

Thyroid status, renal profile and electrolytes in postmenopausal women

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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 (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 necessity to carry out thyroid and renal function tests as routine screening tests in the post menopausal period.

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 (free tetra iodothyronine) 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. As progesterone level drops in menopause, we can expect alterations in renin-angiotensin-aldosterone system (RAAS) 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

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. Confounding factors 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 chosen to be the controls.

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. Plasma 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);

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

Following are the reference ranges for the assayed parameters;

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

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.

Results

The results are expressed as mean $\pm$ standard deviation (sd) for all the parameters and are represented in the Table I. 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. TSH bore a significant negative correlation with sodium as well as with eGFR (Table 4).

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

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

NS : not significant

P<0.05 – significant

P<0.001 – highly significant

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)

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

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)

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

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

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 Rojas et al ,Pearce et al and Hollowell et al(4,5). 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 (9,10). However contradictory reports are available ,which suggest a lower TSH levels in post menopausal women (11,12).

A significant elevation in creatinine ($P<0.05$) and reduction in eGFR ($P<0.01$) observed in our study 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 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.

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.

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.

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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CONSENT FORM

PART 1 of 2

INFORMATION FOR PARTICIPANTS OF THE STUDY

Title of the project: Thyroid status, renal profile and electrolytes in postmenopausal women

Name of the investigator:

Principal Investigator: Dr.Usha Sachidananda Adiga
Professor, Dept of Biochemistry
K.S Hegde Medical Academy,Mangalore
8277781638

Co-investigator:

You are being invited to take part in a research study. Please take some time to read the information presented here, which will explain details of this study. Please ask the researcher any questions about any part of this project that you do not fully understand.

It is very important that you are fully satisfied that you have clearly understood what this research entails and how you would be involved.

Your participation is **entirely voluntary** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever, including health care now or in the future. You are also free to withdraw from the study at any point, even if you do agree to take part.

What is this research study all about?

The study is about studying thyroid and renal status of postmenopausal women.

Why have you been invited to participate?

To compare and find out a probable association between the mentioned parameters.

Why this study is being done?

To establish a panel of investigations as routine screening tests in postmenopausal women.

How the study will be conducted?

Your/your ward's details will be recorded as per the detailed prescribed proforma and kept confidential. Five ml of blood sample will be collected with aseptic precautions for the estimation of thyroid and renal markers .

How long you will be in the study?

You/ your ward will be a part of study for a period of 1 year. If you are enrolled in the study, it is just a single prick.

Will you benefit from taking part in this research?

If we establish a panel of markers , preventive measures can be taken which would be beneficial to you.

In addition to this, it will be definitely beneficial for the community for whom we can take preventive measures.

Are there any risks involved in your taking part in this research?

No, there is no risk involved in your taking part in this research.

Will your participation in this study be kept confidential?

Information obtained about you for this study will be kept confidential to the extent allowed by law.

What will happen to the information collected from this research?

Information obtained from this study will be analyzed and only the results may be published, presented in public talks or written articles, without disclosing the identity of the participants.

Are there any costs involved and will you be paid to take part in this study?

You will not be paid any money or any other incentive.
You are also not required to pay any money for tests.

What if you decide to stop participating in the research before it is over?

You may stop participating in the research at any time you choose. All the services you receive at this hospital will continue even after you quit the research.

Do you have any questions about the research?

If there is anything else that you want to know, if you have any further queries or encounter any problems you can contact any of the investigators.

You will receive a copy of this information and consent form for your own records.

CONSENT FORM

PART 2 of 2- Participant consent form

Participant's name:

Address:

Mobile no.:

Hospital no.:

Title of the project: Thyroid status, renal profile and electrolytes in postmenopausal women

The details of the study have been provided to me in writing and explained to me in my own language. I confirm that I have understood the above study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I have been given an information sheet giving details of the study. I fully consent to participate in the above study.

Signature of the participant : _____ Date: _____

Signature of the witness: _____ Date: _____

PROFORMA

1. Demographic profile:			
Registration Number:		Education status: Illiterate/PS/SS/College	
Age :		Occupation:	
h/o any illness/drug intake		H/o Smoking/ Alcoholism/Tobacco chewing	
Height		Bodyweight	
2. Associated co-morbid conditions (like HTN, CAD ,renal disorders, diarrhea,vomitting etc)			
Disease	Duration	Medication	Complications

3. Investigations

Test	
TSH	
T3	
T4	
Urea	
Creatinine	
Sodium	
Potassium	
Chloride	