



Original Article

Variation of Certain Haemostatic Parameters in Hypothyroidism

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ABSTRACT

Thyroid disorders which has increased incidence in females, were found to effect coagulation-fibrinolytic system. In the present study an effort is made to evaluate the alterations of certain haemostatic parameters in overt hypothyroid patients.

Bleeding time, clotting time & platelet count were estimated in hypothyroid subjects and control group, with sample size of 15 each. Hypothyroid group included subjects with low FT₃, FT₄ & elevated TSH value (mean 14.9 mU/L). Both the groups were age and sex matched. The results showed prolonged bleeding time and clotting time which were statistically significant with p-value of <0.0001 for both the parameters each. In the present study, hypothyroid group showed decreased platelet count when compared to control group which was statistically significant with a p-value of <0.0001. This finding was in contrast to many of the previous studies which showed either increase in platelet count or even if there was decrease, it was statistically not so significant.

This shows increased bleeding tendency or hypocoagulable state in overt hypothyroid patients. The more elevated the TSH levels, the more the deviation of haemostatic parameters from normal.

Key-words: Hypothyroidism FT₃, FT₄, TSH, haemostasis, bleeding time, clotting time, platelet count.

INTRODUCTION

Haemostasis is intricate, well balanced system, maintaining delicate balance between coagulation and fibrinolytic systems. Though haemostasis involves complex multitude of intertwined cascade reactions, ultimately it results in homeostasis. May it be for maintenance of blood in fluid state on one hand or for sealing and containing the injured blood vessel by primary and secondary hemostatic plugs on the other hand, by activating clotting mechanism that too in

a well regulated and sequential manner and resolving of the clot later on by fibrinolytic system, it depicts how well haemostasis is regulated and controlled inspite of involving intricate mechanisms. Such physiological processes are very much essential for maintaining equilibrium. Added to this, haemostasis may be influenced by myriad of factors like autoimmunity, certain drugs and endocrine disorders.

Among the various endocrine abnormalities, thyroid disorders do effect haemostasis. Incidence

of thyroid disorders is more in females than males. Thyroid hormones as such bring about various metabolic and physiological processes including coagulation system. So naturally it implies that thyroid disorders do affect coagulation cascade. Haemostasis is modified by both thyroid disorders and autoimmunity.

In the present study, effort is made to evaluate the effect of hypothyroidism on certain haemostatic parameters.

MATERIALS AND METHODS

Present study included 20 female patients with mean age 32 years (32.4 ± 4.232 years) from medical and endocrinology outpatient clinics and controls included 20 female healthy individuals. Subjects satisfying inclusion and exclusion criteria were enrolled in the study. Prior informed consent was taken from all the subjects participating in the study.

Inclusion criteria

- Females with age group of 25-45 years
- Elevated TSH levels (>20 mU/L)
- Low FT_3 & FT_4 levels.

Exclusion criteria

- H/O DM, HTN, hypotension, coronary heart disease,
- Past or present H/O smoking, alcoholism,
- Past or present H/O bleeding disorders
- Past or present H/O serious medical or endocrine disorders
- Subjects using any medication that may affect haemostatic parameters

METHODS

Blood samples were collected between 9.00 - 10.00 A.M. after overnight fasting and tests were done with only minimal time lapse of $\frac{1}{2}$ hr. to 1hr. Serum FT_3 , FT_4 & TSH levels were measured by automated chemiluminiscence immunoassay (CLIA) method. Haemostatic parameters included in the study were analyzed using Sysmex Coulter automated analyzer.

RESULTS

Descriptive data was analyzed by using SPSS software windows version 21. Results were expressed as means \pm S.D. For comparing study & control groups, unpaired t-test was done and p-value determined by Graphpad software Quickcalcs t-test calculator. Results were assumed to be statistically significant if $p < 0.05$.

Descriptive analysis revealed no significant differences between both the hypothyroid & control groups for gender & mean age.

In the hypothyroid group, mean FT_3 level was 0.142ng/dl, the mean FT_4 level was 1.036ng/dl & the mean TSH level was 14.90mU/L. In the control group, mean FT_3 level was 0.291ng/dl, the mean FT_4 level was 2.117ng/dl & the mean TSH level was 2.7mU/L. P & t-values, degree of freedom are detailed in table-1.

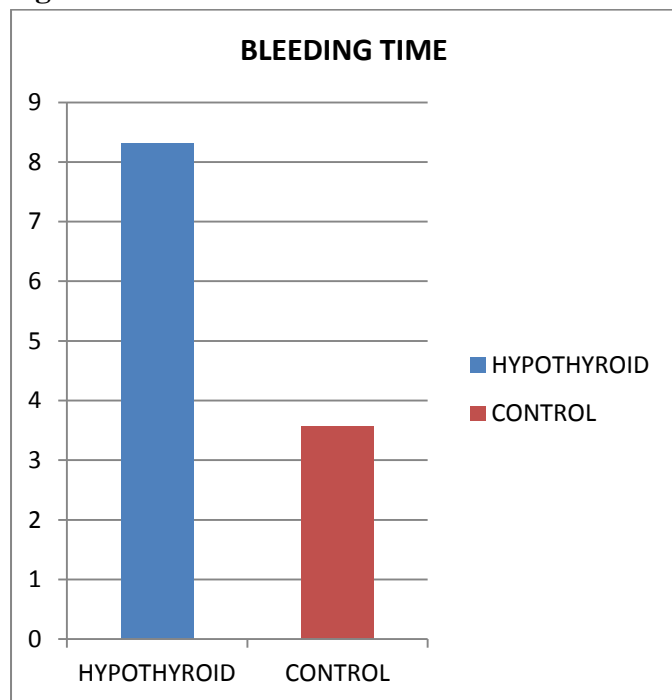
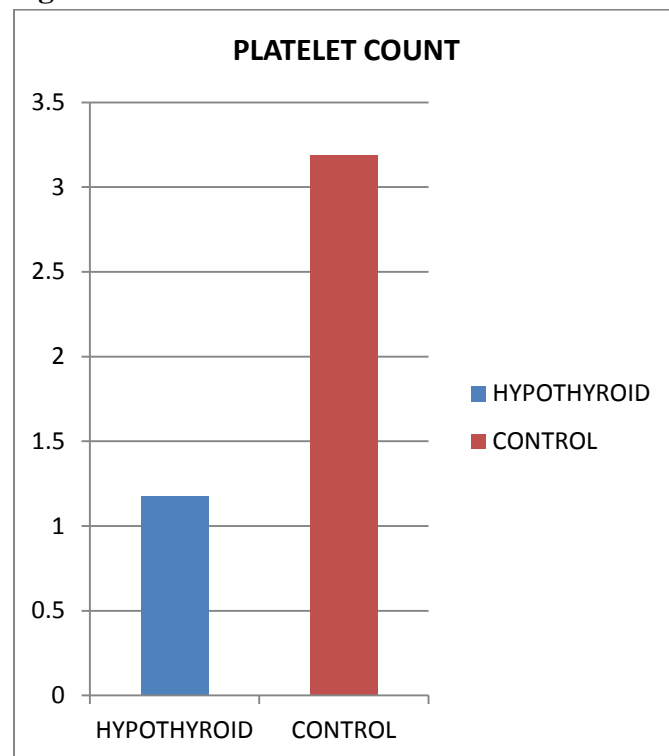
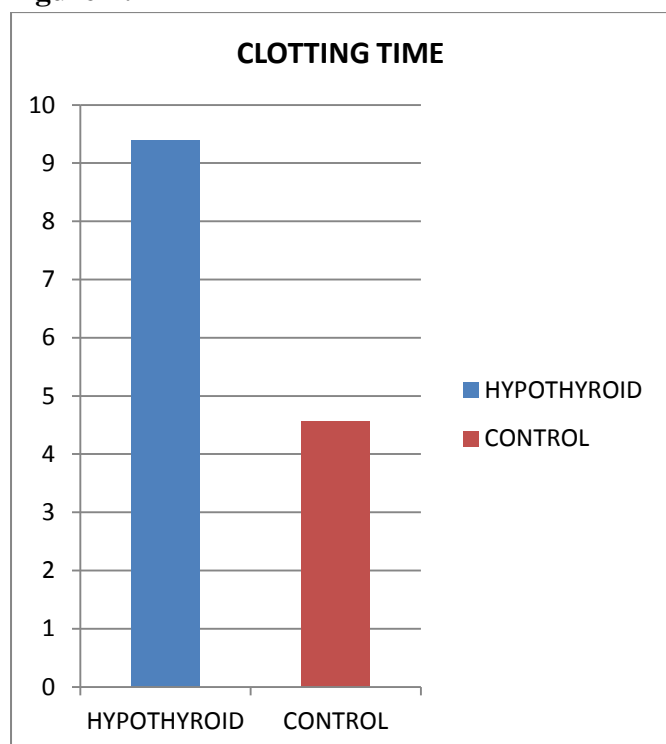
Hypothyroid group showed elevated bleeding time, clotting time when compared to the control group which was extremely statistically significant ($p\text{-value} < 0.0001$) as detailed in table-2. Platelet counts were decreased in the hypothyroid group when compared to control group which was extremely statistically significant. ($p\text{-value} < 0.0001$).

Table-1. Comparison of T_3 , T_4 & TSH levels in hypothyroid and control groups

PARAMETER	HYPOTHYROID		CONTROL		df	P-VALUE	t-VALUE
	MEAN	SD	MEAN	SD			
T_3	0.142	0.018	0.29133	0.017	28	<0.0001	8.215
T_4	1.036	0.274	2.1173	0.153	28	<0.0001	13.34
TSH	14.9	6.949	2.7247	0.955	28	<0.0001	6.723

Table-2. Comparison of haemostatic parameters in hypothyroid and control groups.

PARAMETER	HYPOTHYROID		CONTROL		df	P-VALUE	t-VALUE
	MEAN	SD	MEAN	SD			
BLEEDING TIME	8.324	0.5606	3.5707	0.352	28	<0.0001	27.8085
CLOTTING TIME	9.3907	0.5157	4.5647	1.0099	28	<0.0001	16.4837
PLATELET COUNT	1.1753	0.1239	3.1887	0.5199	28	<0.0001	14.595

Figure-1.**Figure-3.****Figure-2.**

ANALYSIS AND DISCUSSION

Present study revealed alteration of coagulation system in hypothyroid subjects. They had prolonged bleeding time, clotting time & decreased platelet count when compared to the control group. Also it was noted that this change in haemostatic parameters was more pronounced if the disease was more severe. Mostly hypocoagulable state or increased bleeding tendency was found in hypothyroidism. But there was no evidence of overt clinical bleeding in hypothyroid subjects.

Menorrhagia, the most frequent presenting complaint of hypothyroid females, was assumed to be due to oestrogen breakthrough bleeding which was secondary to anovulation^[1-3]. The findings of present study correlated with some of the earlier studies. Decreased platelet count^[4,5],

decreased platelet adhesion to glass beads^[6,7], decreased platelet aggregation^[8,9], decreased platelet factor 3 activity^[10], decreased heat production from platelets^[11] was observed in hypothyroid condition. The decreased platelet count & functions was attributed to altered platelet & arterial wall prostaglandin production or metabolism in hypothyroid state^[12]. Elevated levels of Ig G adherent to platelets in certain autoimmune thyroid disorders was implicated to abnormal platelet aggregation patterns observed in these conditions^[13].

Inspite of varied changes in haemostatic pattern, all the parameters reverted back to normal if treated with thyroxine supplementation^[11].

However certain studies showed contradictory results to present study where the platelet count was increased^[14] or remained unchanged^[15-21] in hypothyroid conditions. It was found that in hypothyroid patients there was decreased megakaryocytes in the bone-marrow inspite of normal peripheral platelet count^[22]. Association between Grave's disease & autoimmune thrombocytopenic purpura was elicited^[23], but contradistinction to that, association between Hashimoto's thyroiditis & autoimmune thrombocytopenia was not established^[24].

Capillary fragility was found to be increased in hypothyroidism^[25]. However there was decreased capillary fragility in one of the studies done in hypothyroid states.

But in majority of the studies, prolonged bleeding time was noted in hypothyroid patients^[6,7,26,27]

Decreased levels of clotting factors like factor VIII^[27,28,29,30], IX, XI^[6,29], XII^[31]^[15-20], factors VII^[6], V, IX^[6,29] & X found in hypothyroid condition was assumed to be due to generalised decrease in protein synthesis observed in hypothyroidism^[32]. Prolonged clotting time was attributed to decreased levels of clotting factors.

Biological half lives of certain clotting factors II, VII, IX & X were increased in hypothyroidism^[33]. It has clinical implications in that the dosage & duration of anticoagulants like heparin, warfarin need to be adjusted in hypothyroid

patients. For optimal anticoagulation, dosage of warfarin need to be increased than usual^[34,35].

Increased fibrinolytic activity observed in hypothyroidism was normalised with thyroxine treatment.^[36,31] There was simultaneous increase in plasminogen which was assumed to be because of increase in plasminogen activator^[31,37,28].

CONCLUSION

To put it in a nut-shell, significant variation of coagulation profile was observed in overt hypothyroidism. Decrease in platelet count was also observed in the subject group. So hypothyroid condition shows hypocoagulable state or increased bleeding tendency. Also in certain studies, subclinical hypothyroidism was associated with hypercoagulable state and episodes of venous thromboembolism was noted. These findings stresses the need for meticulous screening of haemostatic parameters in thyroid disorders to avoid thrombosis or bleeding episodes by instituting appropriate thyroxine therapy.

Also the dosage and duration of anticoagulant therapy need to be adjusted in hypothyroid patients to obtain optimal results.

Unravelling the effect of thyroid hormone variations on haemostatic parameters & the mechanisms involved more precisely may lead to increased options for treatment of altered parameters so as to avoid serious complications.

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