

Original Research Article

# Can high normal TSH level predispose to hypercholesterolemia?


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	International Archives of Integrated Medicine, Vol. 3, Issue 8, August, 2016. Copy right © 2016, IAIM, All Rights Reserved. Available online at <a href="http://iaimjournal.com/">http://iaimjournal.com/</a> ISSN: 2394-0026 (P)                      ISSN: 2394-0034 (O)	
	Received on: 11-07-2016 Source of support: Nil	Accepted on: 18-07-2016 Conflict of interest: None declared.
<b>How to cite this article:</b> Pushkal SR, Shenoy V, Prabhu K. Can high normal TSH level predispose to hypercholesterolemia? IAIM, 2016; 3(8): 248-257.		

## Abstract

**Background:** Thyroid hormone plays an important role in carbohydrate, protein, and lipid and electrolyte metabolism. Studies have demonstrated the association of hypothyroidism with dyslipidaemia. However the impact of high normal TSH on lipid profile is lacking. Also, thyroid hormone is known to influence glomerular filtration rate, and renal electrolyte handling. So, this study compared TSH levels in normal ranges with fasting lipid profile and electrolytes.

**Objectives:** To measure and compare the levels of serum TSH, fasting lipid profile and electrolytes in euthyroid individuals with normal TSH and to correlate serum TSH with lipid profile and electrolytes across different age groups in both sexes.

**Materials and methods:** After obtaining ethical clearance, 2 ml of fasting venous blood sample was drawn from 200 subjects (males=100, females=100) aged between 20-75years who consented to participate. Serum was used for estimation of TSH, lipid profile and electrolytes. TSH was measured by 4<sup>th</sup> generation Immunoassay in Cobas 6000 e601 autoanalyzer (Roche). The lipid profile and electrolytes were assayed in Cobas 6000 c501 autoanalyzer (Roche).

**Results:** Serum TSH values showed significant positive correlation with total cholesterol ( $p < 0.001$ ), triglycerides ( $p < 0.001$ ) and LDL cholesterol ( $p < 0.001$ ), but did not show any significant correlation with HDL cholesterol. Also serum TSH showed significant negative correlation with sodium ( $r = -0.185$ ,  $p = 0.048$ ) and potassium ( $r = -0.205$ ,  $p = 0.028$ ) levels.

**Conclusion:** TSH and thyroid status can influence lipid and electrolyte metabolism. High normal TSH level may predispose to hypercholesterolemia and hypertriglyceridemia. High normal TSH patients can have lower serum electrolytes.

## Key words

Hypercholesterolemia, Hypertriglyceridemia, High normal TSH, Electrolytes, Euthyroid.

## Introduction

Thyroid hormone is a central regulator of body hemodynamics, thermoregulation and metabolism [1-4]. Hypothyroidism is one of the common metabolic disorders in the general population and it is thought to affect around 6–10% of women which may rise up to 25% in women over the age of 65 years [5]. Men are also affected, but less frequently. Hypothyroidism often leads to secondary dyslipidaemia [6]. Thyroid hormone plays an important role in carbohydrate, protein, and lipid and electrolyte metabolism. In recent years, studies have demonstrated that even within the normal range, serum TSH can influence cholesterol, low density lipoprotein, triglycerides and high density lipoprotein metabolism [7]. Even though, existing evidence indicates that decreased thyroid function can lead to reduced activity of HMG CoA reductase, total cholesterol and LDL-C (low density lipoprotein cholesterol) are found to be increased in patients with hypothyroidism [8]. This may be due to decreased LDL receptors activity resulting in decreased catabolism of LDL or a decreased lipoprotein lipase activity resulting in a decreased clearance of triglyceride rich lipoproteins [9]. Therefore, hypothyroid patients may also present with elevated triglyceride levels. Also, Thyroid hormone is known to influence glomerular filtration and renal electrolyte handling [10]. Thyroid hormones are necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of Thyroid hormones indicating a close interplay between them in regulating each other's function.

Hence, the goal of this study evaluated the association between serum TSH levels in normal range with lipid profile and electrolytes in euthyroid individuals.

## Materials and methods

Approval was obtained from institutional Ethics Committee Kasturba Hospital Manipal for this study. Two hundred individuals aged between 20-75years who consented to participate were enrolled in this study. But only 142 subjects were taken as study subjects and the rest were excluded.

**Inclusion criteria:** Both males and females of age group 20-75 years.

**Exclusion criteria:** Individuals aged less than 20 years and more than 75 years. Also individuals suffering from renal, hepatic, bone disorders, thyroid disorders, diabetes mellitus, and subjects on long term medications which might affect thyroid assay, lipid profile and electrolytes were excluded. Fasting serum samples were used for biochemical estimations. TSH was measured by Immunoassay in Cobas 6000 e601 autoanalyzer (Roche). The lipid profile and electrolytes were assayed in Cobas 6000 c501 autoanalyzer.

Based on serum TSH levels study subjects were grouped as follows:

**Group - 1:** 0.3-1.5  $\mu$ IU/mL

**Group - 2:** 1.5-3  $\mu$ IU/mL

**Group - 3:** 3-5  $\mu$ IU/mL

Also to assess the influence of TSH levels on lipid profile and electrolytes across different age groups, the study subjects were sub grouped as follows:

**Group A:** 20-40 years

**Group B:** 40-60 years

**Group C:** >60 years

Data analysis was done using SPSS version 16.0. One way ANOVA was used for intergroup comparisons. All parameters were correlated with TSH levels. P value <0.05 considered to be significant.

## Results

Demographic profile of study subjects was as per **Table – 1**. Comparison of serum lipid profile between the groups was as per **Table – 2**. Correlation of lipid profile with serum TSH was as per **Table – 3**. Comparison of serum TSH and serum lipid profile among different age groups was as per **Table – 4**. Correlation of TSH with lipid profile in males was as per **Table – 5**. Correlation of TSH with lipid profile in females was as per **Table – 6**. Correlation between serum

TSH and electrolytes of whole group was as per **Table – 7**.

**Table - 1:** Demographic profile of study subjects.

Groups	Mean Age in years	Male : Female
1 (n=40)	44.22±15.84	25:15
2 (n= 54)	43.37±13.77	28:26
3 (n=48)	45.37±14.56	30:18

**Table - 2:** Comparison of serum lipid profile between the groups.

Lipid profiles	Group 1	Group 2	Group 3
TC	165.2±35.43	187.1±41.8*	205.7±36.7**
TG	107.30±47.7	138.14±75.9	135.2±37.85
HDL-C	46.97±17.45	45.87±13.36	46.08±13.73
LDL-C	99.35±31.18	113.6±35.2 <sup>#</sup>	132.7±33.3 <sup>##</sup>

TC = Total Cholesterol (mg/dL), TG = Triglycerides (mg/dL), HDL-C = High Density Lipoprotein Cholesterol (mg/dL), LDL-C = Low Density Lipoprotein Cholesterol (mg/dL)

\*TC significant between group 1 & 2(p=0.02)

\*\*TC significant between group 1 & 3(p<0.001)

#LDL-C significant between group 1 & 3(p<0.001)

##LDL-C significant between group 2 & 3(p=0.01)

**Table - 3:** Correlation of lipid profile with serum TSH.

Lipid profiles	r value	p value <sup>*</sup>
Total cholesterol	0.46	<0.001 <sup>*</sup>
Triglycerides	0.25	<0.001 <sup>*</sup>
HDL-C	0.038	0.59 <sup>NS</sup>
LDL-C	0.407	<0.001 <sup>*</sup>
Ratio	0.038	0.59 <sup>NS</sup>

NS - Not significant, <sup>\*</sup> Pearson's correlation

## Discussion

We observed a significant correlation between TSH levels and lipid profile suggesting that individuals with high normal TSH can be predisposed to hypercholesterolemia and hypertriglyceridemia (**Table – 2, 3, Figure – 1 to 4**). When serum TSH and serum lipid profile was compared in different age groups, all the lipid profile parameters showed significant correlation between the groups (**Table – 4**). Only TG

showed a positive correlation in males (**Table - 5, Figure – 5**) whereas in females there was no statistically significant correlation of serum TSH with lipid profile (**Table – 6**) when compared between the sexes.

Subjects with higher normal TSH (TSH 3-5µIU/mL) had significantly higher levels of total cholesterol, LDL-C as compared that of low normal TSH subjects respectively indicating a

strong influence of thyroid hormones on lipid metabolism. We also correlated serum electrolytes with TSH which showed statistically significant negative correlation (**Table - 7, Figure – 6, 7**).

**Table - 4:** Comparison of serum TSH and serum lipid profile among different age groups.

	Group A (n=58)	Group B (n=75)	Group C (n=20)
Age (years)	20-40	40-60	>60
Mean age (mean±SD)	30.9±5.7	49.7±6.1	65.6±3.8
TSH (µIU/ml)	2.5±1.0	3.11±1.9*	3.35±1.7**
TC	188±45.8	203.8±41.0 <sup>#</sup>	186.9±39.2 <sup>##</sup>
TG	133.2±47.2	146.7±52.8	115±43.3 <sup>###</sup>
HDL-C	44±14.9	48.4±13.0 <sup>\$</sup>	51.7±15.7 <sup>\$\$</sup>
LDL-C	119±37.8	125.9±37.4	111.8±30.6 <sup>%</sup>

TC = Total Cholesterol (mg/dL), TG = Triglycerides (mg/dL), HDL-C = High Density Lipoprotein Cholesterol (mg/dL), LDL-C = Low Density Lipoprotein Cholesterol (mg/dL)

# TC significant between group I& II (p=0.02)

##TC significant between group II&III (p=0.05)

###TG significant between group II&III (p=0.02)

\$HDL-C significant between group I&II (p=0.03)

\$\$HDL-C significant between group I& III (p=0.02)

%LDL-C significant between group II&III (p=0.05)

**Table - 5:** Correlation of TSH with lipid profile in males.

	r value	p value
Total Cholesterol	0.206	0.092 NS
Triglycerides	0.294	0.015 *
HDL-C	-0.061	0.621 NS
LDL-C	0.11	0.37 NS

**Only triglyceride was statistically positively correlated with TSH levels in males.**

**Table - 6:** Correlation of TSH with lipid profile in females.

	r value	p value
Total Cholesterol	0.022	0.84 NS
Triglycerides	0.077	0.505 NS
HDL-C	-0.076	0.514 NS
LDL-C	0.033	0.77 NS

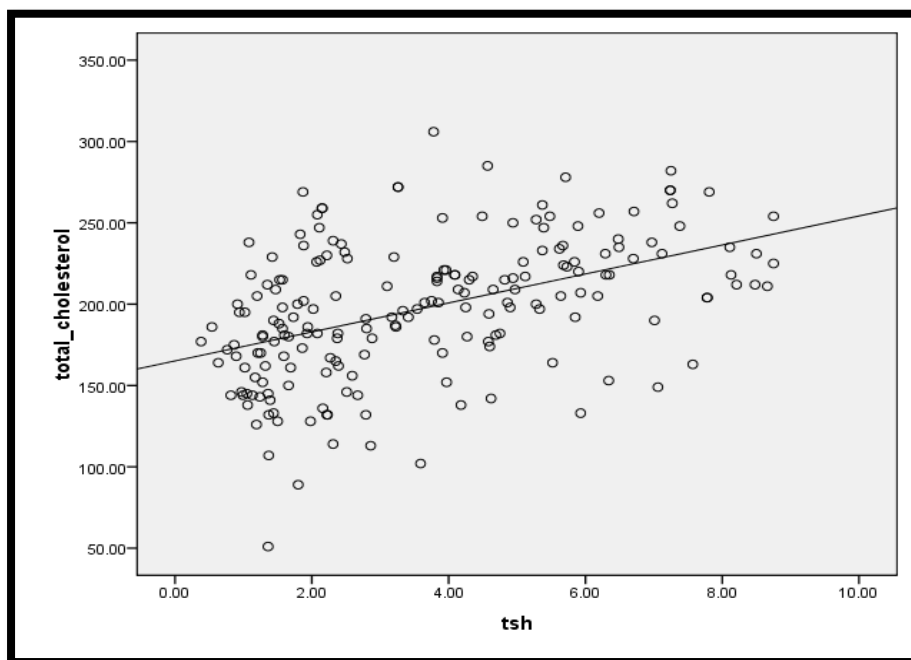
**There was no statistically significant correlation of TSH with lipid profile in females**

**Table - 7:** Correlation between serum TSH and electrolytes of whole group.

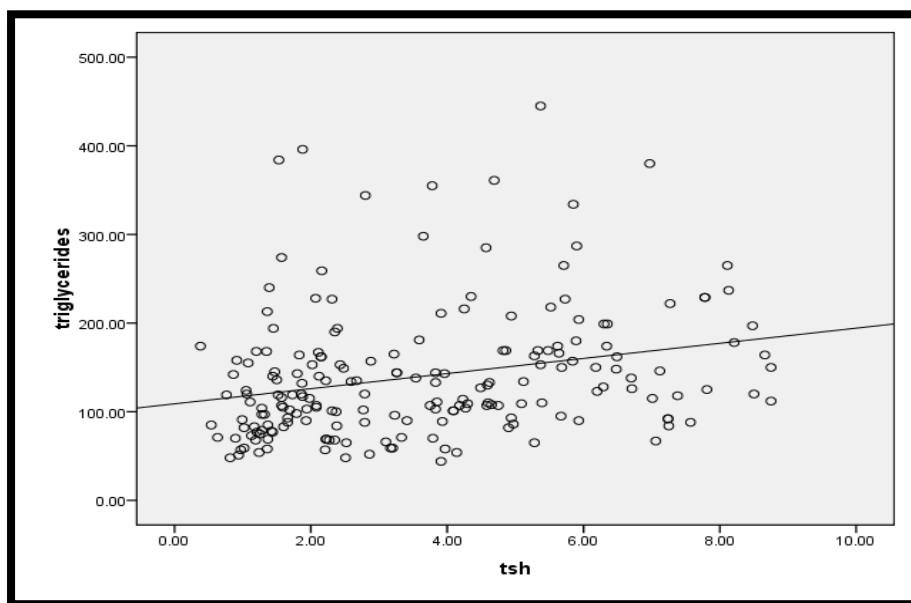
Electrolytes	r value	p value
Sodium	-0.185	0.048 *
Potassium	-0.205	0.028 *

\* significant

**Figure - 1:** Correlation between serum TSH ( $\mu\text{IU/mL}$ ) and total cholesterol (mg/dL).



**Figure - 2:** Correlation between serum TSH ( $\mu\text{IU/mL}$ ) and triglycerides (mg/dL).

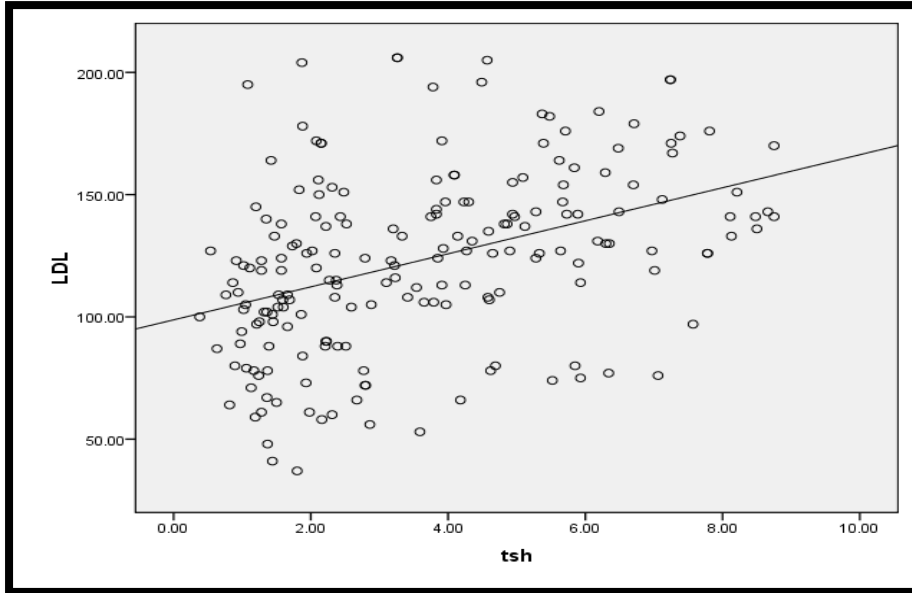


Studies conducted in euthyroid subjects of Korea [11], Latin American [12], and Spanish [13] individuals have shown a significant increase in serum TC, TG and LDL-C levels with TSH levels. Similar result was obtained in the HUNT study performed in Norway [14]. In a large

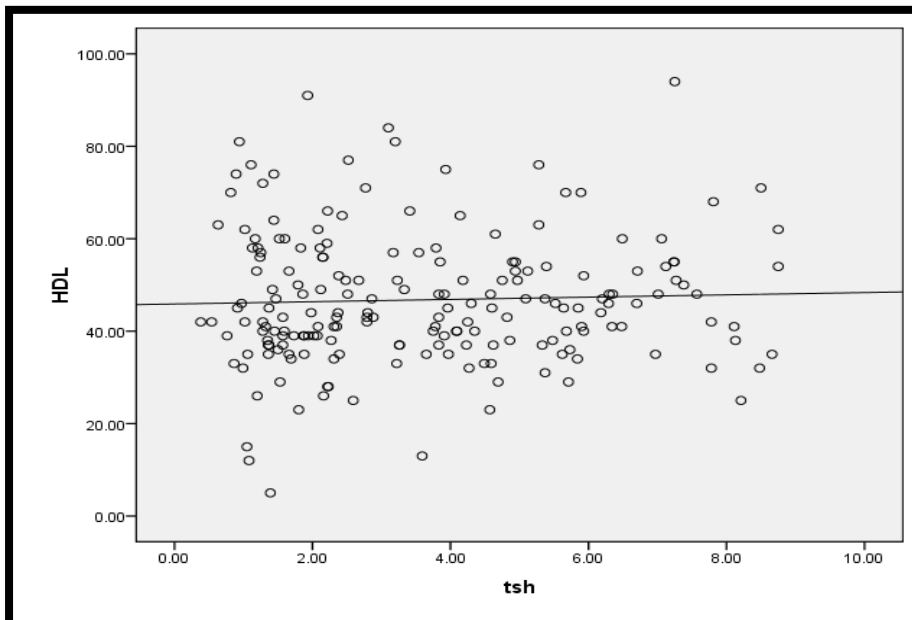
cohort study on euthyroid Indian women [15] suggested that TSH in the upper limits of reference range was associated with increased serum TC. But an Austrian study of 4856 participants with normal thyroid function [16] was contradictory to our study, as it showed no

increase in lipid status with increasing TSH possible influence of genetic and ethnic levels within the normal range indicating a variations among these subjects.

**Figure - 3:** Correlation between serum TSH ( $\mu\text{IU/mL}$ ) and LDL-C (mg/dL).



**Figure - 4:** Correlation between serum TSH ( $\mu\text{IU/mL}$ ) and HDL-C (mg/dL).

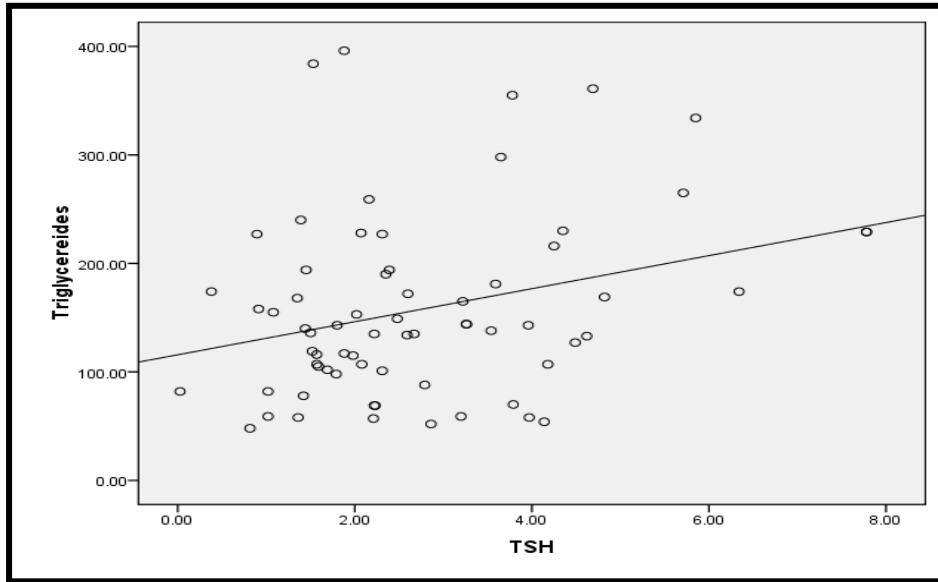


Studies have shown that the TSH receptors were expressed in a variety of extra thyroidal tissues, including the liver, skin, kidney, white and brown adipose tissues [17] suggesting possible

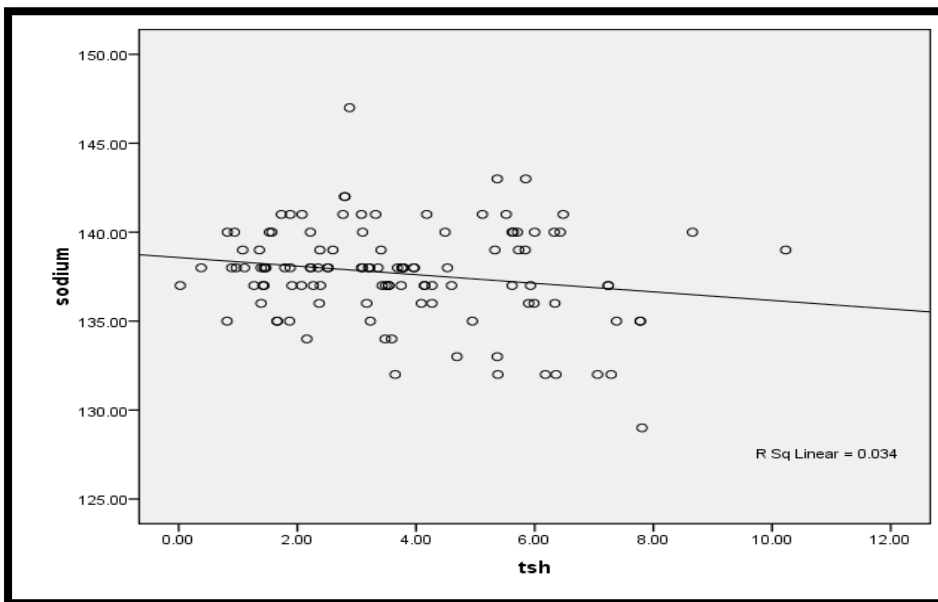
extra thyroidal roles of TSH. This can be further substantiated by studies showing positive correlations between TSH level and waist circumference, body mass index and blood

pressure [18-20]. Zhang, et al. [21] have demonstrated that liver cells express TSH receptor protein and that TSH upregulates the expression of HMG CoA reductase (a rate limiting enzyme in cholesterol biosynthesis) [22].

**Figure - 5:** Correlation between serum TSH ( $\mu\text{IU/mL}$ ) and triglycerides (mg/dL) in males.



**Figure - 6:** Correlation between serum TSH ( $\mu\text{IU/mL}$ ) and serum sodium (mEq/L) levels.



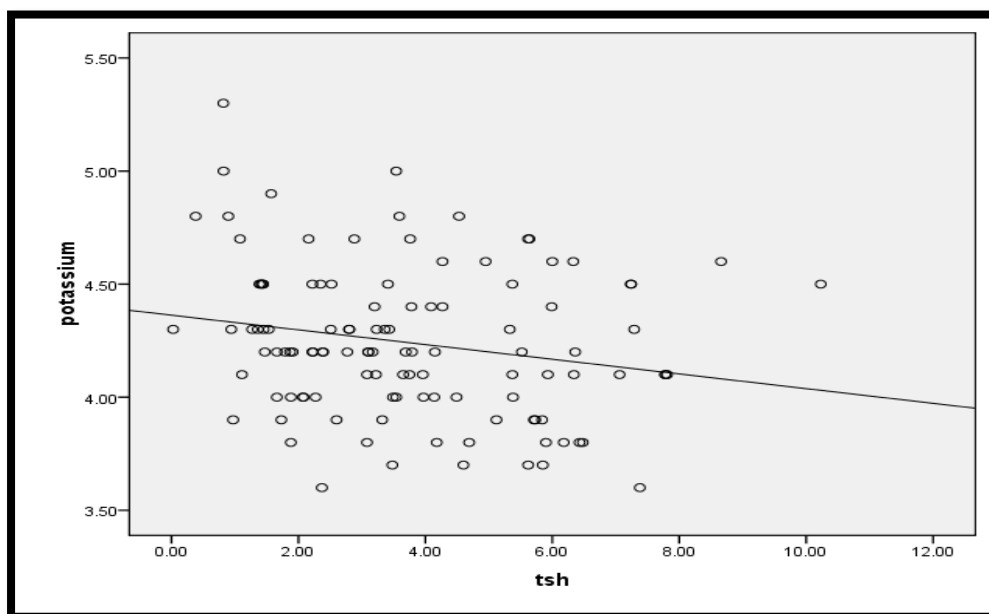
Our data showed that subjects with relatively high normal TSH levels were more likely to have hypercholesterolemia and hypertriglyceridemia. Therefore, according to these results, even within the clinically normal range, subjects with high

TSH levels might be prone to dyslipidaemia. The electrolyte status has an influence on renal haemodynamics, glomerular filtration, as well as the renin angiotensin aldosterone system and renal electrolyte handling [23]. Thyroid

dysfunction has a remarkable effect on glomerular and tubular functions of kidney and therefore on electrolyte and water homeostasis. Some studies show that hypothyroidism is accompanied by hyponatremia and a decrease in

glomerular filtration [24]. Hyponatremia observed in severe hypothyroidism and myxoedema, has been attributed to enhanced renal water retention mediated by vasopressin [27].

**Figure - 7:** Correlation between serum TSH( $\mu$ IU/mL) and serum potassium (mEq/L) levels.



This study also showed a significant negative correlation of TSH with sodium and potassium levels suggesting a possible role for TSH in maintenance of electrolyte balance. Although the weak correlation may suggest that correlation between electrolyte disturbances and thyroid function could be seen in severe cases of hypothyroidism. As electrolyte disorders are common among hospitalised patients, little more attention may have to be given for electrolytes if they are suffering from thyroid disorders [25-26].

### **Conclusion**

High normal TSH levels may predispose to hypercholesterolemia and hypertriglyceridemia. Association of high-normal TSH levels with dyslipidemia may indicate that thyroid hormones can influence lipid metabolism in many ways including receptor uptake and metabolism of lipoproteins, cholesterol and lipoprotein synthesis, activation/inactivation of lipoprotein

lipase etc. TSH and thyroid status can influence lipid and electrolyte metabolism. High normal TSH patients can have lower serum electrolytes. People with high normal Serum TSH levels may require a close monitoring of lipid profiles and electrolytes.

### **Limitations**

As most studies show significant associations of TSH with lipid profiles and electrolytes, it implies a need for a detailed study to understand the exact mechanism of this influence and their clinical implications.

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