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STUDY OF PLATELET ABNORMALITIES IN THYROID DISEASE

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Abstract

Introduction: Disorders related to thyroid function are among the most prevalent endocrine diseases. Certain platelet anomalies can be brought on by thyroid conditions. Patients suffering from hyperthyroidism and hypothyroidism experience varied outcomes. Hence the aim of present research was to study platelets abnormalities in patients with thyroid dysfunction and correlate with level of thyroid dysfunction. **Material and Methods:** Prospective study was conducted among 27 patients attending the Sharda Hospital having clinical and biochemical evidence of thyroid dysfunction were selected for this study and were subjected to relevant investigations including platelet counts and volume, coagulation profile, T3, T4, TSH. 20 subjects matched for age and sex were taken as controls. Results were computed using SPSS version 25.0. **Results:** 47 individuals comprising of 15 hyperthyroid, 12 hypothyroid and 20 normal control were studied and most of the subjects were 15-45 yrs of age and female to male ratio was 3:1. The mean platelet volume was much higher in hyperthyroid cases. Platelet factor 3 availability was increased in hyperthyroid group. Bleeding time, clotting time and prothrombin time was significantly prolonged in hypothyroid group whereas, in hyperthyroid group it was reduced. **Conclusion:** Thyroid hormone evaluation is crucial when dealing with unexplained platelet problems. Therefore, all patients with hypothyroidism and hyperthyroidism should have periodic screening for potential platelet abnormalities.

Keywords: Hormones, Hypothyroid, Hyperthyroid, Platelet Count, Thyroid Disease.

INTRODUCTION

One of the most important hormones is thyroid hormone. Almost all tissues need them for proper growth, differentiation, metabolic balance, and physiological function. Disorders related to thyroid function are among the most prevalent endocrine diseases.[1] Globally, thyroid disorders are prevalent. There is also a notable prevalence of thyroid conditions in India. In India, 10.95% of people have hypothyroidism and 1.3% have hyperthyroidism. There are already 42 million people in our nation who have thyroid diseases in one or more kinds. Thyroid gland problems are highly prevalent, but have not received enough attention. Despite the promotion of iodized salt since 1983, there has been no statistically significant decline in prevalence rates. [2,3]

A number of patients present with subclinical thyroid function derangements, and thyroid hormone evaluations or abnormal results from other investigations, such as blood parameters or lipid abnormalities, cardiac dysfunction, atherosclerosis, and many other clinical manifestations, are used to diagnose thyroid function abnormalities, which have a wide range of clinical spectrums.[4,5]

Patients with excess or insufficient thyroid hormone have been shown to have a variety of alterations in the coagulation and fibrinolytic systems, which can result in coagulation disorders and cardiovascular problems. Recent research indicates that the majority of coagulation/fibrinolytic problems linked to thyroid dysfunction are the

result of thyroid hormones' direct impact on the synthesis of different haemostatic parameters. Additionally, thyroid autoimmunity may alter secondary hemostasis mechanisms. There have been reports of both hypercoagulable and hypocoagulable conditions, including elevated fibrinolytic activity.[6]

In terms of size, density, and reactivity, platelets vary widely. Furthermore, when assessed following myocardial infarction, platelet volume is predictive of both death and another ischemic episode. Megakaryocytes, which are anucleate cells devoid of DNA, are the precursors of platelets. As a result, it is proposed that variations in platelet size may occur prior to acute cardiac events and are dictated by thrombopoiesis in the megakaryocyte. [7,8]

We performed a study to evaluate various platelet abnormalities in individuals with thyroid dysfunction and link them with the degree of thyroid dysfunction in light of these findings.

MATERIAL & METHODS

The present prospective study was conducted among patients having altered thyroid hormone level who visited to Sharda hospital, Medicine Department from January 2022 to December 2022. Patients were asked to signed an informed consent form after explain them the complete procedure.

Total 27 patients with clinical and biochemical evidence of thyroid dysfunction were selected for the study. Total 20 patients matching the same age and sex was taken as controls. The criteria for selection was-

Inclusion criteria-

The patients with age above 15 years of either sex, with altered thyroid level and willing to participate in the study were included in the study.

Exclusion criteria-

Patients with diabetes mellitus (glycemia >126 mg/dl), hypertension (systolic 140 mmHg, diastolic 90 mmHg), and use of medications such as diuretics, beta blockers, corticosteroids, and anti-lipidemic medicines that affect thyroid function tests and platelets were excluded from the study.

Comprehensive medical histories were documented. Patient information, clinical characteristics, biochemical markers, and clinical diagnosis were all part of a strict process that was adhered to. Each patient had two different blood samples drawn: two millilitres in an EDTA-filled vial and three millilitres in a plain vial. The electrochemiluminescence immunoassay method was utilised to measure serum TSH using a sample that was collected in a plain vacuum sealer. Serum TSH levels should range from 0 to 4 2 µIU/ml. Hyperthyroidism was defined as a serum TSH level of less than 0 27 µIU/ml. When the serum TSH level exceeded 4 2 µIU/ml, it was classified as hypothyroidism. From the sample taken in the EDTA vacutainer, a complete blood count and peripheral blood smear preparation were performed. Using an automated cell counter Sysmex 5 part differential for blood cell counts and red cell indices, a complete blood count was performed. To ascertain the haematological alterations, the correlation between serum TSH levels and peripheral blood smear and serum TSH levels and total platelet count was thoroughly examined.

Microsoft Excel was used to enter the data, and SPSS (Statistical Package for Social Sciences) Software 25 was used to analyse it. Continuous variables were expressed as mean and SD, whereas categorical variables were expressed as frequency and percentage. To determine whether the study groups and control group's continuous variables differed significantly from one another, an ANOVA test was used. A value was deemed statistically significant if it was less than 0.05.

RESULTS

Among cases and controls maximum were in the group of 21 to 30 years and 31 to 40 years. the female to male ration was 3:1 in cases group and 2:1 in control group as shown in table 1.

Table 1: Demographic data of patients and controls

Age and gender	Cases (n=27)	Controls (n=20)
15-20 years	2 (7.4%)	3 (15%)
21-30 years	7 (25.9%)	7 (35%)
31-40 years	8 (29.6%)	5 (10%)
41-50 years	5 (18.5%)	3 (15%)
51 - 60 years	3 (11.1%)	2 (10%)
Above 60 years	2 (7.4%)	0
Female: Male	3:1	2:1

Hypothyroid group showed raised mean TSH (20.97±28.1) with depressed T3 (1.08±0.32) and T4 (6.09±3.19) levels and hyperthyroid group showed depressed TSH (0.14±0.061) with raised T3 (2.54±3.61) and T4 (10.87±4.38) levels with significant results as shown in table 2.

Table 2: Comparison of TFT level among groups

Variables	Hyperthyroid (n=15)	Hypothyroid (n=12)	Controls (n=20)	P value
TSH ((µIU/ml)	0.14±0.061	20.97±28.1	2.16±1.13	0.001
T3 (ng/dl)	2.54±3.61	1.08±0.32	1.58±0.4	0.001
T4 (µg/dL)	10.87±4.38	6.09±3.19	8.19±2.09	0.001

In the present study the mean platelet count of Hyperthyroid patients was 298.90±382.79 $Nx10^3$/µl, hypothyroid patients were 189.90±90.01 $Nx10^3$/µl with non significant results. In control group mean platelet count was 259.17±106.32 $Nx10^3$/µl as shown in table 3.

Table 3: Comparison of mean platelet count in groups

Groups	Mean platelet count ($Nx10^3$/µl)	P value
Hyperthyroid (n=15)	298.90±382.79	0.781
Hypothyroid (n=12)	189.90±90.01	0.086
Control (n=20)	259.17±106.32	-

Bleeding time, clotting time and prothrombin time was significantly higher in hypothyroid patients whereas in hyperthyroid group bleeding and clotting time was reduced. Platelet factor III availability was increased in hyperthyroid group as compared to hypothyroid group shown in table 4, figure 1

Table 4: Comparison of clotting factors in groups

Clotting factors	Hyperthyroid (n=15)	Hypothyroid (n=12)	Control (n=20)	P value
Bleeding time (minutes)	3.04±1.5	6.19±3.7	4.07±2.5	0.003
Clotting time (minutes)	8.4±2.4	14.10±7.9	12.09±6.8	0.005
PTT (seconds)	24.67±10.3	37.12±14.3	30.68±15.8	0.001
Platelet factor III (Nx10^3/µl)	299.95±387.78	186.79±88.05	260.19±107.31	0.001

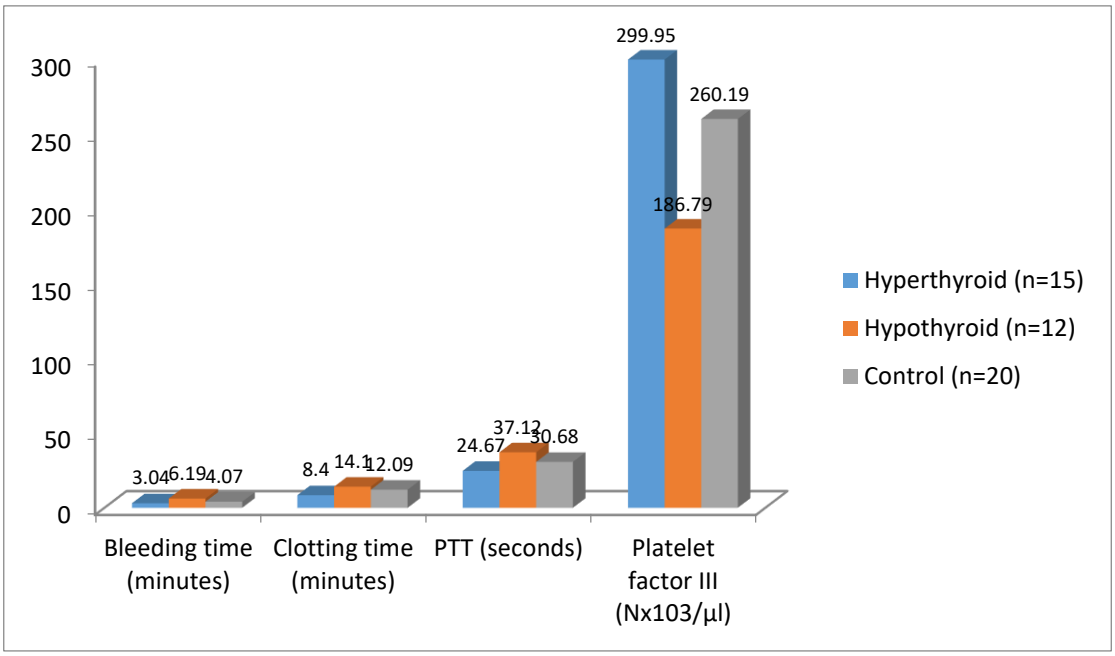

Figure 1: Comparison of clotting factors in groups

DISCUSSION

The largest endocrine gland in the body is the thyroid gland. It has a 14–18 gramme weight. In comparison to men, women have larger thyroid glands. The thyroid gland produces the thyroid hormones, T4 and T3. The hormone T3 is more powerful than T4.[9] Thyroid hormones are essential for maintaining metabolic homeostasis in adults and for cell differentiation throughout development. Erythropoiesis is significantly impacted by the thyroid gland as well. It stimulates the production of erythropoietin and the growth of erythroid progenitors. [10]

Globally, thyroid disorders are prevalent. A considerable number of thyroid disorders are prevalent in India as well. [11] Anaemia is brought on by thyroid malfunction, which impacts red blood cells. Important among these dysfunctions are hyperthyroidism and hypothyroidism. They could also result in pancytopenia. There is additional evidence linking thyroid dysfunction to changes in haematological parameter. [1-3]

In the present study the 27 patients who visited to hospital with altered thyroid levels were included in the study and there platelet volume and factors were taken for the research purpose with same age matched controls (n=20) to evaluate various platelet abnormalities in individuals with thyroid dysfunction and link them with the degree of thyroid dysfunction in light of these findings. In our study the number of hyperthyroid (n=15) patients was higher as compared to hypothyroid (n=12).

Maximum patients belong to age group of 15 to 45 years and females were higher in number as compared to males. These results show the presence of thyroid disease in people of young age and more in female community due to presence of high number of hormonal disturbances during teenage and less availability of nutritional food.

The mean platelet count in hyperthyroid patients was higher as compared to those in hypothyroid group. Our results were similar to a study done by Kadgi NV et al in year 2021 [12]. A measure of platelet activation and function is platelet volume. [13,14] Thrombocytes with high MPV values are more reactive than platelets of normal size. Thromboxane A2, which is exclusive to thrombocytes, may therefore be produced in greater quantities as a result of this circumstance.

In essence, it results in a drop in prostacyclin concentration, vasoconstriction at the vascular vein level, and vein blockage.[13] There are reports of elevated MPV readings in a number of cardiovascular conditions. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease, according to a study by Endler et al [15].

Furthermore, elevated MPV has been shown to be an independent risk factor for myocardial infarction and coronary atherosclerosis by KilicliCamur et al. [16] MPV values have the potential to be a useful indicator of blood glucose levels. Increased mean platelet sizes were recently demonstrated by Coban et al. in both obesity and impaired fasting glucose. [17,18] Additionally, it is mentioned in MPV values are elevated in diabetes mellitus, according to numerous research. [19-22]

Studies assessing platelet volumes in thyroid conditions are scarce. [23,24] Two investigations on hypothyroidism have produced contradicting findings. While it is proven in the study by Ford et al. that long-term hypothyroidism does not result in an increase in small-sized platelets in the bloodstream, the study by van Doormaal et al. asserts that hypothyroidism causes an increase in small-sized platelets. [25,26]

In our study among hypothyroid patients, bleeding and clotting times were much longer, while in the hyperthyroid group, they were shorter. Prothrombin time was also significantly higher. Compared to the hypothyroid group, the hyperthyroid group had higher platelet factor III availability. Increased bleeding time, prothrombin time (PT), activated partial thromboplastin time (aPTT), and clotting time were found in overt hypothyroid individuals compared to control individuals in a study by Gullu S et al. on 15 subclinical hypothyroid, 15 euthyroid, and 15 euthyroid controls.[27]

Reduced levels of factor VIII activity, vWF Antigen, vWF activity, vWF ristocetin, fibrinogen, ristocetin agglutination, factor IX, XI, plasminogen activator inhibitor, factor VIII:C, and vWF:C have also been linked to hypothyroidism. In comparison to the time at which the patient becomes euthyroid after receiving thyroid hormone replacement therapy, hypothyroidism is associated with a significant decrease in FVIII activity, vWF antigen, and vWF activity, as well as increased aPTT in thyroidectomized patients with severe short-term hypothyroidism before and after receiving either levothyroxine.[28]

The limitations of the study include small sample size and study on single center therefore the results cannot be concluded for general population. Future studies on higher number of patients are required to obtain more fruitful results.

CONCLUSION

Our study's strongest component, platelet analysis, revealed that all participants with hypothyroidism and hyperthyroidism directly affect the majority of clotting factors. Thyroid hormones are important regulators of the different parameters in multiple ways. Their existence may indicate subclinical thyroid dysfunction, enabling prompt treatment. Therefore, it's critical to include thyroid hormone screening while treating diseases that remain unexplained in women of reproductive age. Thus, it may be concluded that all patients with hyperthyroidism and hypothyroidism should have routine evaluations for potential platelet alterations.

References

1) Yen PM. Physiological and Molecular Basis of Thyroid Hormone Action. Physiol Rev. 2001;81(3):1097–1142.

2) Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian J Endocr Metab. 2013;17:647–52.

3) Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocr Metab. 2011;15(Suppl S2):78–81.

4) Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC. LThyroxine therapy in subclinical hypothyroidism. A double-blind, placebo-controlled trial. Ann Intern Med 1984; 101: 18–24.

5) Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. J Clin Endocrinol Metab 2003; 88: 2438–2444.

6) Erem C. Thyroid disorders and hypercoagulability. Semin Thromb Hemost.2011; 37: 17-26.

7) Benzaquen LR, Yu H, Rifai N. High sensitivity C-reactive protein: an emerging role in cardiovascular risk assessment. Crit Rev Clin Lab Sci 2002; 39: 459–497.

8) van der Loo B, Martin JF. A role for changes in platelet production in the cause of acute coronary syndromes. Arterioscler Thromb Vasc Biol 1999; 19: 672–679.

9) Das KC, Mukherjee M, Sarkar TK. Erythropoiesis and erythropoietin in hypo and hyperthyroidism. J Clin Endocrinol Metab. 1975;40(2):211–20.

10) Golde DW, Bersch N, Chopra IJ, Cline MJ. Thyroid hormones stimulate erythropoiesis in vitro. Br J Haematol. 1977;37(2):173–7.

11) Kawa MP, Grymuła K, Paczkowska E, Bakiewicz-Masiuk M, D ˛abkowska E, Koziołek M. Clinical relevance of thyroid dysfunction in human haematopoiesis: biochemical and molecular studies. Eur J Endocrinol. 2010;162(2):295–305.

12) Kadgi NV, Chauhan SG, Nakate LA. Hematological changes in hypothyroidism and hyperthyroidism in adults. Indian J Pathol Oncol 2021;8(4):452-456.

13) Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996; 7: 157–161.

14) Greisenegger S, Endler G, Hsieh K, Tentschert S, Mannhalter C, Lalouschek W. Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular events? Stroke 2004; 35: 1688–1691.

15) Endler G, Klimesch A, Sunder-Plassmann H et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. Br J Haematol 2002; 117: 399–404.

16) Kilic¸li-Camur N, Demirtunc¸ R, Konuralp C, Eskiser A, Bas¸aran Y. Could mean platelet volume be a predictive marker for acute myocardial infarction? Med Sci Monit 2005; 11: 387–392.

17) Coban E, Ozdogan M, Yazicioglu G, Akcit F. The mean platelet volume in patients with obesity. Int J Clin Pract 2005; 59: 981–982.

18) Coban E, Bostan F, Ozdogan M. The mean platelet volume in subjects with impaired fasting glucose. Platelets 2006; 17: 67–69.

19) Saigo K, Yasunaga M, Ryo R. Mean platelet volume in diabetics. Rinsha Byar 1992; 40: 215–217.

20) Sharpe PC, Trinick T. Mean platelet volume in diabetes mellitus. Q J Med 1993; 86 (11): 739–742.

21) Hekimsoy Z, Payzin B, Ornek T, Kandogan G. Mean platelet volume in type 2 diabetic patients. J Diabetes Complications 2004; 18: 173–176.

22) Jones RL, Paradise C, Peterson CM. Platelet survival in patients with diabetes mellitus. Diabetes 1981; 30: 486–489.

23) Panzer S, Haubenstock A, Minar E. Platelets in hyperthyroidism: studies on platelet counts, mean platelet volume, 111-indiumlabeled platelet kinetics, and platelet-associated immunoglobulins G and M. J Clin Endocrinol Metab. 1990; 70: 491–496.

24) Marongiu F, Conti M, Murtas ML, Mameli G, Sorano GG, Martino E. What causes the increase in platelet mean volume in thyroid pathological conditions? Thromb Haemost. 1990; 63: 323– 324.

25) van Doormaal JJ, van der Meer J, Oosten HR, Halie MR, Doorenbos H. Hypothyroidism leads to more small-sized platelets in circulation. Thromb Haemost. 1987; 58: 964–965.

26) Ford HC, Carter JM. Moderate, chronic hypothyroidism does not lead to more small-sized platelets in the circulation. Thromb Haemost. 1988; 60: 524.

27) Gullu S, Sav H, Kamel N. Effects of levothyroxine treatment on biochemical and hemostasis parameters in patients with hypothyroidism. Eur J Endocrinol. 2005;152(3):355–61.

28) Yango J, Alexopoulou O, Eeckhoudt S, Hermans C, Daumerie C. Evaluation of the respective influence of thyroid hormones and TSH on blood coagulation parameters after total thyroidectomy. *Eur J Endocrinol.* 2011;164(4):599–603.