

Role of TSH on Urinary Calcium Excretion In Post Menopausal Women of South Indian Population

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ABSTRACT

Background: Unforeseen aberrations in the hormonal status during the early postmenopausal period are responsible for several complications including osteoporosis. Thyroid Stimulating Hormone (TSH) receptors are isolated from various tissues including the bone. A low serum TSH level is known to stimulate osteoclastic activity in bone and accelerate bone resorption. Urinary calcium/creatinine (UCa/Cr) excretion ratio could be an indirect and an early indicator of loss of Bone Mineral Density (BMD). With this background, this study was planned to explore the association of serum TSH levels with the UCa/Cr excretion ratio.

Methods: Forty eight women in the postmenopausal age group, with their menopausal age not more than seven years of duration were included in this study. Based on their TSH val-

ues, these subjects were divided into two groups A (TSH<0.5 mIU/L) and B (TSH>0.5mIU/L). Urinary calcium, UCa/Cr excretion ratio, serum phosphorous, calcium and calcium phosphorous multiplication products were estimated and compared between the two groups.

Results: Twenty two (46%) women were biochemically asymptomatic hyperthyroid cases and Twenty six (54%) were euthyroid. This study documents high UCa/Cr in Group A compared to that of Group B ($p<0.05$). We also observed significant negative correlation of TSH with UCa/Cr excretion ratio ($p=0.041$, $r = -0.43$).

Conclusion: Low serum TSH levels were associated with increased UCa/Cr excretion ratio in postmenopausal women of South Indian population.

Key Words: Thyroid Stimulating Hormone, Post Menopausal Women, Urinary calcium, Urinary Calcium/creatinine ratio

INTRODUCTION

Osteoporosis is a significant global health hazard which affects an estimated 200 million people. A majority of the patients (80% in the US) are Postmenopausal Women (PMW) [1, 2]. In fact, approximately one out of every three women over the age of fifty will experience an osteoporotic fracture during their lifetime. As the mean age of the population keeps increasing, owing to the medical facilities (both qualitative and quantitative), the burden of osteoporosis will continue to escalate in both men and women. By 2050, the worldwide incidence of hip fractures has been projected to increase by 310% in men and by 240% in women [3].

Osteoporosis is a skeletal disorder which is characterized by a reduced bone strength. The loss of the bone strength is related to a decrease in the Bone Mineral Density (BMD) as well as a reduced bone quality, and hence, it is accompanied by an increased risk of fractures, even with trivial injuries. The complications in PMW, especially in the early stages, have been attributed to the aberrations in the statuses of several hormones [4]. The detection and correction of sudden variations in the hormonal status during the early postmenopausal period could help in the prevention of many complications. These complications include bone loss, mood disorders [5], insomnia [6] and the metabolic syndrome [7]. The current therapeutic modalities are aimed at enhancing the BMD and reducing the fracture risk. However, a poor patient compliance compromises the effectiveness of managing osteoporosis successfully.

Previous studies have pointed to the role of the Thyroid Stimulating Hormone (TSH) in the BMD [8], and in other complications

in PMW [4-7]. A normal or high normal TSH level is known to preserve the BMD [9]. Hormone replacement therapy and calcium supplementation are presently available as the therapeutic modalities for the postmenopausal complications [10]. In addition to this, an early detection and correction of the abnormal TSH levels could help in the prevention of these complications which are observed in PMW [4, 8].

The urinary excretion of calcium directly correlates with a decrease in the BMD in PMW [11-13]. The estimation of the urinary calcium/creatinine excretion ratio (UCa/Cr) would be an easy, pragmatic and a feasible marker than the urinary calcium alone. However, there are very few reports, especially in the south Indian population, which pertain to the effect of the TSH on the BMD. With this background, the current study was planned with the following objectives:

1. To evaluate the status of the serum TSH levels during the early postmenopausal period.
2. To explore the association of the serum TSH levels with the UCa/Cr excretion ratio in PMW.

METHODOLOGY

In this prospective, non-randomized, cohort study, forty eight PMW who were in the age group of 45-60 years, with the duration of their menopause not being longer than seven years, were included. This study was approved by the institutional ethics committee. After obtaining informed consents from all the participants, a detailed history was taken and the clinical findings were documented.

The women who were on thyroxine or any other hormone supplementations, oral calcium, Vitamin D, bisphosphonates, statins and antihypertensive therapies were excluded from the study. The women who had undergone total or subtotal thyroidectomies and those with renal or hepatobiliary disorders, hyperparathyroidism and any other clinical features which were suggestive of endocrinal disorders were also excluded from this study.

The serum TSH was estimated by an automated chemiluminescence immunoassay method (on a fully automated analyzer, Hitachi). Alkaline phosphatase, calcium, phosphorous, urea and creatinine were estimated in the serum. The urinary specimens were collected in sterile containers which contained thirty millilitres of 6 mol/L of HCL to prevent the precipitation of calcium and phosphate in the urine. Spot urinary calcium, creatinine and phosphates were estimated by automated procedures which were approved by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). The UCa/Cr excretion ratio and the serum calcium-phosphorus products (serum calcium multiplied by serum phosphorous) were calculated. Forty eight PMW were divided into two groups based on their serum TSH levels. The PMW with a serum TSH of < 0.5 mIU/L were included in Group A and those with a TSH of >0.5 mIU/L were included in Group B. The demographic factors, physical examinations and the biochemical parameters were estimated and compared between the two groups.

All the data were expressed as mean \pm SD; the unpaired Student's 't' test was used for comparing the means between the two groups. Pearson's correlation was used to find the association of the serum TSH levels with the other parameters. A p value of <0.05 was considered as statistically significant for the statistical tests. SPSS, version 18 was used for all the statistical analyses (SPSS Inc., Chicago, USA).

OBSERVATIONS AND RESULTS

The baseline characteristics and the biochemical parameters have been depicted in [Table/Fig-1]. There was no significant difference in the mean age and the duration of the menopause of the participants between the two groups [Table/Fig-1].

Variables	Group A n=22 (TSH < 0.5mIU/L)	Group B n=26 (TSH > 0.5mIU/L)	p value
Age (Years)	53.59 \pm 6.54	53.09 \pm 8.06	0.39
Menstrual age (Years)	5.66 \pm 5.35	6.17 \pm 6.84	0.31
SBP (mm Hg)	134.21 \pm 24.95	134.55 \pm 33.37	0.48
DBP (mm Hg)	82.37 \pm 13.88	81.82 \pm 16.94	0.43
Serum urea (mgs/dl)	31.34 \pm 9.63	32.09 \pm 11.29	0.42
Serum creatinine (mgs/dl)	1.11 \pm 5.59	1.15 \pm 8.02	0.41
Serum calcium (mgs/dl)	8.60 \pm 6.03	9.18 \pm 3.58	0.10
Serum phosphorus (mgs/dl)	4.33 \pm 3.44	4.02 \pm 4.29	0.20
Serum ALP (U/L)	117.0 \pm 28.45	105.0 \pm 37.0	0.06
Spot urinary calcium(mg/dl)	166.09 \pm 39.23	126.89 \pm 55.95	0.03*
UCa/Cr excretion ratio	0.87 \pm 8.06	0.67 \pm 4.67	0.04*
Serum calcium-phosphorus multiplication product (Ca x P)	36.20 \pm 12.21	33.01 \pm 9.74	0.42

[Table/Fig-1]: Baseline characteristics and biochemical parameters

Values expressed as mean \pm standard deviation. *indicates a statistically significant p value (<0.05). SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, ALP=Alkaline Phosphatase, TSH=Thyroid Stimulating Hormone, UCa/Cr ratio=Urinary calcium/creatinine ratio.

In this study, we also documented the statistically significant association between the serum TSH levels with the spot urinary calcium levels and the UCa/Cr excretion ratios by using the *Pearson's correlation method*. There was a significant negative correlation between the serum TSH values and the spot urinary calcium levels [(r = -0.58), (p = 0.035)] as well as the UCa/Cr excretion ratios [(r = -0.43), (p = 0.041)].

DISCUSSION

Since we aimed at finding out the correlation between the serum TSH levels and the UCa/Cr excretion ratios in the early stages of the postmenopausal period; we included only those PMW with less than seven years of menopause [Table/Fig-1]. Although we did not observe many cases with elevated TSH values (>5 IU/L), there were a significant number of cases with TSH values of <0.5 mIU/L (46%). But a greater percentage of the subjects (54%) were euthyroid. Most of these euthyroid (54%) cases were notably in the border line of the reference range of the serum TSH.

We observed significantly high levels of urinary calcium (spot) and UCa/Cr excretion ratios in the Group A subjects in comparison to the Group B subjects. We also observed a significant negative correlation between the serum TSH values and the urinary calcium levels and the spot UCa/Cr excretion ratios, which was in compliance with the previous reports [9].

It was shown in recent past, that besides the thyroid gland, several tissues expressed the TSH receptors [14, 15]. It has been claimed that TSH exerts a critical effect on the components of the skeletal remodeling by interacting with specific receptors which are expressed on the osteoblasts and the osteoclasts. A reduced expression of the TSH receptors on the bone tissue or low levels of serum TSH themselves, could lead to a diminished BMD. TSH has an inhibitory effect on the bone resorption [16]. Low normal TSH values are associated with a high prevalence of multiple fractures in PMW, independent of the thyroid hormone status, age and the BMD [4].

PMW are susceptible to various complications as a result of sudden hormonal variations, which include oestrogen and TSH [4-7]. Osteoporosis in PMW is an important complication, which results from these hormonal changes [8]. The BMD can be assessed by using various sophisticated radiological modalities like the Dual Energy X-ray Absorptiometry (DEXA) scan, which is interpreted in terms of the 'T' scores [17, 18]. These investigations are costly and they are not readily available at the primary and secondary health centres. Moreover, a higher incidence of osteoporosis is seen in the PMW who belong to a lower socioeconomic status and also, they are more susceptible to the fractures which arise due to osteoporosis [19]. In population studies, thyroid abnormalities (both hypo and hyperthyroidism) have both been proved to be associated with an increased risk [20]. In the present study, we observed that most of the cases were asymptomatic hyperthyroid and that the rest were euthyroid. We noted significantly high levels of urinary calcium in the group with TSH levels of <0.5 mIU/L as compared to those in the euthyroid women. Hence, the maintenance of the euthyroid status is very much essential for an optimal bone mineralization and strength. This shows that a mere documentation of the diminished BMD is not comprehensive, but that in addition to this, assessment of the TSH status and its correction is very important. This has been corroborated by our observations. Screening PMW for risk factors such as TSH ab-

normalities and detecting the bone loss by estimating the UCa/Cr excretion ratio have proved to be simple and cost-effective and these can thus afford the possibility of being indirect indicators of the BMD, since most of the hormonal changes are observed in the peri-menopausal age group. An early detection and rectification of the abnormalities in the serum TSH values would certainly help in preventing the development of osteoporosis in the later ages. Even within the reference range, a high normal TSH level could prevent bone loss.

LIMITATIONS OF THE STUDY

A low sample size, along with the insufficiency of the other data like fT3, fT4, FSH, LH and oestradiol, are the few limitations of this short term ICMR Student Fellowship (ICMR STS-2012) project. Further studies with a higher sample size and the inclusion of women who are in their late postmenopausal periods, could provide succinct insight.

CONCLUSION

Low serum TSH levels were associated with increased UCa/Cr excretion ratios in postmenopausal women of the south Indian population when they were compared to those with TSH levels which were within the euthyroid range.

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