MEAN PLATELET VOLUME IN PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM ATTENDING AT A TERTIARY CARE HOSPITAL OF BANGLADESH

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Abstract

Background: *Subclinical hypothyroidism (SCH) is a common endocrine disorder affecting about 3-8% of the general population. On the other hand, mean platelet volume (MPV) is an indicator of platelet activity, and elevated MPV is associated with adverse cardio-metabolic complications. This study was conducted to observe MPV in SCH and to correlate it with thyroid-stimulating hormone (TSH) and free thyroxine (FT4) levels.*

Materials and Methods: *This cross-sectional observational study was conducted in Medicine and Endocrinology OPD of US- Bangla Medical College & Hospital over twelve (12) months from September 2020 to August 2021. This study included forty (40) cases of newly detected SCH and twenty (20) age & body mass index (BMI) matched euthyroid control subjects as per inclusion and exclusion criteria.*

Results: *SCH group had higher TSH and MPV than controls (P value <0.001 and <0.05 respectively) where age, BMI, and FT4 level were comparable (P value>0.05). MPV shows a positive correlation with BMI in SCH & controls (P values <0.05). MPV shows a significant positive correlation with TSH and a negative correlation with FT4 only in SCH (P<0.05) but not in controls (P value>0.05).*

Conclusion: *Patients with SCH have elevated MPV, so they are at increased risk of developing an adverse cardiovascular outcome.*

Keywords: *Subclinical hypothyroidism, mean platelet volume, thyroid stimulating hormone, free thyroxine.*

DOI: https://doi.org/10.3329/jdmc.v31i1.65469
J Dhaka Med Coll. 2022; 31(1) : 61-65

Introduction

Subclinical hypothyroidism (SCH) is a common endocrine disorder in the general population. The prevalence of SCH in people with unknown thyroid status is about 3% to 8%.[1,2] The prevalence increases with age and is relatively higher in females than males.[1] It is a mild form of hypothyroidism or partial thyroid failure, which may progress to overt hypothyroidism. The subjects of SCH are usually asymptomatic, but subtle symptoms may sometimes present. It is a biochemical diagnosis traditionally done

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Received: *15-01-2022* ***Revision:*** *22-03-2022* ***Accepted:*** *30-03-2022*

during routine thyroid function tests. SCH is defined when serum thyroid stimulating hormone (TSH) remains above the reference range with normal free thyroxine (FT4).[3] The most common cause of SCH is autoimmune thyroid disease.[3] The progression to overt hypothyroidism is about 2-5% per year.[4] The presence of TSH> 10mIU/ml and positive thyroid autoantibody increases the chance of developing overt hypothyroidism.

Mean platelet volume (MPV) is a measurement of platelet dimension done in routine blood counts by hematological analyzers. MPV is considered a marker of platelet activity, and increased MPV may be associated with increased reactivity.[5] Larger platelets show a greater content of granules, express more adhesion molecules on the surface and undergo faster activation than smaller platelets, resulting in platelet hyper-reactivity and increasing the chance of thrombus formation.[6] Moreover, elevated MPV may be associated with increased platelet aggregation, enhancing synthesis and release of thromboxane TXA2 and beta thromboglobulin.[7] High MPV is found in diabetes mellitus, hypertension, and dyslipidemia, and all these factors increase the risk of cardiovascular diseases.[8-10]

Thyroid hormone deficiency is commonly associated with weight gain, hyperglycemia, elevated blood pressure, and hypercholesterolemia, which are risk factors for cardiovascular disease. Thus patients with hypothyroidism have an increased chance of developing cardiovascular disease. MPV is an indicator of increased activity of platelets and thrombus formation, so MPV may be elevated in thyroid failure. It is well established that overt hypothyroid patients have elevated MPV and thus associated with adverse cardiovascular outcome and levothyroxine replacement therapy may improve it.[11] The status of MPV in SCH is not well established. To the best of our knowledge, there is no study conducted to observe this association in Bangladesh. So this study was conducted to observe the MPV in SCH and to find the correlation of MPV with TSH & FT4 level.

Materials and methods

This cross-sectional observational study was conducted in Medicine and Endocrinology OPD of US- Bangla Medical College & Hospital over twelve (12) months from September 2020 to August 2021. SCH was diagnosed when TSH was mildly elevated (5-20 mIU/ml) with normal free thyroxine (FT4) level (10.5-25 pmol/L). Patients with abnormal thyroid function tests other than SCH were excluded. Patients with diabetes mellitus, hypertension, dyslipidemia, known cases of hematological, cardiac, renal or liver disease or patient with any acute illness or chronic disease, patients taking antiplatelet drugs or contraceptives and pregnant women were not included. Patients who refused to take part in this study were also excluded. A total of forty (40) newly detected cases of SCH and twenty (20) age & body mass index (BMI) matched euthyroid control subjects were included. After taking informed written consent, detailed history was taken, and relevant physical examination was done for each participant, and relevant information was recorded in a data collection sheet. Thyroid function tests, including TSH & FT4, and complete blood count (CBC), including MPV, were measured in a single reference lab of US-Bangla Medical College Hospital. TSH & FT4 was measured by an Automated Immunoassay Analyzer, Vidas-France. CBC was measured by an Automated Hematology Analyzer XN-350 (Sysmex Corporation, Kobe, Japan).

After proper coding and editing, data were entered into the computer by the software IBM Statistical Packages for the Social Sciences (SPSS) version 22.0. Data were expressed as mean ± standard deviation (SD). A comparison of the two groups was made by student's t test. Correlations between variables were done by the pearson correlation test. A *P* value lees than 0.05 was considered as statistically significant.

Results

This study contained total sixty (60) study subjects which included 40 cases of subclinical hypothyroidism (SCH) and 20 age and BMI

matched controls. Total 42 female (30 cases of SCH & 12 controls) and 18 male (10 cases of SCH & 8 controls) were included.

Mean age of study subjects was 37.22±8.61 years. Table I shows the age distribution of study subjects. Age groups 30-39 years and 40-49 years contained maximum subjects (36.67% and 33.33% respectively).

Table II shows comparison of different characteristics between cases of SCH and controls. It indicates SCH group had higher MPV than controls (*P* value <0.001 and <0.05 respectively) where age, BMI and FT_4 level were comparable (*P* value>0.05).

Table III shows correlation between MPV and different characteristics including age, BMI, TSH and FT_4 level. MPV showed significant positive correlation with BMI in all groups including total study subjects, SCH and controls (*P* values <0.001, 0.016 and 0.044 respectively). MPV showed significant positive correlation with TSH in total subjects and SCH, but not in controls (*P* values 0.001, 0.047 and 0.596 respectively) where MPV showed significant negative correlation with FT_4 level only in SCH, but not in total study subject or controls (*P* values 0.037, 0.228 and 0.138 respectively). MPV showed no significant correlation with age in any group including total subjects, SCH or controls (*P* value >0.05).

Table-I

Age distribution of study subjects

Age Groups (years)	Total (n=60)	SCH (n=40)	Control (n=20)
<30	14 (23.33%)	10	4
30-39	22 (36.67%)	14	8
40-49	20 (33.33%)	14	6
≥50	4 (6.67%)	2	2

Table-II

Comparison of age, BMI, thyroid hormone level and MPV among the SCH and Controls

Characteristics	SCH (n=40)	Control (n=20)	*P* value
Age (years)	37.13±8.40	37.40±9.24	0.908
BMI (kg/m^2)	24.54±3.29	23.06±2.47	0.081
TSH (μIU/ml)	9.26±2.29	2.15±1.07	<0.001**
FT_4 (pmol/L)	14.73±2.18	15.73±2.53	0.116
MPV (fl)	9.94±1.57	8.86±1.44	0.012*

* p<0.05 is significant

**p<0.001 is highly significant

Table-III

Correlation of MPV with different characteristics of study subjects

Total subjects (n=)SCH (n=40)Controls (n=20)

	Characteristics	r	*P* value	r	*P* value	r	*P* value
MPV	Age	0.058	0.661	0.072	0.657	0.054	0.820
	BMI	0.439	<0.001**	0.380	0.016*	0.454	0.044*
	TSH	0.408	0.001*	0.316	0.047*	0.126	0.596
	FT_4	-0.158	0.228	-0.331	0.037*	0.344	0.138

* p<0.05 is significant**p<0.001 is highly significant

Discussion

SCH is a condition of mild thyroid hormone deficiency or partial thyroid failure, which is a very common endocrine disorder. These subjects are at increased risk of developing overt hypothyroidism in the future. Most of cases, symptoms of hypothyroidism may not be present in SCH, in which diagnosis is mainly based on the biochemical finding. As a state of partial thyroid failure, different risk factors of cardiovascular diseases like overweight/obesity, elevated blood pressure, hyperglycemia, and

dyslipidemia may be present in SCH. Hence, patients with SCH are at higher risk of developing cardiovascular diseases.[12,13] MPV is a hematological index of platelet volume. As MPV is an indicator of platelet reactivity, MPV may be altered in SCH.

In this study, MPV was significantly elevated in SCH compared to euthyroid control subjects. Yilmaz et al. also found higher MPV in SCH than in controls which supports our result.[14] That study also found improvement in MPV and metabolic parameters after levothyroxine replacement in SCH.[14] Coban et al. also found significantly higher MPV in SCH, supporting our finding.[15] In contrast to this result, some studies found comparable MPV in different subgroups based on different thyroid function tests.[16]

In this study, MPV showed a significant positive correlation with TSH in total study subjects and subjects with SCH but not in controls. MPV was negatively correlated with Ft4 only in the SCH group, but not in controls or total study subjects. A large study containing 6893 asymptomatic Korean adult volunteers found that MPV is positively correlated with TSH both in healthy subjects and SCH.[17] Another study in a large cohort of 10619 adult individuals in the United States reported that only serum thyroxine (T4) level, but not TSH or triiodothyronine (T3), are independently associated with platelet count and there is no independent association between the hormones of the hypophysis-thyroid axis and MPV.[18] Another study that recruited 13622 healthy Chinese found no association between MPV and thyroid function.[16] Different race/ethnicity, different sample sizes, and different cut-off values for the diagnosis of thyroid functional status may be responsible for the variation of results in diverse populations.

Higher MPV has been found in subjects with cardiovascular risk factors such as smoking, diabetes, obesity, hypertension, and dyslipidemia.[8-10,19,20] Moreover, elevated MPV may be a marker for adverse cardiovascular outcomes in individuals with established cardiovascular disease. The exact mechanism by which higher MPV influence the development or progression of cardiovascular disease is unknown. Larger platelets are enzymatically and metabolically more active than smaller platelets, containing more prothrombotic materials and showing more aggregation in response to ADP.[21,22] So larger platelets are more prothrombotic and increase the risk of adverse cardiovascular outcomes.

Limitations

This study had some limitations. The small sample size was the major limitation. Free triiodothyronine (FT3) and thyroid autoantibodies were not measured in SCH and controls. The effect of thyroxine replacement on MPV was not evaluated.

Conclusions

MPV is elevated in patients with SCH. As multiple risk factors of cardiovascular disease, such as hyperglycemia, elevated blood pressure, obesity and dyslipidemia, are associated with SCH, these patients are prone to develop cardiovascular disease. Elevated MPV further increases the risk of adverse cardiovascular outcomes. Patients with SCH and high MPV should undergo cardiovascular and metabolic screening and appropriate management for better cardiovascular outcomes.

Acknowledgements

We are grateful to Prof. Dr. Swapna Bhattacharjee and Prof. Dr. Shekhar Bhattacharjee, Professors of Medicine, US-Bangla Medical College for their kind supervision. We also express our gratitude to doctors of US- Bangla Medical College Hospital for their cooperation. We are thankful to the all lab stuffs of US- Bangla Medical College Hospital for their technical support. We are grateful to all respondents for their kind participation.

Financial Support:

Nil

Conflicts of interest:

There are no conflicts of interest.

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