



## Frequency of subclinical hypothyroidism and mean serum TSH level in first trimester of pregnancy.

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**ABSTRACT... Objective:** To find out the frequency of subclinical hypothyroidism (SCH) in our pregnant population during 1<sup>st</sup> Trimester and the mean TSH level in first trimester of pregnancy. **Study Design:** Cross Sectional Descriptive study. **Setting:** Dow University Hospital and Dr Ruth KM Pfau CHK. **Period:** June 2015 to May 2016. **Material & Methods:** All Pregnant women with <14 weeks gestation were screened for Serum TSH level. Data were recorded after informed consent and institutional ethical approval. Variables recorded were age, parity, gestational age and serum TSH level. Data were analyzed on SPSS version 16. Mean and SD were calculated for quantitative variables ie. Age, parity, gestational age, serum TSH level and serum free T4 level. Mean TSH level according to age group, parity and gestational age groups were determined by applying ANOVA test. Correlation of Serum TSH level with the maternal age, parity and gestational age groups were also assessed by Pearson Correlation test. Significant P-value was taken as <0.05. **Results:** The frequency of SCH found was 19.35% by taking cut off limit of <2.5 IU/L and 3.55% by taking cut off limit of <4.5 IU/L among total of 310 pregnant women. Mean TSH level was  $1.84 \pm 1.36$  IU/L. The mean maternal age was  $27.22 \pm 4.43$  yrs. while median parity was 1. Mean gestational age of these patients were  $9.41 \pm 2.748$  weeks and out of these 160 (51.61%) were between 4-9 weeks and 150(48.38%) between 10-14 weeks. Majority (74%) of these women belonged to lower middle socioeconomic class. Mean TSH level coorelation between different age groups, parity groups and gestational age groups were found to be insignificant. **Conclusion:** The prevalence of SCH is not so high and mean TSH level in our population was 1.84 IU/L. But to establish reference range for Pakistani population, further studies in population of different backgrounds and geographical distribution needs to be evaluated.

**Key words:** Mean TSH level, Pregnancy, Prevalence, Subclinical Hypothyroidism,

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## INTRODUCTION

Hypothyroidism is a common endocrinological disorder in pregnancy with an estimated prevalence of 2-3% and 0.3-0.5% for subclinical and overt hypothyroidism respectively.<sup>1</sup> According to ACOG guidelines SCH is diagnosed in asymptomatic women when TSH level is > 4.5 IU/ml and free T4 level is within normal range.<sup>2</sup> There has been a wide geographic variation in prevalence of SCH during pregnancy varying from 2.5% in west to 11% from India and other Asian Countries.<sup>3,4</sup> These variations are partly because of different cut off level taken and different laboratories have its own pregnancy specific reference for thyroid test. International guidelines advocate using population based reference ranges, however if

these are unavailable then it is recommended for upper threshold of TSH concentration as 2.5 mIU/L during 1<sup>st</sup> trimester and 3.0 mIU/L during Second and third trimesters.<sup>5</sup>

Endemic iodine deficiency accounts for the most of the hypothyroidism in pregnant women worldwide but chronic autoimmune thyroiditis is responsible for this in iodine sufficient areas.<sup>6</sup>

Changes in thyroid physiology during pregnancy result in the normal ranges of thyroid stimulatory hormones being lower than among non-pregnant adults. In pregnancy thyroid function is modified because of increased thyroid binding globulins, altered thyroid hormones metabolism, increased

loss by kidneys and altered transfer from placenta. Maintenance of true thyroid state is particularly important during pregnancy before the fetal thyroid gland becomes active as in the first trimester maternal thyroid hormone is required for normal fetal neurological development. Several studies reported adverse obstetric outcomes like recurrent miscarriage, anemia in pregnancy, pre-eclampsia, abruptio placenta, preterm delivery, low birth weight, PPH, neonatal respiratory distress and low IQ scores.<sup>7,8</sup>

There is controversy regarding the routine screening of all pregnant mother in first trimester for hypothyroidism as some recommends it but others not.<sup>9,10,11</sup> The use of thyroid functions reference values based on studies using different population and different backgrounds can introduce bias in the evaluation of our local population. Till date no local data is published for pregnant Pakistani women. So studies are needed to establish reference range of TSH in our population for diagnosis of SCH and subsequent need of treatment.

The aim of this study was to find out the frequency of subclinical hypothyroidism and the mean TSH level in first trimester of pregnancy.

## MATERIAL & METHODS

This prospective cross sectional descriptive study was conducted in 310 first trimester (up to 14 week's gestation) pregnant women attending antenatal clinics of outpatient department in Dow University Hospital and Civil Hospital Unit II Karachi from 1<sup>st</sup> June 2015 to 31<sup>st</sup> May 2016.

All pregnant women with singleton pregnancy of < 14 weeks gestation were included in this study for the screening of serum TSH level. Women with medical disorders, multiple gestation, smokers, using drugs affecting thyroid functions (eg methimazole or amiodarone) or already diagnosed as having thyroid disorder and with recent history of fever were excluded. Women were recruited after obtaining informed consent. The study was started after approval from Institutional review boards no. IRB-582/DUHS/Approval/2015.

Data regarding age, gestational age, parity and serum TSH level were recorded on predesigned proforma. Serum TSH level was performed in all patients but serum free T4 level were assessed if Serum TSH level was found to be greater than 2.5 IU/L.

These hormonal assay were performed by chemiluminescent assay using Immolate 2000 analyzer (diagnostic products corporation Los Angeles USA).

The reference range used to diagnose subclinical hypothyroidism was 2.5 IU/L as per American Thyroid Association (ATA) and endocrine society clinical practice guideline (2012) recommendation but we have also analyzed the result using 0.6-4.5 IU/L first trimester range.<sup>2</sup>

Data were analyzed using SPSS version 16. Mean and SD were calculated for quantitative variables ie. age, gestational age and serum TSH level. Mean TSH level according to age group, parity and gestational age groups were determined by applying ANOVA test. Correlation of Serum TSH level with the maternal age, parity and gestational age groups were also assessed by Pearson Correlation test. Significant P-value was taken as <0.05.

## RESULTS

A total of 310 pregnant patients in first trimester (< 14 weeks gestation) who attended antenatal clinic were screened from 1<sup>st</sup> June 2015 to 31<sup>st</sup> May 2016. The serum TSH level in these women ranged from 0.02 to 8.60 IU/L while mean TSH level was  $1.84 \pm 1.36$  IU/L. Frequency of subclinical hypothyroidism came out as 60 (19.35%) with cut off level < 2.5 IU/L and 11(3.55%) with cut off level < 4.5 IU/L as shown in Table-I.

The mean maternal age was  $27.22 \pm 4.43$  yrs. while median parity was 1. Mean gestational age of these patients were  $9.41 \pm 2.748$  weeks and out of these 160 (51.61%) were between 4-9 weeks and 150 (48.37%) were between 10-14 weeks. Majority (74%) of these women belonged to lower middle socioeconomic class.

Mean TSH level according to age group, parity and gestational age groups were also calculated by ANOVA test as shown in Table-II. It showed no significant difference in mean TSH level according to maternal age (P-value 0.3), parity (P-value 0.6) and gestational age (p-value 0.978). Co-relation of TSH level with different age, parity and gestational age groups assessed by Pearson correlation method also depicted the same results. (Age group has Co-relation factor 0.06 and P- value 0.231, parity group has co-relation factor -0.021 and p-value 0.712 and gestational age group has co-relation factor -0.04 and P-value 0.444).

	Max	Min	Mean $\pm$ SD
Age (yrs.)	41	18	27.22 $\pm$ 4.431
Gest Age (weeks)	14	4	9.41 $\pm$ 2.748
S. TSH level (IU/L)	8.6	0.02	1.84 $\pm$ 1.36
Parity (no.)	6	0	Median parity 1

**Table-I. Mean age, parity, gestational age and serum TSH level.**

Age (years)	Mean TSH	P-Value	Pearson Co-relation	
			Cor-relation	P-Value
<21 years	1.704+- 0.571	0.3		
21-30 years	1.902+-1.48		0.06	0.231
>31 years	1.613+-0.917			
Parity (No.)		0.6		
0 (135)	1.799+- 1.028			
1-3 (164)	1.899+-1.617		-0.021	0.712
>3 (10)	1.530+-0.79			
Gestational Age (wks)		0.978		
4-9 (162)	1.842 +-1.441		-0.04	0.444
10-14 (136)	1.846+-1.312			

**Table-II. Relationship of serum TSH level with different ages, parity and gestational age groups.**

## DISCUSSION

There has been a debate for long time regarding the upper limit of normal TSH level in pregnancy. The mean 1<sup>st</sup> trimester TSH value found among 100 pregnant women as reported by Dhanwal and Colleagues from Delhi was 3.68 mIU/L and taking cut off limit of 4.5 mIU/L the prevalence

was 14.3%.<sup>12</sup> This is also evident from our study as the frequency increased from 3.55% to 19.35% when the cutoff limit decreased to 2.5 IU/L.

American Thyroid Association (ATA) thyroid and pregnancy guidelines 2017 recommend strongly that population based trimester specific references should be defined through local population data and should include pregnant women with no thyroid disease optimal iodine intake and negative TPO antibodies status.<sup>13</sup> It also recommends evaluation of anti TPO status in women having TSH level of 2.5 IU/L however we did not perform TPO antibodies unless the level was > 10 IU/L.

Using cut off level of 5 mIU/L as upper limit an Indian study reported SCH in 8.1% women while a Chinese study reported 4% prevalence using 5.08 mIU/L cut off level.<sup>14,15</sup> Studies also suggest variation in TSH level according to geographic region and ethnic origin. ATA 2011 and European Endocrine society 2012 recommended a trimester specific reference range should be established on a local basis as there is a great variation in prevalence according to geographic region and ethnical background.<sup>16</sup>

Recent ATA guideline 2017 also recommends that if local population based pregnancy-specific TSH references are unavailable then take upper limit as 4.0 mIU/L according to current consideration which is 0.5 IU/L less as compared to nonpregnant TSH reference range.<sup>17</sup> Recently an Indian study also stressed to develop reference range for local population for starting therapy.<sup>18</sup> One cohort study from Canada considered serum TSH level <4.0 mIU/L as the upper limit of normal and they found that 67.9% of those having levels between 4.0 mIU/L and 10 mIU/L on repeat testing after 6 weeks were having levels < 4.0mIU/L. They concluded one time test may lead to overdiagnosis and unnecessary treatment.<sup>19</sup>

Incidence of SCH found to be higher in white women and also they were older than controls.<sup>8</sup> Another study also shows higher prevalence of SCH as the age increased.<sup>20</sup> However we found no significant difference in serum TSH level

related to age groups. Similarly difference in TSH level between early and late first trimester was also insignificant.

ATA guideline 2011 recommended not to screen for TPO antibodies among women with miscarriage or universal TSH screening in the first trimester.<sup>9</sup> One of the review article suggested targeted screening to be preferred as it is cost effective and practical while ETA guideline 2014 reports that targeted screening will miss a substantial percentage of women with thyroid dysfunctions.<sup>21</sup> Indian study recommends universal screening for hypothyroidism because of high prevalence there.

As SCH has potential serious adverse effects on mother and fetus, targeted case finding is recommended and if she is taking Thyroxine already then it should be adjusted to keep TSH level not higher than 2.5 mIU/L.<sup>22</sup> Treatment algorithm for patient in 1st trimester of pregnancy is suggested by authors in one study.<sup>5</sup> Some authors recommended treatment with thyroid hormone for women with TSH concentration of 4.1-10.0 mIU/L and not below this level while others recommend second testing before starting treatment.<sup>23,24</sup>

Though this is first study conducted in pregnant woman of our population, there are certain limitations of this study. Firstly, it was hospital based and secondly the number was less, so it may not be representing the true population level.

## CONCLUSION

The prevalence of SCH is not so high in our population and the mean TSH level found is 1.84 IU/L while review of different reports suggest that cut off limit of 2.5 IU/L is too low. Therefore to develop a reference range of TSH level in first trimester further studies should be conducted in women with different ethnic and geographical background Also studies should be conducted to observe the pregnancy outcome at different cut off levels to establish the justification for thyroxine therapy.



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#### AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Fouzia Perveen	Conceived the data, designed written the manuscript and edited.	
2	Lubna Ali	Collected the data and helped in manuscript writing.	
3	Afshan Hasan	Collected the data.	