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Original article

Prevalence of Thyroid Disorders among Pregnant Women in Benha City, Egypt, a Hospital Based Cross Section Study

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Abstract

Background: Thyroid disorders rank as one of the prevailing endocrine disorders frequently observed during the course of pregnancy. **Aim of the work**: This study assessed the thyroid disorders frequency among pregnant women residing in Benha City, Egypt, elucidating the types of disorders, their distribution across trimesters, and potential correlations with demographic factors, obstetric history, and thyroid function test results. **Methods:** This Cross-section study included 173 pregnant females with abnormal thyroid function. A comprehensive history, and a thorough clinical examination- were conducted [demographic data, drugs, obstetric history, previous pregnancy outcome& complication, manifestation on thyroid dysfunction and family history of thyroid diseases], lab investigation [serum TSH serum freeT3 & serum freeT4, TSH value of American Thyroid Association (ATA) 2011]. **Results**: According to abortion history, overt hyperthyroidism is more likely to have a higher number of abortions compared to those with gestational or subclinical hyperthyroidism (p=0.007). There was significant higher median number of abortions in overt hyperthyroidism group compared with gestational hyperthyroidism group (p=0.033), although a significant higher median number of abortions in overt hyperthyroidism group compared with subclinical hyperthyroidism group (p=0.002). Overt hypothyroidism was more likely to have a higher number of abortions compared to those with isolated maternal hypothyroxinemia or subclinical hypothyroidism (p<0.001). **Conclusion:** Demographic factors and obstetric history showed limited associations with the types of thyroid disorders. However, specific thyroid function test parameters [TSH, Free T3, and Free T4] revealed significant correlations with various subtypes of thyroid disorders, showing their diagnostic relevance in identifying and characterizing these conditions during pregnancy.

Keywords: Thyroid Disorders; Pregnant Women; Demographic Factors; Obstetric History.

Introduction

Thyroid disorders are frequently encountered endocrine conditions that are detectable throughout the course of pregnancy. Thyroid dysfunction may arise when the mother fails to adapt adequately to the fluctuations in thyroid function inherent to pregnancy. Factors such as an elevation in thyroglobulin levels resulting from increased estrogen and human chorionic gonadotrophin, modifications in maternal thyroid hormone peripheral metabolism, renal excretion of iodine due to heightened glomerular filtration rate and shifts in iodine transport to the placenta- collectively contribute to these alterations. During the course of pregnancy, there is a notable 50% increase in both the production of thyroid hormones and the demand for iodine (1).

Maternal thyroid dysfunctions exert a significant influence on a myriad of outcomes for both the fetus and the mother (2).

Addressing thyroid disorders in women of reproductive age prior to conception- is of the utmost importance. Hypothyroidism that is not clinically apparent is detected in 2.3% of pregnant women, compared to 0.2% of cases involving overt hypothyroidism (3).

Overt hyperthyroidism commonly leads to complications such as pre-eclampsia, fetal growth restriction, fetal loss, and preterm delivery. Fetal and maternal outcomes have been associated with thyroid disorders that occur in early pregnancy. Fetal complications include low birth weight, prematurity, stillbirth, and perinatal mortality, while, key obstetric complications encompass placental abruption, pre-eclampsia, miscarriage, and premature labor. Offspring born to mothers who are not treated for thyroid disorders can encounter substantial long-term consequences in terms of their intellectual development. Adverse consequences, both occurring during pregnancy and after childbirth, such as attention deficit and hyperactivity syndrome- have been documented in offspring born to mothers afflicted with hypothyroidism (4, 5).

The occurrence of thyroid disorders during pregnancy demonstrates notable geographic diversity. According to Western literature, pregnancy-related hypothyroidism is estimated to affect 2.5% of cases, while the prevalence of hyperthyroidism during pregnancy ranges from 0.1% to 0.4% (6). Insufficient evidence exists on the prevalence of thyroid problems in pregnant women in Egypt. The available data indicates that the prevalence of this condition among pregnant women in Egypt ranges from 4.8% to 11% (6, 7). Benha City is characterized by a diverse population encompassing various cultures and ethnicities. In a preliminary study conducted in Benha City, involving first-trimester pregnant women, a concerning finding emerged, with 43% of the participants experiencing hypothyroidism, including both subclinical and overt forms. This prevalence rate is notably elevated compared to findings in other

studies. Given the well-documented adverse maternal and fetal consequences associated with thyroid disorders during pregnancy- coupled with the evident advantages of early detection and intervention- numerous expert panels worldwide have advocated for the routine screening of thyroid function for every pregnant woman.

The principal goal of this investigation- was to assess the frequency of thyroid disorders among expectant mothers residing in Benha City, Egypt, elucidating the types of disorders, their distribution across trimesters, and potential correlations with demographic factors, obstetric history, and thyroid function test results.

Patients and Methods

This prospective observational study, conducted as a randomized cohort, involved 173 pregnant women exhibiting abnormal thyroid function who attended outpatient clinic at Benha university hospital for antenatal care, during the period from August 2022 to August 2023.

Prior to enrollment in the study, informed consent was acquired from each patient, and approval from the Research Ethics Committee at Benha Faculty of Medicine- was granted (Approval code: Ms-10-8-2022).

Inclusion criteria were pregnant females, patient not known to have thyroid disorder before pregnancy, and the age ranged of patients was 18-40 years.

Exclusion criteria were patients below 18 years and above40 years, and with acute illness or chronic disease which might affect thyroid function, e.g. collagen disease, infection, heart disease, liver disease, CKD.

All studied cases were subjected to the following: all thorough history taking &clinical examination was performed to patient with special stress on; demographic data (marital status, residence & occupation), drugs, obstetric history, previous pregnancy outcome & complication, manifestation on thyroid dysfunction and family history of thyroid diseases, **lab investigation [** serum TSH serum freeT3 & serum freeT4, TSH value of American Thyroid Association (ATA) 2011].

Thyroid hormones assessment (TSH-free t3-free t4)

Blood specimens were aseptically obtained from patients via venipuncture, with 5.0 ml deposited into a vial. A quantity of 2 to 3 ml was reserved in a test tube for coagulation for a duration of 15 minutes. Subsequently, the samples underwent centrifugation at 5000 rpm for 10 minutes. The resulting supernatant serum was isolated and preserved at -70°C until the time of analysis.

The measurement of Serum Free Thyroxine (FT4), Serum Thyroid Stimulating Hormone (TSH), and Serum Free Triiodothyronine (FT3) levels- was conducted using the Accu-Bind ELISA

kit, supplied by Monobind Inc. based in Lake Forest, CA 92630, United States.

ELISA technique

The collected samples were initially stored in a refrigerated environment at 2-8°C, with a maximum storage duration of 5 days. If it was not feasible to analyze the specimens within this timeframe, they were subsequently preserved at temperatures as low as -20°C for a period of up to 30 days. To prevent potential degradation, efforts were made to avoid repetitive freezing and thawing of the samples. During the duplication of assays, 0.100 ml of the specimen was utilized.

The test procedure, executed by a trained professional or proficient individual entailed formatting microplate wells to accommodate serum control, reference, and patient specimens in duplicate, pipetting 0.050 ml (50 µL) of the appropriate samples, adding 0.100 ml (100 µL) of Enzyme Reagent, incubating for 60 minutes at room temperature, followed by decantation or aspiration, three washes with 0.350 ml (350 µL) of wash buffer, incubating with 0.100 ml (100 µL) of working substrate solution for 15 minutes, adding 0.050 ml (50 µL) of stop solution, and finally, reading absorbance at 450nm with a reference wavelength of 620-630nm using a microplate reader. Ensuring results were read within 30 minutes of adding the stop solution while avoiding repetitive freezing and thawing of samples and storing them at 2-8°C for up to five days or at -20°C for a maximum of 30 days if necessary.

Statistical analysis

Statistical analysis was performed using SPSS Version 25.0 (IBM Corp., Armonk, NY). Quantitative variables were represented as mean and standard deviation (SD). To determine the significance of differences between two study group means, the Student's T Test was employed. For comparing more than two study group parametric variables, the One-way ANOVA test was applied. Categorical variables were assessed using the Chi-square test and presented as frequencies and percentages (%). The strength of correlation between two numerical variables was assessed using Spearman's correlation. Statistical significance was defined as a two-tailed P value less than 0.05.

Results

Hyperthyroidism was observed in 50 cases, representing 28.90% of all patients with abnormal thyroid function tests. Subclinical hyperthyroidism was observed, accounting for 17.34% of all abnormal thyroid function cases. Among these patients, 14 (28%) had overt hyperthyroidism, 6 (12%) had gestational hyperthyroidism and 30 (60%) had subclinical hyperthyroidism. On the other hand, hypothyroidism was observed in 123 cases, representing 71.10% of all patients with abnormal thyroid function tests. Overt hypothyroidism was the most prevalent subtype observed, accounting for 60.2% of all abnormal thyroid function cases (**Table 1).**

No significant association was found between gestational age and subtype of thyroid disorder (**Table 2).**

The studied cases had a mean age of 28.1 years with a standard deviation of 5.9 years. The age distribution of the subjects ranged from 18 to 42 years. The average BMI of the subjects was 27.83 kg/m2 with a standard deviation of 3.84 kg/m2. The median BMI was 27.9 kg/m2, with a range of 20.3 to 36.4 kg/m2. The table also shows that 81 of the cases (46.8%) were from urban areas, while 92 cases (53.2%) were from rural areas.

The differences in pregnancy duration and the number of previous pregnancies- were not statistically significant between the two groups.

In the three groups, there were no notable distinctions in the number of pregnancies and pregnancy duration. According to abortion history, overt hyperthyroidism is more likely to have a higher number of abortions compared to those with gestational or subclinical hyperthyroidism (p=0.007). Pairwise comparison showed significant higher median number of abortions in overt hyperthyroidism group compared with gestational hyperthyroidism group (p=0.033), although a significant higher median number of abortions in overt hyperthyroidism group compared with subclinical hyperthyroidism group (p=0.002) (**Table 3).**

There were no notable disparities in the duration of pregnancy and number of pregnancies between the three groups. According to abortion history, overt hypothyroidism was more likely to have a higher number of abortions compared to those with isolated maternal hypothyroxinemia or subclinical hypothyroidism (p<0.001). Pairwise comparison showed significant higher median number of abortions in overt hypothyroidism group compared with subclinical hypothyroidism group (**Table 4).**

Table 1: Classification of thyroid disorders in the studied cases

	Total subjects (№=173)
Type of thyroid disorder	**Count (%)**
Hyperthyroidism	50 (28.9%)
Gestational hyperthyroidism	6 (12%)
Overt hyperthyroidism	14 (28%)
Subclinical hyperthyroidism	30 (60%)
Hypothyroidism	123 (71.1%)
Isolated maternal hypothyroxinemia	2 (1.6%)
Overt hypothyroidism	74 (60.2%)
Subclinical hypothyroidism	47 (38.2%)

Table 2: Association between pregnancy trimester and subtypes of thyroid disorders in studied cases.

	Trimester						
	First		Second		Third		*p*
Type of thyroid disorder	**N**	**%**	**N**	**%**	**N**	**%**	
Hyperthyroidism							
Gestational hyperthyroidism	3	50%	3	50%	0	0%	0.579
Overt hyperthyroidism	6	42.9%	8	57.1%	0	0.0%	
Subclinical hyperthyroidism	16	53.3%	12	40.0%	2	6.7%	
Hypothyroidism							
Isolated maternal hypothyroxinemia	2	100%	0	0%	0	0%	0.206
Overt hypothyroidism	29	39.2%	36	48.6%	9	12.2%	
Subclinical hypothyroidism	15	31.9%	22	46.8%	10	21.3%	

Table3: Comparison of obstetric history between subtypes of hyperthyroid patients.

		Hyperthyroidism				
Variable		**Gestational n=6**	**Overt n=14**	**Subclinical n=30**	***p***	Pairwise comparison
Pregnancy duration (month)	Mean±SD	3.7 ± 0.8	3.9 ± 0.9	4.0 ± 1.6	P=0.936	p1=0.858
	Median	3.5	4.0	3.0		p2=0.928
	(Range)	(3.0 - 5.0)	(3.0 - 6.0)	(2.0 - 8.0)		p3=0.134
gravity	Mean±SD	3.0 ± 0.9	3.4± 1.9	3.3± 1.7	P=0.977	p1=0.961
	Median (Range)	3.0	3.0	3.0		p2=0.888
		(2.0 - 4.0)	(1.0 - 7.0)	(1.0 - 7.0)		p3=0.944
Number of abortions	Mean ±SD	0.3± 0.8	1.3 ± 1.1	0.4± 0.7	P=0.007*	p1=0.033*
	Median (Range)	0.0	1.0 (0.0 - 4.0)	0.0 (0.0 - 8.0)		p2=0.782
		(0.0 - 2.0)				p3=0.002*
No	**Count (%)**	5 (83.3%)	3 (21.4%)	20 (66.7%)	0.026*	p1=0.029*
Once	**Count (%)**	0 (0.0%)	6 (42.9%)	7 (23.3%)		p2=0.407
Recurrent (≥2)	**Count (%)**	1 (16.7%)	5 (35.7%)	3 (10.0%)		p3=0.015*

*: Significant ≤0.05; p1= Mann-Whitney test between gestational hyperthyroidism and overt hyperthyroidism; p2= Mann-Whitney test between gestational hyperthyroidism and subclinical hyperthyroidism; p3 = Mann-Whitney test between overt hyperthyroidism and subclinical hyperthyroidism

Table 4: Prevalence of organic causes in the studied patients according to the individual alarming features

		Hypothyroidism				
Variable		**Isolated Maternal n=2**	**Overt n=74**	**Subclinical n=47**	***p***	**Pairwise comparison**
Pregnancy duration (month)	Mean±SD	3.0± 0.0	4.2 ± 1.9	4.7 ± 1.7	0.111	p1=0.523
	Median	3.0	4.0	5.0		p2=0.274
	(Range)	(3.0 - 3.0)	(2.0 - 9.0)	(2.0 - 7.0)		p3=0.072
gravity	Mean±SD	2.0 ± 0.0	3.1 ± 1.8	2.2 ± 1.1	0.131	p1=0.409
	Median	2.0	2.5	2.0		p2=0.165
	(Range)	(2.0 - 2.0)	(1.0 - 11.0)	(1.0 - 4.0)		p3=0.071
Number of abortion	Mean±SD	0.0 ± 0.0	1.0 ± 1.5	0.0 ± 0.0	<0.001*	p1=0.467
	Median	0.0	0.0	0.0		p2=1.000
	Range)	(0.0 - 0.0)	(0.0 - 8.0)	(0.0 - 0.0)		p3=<0.001*
No	Count (%)	2 (100.0%)	35 (47.3%)	47 (100.0%)	<0.001*	p1=0.339
Once	Count (%)	0 (0.0%)	22 (29.7%)	0 (0.0%)		
Recurrent	Count (%)	0 (0.0%)	17 (23.0%)	0 (0.0%)		p3=<0.001*

*: Significant ≤0.05; p1= Mann-Whitney test between isolated hypothyroxinemia and overt hypothyroidism; p2= Mann-Whitney test between isolated hypothyroxinemia and subclinical hypothyroidism; p3 = Mann-Whitney test between overt hyperthyroidism and subclinical hyperthyroidism

Discussion

In the current study, out of 1440 pregnant females, 173 individuals were identified with abnormal thyroid function, with an overall prevalence of 12.01%.

In line with our investigation, Gupta et al. reported that out of 865 pregnant women, 90 patients exhibited thyroid disorders, yielding a prevalence rate of 10.4%(8) .

likewise, in a study by Dulek et al., it was observed that among 573 pregnant women, 86.7% exhibited normal thyroid function tests, with a frequency of thyroid dysfunction reaching at 13.2% in their study population (9).

Hyperthyroidism was observed in 3.47% of all cases and representing 28.90% of patients with abnormal thyroid function tests. Subclinical hyperthyroidism was observed, accounting for 17.34% of all abnormal thyroid function cases. Among these patients,28% had overt hyperthyroidism, 12% had gestational hyperthyroidism, and(60%) had subclinical hyperthyroidism. On the other hand, hypothyroidism was observed in 8.54% of all cases and representing 71.10% of patients with abnormal thyroid function tests. Overt hypothyroidism was the most prevalent subtype observed, accounting for 60.2% of all abnormal thyroid function cases.

In line with our findings, it is approximated that roughly 4% of pregnancies are affected by hypothyroidism, with 3.5% categorized as subclinical hypothyroidism and 0.5% as overt hypothyroidism. Conversely, hyperthyroidism is identified in approximately 2.4% of pregnancies, with 1.8% classified as subclinical hyperthyroidism and 0.6% as overt hyperthyroidism (10).

A study found that the prevalence of thyroid dysfunction was 29.3% and 24.62%, respectively. Their findings revealed a cumulative prevalence rate of thyroid-related conditions throughout pregnancy of 33.9%, with hypothyroidism (31.6%) being more frequently diagnosed than hyperthyroidism (2.3%)- which aligns with our own data (11,12).

According to our study, the mean age of the studied cases was 28.1 years with a standard deviation of 5.9 years. The age distribution of the subjects ranged from 18 to 42 years. The average BMI of the subjects was 27.83 kg/m2 with a standard deviation of 3.84 kg/m2. The median BMI was 27.9 kg/m2, with a range of 20.3 to 36.4 kg/m2. 81 of the cases (46.8%) were from urban areas, while 92 cases (53.2%) were from rural areas.

Our findings align with Aboelroose's study, in which the age distribution in the study population encompassed individuals aged 18 to 39 years, with a mean age of 28.5 ± 5 years. A majority, or 60%, of the participants were under thirty years old, and urban residents comprised 72 women. Additionally, 81% of the study population were multigravida, mirroring our own results (13). Similarly, Toloza et al. reported that their study encompassed a

final population of 46,528 participants, with an average maternal age of 29.1 years and a standard deviation of 5.2 (14).

Our work studied the relation between obstetric history and different subtypes of hyperthyroid groups. There was no significant difference in pregnancy duration and gravity between the three groups. According to abortion history, overt hyperthyroidism is more likely to have a higher number of abortions compared to those with gestational or subclinical hyperthyroidism (p=0.007). Pairwise comparison showed significant higher median number of abortions in overt hyperthyroidism group compared with gestational hyperthyroidism group (p=0.033), although a significant higher median number of abortions in overt hyperthyroidism group compared with subclinical hyperthyroidism group (p=0.002).

In accordance with Zhang et al.'s research, the occurrence of autoimmune thyroid antibodies- was significantly more pronounced in the overt hyperthyroidism group (25.6%) when contrasted with both the subclinical hyperthyroidism group (14.2%) and the control group (13.9%) ($p < 0.05$). However, there was no statistically meaningful disparity between the subclinical hyperthyroidism group and the control group. Notably, it was observed that the subclinical hyperthyroidism group had a lower miscarriage rate (1.7% vs. 7.2%; odds ratio [OR] = 0.218, $p = 0.016$) in comparison to the control group. Conversely, the overt hyperthyroidism group exhibited a higher prevalence of placenta previa (3.3% vs. 0.8%; OR = 4.366, $p = 0.039$) when compared to the control group (15).

There were no significant differences in pregnancy duration and gravity between the three groups. According to abortion history, overt hypothyroidism was more likely to have a higher number of abortions compared to those with isolated maternal hypothyroxinemia or subclinical hypothyroidism (p<0.001). Pairwise comparison showed significant higher median number of abortions in the group of overt hypothyroidisms in comparison with subclinical hypothyroidism group (p<0.001).

According to thyroid function tests, there was a significant higher level of TSH in the group of overt hypothyroidisms compared to other hypothyroidism subgroups (p<0.001). Free T3 and Free T4 showed significant higher level in subclinical hypothyroidism group compared to compared to other hypothyroidism subgroups (p<0.001). Pairwise comparison showed significant difference in level of TSH in between the three groups of hypothyroidisms (p1=0.017, p2=0.019, p3<0.001). A significantly higher level of Free T3 in Isolated Maternal Hypothyroxinemia compared to overt hypothyroidism group (p=0.017). A significant higher level of Free T3 in subclinical hypothyroidism compared with overt hypothyroidism (p<0.001). Free T4 showed a significant higher level in subclinical hypothyroid group compared to Isolated Maternal

Hypothyroxinemia (p=0.019) and a significant higher level compared to overt hypothyroidism (p<0.001).
Gong et al. discovered that women who had an IMH detected in the first trimester had a considerably elevated level of TSH compared to the control group ($p < 0.01$) (16).

Unlike T3, T4 is regarded as a more dependable marker when assessing the thyroid function in individuals afflicted with hypothyroidism. An examination of five serum markers in hypothyroid patients (TT4, TT3, FT4, FT3, and TSH)- demonstrated a more robust association between TT4, FT4, and TSH, when compared to the relationship between TT3, FT3, and TSH, aligning with the findings from Castellano's investigation. Notably, TSH emerged as the most pivotal parameter for the diagnosis of hypothyroidism (17).

Conclusion

In conclusion, this study in Benha City, Egypt, examined thyroid issues in pregnant women. It was found that hypothyroidism- especially overt hypothyroidism- was more common than hyperthyroidism. While thyroid function varied during pregnancy trimesters, there were no significant differences in thyroid disorder distribution across different stages of pregnancy. Demographic factors and obstetric history- had limited associations with thyroid disorders. However, specific thyroid function tests (TSH, Free T3, and Free T4) showed significant correlations with various thyroid disorder subtypes, demonstrating their diagnostic importance in identifying and characterizing these conditions during pregnancy.

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