



An Association of Vitamin D Insufficiency with Elevated Serum Uric Acid Levels Among Postmenopausal Women

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ABSTRACT

Introduction: Deficiency of vitamin D and raised levels of serum uric acid are considered independent risk factors for causing cardiovascular diseases. **Aims & Objectives:** This study was carried out to study Serum Uric acid and Vitamin D levels in postmenopausal women to find association of hypovitaminosis D with hyperuricemia. **Place and duration of study:** It was a cross-sectional analytical study. Postmenopausal women more than 55 years of age with BMI between 25-30 kg/m² were included in the study. The study was conducted at the Department of Biochemistry and Chemical Pathology, Shaikh Zayed Federal Postgraduate Medical Institute, Lahore over a period of six months. **Material & Methods:** Eighty subjects were included in this study. They were divided into two groups i-e, normouricemic group and hyperuricemic group based on serum uric acid level. Vitamin D levels of both groups were then measured. **Results:** The hyperuricemic group had markedly lower vitamin D levels as compared to normouricemic group. Moreover, vitamin D had a negative correlation with uric acid in the hyperuricemic group i-e, higher the uric acid level, lower was vitamin D. Multiple regression analysis was also performed for studying the relation of vitamin D with uric acid levels in the two groups overall. It was observed that one mg/dl increase in uric acid caused an average decrease of 2.43 ng/ml in vitamin D. **Conclusion:** It may be concluded from this study that association of hypovitaminosis D with hyperuricemia in postmenopausal women can be used for planning an early intervention to prevent cardiovascular diseases in them.

Key words: Hyperuricemia, Hypovitaminosis D, Cardiovascular diseases

INTRODUCTION

Hyperuricemia is considered to be a predictor for cardiovascular diseases¹ and at the same time deficiency of vitamin D is also considered an independent risk factor for the development of cardiovascular diseases.² Hypovitaminosis D and hyperuricemia are being considered major public health concerns worldwide and the prevalence has been increasing in both developed and developing countries.³

Vitamin D deficiency is defined as the serum level of 25-hydroxy vitamin D less than 20ng/ml while a serum level of 25 hydroxy vitamin D in the range 20-29.9ng/ml falls into the category of vitamin D insufficiency.⁴ Approximately 1 billion people throughout the world are suffering from vitamin D deficiency.⁵ A study conducted in Pakistan on about

200 postmenopausal women showed that 59% of these women were vitamin D deficient.⁶ It has been documented that risk of myocardial infarction doubles in patients having vitamin D levels <34ng/ml.⁷ Studies show that serum vitamin D of more than 30ng/ml is implicated in preventing cardiovascular diseases.⁸

Uric acid (2,6,8-trihydroxypurine) is a naturally occurring nitrogenous waste product in the body.⁹ The reference interval in plasma or serum for females is 2.6-6.0 mg/dl and in the twenty four hour urine of adult it is 250-750 mg/dl.¹⁰ Hyperuricemia is a metabolic disorder characterized by either raised uric acid synthesis or decreased renal excretion.¹¹ Women are considered to have hyperuricemia if their serum uric acid level is ≥ 6.0 mg / dl.¹⁵ In Pakistan about 27% of adult females have been found to be hyperuricemic.¹² Hyperuricemia is found to be more prevalent in postmenopausal

women, some ethnic groups like African Americans and patients with renal diseases.¹³ Raised serum uric acid (SUA) in postmenopausal women is linked to the lack of estrogen which is believed to be involved in the excretion of uric acid.¹⁴

Excess uric acid has been related to the risk of hypertension, atherosclerosis and cardiovascular conditions.¹⁵ Relationship of raised SUA level with vitamin D insufficiency is a significant metabolic disorder that is associated with cardiovascular diseases.¹⁶ Low levels of vitamin D cause the release of parathyroid hormone through the activation of parathyroid gland.¹⁷ Some previous studies showed that high levels of parathyroid hormone increase the occurrence of hyperuricemia.¹⁸ It is believed that there are some absorptive and secretory transporters in renal tissue at the basolateral and apical membranes which are involved in the transportation of uric acid.¹⁹ Parathyroid hormone affects some of the transporters of proximal tubules of kidney, for example, its inhibition of sodium/hydrogen ion exchange type 3 isoform is known.²⁰ Renal secretion of uric acid is reduced among hyperuricemic patients having high levels of parathyroid hormone, the severity of which relies on the change in the rate of absorption.²¹

The current study has been designed to study serum uric acid and vitamin D levels and to find out the relationship of low levels of vitamin D with high serum uric acid levels among postmenopausal women in our population. Due to an increasing trend of hyperuricemia and hypovitaminosis D in the middle aged and elderly population, the present study might have significant public health implications and it may also help out in planning an appropriate intervention to prevent cardiac diseases in these patients. Improved exposure to the sun, better diet, supplementation of vitamin D and measures to reduce serum uric acid may therefore be utilized to improve general health, normalize serum uric acid and prevent cardiovascular diseases.

MATERIAL AND METHODS

It was a “cross-sectional analytical study”. The samples were collected from a medical camp in Bajwa Clinic, Kahna, Ferozpure Road, Lahore. Sample size was 80 which was estimated for each group by using 95% confidence level. 90% power of test with expected mean vitamin D levels of 43 ± 12 and 35 ± 10 in uric acid normal and uric acid elevated group respectively.²² This was calculated by using power and precision 3.0 software. The sampling technique was non probability convenient sampling.

Postmenopausal women above 55 years of age and having BMI between 25-30 were included in the study. Patients with self-reported gout or arthritis, self-stated parathyroid or thyroid disease, having used uric acid lowering medicine in last 14 days, deranged liver function tests, history of chronic renal disease, tumours and cardiac disease were excluded from the study. After approval from Institutional Review Board of FPGMI (letter no.F-38/NHRC/ADMIN/IRB/226), consent forms were filled and signed by the participants of study. Serum Uric acid assay was done by uricase method on fully automated chemistry autoanalyzer AU480 by Beckmann Coulter and subjects were divided into two groups based on their uric acid level i.e, normouricemic and hyperuricemic. Each group comprised of 40 postmenopausal women. Vitamin D levels of both groups were then measured by chemiluminescent immunoassay on fully automated analyzer Access 2 by Beckman Coulter.

Statistical analysis:

Data analysis was performed using latest version of SPSS 22.0. Mean \pm SD and median of the two parameters was obtained. Statistical significance was calculated by Student's t-test and Mann Whitney U Test. $P < 0.05$ was considered significant. Step wise regression analysis was done to determine the effect of SUA on Vitamin D.

RESULTS

The study included 80 postmenopausal women, 40 having normal uric acid level and 40 hyperuricemic. The mean age for normouricemic group was 59.4 ± 4.4 years and that of hyperuricemic group was 61.1 ± 3.5 years. On comparing the vitamin D levels of both groups it was found that hyperuricemic group had relatively close range of vitamin D levels while for normouricemic the range was quite wide with a significant p-value of 0.006. In normouricemic group there were 12 cases of vitamin D deficiency while 19 cases were of vitamin D insufficiency. On the other hand in hyperuricemic group there were 19 cases of vitamin D deficiency and 19 cases fell into vitamin D insufficiency. p-value of 0.049 was significant on comparison of both groups.

		Group	
		Normouricemic	Hyperuricemic
Vitamin D (ng/ml)	Mean	24.9	19.5
	SD	12.3	5.0
	Q ₁	18.2	17.3
	Median	23.7	20.1
	Q ₃	28.2	22.2
Mann Whitney = 516.5		P-value* = 0.006	
Vitamin D status	< 20.0 (deficient)	12	19
	20.0 - 29.9 (insufficient)	19	19
	30.0+ (sufficient)	9	2
Chi-square = 6.04		P-value = 0.049	

Table-1: Vitamin D levels of study subjects of both groups based on SUA level.

P * means that p value is < 0.05 (significant)

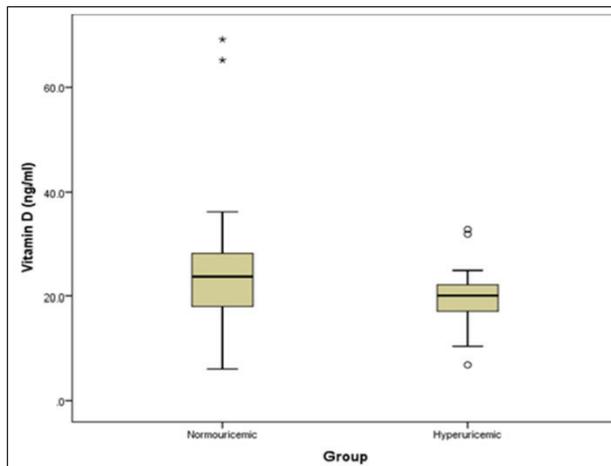


Fig-1: Boxplot presenting distribution for vitamin D levels amongst both group of study subjects.

The correlation analysis was performed to see the association of vitamin D with uric acid. This analysis was carried out within each group and overall. It was noted that overall uric acid had significant negative correlation with vitamin D with $r = -0.471$ with p -values < 0.001. When the correlation analysis was performed in hyperuricemic group it was noted that the uric acid level had a good negative correlation of -0.577 with vitamin D showing that higher the uric acid levels lower the vitamin D levels.

The multiple linear regression analysis was done to see the effect of uric acid on vitamin D. Result found at 17th step showed that the final significant model was decided. It was noted that the uric acid had a significant impact on vitamin D level. When all 80 cases were included, the average vitamin D level was 35.53ng/ml and one unit increase in uric acid caused an average decrease of 2.43ng/ml in vitamin D.

Model		Unstandardized Coefficients		T	P-value
		B	Std. Error		
17	(Constant)	35.53	3.52	10.11	0.000*
	Uric Acid (mg/dl)	-2.43	0.61	-3.94	0.000*

Table-2: Multiple linear regression analysis for studying relation of vitamin D with uric acid by using Backward method in both groups combined ($R^2 = 0.166$ Adj $R^2 = 0.156$)

Dependent Variable: Vitamin D (ng/ml)

The same model was applied on hyperuricemic group and it was noted that in this group serum uric acid had highly significant and negative effect on vitamin D with p -values < 0.050. This model was obtained in 12th step with adjusted R^2 0.555 showing reasonably good fit model. An increase of one mg/dl in uric acid level in this group caused an average decrease of 2.02 ng/ml in vitamin D.

DISCUSSION

Eighty postmenopausal women were included in this study. They were divided into two groups: normouricemic and hyperuricemic groups. The difference between the ages of hyperuricemic and normouricemic groups was insignificant. On comparing vitamin D levels of both groups it came into notice that mean vitamin D level for hyperuricemic group was lower as compared to normouricemic subjects. The difference was significant with p -value of 0.006. The results are similar to a study by Takir M et al in which hyperuricemic group had lower values of vitamin D as compared to normouricemic subjects. There was a negative and important relationship between SUA and vitamin D.²³ Similar findings were also seen in another study done in Turkey. In this research vitamin D and uric acid levels of the patients were obtained. Their findings suggested that subjects having increased SUA levels had low levels of vitamin D. They concluded that low level of vitamin D were correlated with high serum uric acid levels.²⁴ Correlation analysis was performed to see the relationship of vitamin D with uric acid within each group and overall. When multiple regression analysis was performed it was found that uric acid had a significant impact on vitamin D. These results are in agreement with a study done in China in which multiple regression analysis was performed and it was found that there was an independent and significant relationship between vitamin D insufficiency and high SUA levels among the postmenopausal women. The subjects with vitamin

D insufficiency were more likely to have raised SUA compared with those without vitamin D insufficiency among postmenopausal women. Their findings suggested that vitamin D status is negatively associated with elevated serum uric acid. They also summarized that exposure to the sunlight and vitamin D supplementation are easy as well as an inexpensive ways for preventing low levels of vitamin D and other health issues.²² Another study conducted in Saudi Arabia concluded that vitamin D was inversely related with serum uric acid level.²⁵ A study from Egypt also concluded that low level of vitamin D was inversely correlated with high serum uric acid level.²⁶ A study carried out in Turkey suggested that patients who have elevated serum uric acid had lower vitamin D levels.²⁷ Another research carried out on 100 patients for finding out the possible effect of vitamin D on uric acid level concluded that there was an inverse relationship between vitamin D and serum uric acid.²⁸

A systemic review was conducted in 2019 which showed that patients with vitamin D deficiency and insufficiency had a significantly higher level of serum uric acid compared with individuals with normal vitamin D.²⁹

CONCLUSION

It may be concluded from our study that postmenopausal women with higher serum uric acid level had lower level of vitamin D as compared to those who had normal serum uric acid levels. A negative correlation was observed between serum uric acid and vitamin D level in the group with hyperuricemia. Low vitamin D and raised serum uric acid are important risk factors for the development of cardiovascular diseases. By improving vitamin D level, serum uric acid can be normalized. Association of hypovitaminosis D with hyperuricemia in postmenopausal women can be used in planning an early intervention to prevent cardiac diseases in such subjects.

Limitations of study: It was a single center study with a small sample size which may not be sufficient to correlate low levels of vitamin D with elevated SUA. A study should be carried out with larger sample size and in different socio economic strata to get more accurate information.

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