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Original Research Article

PREVALENCE OF HYPOTHYROIDISM IN PATIENTS WITH HYPONATREMIA

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Abstract: *This study evaluated the prevalence of hypothyroidism in hyponatremic patients of varying severity. This prospective cross-sectional study was conducted at the Medicine department of Bakhtawar Amin Trust Hospital Multan from 19th March 2020 to 19th March 2021. Hospital registry data assessed the patient's serum sodium, free thyroxine, and thyrotropin level. The study's primary outcome was free T4 < 1.01 ng/dL and TSH > 10.0 µIU/mL. A total of 243 patients qualified to study criteria. Of them, 20 (8.2%) had overt hypothyroidism, and 50 (20.5%) had hypothyroidism. Hypothyroidism was categorized in terms of the Na levels such that six (12%) patients had Na > 136mEq/L, 16 (32%) had Na=130-135mEq/L, and 28(56%) had Na < 129mEq/L. The number of patients with overt hypothyroidism in similar groups was two patients (10%), eight patients (45%), and 10 patients (50%), respectively. The rate of hypothyroidism increased significantly with an increase in the severity of hyponatremia (p<0.05). Multivariate logistic regression analysis on adjusting confounding factors revealed an increase in overt hypothyroidism rate with an increase in hyponatremia severity. Based on the results, overt hypothyroidism increases significantly with an increase in the severity of hyponatremia. The trend remains the same even after the adjustment of potential confounders.*

Keywords: Hypothyroidism, Hyponatremia, Sodium level, Thyroid hormones

Introduction

The literature is divided into the association of hypothyroidism with hyponatremia, and pathologically low levels of serum sodium, as some studies relate hypothyroidism with hyponatremia, while many reports concluded that thyroid function is weakly associated with serum sodium levels with no clinical significance (Diker-Cohen et al., 2018; Pantalone and Hatipoglu, 2014; Pattanashetti and Krishnappa, 2021). A retrospective cross-sectional analysis reported a similar frequency of hyponatremic patients among hypothyroid and euthyroid cases (de Lemos et al., 2003). According to clinical practice guidelines and a recent review, hypothyroidism can only be considered a possible cause of low serum sodium levels in cases of severe hypothyroidism, such as myxedema coma (Aylwin et al., 2015; Liamis et al., 2017). However, previous research has primarily assessed the prevalence of hyponatremia in patients with hypothyroidism compared with all subjects (Wolf et al., 2017). Additionally, certain confounding factors such as serum albumin level, kidney function, age, and sex are not generally considered related to thyroid function (Chonchol et al., 2008). Moreover, limited literature is available regarding the association of hypothyroidism with varying degrees of hyponatremia. Therefore, the present study was designed to evaluate the prevalence of hypothyroidism in hyponatremic patients of varying severity. Besides, it was also aimed to determine the effect of various confounding factors on the relationship between hypothyroidism and the severity of hyponatremia.

Methodology

The prospective cross-sectional study was conducted at the Medicine department of Bakhtawar Amin Trust Hospital Multan for one year, from 19th March 2020 to 19th March 2021. The study included patients above 18 years with clinically proven low serum Na levels, whereas patients younger than 18 were excluded from the study. All the patients signed informed consent to become a part of the study. The hospital registry was assessed for retrospective data collection regarding initial thyrotropin (TSH) and free thyroxine (T4) levels. Additionally, Na levels were observed, and minimum serum Na level was noted within three days of TSH analysis. As a part of baseline data, information regarding the patient's age, sex, serum creatinine levels, urea nitrogen level, albumin, and total protein level, serum electrolytes, and free triiodothyronine (T3) was also collected such that blood metabolites levels were of the same day when TSH testing was performed. The reference ranges for T4 and TSH were 1.01-1.79 ng/dl and 0.27-4.20 uIU/ml, respectively.

Statistical analysis: SPSS (version 21) was used for statistical analysis. Continuous variables were presented as median with interquartile ranges, while categorical variables were the frequency with percentages. The former variables were compared through the Kruskal-Wallis test and, later, Fisher's exact test. The Cochran-Armitage test was used for assessing linear trends. Correlation analysis was carried out using Pearson's correlation coefficients. Odds ratios were calculated for hypothyroidism in each category of Na levels by considering univariate and multivariate logistic regression models. For each variable, a p-value <0.05 was considered statistically significant.

Results

The study included 243 patients, of which 20 (8.2%) had had overt hypothyroidism, and 50 (20.5%) had hypothyroidism. Hypothyroidism was categorized in terms of the Na levels such that 6 (12%) patients had Na > 136mEq/L, 16 (32%) had Na=130-135mEq/L, and 28(56%) had Na < 129mEq/L. Table-I presents the baseline characteristics of the patients. The number of patients with overt hypothyroidism in similar groups was two patients (10%), 8 patients (45%), and 10 patients (50%). According to the Cochran-Armitage trend test, cases of overt hypothyroidism and hypothyroidism increased significantly with an increase in the severity of hyponatremia. For the whole study sample, Pearson's correlation coefficient for Na and TSH was .021. In the subject with overt hypothyroidism and hypothyroidism, values were .029 and .007. In the entire sample, the correlation between Na and TSH was weak. The comparison of adjusted odd ratio among patients with hypothyroidism showed those with Na=130-135mEq/L and Na < 129mEq/L had an odds ratio of 1.1 while those with Na> 36 mEq/L had 1.3. For overt hypothyroidism, odd ratios were 1.4 and 1.8. In overt hypothyroidism and hypothyroidism, adjusted odds ratios showed an increasing trend (Table II).

Table-I: Baseline characteristics of the patients.

Characteristics	Serum sodium level ≧136mEq/	130-135 mEq/L	≦129mEq/L	*P*
Age years	65 (47-75)	64 (47-74)	71 (60-80)	<0.001
Sodium, mEq/L	139 (138-141)	133 (131-134)	127 (120-129)	<0.001
Potassium mEq/L	4.1 (3.8-4.3)	4.1 (3.8-4.5)	4.1 (3.8-4.6)	<0.001
Chloride, mEq/L	104 (103-106)	99 (96-104)	94 (87-96)	<0.001
Blood urea nitrogen, mg/dL	13.7 10.7-17.9)	15.9 (11.3-24.2)	15.4 (10.1-25.2)	<0.001
Creatinine, mg/dL	0.72 (.61-.80)	0.80 (.61-1.12)	0.70 (.51-1.1)	<0.001
eGFR, mL/min/1.73m²	73.4 (57.8-91.3)	68.2 (44.9-87.9)	73.6 (47.4-65.5)	<0.001
Total protein (g/dL)	7.11 (6.5-7.4)	7.11 (6.5-7.4)	6.5 (6.1-7.4)	<0.001
Albumin (g/dL)	4.25 (3.89-4.4)	3.4 (3.1-4.1)	3.47 (2.65-3.98)	<0.001
TSH (µIU/mL)	1.34 (.84-2.13)	1.41 (.77-2.4)	1.45 (.82-2.67)	<0.001
Free T3 (pg/mL)	2.88 (2.46-3.23)	2.41 (1.92-2.85)	2.11 (1.67-2.55)	<0.001
FreeT4 (ng/dL)	1.05 (.93-1.22)	1.14 (.94-1.33)	1.12 (.95-.131)	<0.001

eGFR=estimated glomerular filtration rate, TSH= thyrotropin, T3=triiodothyronine, T4= thyroxine.

Table II: Association between 3 categories of Na level and hypothyroidism.

Characteristics	Total n=243	Serum sodium level ≧136 mEq/L	130-135mEq/L	≦129mEq/L	*p*
Hypothyroidism %	50 (20.5%)	6 (12%)	12 (32%)	28 (56%)	<0.001
	Un-adjusted	Referent	2.76 (2.58-2.92)	3.29 (2.96-3.66)	<0.001
	Model 1	-	2.41 (2.28-2.56)	2.76 (2.51-3.08)	<0.001
	Model 2	-	1.12 (.98-1.25)	1.31 (1.12-1.57)	<0.001
Overt hypothyroidism	20 (8.2%)	2 (10%)	8 (45%)	10 (50%)	<0.001
	Un-adjusted	Referent	2.96 (2.62-3.37)	3.95 (3.18-4.95)	<0.001
	Model 1	-	2.55 (2.27-2.88)	3.36 (2.75-4.22)	<0.001
	Model 2	-	2.44 (2.14-2.77)	2.88 (2.34-3.67)	<0.001

Model 1 adjusted for estimated glomerular filtration rate, sex, and age.
Model 2 adjusted for serum albumin level and variables in Model 1.

Discussion

The prevalence of hypothyroidism in hyponatremic patients was evaluated in this study. The results showed a very mild relation between Na level and

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TSH; however, overt hypothyroidism and its prevalence were much higher in hyponatremic patients compared to those with a sodium level of 136 mEq/L. Moreover, with an increase in the severity of hyponatremia, the trend of overt hypothyroidism and the prevalence of hypothyroidism significantly increased. According to past studies, the relationship between Na level and TSH is very weak. A study reported that the relationship between TSH and Na in newly diagnosed diseases is mild and not clinically significant (Aylwin et al., 2015). Another study conducted on patients in the emergency department showed a clinically insignificant relation between Na and TSH (Chonchol et al., 2008). This may be because hypothyroid patients were normonatremic. Thus, the weakened relationship between Na and TSH can be because most subjects were hyponatremic at the time of the study. A recent study showed that hyponatremia rarely results from hypothyroidism except in severe cases like myxedema coma (Wolf et al., 2017). According to the result of this study, concurrent hypothyroidism can occur in hyponatremic patients. Considering the pathophysiology of hyponatremia, the results appear credible. The mechanism is that hypothyroidism decreases cardiac output resulting in a compensatory increase of antidiuretic hormone and a decrease in GFR (Elshimy et al., 2022; Nagata et al., 2018). This results in water retention and a reduction in excretion by lowering water input to the nephron (Rashid et al., 2021; Talha et al., 2020). According to a study, elders and females are more affected by hypothyroidism, and its prevalence is higher in subjects with chronic kidney disease (Singh et al., 2021). Moreover, TSH level is also significantly related to levels of serum albumin (Ahmad et al., 2019; Fukata et al., 2022; MuraleedharaN and BeeguM, 2021). After modifying these factors, the relationship between hypothyroidism and hyponatremia was significant. This study's results can be considered reliable. There are many limitations of this study. Firstly, as the subjects suspected of having thyroid disease were tested for free T4 and TSH, the prevalence of hypothyroidism in hyponatremic patients remained unknown. Secondly, patients had various comorbidities which could cause hyponatremia. Third, as the majority of patients were tested for TSH level at the first visit, information about drugs causing hyponatremia was not present. Finally, as it was a cross-sectional study, the cause-and-effect relation between hyponatremia and hypothyroidism could not be investigated, for which a longitudinal study would be needed.

Conclusion

Though there is a fragile relation between Na level and TSH, with an increase in the severity of hyponatremia, there was a significant increase in the prevalence of overt hypothyroidism. Moreover, correlation persisted even after the adjustment of thyroid function confounders.

Conflict of interest

The authors declared absence of conflict of interest.

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