A study on prevalence of sodium and potassium abnormalities in hypothyroidism

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Abstract
Introduction: Medical literature is inundated with incidence of a multitude of electrolyte imbalances in patients with thyroid disorders. However, the cause and association between clinical presentations of thyroid diseases and electrolyte imbalances is still subject to controversies.
Objective: To study the prevalence of abnormal levels of serum Sodium & Potassium amongst men and non-pregnant women with newly detected hypothyroidism.
Materials and Method: Fifty subjects with newly detected hypothyroidism and fifty healthy subjects were identified. Thyroid function tests (serum TSH, T3 and T4) as well as serum sodium and potassium were estimated from the venous blood samples of all the participants.
Results: A statistically significant reduction in levels of serum sodium and potassium was observed in people with newly detected hypothyroidism.

Introduction
Thyroid hormone plays a very central role in regulation of body haemo-dynamics, thermoregulation and metabolism1,7. Thyroid diseases are increasingly being diagnosed in Indian population, especially in the elderly. Recent estimates state around 42 million people to be suffering from thyroid diseases; hypothyroidism being the commonest thyroid disorder. Thyroid hormones influence and regulate routine lipid, carbohydrate and protein metabolism, as well as electrolyte and mineral handling7. Thyroid hormone also affects renal hemo-dynamics, RAAS, salt handling and GFR3,6. Thyroid dysfunction can cause myriad clinical situations including Congestive Heart Failure4, musculo-skeletal dysfunction, electrolyte disturbances and coma5. Electrolytes are important in controlling fluid levels, acid-base balance (pH), nerve conduction, blood clotting and optimal muscle-skeletal activity3,5. The effect of thyroid hormones on electrolytes and minerals is still under much speculation. Several mechanisms are being put forward to attempt to explain this association.
One of the most common electrolyte disturbance seen in patients with thyroid dysfunction in clinical practice is Hyponatremia5.Saruta T et al postulated that in Hypothyroid patients, dysfunction of Juxta-glomerular cells and Glomerulosa cell might suppress Renin Activity (PRA) and Plasma Aldosterone (PA). They also
suggested a correlation between suppression of PRA and PA to exaggerated sodium excretion and decrease in potassium excretion.

Na-K ATPase is an enzyme on the cell membrane important for transport of water and nutrients across the cell membrane. Sodium and potassium are important components of this enzyme. Thyroid hormones are needed for regulating the activity of Na–K ATPase in most of the tissues. One of the several mechanisms of oedema in Hypothyroid patients is believed to be the dysfunction of Na-K-ATPase pump, leading to intracellular accumulation of water and thus causing weight gain.

Yet another possible mechanism being increasingly considered is Vasopressin. Literature reviews reveal increased incidence of hyponatremia in severe hypothyroidism and myxoedema, probably a consequence of non-osmotically released vasopressin, causing impaired urinary dilution capacity, enhanced renal water retention, as well as increased urine sodium loss.

The picture is different and indistinct with regards to potassium level in thyroid dysfunction. Murgod et al found hypokalemia and hypocalcemia in patients with hypothyroidism, while some others like Schwartz et al found hypokalemia along with hypocalcemia in some cases of hyperthyroidism. Possible reasons might be enhanced renal potassium excretion and intracellular potassium shift.

Thyroid dysfunction shows a sex predilection, being more common in women than in men. Oestrogen might play an important role in pathophysiology of thyroid dysfunction. Estradiol shows competitive binding on receptor proteins of T3 and T4, thus, antagonizing their effect. Estradiol also restricts the thermogenic action of T4 and promotes storage of fat. Estradiol might also have a direct effect on thyroid gland. A study by Gantus MA et al demonstrated the effects of oestrogen on Thyroid stromal cells, via the cytokine transforming growth factor beta-1 (TGF-B1) / transcription factor Smad-2 signalling pathway on a homogeneous stromal cell population (TS7 cells) of rat thyroid gland.

Hyponatraemia causes an increased risk of falls and fractures in the elderly, thus adversely affecting to their morbidity and mortality. Hypokalemia is associated with cardiac, renal and musculo-skeletal dysfunction. In the epidemic of CAD and its morbidity and mortality, thyroid dysfunction and its effect on electrolyte handling can have prognostic implications.

Clinically manifesting electrolyte disorders can be seen in even subtle thyroid dysfunction and not necessarily be confined to severe thyroid dysfunction like thyrotoxicosis or myxoedema. Whether the attendant subtle and overt electrolyte dysfunction gets corrected with patient achieving euthyroidism is subject to speculation. Exploration of this aspect of thyroid dysfunction can make an impact on its management. With this background, this study was undertaken to better the management of hypothyroidism and its complications.

**Method**

**Study Design and Subjects**

This study was carried out in the out-patient general medicine department of Government TD Medical College, Alappuzha between July 2018 and July 2019. Fifty patients of either gender and without pregnancy, above 18 years of age, with newly detected abnormally elevated Thyroid function tests, and fifty normal asymptomatic healthy sex and age matched subjects were identified from amongst the patients and bystanders attending the out-patient department. The study was initiated after obtaining clearance from the institutional Research Committee and Ethics committee. Informed consent was obtained from all participants after explaining in detail the aims and objectives of the study.

**Selection Criteria**

Inclusion Criteria: Male and Non-pregnant Female patients of age more than 18 with newly detected abnormally elevated Thyroid function tests were included.
Exclusion Criteria: Patients with history of intake of Thyroid drugs, Anti-Hypertensives, Diabetes Mellitus or Obesity, Current Smokers and alcoholics, Renal Insufficiency or Hepatic Failure, Thyroid malignancy, Anti-Psychotics or Hormone Replacement therapy and critically ill patients.

**Definitions and normal ranges used in the study:**

Thyroid function tests: TSH normal range: 0.35-4.5mU/l, fT4 9.5-25pmol/l, fT3 2.9-6.5 pmol/L, Normal S Sodium: 135-145 mmol/l, Hyponatraemia <135 mmol/l; Hypernatraemia >145 mmol/l

Normal S Potassium: 3.5-4.5 mmol/l, Hypokalaemia <3.5 mmol/l Hyperkalaemia >4.7 mmol/l

**Blood Sample Collection**

5ml of fasting venous blood samples was taken from willing subjects who had given consent. Care was taken during the sample collection by avoiding tourniquets and aggressive venosuction or sample handling. The separated serum was tested for serum electrolytes, RFT, LFT and other clinically relevant investigations. Thyroid hormone levels were measured by Neolumax Chemiluminescence Immune Assay method while serum sodium and potassium were estimated using Easylte selective ion electrodes.

Data was entered into excel sheet and analysis done by using SPSS version 16. Qualitative variables were summarised using proportions. Quantitative variables using mean with standard deviation / median. Associations were checked using Chi-square test. Association between numerical variables was computed using Pearson’s correlation co-efficient.

**Results**

In our study, the mean age of the patients with newly detected hypothyroidism was 34.68± 7.91 years against 34.78 ± 7.85 years of the healthy group and this was of no difference statistically. There were twenty seven female patients and twenty three male patients in the group with hypothyroidism. Twenty two male subjects and twenty eight female subjects with normal TSH were included in the healthy group. The study group of newly detected hypothyroidism had a mean TSH of 51.43 ± 26.14 against the 2.60 ± 1.26 of the healthy group and this was statistically significant (p<.0001). People with hypothyroidism had a mean Serum Sodium of 124 ± 26.14 mmol/l while the normal group had mean values of 138 ± 2.46mmol/l. Again this difference was statistically significant. (p<.0001). Similar difference was noticed in Serum potassium levels with the mean values of 3.38 ± 0.25mmol/l in hypothyroid people and 4.20± 0.55mmol/l in the healthy group (statistically significant p<.0001). Further, the correlation between serum TSH values and Sodium and potassium levels in serum was statistically insignificant and weakly negative.

**Chart No 1: Distribution of Age**

![Age distribution in years](chart1.png)
Discussion
Thyroid Hormone plays a very important and central role in regulation of body hemodynamics, thermoregulation and metabolism. Thyroid diseases are being increasingly detected in India, with a prevalence of about 42 million cases; hypothyroidism being the most common disorder\(^1\). A higher incidence is noted in women, thus potentiating a possible influence of oestrogen on thyroid functions \(^1,2\). Thyroid hormone affects all aspects of body metabolism, including renal electrolyte handling and optimal cardiac functioning and neurological integrity\(^3-6\).

Being a chief regulator of metabolism, thermodynamics and hemodynamics, Thyroid hormone has multiple yet not completely understood actions. Renal blood flow, electrolyte handling and GFR are also influenced by Thyroid hormone. In hypothyroid patients, Plasma renin Activity and plasma aldosterone activity might get suppressed by hypothyroidism which might account for hyponatremia.(Saruta et al). Vasopressin might also get released without an osmotic stimulus in hypothyroid cases and cause renal retention of water and subsequent dilutional hyponatremia. (Schwatz et al). On the other hand, both hypokalemia (Murgod et al) and hyperkalemia (Schwartz et al) have been reported with hypothyroidism.

Na-K-ATPase is a vital and universal enzyme of the human body and is needed for controlling the transcellular shift of water serum electrolytes and nutrients. TSH hormone affects the optimal functioning of the Na-K-ATPase enzyme thus...
accounting for the intra and extra cellular fluid retention.

With this background, the present study was undertaken, to assess the spectrum of sodium and potassium abnormalities in men and non-pregnant women with Hypothyroidism from a coastal area. In our study, majority of the patients were females and the highest numbers belonged to the age group of 30-40 years. Similar findings have been reported in almost all studies (Schwartz et al, Saruta et al, Kaur et al). The research by Gantus et al that postulated that estradiol might directly affect thyroid stromal cells as well as show competitive binding with receptors of T3 and T4.

**Chart 4: Gender Distribution in Hypothyroid vs Healthy Cases**

In our study, a statistically significant negative association was noticed between Serum TSH levels and serum potassium levels (p value <0.001). Similar findings have been reported in other studies also (Kaur et al and Kavitha et al) but studies by some others (Abedelmula et al) failed to show this association.

**Table 1: Association between TSH and Serum Sodium and Serum Potassium**

<table>
<thead>
<tr>
<th>S No</th>
<th>Variable</th>
<th>Hypothyroid (n=50)</th>
<th>Healthy (n=50)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TSH</td>
<td>51.43±26.14</td>
<td>2.60±1.26</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2</td>
<td>Sodium</td>
<td>124.13±1.23</td>
<td>138.03±2.46</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3</td>
<td>Potassium</td>
<td>3.38±0.25</td>
<td>4.20±0.55</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Further, in our study, serum TSH levels and serum Sodium levels were also found to have a negative correlation and this difference was also statistically significant with a p value <0.0001. Similar findings have also been reported by Bharti et al and Derubertis et al.

**Chart 5: Comparison between TSH and Serum Sodium and Serum Potassium**
A highly statistically significant association was seen between TSH levels and serum Sodium and Potassium levels.

**Table 2:** Correlation coefficient (r value), P Value, TSH, Sodium and Potassium

<table>
<thead>
<tr>
<th>S No</th>
<th>Parameter</th>
<th>R Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TSH vs Sodium</td>
<td>-0.03</td>
<td>=0.85</td>
</tr>
<tr>
<td>2</td>
<td>TSH vs Potassium</td>
<td>-0.03</td>
<td>=0.85</td>
</tr>
</tbody>
</table>

**Conclusion**

Our study again reiterated the effect of TSH on serum sodium and potassium. The analysis of all the data in our study revealed that even in a coastal area with high intake of seafood, people with newly detected Hypothyroidism showed lower levels of both serum Sodium and Potassium. Apart from the slowing of thermoregulation, metabolism and hemodynamics, hypothyroidism can also cause hyponatremia which can have deleterious sequelae like falls, fractures and neuro-muscular slowing. Similarly, the hypothyroid individuals had lower levels of serum potassium which in turn might again contribute to cardiac, renal and neuromuscular dysfunction. Further, early recognition and correction of these electrolyte imbalances might help avoid any further decline of health of people with hypothyroidism as well as mitigate some of their symptoms. Thus, a newly detected diagnosis of hypothyroidism warrants a simultaneous baseline screening of serum electrolytes.

**References**

