Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Outcomes of Pregnancy in Euthyroid Women with Positive Thyroid Peroxidase Antibodies

Fatin N. KassabBashi,[a,*] Hazim A. Mohammed,[a]

[a]Department of Biochemistry, College of Medicine,University of Mosul, Mosul, Iraq

Abstract

Thyroid disorders are among the most common endocrine disorders affecting pregnant women. Thyroid autoimmunity has been associated with poor pregnancy outcomes. Thyroid Peroxidase antibodies being the most common of thyroid antibodies and it can be considered as a surrogate marker for thyroid related adverse pregnancy outcomes. The present study was conducted to further elucidate the association between these antibodies and adverse pregnancy outcomes. A case control study including 150 randomly selected participant was carried out at AL-Khansaa Teaching Hospital in Mosul, Iraq. over the period of three months. All participants enrolled in the study were screened for Thyroid Function Tests TFTs including Thyroid Stimulating Hormone TSH, Free thyroid hormones (FT3 and FT4) as well as Anti-Thyroid Peroxidase antibodies ATPO. Pregnant women were then classified depending on their Anti-Thyroid Peroxidase antibodies test results into two groups (positive and negative) groups. All women were followed till delivery to record their pregnancy outcomes. Our results showed that 10% of the screened pregnant women showed positive anti-Thyroid peroxidase antibodies. These women reported a higher incidence of cesarean section and preterm deliveries when compared to negative anti-Thyroid peroxidase antibodies control group. So, a conclusion was drawn to recommend anti-Thyroid peroxidase antibodies as screening test during pregnancy especially those with bad obstetric history or history of thyroid disorders.

***Keywords*:** Pregnancy; TPO; Preterm delivery; Cesarean section

1. Introduction

Thyroid peroxidase (TPO) is a cell membrane-related protein expressed on the surface of thyrocytes. Its principal function is to catalyze the coupling of di-iodo tyrosine and mono-iodo tyrosine forming thyroid hormones [1]. TPO gene is located on chromosome 2p25, it is a Thyroid Stimulating Hormone (TSH) dependent more than thyroglobulin almost loss its expression in the absence of TSH [2]

Anti-thyroid peroxidase antibodies (ATPO) are self-developed antibodies targeting TPO [3]. These antibodies are observed more frequently than thyroglobulin (TG) antibodies and are mostly of Immuno globulin G (IgG) subclass. They Inhibit the action of TPO enzyme so it will not be secreted, thus more readily measurable than TG antibody [1]. The Prevalence of ATPO in association with normal thyroid function varies with ethnicity, gender and iodine status, however, they are considered as markers of auto-immunity [4-6] . Their presence during pregnancy have been proposed to be associated with adverse feto-maternal outcomes such as miscarriage, preterm delivery, subfertility, perinatal mortality, large for gestational age, low birth weight and postpartum hemorrhage [7].The aim of this study is to assess the relationship between ATPO level and maternal obstetric complications.

2. Materials and Methods

Two hundred, apparently healthy pregnant women in their third trimester of pregnancy attending the maternal health care consultation unit at AL-Khansaa Teaching Hospital, Mosul, Iraq between 1st. Jan. to 1st. Apr. 2021 were recruited. Fifty of them were excluded based on the study exclusion criteria which include: personal history of thyroid disorders prior to pregnancy, history of autoimmune disease, any medical illness (cardiac, renal, hepatic, hypertension, diabetes mellitus), twin pregnancy, and history of administrating any thyroid altering drug.

*Corresponding author e-mail: fatin.hmp64@student.uomosul.edu.iq. (Fatin N. KassabBashi)
Receive Date: 22 May 2021, Revise Date: 02 June 2021, Accept Date: 08 June 2021
DOI: 10.21608/ejchem.2021.77119.3775

2.1. Methodology:

Each participant was asked for her permission to be enrolled in the study and her consent was obtained. After explaining the idea from the study. The following were recorded: name, age, parity, gravida, abortions, and gestational age calculated according to the last menstrual period or early ultrasound image. As well weight and height were recorded to calculate body mass index BMI.

General examination and exclusion of goiter for each participant was done. Five milliliters of venous blood were collected, centrifuged at (2000 rpm) for 10 min and serum was obtained.

Thyroid Function Tests (TFTs) were performed to confirm the euthyroid state including measuring levels of TSH, FT3, and FT4 with an electrochemiluminescence (ECL) technique using Access2 (Beckman Coulter), NHANES, USA (www.beckmancoulter.com), with TSH reference interval ranging between (0.24- 5.4 µIU/mL) while free hormones ranges were(2.5-3.9 pg/mL) and(0.6-1.6 ng/dl) for FT3 and FT4 respectively.

ATPO level was measured using ELISA technique by ORGENTEC Diagnostika GmbH, Germany (www.orgentec.com),with measurement range 0-3000 IU/ml and cut off value 75 IU/ml. Any value >75 IU/ml was considered positive, whereas <75 IU/ml was considered negative.

Statistical analysis of the data was done using SPSS version 26.

3. Results

Of the 150 randomly screened women 135(90%) had ATPO level <75 IU/ml, while only 15(10%) where ATPO positive (>75 IU/ml).

The TFTs in both positive and negative groups were as shown in (table 1)

Table (1): The mean ±SD of TFTs between ATPO positive and negative groups

TFT S	ATPO(-ve)	ATPO(+ve)
No. (%)	135(90%)	15(10%)
FT3±SD pg/mL	2.70±0.34	2.73±0.39
FT4±SD ng/dl	0.87±0.19	0.90±0.37
TSH±SD µIU/Ml	1.81±0.94	2.26±1.56

All the screened cases were followed till delivery and their obstetric outcomes were recorded.

Concerning surgical interference at term between the two groups. Four cases from ATPO positive group underwent caesarean section (C.S.) compared to only three cases from the ATPO negative groups (table 2).

Table (2): percent of C.S. between ATPO positive and negative groups.

Mode of delivery	ATPO (-ve) No. (%)	ATPO (+ve) No. (%)
Normal	132(97.8%)	11 (73.3%)
C.S.	3 (2.2%)	4 (26.7%)

*p-value by chi square test was 0.002

Concerning the rate of preterm delivery between the two groups. The study found three cases versus only two preterm deliveries in ATPO positive and ATPO negative groups respectively (table 3).

Table (3): Percentage of preterm deliveries between ATPO positive and negative groups.

Mode of delivery	ATPO (-ve) No. (%)	ATPO (+ve) No. (%)
Full term	133(98.5%)	12 (80.0%)
Preterm	2 (1.5%)	3 (20.0%)

*p-value by chi square test was 0.007

Regarding the mode of delivery only three out of fifteen in ATPO positive group and twenty-three cases in the ATPO negative group were subjected to induction of labor, table (4).

Table (4): Percentage of induction of labor between ATPO positive and negative groups.

Mode of delivery	ATPO (-ve) No. (%)	ATPO (+ve) No. (%)
Normal	112(83.0%)	12 (80.0%)
Induction	23 (17.0%)	3 (20.0%)

Non-significant p-value

No cases of premature rupture membrane, intra uterine growth restriction, postpartum hemorrhage was recorded in both groups.

4. Discussion

The prevalence of the presence of ATPO positive test differs during pregnancy depending on the cut-off point used by each individual laboratory but in general ranging between 10-20%. These variations are due to differences in the sample size and the geographical factors [7].

However, in our study, the ATPO positivity prevalence was 10% among pregnant women.

This figure is slightly low when compared to other studies as it should be taken into account the exclusion of patient previously treated with thyroxine and previous history of thyroid disorders. Evidently, the prevalence of our present study is similar to that reported by [3] who estimated the prevalence of ATPO positive test among 917 pregnant women in Singapore to be about 10.3 %.

Similarly, [8] reported a prevalence of 11.2% from 1500 euthyroid pregnant women in Pakistan. This was greatly approximating the figure noticed by [9] of 11.5% among 400 pregnant women in West Bengal, India.

The relationship between the presence of ATPO and obstetric complications is complicated and reflects a matter of controversy [10]. Several studies examined the association between thyroid autoimmunity and preterm delivery. In our study preterm delivery was 20% among ATPO positive group versus 1.5% in the negative group. This difference was also significant in a study by [10] who reported twice as many preterm deliveries in positive autoimmune pregnancies (16% vs 8%). Another study conducted by [8] revealed a similar association (26.8% vs 8%).

In this regard [11] showed that the chance of preterm deliveries in the positive ATPO group was (13.23) higher than the control group (21% versus 4 %) as well as [12] who found a strong correlation between ATPO positivity and preterm deliveries.

In contrast, a study published by [13], recorded no differences in this respect. As well as [14], who demonstrated a negative association between positive autoimmunity and preterm labor.

The pathophysiological mechanism causing preterm birth by thyroid autoimmunity is still unclear, several factors can contribute such as impaired thyroid response to human chorionic gonadotropin (HCG), inflammation or the presence of other autoimmune diseases. Moreover positivity of ATPO is an indicator of impaired thyroid response to HCG and an inadequate response of FT4 to HCG associated with higher risk of preterm delivery [15]

Fewer data is available about other obstetric complications as C.S.. [12] studied C.S. occurrence rates appearing to be similar in both groups (20.90% in negative group versus 22.40 % in antibody positive women as well as [16] al who noticed no significant difference in incidence between the two groups 25% versus 21.59%.

However, in our study a significant difference was observed between the two groups (26.7% vs 2.2%).

A conclusion was comparable to the 2017 American Thyroid Association Guidelines ATA [6].

Another difference was observed by [2] who noticed 48.4% C.S. rates in hypothyroid pregnancies.

5. Conclusion

The present study provides additional evidence for an association between ATPO positivity and both preterm delivery and C.S. rates.

Thus, we recommend to depend ATPO as screening test during pregnancy especially in those with positive history of thyroid disorders and obstetric complications.

Conflicts of interest:

There are no conflicts to declare

Formatting of funding sources:

The authors received no financial support for the research, authorship, and publication of this article.

Acknowledgments:

The assistance provided by Dr. Rana Raoof in proofreading this paper, Dr.Rana Hani in postpartum follow up, to Dr. Haitham Badr for his help in statistics, and to my family for their support.

References

[1] Balucan F.S., Morshed S.A., and Davies T.F., “Thyroid autoantibodies in pregnancy: their role, regulation and clinical relevance.,” *J. Thyroid Res.*, vol. 2013, p. 182-472,(2013).

[2] Bhat S., Ashwini A.P., Suma A.P., and Umakanth S. “Effect of thyroid peroxidase antibody on pregnancy outcome among hypothyroid women,” *J. Clin. Diagnostic Res.*, vol. 12, no. 8, pp. QC01–QC03, (2018).

[3] Loh T.P. *et al.*, “Association between thyroid function tests and anti-thyroid peroxidase (TPO) antibodies in pregnancy,” *Endocrine*, vol. 53, no. 3, pp. 865–867, (2016).

[4] Lee Y.K., Shin D.Y. Shin H., and Lee E.J., "Sex-specific genetic influence on thyroid-stimulating hormone and free thyroxine levels, and interactions between measurements: KNHANES 2013-2015.," *PLoS One*, vol. 13, no. 11, e0207446, (2018).

[5] Chen C. *et al.*, "Iodized Salt Intake and Its Association with Urinary Iodine, Thyroid Peroxidase Antibodies, and Thyroglobulin Antibodies Among Urban Chinese," *Thyroid*, vol. 27, no. 12, pp. 1566–1573, Dec.(2017).

[6] Alexander E.K. *et al.*, "2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum," *Thyroid*, vol. 27, no. 3, pp. 315–389, Mar.(2017).

[7] ChanS. and Boelaert K., "Optimal management of hypothyroidism, hypothyroxinaemia and euthyroid TPO antibody positivity preconception and in pregnancy.," *Clin. Endocrinol. (Oxf).*, vol. 82, no. 3, pp. 313–326, Mar.(2015).

[8] Ghafoor F. *et al.*, "Role of thyroid peroxidase antibodies in the outcome of pregnancy.," *J. Coll. Physicians Surg. Pak.*, vol. 16, no. 7, pp. 468–471, Jul. (2006).

[9] Bhattacharyya R., Mukherjee K, Das A., Biswas M.R., Basunia S.R., and Mukherjee A., "Anti-thyroid peroxidase antibody positivity during early pregnancy is associated with pregnancy complications and maternal morbidity in later life.," *J. Nat. Sci. Biol. Med.*, vol. 6, no. 2, pp. 402–405, (2015).

[10] Glinoer D., Riahi M., Grün J.P., and Kinthaert J., "Risk of subclinical hypothyroidism in pregnant women with asymptomatic autoimmune thyroid disorders.," *J. Clin. Endocrinol. Metab.*, vol. 79, no. 1, pp. 197–204, Jul.(1994).

[11] Masoomeh M. Ahia K.A., Jamali M., Ebrahimi A., and Mahya V., "Effect of antithyroid peroxidase antibody on pregnancy outcome in euthyroid women," *Perinatology*, vol. 20, no. 1, pp. 10–15,(2019).

[12] Negro R., Schwartz A., Gismondi R., Tinelli A., Mangieri T., and Stagnaro-Green A., "Thyroid antibody positivity in the first trimester of pregnancy is associated with negative pregnancy outcomes.," *J. Clin. Endocrinol. Metab.*, vol. 96, no. 6, pp. E920-4, Jun.(2011).

[13] Tierney K. *et al.*, "Thyroid function and autoantibody status among women who spontaneously deliver under 35 weeks of gestation.," *Clin. Endocrinol. (Oxf).*, vol. 71, no. 6, pp. 892–895, Dec.(2009).

[14] Martínez P.F.*et al.*, "Influence of thyroid peroxidase antibodies on TSH levels of pregnant women and maternal-fetal complications.," *Endocrinol. diabetes y Nutr.*, vol. 65, no. 8, pp. 444–450, Oct.(2018).

[15] Korevaar T.I.M. *et al.*, "Thyroid autoimmunity impairs the thyroidal response to hCG: two population-based prospective cohort studies," *J. Clin. Endocrinol. Metab.*, vol. 102, no. 1, p. jc.2016-2942, Oct.(2016).

[16] Meena A. and Nagar P., "Pregnancy Outcome in Euthyroid Women with Anti-Thyroid Peroxidase Antibodies," *J. Obstet. Gynecol. India*, vol. 66, no. 3, pp. 160–165, Jun. (2016).