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A Study on Correlation between D-Dimer Levels and TSH in Elderly Euthyroid Patients to Evaluate Potential Coagulopathic Tendencies

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Introduction

Thyroid hormones namely T3 (triiodothyronine) and T4 (thyroxine or tetraiodothyronine) primarily sustain basal metabolic rate (BMR) and are essential for growth, neuronal development, reproduction and regulation of carbohydrate, lipid and energy metabolism. Consequently, disorders of the thyroid especially hypothyroidism and hyperthyroidism are common conditions with potentially devastating health consequences that affect all populations worldwide [1]. Hyperthyroidism is characterized by increased thyroid hormone synthesis and secretion from the thyroid gland [2]. It usually manifests with increased excitability and fine tremors, heat intolerance, increased sweating, weight loss, fatigue, etc. Hypothyroidism results from low levels of thyroid hormones with varied manifestations such as cold intolerance, atherosclerosis, insulin resistance, etc [3]. Recent studies suggest that hyperthyroidism enhances coagulation and increases the risk of thrombosis [4]. D-dimer is a soluble fibrin degradation product that results from the systematic degradation of vascular thrombi by fibrinolytic pathway. It functions as an indirect marker of fibrinolysis and displays unique properties as a biological marker of hemostatic anomalies, due to which serves as a valuable marker of activation of coagulation and fibrinolysis in several clinical scenarios [5]. According to recent studies, hyperthyroidism is regarded to be associated with hypercoagulability and hypo-fibrinolysis, whereas the hemostatic profile in hypothyroidism is ambiguous [6]. Low platelet count, aggregation-agglutination, von-Willebrand factor antigen level decreased levels of coagulation factors VIII, IX, XI, VII, and plasminogen activator-1 are detected in overt hypothyroidism, rendering a hypo-coagulable nature; while elevated fibrinogen levels implicated in subclinical hypothyroidism and autoimmune thyroid disease renders a hypercoagulable propensity [7]. Hence, there is ample evidence that indicated hypercoagulable and hypo-coagulable tendencies in hyperthyroidism and hypothyroidism. However, there are almost no studies to our knowledge that have been done on euthyroid subjects to assess whether TSH levels (primarily used in the diagnosis of thyroid disorders) in the extremes of euthyroid reference spectrum can lead to a potential hypercoagulable or hypo-coagulable state, especially in the vulnerable population such as the elderly. Hence, we intend to know more about the risk of a potential hypercoagulable state in the susceptible population (especially the elderly) by studying D dimer levels in a spectrum of elderly euthyroid patients and assessing whether TSH levels (which are primarily used to diagnose thyroid disorders) have any correlation with D-dimer levels (not just in thyroid disorders but also in the euthyroid state). The importance of contributions of such factors can facilitate doctors in developing appropriate treatment regimens for patients with thyroid problems, with suspicion of coagulopathy in mind.

Objective

To study correlation between D-dimer levels and TSH in elderly patients and evaluate coagulopathic tendencies.

Materials and Methods

Type of study: Cross-sectional study.

Sample population: Elderly south Indian individuals aged 50-92 years visiting the respective tertiary care hospital for clinical tests under study.

Criteria for choosing subjects: Subjects were chosen such that they were aged between 50-92 years and not afflicted with any chronic hepatic, pulmonary or renal afflictions, or any inflammatory autoimmune diseases like AIDS or rheumatoid arthritis. Subjects on medications or thyroid supplements were excluded from the study.

Sample size: A total of 30 subjects who met the above-mentioned criteria were chosen.

Duration of study: One month.

Method: Subjects chosen as per inclusion criteria were first informed regarding the study via an informed consent form. Only after receiving their signed approval for participation in the study, the subjects matching selection criteria were taken into consideration.

Results

Normality of the data distribution of D-Dimer levels and TSH levels was first assessed as per Shapiro Wilk test.

Whereas the middle horizontal line represents the median TSH level, the upper and lower bounds of the box represent the 75th and the

Table 1: Case Processing Summary.

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
D-Dimer	30	57.7%	22	42.3%	52	100.0%
TSH	30	57.7%	22	42.3%	52	100.0%

Table 2: Descriptives.

			Statistic	Std. Error
D-Dimer	Mean		2.4660	0.56809
	95% Confidence Interval for Mean	Lower Bound	1.3041	
		Upper Bound	3.6279	
	5% Trimmed Mean		2.2476	
	Median		0.6850	
	Variance		9.682	
	Std. Deviation		3.11156	
	Minimum		0.17	
	Maximum		8.70	
	Range		8.53	
	Interquartile Range		5.05	
	Skewness		1.182	0.427
	Kurtosis		-0.384	0.833
TSH	Mean		1.1893	0.11065
	95% Confidence Interval for Mean	Lower Bound	0.9630	
		Upper Bound	1.4156	
	5% Trimmed Mean		1.1541	
	Median		1.1050	
	Variance		0.367	
	Std. Deviation		0.60606	
	Minimum		0.45	
	Maximum		2.56	
	Range		2.11	
	Interquartile Range		0.95	
	Skewness		0.753	0.427
	Kurtosis		-0.264	0.833

Table 3: Extreme Values.

			Case Number	Value
D-Dimer	Highest	1	41	8.70
		2	45	8.67
		3	44	8.31
		4	23	7.84
		5	48	7.50
	Lowest	1	50	0.17
		2	22	0.18
		3	42	0.21
		4	21	0.21
		5	26	0.30
TSH	Highest	1	25	2.56
		2	24	2.54
		3	27	2.12
		4	46	1.86
		5	51	1.85
	Lowest	1	45	0.45
		2	41	0.48
		3	48	0.52
		4	28	0.52
		5	44	0.62

Table 4: Tests of Normality.

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
D-Dimer	0.335	30	<0.001	0.691	30	<0.001
TSH	0.138	30	0.148	0.915	30	0.020
a. Lilliefors Significance Correction						

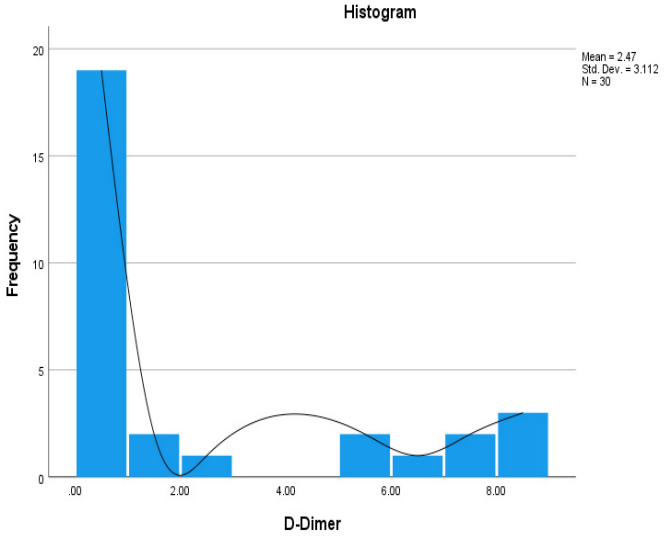

Figure 1: Histogram showing distribution of D-Dimer levels.

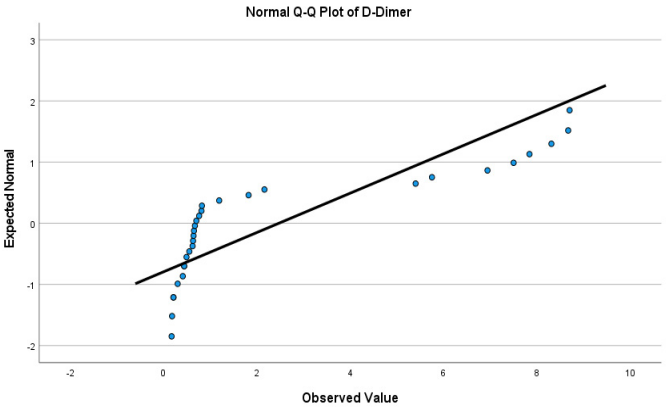

Figure 2: Normal Q-Q Plot of D-Dimer showing relationship between Expected Normal and the Observed values respectively.

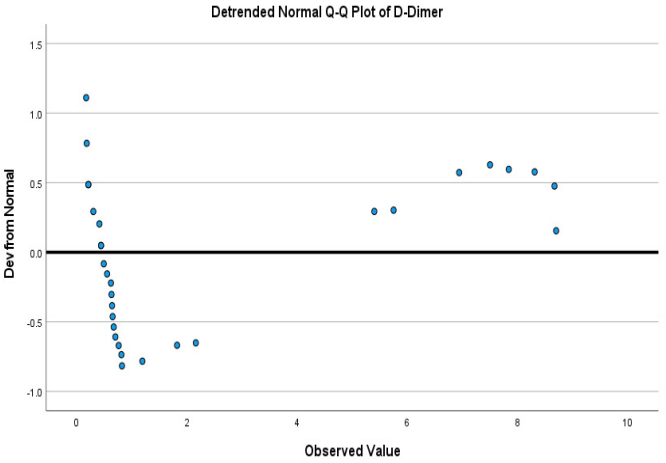

Figure 3: De-trended Normal Q-Q Plot of D-Dimer showing relationship between Deviation from Normal and Observed Values.

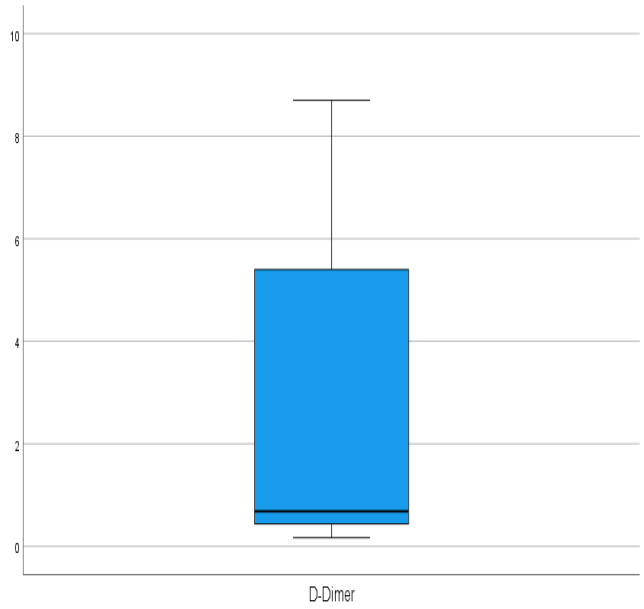

Figure 4: Box-and-Whisker plot depicting the distribution of D-Dimer levels.

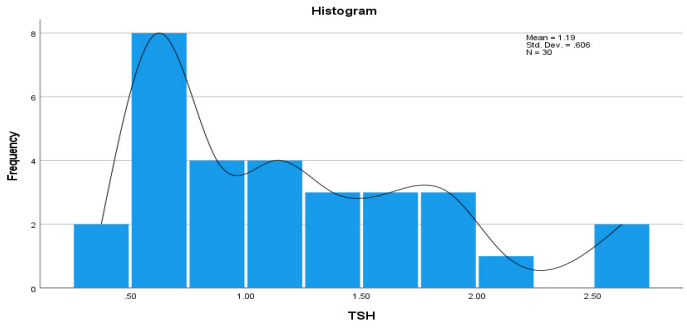

Figure 5: Normal Q-Q Plot of TSH showing relationship between Expected Normal and the Observed values respectively.

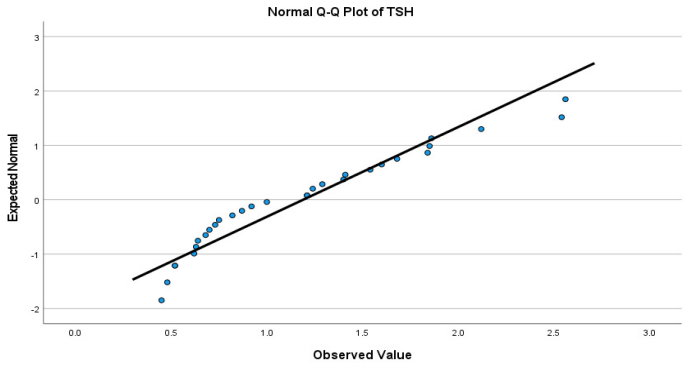

Figure 6:

25th centile of TSH levels respectively, and the upper and lower extent of the whiskers represent the Tukey limits for TSH levels in each of the groups.

The Shapiro-Wilk test indicated that the data distribution was not normal (non-Gaussian) distribution. Hence, Spearman's correlation coefficient (non-parametric test) was employed to check the correlation between TSH levels and D-Dimer levels in elderly euthyroid subjects.

Spearman's rho correlation coefficient test showing a negative correlation between D-Dimer and TSH levels in elderly euthyroid subjects which is statistically significant at the 0.05 level.

The test indicated that there is a negative correlation between D-Dimer and TSH levels in elderly euthyroid subjects which is statistically significant at the 0.05 level, suggesting that a decrease in TSH levels (thus indicating a shift towards hyperthyroidism) is associated with a concomitant increase in D-Dimer levels, implicating a proclivity for a hypercoagulable haemostatic state whereas an increase in TSH levels (thus indicating a shift towards hypothyroidism) are similarly associated with a concomitant decrease in D-Dimer levels, implicating a proclivity for a potential hypo-coagulable state.

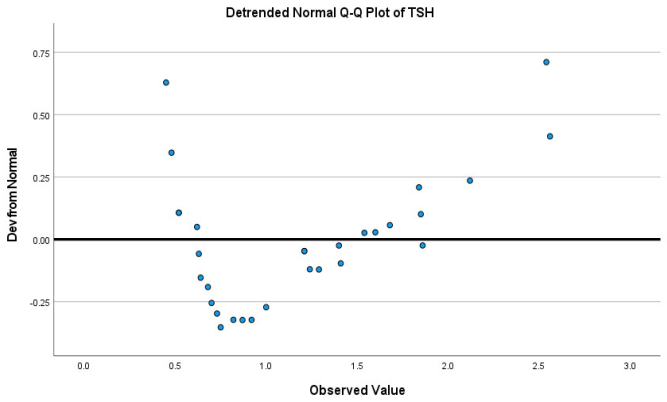

Figure 7: De-trended Normal Q-Q Plot of TSH showing relationship between Deviation from Normal and Observed Values.

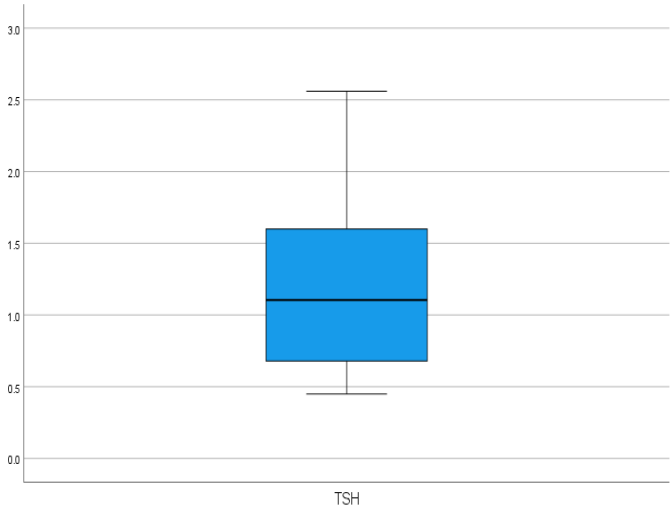

Figure 8: Box-and-Whisker plot depicting the distribution of TSH levels.

Table 5: Correlations.

			D-Dimer	TSH
Spearman's rho	D-Dimer	Correlation Coefficient	1.000	-0.412*
		Sig. (2-tailed)	.	0.024
		N	30	30
	TSH	Correlation Coefficient	-0.412*	1.000
		Sig. (2-tailed)	0.024	.
		N	30	32

*. Correlation is significant at the 0.05 level (2-tailed).

Discussion

Low T3 and T4 levels cause TSH levels to increase via a feedback mechanism. TSH acts on the thyroid gland and stimulates the release of T3 and T4. T3 and T4 in turn exert negative feedback mechanisms on TSH release. As for the elevated D-Dimer dependent procoagulant proclivity, in-vitro and clinical evidence implicate multiple mechanisms for this risk. Genomic functions of T3 via a nuclear thyroid hormone receptor have been suggested, but recent evidence indicates that nongenomic mechanisms initiated at the receptor for L-thyroxine (T4) on platelet integrin, αvβ3 are of a prothrombotic predisposition [4]. It is also possible that thyroid hormone stimulates the platelet-endothelial cell dynamics involved in local thrombus formation. Effects of TSH and resultant release of thyroid hormones not just at the receptor signaling level but at the physiological level on the the heart may also indirectly influence hemostasis. Hyperthyroidism leads to a higher incidence of atrial fibrillation and atrial flutter, and at least partially by that mechanism can result in a higher risk of cerebral arterial thrombosis. In addition, compressive manifestations of goitre on developing venous thrombosis have been ascribed to local stasis of blood because of tumor cell proliferation and neoplastic expansion [8]. Another study reviewed both hyper- and mild-to-moderate hypothyroidism to conclude that they are associated with prothrombotic plasma fibrin clot phenotype and that restoration of euthyroidism had improved fibrin clot properties with a return to normalcy of ex-vivo plasma fibrin clot permeability (Ks) in hyperthyroid and lysis tendency in hypothyroid patients [9]. Thyroxine released after TSH level elevation also increases the activity of HMG CoA reductase leading to increased synthesis of cholesterol. This increased risk of cholesterol-plaque mediated atherosclerosis could also lead to an increase in D-Dimer levels.

Conclusion

Our study confirms that TSH levels in euthyroid elderly individuals correlate negatively with TSH levels. This finding is beneficial for doctors in that they can suspect a risk of potential hypercoagulable state in the euthyroid elderly and provide prompt and appropriate therapy for the same.

Funding

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Conflict of Interest

None declared.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

References

1. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, et al. (2018) Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol 14: 301-316. https://doi.org/10.1038/nrendo.2018.18
2. De Leo S, Lee SY (2016) Hyperthyroidism. Lancet 388: 906-918. https://doi.org/10.1016/s0140-6736(16)00278-6
3. Patil N, Rehman A, Jialal I (2022) Hypothyroidism. StatPearls, StatPearls Publishing, Treasure Island, Florida, United States.
4. Davis PJ, Mousa SA, Schechter GP (2018) New interfaces of thyroid hormone actions with blood coagulation and thrombosis. Clin Appl Thromb Hemost 24: 1014-1019. https://doi.org/10.1177/1076029618774150
5. Johnson ED, Schell JC, Rodgers GM (2019) The D-dimer assay. Am J Hematol 94: 833-839. https://doi.org/10.1002/ajh.25482
6. Erem C (2011) Thyroid disorders and hypercoagulability. Semin Thromb Hemost 37: 17-26. https://doi.org/10.1055/s-0030-1270067
7. Ordookhani A, Burman KD (2017) Hemostasis in hypothyroidism and autoimmune thyroid disorders. Int J Endocrinol Metab 15: e42649. https://doi.org/10.5812/ijem.42649
8. Elbers LP, Squizzato A, Gerdes VE (2018) Thyroid disorders and hemostasis. Semin Thromb Hemost 44: 676-682. https://doi.org/10.1055/s-0038-1666825
9. Mazur P, Sokołowski G, Hubalewska-Dydejczyk A, Płaczkiewicz-Jankowska E, Undas A (2014) Prothrombotic alterations in plasma fibrin clot properties in thyroid disorders and their post-treatment modifications. Thromb Res 134: 510-517. https://doi.org/10.1016/j.thromres.2014.05.041