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Original Research Article

Urinary iodine level assessment during third trimester in a sample of Egyptian pregnant women and its relation to thyroid function

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ABSTRACT

Background: Inadequate intakes of iodine during pregnancy may cause thyroid dysfunctions that adversely affect pregnancy outcomes. Aim of the work was to evaluate the urinary iodine level as a marker of iodine status in a sample of Egyptian pregnant women during 3rd trimester and assess its relation to thyroid functions.
Methods: This cross-sectional study was conducted on 100 pregnant females at their 3rd trimester aged (18-35) years. They were divided according to their urinary iodine concentration into 3 groups; Group (I): Pregnant females with deficient iodine (<150 µg/l), Group (II): Pregnant females with adequate iodine (150-249) µg/l, Group (III): pregnant females including who have above requirements (250-499 µg/l), and excessive (≥500 µg/l). TSH, free t4, free t3, Anti-Thyroglobulin (TgAb) and anti-thyroid perioxidase (TPOAb), medium urinary Iodine concentration (UIC) by ELISA and neck U/S were performed to all participants.
Results: 18% of the pregnant women in our study had iodine deficiency during 3rd trimester (UIC<150 ug/l) whereas 55% of pregnant women had excess iodine level, and adequate iodine level was observed in 27%. Serum TSH was significantly higher in group I with deficient iodine level (p value<0.01). All pregnant women included at group I were suffering from subclinical hypothyroidism. Serum TSH and thyroid volume were inversely correlated with urinary iodine among pregnant females at 3rd trimester (p value<0.01).
Conclusions: Serum TSH and thyroid volume were inversely correlated with urinary iodine level among pregnant females at 3rd trimester.

Keywords: Pregnant, TSH, Thyroid volume, Urinary iodine

INTRODUCTION

Iodine is a fundamental trace element for thyroid hormones production.[1] Iodine deficiency is a significant public health problem; worldwide. Although iodine deficiency was historically marked as a problem of developing nations, observing studies have recently showed rising prevalence of iodine deficiency in developed and industrialized nations.[2] Iodine status during pregnancy impacts maternal thyroid homeostasis.[3] Iodine deficiency during Pregnancy and early neonatal period may adversely affects fetal brain development. While the most observable outcome of iodine deficiency is goiter, health outcomes rely on the degree of iodine deficiency, where moderate-to-severe iodine deficiency during pregnancy increases rates of maternal and neonatal complications specially stillbirth, spontaneous abortion, small for gestational age, and increases perinatal mortality. Newborn of iodine deficient mothers are at increased risk for neurocognitive dysfunctions, with

endemic cretinism being the most severe manifestation caused by in utero irreversible neurodevelopment damage.[1]

Hence, an adequate consumption of dietary iodine during gestation, breastfeeding and early childhood period is essential for ensuring appropriate neurodevelopment and growth of the fetus/newborn. Iodine requirement during pregnancy should be increased to meet the 50% increase in maternal thyroxine synthesis, iodine renal losses and transfer of this micronutrient to the feto-placental unit.[3]

The American Thyroid Association (ATA) recommended increasing the daily iodine supplementation for all pregnant women of at least 250 µg/day. Women who are planning pregnancy should receive iodine supplement 3 months prior the planned pregnancy.[4]

Urine iodine concentration (UIC) is the optimal way to evaluate iodine sufficiency from the diet because 90% of dietary iodine is excreted by the kidney.[5] Therefore, UIC is an excellent marker of recent iodine intake in general population. UIC is assayed in spot urinary samples and termed as a median due to the extreme variability of spot urine samples.[6] The World Health Organization (WHO) revealed that UIC of 100–199 µg/l and 100 and 299 µg/l define adequate iodine nutrition status for adults and non-pregnant women respectively.[5] This UIC of 100–199 µg/l corresponds nearly to a daily iodine consumption of 150 µg/day for adults.[5]

Aim of the work was to assess the urinary iodine concentration as a marker of iodine status in a sample of Egyptian pregnant women during 3rd trimester and assess its relation to thyroid functions.

METHODS

This was cross sectional study was conducted on 100 pregnant females at their 3rd trimester aged (18-35) years, selected from Obstetric out-patient clinics of Ain shams University Hospitals while they were attending their routine antenatal appointment between May 2019 and November 2019. They were divided according to their urinary iodine level into 3 groups; Group (I): Pregnant females with deficient iodine level (<150 µg/l), Group (II): Pregnant females with Adequate iodine level (150-249) µg/l, Group (III): pregnant females including who have above requirements (250–499 µg/l), and excessive (≥500 µg/l).

All pregnant females recruited in this study were subjected to full medical history taking and clinical examination. Gestational age was calculated from the first day of the last normal menstrual period, and gestational age ≥28 weeks defined the third trimester of pregnancy. TSH, free t4, free t3, thyroid autoantibodies ((TgAb and TPOAb), medium urinary Iodine level by ELISA and neck U/S were performed to all participants. Patients taking iodine containing supplements at time of enrolment, those with known thyroid or any other chronic illness, multifetal pregnancies were excluded.

Informed consent was obtained from all participants included in the study. Ethical approval was obtained from Ain Shams University, Faculty of Medicine, research Ethics Committee FWA00017858.

Whole venous blood samples were collected after an overnight fast from all subjects. Blood samples were centrifuged to separate serum for the measurement of: Serum TSH, FT4, FT3 levels using Chemiluminescence Immunoassay (Roche Modular Analytics® E170) and thyroid autoantibodies (TPOAb and TgAb) by ELISA

We used American Thyroid Association third trimester-specific reference ranges for TSH value during pregnancy (3rd trimester TSH: 0.3–3.0 mIU/L).[4] We applied the new criteria proposed by the American Thyroid Association to define subclinical hypothyroidism (SCH) as serum TSH ≥3 mIU/l accompanied by a normal serum FT4 concentration in both trimesters.[4]

A midstream urine was collected from each patient using a sterile container. Centrifuge for 20 minutes at the speed of 2000-3000 rpm. Collect supernatant, if precipitation appeared, centrifuge again. Fluid samples were stored at -80°C to avoid loss of bioactivity and contamination. Iodine status during pregnancy was classified according to the WHO as follows: insufficient: <150 µg/l; sufficient: 150-249 µg/l; more than adequate: 250–499 µg/l; excessive: ≥500 µg/l.[7]

For determination of thyroid volume by US, longitudinal and transverse scans are performed to measure the depth (d), the width (w) and the length (L) of each lobe. The volume of the lobe is calculated by the formula: V (ml) = 0.479 × d × w × l (cm). The thyroid volume is the sum of the volumes of both lobes. The volume of the isthmus is not included.

Statistical analysis

Data were analyzed using IBM© SPSS© Statistics version 23 and MedCalc© version 15. Quantitative data were expressed as Mean±SD; qualitative data were expressed as number and percent of total. Comparative analysis was done using Student t test and Chi square tests for quantitative and qualitative data, respectively. Correlations were done with Pearson's product-moment correlation coefficient. The significance of the test was determined according to the p value to be: Non-significant (N.S) if $p>0.05$; Significant (Sig) if $p<0.05$; highly significant (H.S) if $p<0.01$

RESULTS

All participants were matched for age, BMI, and Gestational age. According to WHO criteria for iodine status: 18% of all participants included in our study had

iodine deficiency, and 55% have excess iodine status, and only 27% had the adequate iodine status Table 1.

There was a high statistical significant difference between the studied groups as regards TSH (p value<0.01), being the highest in group I (4.27 uIU/ml) followed by group II (2.70 uIU/ml), and group III (0.53 uIU/ml). Regarding FT4, there was a high statistical significant difference between the studied groups (p value <0.01), being the highest in group III (1.64±0.11 ng/dl) followed by group II (1.36±0.08 ng/dl), group I (1.07±0.10 ng/dl). While there was no statistically significant difference between the studied groups regarding FT3 (p value>0.089) Table 1.

Table 1: Comparison between the 3 studied groups regarding descriptive and laboratory data.

Variable		Group I Deficient No. = 18	Group II Adequate No. = 27	Group III Above requirement and excessive No. = 55	Test value	P value	Sig.
Age (years)	Mean±SD	29.83±4.27	27.07±4.64	29.00±4.37	2.523	0.085	NS
	Range	22-35	19-34	21-35			
BMI (kg/m^2)	Mean±SD	26.39±2.63	26.73±2.28	27.17±1.93	1.08	0.344	NS
	Range	20-29.4	21.5-29.9	22.1-30			
Gestational Age (weeks)	Mean±SD	32.94±3.28	33.07±3.16	33.31±3.27	0.105	0.9	NS
	Range	28-38	28-38	28-38			
FT3 (pg/ml)	Mean±SD	2.9±0.39	3.13±0.36	3.17±0.42	2.47	0.089	NS
	Range	2.9–3.42	2.58–3.62	3.01–4.29			
FT4 (ng/dl)	Mean±SD	1.07±0.10	1.36±0.08	1.64±0.11	243.979	0.01	S
	Range	0.89-1.21	1.22-1.48	1.29-1.81			
TSH (uIU/ml)	Median (IQR)	4.27 (3.95-4.52)	2.70 (2.55-2.85)	0.53 (0.33-1.56)	194.522	0.01	S
	Range	3.51-5.11	2.15–3.86	0.17-3.13			
Anti-TPO (IU/ml)	Median (IQR)	7.93 (6.6-12.3)	8.2 (6.7-11.2)	10.65 (7.2-12.9)	2.405#	0.3	NS
	Range	4.85–52.05	5.25-60.25	3.95-65.15			
Anti-TG (IU/ml)	Median (IQR)	13.65 (10.1-6.2)	11 (9.8-12.7)	12.9 (9.8–26.4)	4.111#	0.128	NS
	Range	9.1–33.8	8.2-95	7.9-93.5			
Urinary Iodine (µg/l)	Median (IQR)	126.24 (83.53-138.92)	194.15 (168.26-230.31)	476.14 (377.09 – 1363.05)			
	Range	52.51-147.92	151.55-266.11	282.39– 2046.7			

Table 2: Thyroid dysfunction among the studied groups.

Thyroid dysfunction		Group I Deficient (n=18)	Group II Adequate (n=27)	Group III Above requirement and excessive (n=55)
Subclinical	No. of pregnant	18	3	0
Hypothyrodism	Range of TSH	3.9 - 5.1	3.09 - 3.86	-
Euthyrodism	No. of pregnant	0	24	51
	Range of TSH	-	2.15 – 2.91	0.309 - 3.1
Subclinical	No. of pregnant	0	0	4
Hyperthyrodism	Range of TSH	-	-	0.17 - 0.297

There was a non-statistically significant difference between the studied groups regarding Anti-TPO and Anti-TG level (p value>0.05) Table 1. All pregnant women included in group I (Iodine deficient) are suffering from subclinical hypothyroidism; TSH ≥3 mIU/l according to the new criteria proposed by the American Thyroid Association to define subclinical hypothyroidism 4 while Group II included only 3 pregnant women with Subclinical Hypothyroidism and Group III included 4 pregnant women suffering from Subclinical Hyperthyroidism TSH ≤0.3 mIU/l Table 2.

Table 3: Comparison between 3 studied groups regarding total thyroid volume.

Comparison between 3 studied groups		Group I	Group II	Group III	Test value	P value	Sig.
		Deficient	Adequate	Above requirement and excessive			
		(n=18)	(n=27)	(n=55)			
Total thyroid volume (ml)	Mean±SD	11.72±2.24	7.77±1.94	6.11±1.48	68.728	0.01	S
	Range	5.31-16.15	4.45-10.18	4.01-10.27			

As regards Total Thyroid Volume, there was a high statistical significant difference between the studied groups (p value<0.01), being the highest in group I (11.72±2.24 ml) followed by group II (7.77±1.94 ml), group III (6.11±1.48 ml) Table 3.

DISCUSSION

Dietary iodine supplementations during pregnancy should be increased to meet the higher requirements needed for increasing thyroid hormone synthesis, increased urinary iodine excretion, and fetal iodine requirements during pregnancy necessitate.[4,8] Ladies with sufficient iodine consumption before and during gestation have satisfactory intrathyroidal iodine stores required for increasing thyroid hormone production throughout pregnancy which are necessary for neuronal migration, myelination, and fetal brain development.[9]

Insufficient dietary iodine intake has maternal and fetal detrimental effects specially, the fetal neurocognitive function. iodine deficiency in pregnant females may result in reduction of maternal and fetal thyroid hormone synthesis which enhance pituitary TSH production, resulting in maternal and fetal thyroid growth and goiter.[1,7,10] Moreover, severe iodine deficiency during gestation has been correlated with increased rates of abortion, stillbirth, and higher perinatal mortality.[11]

Globally, iodine deficiency is the principal cause of preventable intellectual impairment. Offspring of mothers who were severely iodine deficient during gestation possibly will exhibit cretinism, characterized by marked intellectual dysfunction, deafness and delayed develomental milestone.[7] The best method for evaluation of dietary iodine adequacy is urine iodine concentration (UIC), since 90% of dietary iodine is excreted by the kidney.[5] The present study aimed to evaluate the urinary iodine level as a marker of iodine status in a sample of Egyptian pregnant women during 3rd trimester and assess its relation to thyroid functions.

Our study was conducted on 100 pregnant females at 3rd trimester aged (18-35 years). The participants were assigned into 3 groups based on UIC. Group I: pregnant women with iodine deficiency included 18 females, Group II: pregnant women with adequate iodine level included 27 females, Group III: pregnant women who have above requirement and excess iodine level included 55 females.

Our study found that 18% (n=18) of pregnant women during 3rd trimester had iodine deficiency (UIC<150 ug/l) whereas most of pregnant women 55% (n=55) had excess iodine level, and adequate iodine level was observed in 27% (n=27). Iodine deficiency prevalence is still high in many regions of Egypt despite the implementation of a universal salt iodization program since 1996 12 and Demographic Health Survey (DHS) in 2008, disclosed that generally, 79% of Egyptian families were using adequately iodized salt.[13]

In this study, the higher prevalence excess iodine level (UIC more than 250 µg/l) in our study participants could be referred to the trend for decrease iodine excretion with advancing gestation as in our study population consistent with earlier reports from Iran, Sri Lanka, and Switzerland.[14-16] Moreover, these findings could reflect a significant improvement in iodized salt utilization in Egypt.

In the current study, there was a statistical significant difference between the 3 studied groups regarding FT4 and TSH (p value<0.01) and UIC was positively correlated with serum free T4 and inversely correlated with serum TSH. Group I with deficient iodine status had lower FT4 and higher TSH level compared to group III with excess iodine status who had higher FT4 and lower TSH level. Whereas. FT3 did not differ significantly among the 3 studied groups (p value>0.363).

The results of our study was agreed with a Chinese study which described that pregnant women with a low iodine concentration during were 2.4 times more likely to develop hypothyroxinemia vs. women with a higher iodine concentration, whereas a high iodine concentration during pregnancy was related to risk for thyrotoxicosis.[17] Similarly, an Iranian study conducted on 203 pregnant women at third trimester, assessing UIC and thyroid function, categorized according to UIC into 2 groups:- groups I and II (UIC <150 µg/liter and UIC >150 µg/liter respectively), showed a statistical significant difference between studied groups as regard TSH, as group I had the higher level of TSH and group II had the lower level of TSH.[14]

Interestingly, inconsistent results were reported from studies investigating the correlation between median UIC in pregnant females and maternal thyroid function. Farebrother et al showed a non-statistically significant difference between pregnant females with deficient, adequate or excess iodine status as regard FT4 and TSH. whereas, Abel et al, a study conducted on 2910 pregnant women in Norway who were classified according to UIC into 2 groups deficient 0-150µg/l and sufficient >150µg/l, stated that pregnant women with the lower UIC had the higher FT4 which was the opposite of our study.[18-19] Similarly, Our results disagreed with those reported by Fuse et al who found no correlation between UIE and thyroid function parameters in Japanese pregnant women, in an iodine sufficient area.[20]

In this study, all pregnant women with UIC <150 µg/l (Iodine deficient) have Subclinical hypothyroidism; TSH ≥3 mIU/l according to the new criteria proposed by the American Thyroid Association to define subclinical hypothyroidism while Group II included only 3 pregnant women with subclinical hypothyroidism, whereas 4 (7%) of pregnant women with UIC ≥250 µg/l in Group III have subclinical hyperthyroidism TSH ≤0.3 mIU/l.[4]

This agreed with a previous Egyptian study conducted for assessment of thyroid function in Egyptian pregnant women and it was reported that most of pregnant women (51%) had normal thyroid functions, while subclinical hypothyroidism (39%) was the most prevalent disorder.[21] Similarly, Du et al. a Chinese study conducted on 3rd trimester pregnant females. This study reported that 19.7% of pregnant women with excessive iodine (UIC >500 µg/l) had subclinical hyperthyrodism.[22]

Iodine deficiency results in impaired thyroid hormone production causing hypothyroidism and goiter because despite an increase in thyroid activity to maximize iodine uptake and recycling in this setting, iodine concentrations are still too low to enable production of thyroid hormone 1while thyrotoxicosis has been previously noted following iodine replenishment in iodine-deficient population, and iodine induced Thyrotoxicosis is a well known consequence folllowing the introduction of salt iodization and excess iodine intake.[23,24]

Our study showed no statistically significant difference among the studied groups regarding Anti-TPO level and Anti-TG level which goes in line with several studies.[14,20,25]

Our study showed a significant negative correlation between urinary iodine level and thyroid volume among pregnant females whereas the largest thyroid volume was at the iodine deficient group followed by less thyroid volume at adequate group and then the excess iodine group has least thyroid volume (p value<0.01). This was consistent Gyamfi et al and Mezosi et al reported that the frequency of thyroid enlargement was higher in iodine deficiency group.[26,27]

A persistent low dietatry consumption of iodine may trigger thyroid gland enlargement in pregnant women in order to trap iodine attempting to maintain required plasma concentrations of thyroid hormones.[28,29]

CONCLUSION

Iodine deficiency prevalence is still high in Egyptiant pregnant women despite the application of a universal salt iodization program since 1996 and this consequently could lead to detrimental maternal and fetal complications. Iodine deficiency is the principal cause of preventable intellectual impairment all over the world therefore screening of maternal iodine concentration during pregnancy need to be reinforced by a simple screening test like urinary iodine concentration which is the best method for evaluation of dietary iodine adequacy and adequate iodine supplementation should be maintained during pregnancy without risks of iodine excess or deficiency.

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