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EFFECT OF MENOPAUSE IN URINARY MICROALBUMIN, URINARY CREATININE AND ALBUMIN – CREATININE RATIO

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ABSTRACT

INTRODUCTION: During menopause, i.e. at the age of 40 to 60, women face various physiological, psychological and biochemical changes[1]. Urinary microalbumin is usually considered for diabetic or patients with renal problems [13].

OBJECTIVE: Our aim is to study the usefulness of concurrent urinary micro albumin, urinary creatinine levels is pre and post – menopausal women and to correlate these biochemical as an early marker of osteoporosis in postmenopausal women.

METHODS: Patients attending at Padmashree Diagnostics, Department of Gynaecology, Bangalore, for elective diagnosis and treatment, were belonging to pre and post – menopausal state, among them 70 subjects 35 in each group were recruited for the study. Urinary micro albumin and urinary creatinine were estimated. Urinary albumin creatinine ratio was calculated using standard method.

RESULTS: There was 50% increase in microalbumin excretion in premenopausal woman group. In Post-menopausal woman group shown statistically significant increased excretion to the upper limit of normal reference interval. In substantiating the above-mentioned statement, in current study we observed the microalbumin excretion was steadily increased in contrast to creatinine excretion

CONCLUTION: The derived parameter confirmed that ACR is the most prognostic significant diagnostic marker in pre and post-menopausal patients.

KEYWORDS : Microalbumin, Creatinine, Menopause, Albumin – Creatinine Ratiio (ACR).

INTRODUCTION:

Albumin is the major protein present in the blood; any conditions causing lowering of albumin will lead to reduced total proteins in blood. This condition is called as *Hypoproteinemia.* Albumin is a 585 amino acid polypeptide chain. It is only synthesized in liver [2].

This is produced mainly by salts, which can pass easily from the intravascular to the extravascular space. However, proteins cannot easily escape out of the blood vessels, and therefore proteins exert the **'effective osmotic pressure'**. It is about 25mm Hg and 80% of it is contributed by albumin. The maintenance of blood volume is depends on this effective osmotic pressure [2,10].

Normal Urinary excretion of microalbumin is up to 30mg/L, whereas the increased amount of excretion more than 30mg/L range is called *Microalbuminuria* [12]. The reference range of microalbuminuria is defined as the excretion of 30–300 mg/day. The reference range of normalized microalbumin in urine against the urinary creatinine in men and woman is 17–250 mg/g of creatinine and 25–355 mg/g of creatinine respectively [3]. Microalbuminuria is usually considered as a common risk factor for renal diseases, but recent studies have showed that microalbuminuria could also occur due to general arterial processes [4].Microalbuminuria is usually characterized by arterial hypertension, diabetic nephropathy, peripheral neuropathy and nephropathy. High excretion of albumin in urine could also be one of the risk factors of developing hypertension and chronic kidney disorder [5, 6]. Post-menopausal hormonal variation is also one of the factor that affect albumin abnormal excretion in urine.[7]

MATERIAL AND METHODS:

MATERIALS

Patients who were attending at Padmashree Diagnostics, Department of Gynaecology, Vijayanagar, Main Road, Bengaluru, for elective diagnosis and treatment, who were belonging to pre and postmenopausal woman recruited for this study. After complete explanation of the study to the subjects, a written informed consent was obtained from subjects. A total of **seventy** pre and postmenopausal women (35 each group) was recruited for the present study.

Specimen handling and analysis

Urine specimens received in the laboratory was collected after their routine analysis was done. Remaining specimens were aliquoted, labelled and stored at – 20ºC until further analysis [11]. Aliquots of specimens, once thawed were used for the analysis on the same day and not be subjected to repeat freezing and thawing to avoid any pre-analytical errors.

METHODS

METHODS OF COLLECTION OF DATA

Patient Selection:

A total of **seventy** patients with regular medical follow up record, The Patients were pre and post menopausal woman (35 each) recruited for this study. Patient details like body mass index, education, smoking, alcohol intake, dietary habits and family history was considered before selecting the patients.

Sample Size: Two Groups of 35 Subjects each
Sampling method: Random Sampling
Analytical Methods:

- Urinary micro albumin and Urinary creatinine was estimated by Immunoturbidometric and Spectrophotometric Jaffe's reaction respectively.

SOURCES OF DATA

Available literature information from recent publications was updated during the course of study. The study design to be employed was standardized /modified depending upon the situation before applying the same for the sample analysis. Information with respect to study outcome was procured from the patient medical records and clinical expertise opinion was sought before relating the study outcome.

STATISTICAL ANALYSIS

GraphPad Prism 7 Data analysis package was used and applied to analyse the obtained data. All the values were expressed in mean ± SD. Statistical comparison was performed using unpaired t test. The't' test $*p < 0.05$; $**p < 0.01$; $***p < 0.001$, $****p < 0.0001$ was considered as significant.

RESULTS:

The biochemical investigations such as Urinary micro albumin and urinary creatinine were studied.

Urinary creatinine level in pre and postmenopausal woman was 53.7 ± 14.2mg/dL and 37.0 ± 27.3 respectively (**Fig. 1**).

As shown in (**Fig. 1),** the urinary excretion of microalbumin was significantly high in both the patient group as compared with normal reference interval (10 – 30 mg/L).

There was statistically significant increase ($****p < 0.0001$) in microalbumin excretion in premenopausal woman group. In postmenopausal woman group shown alarmingly 200% statistically significant ($****p < 0.0001$) increased excretion (83.2 ± 19.3 mg/dL) to the upper limit of normal reference interval.

Among the constituent parameters of urinary bio-chemicals urine creatinine, urine microalbumin and Albumin Creatinine ratio, a

derived test parameter proves to be better diagnostic index among the urinary bio-chemicals profiles.

Thus, as shown in the **Fig. 2** albumin: creatinine ratio (ACR) is a better diagnostic parameter as compared to the later urine parameter.

The finding from these two test parameters such as urinary microalbumin and derived test parameter ACR signify that derived test parameter provide better diagnostic index about the underlying pathophysiology of the diseases. Thus, ACR (3.7 ± 1.4) was surprisingly elevated only (****$p < 0.0001$) in postmenopausal group.

Fig: 1 – Urinary Microalbumin & Urinary Creatinine Level

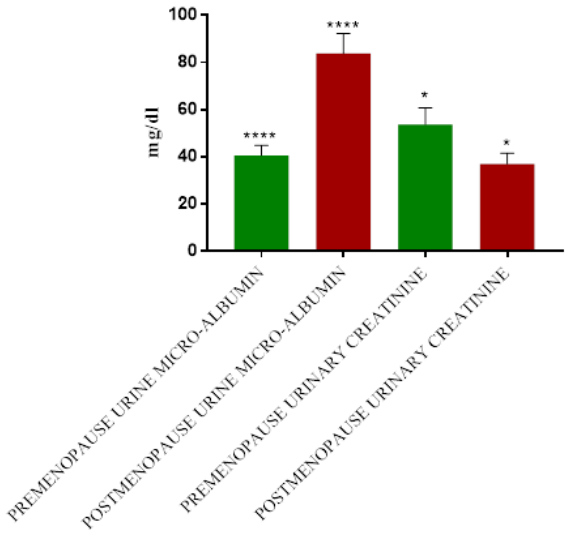

Fig: 2 – Albumin – Creatinine Ratio (ACR)

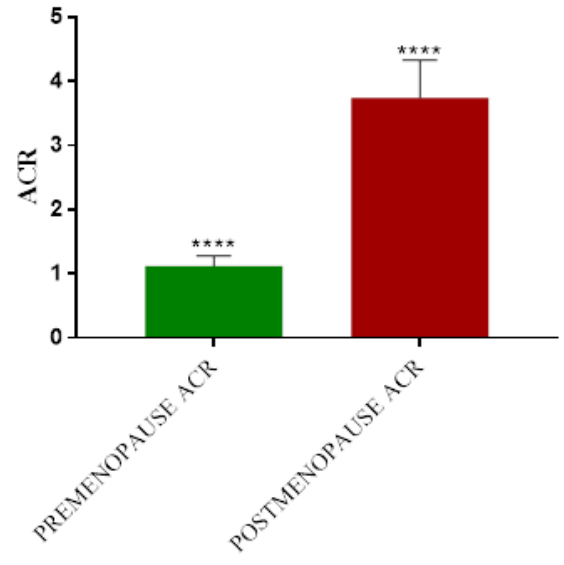

Table: 1 – Urinary Microalbumin, Creatinine and ACR value in Pre and Post – menopausal women

SL No.	Parameter	Premenopause	Postmenopause	Unpaired t – test value
		Mean ± SD	Mean ± SD	
1.	Urinary Microalbumin	40.7 ± 24.8	83.6 ± 49.8	**** p <0.0001
2.	Urinary Creatinine	53.7 ± 41.5	36.9 ± 27.3	* p < 0.0167
3.	ACR	1.1 ± 0.9	3.4 ± 3.4	**** p < 0.0001

Note: p < 0.05 significant at 5% level, p > 0.05 not significant at 5% level.

Table: 2 – Reference ranges of assay parameters

SL No.	Parameter	Reference range
1.	Urinary Microalbumin	10 – 30 mg/L
2.	Urinary Creatinine	30 – 160 mg/dL
3.	ACR	<2.8 mg/g creatinine

STUDY OUT COME:

Increased variations from normal albumin excretion are associated with the development of hypertension in postmenopausal woman, which is a major cause of cardiovascular morbidity and mortality [12]. The findings of this study, in conjunction with the findings of numerous others, including the Framingham Heart Study, suggest that it may be time to reevaluate our current concept of "normal" albumin excretion and to obtain a normal reference interval in Indian sub population by correlating the postmenopausal urinary microalbumin with that of obtained normal reference range of premenopausal woman. In this context, some of the salient feature of study outcomes is as follows.

- Mostly, the observed urinary creatinine level was found to be lower limit of reference interval in both the study group. Fig: 1. Finding suggests that Creatinine elimination in the urine is significantly decreased in both study groups.
- These findings suggest that the prerequisite pharmacotherapy to reduce glomerular filtration pressure and to increase the creatinine excretion significantly. Findings also restate that urinary creatinine clearance could enhance the accuracy and credibility of drug clearance and increase the prognosis.
- Among the urinary profile the derived parameter albumin: creatinine ratio was found to be better diagnostic index. The measurement against to creatinine excretion rate has significantly increased the diagnostic sensitivity of microalbumin measurement.
- The study of ACR as a prognostic marker of cardiovascular risk or renal paucity outcomes in postmenopausal woman has increased; but long-term prospective studies on determinant factors of microalbuminuria are few. The current study states that comparative study between drug naïve pre and post-menopausal patient indicates the various risk factors that affect microalbu minuria in Indian Sub population (Fig: 1 & 2).

CONCLUSION

Our data were obtained between drug naïve pre and postmenopausal woman from Indian sub population. The definition of premenopausal urinary excretion rate of microalbumin level in Indian sub-population has been established. The derived parameter confirmed that ACR is the most prognostic significant diagnostic marker in pre and postmenopausal patients.

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