

# Correlation between Postpartum Depression, Postpartum Thyroiditis and Diabetes Mellitus

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## SUMMARY

**Background:** Women are at a higher risk of depression and thyroid disease in the postpartum period. The risk of these conditions may be increased in diabetic patients. The aim of this study is to review the correlation of depression and thyroiditis in postpartum period and its association diabetes mellitus.

**Methods:** This study included 286 women aged from 20 to 43 years old in postpartum period. All participants were subjected to: History taking, physical examination and laboratory investigations in the form of serum TSH, free T4 and TPO Ab as a thyroid autoantibody 3 months post-partum and were followed up with TSH and free T4 at 6 and 12 month post-partum.

**Results:** We found that prevalence of post-partum thyroiditis is 14% the frequency of autoimmune thyroid disease in the present cohort was 25% and 2.1% of our patients have permanent hypothyroidism. High prevalence of post-partum thyroiditis was noticed in type I diabetes mellitus patients and the prevalence of post-partum depression was higher in post-partum thyroiditis patients.

**Conclusion:** There is correlation of post-partum depression and the postpartum thyroiditis and diabetes mellitus.

**Keywords:** Depression; Postpartum thyroiditis; Diabetes mellitus; Post-partum depression

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## INTRODUCTION

Women are at a higher risk of depression during the postpartum period, with 10 to 15% of postpartum women suffering a severe depressive episode at this time [1]. An episode of depression is termed postpartum onset if it begins within three months following birth [2]. It might harm the woman's social and personal adjustment, marital connection, and mother-infant contact [3]. Furthermore, maternal depression in the early years of a child's life can have a negative impact on the child's psychological development, leading to serious intellectual deficiencies. Postpartum depression is most likely the consequence of a combination of genetic predisposition, hormone changes, and big life events [4].

Postpartum Thyroiditis is defined as thyroid dysfunction that occurs in the year after childbirth in women who had otherwise normal thyroid function prior to pregnancy [5]. About 25% of women have what's considered "classical" postpartum thyroiditis where a period of hyperthyroidism is followed by a period of hypothyroidism, and then normalization of thyroid function within the first year. The hyperthyroid phase typically occurs between 2 and 6 months postpartum, and usually resolves on its own. The hypothyroid phase typically occurs from 3 to 12 months postpartum [3].

Postpartum thyroiditis is more common in women who have other autoimmune disorders. It was reported that postpartum thyroiditis may develop in 25% of women who have Type 1 diabetes mellitus or chronic viral hepatitis, 14% of women with lupus and it affects 44% of women with a prior history of Graves' disease. Also, a history of postpartum thyroiditis in a previous pregnancy carries a 70% chance of developing it in subsequent pregnancies [4].

Complexities associated with universal screening for postpartum thyroiditis are well articulated in the Guide to Clinical Preventive Services which concluded that although there is insufficient evidence to recommend screening all pregnant women, an argument could be made for universal screening based on both the prevalence of the disease and the possibility that symptoms could be overlooked in the postpartum period [5-8].

The aim of this study is to review the correlation of depression and the thyroiditis in the postpartum period and its association with diabetes mellitus.

## MATERIALS AND METHODS

This cross-sectional study was carried out between March 2019 to March 2021 at a university hospital on 284 women in the postpartum period at 3, 6 and 12 months after delivery. A written consent was obtained from all cases.

This study included women aged from 20 to 43 years old in the postpartum period. The study excluded patients with any of the following:

- Present or past history of thyroid diseases or thyroid drug intake.
- Patients receiving drugs affecting thyroid function e.g. amiodarone, interferon.
- Present or past history of severe medical diseases such as liver diseases and renal diseases.

All participants were subjected to:

**I: History taking** about thyroid diseases and family history of thyroid disorders (including first and second degree relatives) history of:

- Symptoms of post-partum thyroiditis (lack of energy, irritability, nervousness, sweating, dry skin, heat intolerance, palpitation, lack of

concentration),

- Symptoms of post-partum depression (sadness, sleep and eating disturbances, exhaustion, low self-esteem, social withdrawal, feeling inadequate in taking care of the baby, history of previous post-partum thyroiditis.

**II: Examination:** This included:

- General examination including body built, blood pressure, pulse, temperature, weight, hand (tremors and sweating), face, eye, chest, abdomen examination.
- Local examination for sign of thyroid enlargement (if any masses assess size, symmetry, consistency, thrill) and neck swellings.

**III: Laboratory investigations:**

- Thyroid gland hormones (TSH and free T4).
- TPO Ab as a thyroid autoantibody 3 months post-partum and follow up with (TSH and freeT4) at 6and 12-month post-partum.

## RESULTS

**Tab. 1.** shows that the age of the studied group ranged

**Tab. 1.** Age of the studied group.

Variables	(n=286)	
	No	%
<b>Age (year)</b>		
Mean ± SD	27.74 ± 5.61	-
Range	20 – 43	-
Variable	No	%
<b>Age groups</b>		
≤ 30	218	76.2
>30	68	23.8
<b>Parity</b>		
1	100	34.9
2	86	30.2
≤ 3	50	17.4
>3	50	17.4
<b>Infant feeding</b>		
Yes	218	76.2
No	68	23.8
<b>Pregnancy desire</b>		
Yes	218	76.2
No	68	23.8
<b>Child sex</b>		
Male	100	35
Female	168	65

PPH		
No	270	96.7
Yes	10	3.3
Methods of delivery		
Vaginal	218	76.2
C.S	68	23.8
PPH :Post-partum Hemorrhage		

**Tab. 2.** PPD & DM among the studied group.

Variables	(n=286)	
	No	%
<b>PPD</b>		
No	212	74.1
Yes	74	25.9
<b>DM</b>		
No	280	97.9
Yes	6	2.1
PPD: Post-partum Depression; DM: Diabetes Mellitus		

**Tab. 3.** TPO of the studied group.

Variables	(n=143)	
	No	%
<b>TPO</b>		
Mean $\pm$ SD	32.93 $\pm$ 13.86	-
Range	9.96 – 76.47	-
-ve ( $\leq$ 40) u/ml	214	74.8
+ve ( $>$ 40) u/ml	72	25.2
TPO: Thyroid Peroxidase Enzyme		

from 20 to 43 with mean 27.74. Regarding age group 76.2% of the studied group were  $\leq$  30 years, PPH in 10% of cases, 65% delivered male, pregnancy was desired in 76.2% and 23.8 delivered by C.S. **Tab. 2.** shows that 25.9% of the studied group had PPD and 2.1% had DM. **Tab. 3.** shows that TPO among the studied group ranged from 409.96 to 76.47 with mean 32.93. Regarding TPO group 74.8% of the studied group was -ve and 25.2% were +ve.  $\geq$  40 u/ml considered positive. **Tab. 4.** shows that there was statistical significance differences in TSH level at different follow up times normal values of kits between 0.4-6 $\mu$ iu/ml. **Tab. 5.** shows that there were statistical significance differences in Free T4 level at different follow up times. Normal value of kits is from 9.0 to 22.2 pmol/l. **Tab. 6.** shows that 14.7% of the studied group had postpartum thyroiditis. **Tab. 7.** shows that there were statistical significance differences between cases with -ve TPO and cases with +ve in TSH level in 3, 6 and 12 months with increase no. of cases had

TSH level more than 6 among +ve cases. **Tab. 8.** shows that there were statistical significance differences between cases with -ve TPO and cases with +ve in Free T4 level in 3, 6 and 12 months with increase no. of cases had T4 level less than 9.0 among +ve cases. **Tab. 9.** shows that there were statistical significance differences between cases with -ve TPO and cases with +ve in PPD, DM and thyroiditis with increase all among +ve cases. **Tab. 10.** shows that there were statistical significance differences between cases had thyroiditis and cases hadn't thyroiditis in PPD and DM with increase both among thyroiditis cases. **Tab. 11.** shows that there were +ve significant correlation between PPD and TSH level at 3 months and 6 months and -ve significant correlation between PPD and Free T4 at 3, 6 and 12 months and no correlation between PPD and parity, PPH, child sex desire of pregnancy, type of feeding and methods of delivery.

Tab. 4. TSH of the studied group.

Variables	(n=286)	
	No	%
<b>TSH: (3 month)</b>		
Mean ± SD	4.37 ± 4.00	-
Range	0.03 – 24.4	-
<b>TSH: (6 month)</b>		
Mean ± SD	4.32 ± 4.44	-
Range	0.8 – 24.89	-
<b>TSH: (12 month)</b>		
Mean ± SD	3.51 ± 3.24	-
Range	0.1 – 23	-
F	5.93	-
P	0.001*	-
<b>TSH: (3 month)</b>		
> 6	32	11.2
0.4 - 6	244	85.3
<0.4	10	3.5
<b>TSH: (6 month)</b>		
> 6	34	11.9
0.4 - 6	252	88.1
<0.4	0	0
<b>TSH: (12 month)</b>		
> 6	6	2.1
0.4 - 6	280	97.9
<0.4	0	0
McNamara	22.1	-
P		<0.001**

Tab. 5. Free T4 of the studied group.

Variable	(n=286)	
	No	%
<b>Free T4: (3 month)</b>		
Mean ± SD	13.16 ± 5.56	-
Range	0.8 – 30	-
<b>Free T4: (6 month)</b>		
Mean ± SD	14.23 ± 5.75	-
Range	0.3 – 21.8	-
<b>Free T4: (12 month)</b>		
Mean ± SD	15.75 ± 4.82	-
Range	2 – 22.1	-
F	22.27	-
P	<0.001**	-
<b>Free T4: (3 month)</b>		
< 9	32	11.2
9 – 22	244	85.3
> 22	10	3.5
<b>Free T4: (6 month)</b>		
< 9	34	11.9
9 – 22	252	88.1
<b>Free T4: (12 month)</b>		
< 9	6	2.1
9 – 22	280	97.9
> 22	0	0
McNamara	22.1	-
P	<0.001**	-

**Tab. 6.** Prevalence of postpartum thyroiditis among the studied group.

Variables	(n=286)	
	No	%
<b>Thyroiditis</b>		
No	244	85.3
Yes	42	14.7

**Tab. 7.** Relation between TPO and TSH of the studied group.

Variables	TPO -ve (n=214)		TPO +ve (n=72)		χ <sup>2</sup>	P
	No	%	No	%		
<b>TSH: (3 month)</b>						
> 6	0	0	32	44.4	-	-
0.4 - 6	214	100	30	41.7	73.16	<0.001**
<0.04	0	0	10	13.9	-	-
<b>TSH: (6 month)</b>						
> 6	0	0	34	47.2	57.35	<0.001**
0.4 - 6	214	100	38	52.8	-	-
<b>TSH: (12 month)</b>						
> 6	0	0	6	8.3	9.1	0.003**
0.4 - 6	214	100	66	91.7	-	-

**Tab. 8.** Relation between TPO and Free T4 of the studied group.

Variables	TPO -ve (n=214)		TPO +ve (n=72)		χ <sup>2</sup>	P
	No	%	No	%		
<b>Free T4: (3 month)</b>						
< 9.0	0	0	32	44.4	-	-
9.0 - 22	214	100	30	41.7	73.16	<0.001**
> 22	0	0	10	13.9	-	-
<b>Free T4: (6 month)</b>						
< 9.0	0	0	34	47.2	57.35	<0.001**
9.0 - 22	214	100	38	52.8	-	-
<b>Free T4: (12 month)</b>						
< 9.0	0	0	3	8.3	9.1	0.003**
9.0 - 22	214	100	66	91.7	-	-

**Tab. 9.** Relation between TPO and PPD, DM and Postpartum thyroiditis of the studied group.

Variables	TPO -ve (n=214)		TPO +ve (n=72)		χ <sup>2</sup>	P
	No	%	No	%		
<b>PPD</b>						
No	168	78.5	88	61.1	4.25	0.04*
Yes	46	21.5	56	38.9	-	-
<b>DM</b>						
No	212	99.1	66	91.7	9.11	0.01*
Yes	1	0.9	4	5.6	-	-
<b>Thyroiditis</b>						
No	214	100	30	41.7	73.16	<0.001**
Yes	0	0	42	58.3	-	-

Variables	No thyroiditis (n=244)		Thyroiditis (n=42)		$\chi^2$	P
	No	%	No	%		
<b>PPD</b>						
No	192	76.9	20	33.3	9.02	0.003**
Yes	52	23.1	22	66.7	-	-
<b>DM</b>						
No	242	99.3	38	77.8	6.61	0.01*
Yes	2	0.7	4	22.2	-	-

Variables	PPD (n=286)	
	R	P
Age	0.09	0.31 NS
TSH (3,6 month)	0.25	0.002*
TSH (6 month)	0.29	<0.001**
TSH (12 month)	0.04	0.57 NS
Free T4: (3 month)	-0.2	0.02*
Free T4: (6 month)	-0.22	0.01*
Parity	0.14	0.43 NS
PPH	0.05	0.33 NS
Child sex	0.11	0.56 NS
Type of feeding	0.08	0.51 NS
Pregnancy desired	-0.22	0.01*
Type of delivery	0.05	0.33 NS

## DISCUSSION

In our research, Younger age and having more children were two risk variables linked to postpartum depression (PPD). The influence of the number of parities on PPD has been the subject of some debate. There was no difference in PPD between primipara and multipara women in one research, however there was a two-fold increase in postpartum psychosis, with no age link [9]. Some research have shown a link between PPD and the first childbirth, while others have found no link between the number of births and PPD, Other demographic and obstetric characteristics, according to our findings, showed no significant link with postpartum depression [10].

Thyroid dysfunction, on the other hand, has been linked to postpartum depression in several studies. Thyroid antibody-positive women are more likely to develop hypothyroidism after birth, which is commonly preceded by transient hyperthyroidism. Furthermore, lower-than-normal total and free thyroxine concentrations during late pregnancy may be linked to postpartum depression symptoms [11].

According to the findings, postpartum depression was not more common among women who had just given birth. The most common postpartum autoimmune disease (AD) is postpartum thyroiditis (PPT), a thyroid dysfunction that occurs within the first year after delivery or miscarriage. Gaberscek and Zaletel et al., PPT occurs during the early

postpartum in approximately half of women who have autoantibodies to the enzyme, thyroid peroxidase, during the first trimester of pregnancy Lazarus, et al. Thyroid peroxidase is a microsomal enzyme that is required in the synthesis of thyroid hormone, but many women who have this autoantibody remain euthyroid. PPT usually has a tri-phasic course, from euthyroidism, to a short hyperthyroid phase (22%) followed by a longer period of Hypothyroidism (48%) and a recovery to euthyroidism Stangaro Green et al. Variants of this course occur [12-14].

Recently this been shown that up to fifty percent of women with PPT remain hypothyroid at one year) Stangaro Green et al. There is significant risk for women with PPT (up to 50%) to develop permanent thyroid disease over time [14].

The pathophysiology involves Th1 cells, autoantibodies, and auto reactive T helper 2 (Th2) cells that promote antithyroid autoantibody production. Cytotoxic T cells and NK cells also participate in a direct destruction of the gland [15]. TPO autoantibodies are able to bind to thyrocytes and activate complement, which sets in motion antibody dependent cytotoxic mechanisms which involve further destruction of the thyrocytes. Symptoms that women with PPT experience are thought to be related to the phase of disease. PPT symptoms during the hyperthyroid phase are usually short-lived and in the hypothyroid phase are particularly likely to be underdiagnosed, as many women consider their experiences as “normal” postpartum

symptoms [15].

Because of the common symptomatic nature of PPT, the availability of a screening test, and the treatable nature of the disease, we devised a decision analytic model to project the clinical impact, cost, and cost effectiveness of screening women for PPT [16].

Those who advocate screening for PPTD cite the following reasons in support of their argument:

avoiding morbidity associated particularly with hypothyroid PPTD, predicting the need for long term thyroxine treatment at the end of the first postpartum year, identifying subjects who might develop PPTD in subsequent pregnancies, identifying subjects for follow up to detect long-term hypothyroidism several years from initial diagnosis [17].

Postpartum thyroiditis has captured the attention of many endocrinologists, various studies have reported thyroid dysfunction in postpartum period. So this study was conducted on 143 women attending primary health care unit for taking vaccine for their infants.

The age of our cases range from 20-43 years old with mean age 27 years old 0.76% of our cases <30 years old and 23% >30 years old.

In this study we document frequency of autoimmune thyroid disease by making TPO. We have 36 patients out of 286 (25%) have TPO positive and we divided our cases into two classes:

- **Group (I):** TPO positive cases with normal thyroid function and they represent 30 patients (41.6%).
- **Group (II):** TPO positive cases disturbed thyroid function and they represent 42 patients (58.3%).

The finding of prevalence of TPO in concordance with Small bridge et al., with prevalence rate 19.6% and Nicholson et al., found that prevalence rate of TPO is 10% lower than our study [18].

This may be due to significant variability of the population studied and the differences in factors known to; increase auto immunity, genetic predisposition, demographic and behavioural characteristic (age, parity, smoking) furthermore these antibodies were tested at variable points during pregnancy and post-partum.

In this study we made TSH and FT4 at 3 month postpartum and as a follow up at 6 month, and at 12 month post-partum.

At 3 month postpartum we found that 32 patients out of 286 cases (11%) had elevated TSH and decreased FT4 (hypothyroidism) and 10 patients had decreased TSH and elevated FT4 (hyperthyroidism) (3.5%) and 244 patients was normal TSH and FT4 (85.3%).

At 6 month 34 patients (13.3%) had elevated TSH and decreased FT4 (hypothyroidism) {2 patient hyperthyroidism and 2 patients hypothyroidism return

normal thyroid function and 4 patients hyperthyroidism became hypothyroidism} and 232 patients was normal (86.7%).

At 12 month 6 patients was elevated TSH and decreased FT4 (hypothyroidism) and 280 patients was normal TSH and FT4.

The thyrotoxic patients had a few mild signs and symptoms such as tremors, tachycardia, and nervousness and none of them required treatment. Although patients with hypothyroidism had moderate to severe signs and required treatment with 50-75 mg.

Levothyroxine after 6-9 month of treatment levothyroxine is discontinued and thyroidal function test reevaluated 6 patients (2.1%) had permanent hypothyroidism and all of our patients become euthyroid at 12 month follow up.

From this result and follow up of patients for 12 month we found that 42 out of 286 patients had post-partum thyroiditis so the prevalence of PPT is 14% and 76% had hypothyroidism and 4.7% had hyperthyroidism and 19% had biphasic course.

This is relatively high prevalence rate in relation to other studies. This may be due to high auto immunity in our study.

Although the reported prevalence of PPT has been between 1.1-16.7% [14].

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 a study by Kita, et al., the incidence of PPT was reported to be 2.4% and among PPT patients 18% had only hyperthyroidism and 40% had hypothyroidism and 42% had biphasic course and in Italian study Flippuu et al. 82% had hypothyroidism and the rest is biphasic course and Husniye Baser et al. Incidence of post-partum thyroiditis was 6% and 90% was in thyrotoxic state and 10% in hypothyroidal phase [19-21].

In lucas, et al., prevalence rate was 7.8%. Japan prevalence rate 5.5%, 90% had transient thyrotoxicosis [22].

In the present study 2.1% 6 patients had permanent hypothyroidism when levothyroxine was discontinued after 1 year this in contrary with Husniye Baser et al., that reported 15.6% permanent hypothyroidism after 40 month follow for 3 years after PPT [21].

In the present study all post-partum thyroiditis patients have TPO positive and this in agreement with Fillippi et al., 90% of patients of TPO positive in pregnancy develop post-partum thyroiditis and the rest of the ppt patients was TPO negative and Husniye Baser et al., found that 60% of ppt patients was TPO positive. He found statistically significant correlation between anti TPO and development

of post-partum thyroiditis [20,21].

In the present study there was no relation between age and development of postpartum thyroiditis but in our study the mean of age is high comparable to other studies considering this may be reason for high auto immunity in our study which increase by age Fillippi et al., who also found no correlation between post-partum thyroiditis occurrence and age [20].

In the present study we have 6 patients had type 1 diabetes mellitus (2%) 4 of these patients develop postpartum thyroiditis (75% developing) and 9% of patient of post-partum thyroiditis. Husniye Baser et al., found those with type 1 DM 19.1% prevalence [21].

Autoimmunity is likely to be the result of the impact of particular environmental factors on genetic susceptible individuals causing loss of self-tolerance and their by triggering disease both PPT and type I DM both are organ specific T cell mediated disease, share a strong genetic susceptibility.

In the present study we assess our patients for postpartum depression they underwent diagnostic evaluation by using structural clinical interview for DSM -IV-TR and EPDS score >30. The diagnosis of PPD was not simultaneous

with that of post-partum thyroiditis but was detected later when the hormone abnormalities was recovering.

The prevalence of PPD in our study is 25.8% and rate of post-partum depression increase in those who develop thyroiditis.

In AnnLucas, et al., PPD incidence rate 1.7% and there was no relationship between the onset and evaluation of both disorder and in Farahnaz et al., found that 25% develop postpartum depression and thyroid function correlated negatively with EPDS scores [23,24].

## CONCLUSION

- Prevalence of post-partum thyroiditis is 14% and 2.1% of our patients have permanent hypothyroidism. We found also that high prevalence of post-partum thyroiditis in type I DM patients and post-partum depression prevalence high in post-partum thyroiditis patients.
- Because hypothyroidism is a potentially reversible cause of depression, women with PPD should be screened for hypothyroidism and appropriately treated.

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