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Thyroid Function Test Screening in Third Trimester of Pregnancy in Eastern Libyan Women

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Abstract

Background: Each trimester have Thyroid Function (TFT) reference range which is still not known in Libya. Our study to determine this range in third trimester of pregnancy in eastern Libya.

Method: Cross sectional study recruited pregnant females at third trimester attending at the anti natal clinic in Benghazi medical center and Ghmenis city during the first 6 months of 2019. TFT and anti-TPO were measured for participants.

Results: A total of 210 pregnant were recruited, their mean duration of gestation was (37 ± 3.2), mean age 32.1 ± 6, mean number of parity was 2.53 ± 1.1, and mean number of abortion was 0.4 ± 0.75. The mean TSH during third trimester in the study participants were (3.33 ± 1.34 mIU/L) and free T4 (17.1 ± 3.3), total T4 (106.9 ± 38.2) while total T3 mean was (1.8 ± 0.7) respectively. The range during third trimester according to 5% to 95% percentile for TSH, free T4, total T4, total T3 were (0.88 to 5.52 mIU/L), (12 to 22.5), (61.6 to 181.2), (1.02 to 3.2) respectively. The number of abortion was strongly correlated with TSH level at third trimester (Pearson correlation = 0.269, P value = 0.000) and with number of parity (Pearson correlation = 0.172, P value = 0.013).

Conclusion: In nearly healthy pregnant females at third trimester in eastern Libyan cities the mean TSH was (3.33 +/- 1.34) and its 5% to 95% range was (0.88 to 5.52) which is higher than the recommended range by many thyroid associations.

Keywords: Thyroid function; Reference range; Gestation; Third trimester; Libya

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Introduction

The thyroid gland originates from a diverticulum located in the median ventral wall of the pharynx (thyroid diverticulum) [1]. The thyroid weighs 15 g to 20 g and consists of two lobes (left and right) and one isthmus that binds them together [2].

The main thyroid hormone which produced by thyroid glands are namely T4 (3,5,30,50-tetraiodothyronine) and T3 (3,5,30-triiodothyronine). TSH regulates and stimulates most stages of thyroid hormones biosynthesis [3]. Other regulator of thyroid hormone synthesis is iodine availability [4]. The deiodinases regulated thyroid hormone activation and inactivation [5]. During pregnancy, there will be many physiological changes in order to accommodate the growing fetus [6]. As regard to thyroid gland the main changes are an increase in the production of Thyroxine-Binding Globulin (TBG) by the liver, resulting in increased levels of thyroxine (T4) and tri-iodothyronine (T3). Serum free T4 (fT4) and T3 (fT3) levels decrease slightly in the second and third trimesters of pregnancy but are usually of no clinical significance [7]. In response to the thyrotropic affects of human chorionic gonadotropin and Human Chorionic Thyrotropin (HCT) during first trimester the Serum concentrations of TSH decreased slightly but start to rise again during second trimester [8]. Active transport of iodine from the mother to the foeto-placental unit and increased iodine excretion in the urine leads to relative iodine deficiency and explain increase iodine requirement during gestation.

That's why in early pregnancy, lower cutoffs TSH are considered normal. There is a controversy between the guidelines regarding the normal cutoff value for TSH during pregnancy the ATA recommends that reference range should be measured locally, and if not available

Table 1: Illustrate the Descriptive statistics of the study sample.

	Mean	Std. Deviation	Range 5% to 95%	N
Age	32.11	6.018	-	210
Duration of pregnancy	37	3.2	-	210
TSH	3.33	1.34	0.88-5.52	210
T3	1.8	0.685	1.02-3.2	210
T4	106.96	38.24	61.6-181.2	210
Anti TPO	18.45	7.922	8-33.2	136
FT4	17.12	3.33	12-22.5	210
Parity	2.53	1.14	-	210
No of abortion	0.42	0.75	-	210

0.4 to 4.5 should be considered normal range in non-pregnant adults. This cutoff should be maintained at 0.1 to 2.5 in the first trimester and at 0.2 to 3.0 in the second trimester and 0.3 to 3 in the third trimester as per ATA, 2011 [9] as well as endocrinology society guidelines, 2012 [10]. ATA revised their recommendations in 2017 they recommended that the first trimester upper normal limit cutoff should be obtained by deducting '0.5 mIU/L' from pre pregnancy TSH value. But if it is not known then '4.0 mIU/' should be taken as upper limit of normal cutoff [11].

The Methodology

Study design

Cross sectional study.

Study population

Pregnant females at Third trimester attending and registered at the anti natal clinic in Ghmenis city and Benghazi medical center.

Study time

During the first 6 months of 2019.

Sample size

210 participants, all participants were tested for thyroid function including FT4, TSH, T3, and T4. Only 136 participants were tested for anti-TPO because of financial issue of the researchers.

Exclusion criteria

These participants were excluded from the study.

- Personal or family history of thyroid disease or History of thyroid swelling before pregnancy.
- History of diabetes or vitiligo or adrenal disease.
- History of taking drugs can affect thyroid function like antipsychotic, steroid, lithium, interferon, amiodarone.
- Acutely sick patient.

Limitation

No ability to do anti-TG antibodies. Anti-TPO were done only for 136 of study participant.

Results

The total number recruited was 210 pregnant females in their third trimester of pregnancy (the mean duration of gestation was 37 ± 3.2 weeks) which attending the anti natal clinic in Benghazi Medical Center and Ghmenis district during the first 6 months of 2019. The mean age of participants was 32.1 ± 6, the mean number of parity was 2.53 ± 1.1 and mean number of abortion was 0.4 ± 0.75.

The mean TSH during third trimester in the study participants were (3.33 ± 1.34 mIU/L) and free T4 (17.1 ± 3.3), total T4 (106.9 ± 38.2) while total T3 mean was (1.8 ± 0.7) respectively. The range during third trimester according to 5% to 95% percentile for TSH, free T4, total T4, total T3 were (0.88 to 5.52 mIU/L), (12 to 22.5), (61.6 to 181.2), (1.02 to 3.2) respectively. Anti-TPO was done for only 136 participants because of financial issues of the researcher and their mean during last trimester was (18.5 ± 7.9) and its 5% to 95% range of was (8 to 33.2) (Table 1).

Interestingly the number of abortion was strongly correlated with TSH level at third trimester (Pearson correlation = 0.269, P value = 0.000) and also with number of parity (Pearson correlation = 0.172, P value = 0.013).

Not surprisingly that Total T3 was positively correlated with Total T4 as the Thyroid binding globulin increase during pregnancy (Pearson correlation was = 0.155, P value = 0.025) but not with free T4.

The age of gestation by weeks (during third trimester) was not correlated with any of thyroid biochemical parameters. Anti TPO was not correlated with any of thyroid biochemical parameters nor with the number of abortion or parity or age of gestation (Table 2).

Discussion

The mean TSH during third trimester in the study participant was (3.33 ± 1.34 mIU/L) TSH range during third trimester according to 5% to 95% percentile was (0.88 to 5.52 mIU/L). In India there is a conflicting result, An early Indian study show that TSH values of 0.6 to 5.0 mIU/L in the first, 0.44 to 5.78 mIU/L in the second and 0.74 to 5.7 mIU/L in the third trimester. They used 5th to 95th percentile as normal reference range [12].

Table 2: Illustrate the correlation statistics of anti TPO with different study variables in pregnant females in their third trimester.

		TSH	**T3**	**Age**	**T4**	**NO. abortion**	**FT4**	**weeks of gestations**	**Parity**
Anti TPO	Pearson Correlation	-0.079	-0.133	-0.046	-0.029	-0.121	-0.006	0	-0.098
	Sig. (2-tailed)	0.358	0.123	0.597	0.734	0.61	0.943	0.996	0.258
		TSH	**T3**	**Age**	**T4**	**NO. abortion**	**FT4**	**weeks of gestations**	**Parity**
Anti TPO	Pearson Correlation	-0.079	-0.133	-0.046	-0.029	-0.121	-0.006	0	-0.098
	Sig. (2-tailed)	0.358	0.123	0.597	0.734	0.61	0.943	0.996	0.258

While a recent systematic review included data from eight Indian studies, stated that TSH cutoffs of up to 5 to 6 mIU/L similar to pre pregnancy stage should be used in all trimesters of pregnancy [13]. TSH reference ranges in large population based Chinese study by taking the 2.5th and 97.5th percentiles were 0.03 mU/L to 3.52 mU/L and 0.39 mU/L to 3.67 mU/L, and the FT4 reference ranges were 11.7 pmol/L to 19.7 pmol/L and 9.1 pmol/L to 14.4 pmol/L, in the first and third trimester, respectively [14].

The range during third trimester according to 5% to 95% percentile for free T4, total T4, total T3 were (12 to 22.5 pmol/L), (61.6 to 181.2), (1.02 to 3.2) respectively. Actually this controversy can lead either to under or over estimation of thyroid dysfunction during pregnancy.

Considering the ATA guidelines 2017 upper cutoffs for TSH in pregnancy which equal to (4 mU/L) around 36.2% in our study participants have Subclinical Hypothyroidism (SCH) while if we take our cutoffs range of our results (5.52 mU/L) only 4.8%| should be diagnose as subclinical hypothyroidism. The ATA recommend that the lower cutoff value should be in pregnancy either 0.1 mU/L or 2.5% of the local pregnancy reference range, the 2.5% TSH level of our study sample was 0.21 mU/L, consequently the rate of sub clinical hyperthyroidism depending of our cutoff level will be 0.5% while depending on 0.11 mU/L level will be 0%. As regard to FT4 level, application of ATA 2017 guidelines or results of our cutoff value will diagnose same rate of clinical hypothyroidism and hyperthyroidism (3.3%, 4.8%) respectively in our study participants.

Our result is comparable to results (Zhang et al. [15]) in Nanjing pregnant women which reveal the trimester-specific reference ranges in Nanjing was in the 3rd trimester. as follows: TSH 0.55 to 4.91 mIU/L, FT4 11.38 to 19.21 pmol/L, TT4 83.54 to 258.12 nmol/L according to the TSH reference range recommended by (ATA), the prevalence of subclinical hypothyroidism, subclinical hyperthyroidism, hyperthyroidism, hypothyroxinemia, and thyroid peroxidase antibody-positive were 12.42%, 0.50%, 0.99%, 1.61%, and 11.80%, respectively, prevalence according to the trimester-specific reference range were 1.99%, 0.25%, 1.61%, 0.37%, and 1.61%, respectively, which showed elevated hypothyroxinemia incidence and declined incidence of subclinical hypothyroidism and hyperthyroidism [15].

Interestingly the number of abortion in our study was strongly correlated with TSH level at third trimester (Pearson correlation = 0.269, P value = 0.000) and also with number of parity (Pearson correlation = 0.172, P value = 0.013) but not with anti TPO level.

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