



PREVALENCE OF HYPOTHYROIDISM IN PATIENTS WITH HYPONATREMIA

Syed Shahzaib Ali¹, Ali Hamza Cheema^{2*}, Muhammad Sadam Hussain³, Hafiz Fahad Ullah Saeed⁴, Sauda Usmani⁵, Saman Siddique⁶

¹Department of Internal Medicine, Punjab Rangers Teaching Hospital Lahore, Pakistan

^{2*}Medical Officer, Department of Internal Medicine, Al-Hajj Nasir Khan Welfare Trust Hospital Gujranwala, Pakistan

³Medical Student, MBBS, Pak International Medical College Peshawar, Pakistan

⁴Resident Physician, Department of Internal Medicine, Icahn School of Medicine at Mount Sinai/Queens

⁵Associate Professor, Department of Physiology, Pak Red Crescent Medical and Dental College Lahore, Pakistan

⁶Medical Officer, General Medicine, Asma Medical Center, Pakistan

***Corresponding author:** Ali Hamza Cheema

*Email: alihamza1039437@gmail.com

Abstract

Objectives: The primary objective of this study was to establish prevalence of hypothyroidism in hyponatremic patients and secondly, to evaluate the relationship between hyponatremia and thyroid dysfunction, and thus emphasizing the necessity of thyroid function checking in patients with hyponatremia.

Results: The study involved 200 patients with hyponatremia out of these 120 (60%) of them had hypothyroidism. Among the hypothyroid patients, the incidence of hyponatremia was stratified by severity: 45 (37.5%) of patients had moderate hyponatremia with serum sodium levels between 130-134mmol 60 (50.0%) had severe hyponatremia with serum sodium levels between 125-129mmol and 15 (12.5%) had severe hyponatremia with serum sodium <125mmol. The mean age of the participants was 55.4 ± 12.3 years, with a male-to-female ratio of 1:1.2. Odds for comorbidity were hypertension at 45%, diabetes mellitus at 30%, and cardiovascular disease at 25%.

Conclusion: The results presented show that hypothyroidism is a very widespread disease among patients with hyponatremia, which points to a definite relationship between these diseases. The evaluation of thyroid function should be done in patients with hyponatremia, as hypothyroidism is often undiagnosed and treatable condition that affects patients' prognosis.

Keywords: Hypothyroidism, Hyponatremia, Thyroid Function, Electrolyte Imbalance, Geriatric Patients, Comorbidities.

INTRODUCTION

Hyponatremia is an electrolyte abnormality in which serum sodium is below 135 mmol/L and is common in several clinical settings. In recent years, thyroid dysfunction, especially hypothyroidism has been implicated as one of the causes of hyponatremia. These findings showed preliminarily that there is a strong connection between hypothyroidism and electrolyte imbalance and further research

is necessary (1). This introduction attempts to determine the extent to which hypothyroidism can be found in hyponatremic patients, establish the existing literature and find out areas that would require further studies.

Hypothyroidism relates to the deficiency of the thyroid hormone produced in the glands that are essential to several metabolic compounds, including those, which regulate fluid and electrolytes. Deficiency of thyroid hormones affects our normal metabolism and creates complications like impaired renal function, and water balance. This impaired renal function can help in the development of hyponatremia because the kidney participates in the regulation of sodium and water (2). Several studies imply that hypothyroidism may contribute to a significant incidence of hyponatremia, especially in elderly customers (3). Both these disorders are especially prevalent in this age group, although hypothyroidism becomes more common as people age. Geriatric patients many a times have multiple health problems, and sometimes chronic diseases, and physiological changes that accompany aging all of which make it complicating to manage their care (4).

Recent studies have been conducted to show that patients with hyponatremia should undergo thyroid function tests. According to Syazana et al. (2020), thyroid hormone levels should be the first investigation to be done any time there is unexplained hyponatremia as early detection will enhance the patient management process (3). In a cross-sectional, multi-centric study from different regions of China Chu et al (2023) also categorized hypothyroidism with hyponatremia coming to the conclusion that thyroid disorder should be looked at in patients with hyponatremia. (1).

Hyponatremia continues to present a major risk in hospitalized patients: the epidemiology. A recent cross-sectional study by Zhang and Li (2020) among old inpatient electrocardiogram patients also pointed to high prevalence of hyponatremia among this group, indicating that electrolyte checking in geriatric wards must considered routine (4). The consequences of these results are quite important, as hypotonias is associated with neurological disorders and higher mortality. Conventional treatment of hyponatremia becomes challenging in patients with hypothyroidism as the treatment itself may involve treatment of the hypothyroidism.

Present clinical manifestations and comorbidities depend on the type of hypothyroidism, and various forms of this pathology have been described in literature. In a tertiary care setting, Bharat and Sasturkar (2022) have outlined different forms of hypothyroidism and have specifically pointed to cardiovascular disease, obesity, and metabolic syndrome (5). Such conditions may also aggravate the clinical presentation and require a combined treatment strategy. Furthermore, Heite (2024) underlines that the ways of organizing the hypothyroidism management in the patients with cirrhosis of the liver should be chosen taking into account possible adverse outcomes such as hyponatremia (6).

The present study is the first to demonstrate the relationships between thyroid function and renal issue are crucial for the understanding the pathways accounting for hyponatremia. Renal blood flow, glomerular filtration rate, and sodium reabsorption by the hormone has been found to be modulated and are clearly important in maintaining electrolyte balance (7). Appears that inhibition of these processes because of hypothyroidism can cause the development of sodium retaining and subsequently hyponatremic. Cao et al. (2021) identified that patients with affected differentiated thyroid carcinoma demonstrated changes in sodium levels, which demonstrated that changes in the levels of thyroid hormones affect sodium balance (8).

Moreover, it is equally important to mention the effect of the adrenal insufficiency on the electrolyte pattern. Khatri et al. (2023) described the case of a patient with adrenal insufficiency and hypothyroidism who had several severe metabolic abnormalities that pointed to a difficult diagnostic approach to electrolyte disorders in patients with multiple endocrinopathies (9). This interplay also confounds treatment of hyponatremia in patients with hypothyroidism and underscores the importance of an interactive evaluation of endocrine function.

This paper's subject makes the etiology of hyponatremia in geriatric patients especially pertinent. Hyponatremia and its causes in frail elderly hip-fractured patients were investigated by Emektar et al., 2024, regarding frail elderly hip-fractured patients, the results suggested that thyroid dysfunction played a particular role. Because the number of the older people is growing, it is crucial to know what makes people react to hyponatremia. The recognition of hypothyroidism as one possible etiology of

hyponatremia in elderly patients may facilitate better patient outcomes as a result of motive treatment plans.

Further, the present studies have mentioned increased incidence of hyponatremia in different groups of patients such as with liver cirrhosis and head and neck cancer. Cirrhotic patients suffering from hypothyroidism admitted within this time were a total of 96 out of 200 a prevalence rate of 48%, Saha and Bhakta 2024 the present study showed us that there is complex interplay between liver function and thyroid function (7). This might be due to change in thyroid hormones metabolism and clearance by liver in cases of liver disorder affecting the general thyroid results. In addition, Pi et al. (2021) also reported that head and neck cancer patients undergoing radiotherapy also show changes of electrolyte levels and the appearance of hyponatremia. In focus, they elucidated the need to monitor these patients' thyroid status more closely, as thyroid disorders can precipitate renal individuals' electrolyte imbalance, and subsequent clinical deterioration (11).

Another issue which is good evidence of the necessity of the complicated clinical approach is the presence of hypothyroidism and its impact on the possibility of hyponatremia management. Dysfunction in the thyroid gland should not be overlooked when patients of healthcare providers present with electrolyte abnormalities, especially among high-risk populations for the disease. According to the literature, treatment of hypothyroidism not only can correct the hyponatremia but also improve metabolic function. (10). This re-emphasizes the need to provide care that is both holistic includes endocrine assessment and electrolyte balance especially from patients with chronic diseases and elderly patients.

Objective: The objective of this study is to evaluate the prevalence of hypothyroidism in patients diagnosed with hyponatremia and to explore the underlying mechanisms linking these two conditions.

MATERIALS AND METHODS:

Study Design: Cross sectional study

Study setting: The proposed study was conducted at Punjab Rangers Teaching Hospital Lahore, Pakistan, which specializes in endocrine and metabolic disorders thus allowing for a good evaluation of the patients.

Duration of the study: The proposed study was conducted in the duration from January 2024 to June 2024 in order to have enough time for patients' enrolment, data collection and data analysis.

Inclusion Criteria:

A participant must be 18 years of age or older, with hyponatremia defined as serum sodium concentration <135 mmol/L and willing to sign the informed consent.

Exclusion Criteria:

All those with an acute illness, those who have recently undergone thyroid surgery, and those who are on thyroid hormone replacement agents will also not be included due to interferences with thyroid test results.

Methods:

This Participants for this study will consist of hyponatremic patients attending the tertiary care hospital endocrine clinic. The participant will be interviewed and once the client gives a formal consent, he/she will be subjected to a detailed medical history and physical examination. Serum sodium will be determined in blood samples and thyroid function will be evaluated by determination of TSH and FT4 levels. Hyponatremia will also be defined as a serum sodium of less than 135mmol/L and hypothyroidism will be diagnosed in patients with increased thyroid-stimulating hormone (TSH) and decreased free thyroxine (FT4). The study will use reference laboratory values to categorize the

level of severity of hyponatremia. Simple descriptive and comparative statistics will be used to establish the occurrence of hypothyroidism among the hyponatremic patients. In descriptive part descriptive analysis of demographic and clinical features will be used, while in inferential part chi-square tests will be applied to compare hypothyroidism and hyponatremia. Level of significance will be set at 0.05 meaning the p-value obtained will be less than 0.05. Analysis of data will be done using statistical software in order to minimize probability of error in the results.

RESULTS:

A total of 200 patients with hyponatremia participated in the study, and of them, 120 patients (60 percent) were screened for hypothyroidism. Table 1 presents the demographic features of the participants in the study. The family caregivers had a mean age of 55.4 years \pm 12.3years which showed that the participants realized and came to the study from a middle-aged population. The male-to-female ratio was 1:1.2, which indicates in turn those females are represented in the participants' group in a somewhat greater measure than males.

The findings of the current study indicate that the commonest coexisting diseases involved hypertension, diabetes mellitus, and cardiovascular diseases they include hypertension 45%, diabetes Mellitus 30% and cardiovascular diseases 25%. Hyponatremia and hypothyroidism may coexist with other diseases, which could worsen clinical outcome of these patients and stress the importance of proper evaluation of health status. These comorbidities indicate the need to more closely evaluate and control risk factors associated with them in patients with the disease.

Table 1: Demographic Characteristics of Participants

Characteristic	Total Participants (N=200)	Hypothyroid (N=120)	Non-Hypothyroid (N=80)
Age (years, mean \pm SD)	55.4 \pm 12.3	57.2 \pm 11.5	52.5 \pm 12.0
Gender (male: female)	90:110	50:70	40:40
Comorbidities			
- Hypertension	90 (45%)	60 (50%)	30 (37.5%)
- Diabetes Mellitus	60 (30%)	40 (33.3%)	20 (25%)
- Cardiovascular Disease	50 (25%)	35 (29.2%)	15 (18.8%)

Exploring the results of the analysis made in the laboratory it became clearly seen that hypothyroid patients manifest a considerable relationship between serum sodium concentration and total and free thyroid hormone level. A significantly lower serum sodium concentration was observed in the hypothyroid group 128.5 \pm 4.2 mmol/L and the non-hypothyroid group 132.1 \pm 3.8 mmol/L $p < 0.001$. Nonetheless, mean TSH was higher in hypothyroid population (8.4 \pm 2.5 mIU/L) than non-hypothyroid group (2.1 \pm 1.2 mIU/L, $p < 0.001$) and FT4 was lower in hypothyroid group (0.8 \pm 0.3 ng/dL) than non-hypothyroid subjects (1.2 \pm 0).

Table 2: Laboratory Findings of Participants

Laboratory Parameter	Hypothyroid (N=120)	Non-Hypothyroid (N=80)	p-value
Serum Sodium (mmol/L)	128.5 \pm 4.2	132.1 \pm 3.8	< 0.001
TSH (mIU/L)	8.4 \pm 2.5	2.1 \pm 1.2	< 0.001
FT4 (ng/dL)	0.8 \pm 0.3	1.2 \pm 0.2	< 0.001

Finally, the incidence of hyponatremia was analyzed based on the degree of hypothyroidism as a source of variation. The hypothyroid patients, 45 (37.5%) had mild hyponatremia with serum sodium concentrations between 130-134 mmol/L. Moderate hyponatremia was defined as sodium level of 125-129 mEq/L, and 60 patients fell into this category (50.0%) severe hyponatremia was defined as sodium level less than 125 mEq/L, and 15 patients (12.5%) met this criterion. Such stratification

shows that hypothyroidism patients can experience mild to severe hyponatremia and calls for progeny observation in electrolyte balance. Knowledge of these differences may help design correct management protocols based on the severity of hyponatremia.

Table 3: Severity of Hyponatremia in Hypothyroid Patients

Severity of Hyponatremia	Frequency (N=120)	Percentage (%)
Mild (130-134 mmol/L)	45	37.5
Moderate (125-129 mmol/L)	60	50.0
Severe (<125 mmol/L)	15	12.5

The analyses of the results of the present clinical investigation show that hypothyroidism was present in a high number of the patients with hyponatremia, which points to the existence of the “strong” relationship between the considered pathologies. This association calls for healthcare providers to endorse assessment of the thyroid status in patients with hyponatremia. Since hypothyroidism makes it easy for a patient to develop low sodium level in the body, if the same is diagnosed early by clinicians, proper management may reduce likelihood of very serious complications that are affiliated to this condition. Therefore, it may be beneficial for utilizing early diagnosis and management of hypothyroidism in the patients to enhance the overall rates of success. The significance of these findings for improving clinical practices is captured in the implications of the summary and further insight of the findings will be discussed in the subsequent section.

Discussion:

The results of this research is comparable to previous studies on hypothyroidism as it pointed out a high incidence of the disease in hyponatremia in that about 60% of the patients with hyponatremia also show symptoms of hypothyroidism. This finding is in conformity with other studies which show there exists a strong correlation between thyroid dysfunctions and electrolyte abnormalities, chiefly hyponatremia (1, 2). The biological credibility for this association may be attributed to kidney dysfunction and water retention resulting from the impact of thyroid hormones on renal handling. It is well understood that hypothyroidism affects the glomerular filtration rate and affects the control of electrolytes such that sodium may be retained and lead to hyponatremia (3).

Therefore, assessing the hypothesis that thyroid hormones are involved in regulation of sodium homeostasis, we found the mean serum sodium levels in hypothyroid patients to be significantly lower than those in patients without thyroid dysfunction. Similar relationship has been documented in previous researches where hypothyroidism has been noted can cause alterations in normal fluid and Kidney functioning ability adding to hyponatremia. (4, 5). These findings of our hypothyroid patients show a raised TSH and low FT4 which strengthens our hypothesis that thyroid hormone deficiency is partially responsible for electrolyte disturbance.

Thus, the data showed that out of the hypothyroid patients approximately 55% experienced moderate hyponatremia, which is critical in clinical practice. Severe hyponatremia results in neurologic manifestations, primarily seizures and compromised mental status, calling for rapid identifiable and treatment (6). In addition, high prevalence of comorbidity like hypertension and diabetes among participants of the study indicates that such factors might worsen the case scenario and the overall handling of hyponatremia and hypothyroidism.

The observed demographic characteristics of the participants reflect what earlier existing literature that inclined towards hypothyroidism as a disease that is common among older people and even more so women (7, 8).

The male-to-female ratio of 1:1.2 in the present study also corroborates the epidemiological pattern of thyroid disorders and the risk factor of being a woman. It is also possible that changes in thyroid function with age and more frequent presence of comorbidities might have an impact on the development of hypothyroidism in patients with hyponatremia of older age.

Another important discovery about the researched topic is that hypothyroidism is strongly linked to hyponatremia as it was established mathematically by comparing TSH/Serum sodium correlation coefficient in patient and control groups. Clinicians might then seek to include routine thyroid function tests in patients presenting with hyponatremia particularly the elderly. This may be due to the fact that early diagnosis and treatment of hypothyroidism may improve sodium status and the patient's general wellbeing since renal function and sodium handling are known to be amplified by normal thyroid hormones (9).

The study also has implications of practical importance emphasizing the management of hyponatremia associated with hypothyroidism. In cases of routine management of hyponatremia, general principles of treatment include fluid restriction, and sodium supplementation but relief of thyroid pathology has to be sought as well. Not only the hormonal deficiency may be corrected by thyroid hormone replacement therapy but also hyponatremia in the patient (10). This fact emphasizes the necessity of a complex medical examination of the patients with the electrolyte abnormalities and the involvement of endocrine and metabolic examinations.

Despite

However, this study has several limitations that need to be acknowledged. Although the present study has yielded substantial findings, the following methods can be used to reduce the limitations of the study. Relative to the study design, the cross-sectional design makes causal relationships between hypothyroidism and hyponatremia difficult to determine. Moreover, the study group was recruited from one tertiary care center and may not reflect the results in other centers. Future longitudinal research must be conducted to describe the associations of thyroid dysfunction and hyponatremia, establish novel treatment modalities and life objectives for patients with both disorders.

Finally, the present work supports the hypothesis about the existence of hypothyroidism in hyponatremic patients. The study calls for hormonal assessment of thyroid hormone levels in those patients with the symptoms of hyponatremia, let alone elderly patients and those with underlying diseases. This way the relationship between these conditions can be understood, and thus adding value to the way diagnostics and treatments are planned and implemented which may benefit clients/patients in the long run. More studies should be directed at examining the pathways by which these two endocrine pathologies are related and assessing the effects of thyroid hormone replacement therapy on the management of hyponatremia.

CONCLUSION

The current findings of this study confirm that patients with hyponatremia are likely to have hypothyroidism, and nearly 60 percent of the participants in this study were found to have some form of thyroid abnormality. Pakistan has strong association between serum sodium levels and TSH which points towards the fact that hypothyroidism could be the main cause of hyponatremia. Based on the observed complications of hyponatremia such as neurological changes, the authors recommend electrolyte disturbances should prompt thyroid function tests because of the high prevalence in older patients with comorbid conditions. It also could also be a learning opportunity because early detection and efficient managing of hypothyroidism will greatly reduce patient morbidity and improve metabolism by stabilizing their sodium levels.

Further clinical and experimental studies are needed to determine how thyroid dysfunction affects sodium balance and to assess whether thyroid hormone supplementation is an effective intervention to treat hyponatremia in hypothyroid patients, in order to enhance clinical management and patients' outcomes.

References

- 1- Chu, C.H., Chien, W.C., Liu, C.C., Chung, C.H., Chen, Y.C., Kuo, F.C., Fang, H.H., Cheng, C.Y., Ding, Y.X., Tien, C.H. and Lin, C.M., 2023. An enigma of hypothyroidism and hyponatremia coexistence: a nationwide population-based retrospective study. *BMC Public Health*, 23(1), p.1889.
- 2- Anghel, L., Baroiu, L., Stefanopol, I.A., Busila, C., Ignat, D.M., Spalatel, O. and Bulza, V., The Role of Hypothyroidism in the Etiology of Hyponatremia-Case Report and a Short Review. *ARS Medica Tomitana*, 29(3), pp.137-143.
- 3- Syazana, N., Sani, H. and Azhar, Z.I., 2020. Thyroid Function Test as First-line Investigation of Hyponatremia: Is It Necessary?. *Asian Journal of Medicine and Biomedicine*, 4(1), pp.12-18.
- 4- Zhang, X. and Li, X.Y., 2020. Prevalence of hyponatremia among older inpatients in a general hospital. *European Geriatric Medicine*, 11, pp.685-692.
- 5- Bharat, B.S. and Sasturkar, M.K., 2022. Clinical Spectrum Of Patients With Hypothyroidism Presenting To Tertiary Care Centre. *Journal of Pharmaceutical Negative Results*, pp.4282-4295.
- 6- Heite, T., 2024. Incidence of hypothyroidism in Coburg Hospital 2018-2023 (Doctoral dissertation, University of Split. School of Medicine).
- 7- Saha, R.D. and Bhakta, S., 2024. PREVALENCE OF HYPOTHYROIDISM IN CIRRHOTIC PATIENTS AND NORMAL INDIVIDUALS. *Int J Acad Med Pharm*, 6(3), pp.268-272.
- 8- Cao, J.J., Yun, C.H., Xiao, J., Liu, Y., Wei, W. and Zhang, W., 2021. Analysis of the incidence and influencing factors of hyponatremia before 131I treatment of differentiated thyroid carcinoma. *World Journal of Clinical Cases*, 9(36), p.11173.
- 9- Ebrahimi, F., Anderegg, L. and Christ, E.R., 2024. Morbidities and mortality among hospitalized patients with hypopituitarism: Prevalence, causes and management. *Reviews in Endocrine and Metabolic Disorders*, pp.1-10.
- 10- Khatri, S., Alom, M., Kashfi, S., Atallah, J. and Goswami, G., 2023. Simultaneous Presentation of Secondary Adrenal Insufficiency and Primary Hypothyroidism due to Pembrolizumab: A Case Report. *Journal of Investigative Medicine High Impact Case Reports*, 11, p.23247096231194401.
- 11- Pi, Y., Li, Y., Shi, Z. and Tang, Y., 2021. Risk factors and causes of hyponatremia in patients after radiotherapy for head and neck cancer: A retrospective study. *Radiation Medicine and Protection*, 2(01), pp.13-16.
- 12- Khan, K.A., Qureshi, S., Hassan, Z. and Faraz, N., 2021. FREQUENCY, RISK FACTORS AND THE OUTCOMES OF PATIENTS ADMITTED WITH HYPONATREMIA IN A TERTIARY CARE SETUP. *Annals of Allied Health Sciences*, 7(1), pp.12-16.
- 13- Kayaokay, K. and Yurtlu, D.A., 2023. The incidence of hyponatremia in hospitalized patients due to hip fracture and its effect on mortality. *Cukurova Medical Journal*, 48(2), pp.601-606.
- 14- Tangsermvong, P., Chamroonrat, W., Vittayachokkitikhun, S. and Sriphrapadang, C., 2024. Serum Potassium in Thyroid Cancer Patients With Hypothyroidism During Thyroid Hormone Withdrawal: A Retrospective Study. *Clinical Medicine Insights: Endocrinology and Diabetes*, 17, p.11795514241278519.
- 15- Emektar, E., Dagar, S., Uzunosmanoğlu, H., Karaaslan, F., Çorbacıoğlu, Ş.K. and Çevik, Y., Etiology and prevalence of hyponatremia in geriatric patients with fragility hip fractures.