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Association of Components of Metabolic Syndrome in Patient with Chronic Kidney Disease with Diabetes Mellitus

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Type 2 Diabetes, Chronic Kidney Disease, eGFR, Fasting Blood Glucose, Albumin

ABSTRACT:

Objective: Patients with diabetes generally suffer from altered components of metabolic syndrome that further promote the risk of chronic kidney disease (CKD). The study will evaluate the association of diabetes with CKD on different metabolic parameters.

Methods: This cross-sectional study included 1,500 adult patients with type 2 DM and healthy controls who sought medical advice in the Department of Medicine at Hind Institute of Medical Sciences between February 2022 to August 2023. The patients considered for the study have gone through different parameters, such as measurement of albumin and eGFR and hence their result is drawn.

Results: The study conducted brings out the result that patients having more than 10 years of diabetes are prevalent to CKD .i.e. around 60%. Also was confirmed that impairment of eGFR with age was more prominent (92.18 ± 2.20 vs 54.19 ± 5.70 $p<0.001$).Low HDL levels of (30.92±4.95, vs 52.47±4.19 $p<0.001$) and high triglyceride levels (228.70 ± 47.82 vs 116.1±29.38 $p<0.001$) were linked to CKD. There were no statistically significant differences in the distribution of smokers and non-smokers between the control and CKD groups ($p=0.687$).

Conclusion: Our study demonstrated that approximately one-half of patients with type 2 DM had CKD. Further studies are necessary to understand this high prevalence and the underlying factors. Future research is needed to assess the effectiveness of implementing targeted community-based intervention.

Introduction

As an urge to become more and more developed, the lifestyle of daily living is also getting worse, and hence such stressful life leads to Diabetes mellitus (DM) which subsequently leads to chronic kidney disease (CKD) and gradually becoming a major healthcare concern worldwide. It has been observed that 20-40% of diabetic nephropathy cases are the consequence of diabetes.[1] which gradually turns into chronic kidney disease which is indicated by increased excretion of urine albumin, decreased glomerular filtration rate (GFR), or can be both.[2] With constant evaluation it can also assumed that association of diabetes with Chronic kidney diseases is regulated individually with each metabolic parameters and hence any alteration in their level can worsen the condition. By the year 2035, it is anticipated that more than 350 million people will be affected by diabetes, which has reached epidemic proportions in several parts of the world.[3] The epidemiology of diabetic kidney disease differs significantly internationally and along racial/ethnic lines, which may be explained by variations in political systems and economic viability. After 15 years of having the condition, about one-third of diabetic individuals had microalbuminuria, and less than half

Journal of Chemical Health Risks
www.jchr.org
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really developed nephropathy. Native Americans, Asian Americans, and African Americans are more susceptible to chronic kidney disease (CKD). In addition to that, despite the fact that type 2 DM patients have a higher overall frequency in the diabetic population, progressive kidney disease (PKD) is more frequent in Caucasian people with type 1 than type 2 diabetes mellitus (DM).[4] The most frequent risk factor for CKD is hyperglycemia, but apart from that, factors such as gender, obesity, hypertension, chronic inflammation, resistance to insulin, hypovitaminosis D, dyslipidemia, and other genetic loci and polymorphisms can have an impact too. In the near future, minimizing its incidence could be made possible by managing its modifiable risk factors.[5] As Patients with diabetic kidney disease are among the most complex patients in diabetes care. They require a multifactorial and multidisciplinary approach with the goal to slow the decline in glomerular filtration rate (GFR) and cardiovascular morbidity. We aimed to evaluate the prevalence, characteristics and correlates of CKD in Jordanian patients with type 2 DM.

Role of Diabetes in Chronic Kidney Disease

Type 2 diabetes has a significant impact on the onset and development of chronic kidney disease (CKD).

- **Diabetic nephropathy**: It is also known as diabetic kidney disease, which is a specific type of kidney damage that results from long-term uncontrolled type 2 diabetes. It is one of the leading causes of CKD.
- **Damage to Glomeruli**: People with type 2 diabetes and always experience high blood sugar levels in individuals can damage the tiny blood vessels in the kidneys, known as glomeruli. These structures are responsible for filtering waste products and excess fluids from the blood. Over time, this damage impairs the kidney's filtration function.
- **Microalbuminuria**: In the early stages of diabetic nephropathy, there is often an elevation of a protein called albumin in the urine, a condition known as microalbuminuria. It is an early sign of kidney damage in people with diabetes and a key indicator of diabetic nephropathy.
- **Hypertension (High Blood Pressure**): Type 2 diabetes is frequently associated with hypertension, which can further stress the kidneys. Hypertension is a significant risk factor for the progression of kidney disease in individuals with diabetes.
- **Inflammation and Oxidative Stres**s: Chronic inflammation and oxidative stress, common in diabetes, can also contribute to kidney damage over time.
- **Advanced Stages of CKD**: If left uncontrolled, diabetic nephropathy can progress to advanced stages of CKD, eventually leading to end-stage renal disease (ESRD), where the kidneys can no longer function adequately to sustain life. At this point, individuals may require dialysis or kidney transplantation for survival.
- **Cardiovascular Complications:** Type 2 diabetes is often accompanied by cardiovascular risk factors such as high cholesterol and triglyceride levels. These factors can further damage blood vessels in the kidneys, exacerbating kidney problems**.**

Chronic Kidney Disease and Glycaemic Control

Hypoglycaemia is linked to a higher risk of lower HbA1c levels and in order for that, specific HbA1c objectives must be developed. The risk of hypoglycemia is greater in the elderly and fragile, in those with erratic eating habits, when using insulin and sulfonylureas, and in those with CKD. Hypoglycaemia can result in renal damage, myocardial infarction, seizures, stroke, or death. For those with shorter life expectancies or those with CKD, those with a history of severe hypoglycemia or hypoglycemia unawareness, and children, higher HbA1c objectives should be considered**.**[6] Suitable glycaemic control objectives were one of the topics covered at the KDIGO-hosted Diabetic Kidney Disease (CKD) Controversies Conference.[7] With reference to the optimum glucose goal in patients with CKD stage 3 or worse, there are not enough studies and data available. According to one study, HbA1c values >9% and 6.5% were linked to higher death rates in those with CKD stage 3 who were not on dialysis.[8] Diabetes patients with ESRD have benefited from keeping their HbA1c levels between 7-8%. Since HbA1c values over 8% or less than 7% increase the risk of cardiovascular and all-cause mortality.[9,10] It has also been found that haemoglobin A1c (HbA1c) >8.5% of individuals had a worse prognosis than those with HbA1c 6.5-7.4%, according to recent observational research; older patients did not vary. Additionally, there

Journal of Chemical Health Risks
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was no difference in survival among those who began dialysis at a younger age (60 years old).[11]

METHODS

The study was conducted over a period of 18 months from February 2022 to August 2023. The study involved diabetes patients from the Inpatients and Outpatients Department of Medicine at the Hind Institute of Medical Sciences in Atariya, Sitapur, U.P., who participated in the study. Patients were selected based on their medical records and confirmed as having DM type 2 during clinic visits. 650 patients are chosen as cases after meeting the criteria, and they are compared to 650 healthy controls. The information was gathered through questionnaires directly with the patient in order to cover their medical history, which comprises the onset of hypertension and diabetes, their current diabetes status, including any complications and their glycaemic control, including their most recent fasting blood sugar and hemoglobin A1C values, as well as their smoking status. The patient's height, weight, waist circumference, and blood pressure have all been measured. We also collected data on fasting blood sugar, fasting lipid profile, including High density lipoprotein (HDL) and triglyceride, Low-density lipoprotein (LDL), and serum albumin levels up to 3-6 months following the clinic visit using the most current blood test results, when available. We examined blood creatinine, BUN, urea, and uric acid within six months of the planned clinic visit to assess kidney function. Using a standard blood creatinine level and the Chronic Kidney Disease Epidemiology Collaboration methodology, the estimated glomerular filtration rate (eGFR) for each patient was determined.

Selection Criteria

Inclusion Criteria

1. Patient above age ≥ 30 years are included
2. Having Diabetes 2 Mellitus

Exclusion Criteria

1. Type 1 Diabetes Mellitus
2. Pregnant Female

Statistical Analysis

The collected data was meticulously organized, tabulated, and subjected to comprehensive statistical analysis utilizing SPSS statistical software. For the qualitative data in this study, numerical and percentage representations were employed. Quantitative data were presented in terms of mean values along with their corresponding standard deviations (SD). To determine the significance of the findings, P-values associated with the relevant test statistics were evaluated, with a significance level set at 0.05. P-values exceeding 0.05 were regarded as statistically insignificant, while those equal to or less than 0.05 were considered significant. To assess the normality of the quantitative data, the unpaired t-test was employed to compare biochemical parameters between the case and control groups.

Result

In this comparative analysis between the control group (Group I) and individuals with Chronic Kidney Disease (CKD), several crucial variables were examined to understand the differences between the two groups. The data is presented as follows:

Age (Years): Individuals in the CKD group (55.27 ± 17.22) were notably older compared to the control group (40.25 ± 10.22), and this age difference was statistically significant ($t=19.12$, $p<0.001$).

Sex: There was no significant difference in the gender distribution between the control and CKD groups ($p=0.653$).

Duration of DM: The duration of diabetes (DM) in the CKD group differed significantly from the control group (chi sq=74.7, $p<0.001$). A substantial portion of the CKD group had diabetes for more than 10 years.

HbA1c (%): HbA1c levels were markedly higher in the CKD group (9.44 ± 0.83) compared to the control group (4.48 ± 0.72), and this difference was highly significant ($t=115.10$, $p<0.001$).

Antidiabetic Medications: A significantly higher proportion of the CKD group was using insulin and metformin (chi sq=23.4, $p<0.001$, chi sq=18.7, $p<0.001$, respectively).

Waist circumference (cm), Body mass index (Kg/m2), Systolic and Diastolic Blood Pressure (mmHg): All of these parameters were substantially higher in the CKD group compared to the control group, with highly significant differences ($p<0.001$).

BUN (mg/dl), Serum creatinine (mg/dl), Albumin (gm/dl), eGFR (ml/min/1.73 m2): The CKD group exhibited significantly different values in all these variables, indicating the presence of kidney dysfunction ($p<0.001$).

Journal of Chemical Health Risks
www.jchr.org
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Fasting blood glucose (mg/dl), Urea (mg/dl), Uric acid (mg/dl), TC (mg/dL), TAG (mg/dL), LDL-C (mg/dL), TC/HDL-C, HDL-C (mg/dL), VLDL-C (mg/dL): In all these parameters, the CKD group showed substantial differences compared to the control group, signifying significant alterations in glucose metabolism, lipid profiles, and renal function.

Smoking: There were no statistically significant differences in the distribution of smokers and non-smokers between the control and CKD groups (p=0.687).

Medical History: The CKD group had a significantly higher prevalence of hypertension compared to the control group (chi sq=25.3, p<0.001).

These findings provide valuable insights into the disparities between the control and CKD groups, especially concerning age, diabetes duration, glycemic control, medication use, anthropometric measures, blood pressure, renal function, and lipid profiles. These disparities are critical for understanding and managing chronic kidney disease in individuals with diabetes. To bring out clear significance data is been tabulated in Table 1 and certain parameters such blood urea nitrogen serum creatinine, albumin, urea are plotted in respective graphs.

Table 1: Intergroup Comparison of Study Parameters between Control & CKD Cases

Variable	Category	Group I [Control] (n =650)	CKD (n =650)	p-value
Age (Years)	<60	40.25 ± 10.22	55.27 ± 17.22	**p<0.001**
Sex	Male	376 (57.8%)	384 (59.1%)	p=0.653
	Female	274 (42.2%)	266 (40.9%)	
Duration of DM	<5 years	249 (38.3%)	147 (22.6%)	**p<0.001**
	5–10 years	178 (27.4%)	126 (19.4%)	
	>10 years	223 (34.3%)	377 (58.0%)	
HbA1c (%)		4.48 ± 0.72	9.44 ± 0.83	**p<0.001**
Antidiabetic medications	Insulin	302 (46.5%)	389 (59.8%)	**p<0.001**
	Metformin	200 (30.8%)	275 (42.3%)	**p<0.001**
Waist circumference (cm)		106.4 ± 13.6	111.2 ± 15.6	**p<0.001**
Body mass index (Kg/m2)		24.73 ± 2.20	31.76 ± 3.82	**p<0.001**
Systolic Blood Pressure (mmHg)		123.67 ± 9.87	144.32 ± 21.90	**p<0.001**
Diastolic Blood Pressure (mmHg)		72.67 ±10.45	80.00 ± 12.30	**p<0.001**
BUN (mg/dl)		14.45 ± 2.53	64.90± 4.45	**p<0.001**
Serum creatinine (mg/dl)		0.97 ± 0.12	8.83 ± 0.40	**p<0.001**
Albumin (gm/dl)		3.02± 0.48	4.50 ± 0.17	**p<0.001**
eGFR (ml/min/1.73 m2)		92.18 ± 2.20	54.19 ± 5.70	**p<0.001**
Fasting blood glucose (mg/dl)		96.74 ± 9.89	210.40 ± 17.69	**p<0.001**
Urea (mg/dl)		23.75 ± 3.96	116.58 ± 42.49	**p<0.001**
Uric acid (mg/dl)		3.83 ± 0.47	6.96 ± 2.96	**p<0.001**
TC (mg/dL		160 ±17.35	253 ± 58.84,	**p<0.001**
TAG (mg/dL)		116.1±29.38	228.70 ± 47.82,	**p<0.001**
LDL-C (mg/dL)		80.22± 24.49	190.40 ± 49.82	**p<0.001**
TC/HDL-C		3.25 ±2.6	3.79 ± 9.8	p=0.175
HDL-C (mg/dL)		52.47±4.19	30.92±4.95,	**p<0.001**
VLDL-C (mg/dL)		33.55±5.03	48.33±8.99	**p<0.001**
Smoking	Never smoker	402 (61.8%)	401 (61.7%)	p=0.687
	Current smoker	104 (16.0%)	114 (17.5%)	
	Ex-smoker	144 (22.2%)	135 (20.8%)	
Medical history	Hypertension	240 (36.9%)	330 (50.8%)	**p<0.001**

Journal of Chemical Health Risks
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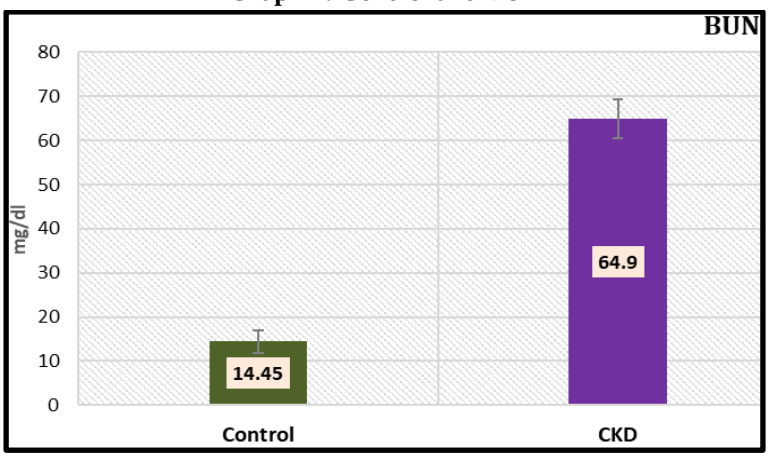
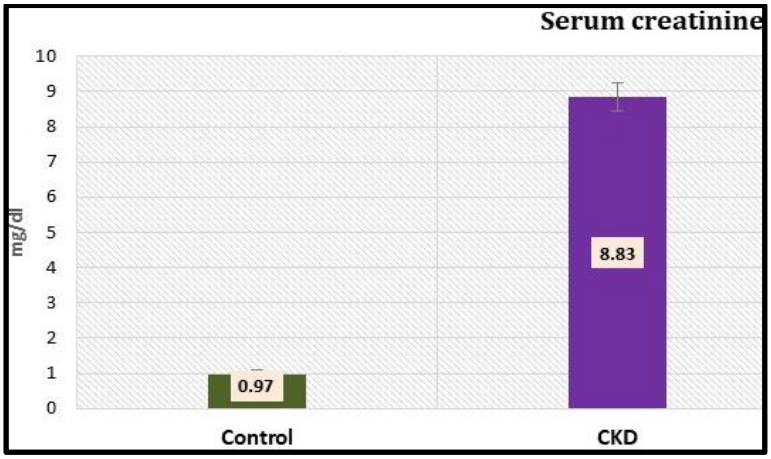
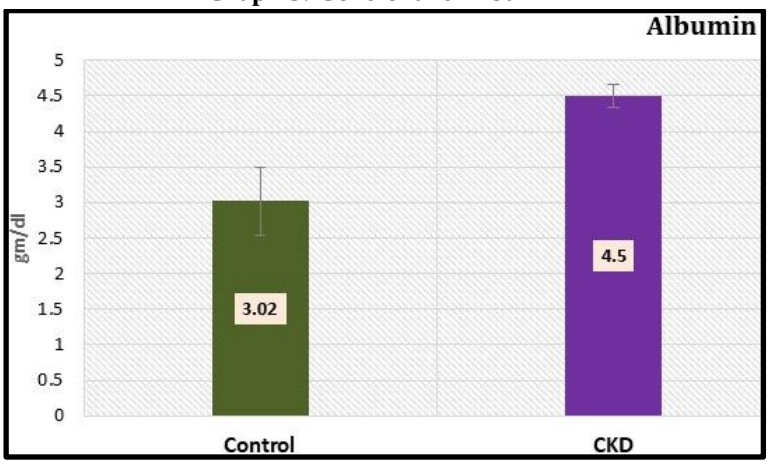
Graph 1: Control and BUN



Graph 2: Control and Serum Creatinine



Graph 3: Control and Albumin



Journal of Chemical Health Risks
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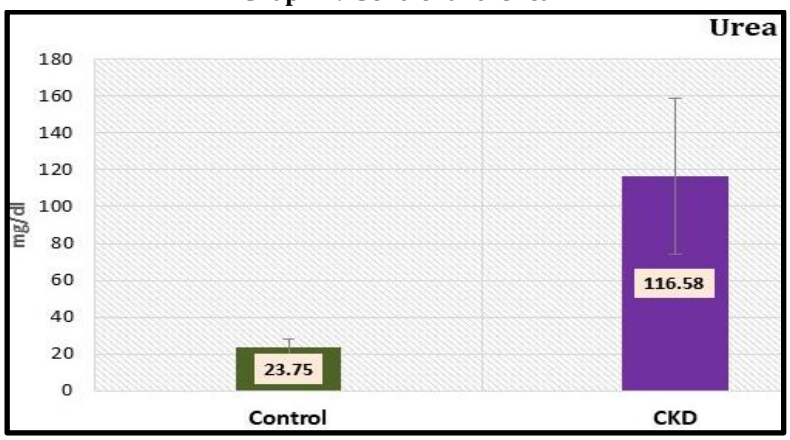
Graph 4: Control and Urea



Discussion

The study conducted shows that the patientswho visited the clinic that have chronic kidney disease have a clear association with the duration of diabetes. Most of the patients who are diabetic of more than five years are having kidney issues with a significance of p<0.001. The patients with diabetes of more than 10 years are around 60% that suffer from CKD. Low eGFR is a more significant indicator of CKD prevalence than albuminuria as people age. This is comprehensible in light of the physiological reduction in renal function that occurs with aging and is connected to a steady decline in eGFR.[12] This observation was confirmed in our study, wherein the impairment of eGFR with age was more marked (92.18 ± 2.20 vs 54.19 ± 5.70, **p<0.001**). According to our research, metformin users had a lower chance of developing proteinuria and CKD. Metformin, the main drug used to treat type 2 diabetes, was discovered to have a bad relationship with advanced CKD, albuminuria, and CKD. The reason behind these observations is yet unknown, though.[13] In the majority of animal model studies conducted in both diabetes and non-diabetic conditions, metformin has been shown to have potent inhibitory effects on tubulointerstitial fibrosis.[14] HbA1c levels were markedly higher in the CKD group (9.44 ± 0.83) compared to the control group (4.48 ± 0.72), and this difference was highly significant (p<0.001). Typically, the screening method for diabetic kidney disease is albuminuria and is regarded as the first clinical sign of the disease. However, there is growing evidence that, since the normal progression of CKD is now well understood, many adult diabetics who also have low eGFR are normo-albuminuric.[15] Among the different studies performed on diabetes patients of various racial/ethnic backgrounds, 14.29 to 56.6% of people have normoalbuminuric CKD, depending on the individual.[16,17] Although the link between albuminuria and hypertension is well known, the exact mechanism is still up for debate. It is believed to be an endothelial malfunction that results in renal manifestation and is closely linked to an elevated cardiovascular risk. When the diagnosis was made, 70–80% of people with diabetes mellitus reported having hypertension, which has been found to worsen diabetic nephropathy.[18] Our study also showed that hypertension was associated with higher degrees and CKD in patients with DM type 2 i.e. (50.8% vs 36.9%, **p<0.001).** Numerous investigations examined the connection between dyslipidemia and the onset of CKD, and numerous epidemiological studies found evidence of a link between diabetic dyslipidemia and CKD.[19] Low HDL levels of (30.92±4.95, vs 52.47±4.19**p<0.001**) and high triglyceride levels (228.70 ± 47.82 vs 116.1±29.38 **p<0.001)** were linked to CKD, according to the after-event analysis of large interventional trials of high-risk diabetic patients.[20,21] Baseline HDL levels that were lower were shown to be a substantial and significant indicator of CKD by the ADVANCE trial. However, no correlation was seen with the smoking, risk of diabetic retinopathy, indicating these microvascular problems may have different pathophysiology from the studies available.[19] In summary, diabetes type II significantly increases the risk of developing chronic kidney disease, primarily through damage to the kidney's filtering units

(glomeruli) and other associated factors. However, with careful management of blood sugar levels and blood pressure, as well as early detection and intervention, In those with type 2 diabetes, kidney disease development is frequently delayed or even stopped. Also, it's crucial to comprehend that not everyone with type 2 diabetes will develop kidney damage and that each person's course of diabetic nephropathy will be different. However, effective blood pressure and sugar management are crucial for lowering the risk of renal problems in diabetics.

Conclusion

Our results showed that more than half of the type 2 patients developed CKD, and around one-third were at intermediate risk of major adverse outcomes. CKD was linked to age, the duration of diabetes, the frequency of diabetic comorbidities, and dyslipidemia. Patients who used metformin or insulin had lower rates of CKD and proteinuria. Important information on the risk factors, epidemiological characteristics, and prevalence of CKD is provided by albuminuria. Future studies should focus on the effects of raising CKD knowledge in patients with DM type 2 by undertaking prospective studies with extensive follow-up duration in order to implement a more targeted community-based intervention.

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