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INFLUENCE OF SERUM ESTRADIOL ON SERUM URIC ACID LEVEL IN PRE AND POSTMENOPAUSAL WOMEN.

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ABSTRACT… Background: Hyperuricemia develops when serum uric acid level exceeds the normal value. Estrogen may influence the level of serum uric acid. Postmenopausal females have a remarkable reduction in its level, so serum estradiol is studied in relation to serum uric acid levels in pre and post-menopausal women. **Objective:** To find out the relationship of serum Estradiol with serum uric acid level in premenopausal and postmenopausal women in local population. **Study Design:** Case control study. **Setting:** This study was conducted in Lady Aitchison Hospital Lahore. **Period:** March 2017- August 2017. **Material and Methods:** 134 females were enrolled in total and were grouped in to two. Group A comprised of premenopausal and Group B included postmenopausal females. After complete history and general physical examination, 5 ml venous blood sample under aseptic measures was taken. Serum uric acid was measured by enzymatic and serum estradiol by Enzyme-linked immunosorbent assay method. **Results:** The mean age of pre and postmenopausal women was 32 and 57 ± 7 years, with significantly lower in premenopause. The mean serum E2 was 91.86 ± 26.71 mg/dL in premenopause and 22.04 ± 9.28 mg/dL in postmenopause, with significantly lower mean in postmenopause. Mean serum uric acid was statistically higher in postmenopause that was 6.04 ± 0.58 mg/dL, when compared to premenopause that was 4.22 ± 0.90 mg/dL. **Conclusion:** Serum uric acid levels increased due to decreased serum estradiol in postmenopausal women as compared to premenopausal women.

Key words: Hyperuricemia, Postmenopause, Premenopause, Serum Estradiol, Serum Uric Acid.

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INTRODUCTION

Uric acid is the byproduct of purine metabolism.[1] Hyperuricemia is a pathological condition in which the uric acid levels exceed the normal values of 3.5-7.0 mg/dL in males and 2.5-5.7 mg/dL in females.[2] Worldwide the prevalence of hyperuricemia has increased steadily over the last 40 years.[3] In United State general population it's prevalence is 21%.[4] Moreover, hyperuricemia may be associated with various morbidities like metabolic syndrome[5], diabetes mellitus[6], gout[7] and hypertension.[8] As reactive oxygen species are being produced by increased uric acid level so it is considered to be the source of vascular diseases.[9]

Levels of estradiol (E2), which is one of the three forms of serum estrogen vary in premenopause and postmenopause. It is synthesized by the aromatization of androstenedione in ovaries and adrenal glands during reproductive age. Though, females also produce E2 in the peripheral tissue by aromatization of testosterone after menopause, still they have the lowest levels as compared to that in premenopause. Normal level of E2 is 30-400 ng/L in premenopause and 5-25 ng/L in postmenopause.[10]

Estradiol has uricosuric effect. It eliminates uric acid from the body through kidneys.[11] But when the estradiol falls below the normal levels, excretion of uric acid halts. Hence a considerable prevalence of hyperuricemia in postmenopausal women may be due to changes in the normal levels of estradiol.[12]

However, data in context of Pakistan regarding the effect of serum E2 on serum uric acid level in postmenopausal women is scarce. This research is, therefore, designed to study the relationship of serum estradiol with serum uric acid in premenopausal and postmenopausal women in local population. The study will help improve the quality of life in postmenopausal women by making strategies to overcome hyperuricemia and its related morbidities at an early stage.

MATERIALS AND METHODS

After approval from hospital and ethical committee, Case control study was conducted in Lady Aitchison Hospital Lahore Written informed consent was taken prior to data collection. Sample size of 134 subjects (67 subjects in each group) was estimated by using 5% level of significance, 95% confidence level, 90% power of test for expected percentage of uric acid level by taking premenopausal as 37% and postmenopausal as 62%.[13] Group A comprised of premenopausal and Group B included postmenopausal females. Detailed history was taken from the participants. Participant's age was asked and grouped accordingly. History of menstrual cycle was taken from group A. Duration of postmenopausal period was asked from group B. Blood samples were taken under aseptic measures, serum was separated after centrifugation and was kept in two separate serum cups for measurement of serum uric acid and estradiol. Cups were numbered and stored in freezer at -70° c. Serum estradiol was measured by ELISA and uric acid was measured by uricase method.

Data was analyzed using SPSS version 21. For comparison of serum estradiol and serum progesterone with serum uric acid level in two groups, independent sample t-test was applied. Simple regression technique was used to predict the relationship of serum uric acid and serum estradiol. p-value ≤ 0.05 was taken as significant.

RESULTS

Mean age in premenopausal females was found to be 32±7 years and in postmenopausal 57±7 years (Table-I). Mean serum E2 in premenopausal females was found to be 91.86± 26.71 mg/dL and in postmenopausal 22.04± 9.28 mg/dL (Table-II). Mean serum uric acid in premenopausal females was 4.2±0.96 mg/dL and in postmenopausal 6.04± 0.58 mg/dL (Table-III). We significantly observed that there will be 0.021 units decreases in the serum uric acid with one unit increase in serum estradiol with p -0.0004 (Table-IV).

To examine how much of the total variation in serum uric acid level of the patients under study is explained by serum estradiol, the R^2 for the final model is calculated which is 0.43 it shows that 43% of the total variation in serum uric acid level is explained by serum estradiol.

	Age		P-Value
	Mean	Standard Deviation	
Group A N=67	32	7	0.0001
Group B N=67	57	7	

Table-I. Age difference between group A and B

	Serum Estradiol		P-Value
	Mean	Standard Deviation	
Group A n=67	91.8612	26.7150	0.0004
Group B n=67	22.0448	9.2839	

Table-II. Difference of serum estradiol levels between groups

	Serum Uric Acid		P-Value
	Mean	Standard Deviation	
Group A n=67	4.2209	0.9063	0.001
Group B n=67	6.0493	0.5899	

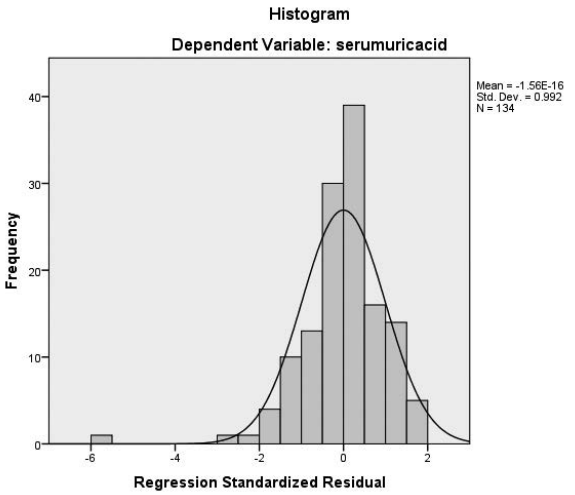
Table 3: Difference between serum uric acid levels of two groups

Model	Coefficient	Sig. (P-Value)
	b	
(Constant)	6.258	0.0002
Serum estradiol	-0.021	0.0004

Table-IV. Significance of serum estradiol

NORMALITY TEST

In order to check the normality of the error term a simple technique is adopted in which the histogram of the distribution of error term is plotted and this shows that residuals are normally distributed.



DISCUSSION

Postmenopausal females are more prone to have high serum uric acid levels as compared to premenopausal females. Estradiol is markedly decreased in postmenopausal females. This could be considered as the causative factor for the hyperuricemia.

Present study denotes that mean serum estradiol in premenopause is 91.86 ± 26.7 ng/dL as compared to postmenopause, where it is 22.04 ± 9.2ng/dL., serum uric acid, has its mean value of 4.2 ± 0.90 mg/dL in premenopause and 6.04 ± 0.58 mg/dL in postmenopause. So, in postmenopausal women there is increase in serum uric acid as compared to premenopausal women.

Yahyaoui et al[14]., 2008, demonstrated the uricosuric effect of E2 by decreasing the post secretary reabsorption of uric acid. They also supported the fractional excretion of uric acid. J H Jung et al.[15] found high serum uric acid in postmenopausal women and a decrease in its level was noticed by giving progesterone rather than estrogen. Reproductive events over the life were found to be causative factor of hyperuricemia (Stockle D et al.).[13] Rukzan M Dawood[16] noticed that there is a high level of serum uric acid in postmenopausal women but the cause remained unknown. Bachmann G[17] documented an increase threat of gout after surgical menopause.

An increase in serum uric acid level was studied from fourth decade of life in females and from second decade in males by Masafumi Kuzuya et al.[18] Sunny et al.[19] further favoured our observation by studying the serum uric acid levels in different phases of menstrual cycle. They declared a high serum uric acid level in proliferative phase and lower in secretary phase depicting an inverse relationship. Furthermore they observed a 1.1% decrease in serum uric acid level with every 1 log unit increase in estradiol. Similar kind of findings were noticed Das et al.[20] 26 % increase chances of gout after menopause and having relieving effects with female hormones were studied by A E Hak et al.[21]

Our study showed that serum uric acid is more closely related to female advancing age consistent with the study showing the prevalence of hyperuricemia to be 21.9% in Thai postmenopausal females.[22] Majority of the above mentioned studies indicated a similar effect as our study. With the advancing age of females, serum estradiol declines with increase in serum uric acid levels.

CONCLUSION

Our study used multiple regression technique to predict the relationship of serum uric acid and serum estradiol. We concluded a significant effect of serum estradiol in decreasing serum uric acid levels. Our analysis further revealed that with the unit increase in serum estradiol, there is a decrease in serum uric acid level up to 0.021 units (p - 0.0004).

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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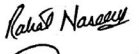
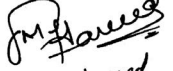
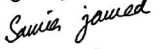
1	Rahat Naseem	Study design, Collection of data, statsitical analysis, article writing.	
2	Sardar Muhammad Al-Fareed Zafar	Article writing and Proof reading.	
3	Samia Jawed	Research idea, Literature Search, Final drafting.	
4	Saima Mukhtar	Literature search, Proof reading.	
5	Farhat Ijaz	Drafting, Proof reading of article and references writing.	
6	Rana Khurram Aftab	Data collection, drafting and proof reading of article.