester, 25.07 ± 3.15 in second trimester and 23.7 ± 3.47 in third trimester. However, maximum numbers of study subject was in age group of 25-29 years. A statistically significant differences was found for serum total T3 ($p<0.001$), serum total T4 ($p<0.01$) and serum TSH ($p<0.001$) levels among trimester groups were found as shown in Table-2.

Conclusion: The clinical relevance of this study showed that the cases of hypothyroidism were found to be increased particularly in second trimester during the pregnancy.Uncontrolled or inadequate control of thyroid dysfunctionin pregnancy is associated with adverse fetal and maternaloutcomes.So only diagnosis and treatment should be started based on the lab diagnosis due to present complains in pregnancy as well as in newborn.

Keywords:FT3, FT4, TSH

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Introduction

Pregnancy is a physiological phenomenon in which there is the maternal adjustment of multiple organ systems, including metabolic and hormonal adjustments, to supply adequate nutrition to the fetus [1, 2]. During this process, the thyroid gland adapts through regulating thyroid hormones via the hypothalamic pituitary- thyroid axis [3]. Thyroid hormones are necessary to ensure the healthy development of the fetus, especially during the first trimester, during which the fetus is entirely dependent on the maternal thyroid supply delivered through the placenta [4]. Moreover, during pregnancy, there is increased maternal renal iodide loss, increased levels of serum total thyroxine binding globulin (TBGs), and increased degradation of thyroid hormone by placental enzymes [5]. Human chorionic gonadotropin (HCG) has a striking structural resemblance with thyroid-stimulating hormone (TSH), leading to an increase in thyroid hormone production during pregnancy followed by a plateau phase around 16 weeks of gestation [6]. Thyroid disease is one of the most common endocrine disorders worldwide. Thyroid disorders are also common problem in pregnancy and hypothyroidism is widely prevalent in pregnant women. If pregnancy is associated with hypothyroidism, the prospective for maternal and foetal adverse outcomes can be huge [7,8]. Maternal hypothyroidism occurs in 2-5% of pregnant women and associated with the adverse pregnancy outcomes [9]. Prevalence of hypothyroidism was found to be more prominent in the Asian countries than that in the west [10]. In the west, the prevalence of hypothyroidism in pregnancy is 2.5%, Overt Hypothyroidism (OH) and Subclinical Hypothyroidism (SCH) is 0.3-0.5% and 2-3%, respectively [11,12], whereas the prevalence of OH (3-4%) and SCH (4.8 to 12%) is much higher in the East [13]. Therefore, the Indian Thyroid Society recommends screening of TSH levels in all pregnant women during the first antenatal check-up [14].

Over the past several years it has been proved that maternal thyroid disorder influence the outcome of mother and fetus, during and also after pregnancy. The most frequent thyroidabruptions, pre-eclampsia, preterm delivery and reduced intellectual function in the offspring. [15] In pregnancy, overt hypothyroidism is seen in 0.2% cases and sub clinical hypothyroidism in 2.3% cases[16,17]. Fetal loss, fetal growth restriction, pre-eclampsia and preterm delivery are the usual complications of overt hyperthyroidism (low TSH and high T3, T4) seen in 2 of 1000 pregnancies whereas mild or sub clinical hyperthyroidism (suppressed TSH alone) is seen in 1.7% of pregnancies and not associated with adverse outcomes[18]. Autoimmune positive euthyroid pregnancy shows doubling of incidence of miscarriage and preterm delivery. Worldwide more than 20 million people develop neurological sequel dueto intra uterine, iodine deprivation[19].

Material and methods -

This study was conducted in Department of Biochemistry, Sarojini Naidu Medical College & Hospital, AGRA.

Sample was collected from Gynae OPD of SNMC.

Study subject

100 patients with thyroid during pregnancy will be recruited from OPD of Sarojini Naidu medical college & hospital.

This was a case control study.

Case: 100 patients of thyroid during pregnancy.

Control: 100 normal healthy person will be included.

Inclusion Criteria:

1. Patients diagnosed with thyroid in age range 20-40 years.
2. Age matched healthy indivisuals.
3. Duration of pregnancy different trimester.

Exclusion Criteria:

1. Age below 20 years and above 40 years.
2. Patients having any other systemic disease and on regular medication for the same.
3. patients undergoing laparoscopic surgery.
4. Patients with habits of tobacco or alcohol and smoking.

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Specimen Collection:
5 ml of blood sample was collected from antecubital vein in which collected in Plain vial (red cap) for thyroid profile estimation.

Speciemenprocessing:
Serum will be saperated by centrifugation at 3000 rpm (rotation per minute) for 5 minutes then serum will be conducted. The serum sample will be stored at 80°Cuntill assayed.

Thyroid Estimation:
Thyroid profile FT_3, FT_4 and TSH was estimated on Architech - plus analyzer by CMIA method.

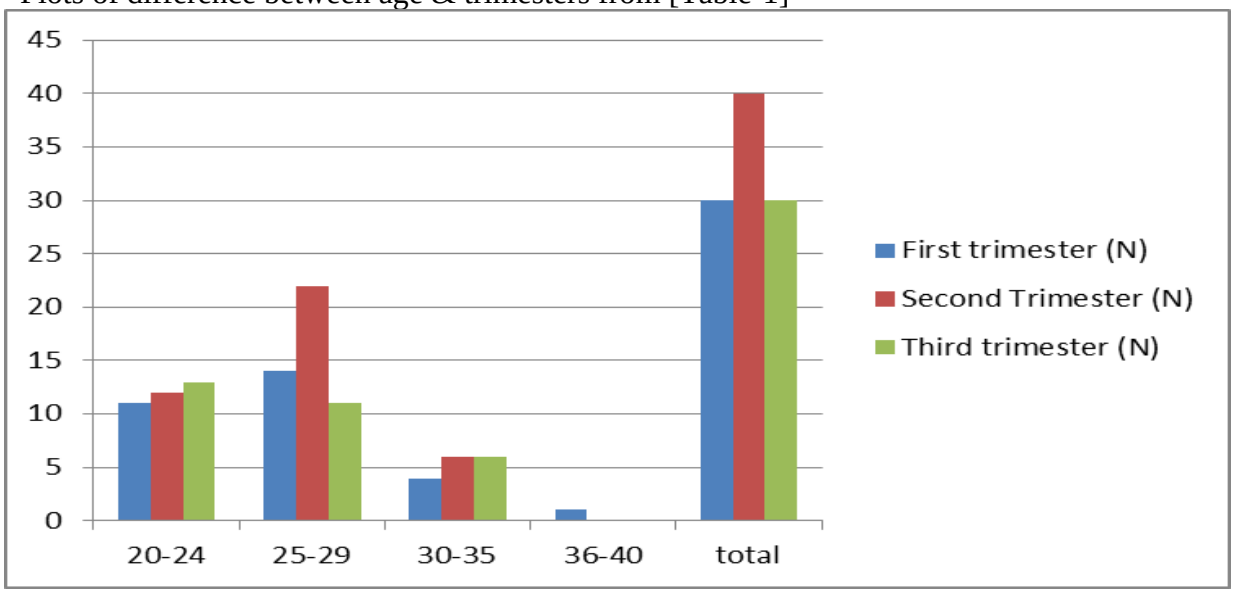
Principle:
The ARCHITECH Free T_3 assay is a two step immunoassay to determine the presence of free (unbound) T_3 in human serumand plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex. [Principle of FT_4 and TSH as well as FT_3 assay].

STATISTICAL ANALYSIS:

*[Table-1] Age wise comparison of study subject among trimester groups.

Age (year)	First trimester (N)	Second Trimester (N)	Third trimester (N)	p - value
20-24	11	12	13	
25-29	14	22	11	
30-35	4	6	6	
36-40	1	0	0	
total	30	40	30	
Mean ± SD	22.44 ±3.60	25.07 ± 3.15	23.7 ± 3.47	0.929

*Plots of difference between age & trimesters from [Table-1]



*Graph of Mean & SD trimester wise from [Table-1]

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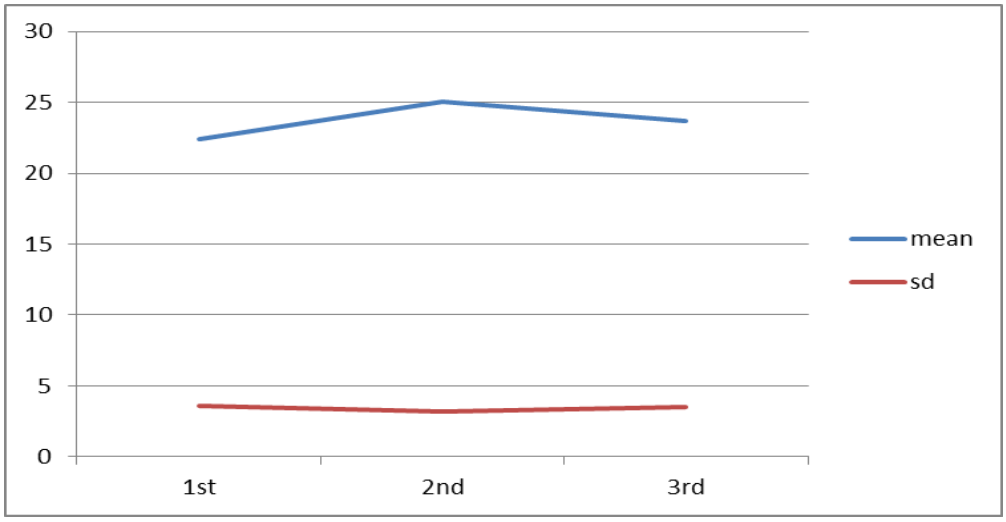
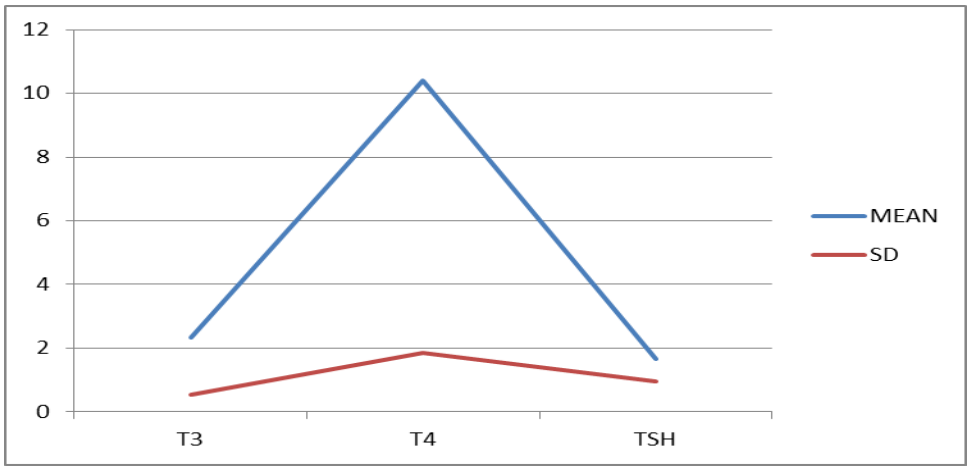


*[Table-2] Status of thyroid profile parameters among pregnant women trimester wise.

Parameter	First trimester (N=30)	Second Trimester (N=40)	Third trimester (N=30)	p - value
T_3	2.33±0.54	2.98±0.76	3.07±0.86	<0.001
T_4	10.41±1.85	10.57±1.84	11.99±2.70	<0.01
TSH	1.67±0.95	3.11±1.79	2.90±1.20	<0.001

*Graph of first trimester from [table-2]



*Graph of second trimester from [table-2]

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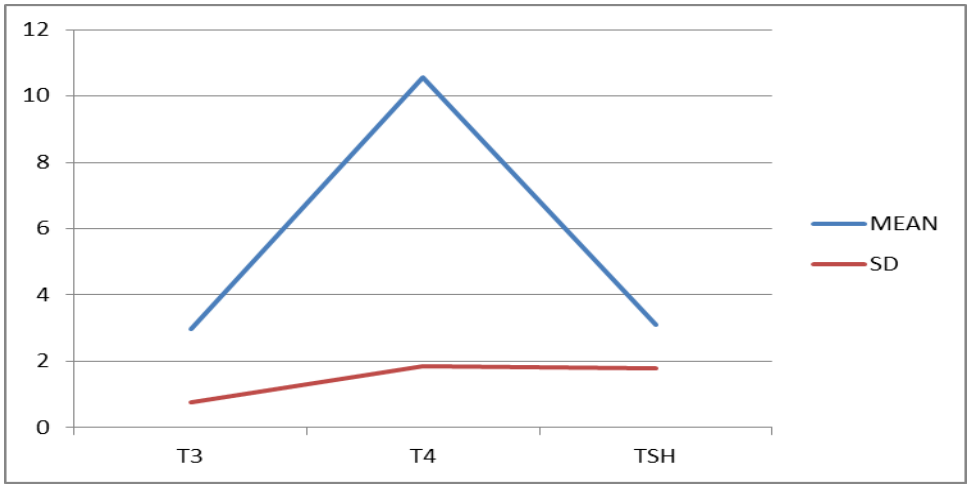
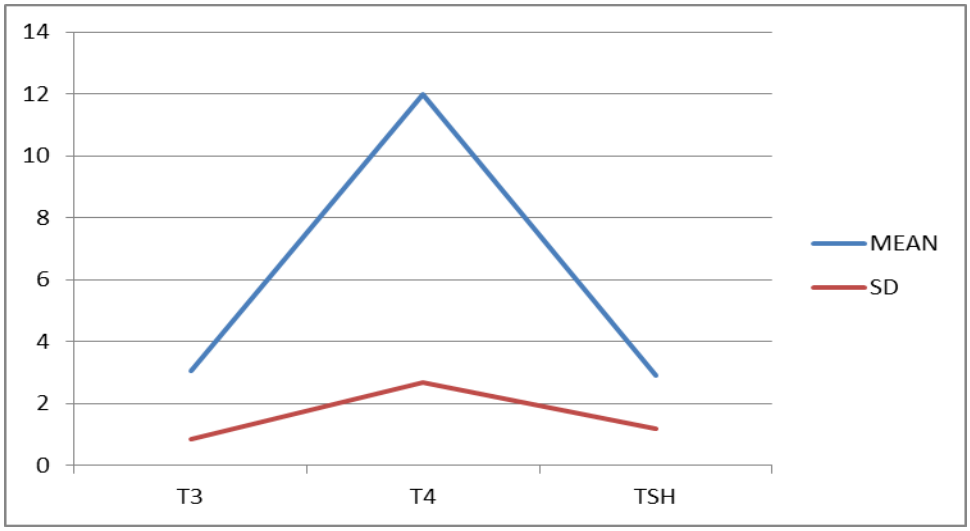


Graph of third trimester from [table-2]



Anova: Single Factor						
SUMMARY						
Groups	*Count*	*Sum*	*Average*	*Variance*		
Column 1	100	97.14	0.9714	0.040270747		
Column 2	100	64.48	0.6448	0.00160097		

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Column 3	100	527.29	5.2729	0.032976354		
ANOVA						
Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	*F crit*
Between Groups	1334.295981	2	667.1479903	26740.08765	0	3.026153369
Within Groups	7.409959	297	0.024949357			
Total	1341.70594	299				

RESULT

The number, percentage and mean and Standard deviation (SD) levels of both the parameters as well as the clinical characteristics of the study subjects are mentioned in Table-1 out of 100 pregnant women across all trimesters, the mean age of pregnant women was 22.44 ± 3.60 in first trimester, 25.07 ± 3.15 in second trimester and 23.7 ± 3.47 was third trimester, significant (p =0.929). However, maximum numbers of study subject was in age group of 25-29 years. A statistically significant differences was found for serum total T3 ($p<0.001$), serum total T4 ($p<0.01$) and serum TSH ($p<0.001$) levels among trimester groups were found as shown in Table-2.

DISCUSSION

Mandel SJ et al., have suggested that TSH should be used as a marker for diagnosis of hypothyroidism in pregnancyand the effect of the thyroid dysfunction on the obstetric outcomes appear to manifest when TSH cut-off >2.5 mIU/L in the first trimester. Therefore, National guideline (2014) and American Thyroid Association (2011) have suggested >2.5 and >3 mIU/L cut-off range of TSH for the diagnosis of hypothyroidism in the first and second-third trimester, respectively. In the present study, the serum total T3, T4 and TSH levels were found statistically significant in all trimesters of pregnancy. In this study, trimester wise raised total T3 and total T4 values were observed during pregnancy and in third trimester maximum rise was observed for total T3 and total T4. Another interesting finding was that TSH cut-off >3 mIU/L observed in the second trimester only. The slight decrease in the values of TSH in the third trimester might be a reflection of proper clinical screening and management done by the clinician. In support to present results, Nepalia R and Verma AK, have also observed high serum T3 and T4 values during pregnancy. [20,21,22]

In contrast to the present findings, Kumar A et al., have observed a rise in mean value of T4 levels in second trimester and after that decline in third trimester and gradual increase in TSH levels during all trimesters of pregnancy.[23,24]

Zarghami N et al., have also observed the declining mean FT3 and FT4 levels during the pregnancy.

The important finding in the present study was the highest prevalence of hypothyroidism (40.0%) found in second trimester's women in comparison to first and third trimester when the trimester

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specific TSH cut-off values were used. The overall prevalence of hypothyroidism in this study was 24% which is higher than the Western studies as well as previous published Indian studies. The difference in the prevalence rate of various studies in India because of different cut-off values of TSH level were used in these studies. Most of the studies had much higher prevalence of hypothyroidism in first trimester when compared to the present study results. In this study, the prevalence of hypothyroidism in second trimester was higher in comparison to previous published Indian studies. Very few Indian studies have reported the prevalence of hypothyroidism in second trimester. In third trimester, 23.31% prevalence of hypothyroidism was observed among pregnant women which was lower as compared to the Panda J et al., and Rajput R et al., study prevalence 75% and 25.8%, respectively. In first trimester, 3.33% prevalence of hyperthyroidism observed in the present study which was similar to the other studies. Based on trimester-specific TSH cut-off values, a trimester wise comparative prevalence of thyroid disorders in pregnant women of different studies of India. [25,26,27,28,29].

Haddow JE et al., have also reported no association between TSH value and body weight but showed negative correlation between body weight and T4 during pregnancy [30].

CONCLUSION

The clinical relevance of this study showed that the cases of hypothyroidism were found to be increased particularly in second trimester during the pregnancy.Uncontrolled or inadequate control of thyroid dysfunctionin pregnancy is associated with adverse fetal and maternaloutcomes.Propylthiouracil is the preferred antithyroid drug inpregnancy although methimazole can be used whererepropylthiouracil is unavailable.Synthetic levothyroxine is the treatment of choice inhypothyroidism. Patients with pre-existing hypothyroidism usually requirean increase in thyroxine dose in pregnancy. Long-term follow-up of patients with this syndrome isessential owing to the risk of permanent hypothyroidism. Subclinical hypothyroidism in pregnancy requiresreplacement treatment. Excellent maternal and fetal outcomes can be achievedwith appropriate management of thyroid dysfunction in pregnancy.

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