Thyroid Status, Renal Profile and Electrolytes in Postmenopausal Women

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Introduction: Diminished gonadal hormones after menopause are found to influence thyroid status, renal functions as well as electrolyte balance. There are a few published data in this area, to the best of our knowledge. Aim of our study was to compare thyroid status, renal profile and serum electrolytes in postmenopausal women with those in reproductive age group as well as to find the association between them.

Methods: A case control study, which included fifty post menopausal and fifty women in reproductive age group were compared with respect to their thyroid status, renal profile and electrolytes. Statistical analysis was done using Student's 't' test, Pearson's correlation coefficient and Odd's ratio.

Results: Postmenopausal women had a significantly higher TSH (thyroid stimulating hormone) levels (P<0.05), elevated creatinine (P<0.05), lower eGFR (P<0.001) and sodium levels (P<0.05) as compared to controls. Post menopausal women with higher TSH levels were at greater risk of developing low GFR (glomerular filtration rate) and hyponatremia. A significant positive correlation was observed between age and TSH. A significant negative correlation was observed between TSH and sodium as well as eGFR in post menopausal women.

Conclusion: Subclinical hypothyroidism, altered renal functions and hyponatremia observed in post menopausal women suggest a need for routine screening panel, which includes thyroid and renal function tests.

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Keywords: Menopause; thyroid functions; renal profile; electrolytes.

1. INTRODUCTION

Endocrine glands exhibit changes as the age advances. Age related fall in circulating T4, reduction in TSH bioavailability, reduced responsiveness of thyroid gland to TSH resulting in increased TSH secretion in the absence of overt thyroid disease are reported. Subclinical hypothyroidism with normal free T4 and raised TSH is found to be common in elderly [1,2]. Gender specific alterations in TSH and FT4 (free tetra iodothyronine) has also been reported in elderly women, who had elevated TSH, unaltered FT4 [3]. Menopause is a condition where there is cessation of menstruation under the influence of reproductive hormones. These hormones influence various systems in the body. Thyroid gland is one among them. Thyroid hormone regulates body metabolism, including reproductive functions. Disorders of thyroid gland are common in women.

We could review a few American studies in which higher TSH levels were reported in post menopausal women [4,5]. There is a scarcity of literature in Indian settings which focus on thyroid status in post menopausal women.

There are reports suggesting an association between chronic kidney disease (CKD) and low T3 syndrome, thyroid dysfunction and glomerulonephritis of auto immune etiology. Association of thyroid functions with renal profile is not much explored to the best of our knowledge.

Diminished estrogen and progesterone in the post menopausal period, may be associated with alterations in electrolytes. Evidence suggests that estrogen related sodium retention is mediated through aldosterone [6]. Progesterone is important in fluid and electrolyte regulation. As progesterone level drops in menopause, alterations in renin-angiotensin-aldosterone system (RAAS) in turn alters serum electrolytes.

As there is scarcity of published data in this area, we aimed to compare thyroid status, renal profile and serum electrolytes in post menopausal women.

1.1 Objectives

Aim of our study was to compare thyroid status, renal profile and serum electrolytes in postmenopausal women with those in reproductive age group as well as to find the association between those three biochemical profiles if any.

2. METHODOLOGY

2.1 Study Design

A case control study was conducted in the Department of Biochemistry, Karwar Institute of Medical Sciences, Karwar from June 2015 to May 2016. Institutional ethics committee approval was obtained.

Blood samples of fifty post menopausal women who were asymptomatic of thyroid disorders and fifty women of reproductive age group (controls) were identified from patient bystanders in our hospital and analyzed for thyroid status, renal functions and electrolytes.

Post menopausal women with a mean age of 56.3±5.7 years, who were bystanders of admitted patients were included in the study. Diabetics, hypertensives, known thyroid and renal disorders, electrolyte disturbances, those on diuretics, steroids were excluded based on the history. Healthy women in the age group of 25.5±3.2 yrs, non diabetic, not suffering from thyroid disorders were taken as controls.

2.2 Data Collection and Analysis

Five ml of venous blood sample was collected in plain tubes by puncturing antecubital vein with aseptic precautions. Samples were centrifuged at 3000 rpm for 15 minutes. Serum was analyzed for thyroid hormones and TSH with commercially available kits in hormone analyzer Maglumi, which works on the principle of electrochemiluminescence. Blood urea and serum creatinine were estimated using fully automated chemistry analyzer, XL-640 and electrolytes were assayed with Roche electrolyte analyzer which works on the principle of ion selective electrodes. Estimated GFR (eGFR) was calculated by using MDRD formula [7]:

\[ \text{eGFR} = 186 \times (\text{serum creatinine})^{1.154} \times (\text{Age})^{-0.203} \times 0.742 \times 0.742 \] (Multiplied by 0.742 only in females).

Following are the reference ranges for the assayed parameters:
2.3 Statistical Analysis

Data was analyzed by Graph pad Instat, version 3 software using Student’s unpaired ‘t’ test for comparison of means. P< 0.05 is taken as significant. Pearson’s correlation coefficient, r (between -1 and +1) was calculated for the correlation studies. Odd’s ratio was calculated to find the relative risk.

3. RESULTS

The results are expressed as mean ± standard deviation (sd) for all the parameters as represented in Table 1. We observed that postmenopausal women had a significantly higher TSH levels (P<0.05), elevated creatinine (P<0.05), lower eGFR (P<0.001) and sodium levels (P<0.05) (Table 1).

Post menopausal women with high TSH levels were at higher risk of developing low GFR and hyponatremia (Table 2 and 3). A significant positive correlation was observed between age and TSH. A significant negative correlation was found between TSH and sodium as well as TSH and eGFR (Table 4).

4. DISCUSSION

We found a significant elevation in TSH levels (P<0.05) as well as nonsignificant decline in thyroid hormones in post menopausal women compared to those in reproductive age group. A positive correlation has also been found between TSH and age. Similar results were observed by Pearce et al. [4] and Hollowell et al. [5]. Altered thyroid functions can be explained as an age related fall in thyroid hormones or reduced responsiveness of thyroid to TSH in the absence of overt thyroid disease. It also may be an occult thyroid disease or just an age related alteration in TSH set point [8-10]. However contradictory reports are available, which suggest a low TSH levels in post menopausal women [11,12].

A significant elevation in creatinine (P<0.05) and reduction in eGFR (P<0.01) was observed in our study, which could be attributed to prerenal and intrinsic renal effects of thyroid hormones. These hormones increase renal blood flow and glomerular filtration rate as well as activate renin angiotensin aldosterone system. Subclinical hypothyroid status in postmenopausal women could be the reason for observed decreased eGFR. Hypothyroidism is found to be associated with 40% diminished GFR, low angiotensin II levels and impaired RAAS system [13-15]. These reports explain observed low GFR in subclinically hypothyroid post menopausal women. It was also found that post menopausal women with high TSH were 3 times at higher risk of renal impairment. There was a significant negative correlation between TSH and eGFR, suggesting a risk of renal impairment in hypothyroid postmenopausal women.

Table 1. Comparison of thyroid and renal profiles of post menopausal women and women of reproductive age group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Post menopausal women</th>
<th>Women of reproductive age group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3 (ng/ml)</td>
<td>0.98±0.09</td>
<td>1.10±0.03</td>
<td>NS</td>
</tr>
<tr>
<td>T4 (ng/ml)</td>
<td>84.98±2.5</td>
<td>86.01±10.97</td>
<td>NS</td>
</tr>
<tr>
<td>TSH (µIU/ml)</td>
<td>5.67±0.76</td>
<td>2.2±1.5</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>36.45±2.8</td>
<td>35.67±3.4</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.7±0.2</td>
<td>0.91±0.23</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>eGFR</td>
<td>67.45±5.8</td>
<td>98.23±4.78</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
<td>130.06±2.3</td>
<td>138.98±4.5</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>3.7±0.43</td>
<td>3.8±0.51</td>
<td>NS</td>
</tr>
<tr>
<td>Chloride (mEq/L)</td>
<td>98.72±8.7</td>
<td>99.11±7.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS: Not significant  
P<0.05 – significant  
P<0.001 – highly significant
Table 2. Contingency table for TSH and eGFR in post menopausal women

<table>
<thead>
<tr>
<th></th>
<th>High TSH</th>
<th>Normal TSH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low eGFR</td>
<td>29 (a)</td>
<td>15(b)</td>
</tr>
<tr>
<td>Normal eGFR</td>
<td>21(c)</td>
<td>35(d)</td>
</tr>
</tbody>
</table>

Odd’s ratio = \(ad/bc = 3.22\)

Table 3. Contingency table for TSH and sodium levels in post menopausal women

<table>
<thead>
<tr>
<th></th>
<th>High TSH</th>
<th>Normal TSH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low sodium</td>
<td>28 (a)</td>
<td>10(b)</td>
</tr>
<tr>
<td>Normal sodium</td>
<td>22(c)</td>
<td>40(d)</td>
</tr>
</tbody>
</table>

Odd’s ratio = \(ad/bc = 5.09\)

Table 4. Correlation studies

<table>
<thead>
<tr>
<th></th>
<th>Pearson’s correlation coefficient (r)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age and TSH</td>
<td>0.48</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TSH and sodium</td>
<td>-0.53</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TSH and eGFR</td>
<td>-0.41</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Significant reduction in sodium levels as well as statistically insignificant diminution of potassium and chloride levels suggest that, influence of thyroid hormones on renal system is reflected as electrolyte disturbance. A significant negative correlation between TSH and sodium supports this finding. Subclinically hypothyroid post menopausal women were five times at higher risk of hyponatremia. Net decrease in reabsorption of sodium and chloride in proximal convoluted tubules as well as increased excretion of sodium reported in hypothyroid patients supports hyponatremia found in our study subjects [16]. In another study, Schwarz et al. [17] reported hyponatremia and altered potassium levels in hypothyroid patients. However serum TSH did not correlate with sodium levels. A study by Schmitt et al reported that impaired urinary dilution capacity due to non osmotic release of ADH and increased urine sodium loss were the major mechanisms for hypothyroidism induced hyponatremia in rats [18]. Hyponatremia in severe hypothyroidism and myxedema was attributed to enhanced renal water retention due to ADH [19].

Hyponatremia in post menopausal women with high TSH can also be explained by another possible theory. Menopause is a condition with lowered estrogen and progesterone levels. Estrogen stimulates liver to synthesize angiotensinogen, which when activated to angiotensin II, stimulates aldosterone secretion. Study by Boschitsch et al. [6] suggest that estrogen related sodium retention is mediated through aldosterone. Electrolyte disturbances due to lowered estrogen levels could be a consequence of changes in binding sites of aldosterone or due to the direct effect of estrogen on PCT.

Progesterone is another important hormone which has a role in fluid electrolyte balance [6]. It is found to be the primary mediator of sodium regulation as it influences RAAS. As progesterone level drops in menopause, hyponatremia may develop.

5. LIMITATION OF THE STUDY

We have not obtained the details of social status, dietary interventions and previous risk factors. Smaller sample size is also a limiting factor, because of which it is not possible to generalize the findings.

6. CONCLUSION

Subclinical hypothyroidism, altered renal functions and hyponatremia observed in post menopausal women suggest that a panel of biochemical tests have to be performed as routine screening tests to assess thyroid and renal functions. This can ensure early detection of subclinical thyroid dysfunction and early renal impairment.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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