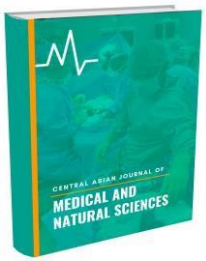

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*Article*

# Study of the Relationship of Kim-1 Correlation with Some Physiological and Biochemical Indicators in Males with Diabetic Nephropathy in Kirkuk City

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**Abstract:** This study aimed to evaluate the relationship between KIM-1 protein and biochemical markers associated with diabetes, to determine its potential role as a biological indicator of the development of diabetic nephropathy. The study was conducted in Kirkuk Governorate during the period from December 2023 to May 2024, where 90 samples were collected from government and private hospitals and specialized medical clinics, including 70 patients with diabetic nephropathy and 20 non-diabetic nephropathy. Diabetic nephropathy is a chronic complication of diabetes, characterized by a gradual deterioration in kidney function due to damage to small blood vessels due to high blood glucose levels. The KIM-1 protein (known as Kidney Injury Molecule-1) is linked to kidney damage, as it is secreted from the cells of the renal tubules in response to damage, making it a potential indicator for monitoring the progress of kidney damage in people with diabetes. In this study, the KIM-1 levels were analyzed along with variables such as HBA1C, the level of cells in the blood, insulin level, and insulin resistance, using Pearson's connection coefficient. The results showed that there is a positive overwhelming connection between the KIM-1 and the levels of cake, HBA1C, and insulin resistance at the possibility of 0.000, as well as with the level of insulin at the possibility of 0.005. These results indicate that the Kim-1 may be a useful biological indicator to assess the progress of diabetic kidney disease, which calls for more research to explore its role in improving the diagnosis and control of the disease. The study aims to contribute to the development of better treatment and monitoring strategies for diabetic patients, with the aim of reducing the complications of the disease and improving the quality of health care provided to them.

**Keywords:** Diabetic nephropathy, HbA1C, Glucose-Insulin, Insulin resistance, Renal oxidative stress

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## 1. Introduction

Diabetes Mellitus (DM) is a chronic condition that occurs as a result of the failure of the pancreas in the production of sufficient amount of insulin or when the body's production of insulin is ineffective or an insulin receptor imbalance [1]. Insulin is a hormone produced by beta cells in the pancreas and is necessary for the body to use glucose from digested food as a source of energy for [2]. DM diabetes is the most prevalent endocrine disease and is a source of health anxiety around the world in developing countries in particular and which is increasingly spread along with poor control, serious complications lead to the most common causes of diabetes and the increased death rate [3]. Diabetic nephropathy (DN) is one of the most common chronic microvascular complications of di-

abetics and the main cause of end-stage kidney disease (chronic kidney disease (CKD disease), DN diabetic nephropathy is characterized by over-filtration and albuminuria in the early stages followed by a gradual decline in kidney function [4]. It is a very prevalent condition worldwide and represents one of the most common complications of diabetes mellitus DM, and the main cause of end-stage kidney disease (ESKD) End stage kidney disease Its development includes three main axes: circulatory axes, metabolism and inflammation, clinically persistent albuminuria associated with a gradual decrease in glomerular filtration rate GFR determines this disease [5, 6]. It represents approximately 50 % of all cases of chronic or final kidney disease that require dialysis or kidney transplantation, about 40 % of patients with T2DM and 30 % of those who suffer from T1DM ultimately develop CKD (CKD (CKD) [6].

KIM-1 kidney infection is a sugar protein that is expressed by the cells of nearby tabs and is known as an early, sensitive, and specific biological sign associated with KIM-1 in the blood recently with the severity of severe and chronic renal damage [7]. The current study aims to find the correlation between KIM-1, HBA1C diabetic, glucose, insulin and insulin resistance.

## 2. Materials and Methods

### Study Design

This study was conducted for the period from December 2023 until the end of May 2024 in government and private hospitals and specialized medical clinics in the city of Kirkuk, and included (70) male patients who suffer from complications of diabetes after confirming that they are infected with ages of (40-70) years, as well as (20) healthy people with the same average age of patients.

### Blood Samples

Blood samples were collected from patients by (5) ml of vein, (1) ml of blood was placed in glass tubes containing an edta tubes, to find out the percentage of cumulative HBA1C cumulative hemocopin. The remaining amount of blood is placed (4) ml in glass tubes containing the gel and without the vaguum tube with gel and Clot Activator The sample left room temperature for 30 minutes for clotting, then the tubes were placed in the centrifugal device for (15) minutes and quickly (3000) a minute course for the serum.

### Physiological and Biochemical Tests

The concentrations of physiological and biochemical indicators of the studied groups were estimated and included the determination of the concentration of kidney injury molecule Kim-1 and the hormone insulin through the use of ready-made analysis kits (Kits) from the manufacturer Sunlong of Chinese origin using ELISA type ELISA technology as a method, and the estimation of the percentage of glycated hemoglobin HbA1c using the ready-made I analysis number (Kits) from the manufacturer Boditech of Korean origin according to the immunoassay method [8]. Serum glucose was estimated using a special ready-made kit from the French-origin Biolabo manufacturer according to [9]. It is an enzymatic method in which glucose oxidation occurs, and insulin resistance is calculated by multiplying the fasting glucose concentration mg / 100 ml by the level of fasting insulin in the blood serum and dividing it by 405 to produce a HOMA-IR index, according to the following equation [10].

$$\text{Homa-IR} = (\text{Fasting Blood Glucose} \times \text{Fasting Insulin}) \div 405$$

**Statistical Analysis**

The results obtained from the present study were analyzed statistically using SPSS software and Pearson's correlation coefficient was applied to the data to find the direction and strength of the correlation between the variables studied [11].

## 3. Results

This study, which included 90 samples, is highlighted, of which 70 are diabetic kidney disorder and 20 uninfected, an important correlation relationship between the levels of Kim-1 protein and a set of indicators associated with diabetes, as the study found positively average strength between KIM-1 and the level of both kimos and HBA1C and insulin resistance, at the probability level (P≤0,000), as well as a positive interconnection between KIM-1 and insulin level at the possibility (P≤0.005) as shown in Table (1).

**Table 1**. The correlation between KIM-1 and a number of physiological indicators in males with diabetic nephropathy.

| Correlations between KIM-1 and some parameters | | Glucose | HbA1C | Insulin | Insulin resistance |
|---|---|---|---|---|---|
| KIM-1 | r | 0.403** | 0.522** | 0.292** | 0.470** |
| | Sig | 0.000 | 0.000 | 0.005 | 0.000 |

**Correlations is significant at the 0.01 level

## 4. Discussion

**Correlation between kim-1 and HbA1C level**

The results of the study indicated in schedule (1) of the presence of an obligatory connection (r = 0.522) with statistical significance (P≤0,000) between Kim-1 and the level of HBA1C in the study samples. These results came in compliance Answer (r = 0.88) between the two variables in the patients of diabetic (Nephropathy). Several other studies, including the study of both [12], and the study [13] indicated that patients with high levels of Hb1AC (higher than 7 % From the normal limit) they show a higher level than Kim-1 This rise in KIM-1 reflects an increase in kidney tissue damage as a result of poor control of sugar levels. This association may also be attributed to inflammation, as an increase in Hb1AC leads to increased inflammation, oxidative stress through increased production of free radicals in the kidneys, which contributes to an increase in KIM-1 levels, which plays a vital role in the development of diabetic nephropathy [14, 15]. Persistent high glucose level leads to abnormal activation of mitochondrial stress and intracellular signaling pathways, leading to stress Cells and their dysfunction Furthermore, abnormal activation promotes additional activation of inflammatory factors, leading to primary damage to renal tissue and tubules [16].

**Correlation between KIM-1 and glucose level**

The results of the study shown in Table (1) showed a statistically significant positive association (r≤0.403) between KIM-1 and the level of glucose in the study samples, and

these results were consistent with what [17] came out, as they revealed a positive association ($P < 0.001$) between KIM-1 and diabetes and fasting blood glucose As high blood sugar causes a cellular injury, which leads to the release of inflammatory media that include chemical compounds, including cytokines and kimokins such as tumor necrosis factor ((TNF-$\alpha$ Interleukin-1 , adhesion Particles and associated molecular patterns and molecular patterns. The damage that attracts the immune cells to the location of the injury, which leads to the enhancement of inflammatory reactions, reduces the level of oxygen and damages the cells, in addition to that causes a high level of kidney infection molecule in conditions of hypoxia causes a cellular balance disorder, and leads to diabetic kidney disease [18] . The high level of glucose in the blood leads to the damage of the cabinet cells directly, which leads to a wide range of metaphysical and cellular imbalances, and excessive production of interactive oxygen types ROS and stimulating the path of programmed cell death are interconnected mechanisms that perform pivotal roles in the development of DKD, although that Epual tuberculosis cells contain large numbers of mitochondria, but the ancient cells, mabareg cells and cabinian ventricular cells may all be affected by the infection of the mitochondria caused by diabetes [19, 20].

**Correlation between Kim-1 and the level of insulin**

The results of the study shown in schedule (1) showed a positive correlation ($r = 0.292$) with statistical significance ($P \leq 0.005$) between Kim-1 and the level of insulin in the study samples. These results came compatible with [21] as they showed the link The big and positive between Kim-1, obesity indicators, insulin state, signs of oxidative stress, and their potential effect in causing kidney abnormalities, as the increasing inflammatory activity as a result of continuous renal damage to weakening the body's sensitivity to insulin and as a result, the levels of kidney infection are significantly increasing in the case of kidney inflammation, as patients are Those who suffer from kidney dysfunction are very vulnerable to oxidative stress, leading risk factors such as diabetes, kidney hypotension, dialysis and aging to increase the levels of interactive oxygen types and then increase the kidney infection molecule [22]. The most common cause of the high concentration of insulin in people with diabetes is that insulin resistance (resistance to insulin in enhancing the absorption of glucose by muscle and fatty cells) preceded and caused an overall insulin from the blood. Blood sugar and type 2 diabetes after years or even later contracts, yet in the studies of association at the genome level, insulin resistance is referred to as the main cause of type 2 diabetes, in addition to that, some of them are due to defects in the beta cell in the pancreas [23].

**Correlation between Kim-1 and insulin resistance**

The results of the study shown in schedule (1) showed a positive correlation (0.470 R = statistical significance ($P \leq 0{,}000$) between Kim-1 and the level of insulin resistance in the study samples. These results came in compliance with the [24] and the study of [25], which indicated the existence of a great positive connection between the Kim-1 and the level of insulin resistance in patients with diabetic kidney disease, while insulin resistance cannot secrete the hormone from beta cells in the pancreas that leads to the absorption of glucose in the tissues, which leads to high levels of glucose in the blood , Type 2 diabetes begins to decrease a gradual decrease in the work of insulin. Which leads to the removal of insulin receptors 'sensitivity to compensate for insulin resistance. The body produces additional insulin to facilitate the balance of glucose, which leads to a high level of insulin in the blood [26]. The high levels of the KIM-1 kidney infection in patients with diabetic kidney disease are attributed to a disorder in the renal tabs and also due to the kidney inflammation caused by the high level of sugar, as its levels increase in diabetics. Disorder in the kidney tubes, even if the albumin night levels are within Natural limits [27]. In addition, KIM-1 levels increase as a result of insulin resistance, which is closely related to oxidative stress resulting from high blood sugar level, as the increased levels of reactive

oxygen species (ROS) in the kidneys lead to damage to essential cellular components and DNA, as well as dysfunction in the endothelium, which is a characteristic feature of T2DM and diabetic kidney disease (DKD) [28].

## 5. Conclusion

These results indicate that Kim-1 may play a decisive role as a biological indicator to assess the risk or progress of diabetic kidney disease. These connections may reflect pathological changes in kidney function associated with poor control of blood sugar levels and insulin resistance. Therefore, it may be important to explore the role of Kim-1 in a deeper way in future studies, to verify its effectiveness as a diagnostic tool or as a standard for estimating the development of the disease, which may help improve treatment and monitoring strategies for diabetics at risk of kidney disease.

## REFERENCES


[1] N. M. Jasem and A. S. Abdul-Razaq, 'Evalution of Biomarkers in Iraq Patients with Diabetes Mellitus Type 2', *Egypt. J. Hosp. Med.*, vol. 90, no. 2, pp. 3062–3066, 2023.

[2] N. Rachdaoui, 'Insulin: the friend and the foe in the development of type 2 diabetes mellitus', *Int. J. Mol. Sci.*, vol. 21, no. 5, p. 1770, 2020.

[3] F. Bandarian, M. Omidvar, R. Farideh, E. Nasli-Esfahani, S. Saeedi, and B. Larijani, 'Iran diabetes research roadmap (IDRR) study; knowledge gap in Ge-netic research on diabetes mellitus in Iran: a review article', *Iran. J. Public Health*, vol. 46, no. Supple 1, pp. 53–59, 2017.

[4] M. K. Sagoo and L. Gnudi, 'Diabetic Nephropathy: An Overview', in *Diabetic Nephropathy*, vol. 2067, L. Gnudi and D. A. Long, Eds., in Methods in Molecular Biology, vol. 2067. , New York, NY: Springer US, 2020, pp. 3–7. doi: 10.1007/978-1-4939-9841-8_1.

[5] J. Rico-Fontalvo *et al.*, 'Novel biomarkers of diabetic kidney disease', *Biomolecules*, vol. 13, no. 4, p. 633, 2023.

[6] V. Vallon and S. C. Thomson, 'The tubular hypothesis of nephron filtration and diabetic kidney disease', *Nat. Rev. Nephrol.*, vol. 16, no. 6, pp. 317–336, 2020.

[7] B. Brilland *et al.*, 'Kidney injury molecule 1 (KIM-1): A potential biomarker of acute kidney injury and tubulointerstitial injury in patients with ANCA-glomerulonephritis', *Clin. Kidney J.*, vol. 16, no. 9, pp. 1521–1533, 2023.

[8] D. E. Goldstein *et al.*, 'Tests of glycemia in diabetes', *Diabetes Care*, vol. 27, no. 7, pp. 1761–1773, 2004.

[9] P. Trinder, 'Determination of Glucose in Blood Using Glucose Oxidase with an Alternative Oxygen Acceptor', *Ann. Clin. Biochem. Int. J. Lab. Med.*, vol. 6, no. 1, pp. 24–27, Jan. 1969, doi: 10.1177/000456326900600108.

[10] T. M. Wallace, J. C. Levy, and D. R. Matthews, 'Use and abuse of HOMA modeling', *Diabetes Care*, vol. 27, no. 6, pp. 1487–1495, 2004.

[11] C. Heumann, M. Schomaker, and Shalabh, *Introduction to Statistics and Data Analysis*. Cham: Springer International Publishing, 2016. doi: 10.1007/978-3-319-46162-5.

[12] K. Siddiqui, S. S. Joy, T. P. George, M. Mujammami, and A. A. Alfadda, 'Potential Role and Excretion Level of Urinary Transferrin, KIM-1, RBP, MCP-1 and NGAL Markers in Diabetic Nephropathy', *Diabetes Metab. Syndr. Obes. Targets Ther.*, vol. Volume 13, pp. 5103–5111, Dec. 2020, doi: 10.2147/DMSO.S282166.

[13] A. A. Yahya, D. J. Kadhim, and N. A. Abdalhadi, 'Kidney injury molecule-1 and cystatin C as early biomarkers for renal dysfunction in Iraqi type 2 diabetes mellitus patients', *J. Adv. Biotechnol. Exp. Ther.*, vol. 6, no. 3, 2023, Accessed: Aug. 17, 2024. [Online]. Available: https://www.academia.edu/download/106723075/178_1686643151.pdf

[14] H. A. El-Attar, G. I. Khalil, and E. W. Gaber, 'Human kidney injury molecule-1 (Kim-1) level as an early marker for diabetic nephropathy in Egyptian type 2 diabetic patients', *J. Ren. Med.*, vol. 1, no. 3, pp. 1–13, 2017.

[15] H. Ghasemi, B. Einollahi, N. Kheiripour, S.-R. Hosseini-Zijoud, and M. F. Nezhad, 'Protective effects of curcumin on diabetic nephropathy via attenuation of kidney injury molecule 1 (KIM-1) and neutrophil gelatinase-associated lipocalin (NGAL) expression and alleviation of oxidative stress in rats with type 1 diabetes', *Iran. J. Basic Med. Sci.*, vol. 22, no. 4, p. 376, 2019.

[16] G. H. Tesch, 'Diabetic nephropathy–is this an immune disorder?', *Clin. Sci.*, vol. 131, no. 16, pp. 2183–2199, 2017.

[17] D. Balu, V. Krishnan, V. Krishnamoorthy, R. S. Singh, S. Narayanasamy, and G. Ramanathan, 'Does serum kidney injury molecule-1 predict early diabetic nephropathy: A comparative study with microalbuminuria', *Ann. Afr. Med.*, vol. 21, no. 2, pp. 136–139, 2022.

[18] J. Barrera-Chimal and F. Jaisser, 'Pathophysiologic mechanisms in diabetic kidney disease: A focus on current and future therapeutic targets', *Diabetes Obes. Metab.*, vol. 22, no. S1, pp. 16–31, Apr. 2020, doi: 10.1111/dom.13969.

[19] S. M. Abdullah, S. J. Abdulrahman, and A. A. Hayder, 'Assessment of the Effect of Propolis Extract on Enzymatic Antioxidants and Lipidperoxidation', 2024, Accessed: Apr. 24, 2024. [Online]. Available: https://www.researchgate.net/profile/Adil-Hassan-5/publication/378976972_Assessment_of_the_Effect_of_Propolis_Extract_on_Enzymatic_Antioxidants_and_Lipidperoxidation/links/65f49a39c05fd2688015d229/Assessment-of-the-Effect-of-Propolis-Extract-on-Enzymatic-Antioxidants-and-Lipidperoxidation.pdf

[20] P. Z. Wei and C. C. Szeto, 'Mitochondrial dysfunction in diabetic kidney disease', *Clin. Chim. Acta*, vol. 496, pp. 108–116, 2019.

[21] N. Polidori *et al.*, 'Role of urinary NGAL and KIM-1 as biomarkers of early kidney injury in obese prepubertal children', *J. Pediatr. Endocrinol. Metab.*, vol. 33, no. 9, pp. 1183–1189, Sep. 2020, doi: 10.1515/jpem-2020-0138.

[22] S. Verma *et al.*, 'Implications of oxidative stress in chronic kidney disease: a review on current concepts and therapies', *Kidney Res. Clin. Pract.*, vol. 40, no. 2, p. 183, 2021.

[23] R. N. Bergman, F. Piccinini, M. Kabir, C. M. Kolka, and M. Ader, 'Hypothesis: role of reduced hepatic insulin clearance in the pathogenesis of type 2 diabetes', *Diabetes*, vol. 68, no. 9, pp. 1709–1716, 2019.

[24] M. H. Ahmed, N. H. Abdullah, S. O. Mostafa, A. T. Abd Elaal, and H. S. Matar, 'Relation Between Kidney Injury Molecule 1 (KIM 1) And Diabetic Nephropathy', *Egypt. J. Med. Res.*, vol. 5, no. 1, pp. 80–91, 2024.

[25] R. H. H. Al-Abbadi and S. J. Abdulrahman, 'Assessment the role of Kidney injury molecule-1, Endostatin, and Insulin resistance in patients with Diabetic nephropathy in Kirkuk/Iraq', *Afr.J.Bio.Sc.*, vol. 6, no. 4, pp. 155–164, 2024.

[26] L. Dilworth, A. Facey, and F. Omoruyi, 'Diabetes mellitus and its metabolic complications: the role of adipose tissues', *Int. J. Mol. Sci.*, vol. 22, no. 14, p. 7644, 2021.

[27] J. Geng, Y. Qiu, Z. Qin, and B. Su, 'The value of kidney injury molecule 1 in predicting acute kidney injury in adult patients: a systematic review and Bayesian meta-analysis', *J. Transl. Med.*, vol. 19, no. 1, p. 105, Dec. 2021, doi: 10.1186/s12967-021-02776-8.

[28] T. Honda, Y. Hirakawa, and M. Nangaku, 'The role of oxidative stress and hypoxia in renal disease', *Kidney Res. Clin. Pract.*, vol. 38, no. 4, p. 414, 2019.