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Evaluation and Correlation of Urinary Micro Albumin in Early Diagnosis of Patients with Hypertension Related Chronic Kidney Disease

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Abstract

One of the main organs targeted by hypertension, which is now understood by science to be an inflammatory disease, is the kidney. Urinary microalbumin, serum blood urea nitrogen, and creatinine are examples of clinical biochemical indicators for kidney illness that are often employed. This study aimed to study the role of Urinary microalbumin as a marker of inflammation in hypertensive chronic kidney disease patients. Evaluate the association of Urinary microalbumin levels in chronic kidney disease with/without hypertension. Possible usage of this marker as a predictive index for regular kidney disease occurrence. A case–control study was conducted on 100 participants, including 48 individuals identified as male and 52 individuals identified as female; in addition, their ages ranged from (20 to 70), these 100 participants, including (35) chronic kidney disease patients with hypertension (35) chronic kidney disease patients without hypertension, and (30) healthy control group, were evaluated concerning Urinary Micro Albumin using an immunochromatographic test kit. The results illustrated that Urinary microalbumin, Urea and Creatinine in CKD with the HBP group showed a highly significant increase ($p<0.05$) compared to the control group according to case/ control, sex and age. In contrast, the most negligible value was in the Control group.

In conclusion

The research findings indicate a correlation between hypertension and chronic kidney disease (CKD). The presence of hypertension resulted in elevated levels of Urinary microalbumin, urea, and creatinine in patients as compared to the control group. Urinary microalbumin has the potential to serve as a marker for the assessment of glomerular and tubular function in adults. It performs comparably to the Cr-based estimating equations as an indicator of renal function.

تقييم وارتباط الزلال البولي الدقيق في التشخيص المبكر للمرضى الذين يعانون من مرض الكلى المزمن المرتبط بارتفاع ضغط الدم

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الملخص

أحد الأعضاء الرئيسية المستهدفة بارتفاع ضغط الدم، والذي يُفهم الآن على أنه مرض التهابي، هو الكلية. الميكروبومين البولي، نيتروجين اليوريا في مصل الدم، والكرياتينين هي أمثلة على المؤشرات الكيميائية الحيوية السريرية لأمراض الكلى. كان الهدف من هذه الدراسة هو دراسة دور الميكروبومين البولي كعلامة على الالتهاب في مرضى أمراض الكلى المزمنة المصابين بارتفاع ضغط الدم، وتقييم ارتباط مستوى الميكروبومين البولي في أمراض الكلى المزمنة مع أو بدون ارتفاع ضغط الدم، واستخدامه كمؤشر تنبؤي لحدوث أمراض الكلى المزمنة. أجريت دراسة حالات مراقبة على ١٠٠ مشارك، بينهم ٤٨ ذكور و٥٢ إناث، تراوحت أعمارهم بين ٢٠ و٧٠ سنة. تضمنت الدراسة ٣٥ مريضًا بأمراض الكلى المزمنة المصابين بارتفاع ضغط الدم، ٣٥ مريضًا بأمراض الكلى المزمنة بدون ارتفاع ضغط الدم، و٣٠ فردًا كمجموعة تحكم صحية. تم قياس الميكروبومين البولي باستخدام اختبار مناعي. أظهرت النتائج أن الميكروبومين البولي، اليوريا، والكرياتينين كانت مرتفعة بشكل كبير ($p<0.05$) في مجموعة مرضى الكلى المزمنة مع ارتفاع ضغط الدم مقارنة بمجموعة مرضى الكلى المزمنة بدون ارتفاع ضغط الدم، بناءً على الحالة/السيطرة، الجنس، والعمر، بينما كانت أقل قيمة في مجموعة التحكم.

1. Introduction

Hypertension is one of the top five global killers and a significant risk factor for cardiovascular and renal illnesses, which kill more than 40% of people worldwide (Nahimana et al., 2018).

Hypertension is a frequent condition encountered during kidney disease development and a leading cause of its progression. Multiple crosstalk mechanisms are involved in sustaining the inevitable high blood pressure (BP) state in CKD, and these play an essential role in the pathogenesis of increased cardiovascular (CV) events associated with CKD (Ameer, 2022).

Primary hypertension, sometimes known as essential hypertension, is the prevailing kind of hypertension. Secondary hypertension may be ascribed to several reasons, including chronic kidney disease, renal artery stenosis, and sleep apnea. The symptoms of hypertension are often not apparent until severe or chronic signs mark the disorder. *Sphygmomanometry* is a diagnostic procedure used in medical settings. Testing may be performed to ascertain the aetiology, evaluate the extent of organ impairment, and ascertain other risk factors associated with cardiovascular well-being(Carey et al., 2018).

A kidney typically contains around one million nephrons, contributing to the glomerular filtration rate (GFR). In cases of kidney damage, the kidney may maintain a glomerular filtration rate (GFR) via the mechanisms of hyperfiltration and compensatory hypertrophy of the unaffected nephrons (C. Shima et al., 2022).

Signs of kidney damage (albuminuria and structural abnormalities on ultrasonography) high urea and creatinine levels and were used to identify chronic kidney disease (Eka et al., 2021)

Microalbumin, with a molecular weight of 68,000 Daltons, indicates aberrant permeability in the glomerulus. One of the first signs of chronic kidney disease (CKD) is the presence of urine albumin excretion ranging from 20 to 200 mg/L. This particular range is also associated with an increased susceptibility to metabolic diseases, cardiovascular illness, and death from any cause (Gaeini et al.,2022).

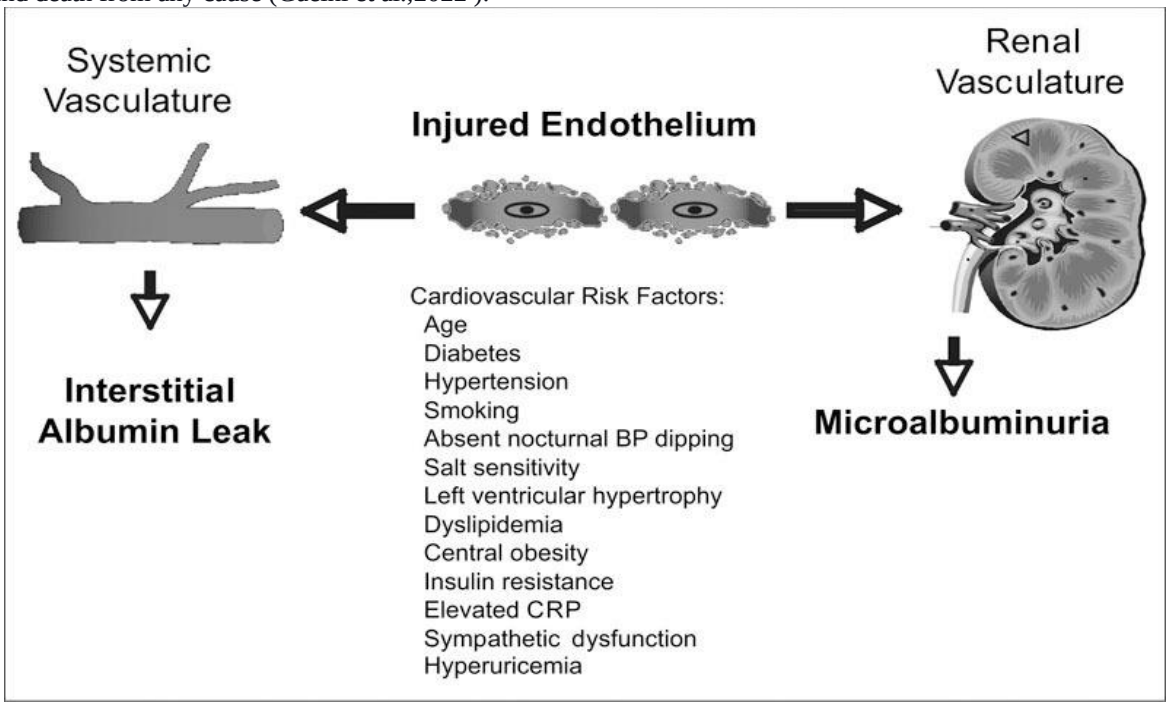

Figure 1: Microalbuminuria: Manifestation of Diffuse Endothelial Cell Injury. BF=Blood Pressure; CRF=C-Reactive Protein (Toto, 2004)

Numerous obstacles impede the passage of albumin through the glomerular filtration system of the nephron. At pH, characteristic of physiological conditions, the glomerular capillary wall and endothelial cells exhibit a repulsive interaction with albumin due to opposing charges on their surfaces. , Its porous nature characterizes the glomerular basement

membrane (GBM), yet the size of these openings is often insufficient to allow the passage of albumin. Furthermore, the megalincubulin complex is responsible for the albumin degradation inside the nephron, especially in the proximal convoluted tubule. The primary purpose of this mechanism is to save amino acids for subsequent use while concurrently serving as an additional means of impeding the translocation of albumin. The presence of albumin in urine may be attributed to the malfunction of the glomerular basement membrane (GBM) filtration barrier, and the quantity of albumin excreted has significance (Waghmare & Goswam, 2016).

The Steno hypothesis proposes that the initiation of microalbuminuria and cardiovascular disease is attributed to systemic vascular endothelial dysfunction since a robust link exists among these three variables. Hence, the presence of comorbidities that induce endothelium degradation is regarded as a risk factor. The factors contributing to this phenomenon include hypertension, advanced age, insulin resistance and dyslipidemia (Prasad et al., 2023).

Therefore, in addition to the renal system, albumin has the potential to either extravasate from or permeate into the artery wall at many vascular sites. In instances of occurrence, albumin has the potential to incite inflammation, lipid buildup, and atherosclerosis, ultimately leading to persistent albuminuria and a decline in renal function (Abdelhafiz et al., 2011).

The primary purpose of assessing the urine microalbumin level is to examine the patient's potential susceptibility to future issues. Nevertheless, it is essential for healthcare practitioners to not just see microalbuminuria as a simple indicator of kidney damage but rather as a prognosticator of the pace at which kidney dysfunction may proceed, as well as an indicator of the impact of systemic illnesses on renal function (Waghmare & Goswami, 2016).

The Study Aims to evaluate and correlate urinary microalbumin (mAlb) in chronic kidney disease patients with/without hypertension.

2. Materials and Methods

The case-control study has been conducted at Al-Imam Al-Sadiq Teaching Hospital in Babylon Governorate, spanning from January

2023 to April 2023. The study population consisted of seventy individuals diagnosed with chronic kidney disease (CKD), with 35 of them presenting with CKD and Hypertension, while the remaining 35 had CKD without Hypertension. Additionally, a control group of 30 healthy individuals was included for comparison. The ages of the individuals ranged from 20 to 70 years. Regarding sex, there were 48 individuals identified as male and 52 individuals identified as female.

The urinary microglobulin level of participants was measured by immunochromatographic test kit after the urine was collected using the traditional technique and conversed in a screw cup. The fluorecare® mAlb is a diagnostic tool that utilizes the immunochromatographic assay concept to measure the content of mAlb in human urine using a competitive immunodetection approach. The urine sample is introduced into the designated aperture for specimen addition. Within the specimens intended for analysis, the monoclonal anti-mAlb antibody interacts with the fluorescently labelled mAlb antibody on the bonding pad, forming the mAlb antibody complex—the diffusion of the mAlb antibody complex along the nitrocellulose membrane results from the chromatographic action.

3. Exclusion Criteria

Patients were excluded from the study if they had any of the following: hepatitis, autoimmune disease, pregnant women, elevated blood pressure due to cancer, diabetic patients, kidney stones disease and other types of renal diseases, except CKD with hypertension.

4. Inclusion Criteria

CKD patients with/without hypertension served as the case group, and Healthy subjects served as the control group.

5. Ethics Approved

The College of Applied Medical Sciences Ethical Committee, which has its headquarters in Karbala, gave the study's protocol their stamp of approval. Patients or their guardians provided their approval for samples to be collected. Additionally, a questionnaire designed by the researcher was used to interview participants.

6. Statistical Analysis

Independent T-Test and Mann-Whitney U tests have been utilized to conduct a comparative analysis between two groups on the same continuous variable and the
results have been
considered to have
statistical significance at ($p \leq 0.05$).

7. Results

1-Correlation of Urinary Microalbumin on study groups

The findings shown in Table (1) demonstrate a highly significant statistical distinction ($P<0.05$) in the levels of urine albumin between the CKD with HBP group and the CKD without HBP group, as compared to the control group. This distinction was seen when considering factors such as case, sex, and age.

The group with chronic kidney disease (CKD) and high blood pressure (HBP) exhibited the most significant Urinary microalbumin level, with a mean value of 114.49 in the case/control group. The group with CKD followed this without HBP, with a mean level of 56.62 in the same category. The average degree of control is 8.68.

Furthermore, it was observed that the concentration of Urinary microalbumin was found to be the greatest in both male and female individuals belonging to the chronic kidney disease (CKD) with high blood pressure (HBP) category. The mean values for this group were recorded as 113.41 and 115.52, respectively. In contrast, the mean levels of urinary Microalbumin in the CKD without HBP category were lower, with values of 51.80 and 60.68 for males and females, respectively. The mean degree of control is 8.51 and 8.77, respectively.

Table 1: Relation of Sex and Age Group on Microalbumin in the Patients Compared with the Control Group

Disease Status	Variable	Variable Level	Patients		Control		P. Value
			Mean	Std. Deviation	Mean	Std. Deviation	
CKD with HBP	**Case**	**Case/ Control**	**114.49**	**32.98**	**23.42**	**8.68**	**0.001****
	Sex	**Male**	**113.41**	**41.56**	**21.65**	**8.51**	**0.007****
		Female	**115.52**	**23.40**	**25.20**	**8.77**	**0.003****
	Age Group	**20 - 40**	**107.18**	**36.72**	**٢٦.٢٠**	**9.٢٨**	**0.007****
		41 - 70	**118.31**	**31.03**	**٢٢.٠٣**	**٨.٢٥**	**0.007****
CKD without HBP	**Case**	**Case/ Control**	**56.62**	**31.97**	**23.42**	**8.68**	**0.007****
	Sex	**Male**	**51.80**	**32.59**	**21.65**	**8.51**	**0.002****
		Female	**60.68**	**31.74**	**25.20**	**8.77**	**0.001****
	Age Group	**20 - 40**	**49.66**	**29.52**	**٢٦.٢٠**	**9.٢٨**	**0.004****
		41 - 70	**61.27**	**33.39**	**٢٢.٠٣**	**٨.٢٥**	**0.001****

-Independent T-Test and Mann-Whitney U tests have been used to compare two groups on the same continuous variable.

-****** The mean difference is significant at the 0.05 level

2-Correlation of Biochemical Parameters (Urea and Creatinine) on study groups

Table (2) illustrated that Urea and Creatinine in CKD with the HBP group showed a highly significant increase ($p<0.05$) when compared with the control group according to case/ control, sex and age. In contrast, the most negligible value was in the Control group.

Also, Urea and Creatinine in CKD without the HBP group showed a highly significant increase ($p<0.05$) compared to the control group according to case/ control, sex and age. In contrast, the most negligible value was in the Control group.

Generally, in comparisons among all groups of chronic kidney disease, the results showed significantly higher differences ($p<0.05$), as illustrated in the table below.

Table 2: Relation of Sex and Age Group on the Biomarker Levels (Urea, Creatinine) in the Patients Compared with the Control Group

Disease Status	Parameters	Variable Level	Patients		Control		P. Value
			Mean	Std. Deviation	Mean	Std. Deviation	
CKD with HBP	Urea	Case/Control	22.82	10.99	4.62	1.40	0.005**
		Male	25.86	11.83	4.77	1.24	0.002**
		Female	19.95	9.59	4.47	1.58	0.002**
		20 - 40	23.43	10.98	٤.٢٦	١.١٦	0.00٧**
		41 - 70	22.51	11.23	٤.٨0	١.٥٥	0.00١**
	Creatinine	Case/Control	216.05	114.93	65.82	11.51	0.005**
		Male	247.79	125.69	66.73	13.28	0.002**
		Female	186.08	97.93	64.90	9.81	0.006**
		21 - 40	235.49	133.58	٦٦.٩٧	١٠.٥٥	0.001**
		42 - 70	205.91	105.73	٦٥.٢٤	١٢.١٨	0.002**
CKD without HBP	Urea	Case/Control	19.64	10.17	4.62	1.40	0.003**
		Male	21.07	11.89	4.77	1.24	0.006**
		Female	18.43	8.61	4.47	1.58	0.001**
		20 - 40	20.58	11.16	٤.٢٦	١.١٦	0.002**
		41 - 70	19.01	9.68	٤.٨0	١.٥٥	0.001**
	Creatinine	Case/Control	213.46	99.64	65.82	11.51	0.003**
		Male	221.14	126.44	66.73	13.28	0.005**
		Female	206.99	73.03	64.90	9.81	0.009**
		20 - 40	216.69	96.68	٦٦.٩٧	١٠.٥٥	0.005**
		41 - 70	211.31	103.87	٦٥.٢٤	١٢.١٨	0.003**

Independent T-Test and Mann-Whitney U test have been used to compare two groups on the same continuous variable.

-. The mean difference is significant at the 0.05 level.**

3-The Relationship Between Research Parameters in Patients with CKD and Their Controls

Table (3) demonstrates that the levels of Urea and Creatinine were significantly higher ($p<0.05$) in the group with Chronic Kidney Disease and High Blood Pressure. In contrast, the Control group had the lowest values.

Table 3: The Relationship Between Research Parameters in Patients with CKD and Their Controls

Parameters	Disease Status	Mean	Std. Deviation	P. Value
Urea	CKD with HBP	22.82	10.99	0.0002**
	CKD without HBP	19.64	10.17	
	Control	4.62	1.4	
Creatinine	CKD with HBP	216.05	114.93	0.0003**
	CKD without HBP	213.46	99.64	
	Control	65.82	11.51	
Urinary Microalbumin	CKD with HBP	114.49	32.98	0.0002**
	CKD without HBP	56.62	31.97	
	Control	23.42	8.68	

-ANOVA and Kruskal-Wallis tests have been utilized to discern statistically significant differences across multiple independent groups.

- The mean difference is significant at the 0.05 level.**

In contrast, the levels of Urinary microalbumin were found to be significantly higher ($p<0.05$) in the group of individuals with chronic kidney disease (CKD) and high blood pressure (HBP) compared to the other groups included in the research. Notably, the control group exhibited the lowest value of these biomarkers.

In the analysis of chronic Kidney disease across various categories, the findings indicated significantly higher differences ($p < 0.05$), as shown in the table above.

8. Discussion

The results of the present study are shown in Table (1), where screening for Urinary Microalbumin is a sensitive and trustworthy way to detect renal disease and mortality in hypertension. Additionally indicative of end-stage renal illness is Urinary Microalbumin.

According to Yang's 2021 results, there was a significant difference ($P<0.05$) in the Urinary microalbumin levels between the groups with hypertension and hypertensive nephropathy and the control group. Comparability was shown by the lack of statistically significant differences in age and gender between the three groups of people ($P>0.05$).

In contrast to ordinary persons, most cases developed mAlb. Overt mAlb was present in more than half of the cases. This demonstrated a correlation between CKD and mAlb, according to the research by Chin'ombe et al. 2013.

Hwang et al. 2000 Compared to women with normotension, hypertensive women had a significantly greater prevalence of mAlb (16% vs. 4%, $P < 0.001$). These findings imply that whereas hypertension is often the primary cause of mAlb, other illnesses may also play a role.

As time went on, more cases of microalbuminuria were discovered, and in women, the condition was once more severe. There is a strong correlation between hypertension and microalbuminuria. It has been reported that mAlb is linked to excess body weight. The prevalence of mAlb in the hypertensive female population was higher than that of the male population. This difference in prevalence may be related to the fact that women have lower muscle mass than men—roughly 15% less—and, therefore, lower levels of creatinuria. A

research by Poudel et al.,2012 indicated obesity to be an independent risk factor for microalbuminuria, which is consistent with the current finding.

The higher level of mAlb and creatinine may be due to subclinical ultra-structural changes in the glomeruli of hypertensive patients. The presence of microalbuminuria in the early stage of hypertension can be taken as a significant independent predictor for the progression of renal disease.

So, mAlb in hypertensive subjects may prove to be a valuable marker in the evaluation of target organ damage and control of risk factors amenable to prevention (regular treatment of HT, weight control, normal lipid levels) may have a favourable effect in preventing, delaying and lessening prevalence of mAlb.
In conclusion, mAlb should be used as a marker of renal dysfunction in CKD. It may also be a marker for other metabolic problems associated with CKD.
The levels of the routine chemistries (creatinine and urea) were consistent with the expected pattern in CKD. They were significantly different from those of the control group, according to Chin'ombe et al. 2013 study. This agrees with our study's findings in Table (2).
A Hanratty et al. 2011 study found that higher treated BP was associated with early kidney function decline (a rise in serum creatinine ≥0.6 mg/dl).
Also, the present study's findings align with Hussein's 2022 study, which also examined renal function tests. The results showed statistically significant differences ($p<0.01$) in serum urea and creatinine across all groups studied.
The present research's findings are consistent with those of a previous study done by Yang, 2021 whereby the results of biochemical index detection indicated that levels of BUN and creatinine were significantly elevated in the hypertensive nephropathy group compared to both the control group and the hypertension group ($P<0.05$). This agrees with our study's findings in Table (3).
Bae et al. 2022 study showed higher hazard ratios for CKD among males younger than 40 years compared to females younger than 40.
Hasan et al.,2013 study found that hypertension is higher among men than women. Age was shown to be a significant associated risk factor for hypertension.
Abd Allah et al. 2021 study observed that age had a positive association with serum urea and also negative with diastolic pressure. Diastolic pressure had a positive correlation with systolic pressure and also a positive correlation with serum urea. No significant differences between serum parameters in the study population were found. The serum creatinine was significantly increased in males than females.
In light of the given information, the findings suggest clinical implications associated with higher urinary albumin levels in the general population. These elevated levels should be considered as potential risk factors for the future onset of hypertension and related complications, such as chronic kidney disease. The timely identification and intervention of hypertension are anticipated to mitigate the advancement of renal impairments and hypertension.

9. Conclusion

1. The study showed that there was a strong relationship between Urinary microalbumin and chronic renal disease and hypertension, and the nature of the relationship was synergistic between them.
2. Creatinine and Urea, routine markers for CKD, were increased in CKD with/without hypertension, while average values were in the control group.

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