

Thyroid status, renal profile and electrolytes in postmenopausal women

Abstract

Introduction : Diminished gonadal hormones after the menopause is found to influence thyroid status, renal functions as well as electrolyte balance. There are a few published literature 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 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 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 necessity to carry out thyroid and renal function tests as routine screening tests in the post menopausal period.

Key words: Menopause, thyroid functions, renal profile, electrolytes

Introduction

Endocrine glands exhibit changes as the age advances. Hence it is possible to have age related fall in circulating T₄, reduction in TSH bioavailability, reduced responsiveness of thyroid gland to TSH can result in increased TSH secretion in the absence of overt thyroid disease. 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 has also been reported in which elderly women had elevated TSH, without any alterations in FT4(3). Menopause is a condition where there is cessation of menstruation under the influence of reproductive hormones. These hormones influence other systems in the body as well. Thyroid gland is one among them. Thyroid hormone regulates body metabolism, including reproductive functions. Disorders of thyroid gland are common in women.

We could find 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.

Thyroid dysfunction affects renal physiology and development and kidney disease results in thyroid dysfunction. There are reports suggesting that CKD is associated with low T3 syndrome, thyroid dysfunction is associated with glomerulonephritis of autoimmune 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. There is an evidence that estrogen related sodium retention is mediated through aldosterone (6). Progesterone is important in fluid and electrolyte regulation (42-10.11). As progesterone level drops in menopause, we can expect alterations in renin-angiotensin-aldosterone system which in turn can alter serum electrolytes.

As there are not much published data in this area, we aimed to compare thyroid status, renal profile and serum electrolytes in post menopausal women.

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.

Methodology

Study design

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

58 Blood samples of fifty post menopausal women who were asymptomatic of thyroid disorders
59 and fifty women of reproductive age group (controls) were analyzed for thyroid status, renal
60 functions and electrolytes.

61 Inclusion criteria: Post menopausal women with a mean age of 56.3 ± 5.7 years.

62 Exclusion criteria: diabetics, hypertensives, known thyroid and renal disorders, electrolyte
63 disturbances, those on diuretics, steroids

64 Inclusion criteria for controls: healthy women in the age group of 25.5 ± 3.2 yrs, non diabetic, not
65 suffering from thyroid disorders

66 **Data collection and analysis**

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

74
$$eGFR = 186 \times (\text{serum creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times 0.742$$
 (Multiplied by 0.742 only in females).

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76 Following are the reference ranges for the assayed parameters;

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78 T3 - 0.69-2.15 ng/ml	Sodium – 135-145 mEq/L	Urea – 15-40 mg/dl
79 T4 - 52-127 ng/ml	Potassium – 3.5 -5 mEq/L	Creatinine – 0.5 -1.5mg/dl
80 TSH - 0.3-4.5 μ IU/ml	Chloride – 97 -104 mEq/L	

81 Statistical analysis:

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

86 87 Results

88
89 The results are expressed as mean $\pm$ standard deviation (sd) for all the parameters and are
90 represented in the Table I. We observed that postmenopausal women had a significantly higher
91 TSH levels ($P < 0.05$), elevated creatinine ($P < 0.05$), lower eGFR ($P < 0.001$) and sodium levels
92 ($P < 0.05$)(Table 1).

93 Post menopausal women with high TSH levels were at higher risk of developing low GFR and
94 hyponatremia (Table 2 and 3). A significant positive correlation was observed between age and
95 TSH. TSH bore a significant negative correlation with sodium as well as with eGFR (Table 4).
96

97 Table 1: Comparison of thyroid and renal profiles of post menopausal women with that of
98 women in reproductive age group

	Postmenopausal women	Women of reproductive age group	P value
T3 (ng/ml)	0.98 $\pm$ 0.09	1.10 $\pm$ 0.03	NS
T4 (ng/ml)	84.98 $\pm$ 2.5	86.01 $\pm$ 10.97	NS
TSH (μ IU/ml)	5.67 $\pm$ 0.76	2.2 $\pm$ 1.5	<0.05*
Urea(mg/dl)	36.45 $\pm$ 2.8	35.67 $\pm$ 3.4	NS
Creatinine (mg/dl)	1.7 $\pm$ 0.2	0.91 $\pm$ 0.23	<0.05*
eGFR	67.45 $\pm$ 5.8	98.23 $\pm$ 4.78	<0.001**
Sodium (mEq/L)	130.06 $\pm$ 2.3	138.98 $\pm$ 4.5	<0.05*

Potassium (mEq/L)	3.7±0.43	3.8±0.51	NS
Chloride (mEq/L)	98.72±8.7	99.11±7.6	NS

99

100 NS : not significant

101 P<0.05 – significant

102 P<0.001 – highly significant

103 Table 2: Contingency table for TSH and eGFR in post menopausal women

	High TSH	Normal TSH
Low eGFR	29 (a)	15(b)
Normal eGFR	21(c)	35(d)

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105 Odd's ratio = $ad/bc = 3.22$

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

	High TSH	Normal TSH
Low sodium	28 (a)	10(b)
Normal sodium	22(c)	40(d)

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109 Odd's ratio = $ad/bc = 5.09$

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115 Table 4:Correlaton studies

	Pearson's correlation coefficient (r)	P value
Age and TSH	0.48	<0.05
TSH and sodium	-0.53	<0.01
TSH and eGFR	-0.41	<0.05

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117

118 **Discussion**

119 We found a significant elevation in TSH levels ($P<0.05$) as well as nonsignificant decline in
 120 thyroid hormones in post menopausal women compared to those in reproductive age group. A
 121 positive correlation has also been found between TSH and age. Similar results were observed by
 122 Rojas et al (10-A15), Pearce et al and Hollowell et al(4,5). Altered thyroid functions can be
 123 explained as an age related fall in thyroid hormones or reduced responsiveness of thyroid to TSH
 124 in the absence of overt thyroid disease. It also may be an occult thyroid disease or just an age
 125 related alteration in TSH set point (9,10). However contradictory reports are available, which
 126 suggest a lower TSH levels in post menopausal women (11,12).

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

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 reported hyponatremia and altered potassium levels in hypothyroid patients (17). 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 was the major mechanism 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 is activated to angiotensin II, stimulates aldosterone secretion. Study by Boschitsch et al suggest that estrogen related sodium retention is mediated through aldosterone (6). Electrolyte disturbances due to lowered estrogen levels in our subjects 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 can be expected.

Conclusion

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

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