Correlation between Microalbuminuria Creatinine Ratio and severity of Vasomotor symptoms among Postmenopausal Women

Ibrahim Adel ELnaptiti[1], Mohamed sallam Soliman[1], Amany Mohamed Ahmed Abdelghany[2], Azza Hassan Abdelfattah[1]

1 Internal Medicine Department, Faculty of Medicine, Zagazig University, Egypt
2 Obstetrics and Gynecology Department, Faculty of Medicine, Zagazig University, Egypt

Email: ibrahim.adel693@gmail.com

Article History: Received 10th June, Accepted 5th July, published online 10th July 2023

Abstract

Background: Microalbuminuria creatinine ratio, on the other hand, is a marker of kidney dysfunction and cardiovascular risk. It has been suggested that microalbuminuria may reflect endothelial dysfunction, which is characterized by impaired blood vessel function. Endothelial dysfunction has been implicated in the pathogenesis of Vasomotor symptoms (VMS).

Aim: assessment of the Correlation between Microalbuminuria Creatinine Ratio with severity of Vasomotor symptoms in Postmenopausal Women.

Methods: This Comparative cross-sectional study was conducted at the Endocrinology unit & clinic, Internal Medicine Department, Zagazig University Hospital, on 74 cases with Postmenopausal status Patients were divided into to 2 groups: Group I: Postmenopausal women without VMS, Group II: Postmenopausal women with VMS. The MVS survey was done to all cases, creatinine, albumin in urine, urinary albumin to creatinine ratio (UACR) Measurement were assessed.

Results: there are statistical significant differences in studied groups regarding UACR , Mean± SD was (8.45 ± 5.29 vs 236.54 ± 406.55) in Group I and Group II respectively p-value <0.001, that were higher in Group II, vasomotor symptoms were present in (0% VS 100%, in Group I and Group II respectively p-value <0.001), 45% of the cases in Group II had UACR 7.35+0.39, 35% of the cases in Group II had UACR 3.24+0.33 and, 7% of the cases in Group II had UACR 17.52+0.55. There are positive Correlation between UACR, and VMS severity (P<0.05). This table shows that there were statistically significant positive correlations between HOMA-IR score and: body mass index, UACR, Fasting Insulin, HBA1C, FBS, PBS, HDL, TGs, cholesterol and e FGR to VMS (P<**0.001)** also statistically significant negative correlation between VMS and age. (P<**0.05).** Receiver operating characteristics (ROC) curve was used to Analysis of UACR as predictor test for the severity of VMS the best cut off value of UACR was ≥3.25, with sensitivity of 100%, specificity of 92% positive predictive value of 91.6%, negative predictive value of 90%. We concluded that UACR at cutoff value = 3.25 was a good predictor test for the severity of VMS in postmenopausal women.

Conclusion:

Keywords: Microalbuminuria Creatinine Ratio, Vasomotor symptoms, Postmenopausal Women

DOI: 10.53555/ecb/2023.12.Si12.334

Introduction

Menopause is the permanent cessation of menstrual cycles following the loss of ovarian follicular activity". Climacteric is the transitional phase from the first signs of ovarian senescence until its complete installation. Among the various endocrine changes that characterize the progressive loss of ovarian function and ultimately lead to menopause, the most important is the decrease of circulating levels of ovarian steroids. The loss of luteal phase progesterone due to missed ovulation may cause menstrual irregularity and heavy menstrual bleeding in the late premenopausal years, while the subsequent decrease of estradiol levels due to follicular exhaustion is related to vasomotor symptoms, and the cause of urogenital atrophy, bone loss, and increased cardiovascular and metabolic risk **(1).**

One of the primary factors contributing to the severity of vasomotor symptoms is hormonal fluctuations, particularly the decline in estrogen levels that accompanies menopause. Estrogen plays a central role in regulating body temperature and the body's response to temperature changes. As estrogen levels decline, the body's thermostat becomes dysregulated, leading to the hallmark heat surges of hot flashes. However, while hormonal changes are a key factor, they do not tell the full story **(2).**

Estrogen is known to be anti-inflammatory and mildly immunosuppressive. Its role as a steroid hormone of pregnancy requires this. (Younger) rheumatoid arthritis patients routinely note improvement or even remission during pregnancy, and much of this effect is attributed to the anti-inflammatory properties of estrogen. Joint damage in arthritis is driven by activation of inflammatory signaling pathways inducing proteinases. HRT and SERMs such as levormeloxifene and raloxifene have been reported to reduce levels of inflammation and markers of subsequent matrix degradation **(3).**

Among the most prominent and frequently reported symptoms experienced by postmenopausal women are vasomotor symptoms, which include hot flashes, night sweats, and flushes. Vasomotor symptoms are often described as sudden, intense sensations of heat that radiate through the body, frequently accompanied by sweating and flushing of the skin. These symptoms can occur during both the day and night, leading to sleep disturbances and a reduced overall quality of life **(4).**

Microalbuminuria creatinine ratio, on the other hand, is a marker of kidney dysfunction and cardiovascular risk. Microalbuminuria refers to the presence of small amounts of albumin, a protein, in the urine. It has been suggested that microalbuminuria may reflect endothelial dysfunction, which is characterized by impaired blood vessel function. Endothelial dysfunction has been implicated in the pathogenesis of VMS, as it may affect the regulation of blood flow and temperature control mechanisms in the body **(5)**

The aim of this study was assessment of the Correlation between Microalbuminuria Creatinine Ratio with severity of Vasomotor symptoms in Postmenopausal Women.

Methods

This Comparative cross-sectional study study was conducted at the Endocrinology unit & clinic, Internal Medicine Department, Zagazig University Hospital.

c- Inclusion criteria:

(1) Postmenopausal status was defined as at least 12 consecutive months of amenorrhea.
(2) Patients' age more than 40 years old.
(3) Each participant provided written informed consent.

d- Exclusion criteria:

(1) Current hormone use: current medication for diabetes mellitus or dyslipidemia; overt thyroid. surgical menopause; bilateral oophorectomy.
(2) Past history of chemotherapy or pelvic radiotherapy due to malignant diseases.
(3) Patients who had undergone hysterectomy or bilateral oophorectomy.
(4) Patients with a history of polycystic ovary syndrome.
(5) Presence of cardiovascular disease such as prior myocardial infarction, angina, stroke, and peripheral arterial diseases; and presence of chronic diseases such as renal failure, liver cirrhosis.

e- Sample size:

Assuming the mean UACR was 4.357 ± 0.677 vs 5.043 ± 1.004 in IR m vs IR h. The estimated sample will be 74 cases (37 in each group) at 80% power and 95% CI. Open Epi.

Patients were divided into to 2 groups:

- **Group I**: Postmenopausal women without VMS.

- **Group II:** Postmenopausal women with VMS.

II- Operational design:

a) Process:

All patients included in this study were subjected to the following: Complete history taking in the form of:
Personal history: including age, sex and BMI of each case, History of present condition to fulfill inclusion and exclusion criteria, Medical history: including present or past history of any comorbidities and chronic illnesses. Detailed history about Menopausal Vasomotor Symptoms (MVS) **(1)**: questionnaire designed specifically for subjective assessment of hot flashes, the MVS survey, was administered to all study participants.
The MVS survey was designed to be short, simple, clear, easy to respond to, and easy to administer. The one-page form had 39 questions addressing the various dimensions of hot flashes and associated conditions.
The questions were mutually exclusive. Thirty-five survey questions were closed response and required either a Yes or No answer (nominal measurements). For 3 of the 39 questions, the participant needed to provide a number reflecting the age or year when a specific hot flash-associated event occurred (numerical measurements), and one question asked for the name of the hormonal preparation used to treat hot flashes. In the MVS survey, each specific dimension of hot flashes was addressed by a group of questions: duration of the period with hot flashes (questions 2–5), frequency (questions 6–8), timing—day or night (questions 9, 10), duration of one episode (questions 11–13), intensity (questions 14–16), and quality of life (question 17). Questions within each group addressed the quantitative and qualitative measures of hot flashes.
In addition to questions on various measures of hot flashes, the MVS survey included a set of questions about conditions associated with hot flashes, such as hysterectomy (questions 19, 20), hormone therapy (HT) and its type (questions 21–27), duration of HT (questions 28–32), effectiveness of HT in relieving hot flashes (questions 33–35), age HT was started (question 36), nonhormonal therapies for hot flashes (question 37), and history of use of hormonal contraceptives (questions 38,39). If a woman did not remember the name of a medication, she was asked to identify her medication on a color chart from the Physician's Desk Reference (PDR) with currently available hormonal preparations (question 23). If she could not recognize the hormonal preparation on the chart, she was asked to provide the dose form (pill, patch, cream, or injection) of the drug (questions 24–27). Reponses to survey questions were marked in the ANSWER column. A separate column on the survey form (NOTES) was designated for additional comments to be written by the person conducting the survey.
A detailed medication history was taken. Full clinical examination (Hight, Weight, body mass index, vital signs, local examination). Laboratory investigations including:

- HbA1c
- Kidney function tests: the most practical tests to assess renal function to get an estimate of the glomerular filtration rate (GFR) and to check for proteinuria (albuminuria).

Creatinine

The most commonly used endogenous marker for the assessment of glomerular function is creatinine. The calculated clearance of creatinine is used to provide an indicator of GFR. This involves the collection of urine over a 24-hour period or preferably over an accurately timed period of 5 to 8 hours since 24-hour collections are notoriously unreliable. Creatinine clearance is then calculated using the equation:
[C = (U x V) / P]
(C = clearance, U = urinary concentration, V = urinary flow rate (volume/time i.e. ml/min), and P = plasma concentration).

Albuminuria

Albuminuria refers to the abnormal presence of albumin in the urine. Microalbumin, considered an obsolete term as there is no such biochemical molecule, is now referred to only as urine albumin. Albuminuria is used as a marker for the detection of incipient nephropathy in diabetics. It is an independent marker for the cardiovascular disease since it connotes increased endothelial permeability, and it is also a marker for chronic renal impairment. Urine albumin may be measured in 24-hour urine collections or early morning/random specimens as an albumin/creatinine ratio. The presence of albuminuria on two occasions with the exclusion of a urinary tract infection indicates glomerular dysfunction. The presence of albuminuria for three or more months is indicative of chronic kidney disease. Frank proteinuria is defined as greater than 300 mg per day of protein. Normal urine protein is up to 150 mg per day (30% albumin; 30% globulins; 40% Tamm Horsfall protein).
Urine protein may be measured using either a 24-hour urine collection or random urine protein: creatinine ratio (early morning sample is preferred since it is a near representative of the 24-hour sample).
The KDIGO classification defines three stages of albuminuria:

- A1: Less than 30 mg/g creatinine
- A2: 30 to 300 mg/g creatinine
- A3: Greater than 300 mg/g creatinine

    - Fasting blood glucose (FPG)
    - Fasting insulin (FINS)
    - HOMA index

UACR Measurement: The first morning urine or the second morning urine of subjects was taken, after which MAU was determined; urine creatinine was assessed using an automatic biochemical detector (sarcosine oxidase method); UACR (mg/g) = MAU/urine creatinine.

b) Data analysis

The results for categorical variables were presented as numbers and percentages and the results for continuous variables as median (95% confidence interval). Data were analyzed statically by SPSS program version 26.
The Chi square test was used for categorical variables and an independent samples *t*-test was used to compare the means of the groups, and a one-way analysis of variance (one-way ANOVA) was used for comparison between multiple groups. Pearson correlation analysis was employed to analyze the association between HOMA-IR and UACR, and multiple linear regression was used to analyze the related influencing factors of UACR. Nonnormally distributed data were log-transformed to facilitate statistical analysis. Rates were compared using the $\chi 2$ test. $P < 0.05$ was considered a statistically significant difference.

Results

Table (1): Distribution of the studied groups regarding demographic data.

	Group I N=37		**Group II N=37**		**Test of Sig.**	**p-value**
Age(years) Mean± SD	**53.0±2.83**		**51.0±2.23**		χ^2=0.580	**0.876 NS**
Parity :	**Group I N=37**		**Group II N=37**		**Test of Sig.**	**p-value**
	N	**%**	**N**	**%**		
Nullipara	**10**	**27**	**11**	**30**	t=1.332	**0.421 NS**
Multipara	**27**	**73**	**26**	**70**		

This table showed no significant data between studied groups as regard age Mean± SD was (53.0±2.83 vs 51.0±2.23) in Group I and Group II respectively p-value = 0.876 and also no significant data between studied groups as regard Parity p-value = 0.421.

Table (2): Biochemical characteristics of the studied subjects.

Variable	**Group II N=37 Mean±SD**	**Group I N=37 Mean±SD**	**T test**	**P value**
Cholesterol (mg/dl)	158.6±19.8	226.3±53	6.29	<.0.003 HS
Range	120-188.4	114.8-304.7		
TG(mg/dl)	99.4±24	116.7±44	12.7	<0..001 HS
Range	60.3-163	75.5-267		
HDL(mg/dl)	43.1±13	43.9±5.7	3.6	<0.008

Range	23.7-92	27-43		HS
LDL(mg/dl) **Range**	95. ±5+20 54-127.5	168±53.9 49.6-251-9	7.75	<.0.001 HS
Urea (mg/dL) **Range**	20.84±4.78 17-22.5	22.74±7.73 20-26.5	1.85	0.12 NS
Creatinine (mg/dL) **Range**	0.526±0.170 0.6-0.95	0.850±0.151 0.7-1.35	10.03	<0.001 HS
e FGR (mg/mmol) **Range**	110±14.78 110-130	100.74±7.73 85-95	16.5	<.0.001 HS
UACR(mg/g) **Range**	8.45 ± 5.29 5.54 ± 9.55	236.54 ± 406.55 220- 255	10.03	<0.001 HS

This table shows that:
there are statistical significant differences in studied groups regarding UACR , Mean± SD was (8.45 ± 5.29 vs 236.54 ± 406.55) in Group I and Group II respectively p-value <0.001, that were higher in Group II, there are statistical significant differences in studied groups regarding, Cholesterol : Mean± SD was (158.6±19.8 vs 226.3±53) in Group I and Group II respectively p-value <0.003, that were higher in Group II, there are statistical significant differences in studied groups regarding, **TG** : Mean± SD was (99.4±24 ± 5.29 vs 116.7±44) in Group I and Group II respectively p-value <0.001, that were higher in Group II, there are statistical significant differences in studied groups regarding, LDL : Mean± SD was (95. ±5+20 vs 168±53.9) in Group I and Group II respectively p-value <0.001, that were higher in Group II, there are statistical significant differences in studied groups regarding, Creatinine : Mean± SD was (0.526±0.170 vs 0.850±0.151) in Group I and Group II respectively p-value <0.001, that were higher in Group II. there are statistical significant differences in studied groups regarding, e FGR : Mean± SD was (110±14.78 vs 100.74±7.73n) in Group I and Group II respectively p-value <0.001, that were lower in Group II

Table (3): Menopausal symptoms scores according to menopause rating scale in in studied Groups.

Menopausal symptoms scores	**Group I(n=37) Mean(SD)**	**Group II(n=37) Mean (SD)**	**T**	**p-value**
Vasomotor symptoms score		8.03(3.22)		
Somato-vegetative symptoms	5.16(3.01)		9.9	<0.001 HS
Uro-genital symptoms	1.77(2.21)	3.77(2.21)	4.6	<0.001 HS
Overall MRS score(menopause rating scale)	6.93(5.22)	18.99(8.44)	7.8	<0.001 HS

This table shows that:
Menopausal symptoms scores according to menopause rating scale (Vasomotor symptoms score (0 VS 8.03(3.22) (p <0.001), Somato-vegetative symptoms (5.16(3.01) VS 7.16(3.01) (p <0.001), Uro-genital symptoms (6.93(5.22) VS

18.99(8.44) (p <0.001) and Overall MRS score6.93(5.22) VS 18.99(8.44) (p <0.001) all were statistically significant higher in Group II.

Table (4): Distribution of cases in Group II according UACR.

UACR	**Group II N=37**	
	N	**%**
3.24+0.33	13	35
7.35±0.39	**17**	45
17.52+0.55	7	30

This table demonstrates that 45% of the cases in Group II had UACR 7.35±0.39, 35% of the cases in Group II had UACR 3.24+0.33 and, 7% of the cases in Group II had UACR 17.52+0.55.

Table (5): Correlation between UACR, HOMA-IR and severity of vasomotor symptoms in Group II.

vasomotor symptoms severity	**UACR**	**R**	**P**
mild (5–8)	**3.24±0.33**	**0.15**	**<0.05 (S)**
moderate (9–15)	**7.35±0.39**	**0.31**	**<0.05(S)**
severe (more than 16 points)	**17.52±0.55**	**0.29**	**<0.05(S)**

This table shows that there are positive Correlation between **UACR,** and VMS severity (P<**0.05).**

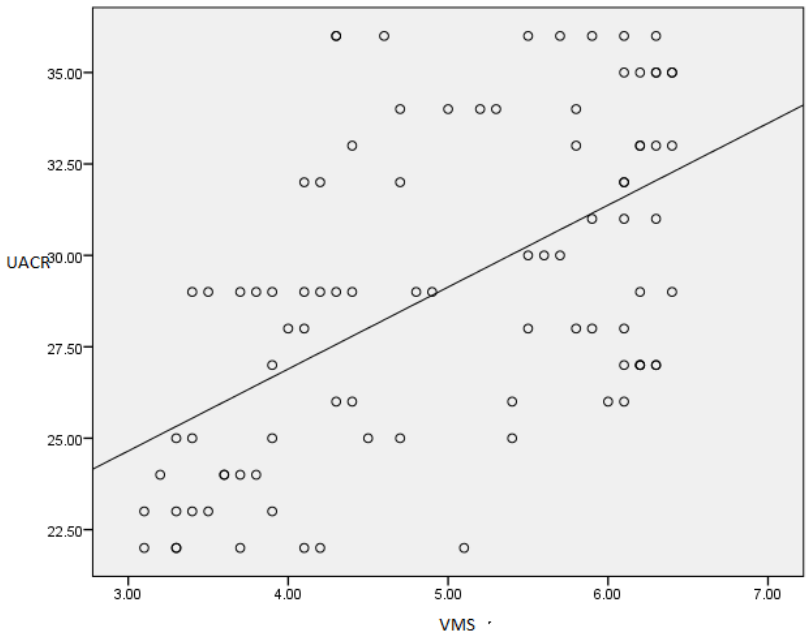

Fig. (1): Scatter plot between VMS and UACR among Group II there was statistically significant positive correlation between VMS and UACR.

Table (6): ROC Curve Analysis of UACR as predictor test for the severity of VMS.

Cut-off values	**Senstivity %** (95% CI**)**	**Specificity %** (95% CI**)**	**PPV %** (95% CI**)**	**NPV %** (95% CI**)**	**AUC** (95% CI**)**
> 3.25	100 %	92 %	91.6 %	90 %	0.768

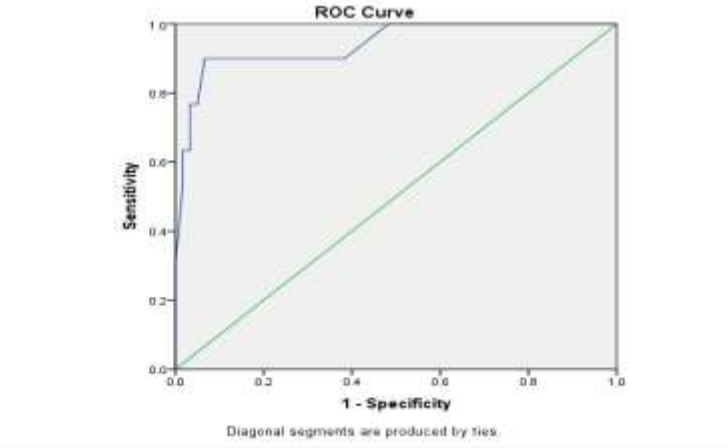

Fig (1): ROC Curve of UACR as predictor test for the severity of VMS in postmenopausal women.

This table shows that Receiver operating characteristics (ROC) curve was used to Analysis of UACR as predictor test for the severity of VMS the best cut off value of UACR was ≥3.25, with sensitivity of 100%, specificity of 92% positive predictive value of 91.6%, negative predictive value of 90%. We concluded that UACR at cutoff value = 3.25 was a good predictor test for the severity of VMS in postmenopausal women.

Table (7): Logistic regression analysis for predictors for the severity of VMS in postmenopausal women.

	Regression Coefficient	**SE**	**OR**	**95% CI**	**P**	**Sig.**
Age	- 0.330	0.124	1.719	0.564 – 0.917	0.008	**S**
UACR	+ 0.234	0.289	8.264	0.717 – 2.227	0.008	**HS**
BMI	+ 0.221	0.245	9.247	0.771 – 2.016	0.004	**HS**
HbAlc	+ 0.485	0.761	7.719	0.564 – 0.917	0.008	**HS**

This table shows that, Age, UACR, BMI and HbAlc are independent predictors for the severity of VMS in postmenopausal women($P<0.05$).

Discussion

Generally, insulin resistance results in the development of type 2 diabetes mellitus and increases the risk of life-threatening complications such as cardiovascular diseases, renal failure, and infections. (**4**).

The evidence suggests that IR probably precedes the onset of CVD, type 2 diabetes mellitus conditions in which there are metabolic Inflammation and thrombosis disorders. Many factors increase the risk for a subject to develop IR including obesity, diabetes and atherosclerosis. Considering that prevention is the top priority, we must find and identify the patient who acquires or is at risk of developing IR prior to the onset of the disease in order to delay or prevent its onset **(6).**

Microalbuminuria, which is defined as a urinary albumin to creatinine ratio (UACR) between 30 to 300 mg/g, is a known predictive marker of cardiovascular disease (CVD) and mortality in individuals with and without diabetes **(6).** The presence of microalbuminuria (MAU) reflects the state of endothelial damage in the whole body; MAU can predict the development of microvascular events, such as diabetic nephropathy (DN), as well as macrovascular events. In this study, the HOMA-IR index was used to assess IR, and the urine albumin-creatinine ratio (UACR) was used as an indicator of MAU **(7).**

Regarding the Clinical characteristic of the studied groups in the current study: there are statistical significant differences in studied groups regarding BMI , waist ,SBP and DBP that were higher in Group II ($p < 0.05$) , there are no statistical significant differences in studied groups regarding height , weight and pulse. ($p > 0.05$)

Our study was inconsistent with the study results of Na et al., (2022), they evaluated the relationship between insulin resistance and urinary microalbumin creatinine ratio in postmenopausal women. with type 2 diabetes The age, body mass index, systolic blood pressure (SBP), diastolic blood pressure (DBP), there are statistical significant differences in studied groups regarding BMI, waist, SBP and DBP that were higher in postmenopausal women

Regarding biochemical characteristics of the studied subjects in the current study: there were statistical significant differences in studied groups regarding (lipid profile, urea & Creatinine) ($p < 0.001$) that were higher in Group II, however eFGR was lower in Group II ($p < 0.001$).

In agreement with our findings Thurston et al. [8], Studied of Women's Health Across the Nation participants (N=3,201), aged 42-52 years at entry, completed interviews on frequency of hot flushes and night sweats, physical measures (blood pressure, height, weight), and blood draws (low-density lipoprotein [LDL], high-density lipoprotein [HDL], apolipoprotein A-1, apolipoprotein B, lipoprotein[a], triglycerides, serum estradiol, follicle-stimulating hormone) yearly for 8 years. Relations between symptoms and lipids were examined in linear mixed models adjusting for cardiovascular risk factors, medications, and hormones. They reported that Vasomotor symptoms were associated with higher LDL, HDL, apolipoprotein A-1, apolipoprotein B, and triglycerides. Lipids should be considered in links between hot flushes and cardiovascular risk.

Our findings of increased LDL-C, apoB, and triglycerides were broadly consistent with the two other population-based studies. In one large cross-sectional study, vasomotor symptoms were associated with elevated total cholesterol [9].

Another study (n=150) of very healthy women found no associations between hot flashes and lipids [8]. The reasons for differences between studies are not immediately apparent but may be due to differences in sample size and selection of women to be low on cardiovascular risk factors yet highly symptomatic. The physiology linking vasomotor symptoms to lipids is not entirely clear.

VMS are the main indication for menopausal hormone therapy (MHT) in postmenopausal women. An important implication can be drawn from this statement. If VMS are significantly associated with insulin resistance, as shown in our study, we can postulate that women with insulin resistance would have a greater need for MHT than those without insulin resistance. From this context, the possibility of the curative effect of MHT in patients with insulin resistance should be considered. (**8).**

In the present study, Correlation between UACR, HOMA-IR and severity of vasomotor symptoms in Group II were positively correlated; Logistic regression analysis for predictors for the severity of VMS in postmenopausal further showed that HOMA-IR and UACR were positively correlated, suggesting that HOMA-IR is a risk factor for UACR in postmenopausal. Also ROC Curve Analysis of HOMA-IR as predictor test for increase of UACR, the best cut off value of HOMA-IR as predictor test for increase of UACR which was ≥ 1.67, with sensitivity of 98% specificity of 95% positive predictive value of 92%, negative predictive value of 100% with diagnostic accuracy of 93%.

Our study was inconsistent with the study results of Na et al., (2022), urinary albumin-creatinine ratio (UACR) was analyzed and. The insulin resistance index (HOMR-IR) was calculated, in postmenopausal and the correlation between IR and UACR was analyzed. They found that Levels of HOMA-IR and UACR in postmenopausal group were higher than those in the control group, Pearson correlation analysis showed that UACR was positively correlated with HOMA-IR and HbA. Multiple linear stepwise regression analysis further showed that HOMA-IR and age were positively correlated with UACR.

It was also confirmed that podocytes in the glomerular filtration barrier are insulin-sensitive cells, and insulin-specific antibodies have appeared on podocyte. Podocyte injury is positively correlated with IR, and MAU gradually appears as podocyte injury increases, and podocytes play a key role in the progression of DN **(8).**

Concerning distribution of cases in Group II according UACR 45% of the cases in Group II had UACR 7.35 ± 0.39 , 35% of the cases in Group II had UACR 3.24+0.33 and , 7% of the cases in Group II had UACR 17.52+0.55

This in agreement with Yao et al., (9). There is a close correlation between menopausal symptoms and cardiovascular disease (CVD) risk and (UACR), A total of 21,672 postmenopausal women , they reported that those with an earlier onset of menopause exhibited an increased risk of menopausal symptoms and cardiovascular disease (CVD) risk and

(UACR), UACR elevation following adjustment for confounding variables (OR: 1.18, 95% CI: 1.04-1.33), whereas the opposite was true for women with a later age of menopause onset (>50 years) (OR: 0.86, 95% CI: 0.78-0.94). For every 1-year delay in the onset of menopause, UACR risk fell by 3% (OR: 0.97, 95% CI: 0.96-0.98).
In agreement also with our result Tang et al. (10), examined A total of 4821 subjects with type 2 diabetes mellitus (T2DM), an estimated glomerular filtration rate >60 ml/min/1.73 m^2 and UACR <30 This study demonstrated that a cutoff UACR value of >4 mg/g could significantly predict the cumulative incidence and progression of CKD.

Conclusion
In postmenopausal women, the VMS increased with the aggravation of Microalbuminuria Creatinine Ratio, A correlation was observed between Microalbuminuria Creatinine Ratio and VMS; moreover, Microalbuminuria Creatinine Ratio was an independent risk factor for the severity of VMS in postmenopausal women, providing a strong basis for clinical diagnosis and treatment

References

1. Santoro, N., Roeca, C., Peters, B. A., & Neal-Perry, G. (2021). The menopause transition: signs, symptoms, and management options. The Journal of Clinical Endocrinology & Metabolism, 106(1), 1-15.
2. Talaulikar, V. (2022). Menopause transition: Physiology and symptoms. Best practice & research Clinical obstetrics & gynaecology, 81, 3-7.
3. Clark, A. L. (2022). Overactive bladder, stress urinary incontinence, and menopause—what are the associations?. Menopause, 29(2), 125-126.
4. Stuenkel, C. A. (2021). Managing menopausal vasomotor symptoms in older women. Maturitas, 143, 36-40.
5. Prasad RM, Bali A, Tikaria R. Microalbuminuria. [Updated 2023 May 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563255/
6. Lambrinoudaki, I., Paschou, S. A., Lumsden, M. A., Faubion, S., Makrakis, E., Kalantaridou, S., & Panay, N. (2021). Premature ovarian insufficiency: a toolkit for the primary care physician. Maturitas, 147, 53-63.
7. Solbu, M. D., Kronborg, J., Jenssen, T. G., Njølstad, I., Løchen, M. L., Mathiesen, E. B., ... & Toft, I. (2009). Albuminuria, metabolic syndrome and the risk of mortality and cardiovascular events. Atherosclerosis, 204(2), 503-508.
8. Cho, Y., Chang, Y., Choi, H. R., Kang, J., Kwon, R., Lim, G. Y., ... & Ryu, S. (2022). Nonalcoholic Fatty Liver Disease and Risk of Early-Onset Vasomotor Symptoms in Lean and Overweight Premenopausal Women. Nutrients, 14(14), 2805.
9. Yao M, Liu H, Li B, Liu Y, Mu Y. The Relationship Between Earlier Onset of Natural Menopause and Elevated Urinary Albumin-Creatinine Ratio in Postmenopausal Chinese Women. Diabetes Metab Syndr Obes. 2021;14:847-856.
10. Tang WH, Hung WC, Wang CP, et al. The Lower Limit of Reference of Urinary Albumin/Creatinine Ratio and the Risk of Chronic Kidney Disease Progression in Patients With Type 2 Diabetes Mellitus. Front Endocrinol (Lausanne). 2022;13:858267.