CHARACTERISTICS OF THYROTOXICOSIS DURING THE POSTPARTUM PERIOD

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ABSTRACT

Introduction: Thyrotoxicosis occurs with increased frequency during the postpartum period and may be caused by either destructive thyrotoxic phase of postpartum thyroiditis (PPT) or onset or relapse of Graves disease (GD). Both have similar pathogenesis, clinical manifestations, hormonal and immunological changes leading to some difficulties in the differential between the two conditions. Making proper diagnose is important regarding the different treatment strategy and prognosis for long-term thyroid status.

Objective: To investigate the functional, immunological and morphological characteristics of the thyroid in patients with thyrotoxicosis in the postpartum period.

Patients and methods: The study included 36 patients with thyrotoxicosis after delivery or abortion (mean age 30.17 years, from 23 to 38). Serum levels of thyroid stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), thyroperoxidase antibodies (TPOAb), thyroglobulin antibodies (TgAb), TSH-receptor antibodies (TRAb) were measured and ultrasound (US) evaluation of the thyroid gland was performed. 13 patients had pre-existing autoimmune thyroiditis (AIT) receiving levothyroxine (LT4) during pregnancy. The dose of LT4 after parturition was reduced to pre-pregnancy values according to the current recommendations.

Results: 29 (80,6 %) of the women studied presented with clinically overt form of thyrotoxicosis. In the remaining seven (19,4%) patients the diagnosis was based on hormonal criteria. Complex clinical and laboratory evaluation distinguished two main forms of thyrotoxicosis: PPT (n=27) and GD (n=9). Thyrotoxic phase of PPT manifested earlier – 3,8 months (from 1 to 7) following parturition compared to GD – 5,6 months (from 3 to 9) postpartum. The analysis of the hormonal, immunological and ultrasound characteristics found significantly lower TSH values, higher FT3 levels, higher titers of TRAb and a larger thyroid volume in the patients with GD compared to those with PPT. In the patients experiencing thyrotoxic phase of PPT specific treatment was not initiated and those receiving LT4 had their dose reduced according to the clinical and laboratory findings. On follow-up visit marked changes of the thyroid functional parameters were observed. 9 (33,3 %) of the women with PPT had restored their euthyroid state (transient thyrotoxicosis) by the end of the postpartum period. 16 (59,3 %) of the affected women experienced a subsequent hypothyroid phase (biphasic course of PPT) and in 2 (7,4 %) thyrotoxic syndrome persisted. Patients who developed postpartum Graves' disease required long-term antithyroid therapy and close follow-up.

Conclusion: Postpartum thyrotoxicosis manifests with clinical and laboratory abnormalities depending on the pathogenetic mechanisms (destructive or stimulating processes). Thyrotoxic phase of PPT is often transient, does not require specific treatment and in some cases may be followed by hypothyroidism. Graves' disease is characterised with more pronounced functional alterations and prolonged antithyroid treatment is commonly required to maintain optimal hormonal balance. The differential diagnosis between the thyrotoxic phase of PPT and GD is essential in patients with postpartum thyrotoxicosis regarding the different approach to treatment and monitoring.

Key words: *thyrotoxicosis, postpartum thyroiditis, Graves' disease*

Introduction: Thyrotoxicosis occurs with increased frequency during the postpartum period and may be caused by either destructive thyrotoxic phase of postpartum thyroiditis (PPT) or onset or relapse of Graves disease (GD) (1). Both have similar pathogenesis, clinical manifestations, hormonal and immunological changes leading to some difficulties in the differential diagnose

between the two conditions. Making proper diagnosis is important regarding the different treatment strategy and prognosis for long-term thyroid status.

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Results: Complex clinical and laboratory evaluation distinguished two main forms of thyrotoxicosis occuring during the postpartum period - PPT in 27 (75%) and GD in 9 (25%) of the patients studied. 29 (80.6%) of the women presented with clinically overt form of thyrotoxicosis. In the remaining seven (19.4%) patients the diagnosis was made on hormonal criteria (tab. 1).

Table 1. Distribution of cases according to clinical form and type of thyroid dysfunction

Thyroid dysfunction	Subclinical form	Clinical form	Total
PPT	**7 (25,9 %)**	**20 (74,1 %)**	**27**
Graves' disease	**0 (0 %)**	**9 (100 %)**	**9**
Total	**7 (19,4 %)**	**29 (80,6 %)**	**36**

Clinical manifestations of postpartum thyrotoxicosis were observed in the majority of patients with PPT (74.1%) while all patients with Graves' disease experienced clinically overt form of thyrotoxicosis. The most common complaints were related to fatigue, unmotivated anxiety and nervousness, palpitations and heat intolerance. In patients with new onset or recurrence of Graves' disease weight loss as a consequence of the hypermetabolic state was also reported.

Comparative analysis of several parameters between the two groups of patients found that thyrotoxicosis as a manifestation of PPT presents earlier in the postpartum period than GD (tab. 2). An older age at pregnancy in postpartum patients with Graves' disease compared to those who developed thyroiditis was observed, but the difference was not statistically significant.

Table 2. Comparison between patients with postpartum thyroiditis and Graves' disease

parameter		PPT (n=27)	Graves' disease (n=9)	P
Age (years)	$x \pm Sx$	**30,48±0,83**	**33,22±0,81**	**0,079**
Months postpartum	$x \pm Sx$	**3,8±0,31**	**5,6±0,71**	**0,011***
TSH (mIU/l)	$x \pm Sx$	**0,06±0,01**	**0,02±0,01**	**0,017***
FT4 (pmol/l)	$x \pm Sx$	**23,87±2,54**	**33,31±6,01**	**0,168**
FT3 (pmol/l)	$x \pm Sx$	**8,78±1,35**	**16,31±3,28**	**0,027***
TPOAb (IU/ml)	- + $x \pm Sx$	**8** **19** **363,96±70,15**	**2** **7** **750,81±157,35**	**0,016***
TgAb(IU/ml)	- + $x \pm Sx$	**19** **8** **119,60±47,08**	**6** **3** **71,13±44,93**	**0,575**
TRAb (U/l)	$x \pm Sx$	**0,32±0,08**	**10,33±3,00**	**0,000***
Thyroid volume (ml)	$x \pm Sx$	**11,14±0,95**	**15,57±1,57**	**0,009***
Hypoechogenicity				**0,396**
	mild	**8**	**1**	
	moderate	**19**	**8**	

Analysis of the data showed significantly lower values of TSH in combination with higher levels of FT3 in patients with Graves' disease. Furthermore, in those patients higher titres of TPOAb and a larger volume of the thyroid gland was observed compared with patients with PPT. With regards to TgAb we did not find differences in the incidence and serum levels in both groups of patients.

In order to verify the cause of the thyrotoxic syndrome in the postpartum period levels of TSH-receptor antibodies were measired. Positive titers of TRAb are useful in the diagnostic algorhythm and their presence is considered a specific immunological marker for the diagnosis of Graves' disease. The analysis found significantly higher levels of TRAb in patients with Graves' disease which in combination with the clinical, hormonal and ultrasound abnormalities contributed to the diagnosis.

In patients experiencing thyrotoxic phase of PPT specific treatment was not initiated because of the destructive nature of the disorder. In women receiving LT4 the dose of the medication was reduced according to the hormonal tests. In women with Graves' disease antithyroid treatment was instituted according to the clinical and laboratory findings. Patients with complaints from the cardiovascular system were recommended low dose beta-blocker treatment to control the disturbing symptoms.

During follow-up at the end of the postpartum period (8,36 ± 0,36 months after delivery) significant changes of thyroid hormone tests was observed (Fig. 1)

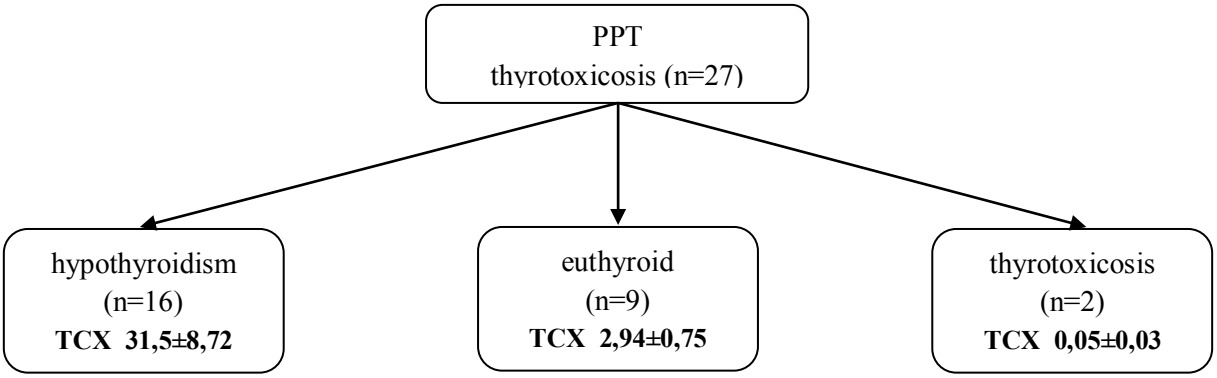
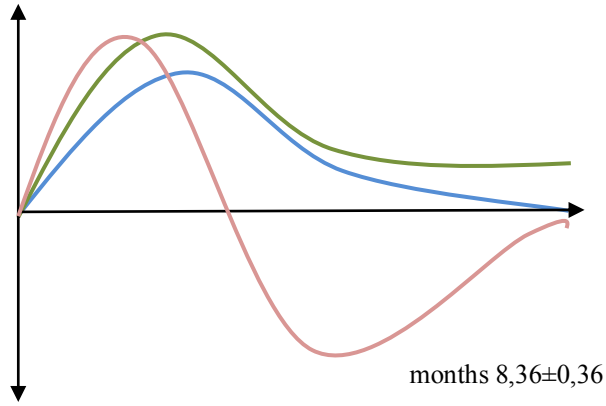


Figure 1. Changes of the thyroid hormone tests in patients with PPT.

In the patients with PPT the following models of evolution of thyrotoxic syndrome were observed (Fig. 2).



Transient thyrotoxicosis with spontaneous recovery of euthyroid state was observed in 9 patients (a). Biphasic course developed in 16 cases in which thyrotoxicosis was followed by a hypothyroid phase (b). Persistent thyrotoxicosis at the end of the postpartum period was found in 2 of women with PPT (c).

Figure 2. Evolution of thyrotoxicosis in patients with PPT

In all patients with Graves' disease the chronic thyrotoxicosis required prolonged antithyroid treatment to maintain clinical and hormonal euthyroid state.

Discussion: Thyrotoxicosis occurs more commonly in the period following delivery in women of reproductive age compared to other periods of life. Postpartum period is characterized by exacerbation of immune processes and leads to increased risk of onset, recurrence or aggravation of autoimmune thyroid diseases. Postpartum thyroiditis and Graves'disease are the two main causes of thyrotoxicosis in the postpartum period (1). From an epidemiological view thyrotoxic phase of PPT occurs 20 times more often than postpartum Graves' disease (4), but incidence of new onset of the latter is greater in postpartum compared than other periods (3).

Similar pathogenesis, clinical manifestations, hormonal and immunological findings pose some difficulties in the differential diagnosis and require proper assessment of the two conditions due to the different approach to treatment and monitoring. In this study, thyrotoxicosis as a part of PPT (with or without prior AIT) was found in 75% of the patients. In 25% of the cases thyrotoxic syndrome was caused by new onset or relapse of Graves' disease in the postpartum period. Thyrotoxicosis as a result of PPT is more common and occurs earlier in the postpartum than GD in the studied group of patients.

The clinical picture is similar and both diseases manifest with clinically overt symptoms in a significant number of the affected patients. Thyrotoxic form of PPT is usually transient and self-limiting in nature, and in 30% of the cases is asymptomatic and the abnormalities may remain unrecognized (4). Analysis of the results found subclinical course of hormonal dysfunction in

25.9% of patients with thyrotoxic phase of PPT. All patients with Graves' disease experienced clinically overt form of thyrotoxicosis with different severity of signs and symptoms.

Thyrotoxicosis in the postpartum period runs with pronounced alterations in thyroid laboratory and morphological parameters. Thyrotoxicosis due to onset or recurrence of Graves' disease is characterized by more pronounced hormonal (TSH, fT3), immunological (TPOAb, TRAb) and morphological (thyroid gland volume) abnormalities compared to thyrotoxic phase of PPT, being an expression of the increased hormone production by stimulatory effects on thyroid parenchyma. It is important to note that in some patients with PPT thyroid dysfunction developed in the absence of thyroid autoantibodies, which raises the question of the role of the autoimmune mechanisms in the pathogenesis of postpartum thyroid disorders.

Thyrotoxicosis as a part of PPT can undergo dynamic changes in the first year after delivery. Thyroid disorders may be transient with spontaneous restoration of euthyroid state, which was observed in 33.3% of the studied patients. In other cases (59.3%) thyrotoxicosis was followed by hypothyroidism, often requiring initiating of replacement therapy. At the end of the postpartum period unusual persistence of suppressed TSH values was found in 7.4% of the cases with PPT. Thyroid hormone levels in those patients were slightly elevated and due to the lack of clinical complaints they did not require drug treatment and were recommended frequent monitoring of clinical and hormonal state.

Thyrotoxicosis resulting from onset or relapse of Graves' disease is a chronic condition characterised by pronounce hormonal, immunological and morphological changes in the thyroid gland. This disease requires long-term treatment and close follow-up to maintain optimal hormonal balance.

Conclusion: Postpartum thyrotoxicosis manifests with clinical and laboratory abnormalities depending on the pathogenetic mechanisms (destructive or stimulating processes). Thyrotoxic phase of PPT is often transient, does not require specific treatment and in some cases may be followed by hypothyroidism. Graves' disease is characterised with more pronounced functional alterations and prolonged antithyroid treatment is commonly required to maintain optimal hormonal balance. The differential diagnosis between the thyrotoxic phase of PPT and GD is essential in patients with postpartum thyrotoxicosis regarding the different approach to treatment and monitoring.

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