Research Article

Postpartum Thyroiditis; is it a flare of lucent autoimmune thyroiditis?

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Abstract
The postpartum period is a vulnerable period for the flare or development of autoimmune diseases, Postpartum thyroiditis is a new onset inflammation of previously normal thyroid gland that occurs within 1 year after delivery or pregnancy loss.it may be complicated with permanent hypothyroidism; in this study we aimed to investigate the role of Thyroid peroxidase antibody for diagnosis of thyroid autoimmunity and so prediction of Postpartum thyroiditis among Egyptian women. patients and methods: This prospective cohort study was conducted at randomly selected primary health care unit at Zagazig City, Egypt. 143 women just after labor were included in the study with follow up for one year, all were subjected to detailed history, General and Thyroid gland examination, Laboratory investigations included thyroid peroxidase antibody and TSH and free T4 at 3, 6 and 12 month post-partum. Results: all patients who developed PPT in our study were anti TPO positive and only 3 of them complicated permanent hypothyroidism. conclusion: postpartum thyroiditis is a flare of previously asymptomatic autoimmune thyroiditis, may complicated with permanent hypothyroidism.
Key words: Postpartum; thyroiditis; autoimmune; Thyroid peroxidase antibody.

Introduction
Postpartum thyroiditis is an autoimmune inflammation of the thyroid gland that occur within 1 year after delivery. It may present as new-onset, painless hypothyroidism, transient thyrotoxicosis, or thyrotoxicosis followed by hypothyroidism[1]. It occurs in about 5% of women without preexisting thyroid disease and may also occur after early pregnancy loss[2].

About 25% of patients present as classic postpartum thyroiditis where thyrotoxic phase is followed by hypothyroidism stage, and then euthyroid again within one year. Thyrotoxicosis typically occurs between 2 and 6 months after delivery, and usually resolves spontaneously. The hypothyroid phase typically occurs from 3 to 12 months[3]. while most cases (about 50%) with postpartum thyroiditis have isolated hypothyroidism, and about one third experience isolated thyrotoxicosis[4].

As an autoimmune disorder Postpartum thyroiditis is associated with the presence of thyroid antibodies (TPOAb and TgAb), lymphocyte abnormalities, complement activation, increased levels of IgG1, increased NK cell activity, and specific HLA haplotypes[5].

One of each two or three women having antithyroid antibodies in the first trimester will develop postpartum thyroiditis, compared to 8% of all pregnant women[6].

Subjects and Methods
Prospective cohort study was conducted at randomly selected primary health care unit at Zagazig City, Egypt. 143 women in postpartum period aged from 20 to 43 years old with a mean age of 27.74±5.61 years were included, after Exclusion of Patients with Present or past history of thyroid diseases or Patients receiving drugs affecting thyroid function e.g. levothyroxine, anti-thyroid drugs, amiodarone, interferon. also patients with advanced liver diseases or renal diseases were excluded. Written informed consent was obtained from all participants, and all protocols were approved by Zagazig Institutional Review Board (IRB).The study was carried out during the period January 2016 to January 2017.

All women of the study were subjected to detailed history about thyroid diseases and family history of thyroid disorders. Thorough General and Thyroid gland examination for signs of thyroid disease with Laboratory investigations included TPO Ab as a thyroid autoantibody and Thyroid function test (TSH and free T4) at 3, 6 and 12 month post-partum.

Statistical Analysis

After data collection, data were coded, entered and analyzed using SPSS (Statistical Package for Social Science) version 19. Chi-squared test and fisher exact test was used for comparing descriptive data. A Pearson's correlation is used to find a linear relationship between quantitative variables. P value (≤0.05) was considered significant difference and P value (≤0.01) was considered highly significant difference.

Results:

Table (1): Thyroid function test in anti-TPO +ve and anti-TPO –ve group:

Variable	TPO AB –ve (n=107)		TPO AB +ve (n=36)		P
	No	%	No	%	
TSH: (3 month)					
> 6 mU/L	0	0	16	44.4	
0.4 – 6 mU/L	107	100	15	41.7	<0.001**
<0.04 mU/L	0	0	5	13.9	
TSH: (6 month)					
> 6 mU/L	0	0	17	47.2	<0.001**
0.4 – 6 mU/L	107	100	19	52.8	
TSH: (12 month)					
> 6 mU/L	0	0	3	8.3	0.015**
0.4 – 6 mU/L	107	100	33	91.7	
Free T4: (3 month)					
< 9.0 pmol/L	0	0	16	44.4	
9.0 – 22 pmol/L	107	100	15	41.7	<0.001**
> 22 pmol/L	0	0	5	13.9	
Free T4: (6 month)					
< 9.0 pmol/L	0	0	17	47.2	<0.001**
9.0 – 22 pmol/L	107	100	19	52.8	
Free T4: (12 month)					
< 9.0 pmol/L	0	0	3	8.3	0.015**
9.0 – 22 pmol/L	107	100	33	91.7	

Fisher exact test was used

This table shows significant increase in cases with abnormal thyroid function test at 3,6 and 12 month among TPO AB +ve group.

Table (2): Relation between anti-TPO stat and Postpartum Depression, new onset DM and Postpartum thyroiditis**:**

Variable	TPO AB –ve (n=107)		TPO AB +ve (n=36)		χ^2	P
	No	%	No	%		
PPD:						
No	84	78.5	22	61.1	4.25	0.04*
Yes	23	21.5	14	38.9		
DM:						
No	106	99.1	33	91.7	9.11	0.01*
Yes	1	0.9	2	5.6		
Thyroiditis:						
No	107	100	15	41.7	73.16	<0.001**
Yes	0	0	21	58.3		

Chi-squared test was used

This table shows significant increase in thyroiditis, new onset DM and percentage of **Postpartum D**epression among TPOAB +ve group.

Table (3): Relation between PPD & DM and Postpartum thyroiditis of the studied group:

Variable	No thyroiditis (n=122)		Thyroiditis (n=21)		χ^2	P
	No	%	No	%		
PPD:						
No	96	76.9	10	33.3	9.02	0.003**
Yes	26	23.1	11	66.7		
DM:						
No	121	99.3	19	77.8	6.61	0.01*
Yes	1	0.7	2	22.2		

This table shows that both PPD and DM were significantly higher in patients with thyroiditis.

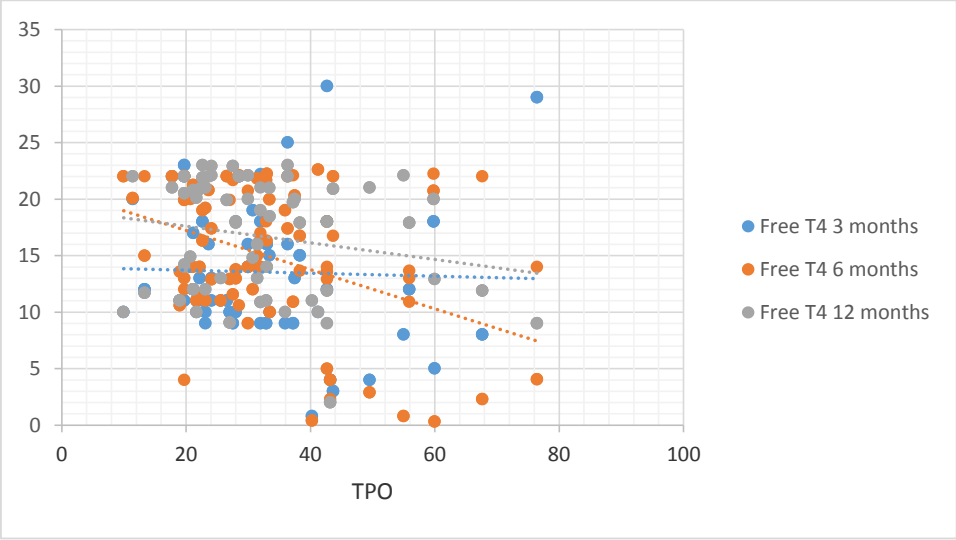

Figure (1): Correlation between TPO and T4 of the studied group: There is a significant negative correlation between TPO and T4 of the studied group

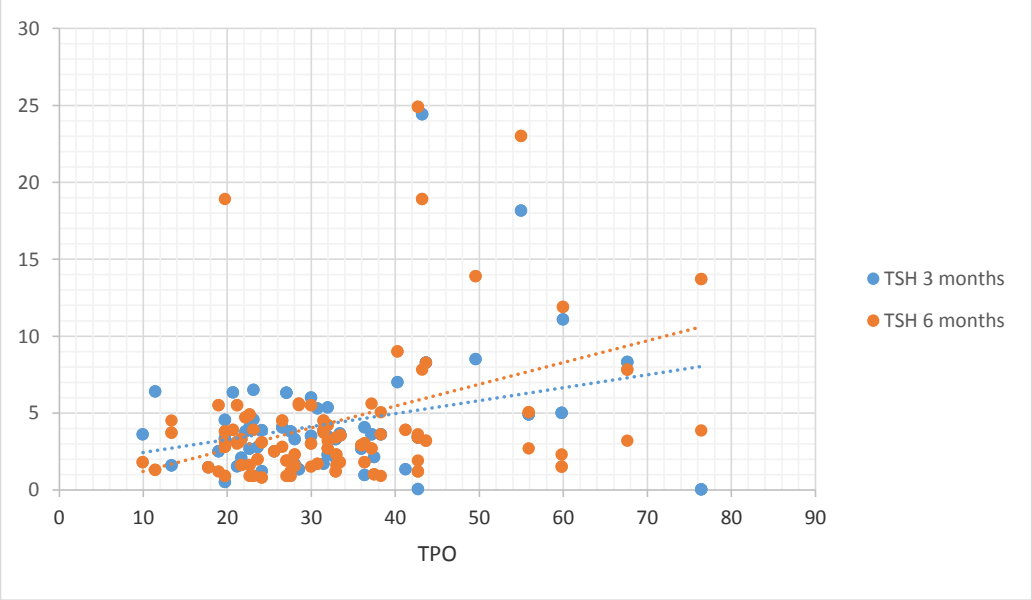

Figure (2): Correlation between TPO and TSH of the studied group:There is a significant positive correlation between TPO and TSH of the studied group of the studied group

Discussion

The postpartum period is considered a vulnerable period for the flare or development of some autoimmune diseases which ameliorate during pregnancy, especially those caused by excessive Thelper 1 (Th1) lymphocyte mediated processes. This is may be due to the rebound of the previously suppressed Th1 mediated immunity during pregnancy[7].

Postpartum thyroiditis is The most common postpartum autoimmune disease[8]. It occurs in about 50% of thyroid peroxidase positive women. TPO autoantibodies are able to bind to thyrocytes and activate complement mediated cell destruction[9].

This study was conducted on 143 women just after child birth, thyroid autoimmunity was proved in 25% of our patients (36 patients anti TPO positive).

TSH and FT4 were done at 3 month postpartum and as a follow up at 6 month, and at 12 month.
At 3 month after delivery we found that 16 patients out of 143 cases (11%) had elevated TSH and decreased FT4 and 5 patients had decreased TSH and elevated FT4 (3.5%) and 122 patients was normal TSH and FT4 (85.3%). At 6 month 17 patients (13.3%) had elevated TSH and decreased FT4 {1 patient hyperthyroidism and 2 patients hypothyroidism return normal thyroid function and 4 patients hyperthyroidism became hypothyroidism} and 126 patients was normal (86.7%). At 12 month 3 patients only was elevated TSH and decreased FT4 (primary hypothyroidism) and 140 patients was normal TSH and FT4. see table no.1

Patients with thyrotoxicosis had a few mild signs and symptoms such as tremors, tachycardia, and nervousness and received propranolol on demand. Although patients with hypothyroidism had moderate symptoms and required treatment with 50-75 µg. after 6-9 month of treatment with levothyroxine is discontinued and thyroid function test reevaluated 3 patients only (2.1%) had permanent hypothyroidism and all of our patients return euthyroid at 12 month follow up.

From this result and follow up of patients for 12 month we found that 21 out of 143 patients had postpartum thyroiditis so the prevalence of PPT in our study 14% and of them 76% had hypothyroidism and 4.7% had thyrotoxicosis and 19% had biphasic course see table no. 2.

This is relatively high prevalence rate in relation to previous studies, prevalence of PPT has been between 1.1-16.7% [10].while other studies found higher prevalence more than our study[11,12,13]. The wide range of prevalence in various studies may be due to: Differences in ethnic groups, Geographical area, Iodine intake, Methodology, population size, Length of follow up.

In the present study 3 patients only (2.1%) had permanent hypothyroidism when levothyroxine was discontinued after 1 year this in contrary with Lucas, et al., reported 15.6% permanent hypothyroidism after 40 month follow up[14] and Lazarus, et al., (2002) prevalence of permanent hypothyroidism after 6.5 year follow up was 26%[15].

In our study; There is a significant negative correlation between anti TPO and T4 and a significant positive correlation between anti TPO and TSH of the studied group of the studied group, this may reflect the strong relation between anti TPO and thyroid dysfunction see figure no.1 and 2.

Also In our study 58% of Anti TPO positive patients developed PPT. All postpartum thyroiditis patients in our study have Anti TPO positive and this in agreement with zagar, (2002) as 75% were TPO positive at 1 and 6 month at pregnancy[16], and Fillippi, (2008) 90% of patients of TPO positive in pregnancy develop postpartum thyroiditis and the rest of the PPT patients was TPO negative[11], and Husniye Baser, et al., (2011) found that 60% of PPT patients was TPO positive . He found statistically significant correlation between anti TPO and development of postpartum thyroiditis[17].

In the present study we have 3 patients had type 1 diabetes mellitus (2%) 2 of these patients develop postpartum thyroiditis (75% developing) and 9% of patient of postpartum thyroiditis had DM . this in agreement with many previous studies which stat that women with type I DM have increased incidence of postpartum thyroiditis. This can be explained by shared genetic susceptibility and Autoimmunity[18,19,20].

In the present study we assessed our patients for postpartum depression by using structural clinical interview for DSM -IV-TR and EPDS score >30. The diagnosis of PPD was not simultaneous with that of postpartum thyroiditis but was detected later when the hormone abnormalities was recovering.

The prevalence of PPD in our study is 25. 8% and rate of postpartum depression was statically higher in those who develop thyroiditis. also PPD was significantly higher in anti TPO positive group. see table no. 2 and 3. This is in agreement with Kuijpens et al., 2001[21], and also in agreement with Farahnaz, et al., (2011) who found the same prevalence postpartum depression and thyroid function correlated negatively with EPDS scores[22],

Though in contradictory with Pop et al., 1993 who showed no association between the presence of anti TPO and postpartum depression[23]. Also lucas, et al., found that PPD incidence rate was 1.7% and there was no relationship between the onset of both disorder[24] .

We can conclude that Postpartum Thyroiditis is a flare of previously asymptomatic autoimmune thyroid disease. Thyroid peroxidase antibody is a good predictor of postpartum thyroiditis and it can be used for early screening test.

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Conflicts of interest:
The authors declare that they have no competing interests.

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