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STUDY OF PREVALENCE OF HYPONATREMIA IN HYPOTHYROIDISM

Internal Medicine

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ABSTRACT

Background: Hypothyroidism is a common endocrine disorder encountered in clinical practice. Hypothyroidism has been classically considered as a cause of hyponatremia. **Objective:** To study the prevalence of hyponatremia among hypothyroid patients and correlation between serum TSH and serum sodium in hypothyroid patients. **Methods:** It is a cross sectional study conducted among 300 hypothyroid patients, both previously diagnosed as well as newly diagnosed in a tertiary care hospital. The prevalence of hyponatremia and the correlation between serum TSH and serum sodium was assessed. **Results:** The mean TSH value among hypothyroid patients in the current study was 7.7 µIU/L and the mode of 6.5 µIU/L. Overt hypothyroidism was seen only in 22% of cases, while 73.7% had mild hypothyroidism and the rest 4.3% had severe hypothyroidism. The mean serum sodium concentration was 137.3 mmol/L with 79% of the participants had normal serum sodium concentration, 18.3% had mild hyponatremia (130-135mmol/L) and 2.7% of participants had moderate hyponatremia (125-130mmol/L). No case of severe hyponatremia was found. The current study showed negative, poor and nonsignificant correlation (rho = 0 = 0.073, p=0.208) between TSH and serum sodium level. **Conclusion:** The current study revealed no significant correlation between TSH and serum sodium levels in patients with hypothyroidism. So alternate cause should be sought for hyponatremia in patients with hypothyroidism.

KEYWORDS

Hypothyroidism, Hyponatremia, Sodium levels, Thyroid levels

INTRODUCTION

Thyroid gland is a butterfly shaped endocrine gland weighing between 20-60 grams and located at the front of the neck[1]. Under the influence of Thyroid stimulating hormone (TSH) released from the anterior pituitary gland, thyroid gland releases the only iodine containing hormones in the vertebrates i.e. triiodothyronine (T3) and thyroxine (T4), which are endocrine messengers which act as key regulators of metabolism and development in the body[2] and moderator for gene expression of virtually every tissue[3]. They act synergistically with growth hormone for growth and development, increase oxygenation through stimulation of respiratory centers, increase contractility through type II muscle fibers, increases metabolism mainly through Na-K ATPase activity and increase heart rate, stroke volume and cardiac output through permissive effect on catecholamines[4]. The overall mechanism of thyroid hormone release is down-regulated to normal range by negative feedback mechanism by circulating T3 and T4 on TSH regulation[2]. Any failure of the thyroid gland to produce these thyroid hormones to meet the metabolic demands of the body is called hypothyroidism[5].

Hypothyroidism can occur due to primary gland failure or insufficient thyroid gland stimulation by the hypothalamus or pituitary gland[5]. They can present with nonspecific symptoms like weight gain, fatigue, poor concentration, depression, diffuse muscle pain, and menstrual irregularities or highly specific symptoms like constipation, cold intolerance, dry skin, proximal muscle weakness, and hair thinning or loss[5]. Among the many effects of hypothyroidism, one of the parameters that have been of scientific interest has been its role in hyponatremia[6]. Hypothyroidism is noted to reduce cardiac output which in turn reduces the renal perfusion.This will lead to reduced glomerular filtration rate (GFR) and hence retention of fluids leading to hyponatremia[7]. Certain studies have theorized that excess vasopressin secretion may lead to hyponatremia secondary to hypothyroidism[8]. But there is contradictory evidence on causation of hyponatremia in hypothyroid patients[5]. On one hand, there are case reports which show diagnosis of severe primary hypothyroidism in case of infants with hyponatremia[9].Some retrospective studies show significantly higher prevalence of overt hypothyroidism with severity of hyponatremia[10], whereas there are studies which show negligible correlation between serum sodium and hypothyroidism[11] and they suggest other potential reasons for hyponatremia in hypothyroid patients[12]. There are also studies which suggest the need to monitor serum sodium only in settings of impaired renal functions[13]. Hence the role of hypothyroidism in hyponatremia is debatable. But as hyponatremia is a serious and often overlooked electrolyte imbalance which can lead to increased mortality and morbidity due to conditions like cerebral oedema[14], there is a need for further studies to find out the correlation between of hyponatremia and hypothyroidism.

METHODS:

This cross sectional study included 300 patients aged more than 18 years and with a TSH value more than 5.5 µIU/L and who did not have a documented cause for hyponatremia**.** Patients with diabetes mellitus, renal , cardiac or hepatic disorders were excluded from the study. Laboratory parameters like TSH and serum sodium were assessed using laboratory reports and the values which were taken within 3 week interval of each other were selected. Patients were continuously selected for the study by convenient sampling until the required sample size was met.

Statistical Analysis : Qualitative data was analyzed using frequency, percentage and association using chi square test and Fischer exact test wherever deemed necessary and p- value less than 0.05 was taken as statistically significant. Quantitative data was analyzed using measures of central tendency like mean, median, mode and measures of dispersion like range, standard deviation and 95% confidence interval. Correlation between TSH and serum sodium was done using spearmanns correlation tests. Tabulations was done using tables and graphical representation was done using bar graphs, pie charts and box.

RESULTS

The 300 study participants belonged to the age group of 19 – 87 years with mean age group of 53.6 ± 15.8 years. Majority of the participants belonged to above 60 years of age (114, 38%), followed by 45 – 60 years (82, 27.3%), 30 – 45 years (73, 24.2%) and 18 – 30 years (31, 10.3%) (Table 1 / Figure 1)

Table No.1: Distribution of participants based on age

Age group	Frequency	Percentage
18 - 30 yrs	31	10.3
30 – 45 yrs	73	24.3
45 – 60 yrs	82	27.3
Above 60 yrs	114	38.0
Total	300	100

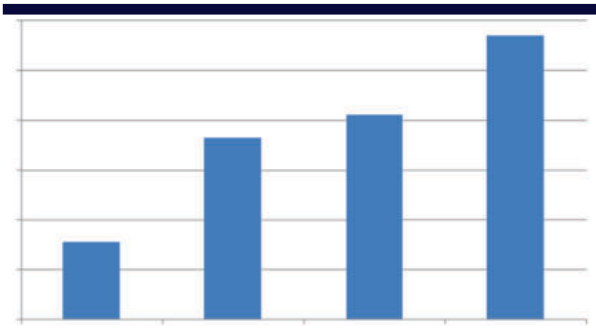


Figure 1
In this study, 77.3% (232) participants were female and rest 22.7% (68) were male (Table 2 / Figure 2)

Table No.2 : Distribution of participants according to gender

Gender	Frequency	Percentage
Female	232	77.3
Male	68	22.7
Total	300	100

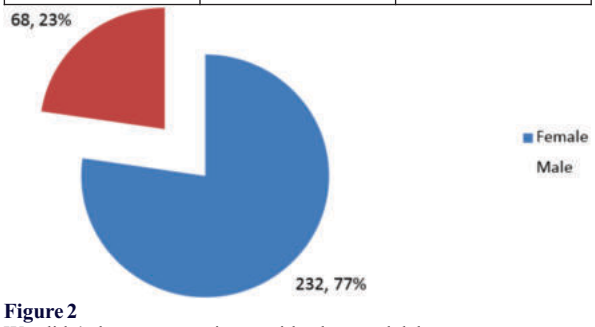


Figure 2
We didn't have any patients with abnormal laboratory parameters suggestive of kidney disease. Affect. 87.7% and 92.4% participants had normal urea and creatinine level respectively and rest had low levels of these parameters.

None of the participants (Table 3)

Table No.3: Distribution of study participants based on renal profile

Renal profile	Low	Normal	High
Urea	37 (12.3%)	263 (87.7%)	0
Creatinine	23 (7.6%)	277 (92.4%)	0

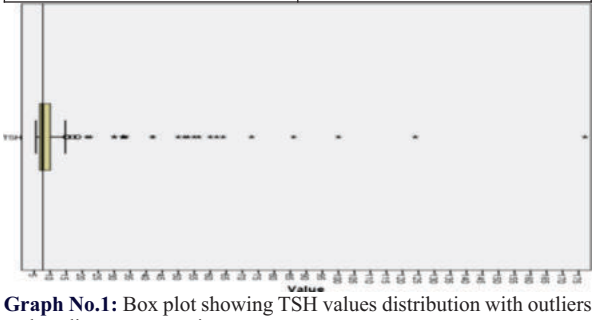
All participants had normal liver function during study (Table 4)

Table No.4 : Distribution of participants based on liver function tests

Liver function tests	Normal	High
SGOT	300	0
SGPT	300	0
Albumin/globulin ratio	300	0

Table No.5 : TSH level status among study participants

Characteristics	TSH value (µIU/L)
Median	7.7
Mode	6.5
Minimum	5.53
Maximum	177



Graph No.1: Box plot showing TSH values distribution with outliers and median representation

The study was conducted among cases of hypothyroidism with TSH value above 5.5 µIU/L. TSH value in our study showed a non parametric distribution with minimum value of 5.53 and a maximum value of 177 µIU/L. The median TSH value was 7.7 µIU/L and the mode was 6.5 µIU/L (Table 5 / Graph 1)

In addition, it was noted that majority of the participants had mild hypothyroidism (221, 73.7%), followed by moderate (66, 22%) and severe hypothyroidism (13, 4.3%) (Table 6 / Figure 3).

Table No.6 : Classification of participants based on TSH status

Thyroid status	TSH range (Miu/l)	Frequency	Percentage
Mild hypothyroidism	5 - 9.99	221	73.7
Overt hypothyroidism	10 - 49.99	66	22.0
Severe hypothyroidism	> 50	13	4.3
Total		300	100

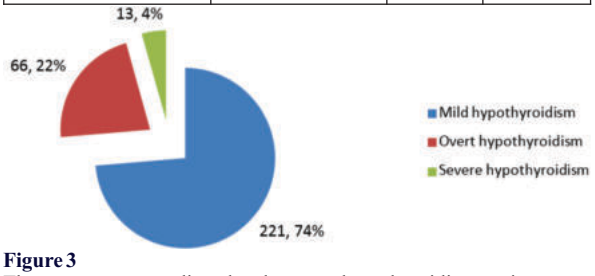
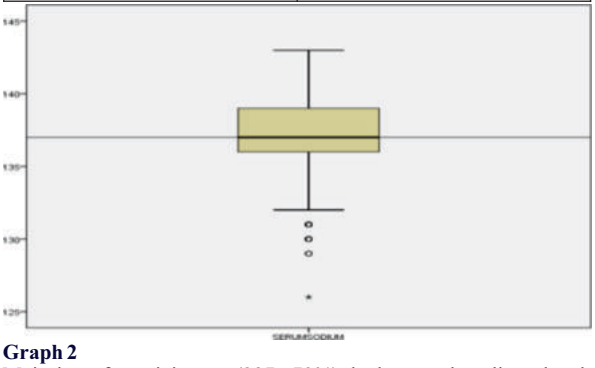


Figure 3
The mean serum sodium level among hypothyroidism patients was 137.3 mmol/ (at 95% CI is 131.8 – 142.8) with values ranging from 126 – 143 mmol/L (Table 7 / Graph 2)

Table No.7: Serum sodium levels among cases of hypothyroidism

Distribution	Serum sodium level (mmol/L)
Mean	137.3
Median	137
95% Confidence interval	131.8 -142.8
Minimum value	126
Maximum value	143



Graph 2
Majority of participants (237, 79%) had normal sodium level, followed by mild hyponatremia (55, 18.3%) and moderate hyponatremia (8, 2.7%). None of the participants had hypernatremia and severe hyponatremia. (Table 8 / Figure 4)

Table No.8 : Distribution of participants based on their sodium status

Sodium status	Sodium range	Frequency	Percentage
Normal	135 - 145	237	79
Mild hyponatremia	130 – 135	55	18.3
Moderate hyponatremia	125 – 130	8	2.7
Total		300	100

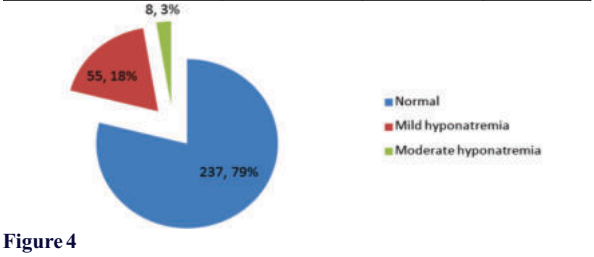


Figure 4

When the association between hyponatremia and type of hypothyroidism was assessed, it was found that mild hyponatremia was noted that 14.5%, 30.3% and 23.1% of mild, overt and severe hypothyroidism respectively. Similarly, moderate hyponatremia was seen in 0.4%, 7.6% and 15.4% of mild, moderate and severe hypothyroidism respectively. This difference was found to be of statistical significance (p= 0.000). Rest of the participants had normal serum sodium levels. (Table 9)

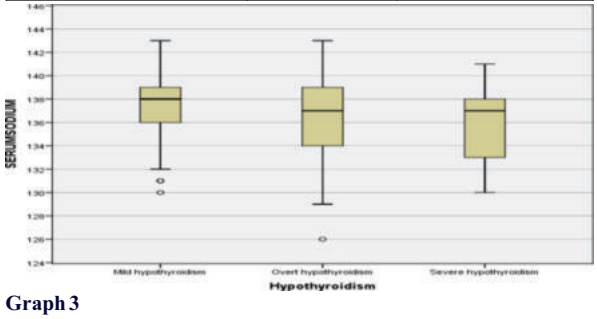
Table No.9 : Association between Hyponatremia and hypothyroidism

Status	Normal sodium level		Mild hyponatremia		Moderate hyponatremia		Total	p value
	N	%	N	%	N	%		
Mild hypothyroidism	188	85.1	32	14.5	1	0.4	221	0.000 *
Overt hypothyroidism	41	62.1	20	30.3	5	7.6	66	
Severe hypothyroidism	8	61.5	3	23.1	2	15.4	13	

The mean serum sodium level among mild, overt and severe hypothyroidism was 137.6 (at 95% CI: 133.2 – 142) , 136.4 (128.8 – 144) and 135.0 mmol/L (128.3 – 143.5 mmol/l) respectively (Table 10 / Graph 3).

Table No.10 : Mean serum sodium level among different classes of hypothyroidism

Classification of hypothyroidism	Mean sodium level	95% Confidence interval
Mild hypothyroidism	137.6	133.2 - 142
Overt hypothyroidism	136.4	128.8 - 144
Severe hypothyroidism	135.9	128.3 - 143.5
Total	137.3	131.8 -142.8

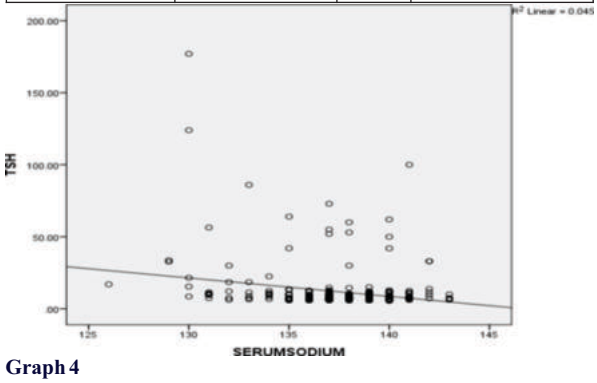


Graph 3

The current study showed negative, poor and non significant correlation (-0.073 at p=0.208) between TSH and serum sodium levels (Table 11 / Graph 4)

Table No.11 : Correlation between TSH and serum sodium level

Parameters	Correlation value (rho)	p value	Inference
Correlation between TSH and Serum sodium	- 0.073	0.208	Negative, poor and non significant significance



Graph 4

DISCUSSION

Our study was a cross sectional study done to assess correlation between hypothyroidism and hyponatremia among 300 participants. This was done by selecting 300 patients with hypothyroidism , including newly and previously diagnosed with TSH values more than 5.5 µIU/L. All other causes which would cause hyponatremia were excluded by detailed drug history and liver function and renal function tests.

The age group of patients was between 19 years and 89 years. The mean age group of participants with hypothyroidism was 53.6 ± 15.8 years. They were within normal limits . The mean TSH value among hypothyroid patients in the current study was 7.7 µIU/L, but as it was a non parametric data with extreme outliers, mode of 6.5 µIU/L was taken as a better indicator of central tendency. Moderate hypothyroidism was seen in 22% of cases while 73.7% had mild hypothyroidism and the rest 4.3% had severe hypothyroidism.

Of the 300 participants included in the study 232 participants were females and 68 participants were males. Prevalence of hypothyroidism is more in females (22.7%) than males (77.3%) . This is in line with previous studies[15] stating higher prevalence of hypothyroidism in female subjects.

The mean serum sodium concentration was 137.3mmol/l which was within normal limits with 79% of the participants had normal serum sodium concentration, 18.3% had mild hyponatremia (130-135mmol/l) and 2.7% of participants had moderate hyponatremia (125- 130mmol/L No case of severe hyponatremia in the current study.

The proportion of cases with hyponatremia was more in cases of moderate and severe hypothyroidism compared to mild hypothyroidism and this difference was of statistical significance (at p <0.05). Hence there were higher chances of hyponatremia with severity of hypothyroidism, but the mean sodium level among mild, overt and severe hypothyroidism was 137.6, 136.4 and 135.9 mmol/l respectively.That is the values were within the normal limits.

So this study showed negative, poor and non significant correlation (rho = 0=- 0.073, p=0.208) between TSH and serum sodium level.

Hence according to the current study, even though there is an increase of hyponatremia with severity of hypothyroidism, the mean serum sodium concentration remains within normal limits and there was no significant correlation between TSH and serum sodium level.

CONCLUSION

The results of our study showed slight increase in prevalence of hyponatremia with increased progression of hypothyroidism, but more than half the patients in all stages of disease had normal serum sodium. More over there was no significant correlation between serum sodium and TSH level. Hence we conclude that there is need to look for alternate causes of hyponatremia in hypothyroidism especially in mild and moderate cases.

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