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The Role of Kidney Injury Molecule-1(KIM-1) In Early Location Nephropathy of Iraqi Diabetic Patients

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Abstract

Background: Serum KIM1 is the most effective diagnostic method for type 2 diabetes with microalbuminuria (increasing the level of albumin in urine). About 50% of diabetics develop diabetic nephropathy, which is another typical consequence of hyperglycemia.

Objective: This study evaluates the impact of serum renal damage in the initial stages of diabetic nephropathy.

Study design: The current study was conducted at the Department of Medical Laboratories at Osol AL- Elm University and Baghdad Hospital in the Medical City between December 2023 and June 2024. There were 90 participants in the trial, 60 of whom had type 2 diabetes and 30 of whom were controls. The participants, who vary in age from 51 to 53, were split into three groups: 30 individuals with microalbuminuria from type 2 diabetes, 30 individuals with macroalbuminuria from type 2 diabetes, and 30 healthy controls.

Results: There was no difference significant in body mass index (BMI) and age between the study groups ($p > 0.05$), correlation analysis of the study analysis in diabetic patients with microalbuminuria, the serum KIM 1 shows a significant positive correlation with 0.708 of HbA1c% (r), P value ≤ 0.001) and urinary albumin ($r = 0.893$, P value ≤ 0.05). Serum KIM-1 shows a significant positive correlation with serum creatinine ($r = 0.792$, p-value ≤ 0.001) but a significant negative correlation with the GFR amount ($r = - 0.338$, p-value ≤ 0.001).

Conclusion: Serum KIM-1 increases significantly as eGFR decreases. Serum KIM-1 is a kidney damage marker related to the decline of kidney function in type 2 diabetes mellitus.

Keywords: Diabetes Mellitus, Type 2 Diabetes, Diabetic Nephropathy, And Serum Kidney Injury Molecule 1 (KIM-1).

1. Introduction

High levels of glucose, or blood sugar, are a hallmark of diabetes mellitus, a condition in which the body either fails to produce enough insulin or cannot react appropriately to the insulin that it does produce [1]. The two main types of diabetes are non-insulin-dependent diabetes mellitus (type 2 diabetes mellitus, or T2DM) and insulin-dependent diabetes mellitus (type 1 diabetes mellitus, or T1DM). Type 2 diabetes is the most common form of the disease, affecting 90 – 95% of its patients. Severe hyperglycemia can result in polyuria, polydipsia, weight loss, visual impairment, and even polyphagia. Chronic hyperglycemia can also hinder growth and increase susceptibility to specific illnesses [2].

A sedentary lifestyle, lack of physical exercise, smoking, and alcohol use are among the many lifestyle factors that greatly contribute to the onset of type 2 diabetes. According to extensive epidemiological studies, obesity is the main cause of type 2 diabetes. Being overweight may affect

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how insulin resistance develops and how the problem progresses. Insulin is a peptide hormone secreted by the beta cells in the pancreatic islets of Langerhans that regulates blood sugar levels. Medical intervention is required when the body requires more insulin than it produces or when its needs are greater. Because of its special characteristics, insulin is elevated in obese individuals, decreases the absorption of glucose by muscles and fat, and damages liver function [3]. Research indicates that obesity is associated with insulin resistance and beta-cell dysfunction. Because of alterations in adipose tissue biology, abdominal obesity and BMI distribution raise the risk of type 2 diabetes [4]. Additionally, diabetic neuropathy is another common outcome among diabetics, and around 50% of diabetic individuals develop diabetic nephropathy [5].

Diabetes is the primary cause of diabetic nephropathy, along with end-stage renal disease. According to statistics, 30% of diabetics have DN, which poses a serious risk to public health [6]. The complicated thing about it is the progression and development of DN with multifactorial involvement and the involvement of multiple pathways and mediators [7]. As a result, the development of diabetic nephropathy of the mechanism is conventionally thought to include hemodynamic factors, which are homeostasis abnormalities, as well as the synthesis of hormonal and metabolic abnormalities [8]. The renin-angiotensin-aldosterone system, the synthesis of advanced glycation end products (AGEs), connective tissue growth factor, protein kinase C, and the pathway are all significant contributors to the onset and progression of diabetic nephropathy [9].

People with diabetes mellitus frequently develop the clinical condition known as diabetic nephropathy. It is characterized by a decline in GFR, a progression to hypertension, and continuous albuminuria (> 200 mg/l) in two out of three exams during a period of three to six months [10]. The development and progression of diabetic nephropathy are significantly influenced by factors such as gender, race, smoking, obesity, hypertension, and hyperglycemia [11]. Usually, diabetic nephropathy develops in five stages. A higher risk of cardiovascular disease and gradual renal impairment is linked to proteinuria, whereas microalbuminuria is the result of an albumin excretion rate that varies between 20 and 200 mg/min [12].

It is more common in African Americans and Americans than in Caucasians. Since the onset of diabetic nephropathy, individuals with type 1 and type 2 diabetes have experienced adverse outcomes, including decreased GFR and hypertension [13]. Kidney injury molecule 1, a transmembrane glycoprotein present in the proximal tubular cells, is an effective biomarker with promising curative potential for acute kidney injury. If damage is sustained at this level, it escapes in the urine [14]. Early proximal tubular injury is seen in people with type 2 diabetes who have normal albuminuria and high urine KIM-1 levels. Urine production is higher overall in those with microalbuminuria. In individuals with urine albumin, KIM-1 levels eventually exceed those of those with normal albuminuria [15]. Additionally, filtration is increased in type 2 diabetics due to their higher KIM-1 clearance compared to those with normal GFR. These indicators suggest that the hyperfiltration lesion could harm the KIM1 proximal tubule [16].

2. Subjects and Methods

The current study was done at the Department of Medical Laboratories at Osol ALElm University an d Baghdad Hospital in the Medical City between December 2023 and Jun 2024. There were 90 participants in this study: 60 had type 2 diabetes and 30 served as controls. The age range of the

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participants was 51 – 53 years. Thirty type 2 diabetic patients with microalbuminuria (urinary albumin excretion < 200.0 mg/L), thirty patients with macroalbuminuria (urinary albumin excretion > 200.0 mg/L), and thirty controls were added to the three groups. According to the clinical interview, none of the patients had a history of thyroid, liver, or other endocrine diseases.

Each participant was given an appropriate disposable snap freeze container to store in a 20°C freezer as part of the urine sampling protocol. A separate urine sample was examined under the microscope, chemically, and physically to validate the ultimate choice of a subject's inclusion or exclusion from the research. To calculate body mass index (BMI), which is based on a person's weight divided by their height (kg/m^2), the weight and hypertension of all patients and controls were assessed.

3. Results

The ANOVA test revealed no statistically significant differences in Age and BMI (P value > 0.05) among the groups studied. However, Systolic & Diastolic blood pressure exhibited statistically significant differences (P value < 0.001) across the study groups, as shown in Table 1. Individuals who had macroalbuminuria had significantly greater fasting blood sugar levels (P value < 0.001) compared to those with microalbuminuria & control subjects. Additionally, HbA1c% was significantly elevated in macroalbuminuria (P value < 0.001) relative to microalbuminuria and healthy individuals. The subject is illustrated in Fig. 1. Whereas, Fig. 2 illustrates that urinary albumin was considerably greater in macroalbuminuria (P value < 0.001) than in microalbuminuria and healthy patients. Furthermore, compared to microalbuminuria and healthy participants, blood urea levels were considerably higher in macroalbuminuria (P value < 0.05).

Additionally, as shown in Fig. 3 and Table 2, serum creatinine levels were significantly higher in macroalbuminuria (P value < 0.05) compared to microalbuminuria and healthy subjects, while eGFR significantly decreased in macroalbuminuria (P value < 0.05) compared to microalbuminuria and healthy subjects. Additionally, serum kidney injury molecule-1 (S. KIM1) was significantly higher in macroalbuminuria (P value < 0.001) compared to microalbuminuria and control subjects. Serum KIM1 concentration and HbA1c% have a strong positive association, according to the Person correlation analysis ($r = 0.807$, P value ≤ 0.001) as show in Fig. 4, and significant correlation between Serum KIM1 and Urinary albumin ($r = 0.839$, P value ≤ 0.001) as show Fig. 5, also significant correlation between Serum KIM1 and serum creatinine ($r = 0.792$, P value ≤ 0.001) as shows Fig. 1.

There was a significant negative correlation between serum KIM1 and eGFR ($r = 0.338$, P value ≤ 0.001) as shown in Fig. 6, and there was a significant positive correlation between serum KIM1 and duration of diabetes ($r = 0.414$, $p = 0.02$). As shown by serum KIM1, it is the most useful diagnostic tool for type 2 diabetes with microalbuminuria, as it has a higher sensitivity (96%) than urine albumin (93%). While serum creatinine was found to be the most specific tool in the diagnosis of type 2 diabetes with microalbuminuria (96%), which is higher than GFR (73%), as shown in Table 3, with Fig. 7.

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Table 1: The study group (mean ± SD) of Age, BMI, systolic & diastolic blood pressure & duration of diabetes

Characteristics	Healthy subject	micro albuminuria	Macro albuminuria	ANOVA
Age (year)	53.5 ± 11.7	51.4 ± 10.7	51.1 ± 10.2	> 0.001
BMI (Kg/m^2)	28.5 ± 4.1	29.21 ± 3.8	30.4 ± 5.5	≥ 0.001
BP mm/Hg	123.2 ± 12.7	132.0 ± 17.1	142.0 ± 16.2	< 0.001
BP mm/Hg	75.4 ± 8.1	84.0 ± 4.8	90.5 ± 4.0	< 0.001
Duration diabetic	_	8.9 ± 2.0	10.7 ± 5.6	< 0.05

Table 2: The (mean±SD) of FBS, HbA1c%, urinary albumin, urea, creatinine, eGFR, and S.KIM-1

Characteristics	Healthy subject	micro albuminuria	Macro albuminuria	ANOVA
FBS (mg/dl)	88.33 ± 8.6	188.47 ± 13.21	239.83 ± 12.23	< 0.001
HbA1c (%)	4.9 ± 0.6	8.0 ± 1.9	12.17 ± 2.1	< 0.001
Urine albumin (mg/l)	17.83 ± 2.4	136.80 ± 28.37	224.30 ± 26.34	< 0.001
Serum urea(mg/dl)	34.4 ± 8.0	60.8 ± 12.8	67.55 ± 13.65	< 0.05
Serum Cr (mg/dl)	0.8 ± 0.20	1.53 ± 0.18	1.8 ± 0.17	< 0.05
GFR((ml/min/1.73m^2)	95.05 ± 19.0	72.37 ± 12.2	58.63 ± 12.5	< 0.05
S.KIM-1 ng/l	18.3 ± 2.9	34.50 ± 2.3	45.16 ± 2.43	< 0.001

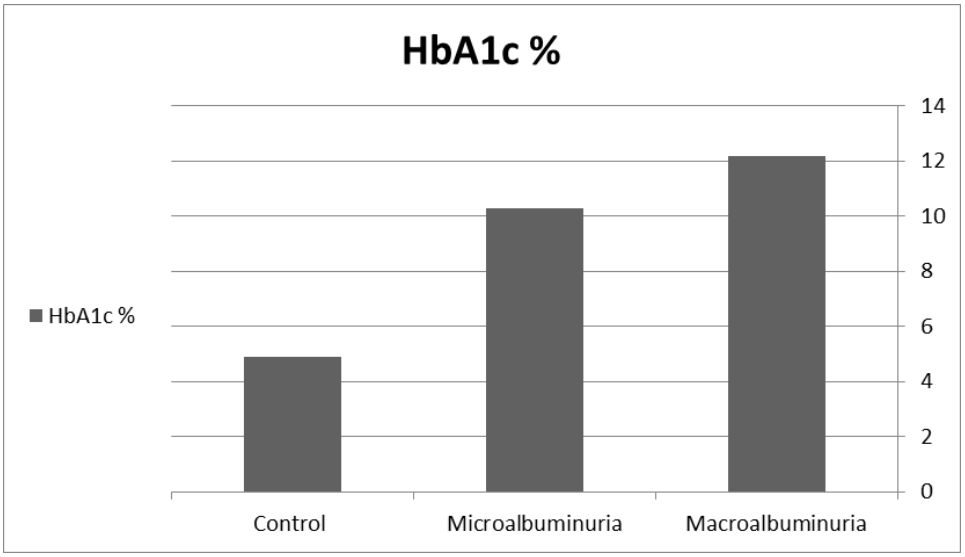

Fig. 1 The mean level of glycated hemoglobin

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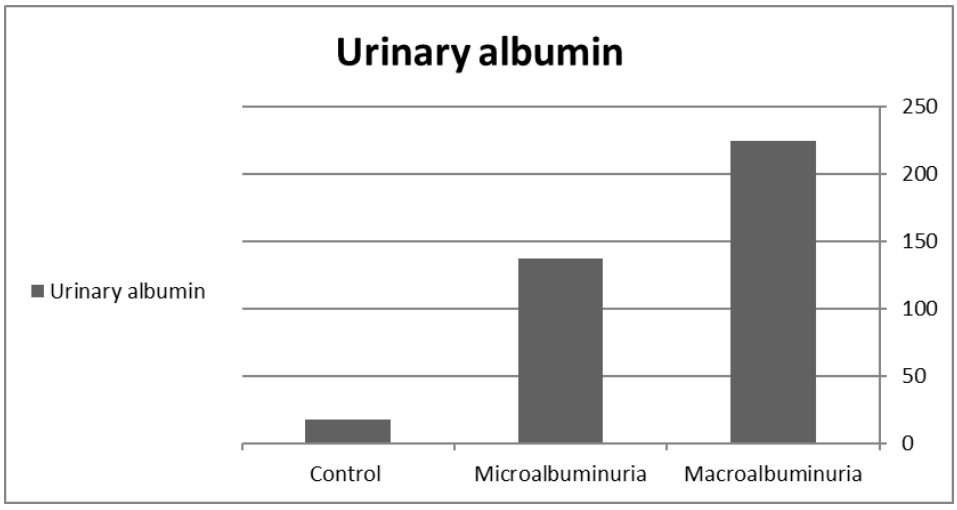

Fig. 2 The mean level of urinary albumin

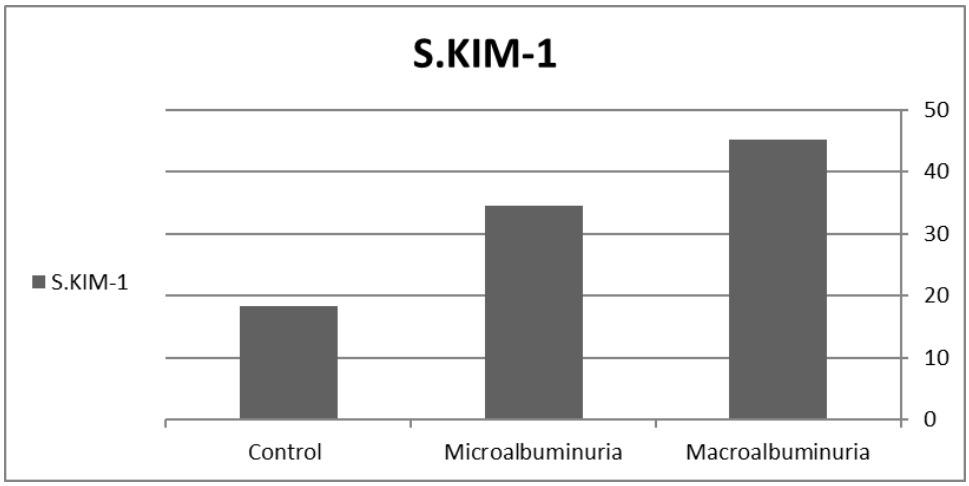

Fig. 3 The mean level of SKIM-1 of all study groups

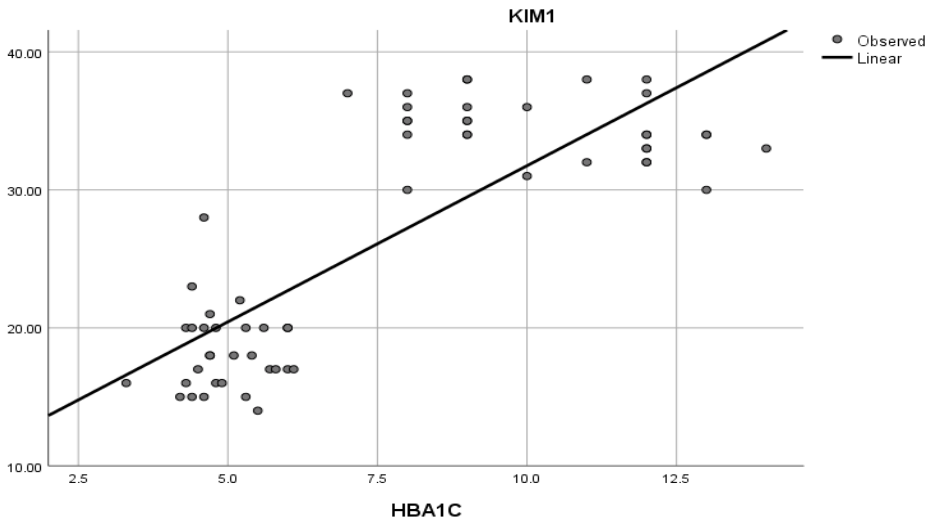

Fig. 4 The positive correlation between S.KIM-1 & HbA1c%

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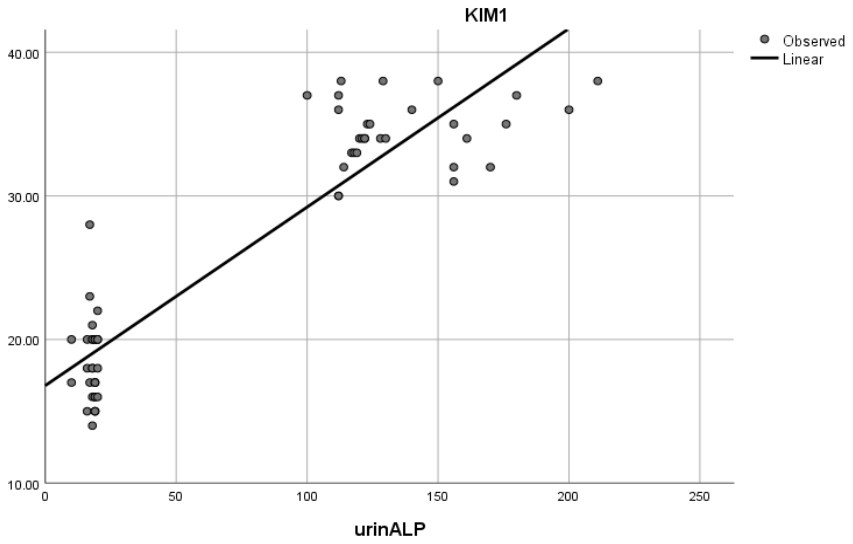

Fig. 5 The positive correlation between SKIM-1 with urinary albumin

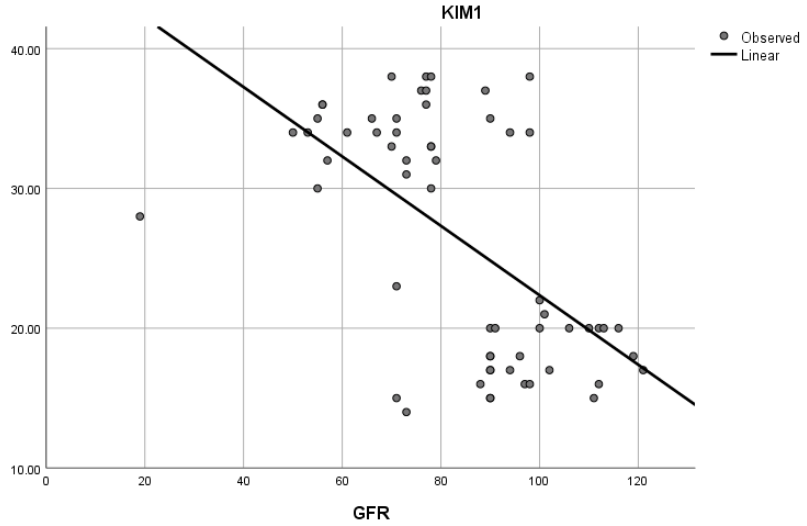

Fig. 6 The negative correlation between SKIM-1 with GFR

Table 3: Sensitivity and specificity, the area under the curve, and cut-off point of the studied marker between type 2 diabetes with microalbuminuria and healthy subjects (serum KIM-1, Urinary albumin, serum creatinine, and GFR).

Parameters	Cut-off value	Sensitivity	Specificity	AUC
Urine albumin	13.0	93 %	100 %	**1.000**
S.KIM-1	14.5	96 %	100 %	**1.000**
GFR	63.5	96 %	73 %	**0.868**
S. Creatinine	1.2	100 %	96 %	**0.014**

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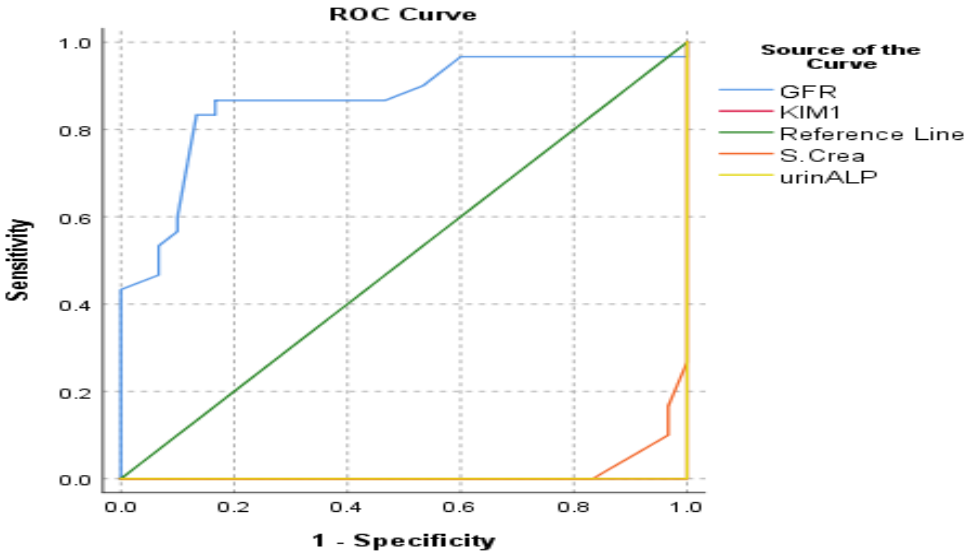

Fig. 7 The ROC between type 2 diabetes with microalbuminuria and healthy subjects

4. Discussion

One biomarker that can be suggested for identifying diabetic nephropathy early on is serum KIM-1. The longer the patient had diabetes, the more slowly the KIM-1 level rose. demonstrates that there is a detectable increase in serum KIM-1 with the duration of diabetes, indicating renal damage and the advancement of renal inflammation. It is most frequently diabetic nephropathy that causes end-stage kidney disease. Hyperglycemia is the first cause of renal damage because it activates a variety of metabolic pathways and increases oxidative stress, which leads to enhanced renal lengthening and renal damage. Given the finding that in people with type 2 diabetes, microalbuminuria is a predictor of diabetic nephropathy, associated with significant glomerular dysfunction, and a sign of the onset of renal and cardiovascular problems [17].

It is proposed that typical albuminuria may show early tubular and glomerular structural damage since renal resistance in expansion is not always represented in the dose of miniaturized albuminuria [18]. Thus, it is necessary to identify biomarkers that may be used to assess the patient's risk of infection and to search for positive and preventive effects. The results of the study showed that diabetic patients with miniaturized scale albuminuria had significantly higher serum KIM1 levels than diabetic patients with traditional albuminuria, among healthy volunteers.

Diabetes is associated with renal impairment that may not be noticed. Even when all other measures, such as urea or creatinine levels, stay within normal ranges, we have repeatedly demonstrated that KIM1 levels rise as kidney infections worsen. According to this, KIM1 levels can be utilized to detect diabetic nephropathy in diabetic patients at an early stage, since more KIM1 is released as kidney damage worsens. When the microalbuminuria in the urine is not identified in this manner, it is usually too real. Some studies have shown that people with normal albuminuria and those with diabetes have higher levels of SKIM1 and other indicators of early renal tubular damage [19].

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In this study, KIM1 levels showed a strong positive correlation with the percentage of HbA1c, a measure of glycemic control in diabetes ($r = 0.807$; P value = < 0.001). S KIM1 increased and was associated with the long-term course of diabetes mellitus, and poor glycemic control is thought to contribute to the progression of diabetic nephropathy [20].

The results of this investigation demonstrated a factually significant positive correlation between serum creatinine and urine egg white excretion and serum KIM-1. Long-term diabetes mellitus is associated with increased excretion of egg whites, and poor glycemic management is thought to contribute to the development of diabetic nephropathy [20]. It seems from this study that it found a statistically significant unfavourable connection between serum KIM1 and GFR in individuals with microalbuminuria and diabetes. In patients with type 2 diabetes mellitus and macroalbuminuria, a longitudinal study found that standard urinary KIM1 predicted either a faster fall in eGFR or a progression to end-stage renal disease [21].

5. Conclusion

This discusses elevated KIM1 levels in conjunction with dynamic renal damage, microalbuminuria, and impaired renal function. The total serum KIM1 rises as GFR declines. In type 2 diabetes mellitus, serum KIM1 is thought to be a sign of renal damage associated with decreased renal function. In diabetes mellitus, serum KIM1 is also thought to be a biomarker for the early identification of diabetic nephropathy.

Conflict of Interest

There is no conflict of Interest

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