

A Correlative Study of MPV, PDW and Plateletcrit in Patients with Hyperthyroidism, Hypothyroidism and Euthyroid in Tertiary Care Centre

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Abstract

Aims: Thyroid gland is composed of spherical follicles and thyroid parenchyma includes two major cell types, the thyrocytes releasing thyroid hormones and C cells secreting mature calcitonin. Hypothyroidism and Hyperthyroidism both have been, known to be associated with the various abnormalities of the coagulation system. Our study, had been purposed to investigate the relationship between Mean platelet volume, platelet distribution width and plateletcrit with T3, T4, TSH levels of the patients. **Methods:** A retrospective evaluation was conducted on 90 patients (age group from 30 to 45 years) diagnosed with hypothyroidism (n=30), hyperthyroidism (n=30) and euthyroid (n=30) for over 6 months from October 2020 – March 2021. The demographic data and T3, T4, TSH values was obtained from the patients lab reports in Saveetha Medical College and Hospital. These values was correlated with platelet indices of MPV, PDW and PCT obtained by Sysmex-XN 1000 automated analyser. **Result:** Females population was predominant in both hypothyroidism and hyperthyroidism. On comparison of hypothyroid patients with euthyroid revealed statistically increase significant difference in plateletcrit. On comparison of hyperthyroid patients with euthyroid revealed statistically significant increase in Platelet count, MPV and plateletcrit. **Conclusion:** The present study, suggest that platelet parameters can be considered as a reliable markers and can be used as CVD risk evaluation parameters in hypothyroid and hyperthyroid patients due to abnormal thrombovascular activity.

Keywords: Platelet indices, mean platelet volume, platelet distribution width, plateletcrit, hypothyroidism, hyperthyroidism and euthyroid.

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INTRODUCTION

Thyroid hormones play a vital role in the normal development, differentiation, metabolic balance, and physiological functioning of tissues in the human body. Thyroid disorders constitute a major category of endocrine disorders in clinical practice. Thyroid gland has follicular cells that iodinate the tyrosine residues of thyroglobulin glycoprotein. Thyroid parenchyma has thyrocytes that produce thyroid hormones that is L-thyroxine (T4) and triiodothyronine (T3) and C cells producing calcitonin [1]. Thyroid production is regulated by a negative feedback mechanism through the hypothalamus – pituitary axis. TSH from anterior pituitary bind to its receptor on the thyroid follicular cell and regulates the iodine uptake [3]. Thyroid hormones have receptors within the nucleus. These intranuclear thyroid receptors join with the retinoid X receptors (RXR) and forms a heterodimer that causes modulation of gene expression through thyroid

response elements (TRE) which are the regulatory genes of DNA. Receptors of thyroid hormones are expressed on the hematopoietic stem cells too. So these hormones in turn affect blood cell production including Megakaryopoiesis in bone marrow activity [2]. Changes in Mean platelet volume, platelet distribution width and plateletcrit can be related to thyroid dysfunction. MPV describes the average PLT size, PDW is a measure of PLT size heterogeneity, and PCT shows percentage of blood occupied by platelets. Increase in the size of platelets indicates increase in metabolic and enzymatic activity. Mean Platelet volume and PDW are found to be the markers of activated platelets. Conditions such as metabolic syndrome, obesity and hypertension show alterations such as increase in the MPV along with other platelet parameters [4]. These alterations can also be related to increased incidence of venous thromboembolism and vascular disease. It was shown in the previous studies that MPV which is an indicator of platelet activity can act as an individual independent

risk factor for cardiovascular complications. These parameters using automated cell counters are proved to be cost effective and routinely ordered by clinicians during clinical practice [3]. These markers are mostly underutilized or ignored though it is easily available. To the best of our knowledge there are few studies available relating hypothyroidism and platelet parameters especially concentrated on platelet parameters such as platelet count, MPV, PDW and plateletcrit. Previous research studies suggest there is a strong link between PLT parameters and thyroid disorders which should be perceived as an interdisciplinary phenomenon.

Inclusion Criteria: Includes Age group between 30–45 years.

Exclusion Criteria: Includes malignancy, surgery, major trauma within the previous six months, chronic diseases, pregnant women and history of bleeding disorders.

MATERIALS AND METHODS

A retrospective study was carried out in line with research regulations, including the approval of the Ethical Committee .In total, 90 subjects of age-matched group 30 to 45 years were taken for the study. 60 patients with thyroid diseases, who were admitted to Saveetha medical college and hospital under various clinical departments were taken up for this study. Patients were classified, as having hyperthyroidism (n=30) and hypothyroidism (n=30). Out off 30 hyperthyroid patients males were 8 and females were 22. Out off 30 hypothyroid patients males were 11 and females were 19. Diagnosis of hyperthyroid patients were made on the basis of clinical features such as diffuse thyroid swelling , tachycardia, heart intolerance, tremor, palpitations and sweating, with supporting

laboratory data of reduced levels of serum TSH and elevated levels of serum T3 and T4 .The existence of symptoms and signs of hypothyroidism like weight gain, dry skin, cold intolerance with laboratory data showing low levels of T3 and T4 and elevation levels of TSH were taken as criteria in diagnosing of hypothyroidism. Both clinically and laboratory investigation proven euthyroid subjects (n=30) were taken as control for this study. Patients who had serum T3, serum T4 and TSH tested were taken up for categorization as hyperthyroid and hypothyroid. Serum concentrations of T3, T4 and TSH were measured using VITROS integrated system 5600 auto analyser. Platelet indices were generated from Sysmex XN 1000 autoanalyser. These parameters (Platelet count, Mean platelet volume, platelet distribution width and plateletcrit) were standardized by routine external and internal quality control checks.

Statistical Analysis

The results were expressed as mean \pm SD. Microsoft word and Excel were used to generate graphs, and tables. Statistical methodology were used to evaluate the significance of differences between two groups. P-value <0.05 was considered as a significant change. The study was approved by the institutional ethical committee.

RESULT

On gender distribution, female patients were predominant in both hypothyroidism and hyperthyroidism disorders (Fig 1). On comparing hypothyroidism with euthyroid group T3 and T4 values showed statistical decrease and TSH value shows statistical increase. On comparing of hyperthyroidism with euthyroid group T3 and T4 values showed statistical increased and TSH value shows statistical decreased (Table 1).

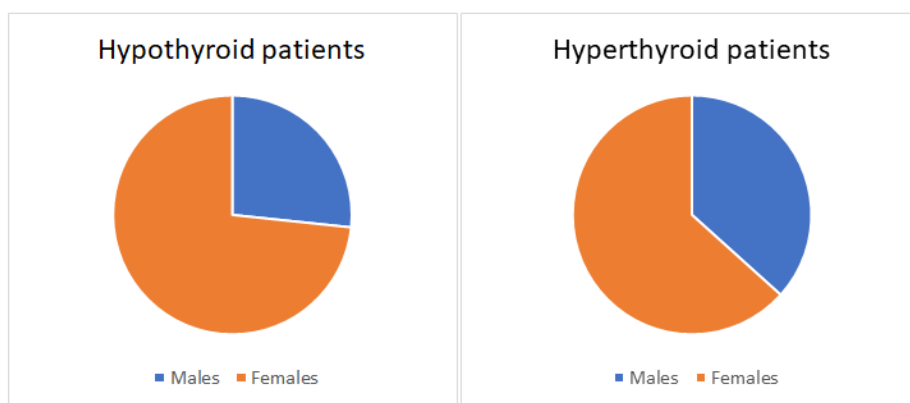


Fig 1: Gender distribution in Hypothyroid and Hyperthyroid patients

Table 1

Parameters	Hypothyroid (n=30) Mean \pm SD	Euthyroid (n=30) Mean \pm SD	Hyperthyroid (n=30) Mean \pm SD
Age (Years)	38.6 \pm 12.3	40.23 \pm 9.2	42.1 \pm 7.9
Serum T3 (μ IU/mL)	0.92 \pm 0.11	2.84 \pm 0.41	3.08 \pm 1.21
Serum T4 (ng/ml)	1.10 \pm 0.81	1.86 \pm 0.20	8.92 \pm 2.17
TSH (μ g/dL)	11.32 \pm 2.89	2.81 \pm 0.64	0.8 \pm 0.21

In our study, comparison of platelet parameters between euthyroid and hypothyroid groups were shown in Table 2. Statistical increase in plateletcrit was seen in hypothyroid patients. Statistical decrease in platelet count was seen in hypothyroid patients (2.16 ± 0.47) when compared with euthyroid group (2.64 ± 0.24). Statistically significant decrease in platelet count (p value = 0.001) and increase in plateletcrit (p value =

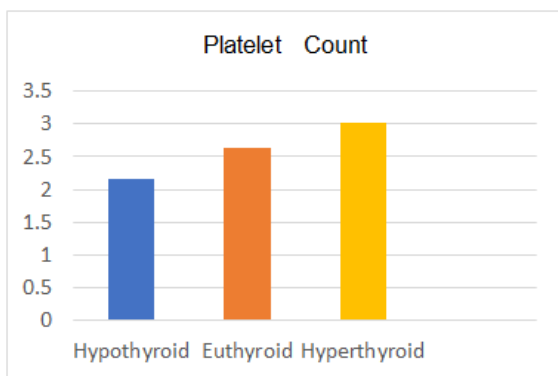
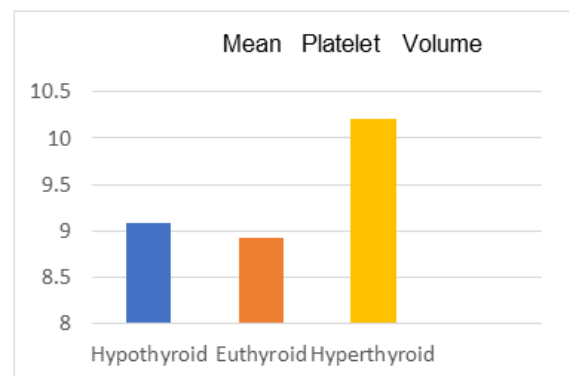
0.001). Significant p values were not found in mean platelet volume and Platelet distribution width. Comparison of platelet indices in hyperthyroid patients with euthyroid groups were shown in Table 3. Statistically significant increase was noted in platelet count (p value = <0.003), mean platelet volume (p value = 0.001), and plateletcrit (p value = 0.001) on comparing with euthyroid (Fig 2 a,b,c,d).

Table 2:

Parameter	Hypothyroid Mean \pm SD	Euthyroid Mean \pm SD	P- value
Platelet count	2.16 \pm 0.47	2.64 \pm 0.24	0.001
Mean platelet volume	9.08 \pm 0.91	8.93 \pm 0.42	0.41
Platelet distribution width	14.2 \pm 1.81	13.31 \pm 2.14	0.08
Plateletcrit	0.40 \pm 0.05	0.22 \pm 0.04	0.001

Table 3:

Parameter	Hyperthyroid Mean \pm SD	Euthyroid Mean \pm SD	P- value
Platelet count	3.02 \pm 0.62	2.64 \pm 0.24	0.003
Mean platelet volume	10.20 \pm 0.38	8.93 \pm 0.42	0.001
Platelet distribution width	8.02 \pm 0.68	13.31 \pm 2.14	0.001
Plateletcrit	0.28 \pm 0.03	0.22 \pm 0.04	0.001

**Fig 2a****Fig 2b**

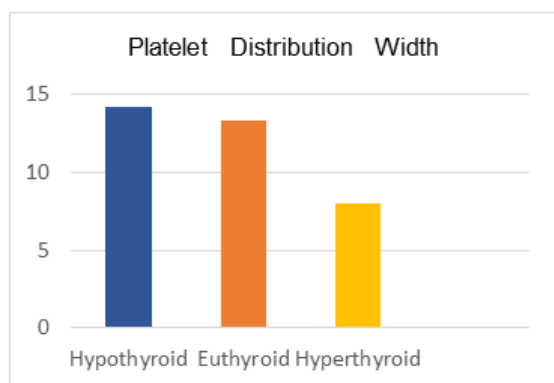


Fig 2c

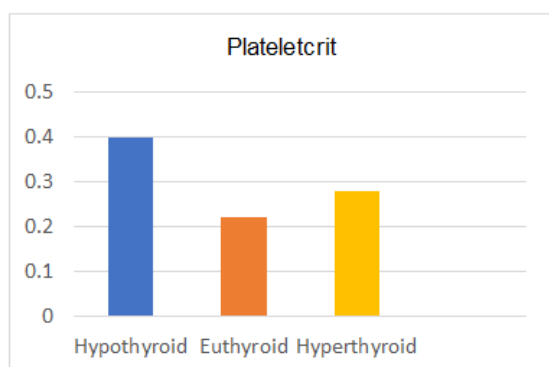


Fig 2d

DISCUSSION

Thyroid hormone imbalances are one of the commonest endocrine disorders prevalent worldwide at an estimated frequency of 2-5% population. The most common thyroid dysfunctions, hypothyroidism and hyperthyroidism affect blood cells and cause thrombocytopenia and even in rare cases cause pancytopenia. Platelets play an important role in atherothrombosis. Larger platelets are likely to be more reactive, contain more granules and produce greater amounts of vasoactive and prothrombotic factors. As mean platelet volume, platelet distribution width and plateletcrit can reflect the platelet activity [7]. MPV is average size of the platelets in blood reported in femto litre (fL) and is available on most hematology auto analyzers. $MPV = (\text{mean} \pm \text{SD}), MPV = (9.7 \pm 1.48) \text{ fL}$. Variation in platelet size comprising of both small platelets and giant/ mega platelets is an indication of over production of platelets in bone marrow is calculated as PDW (Mean \pm SD), $PDW = (14.46 \pm 1.68) \%$. Plateletcrit is a measure of total platelet mass. Normal range of PCT is 0.1 - 0.31%. So, we need to evaluate the value of these parameters in patients with hypothyroidism and hyperthyroidism. We thought to analyse the impact of hypothyroidism and hyperthyroidism on platelet indices may be helpful in understanding the pathogenesis of coagulation abnormalities or thrombotic events occurring in these patients. Our study aimed to assess relation between the effects of hypothyroidism and hyperthyroidism with

platelet indices like mean platelet volume, platelet distribution width and plateletcrit parameters with euthyroid.

By studying baseline characteristics, study found that majority of the subjects were females; this was in agreement with Manji *et al.*, who proved that the incidence of thyroid disorders is reported to be higher in women than in men. In our study, comparison of hypothyroid patients group with control group (euthyroid) revealed statistically significant difference in Platelet count and plateletcrit but no significant seen in mean platelet volume and platelet distribution width. Though, our study have not shown any significant change in MPV and PDW [9], many research studies have found significant change in MPV and PDW. An study done by Slavka *et al.*, patients who showed increased mean platelet volume levels ($\geq 11.01 \text{ fL}$) were seen with increased risks of mortality due to ischemic heart conditions [16]. The researchers discussed that increase in Mean platelet volume levels would have contributed to the risk identified and they proposed pathogenesis behind these effects such as larger platelets were more active and had more alpha granules which can induce blood vessel intima layer proliferation than smaller platelets due to increased metabolic and biochemical activity. As it contains prothrombotic activators like thromboxane A2 and also having pro-coagulant surface proteins it acts in enhance thrombus formation which might lead to myocardial infarction [4]. So, they concluded that mean platelet volume was considered as a reliable marker, which can assess functional activity of the platelet and its effects on blood vessels. Over activation of platelets produces increase in size as well as irregular shape with increase number of pseudopodia formation in turn causes increased aniso-poikilocytosis which contributes to increase platelet distribution width in hypothyroid patients [13]. Plateletcrit (PCT) refers to the percentage of platelet volume in the blood and has been considered as a better prognostic factor than MPV in inflammatory conditions. In our study, plateletcrit values were slightly higher in hypothyroid group than euthyroid group and statistically significant difference was identified between the groups. In our study correlated with Dincel O *et al.*, PCT was found to be significantly higher in patients with malignant thyroid tumours than multinodular goitre patients. Another study done by Oncel M *et al.*, also proposed that platelet indices would be useful to identify and to follow-up, thromboembolic activity as well as inflammatory diseases.

In our study, comparison of hyperthyroid patients group with control group (euthyroid) revealed statistically significant difference in Platelet count, MPV, PDW and plateletcrit. We also found that the platelet count, mean platelet volume and plateletcrit were significantly higher and platelet distribution width

significantly lower in the hyperthyroid patient group. In another research study showed bone marrow aspirates from the sternum were obtained from 26 hyperthyroid patients and 16 healthy subjects. Individuals with hyperthyroidism disorder had a significantly higher number of megakaryocytes in bone marrow aspirates as compared to euthyroid subjects. One possible mechanism through which thyroid hormones may increase the proliferation of megakaryocytes may include modulation of bone marrow matrix proteins, such as Fibronectin [13]. In several cell lines, thyroid hormones increase the expression of Fibronectin gene [11]. Moreover, individuals with hyperthyroidism have elevated blood levels of fibronectin. Fibronectin appears to affect megakaryocyte maturation and thrombopoiesis through interaction with integrin $\alpha 4\beta 1$. Apoptosis is the major mechanism through which platelets destruction and thyroid hormones have been shown to inhibit apoptosis in several cell lines. This finding, helps to conclude that increase thyroid hormone also increase the mean platelet volume in accordance with claims of Bagir *et al.*, In our study plateletcrit gives an idea of platelet mass, had the highest sensitivity and specificity among all the indices and significantly higher in the hyperthyroid patients than the euthyroid patients (0.28 ± 0.03 , 0.22 ± 0.04 ; p value 0.001, respectively). However, a single measurement of thyroid hormones may not provide the significant results. So, thyroid hormone profile status of an individual over a longer time-period is essential.

CONCLUSION

In this research study, on comparison of hypothyroid patients with healthy euthyroid subjects we found statistically significant increase in plateletcrit in hypothyroid patients. However, there is no significant difference found in the mean platelet volume and platelet distribution width between these groups. On comparison of hyperthyroid patients with healthy euthyroid subjects we found statistically significant increase in Platelet count, mean platelet volume and plateletcrit in hyperthyroid patients. Measurement of these platelet indices are cost effective and routinely available laboratory investigation. Our research studies also suggest that platelet indices are the reliable markers among the platelet parameters, thus can be used for risk evaluation of atherothrombotic complications in future in both hypothyroid and hyperthyroid individuals [16]. However, confounding factors are always present at any point of period, more large scale studies with longer duration of time would contribute more towards the understating the mechanism between platelet indices and thyroid hormones.

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Statement of Ethics

This study was approved by Ethics Committee of Saveetha Medical and Hospital. As this study was a retrospective study, there was no patient's privacy data such as patient name, ID number, telephone and address were involved. Only demographic information and laboratory testing data of patients were collected and analyzed in this study.

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