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A STUDY TO ASSESS THE CARDIO-VASCULAR RISK IN HYPOTHYROIDISM INDIVIDUALS BY USING PLATELET INDICES

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Abstract

Background: Hypothyroidism is a disorder characterized by elevated TSH and reduced FT3 and FT4. Studies on subjects with hypothyroidism have showed positive correlation of thyroid hormone status to Mean platelet volume and studies have shown that Thyroid stimulating hormone can have a prothrombotic effect on platelets. Mean platelet volume, which is a determinant of platelet function, is a risk factor for cardiovascular disease. **Aims and Objectives:** The aim of this study is to compare the platelet count and other platelet parameters in hypothyroid and euthyroid healthy control group. **Materials and Methods:** It is a hospital based Case control study, done on 40 female subjects aged between 14 to 50 years over a period of 6 months. Fasting Blood sample was collected to determine thyroid profile, lipid profile and complete blood count. **Results:** Out of 20 diagnosed hypothyroidism cases and 20 controls, Total cholesterol values and LDL-cholesterol of cases were significantly higher. TSH levels of cases were significantly elevated. Mean platelet volume and platelet distribution width of cases were significantly high. Platelet distribution width showed significant positive correlation with cardiac risk. **Conclusion:** Platelet distribution width could be a definitive cardiac risk marker among hypothyroid individuals.

Keywords: Platelet Indices, Hypothyroidism, Cardiac Risk, Platelet Distribution Width.

INTRODUCTION

Hypothyroidism is a disorder of the thyroid gland characterized by elevated TSH and reduced fT3 and fT4. To a certain extent, normal haematopoiesis especially the coagulation system is influenced by various endocrine organs. Thyroid hormones have an important and influential role on haematopoiesis. The effect of thyroid dysfunction on coagulation cascade is complex and yet to be established. Few types of acquired abnormalities of coagulation system have been reported in patients with thyroid functional abnormalities, patients with hypothyroidism are at increased risk of haemorrhage and there is a tendency to develop thromboembolic complications. Long-term follow-up studies have pointed out that there was increased mortality due to cardiovascular and cerebrovascular complications in patients with hypothyroidism[1]. In case of thyrotoxicosis the important finding is significant thrombocytopenia associated with immune-mediated lytic mechanisms. In hypothyroidism decreased production of proteins causes decreased levels of multiple coagulation factors. However, these changes do not cause any significant coagulation manifestations[2]. Studies on subjects with hypothyroidism have showed positive correlation of thyroid

hormone status to Mean platelet volume (MPV) and it has been postulated in literature that Thyroid stimulating hormone (TSH) can have a prothrombotic effect on platelets[3].

Consequences of hypothyroidism include increased risk of cardiovascular disease such as coronary artery disease, dyslipidemia, liver disease, neuropsychiatric symptoms and infertility, low birth weight and miscarriages. On the other hand, mean platelet volume (MPV), which is a determinant of platelet function, is an independent risk factor for cardiovascular disease.

Platelets play a crucial role in the mortality, morbidity and pathophysiology of CAD. Studies have demonstrated that total serum T4 levels are independently associated with increased platelet count and MPV.[3] But in some studies, like the one done by van Doormaal et al., it is stated that hypothyroidism leads to more small-sized platelets[2]. In this study, we try to establish a relationship between hypothyroidism and platelet parameters which in turn reflects the cardiovascular status of an individual.

AIMS & OBJECTIVES

The aim of this study was to compare the platelet count and other platelet parameters (Platelet count, MPV, PDW) as a marker for cardiovascular risk factors in hypothyroid and euthyroid healthy control group.

MATERIALS AND METHODS

It is a prospective hospital based cross sectional study done over a period of 6 months from February 2021 to July 2021 at AIMSR, Chittoor. The study was done on 20 hypothyroid subjects as a study population and 20 normal adults as a control group. Institutional scientific and Ethical Committee permission and approval were obtained (No. 011/IEC/AIMSR/2021). Informed consent was taken after explaining the purpose and objective of the study.

Sample Size: 40, Open Epi was used to calculate the sample size with Mean platelet volume as a parameter obtained from previous study[4].

Demographic details such as socioeconomic status, age and weight were obtained. All females in the age group of 14-50 years and patients with hypothyroidism were included in the study.

Subjects with history of coagulation disorders, diabetes mellitus, hypertension, peripheral vascular disease, hyper/dyslipidaemia, chronic kidney disease, hepatic disease and those who are on any drugs influencing coagulation were excluded from the present study. The study subjects were examined thoroughly and parameters like BP and anthropometric measurements were measured.

Random blood sugar, Thyroid profile (T3,T4 and TSH) and Lipid profile were measured.

Fasting blood sample was collected to exclude diurnal variation. Blood samples were studied within half an hour, in order to avoid the platelet swelling induced by EDTA which is time-dependent.

Enzyme Linked Immunosorbent Assay (ELISA) was used to quantitatively determine Triiodothyronine hormone (T3), thyroxine hormone (T4), and thyroid stimulating hormone (TSH) levels in subjects' serum/ plasma. All patients with established thyroid dysfunction were included in the study and then patients with local or systemic

diseases that could affect platelet indices and also inadequate samples/ samples with clots were excluded from the study. Reference range for thyroid stimulating hormone was 0.03 –5.5µIU/mL, and according to this range hypothyroid (TSH> 5.5µIU/mL) patients were selected for study group[5]. Automated blood counter was used to measure platelet parameters after calibration. Venous blood sample was collected from all test and control subjects in ethylene diamine tetra acetate (EDTA) coated vacutainer and analysed using automated analyser to measure complete blood count (CBC) and platelet indices such as platelet count (PLT), plateletcrit (PCT), MPV, PDW, and platelet large cell ratio (P-LCR).

STATISTICAL ANALYSIS

Data was entered in MS excel and analyzed using SPSS 22 version software.

Data is presented as mean and standard deviation. Student's t test was used as test of significance for quantitative data and chi-square test was used as test of significance for qualitative data.

p value <0.05 was considered as statistically significant.

RESULTS

Out of 20 diagnosed hypothyroidism cases and 20 controls, mean age of the cases and controls was 38.5 ± 8.88years and 36.1 ± 9.78 years respectively and the difference was not significant statistically. Anthropometric parameters such as body mass index and waist hip ratio were significantly higher in cases compared to controls (Table 1).

In lipid profile, total cholesterol values and LDL-cholesterol of cases were significantly higher compared to controls. Other lipid parameters such as HDL-cholesterol and triglycerides were almost similar in cases and controls, so the difference in mean values was not significant statistically. There was no significant difference in the values of Random blood sugar levels between cases and controls. Mean systolic blood pressure of cases was significantly elevated compared to controls, but diastolic blood pressure was not showing significant difference between cases and controls.

Among platelet parameters (Table 1), mean platelet volume (MPV) and platelet distribution width (PDW) of cases were abnormally high compared to controls and their difference was significant. But, platelet count and plateletcrit of both cases and controls were in normal range.

Among thyroid profile of cases and controls (Table 1), only TSH levels of cases were elevated abnormally compared to controls and their difference was significant. Free T3 and T4 levels of both cases and controls were in normal ranges, without any significant difference between their mean values.

On assessing the absolute Cardiac risk for 10 years by using NCEP III (modified from Framingham risk score), it was found to be low risk(<10%) for both cases and controls, but it was comparatively higher for cases than controls (Table 1).

Platelet distribution width (PDW) of cases showed significant positive correlation with cardiac risk (Pearson's correlation, r = 0.485; p<0.05). Total platelet count of cases missed marginally to have significant positive correlation with cardiac risk (Pearson's

correlation, r = 0.433; p=0.053). But in controls, none of the platelet parameters showed significant correlation with cardiac risk scores (Table 2).

Table 1: Demographic and clinical characteristics of cases and controls

Variable	Normal range	Cases	Controls	p-value
Age (in years), Mean ± SD	-	38.5 ± 8.88	36.1 ± 9.78	0.422; NS
Body mass index (in kg/m^2)	18.5 – 24.9	26.2 ± 2.13	23.1 ± 0.69	**<0.001; S**
Waist-Hip ratio (in cms)	≤0.80	0.87 ± 0.01	0.80 ± 0.03	**<0.001; S**
Total cholesterol (mg/dl)	125 - 200	212.5 ± 15.6	183.6 ± 11.5	**<0.001; S**
Mean HDL (mg/dl)	35 -80	51.3 ± 11.7	50.9 ± 10.3	0.909; NS
Mean LDL (mg/dl)	85 - 130	120.5 ± 22.9	101.5 ± 12.1	**0.002; S**
Mean Triglycerides (mg/dl)	25 – 200	173 ± 29.6	160.5 ± 22.2	0.139; NS
Random blood sugar (gm%)	<200	117.1 ± 8.0	116.6 ± 6.23	0.827; NS
Systolic Blood Pressure (mm of Hg)	<120	136.1 ± 9.57	128.4 ± 5.34	**0.003; S**
Diastolic Blood Pressure (mm of Hg)	<80	70.2 ± 6.01	72.2 ± 4.40	0.237; NS
Platelet count (lakh/mm^3)	1.5-4	3.45 ± 0.73	3.43 ± 0.70	0.948; NS
Mean platelet volume (fL)	6.5 -12	13.5 ± 1.68	9.86 ± 1.51	**<0.001; S**
Platelet distribution width (fL)	9.6 – 15.2	17.2 ± 1.15	12.1 ± 1.34	**<0.001; S**
Plateletcrit (%)	0.19-0.39	0.25 ± 0.04	0.24 ± 0.03	0.824; NS
Mean T_3 (ng/dl)	60 – 200	131.2 ± 17.9	130.4 ± 16.8	0.885; NS
Mean T_4 (ng/dl)	4.5 – 12	7.46 ± 1.10	7.32 ± 1.01	0.688; NS
Mean TSH (micro-IU/ml)	0.3 - 5.5	8.26 ± 1.08	3.80 ± 0.74	**<0.001; S**
Mean cardiac risk (%)	-	0.49 ± 0.51	0.22 ± 0.28	**0.040; S**

S = Significant; NS = Not significant

Table 2: Correlation of platelet parameters with cardiac risk in cases and controls

Correlation between	Cases		Controls	
	Pearson's correlation co-efficient	p-value	Pearson's correlation co-efficient	p-value
Platelet count and cardiac risk	0.433	0.056; NS	0.435	0.055; NS
Mean platelet volume and cardiac risk	-0.349	0.132; NS	-0.200	0.397; NS
Platelet distribution width and cardiac risk	0.485	**0.030; S**	-0.064	0.788; NS
Plateletcrit and cardiac risk	0.260	0.269; NS	-0.233	0.322; NS

DISCUSSION

Thyroid hormones are essential for the normal development, differentiation, metabolic balance and physiological function of all tissues including blood cells. Mean platelet volume (MPV) indicates mean platelet size and reflects platelet production rate and stimulation. Increased platelet size has been observed in association with known cardiovascular risk factors[6]. Evaluation of the effect of hypothyroidism on platelet parameters may be useful in understanding the pathogenesis of the thrombotic events occurring in these patients. In this study we aimed to compare the platelet count and other platelet parameters (Platelet count, MPV, PDW) as a marker for cardiovascular risk factors in hypothyroid and euthyroid healthy control group.

Twenty patients with hypothyroidism and 20 healthy subjects with euthyroid state were enrolled for this current study. None of the study subjects had hyper/dyslipidaemia, diabetes mellitus, hypertension or with the history of previous cardiovascular illness or coagulation abnormalities. All the study subjects were evaluated for biochemical and platelet parameters. In our study, mean platelet volume (MPV) and platelet distribution width (PDW) of cases were abnormally high compared to controls. This is in accordance with a study done by Kutluturk, Faruk & Gul et al, in which they concluded that levels of MPV significantly increased in patients with hypothyroidism[7].In comparison to normal sized platelets, thrombocytes with high MPV values are more reactive. Therefore, this situation may lead to an increase in production of tromboxane A2, which is specific to thrombocytes. It basically causes vasoconstriction and vein occlusion, a decrease in prostacylin concentration and results in vasoconstriction at vascular vein level[8]. It was also found out in our study that Total cholesterol values and LDL-cholesterol of cases were significantly higher compared to controls. Increased MPV values are also reported in various cardiovascular diseases. In a study done by Endler et al., it is reported that mean platelet volume is an independent risk factor for myocardial infarction[9]. In another study done by Kilicli Camur et al. it was stated that high MPV is an independent risk factor for coronary atherosclerosis and myocardial infarction[10]. Some studies have contradicting results. In a study done by van Doormaal et al., it is stated that hypothyroidism leads to more small-sized platelets[11]. In another study done by Ren X, Meng Z et al, it was concluded that there was no association between hypothyroidism and platelet parameters[12].

In a study done by Ford et al., it is shown that chronic hypothyroidism does not affect the size of platelets in the circulation[13]. Recently, in a study done by Coban et al. it was reported that MPV values were high in hypothyroid cases[14].

In our study platelet distribution width (PDW) of cases were abnormally high compared to controls and Platelet distribution width (PDW) of cases showed significant positive correlation with cardiac risk. A similar finding was obtained in a study done by Sato Y et al, in which it was found that high PDW is an important predictor of adverse prognosis in patients with heart failure [15]. In another study done by Izzi, B., Costanzo, S et al, it was concluded that PDW-associated increase in CVD mortality risk could be related to activation, production, or destruction of platelets[16]. In the process of atherosclerosis and cardiovascular disease, endothelial dysfunction is a significant factor leading to platelet aggregation. Some novel inflammatory markers have been proposed by recent studies which are costly and involve complex processing techniques[17]. Hence, platelet parameters which are easily measurable can be used as markers of endothelial dysfunction and for Cardiovascular disease (CVD) risk assessment.

CONCLUSION

In our study, it was concluded that there was a statistically significant increase in MPV and PDW in hypothyroid patients when compared to healthy euthyroid subjects. However, platelet distribution width (PDW) of cases showed significant positive correlation with cardiac risk. That means elevated platelet distribution width could be a definitive cardiac risk marker among hypothyroid cases. Total platelet count can be a suggestive parameter for cardiac risk. The findings of our study are in accordance with a study done by Ericki et al, which showed that patients with subclinical

hypothyroidism had increased mean platelet volume (MPV) and platelet distribution width (PDW) values compared to the healthy control group, which were statistically

significant and concluded that MPV and PDW values have played significant predictive role in case of subclinical hypothyroidism[18].

However, there was no significant difference found in the platelet count and plateletcrit between the two groups. Our results suggest that MPV and PDW are the reliable markers among the platelet parameters, thus can be used as a CVD risk evaluation parameters in hypothyroid patients. Measurement of platelet parameters are done routinely as part of CBC (Complete blood count) and are affordable. Therefore, they can be used as a predictive marker to identify hypothyroid patients who are at increased risk of atherothrombotic complications in future.

Conflicts of Interest: Nil

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