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Protective role of serum uric acid for bone loss in postmenopausal women

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ABSTRACT

Researchers had found that there is an association between oxidative stress and osteoporosis. Postmenopausal osteoporosis causes major public health problems. Since Uric acid has strong antioxidant properties, it will improve bone quality. This cross-sectional observational study was done to determine the association of Uric Acid and Bone Mineral Density of 75 healthy post-menopausal women who came for a master health checkup. The mean age was 60.5 years. After ethical clearance and informed consent, women were recruited for the study at Saveetha Medical Hospital Chennai. Women with medical conditions or who were using drugs affecting bone metabolism or uric acid were excluded. Basic investigations were Hb, serum UA, blood urea, serum creatinine, serum calcium and alkaline phosphatase, blood glucose and glycosylated Hb. Total Cholesterol, HDL, LDL, VLDL, 25 hydroxy Vitamin D were also done. Serum UA levels were graded as <3.9, 3.9–4.9, 5–6.1, and ≥6.2 mg/dl. Bone Mineral Density (BMD) was calculated with Dual Energy X-ray Absorptiometer (DXA). Osteoporosis was defined as BMD T-score −2.5 and below. BMD with a T-score of -1 −2.5 was classified as osteopenia (WHO). In women with high UA, there were significantly higher levels of low-density lipoprotein, and calcium, as compared to women with low UA group ($p<0.05$). High UA group, as compared to the low UA group, also had lower levels of high-density lipoprotein ($p<0.001$). Women with higher Uric acid levels had lower BMI, lesser years of duration of Menopause and increased BMD. Serum UA level had a positive correlation with the Lumbar BMD T score and Right Femoral Neck BMD T Score. In UA >5.4mg/dl group Osteoporosis was nil.

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INTRODUCTION

In Postmenopausal women incidence of osteoporosis increased and it is a major health concern (O'Neil *et al.*, 2004). Aging also contributes to the incidence of osteoporosis (Grzibovskis *et al.*, 2010). Age has an important association with osteoporosis along with certain other factors like BMI, blood glucose, lipid profile (Zhang *et al.*, 2016). There is ample evidence stating that uric acid (UA) is an antioxidant because of its free radical scavenging properties (Sautin and Johnson, 2008).

UA concentrations contribute to about half of the antioxidant levels in serum. Oxidative stress can result in reduced bone mineral density. Free radicals can reduce osteoblast proliferation and activate osteoclasts. Plasma UA may promote fracture healing due to its antioxidative action. Bone metabolism is also likely to be altered by uric acid.

Table 1: Study Population- Basic Characteristics and Laboratory parameters stratified by Uric acid status

Demographic details	Serum Uric Acid (<5.4mg/dl) N1 - 34	Serum Uric acid (>5.4mg/dl) N2-41	P-value
Lifestyle Parameters			
No exercise	19.1	2.7	0.818
Exercise Present	18.2	60.7	
Vegetarian diet	28.1	13.7	
Non vegetarian diet	27.1	31.1	0.556
Serum Parameters			
Alkaline phosphatase (mg/dl)	65.3±21.8	68.9±18.9	0.470
Calcium(mg/dl)	9.1±0.3	9.4±0.4	0.017
Phosphorous mg/dl	3.4±0.5	3.4±0.5	0.503
Glucose –fasting (mg/dl)	103.5±25.4	101±23.8	0.910
Glycosylated Hb %	5.6±0.8	5.5±0.7	0.787
Total Cholesterol (mg/dl)	178.7±38	186.7±36.9	0.072
HDL (mg/dl)	44.8±11.1	39.2±7.4	<0.001
LDL (mg/dl)	114±32.9	128.7±31.8	<0.001
VLDL(mg/dl)	26.8±24.8	32.5±12.9	<0123
Urea (mg/dl)	24±10.1	27±09	<0.017
Uric Acid (mg/dl)	4. 4±0.7	6.3±0.7	<0.001
25 hydroxy Vit.D (ng/dl)	18.9±11.8	23.7±18.9	<0.285

Table 2: Physical Examination Findings in various Uric acid quartiles (Values as Mean±SD)

Characteristic Serum UA levels(mg/dl)	$Q1_{n-14}$ 3.9-.4-8	$Q2_{n-20}$ 4.9- 5.3	$Q3_{n-35}$ 5.4 – 6.1	$Q4_{n-6}$ >6.2	P-value
Age - years	50.5±9.8	57.4±7.2	58.8±8.8	55.7±7.8	0.06
Weight (kg)	83.7±11	82.4±7.9	81.4±8.1	80.1±7.3	0.64
Height (cm)	159.7±11	162.9±9	165.4±10	161.9±8	0.03
BMI	32±2.7	31.8±3.1	30.6±3.8	29.1±4	0.1
Years after Menopause	8.8±2	7.8±1.2	4.1±2	2.5±0.5	0.01
L1-L4 Bone Mineral Density (g/cm^2)	0.92±0.11	0.92±0.13	0.96±0.12	0.98±0.14	0.32
Rt Femoral Neck Bone Mineral Density (g/cm^2)	0.8±0.15	0.86±0.14	0.89±0.313	0.97±0.24	0.04
L1-L4 (T score)	-1.43±0.99	-1.5±1.09	-1.23±0.15	0.96±0.36	0.35
Rt Femoral Neck T score	-2.03±0.14	-2.13±0.01	-1.18±0.03	0.93±0.06	<0.0001

MATERIALS AND METHODS

This is a cross-sectional observational study to determine the association between UA and BMD. Seventy-five healthy postmenopausal women, with a mean age of 60.5 years (range from 45 -65), were recruited for the study at Saveetha Medical Hospital Chennai. Healthy Postmenopausal women who came for a routine master health check-up to rule out age-related diseases like malignancy, diabetes, and Hypertension and osteoporosis were included. The study was conducted after Ethical Committee approval and obtaining informed written consent in the local language from all participants. Women with a medical condition or who were using drugs affecting bone metabolism or uric acid levels were not included. Serum UA, blood urea, serum Creatinine, serum calcium and alkaline phosphatase and blood glucose, glycosylated Hb, Total Cholesterol, HDL, LDL, VLDL, and 25 hydroxy Vitamin D levels

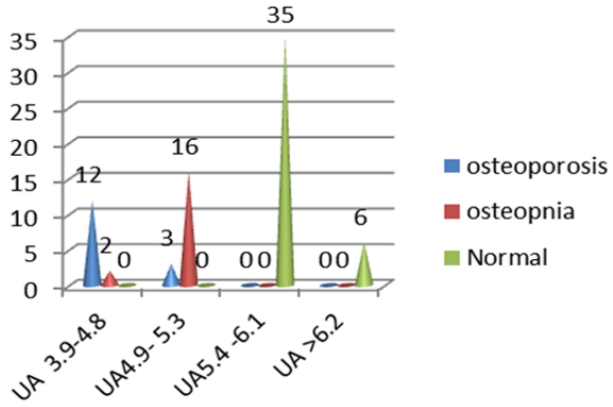

Figure 1: Distribution of Normal, Osteopenia, and Osteoporosis according to Uric acid quartiles

were measured early morning after 8 hrs. of fasting. Measured were made with an automated biochemical analyzer. Two repeated measurements of Uric acid were made and the mean was considered categorical. Analysis. Serum UA levels were grouped as percentiles as <3.9, 3.9–4.9, 5–6.1, and ≥6.2 mg/dl. Dual-energy x-ray absorptiometer (DXA) was used to measure BMD at the L1-L4 spine and right femoral neck (RFN) in gram/cm2. Osteoporosis was defined as BMD T-score −2.5 and below. BMD with a T-score of -1 −2.5 was classified as osteopenia (WHO). Parametric variables were expressed as mean + SD. ANOVA was used to compare the means across percentiles; the Pearson coefficient calculator was used for the analysis of correlation.

RESULTS AND DISCUSSION

Table 1 Indicates the study population's basic Characteristics and Laboratory parameters stratified by Uric acid status. Based on a uric acid level, they were grouped as Low serum values of uric acid (≤5.4 mg/dL) (N1 -34) and high serum values of uric acid (5.4 mg/dL) (N2- 41). In women with high UA, there were significantly higher levels of low-density lipoprotein, and calcium, as compared to women with low UA group ($p<0.05$). High UA group, as compared to the low UA group, also had lower levels of high-density lipoprotein ($p<0.001$). The two groups had similar alkaline phosphatase, calcium, phosphorus, vitamin D, glucose (fasting), and glycosylated hemoglobin ($p>0.050$, nonsignificant). Table 2 shows the population characteristics of the women & DXA report in various Uric acid groups. Women with higher Uric acid levels had lower BMI, lesser years of duration of Menopause and increased BMD. Serum UA level had positive correlation with Lumbar BMD, T score (Nabipour *et al.*, 2011; Han *et al.*, 2017) and Right Femoral Neck BMD T Score (Hernández *et al.*, 2015) In the study distribution of Normal, Osteopenia, Osteoporosis according to Uric acid quartiles depicted in Figure 1 Osteoporosis was nil when UA >5.4mg/dl. (Zhao *et al.*, 2016) When UA >5.4mg/dl to 6.1mg/dl group, 35 women had normal BMD and in >6.2mg/dl group, 6 women had normal BMD. A few studies (Makovey *et al.*, 2013) and (Ahn *et al.*, 2013) have shown that high serum UA levels are associated with better Lumbar spine BMD in postmenopausal women. In the study, UA had a positive correlation with Lumbar spine BMD (Dong *et al.*, 2016) in his study stated that there is a comparable effect of UA and BMD in Chinese people and attributed to the antioxidant effect of UA. In this study when UA was>5.4mg/dl 54.6% had normal BMD when uric acid <5.4 mg/dl, 24% Osteopenia and 20.4% osteoporosis (Xiao *et al.*, 2017) study demonstrated positive correlation of Serum UA with BMD in healthy Chinese male UA level had positive correlation with BMD (T score) of Lumbar spine and Right Femoral Neck.

Strength & Limitation of the study

We had strict exclusion criteria, though it was adjusted to possible confounding factors & Small cross-sectional study cannot extrapolate to the different genetic, ethnic and environmental group

CONCLUSION

This study concludes that high serum Uric acid levels correlate with high BMD. High Uric acid levels will have a better quality of bone. A hence higher level of uric acid will have a protective effect in postmenopausal osteoporosis

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