Transforming growth factor β1 in postpartum thyroiditis

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BACKGROUND

Transforming growth factor β1 (TGF β1) is a polypeptide formed of 112 aminoacids, synthesised by almost all cells and produced mainly by platelets, lymphocytes and fibroblasts. TGF β1 has influence on a number of physiological and pathophysiological processes. It has been shown that it participates in the development of foetus, regulation of cell growth and differentiation as well as the process of wound healing and scarring. Its most crucial functions include regulation of both proliferation of cell growth and cell differentiation, immunomodelling and profibrinogenic effects. TGF β1 participates in the pathogenesis of numerous autoimmune and neoplastic disorders as well as the diseases related to organ fibrosis. According to reports, TGF β1 plays a crucial role in diabetes and its complications (retinopathy, nephropathy, diabetic foot), autoimmune thyroid diseases (Hashimoso disease) and digestive system disorders (Colitis ulcerosa, Crohn's disease, coeliac disease), cirrhosis, bronchial asthma, pulmonary hypertension and Alzheimer's disease. Postpartum thyroiditis (PPT) develops after giving birth in predisposed patients as increased severity or manifestation of autoimmune thyroid disorders as a result of resolving of the immunosuppressive impact of pregnancy. The group particularly predisposed to develop postpartum thyroiditis are women with increased titre of anti-thyroid peroxidase (ATPO) and anti-thyreoglobulin antibodies (ATG). 40-60% of these women develop thyroid disorders after delivery. To date, only one research has demonstrated the vital role of TGFβ1 in PPT.

AIM

The aim of our study was to evaluate TGF-β1 levels during pregnancy and after childbirth in women who developed postpartum thyroiditis (PPT) in comparison to the healthy control group (CG) and women with positive anti-thyroid antibodies (ATA+) who did not develop PPT.

SUBJECTS AND METHODS

96 women were examined in 1st and 3rd trimester of pregnancy (T1, T3) and 3, 6 months postpartum (3MPP, 6MPP): 47 ATA+ without Hashimoto disease (28 with PPT, 19 ATA+ without PPT) and 49 healthy controls (HC). We measured TGF-β1 (ELISA), TSH, FT3, FT4, ATG, ATPO with the clinical chemistry analyzer Architect Chemistry System, TRAbs (RIA), fasting glucose, OGTT (enzymatic method with hexokinaze) and HbA1c (HPLC). All women underwent thyroid ultrasound examination. The median age of women in each group was similar – precise data are shown in table.

	HC	PPT	ATA+ (without PPT)
N	49	28	19
Median age (IQR)	30 (7)	30 (3.5)	29 (4)
Median BMI (IQR) before pregnancy	21.97 (2.88)	22.67 (3.45)	23.35 (4.84)

RESULTS

CORRELATIONS

HC	I trimester	III trimester	3 months postpartum	6 months postpartum
TGFβ1&fT3	ns	r=0.34 p=0.016	ns	ns
TGFβ1&TSHR-Ab	ns	ns	r=0.32 p=0.034	ns
TGFβ1&ATPO	ns	ns	ns	r=0.32 p=0.045

PPT	I trimester	III trimester	3 months postpartum	6 months postpartum
TGFβ1&glucose	ns	r=0.43 p=0.03	ns	ns

ATA+ without PPT	I trimester	III trimester	3 months postpartum	6 months postpartum
TGFβ1&fT3	ns	ns	r=0.64 p=0.01	ns

All women	I trimester	III trimester	3 months postpartum	6 months postpartum
TGFβ1&fT3	ns	r=0.33 p=0.001	r=0.37 p<0.001	ns

RESULTS

Serum level of TGF β1	Value ng/ml Median (IQR)	Significance
Healthy Control (HC)		
I trimester	14.7 (6.7)	
III trimester	13.7 (7.0)	
3 months postpartum	15.6 (6.2)	
6 months postpartum	13.8 (5.8)	
Postpartum Thyroiditis (PPT)		
I trimester	**15.2 (6.6)**	
III trimester	**16.1 (7.8)**	
3 months postpartum	**18.4 (9.3)**	**I trimester vs 3MPP P=0.0003 (P=0.0009 after Bonferroni correction) only in PPT group**
6 months postpartum	**16.4 (8.5)**	
ATA+ (without PPT)		
I trimester	18.8 (11.0)	
III trimester	20.2 (7.0)	
3 months postpartum	19.6 (9.6)	
6 months postpartum	18.3 (9.2)	

Significantly higher TGF-β1 levels were observed in 3MPP between PPT and CG (p=0.02), in T1 and T3 between ATA+ without PPT and CG (p=0.049; p=0.017, respectively).

Serum level of TGF β1 (ng/ml)	HC	All ATA+	P value
I trimester	14.7 (6.7)	16.8 (8.9)	P=0.078
III trimester	13.7 (7.0)	17.2 (8.2)	**P=0.012**
3 months postpartum	15.6 (6.2)	18.5 (9.1)	**P=0.015**
6 months postpartum	13.8 (5.8)	17.1 (8.6)	**P=0.034**

Healthy Control (HC)	I trimester Median (IQR)	3 months postpartum Median (IQR)	P value
TSH µIU/ml	0.7 (1.1)	1.3 (0.8)	**P<0.001**
fT3 pg/ml	3.2 (0,4)	2.9 (0.4)	**P<0.001**
fT4 ng/ml	1.1 (0.3)	1.0 (0.1)	**P<0.001**
ATPO IU/ml	0.2 (0.3)	0.2 (0.4)	P=0.3
ATG IU/ml	1.0 (0.6)	0.9 (1.5)	P=0.08
TSHR-Ab IU/l	0.4 (0.7)	0.1 (0.5)	**P=0.008**
Glucose mg/dl	83.0 (9.0)	87.0 (10.0)	**P<0.001**
HbA1c %	5.0 (0.4)	5.2 (0.5)	**P<0.001**

Postpartum thyroiditis (PPT)	I trimester Median (IQR)	3 months postpartum Median (IQR)	P value
TSH µIU/ml	1.4 (1.2)	0.1 (0.6)	**P<0.001**
fT3 pg/ml	3.0 (0.5)	3.5 (1.5)	**P<0.001**
fT4 ng/ml	1.2 (0.2)	1.2 (0.6)	**P=0.016**
ATPO IU/ml	45.7 (138.7)	97.9 (412.3)	**P=0.001**
ATG IU/ml	20.8 (53.9)	21.2 (114.1)	**P=0.012**
TSHR-Ab IU/l	0.6 (0.7)	0.5 (0.4)	P=0.5
Glucose mg/dl	82.5 (11.0)	87.0 (9.0)	P=0.052
HbA1c %	5.0 (0.3)	5.1 (0.5)	**P<0.001**

Women with PPT had significantly higher ATPO level than healthy control.

ATA+ (without PPT)	I trimester Median (IQR)	3 months postpartum Median (IQR)	P value
TSH µIU/ml	0.8 (0.6)	1.0 (1.1)	P=0.09
fT3 pg/ml	3.1 (0.6)	3.0 (0.3)	P=0.4
fT4 ng/ml	1.1 (0.2)	1.0 (0.2)	P=0.13
ATPO IU/ml	6.8 (31.0)	0.5 (13.7)	**P=0.034**
ATG IU/ml	4.2 (14.2)	5.0 (8.3)	P=0.6
TSHR-Ab IU/l	0.6 (0.7)	0.3 (0.6)	P=0.3
Glucose mg/dl	86.0 (8.0)	85.5 (10.0)	P=0.3
HbA1c %	5.0 (0.4)	5.3 (0.5)	**P=0.016**

ATA+ women who did not develop PPT had lower APTO level than women who developed PPT.

CONCLUSIONS

Our results may suggest that TGF-β1 plays an important role in the pathogenesis of PPT. Significantly higher TGF-β1 levels between ATA+ women and CG suggest that this cytokine may play a crucial role in autoimmune thyroid disorders. This is the second study on the role of TGF-β1 in PPT and it confirms that TGF-β1 increases in postpartum period in women with PPT. Pregnant women with even slighty elevated ATPO levels in I trimester should be observed for PPT after delivery.

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