

The Link between Body Mass Index and Maternal Thyroid Autoimmunity in Early Pregnancy

Original Article

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ABSTRACT

Background: Maternal thyroid autoimmunity has hazardous effects on the mother and fetus. There are controversies regarding screening obese women during pregnancy for thyroid antibodies.

Objectives: We investigated the association between body mass index (BMI) in early pregnancy and thyroid peroxidase antibody (TPO Ab).

Patients and methods: We recruited 225 women at 4th-8th weeks of gestation. 75 women of them had normal weight (Group I), 75 were overweight (group II) and 75 had obesity (group III). We investigated Thyroid Stimulating Hormone (TSH), TPO Ab, Anti thyroglobulin antibody (Tg Ab) for all participants and compared them across the 3 groups.

Results: TPO Ab was significantly the highest in obese women and on post hoc analysis, it was significantly more in each of obese, and overweight women compared to ladies with normal BMI. On comparing the 3 groups a significant difference was found as regards the distribution of each of TPO Ab and Tg Ab positivity being the highest in the group with maternal obesity. All participants with normal BMI had normal TPO Ab and Tg Ab antibodies. In the overweight women, 8% had positive TPO Ab and 3% had positive Tg Ab. In women with obesity 16% had TPO positivity and 12% had Tg Ab positivity. TSH was significantly the highest in maternal obesity. BMI was positively correlated with TPO Ab only in obese women.

Conclusion: An association exists between maternal BMI and each of TSH, TPO Ab levels, distribution of TPO Ab and Tg Ab positivity in early pregnancy.

Key Words: Body mass index, early pregnancy, thyroid peroxidase antibody.

Received: 04 May 2025, **Accepted:** 19 June 2025.

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ISSN: 2735-3540, Vol. 76, No. 3, Sep. 2025.

INTRODUCTION

Hypothyroidism affects 3–5% of pregnant women and it is the most common thyroid dysfunction during pregnancy with subclinical hypothyroidism being more prevalent than overt hypothyroidism^[1]. Hashimoto's thyroiditis (HT) is the commonest cause of hypothyroidism in iodine-sufficient areas. TPO Ab and Tg Ab are prevalent in 10–20% of ladies in the reproductive period^[2].

Thyroid autoimmunity increases the possibility of adverse pregnancy outcomes. They could lead to abortion, premature birth, and low IQ even if it's associated with an euthyroid or a subclinical hypothyroid status^[2-4].

Controversies exist about which ladies deserve a screen for TPO Ab in pregnancy^[4]. Some guidelines recommend the autoimmune screen during pregnancy only in obese pregnant women^[5]. There are suggestions that increased body mass index (BMI) predisposes to HT^[6].

THE AIM OF THE WORK

We searched for the association of TPO Ab and BMI in early pregnancy. And explored the distribution of TPO Ab positivity across ladies with different BMI.

ETHICS COMMITTEE

Our work was approved by the Medical Ethics Committee of Ain Shams University MSO 48/2023. All participants provided written informed consent.

SUBJECTS AND METHODS

Participants were recruited from Ain Shams University Hospital and the National Institute of Diabetes and Endocrinology.

The study was conducted on 225 women who were pregnant at the 4th–8th weeks of gestation. We included those aged between 19–40 years and divided the participants according to their BMI in line with World Health Organization (WHO) criteria into three groups, each including 75 subjects. Group I: included women with normal BMI between 18.5 and 24.9 kg/m². Group II consisted of overweight participants with BMI between 25.0 and 29.9 kg/m². Group III: women with obesity with BMI $\geq$ 30.0 kg/m².

We excluded women who were >8 weeks pregnant and patients with a history of thyroid disease or any other chronic diseases. Smokers and patients on any medical regimen that may affect thyroid function, such as glucocorticoids, amiodarone, or antiepileptic drugs were also ruled out.

We took full history and preformed clinical examination with special emphasis on thyroid gland examination, and measurement of weight, and height for all participants. BMI was calculated by dividing weight in kilograms by squared height in meters.

We measured serum TSH for all participants using Calset TSH.

TPO Ab and Tg Ab were measured for all women using NOVA Lite thyroid kits with immunofluorescence

technique. The reference range for TPO Ab was 0–34 IU/mL and Tg Ab was 0–115 IU/mL with TPO Ab considered positive if > 34 IU/mL and Tg Ab positive if > 115 IU/mL.

Statistical Analysis: Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges when parametric distribution. The comparison between groups with qualitative data was done by using Chi-square test. The Analysis of Variance (ANOVA) was used to compare quantitative data between more than two independent groups followed by post hoc analysis using TUKEY'S test, which was used for comparisons of all possible pairs of group means. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. Probability (*p-value*) was considered significant if it was less than 0.05 and considered highly significant if less than 0.001.

RESULTS

Group I included 75 pregnant females with a normal BMI of a mean 21.264 ± 1.908 kg/m² and a mean age of 27.240 ± 4.226 years. Our results showed they all had negative TPO and TgAb antibodies (Table 1).

Group II consisted of 75 overweight pregnant females with mean BMI of 26.284 ± 1.886 kg/m² and a mean of age 27.64 ± 3.55 years. TPO Ab was positive in 8% and Tg Ab positive in 3% (Table 1).

Group III included of 75 obese pregnant females with a mean BMI of 32.320 ± 2.255 kg/m² and a mean age of 29.66 ± 2.150 years and 16% had positive TPO Ab and 12% had Tg Ab positive (Table 1).

Table 1: Distribution of TPO Ab positivity and Tg Ab positivity in each group.

	Groups					
	Group I		Group II		Group III	
	N	%	N	%	N	%
TPO Ab positivity	0	0.00	6	8%	12	16 %
Tg Ab positivity	0	0.00	3	3%	9	12 %

We demonstrated a significant difference between the 3 groups as regards TPO Ab levels being the highest in maternal obesity (group III). Post hoc analysis showed that it was significantly higher in each of overweight women (group II) and those who had obesity (group III) compared

to ladies with normal BMI (group I) but not significantly different between obese and overweight participants as shown in (Table 2). No significant difference was detected between the 3 groups regarding Tg Ab levels.

Table 2: Comparing TPO Ab levels among the 3 groups.

Groups	TPO Ab (Iu/ml)		ANOVA	
	Range	Mean $\pm$ S D	F	<i>P-value</i>
Group I	10-33	23.312 $\pm$ 7.500	5.508	0.005*
Group II	13-36	26.080 $\pm$ 7.050		
Group III	14-37	27.080 $\pm$ 7.050		
TUKEY'S Test				
I&II		I&III	II&III	
0.051 *		0.004*	0.672	

On comparing the 3 groups, we reported a significant difference regarding the percentage of women having positive TPO Ab (Table 3) and as regards percentage of

women having positive Tg Ab (Table 4) being both the highest in subjects with maternal obesity (group III)

Table 3: A comparison between the three groups as regards the distribution of TPO Ab positivity.

TPO	Groups								Chi-Square	
	Group I		Group II		Group III		Total		X ²	P-value
	N	%	N	%	N	%	N	%		
Negative	75	100.00	69	92.00	63	84.00	207	92.00	13.043	0.001*
Positive	0	0.00	6	8.00	12	16.00	18	8.00		
Total	75	100.00	75	100.00	75	100.00	225	100.00		

X² Chi-square test, N-Number

Table 4: Comparison between the three groups studied as regards the distribution of TgAb positivity.

TgAb	Groups								Chi-Square	
	Group I		Group II		Group III		Total		X ²	P-value
	N	%	N	%	N	%	N	%		
Negative	75	100	72	96.	66	88.	213	94.67	11.092	0.004*
Positive	0	0	3	4.	9	12	12	5.33		
Total	75	100	75	100	75	100	225	100		

X² Chi-square test, N-Number

TSH showed a significant difference between the 3 groups being the highest in maternal obesity (group III). Post hoc analysis showed a significant difference between

ladies with normal BMI (group I) and women with maternal obesity (group III) (Table 5)

Table 5: A Comparison of TSH between the 3 groups.

Groups	TSH (mIU/ml)		ANOVA	
	Range	Mean $\pm$ S D	F	P-value
Group I	1.2 - 3.4	2.252 $\pm$ 0. 57	5.078	0.007*
Group II	1.4 - 3.6	2.508 $\pm$ 0. 84		
Group III	1.5 - 3.7	2.588 $\pm$ 0. 82		
TUKEY'S Test				
	I&II	I&III	II&III	
	0.055	0.007*	0.748	

In subjects with maternal obesity (group III), BMI had a positive correlation with anti TPO Ab and no correlation with TSH and anti Tg Ab. However, the other 2 groups (I

and II) had a positive correlation between BMI and Tg Ab but no correlation with TSH, and TPO Ab (Table 6)

Table 6: Correlation of BMI with different parameters in the studied groups.

	Correlations BMI (kg/m ²)					
	Group I		Group II		Group III	
	R	P-value	R	P-value	R	P-value
TSH (mIU/ml)	0.129	0.272	0.069	0.559	0.129	0.270
TPO (IU/ml)	-0.207	0.075	-0.080	0.493	0.264	0.022*
TGAb (IU/ml)	0.290	0.012*	0.268	0.020*	0.141	0.226

DISCUSSION

In our study pregnant women with normal weight had negative anti TPO and TgAb. In overweight pregnant females 8% had positive TPO Ab and 3% had Tg positive Ab. In obese pregnant females TPO Ab positivity was 16% and Tg Ab positivity 12%. A significant difference was noted between the 3 groups regarding the distribution of patients with positive TPO Ab or Tg Ab being the highest with maternal obesity in line with *Marzullo et al.*^[7] who showed greater prevalence of TPO positivity in the obese subjects.

Additionally, our results showed that TPO Ab was significantly the highest in obese women and on post hoc analysis, it was significantly more in women with obesity, and those who are overweight in comparison to ladies having a BMI within normal which agrees with *Han et al.* who found that obesity was linked to thyroid autoimmunity during the period of early pregnancy^[8].

Moreover, in our study BMI had a positive correlation with anti TPO Ab in accordance with *Song et al.*^[9]. There are suggestions that the inflammatory -derived cytokines in obesity could trigger thyroid autoimmunity. Addressing this possibility could offer new targets therapeutic in thyroid autoimmunity and obesity^[10].

We found a significant difference as regards TSH between women with maternal obesity and those with normal BMI which agrees with *Bastemir et al* who on comparing lean and obese women found a higher TSH in obese females^[11] and with other studies which showed that weight affected TSH in early pregnancy^[12]. On the other hand, BMI was not correlated to TSH in women enrolled in our study which disagreed with *Pop et al.* and *Gowachirapant et al.*^[13,14] and disagreed with *Iacobellis et al.* who concluded that BMI and TSH were related positively^[15].

At time there were suggestions that hypothyroidism caused obesity. Yet, the correction of severe hypothyroidism resulted in only minimal weight loss. On the other hand, losing weight after bariatric surgery or low caloric diet significantly reduced TSH. Accordingly, an elevated TSH could be an outcome of increased body weight and not a cause^[16].

Screening for autoimmune disease during pregnancy is still controversial. Some countries choose targeted screening for women with higher risk of thyroid dysfunction^[4]. Many studies suggest that the higher leptin in subjects with increased BMI helps the development of thyroid autoimmunity^[17].

CONCLUSION

We found an association between thyroid autoimmunity in mothers and their BMI early in pregnancy. Our study supports considering screening for thyroid autoimmunity not only in obesity but also in overweight women. Detecting TPO Ab early in pregnancy would indicate closer thyroid function and obstetric follow up to during pregnancy decreasing the risk of thyroid autoimmunity related adverse events in pregnancy. Given that our study was cross-sectional, we recommend further studies to establish causal effect relationship between higher BMI and thyroid autoimmunity

LIST OF ABBREVIATIONS

ANOVA: Analysis of Variance

BMI: Body mass index

TSH: Thyroid Stimulating Hormone

TPO Ab: Thyroid Peroxidase Antibodies

TgAb: Thyroglobulin Antibodies

WHO: World Health Organization

P value: Probability Value

DECLARATIONS

Our work was not funded. We have no competing interests to declare

AUTHORS' CONTRIBUTIONS

Hanan Mohammed Ali Amer and Mona Mohammed Abdelsalam and Caroline Adel Girgis Bishay formulated the question designed the research. Marwa Mohamed Alsayed Algalal did the data collection and analysis. Caroline Adel Girgis Bishay is the main contributor in manuscript writing.

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الرابط بين مؤشر كتلة الجسم ومناعة الغدة الدرقية الذاتية للأم في المرحلة المبكرة من الحمل

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المقدمة: لمرض المناعة الذاتية للغدة الدرقية لدى الأمهات آثار خطيرة على الأم والجنين. هناك جدل حول فحص النساء البدينات خلال الحمل للأجسام المضادة للغدة الدرقية.

الأهداف: تحققنا من العلاقة بين مؤشر الكتلة الجسم في المراحل المبكرة من الحمل ووجود أجسام مضادة لبيروكسيدياز الغدة الدرقية.

المرضى والطرق: قمنا بتجنيد ٢٢٥ امرأة في الأسابيع ٤-٨ من الحمل. كان لدى ٧٥ امرأة وزن طبيعي (المجموعة الأولى)، و ٧٥ يعانون من زيادة الوزن (المجموعة الثانية) و ٧٥ يعانون من السمنة (المجموعة الثالثة). قمنا بفحص هرمون تحفيز الغدة الدرقية والأجسام المضادة لبيروكسيدياز الغدة الدرقية والأجسام المضادة للثيروجلوبولين لجميع المشاركات وقارناها عبر المجموعات الثلاث.

النتائج: كانت مستويات الأجسام المضادة لبيروكسيدياز الغدة الدرقية أعلى بشكل ملحوظ في النساء السمينات، وعند إجراء تحليل للمجموعات، كان الأجسام المضادة لبيروكسيدياز الغدة الدرقية أعلى بشكل ملحوظ في كل من النساء البدينات وذوات الوزن الزائد مقارنة بالنساء ذوات مؤشر كتلة الجسم الطبيعي.

عند مقارنة المجموعات الثلاث، وجد فرق كبير فيما يتعلق بتوزيع كل من إيجابية الأجسام المضادة لبيروكسيدياز الغدة الدرقية والأجسام المضادة للثيروجلوبولين في المجموعة التي تعاني من السمنة أثناء الحمل.

كان لدى جميع المشاركات ذوات مؤشر كتلة الجسم الطبيعي مستويات طبيعية من الأجسام المضادة لبيروكسيدياز الغدة الدرقية والأجسام المضادة للثيروجلوبولين.

في النساء ذوات الوزن الزائد، كانت نسبة ٨٪ لديهن أضداد بيروكسيدياز الغدة الدرقية إيجابية و ٣٪ لديهن أضداد للثيروجلوبولين إيجابية. بيروكسيدياز الغدة الدرقية إيجابية في النساء المصابات بالسمنة، كانت نسبة ١٦٪ لديهن أضداد.

و ١٢٪ لديهن أضداد للثيروجلوبولين إيجابية.

كانت مستويات هرمون تحفيز الغدة الدرقية مرتفعة بشكل ملحوظ في حالات السمنة.

كان مؤشر كتلة الجسم مرتبطاً إيجابياً بأضداد بيروكسيدياز الغدة الدرقية فقط في النساء البدينات.

الخلاصة: يوجد ارتباط بين مؤشر كتلة الجسم للأم و كل من هرمون تحفيز الغدة الدرقية ومستويات أضداد بيروكسيدياز الغدة الدرقية وتوزيع إيجابية أضداد بيروكسيدياز الغدة الدرقية و أضداد الثيروجلوبولين في المراحل المبكرة من الحمل.