Effect of Subclinical Hypothyroidism on the Mean Platelet Volume of Pregnant Women

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Abstract

Subclinical hypothyroidism (SH) is a frequently seen clinical disorder, which needs to be managed strictly in the pregnant population. SH is closely related with newborn complications and also suggested to be risk factor for cardiovascular events. Mean platelet volume (MPV), a determinant of platelet function, is a newly emerging risk marker for cardiovascular events. The aim of this study was to evaluate how MPV values and other hematological parameters are influenced in pregnants with subclinical hypothyroidism. A total of 70 subclinical hypothyroidic pregnants and 40 euthyroid pregnant controls were enrolled in our study. Age, body mass index (BMI), erythrocyte and platelet parameters were all evaluated. Erytocyte parameters and thrombocyte parameters, including MPV, were not statistically significantly different between pregnants with SH and healthy pregnants ($p>0.05$). Mean free T3 and TSH levels of subclinical hypothyroidic pregnants were statistically significantly different from healthy pregnant ($p=0.04$ and $p<0.01$ respectively).Our results suggest that pregnants with subclinical hypothyroidism do not tend to have increased platelet activation, in other words platelet parameters are not different in pregnants with subclinical hypothyroidism in comparison with healthy pregnants.

Keywords: Mean platelet volume, subclinical hypothyroidism, erytocyte parameters, platelet parameters

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Introduction

Subclinical hypothyroidism is defined as elevated serum thyrotropin (TSH) levels with normal free T4 levels. Prevalence of subclinical hypothyroidism has a range of 2% to 5% in pregnant women [1-4]. This clinical condition has a clear importance because the spectrum of thyroid disorders begins with subclinical hypothyroidism. SH is the first step of overt hypothyroidism and overt maternal hypothyroidism is directly associated with intellectual disorders during childhood in addition to severe pregnancy complications [5,6]. Furthermore, hypothyroidism has adverse effects in almost all steps of lipid metabolism, causes hypercholesterolemia [7,8] as another risk factor of atherosclerosis. So as a conclusion, hypothyroidism is suggested as a risk factor of cardiovascular events for whole population. Although it is not clear the cutoff values for increased mean platelet volume (MPV) in prediction of cardiovascular risk but large platelets may casting in the pathogenesis of cardiovascular disease [9-11] In the literature, there is conflicting data about how SH affects MPV [12-14]. The aim of this study was to evaluate the MPV levels in pregnants with SH who have low cardiovascular risk.

Materials and Methods

A total of 70 pregnants with SH and 40 healthy pregnants who were followed up by the Department of Obstetrics and Gynecology at the Gulhane Military Medical Faculty, between January 2011 and March 2013, without known cardiovascular risk factors were included in our study, retrospectively. Patients with hypertension, diabetes mellitus, anemia, smoking, ongoing infection, having a history for antiplatelet and antilipid therapy or any of chronic diseases were excluded. Age, height, pre-pregnancy weight, pre-pregnancy body mass indexes (BMI), platelet count (PLT), mean corpuscular volume (MCV), hemoglobin (Hgb), hematocrit (Hct), red blood cell (RBC), red cell distribution width (RDW), mean platelet volume (MPV) , platelet distribution width (PDW), TSH, fT3, fT4 levels were all recorded.

SPSS for windows 15.0 software was used for statistical analysis. Data were defined as mean + standard deviation (SD). Groups were compared with one-way (ANOVA) for variables that show a normal distribution and with Mann-Whitney U test for variables that did not show a normal distribution. Bonferoni correction was also performed. Pearson correlation test was used for correlation analysis. Statistical significance was defined as $p < 0.05$.

The study turned into a project, approved by the Helsinki Declaration through general and ethical council.

Results

A total of 70 pregnants with SH and 40 healthy pregnants were included in the study. Mean age was 32.03±4.53 for pregnants with SH and 30.08±5.12 for the healthy pregnant (p=0.041). BMI was 25.24±3.98 for subclinical hypothyroidic pregnants and 24.75±4.09 for healthy pregnants (p=0.547) (Table 1). Erytocyte parameters (RBC, Hgb, Hct, MCV, RDW) and thrombocyte parameters (Plt, MPV, PCT, RDW, PDW) were not statistically significantly different between pregnants with SH and healthy pregnants (p>0.05) (Table 2). Mean fT3 and TSH levels of subclinical hypothyroidic pregnants were statistically significantly different from healthy pregnant (p=0.04 and p<0.01 respectively). In first trimester; Hgb, Hct, MCV, fT3 and TSH levels were statistically significantly different between two groups (p<0.05). In second trimester only TSH levels were statistically significantly different between two groups (p<0.05) and in the third trimester, there was no difference between two groups (p>0.05) (Table 3).

Table 1. Mean age and BMI vales of patient and control pregnant groups

Parameters		n	Mean-SD	Median	Minimum-maximum	p
Age	SH	70	32.03±4.53	32	20-42	0.060
	Control	40	31.08±5.12	31	21-42	
BMI (Body Mass Index)	SH	70	25.24±3.98	24.87	17.30-35.84	0.547
	Control	40	24.75±4.09	24.88	17.36-37.74	

SH: Subclinical hypothyroidism

Table 2. Mean values of erythrocyte parameters, thrombocyte parameters and thyroid function tests

Parameters			**Mean-SD**	**Median**	**Minimum-maximum**	**p value**
Erythrocyte parameters	RBC	Patient	4.14±0.38	4.19	3.22-5.11	0.955
		Control	4.14±0.39	4.09	3.36-5.00	
	Hgb	Patient	12.57±1.19	12.13	8.75-15.10	0.183
		Control	11.70±1.08	11.69	9.49-13.91	
	Hct	Patient	36.27±3.43	36.45	27.8-44.1	0.125
		Control	35.29±2.79	35.20	28.4-40.9	
	MCV	Patient	87.78±6.94	89.00	64.0-99.0	0.093
		Control	85.52±6.32	86.00	67.5-95.0	
	RDW	Patient	14.81±2.13	14.55	10.9-23.5	0.506
		Control	15.10±2.36	14.65	11.4-21.6	
Thrombocyte parameters	Plt	Patient	253.76±66.89	251.0	123-462	0.878
		Control	255.73±59.68	246.50	139-368	
	MPV	Patient	8.75±0.97	8.80	6.7-11.1	0.564
		Control	8.86±0.86	8.70	7.4-11.6	
	PCT	Patient	0.23±0.09	0.21	0.11-0.70	0.756
		Control	0.22±0.04	0.21	0.15-0.34	
	PDW	Patient	16.20±3.14	16.50	0.1-22.8	0.512
		Control	15.81±2.61	15.80	11.0-22.8	
Thyroid function tests	fT3	Patient	2.76±0.36	2.74	2.04-4.37	**0.004**
		Control	3.02±0.43	2.95	2.21-4.30	
	fT4	Patient	1.05±0.22	1.08	0.56-1.71	0.230
		Control	1.11±0.20	1.13	0.55-1.63	
	TSH	Patient	4.58±4.27	4.12	0.35-22.0	**0.001**
		Control	1.88±1.02	1.86	0.27-3.95	

Table 3. Comparison of haematological parameters and thyroid functions in view of trimesters between subclinical hypothyroidic pregnants and control pregnants

Trimester	Parameters		95% Confidence interval		p value
1.Trimester	Erythrocyte parameters	RBC	-.13262	.26599	.503
		Hgb	.00428	1.50187	**.049**
		Hct	.6712	4.5942	**.010**
		MCV	.2770	9.6495	**.038**
		RDW	-1.9717	.9269	.471
	Platelet parameters	PLT	-68.568	4.232	.082
		MPV	-.6062	.6755	.914
		PCT	-.07389	.04226	.585
		PDW	-1.5354	2.8105	.557
	Thyroid Functions	T3	-.53969	-.02586	**.032**
		T4	-.14718	.09903	.695
		TSH	.64007	6.04678	**.017**
2.Trimester	Erythrocyte parameters	RBC	-.25552	.20885	.840
		Hgb	-.64853	.70786	.930
		Hct	-2.0106	1.6049	.822
		MCV	-4.3529	4.1352	.959
		RDW	-1.4032	1.2311	.896
	Platelet parameters	PLT	-25.905	59,800	.429
		MPV	-.8061	.3720	.461
		PCT	-.02771	.04241	.674
		PDW	-1.2164	2.0354	.614
	Thyroid Functions	T3	-.41443	.00226	.052
		T4	-.22054	.05515	.231
		TSH	.91206	5.6046	**.007**
3.Trimester	Erythrocyte parameters	RBC	-.38991	.29277	.771
		Hgb	-.86041	.98755	.888
		Hct	-2.4995	2.8309	.899
		MCV	-3.5450	6.5302	.545
		RDW	-2.5385	1.7516	.707
	Platelet parameters	PLT	-41.099	72.099	.576
		MPV	-.9494	.6937	.750
		PCT	-.04645	.12511	.352
		PDW	-2.3086	2.6000	.903
	Thyroid Functions	T3	-.82134	.44134	.531
		T4	-.43551	.31718	.742
		TSH	-2.68377	3.32144	.824

Discussion

Our study has shown that platelet, MPV, PCT, PDW levels are not different in pregnants with subclinical hypothyroidism, who have no confounding factors such as hypertension, diabetes mellitus, anemia, smoking, ongoing infection, having a history for anti-platelet and anti-lipid therapy or any of chronic diseases, in comparison with healthy pregnants. Therefore, including only subclinical hypothyroid pregnants free from any confounding factor is an important feature of the present study.

In normal pregnancy, an increase in platelet aggregation and a decrease in the number of circulating platelets with gestation occur [15,16]. Also, platelet lifespan declines and the MPV increase minimally during pregnancy. These physiological changes are related to increased consumption of platelets in the uteroplacental circulation [17,18]. Thyroid hormones affect the MPV levels of general population as normal pregnant women. To our knowledge, there has not been any previous study about MPV levels in subclinical hypothyroidic pregnants. So, this is the first study which evaluates MPV levels in pregnants with subclinical hypothyroidism.

Studies concerning about the prognostic and diagnostic usefulness of MPV is still ongoing. Platelet volume is a marker of platelet function and activation and measured as MPV by hematological analyzers [19]. Larger platelets are more reactive than smaller ones and produce more tromboxane A2, which is specific to thrombocytes and then it finally causes vasoconstriction and vein occlusion, prostacylin concentration decrease and vasoconstriction at vascular vein can occur [20]. These alterations can threaten both maternal and fetal life seriously.

According to our results, MPV levels were not statistically significantly different in the, age and BMI matched (Table 1), subclinical hypothyroidic pregnants group than in euthyroidic control pregnants group. Also platelet counts, RDW, PCT, PDW levels were not different between two groups (Table 2). These results let us to think that, subclinical hypothyroidism may not affect the platelet functions of pregnants. Also in subclinical hypothyroidic pregnant group, platelet counts, RDW, PCT, PDW levels were not different between all trimesters (Table 3). Only, tyhroid functions and erythrocyte parameters were different between all trimesters. These differences may be related to subclinical hypothyroidism and physiological

changes in the course of normal pregnancy. After Bonferroni correction, statistical significancy of our results was not changed ($p>0.05$).

There are some limitations of the present study. Firstly, this is a retrospective observational study and we included only one cross-sectional value of MPV. Secondly, the results are valid for only Caucasians. Further epidemiological studies are needed to reveal exact values in different races and societies. Thirdly, because of limited sample size and the strict inclusion criteria, our findings are not representative for all subjects with SH. Fourthly, in most of our patients with subclinical hypothyroidism had autoimmune thyroiditis. Also, the best time interval for MPV determination is within 2 hours after obtaining of blood samples but this interval could not be achieved. Despite the limitations, our study is the first study to date evaluating the MPV levels in pregnants with SH.

In conclusion, our results suggest that pregnants with subclinical hypothyroidism do not tend to have increased platelet activation, in other words platelet, MPV, PCT, PDW levels are not different in pregnants with subclinical hypothyroidism in comparison with healthy pregnants. Further prospective researches including large numbers of patients are required to evaluate the platelet activation in pregnants with subclinical hypothyroidism.

Conflict of Interest

The authors declare that they have no conflict of interest. We certify that we had no relationship with companies that may have a financial interest.

References

1. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG.. Subclinical hypothyroidism and pregnancy outcomes. Obstet Gynecol. 2005;105(2):239-45.
2. Jacob JJ. Subclinical hypothyroidism in the first trimester of pregnancy in North India. Indian J Endocrinol Metab. 2013; 17(1):160-1.
3. Nelson DB, Casey BM, McIntire DD, Cunningham FG. Subsequent pregnancy outcomes in women previously diagnosed with subclinical hypothyroidism. Am J Perinatol. 2014; 31(1):77-84.
4. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000;160(4):526-34.

5. Leung AS, Millar LK, Koonings PP, Montoro M, Mestman JH. Perinatal outcome in hypothyroid pregnancies. Obstet Gynecol. 1993;81(3):349-53.
6. Casey BM, Dashe JS, Spong CY, McIntire DD, Leveno KJ, Cunningham GF. Perinatal significance of isolated maternal hypothyroxinemia identified in the first half of pregnancy. Obstet Gynecol. 2007; 109(5):1129-35.
7. Sari O, Tanoglu A, Aydogan U, Simsek A, Serdar AM, Akbulut H, Kurtulus O, Saglam K. Serum visfatin levels before and after levothyroxin treatment in cases with hypothyroidism and subclinical hypothyroidism and their relationships between the lipid levels. Biomedical Research. 2012;23(1):55-9.
8. Duntas LH. Thyroid disease and lipids. Thyroid. 2002;12(4):287-93.
9. Torun AN, Uzum AK, Aksoy N. Overt and mild subclinical hypothyroidism do not ınfluence mean platelet volume in premenopausal women having low cardiac risk. Clin Appl Thromb Hemost. 2012;18(3):312-5.
10. Van der Loo B, Martin JF. Megakaryocytes and platelets in vascular disease. Baillieres Clin Haematol. 1997;10(1):109-23.
11. Halbmayer WM, Haushofer A, Radek J, Schön R, Deutsch M, Fischer M. Platelet size, fibrinogen and lipoprotein (a) in coronary heart disease. Coron Artery Dis. 1995;6(5):397-402.
12. Yilmaz H, Ertugrul O, Ertugrul B, Ertugrul D. Mean platelet volume in patients with subclinical hypothyroidism. Platelets. 2011;22(2):143-7.
13. Erikci AA, Karagoz B, Ozturk A, Caglayan S, Ozisik G, Kaygusuz I, Ozata M. The effect of subclinical hypothyroidism on platelet parameters. Hematology. 2009;14(2):115-7.
14. Coban E, Yazicioglu G, Ozdogan M. Platelet activation in subjects with subclinical hypothyroidism. Med Sci Monit. 2007; 13(4):211-4.
15. Juan P, Stefano G, Antonella S, Albana C. Platelets in pregnancy. J Prenat Med. 2011;5(4):90-2.
16. Ahmed Y, van Iddekinge B, Paul C, Sullivan HF, Elder MG. Retrospective analysis of platelet numbers and volumes in normal pregnancy and preeclampsia. Br J Obstet Gynaecol. 1993;100(3):216-20.
17. Valera MC, Parant O, Vayssiere C, Arnal JF, Payrastre B. Physiologic and pathologic changes of platelets in pregnancy. Platelets. 2010; 21(8):587-95.
18. Gioia S, Piazze J, Anceschi MM, Cerekja A, Alberini A, Giancotti A, Larciprete G, Cosmi EV. Mean platelet volume: association with adverse neonatal outcome. Platelets. 2007;18(4):284-8.
19. Park Y, Schoene N, Harris W. Mean platelet volume as an indicator of platelet activation: methodological issues. Platelets. 2002;13(5-6):301-6.
20. Vizioli L, Muscari S, Muscari A. The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. Int J Clin Pract. 2009;63(10):1509-15.