

## **Study of Micro albuminuria and HbA1c in type 2 Diabetes Mellitus Patients in Shendi town\_sudan- case control based study**

### **Abstract:**

**Background:** Diabetes mellitus (DM) is a systemic metabolic disorder that can lead to diabetic nephropathy (DN), a leading cause of end-stage renal disease around the world.

**Objectives:** The purpose of this study was to compare microalbuminuria and glycosylated hemoglobin (HbA1c) levels in patients with diabetes mellitus to healthy normal controls in Shendi, Sudan.

**Materials and Methods:** This hospital-based case-control study was carried out in Shendi, Sudan. Between June and October of 2021 This study included 50 participants, 30 of whom had clinically confirmed diabetes as cases and 20 who appeared to be healthy as controls. In this study, blood and random urine samples were collected from each case and control, and the levels of microalbuminuria and hemoglobin A1C (HbA1C) were estimated using an A25 chemistry analyzer and an Ichroma immuno-analyzer, respectively. The data was collected with a structured questionnaire and analyzed with SPSS version 20.

**Results:** In our study, patients had higher mean microalbuminuria than controls (26.438.2 vs 11.4 9.2 mg/l, P value = 0.000). This study found a significant increase in mean hemoglobin A1C levels in the case group compared to the control group (7.382.2 vs5.7 0.76% P value = 0.001). Our findings also revealed that there was no relationship between microalbuminuria and disease duration.

**Conclusions:** Microalbuminuria levels were higher when compared to controls. In comparison to the control group, HbA1c levels were higher. Microalbuminuria and patient age had a weak positive correlation in our study group.

**Keywords:** diabetes mellitus type 2, Microalbuminuria, HbA1C.

## **Introduction:**

Diabetes is a metabolic disorder of global importance, characterized by varying degrees of insulin resistance, impaired insulin secretion, and increased glucose production. The International Diabetes Federation (IDF) estimates that 536.6 million adults worldwide had T2DM in 2021 and that by 2045, 783.2 million people would have the disease (12.2% of the population). The World health organization (WHO) determined that the Eastern Mediterranean region has the highest prevalence of DM. In this region, DM is highly prevalent in seven countries and is moderately prevalent (9–12%) in another seven countries, including Sudan. Type 2 diabetes mellitus (T2DM), accounts for about 90% of all cases in Africa. Sudan was one of the nations with a prevalence of DM of more than 12%, with an estimated 3.3% prevalence in Africa in 2017.[1]. “The consequences of diabetes mellitus include long-term damage, dysfunction, and dysfunction of various organs. The two main types of this syndrome are type 1 (usually onset in childhood and adolescence and patients require lifelong insulin injections for survival), and patients with type 2 diabetes mellitus have high It has a long asymptomatic glyceimic period and often develops many complications by the time of diagnosis” [2]. “Diabetic nephropathy is a common consequence of long-standing diabetes mellitus. It is characterized by the presence of large amounts of proteins, mainly albumin, in the urine. Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD) in the United States and the leading cause of diabetes-related morbidity and mortality” [3].

“Glycosylated hemoglobin (HbA1c) is a glyceimic control marker in diabetic patients. HbA1c is the result of post-translational alterations in the hemoglobin molecule, and its levels correlate well with blood glucose levels over the past 6-10 weeks. Glycosylation of hemoglobin occurs under physiological conditions by a reaction between glucose and the N-terminal valine of the beta chain of the molecule” [4]. “Higher HbA1C levels are

associated with the risk of developing microangiopathy in diabetic patients. associated with an increase. This may be due to the fact that HbA1c has a specific affinity for oxygen, causing tissue anoxia and being involved in the development of micro- and macroangiopathy” [5]. “Several studies have shown a positive correlation between microalbuminuria and HbA1c” [6,7]. “347 million people worldwide have diabetes” [8]. “An estimated 3.4 million people died in 2004 from high fasting blood sugar” [9]. “More than 80% of deaths from diabetes” [10]. “Recent statistics from the World Health Organization (WHO) predict that the prevalence of diabetes will increase worldwide, especially in developing countries” [11]. “India currently has the highest number of people with diabetes, and this number is expected to increase further in the coming years” [11,12].

“In diabetic patients, microalbuminuria is an early sign of nephropathy or renal damage. The increase in urine albumin excretion (30–300 mg/day) or (20–200 mg/day) is known as microalbuminuria. The screening method of choice is urine albumin/creatinine ratio (urine ACR). When urine ACR levels range from 30 to 300 mg/g, microalbuminuria is identified” [13-16]. Identification of these patients for prompt implementation of appropriate therapeutic measures should therefore be a key factor. Patients with type 2 DM will likely find that therapeutic measures to improve blood pressure control and decrease microalbuminuria are the most effective means of delaying the progression of both renal and cardiovascular diseases or complications [17-20].

Despite increased attention in various parts of the world on the role of biochemical parameters in the progression and management of diabetes mellitus, there is still a scarcity of information in Sudan on the inter-relationship between these markers and the presence of microvascular complications, particularly in relation to disease duration. Therefore, The purpose of this study was to compare microalbuminuria and glycosylated hemoglobin (HbA1c) levels in patients with diabetes mellitus to healthy normal controls in Shendi, Sudan.

## **Materials and methods:**

### **Study design:**

Case-control study conducted in Shendi City from June to October 2021. In this study, a total of 50 subjects were included of which 30 are diabetic patients as cases and 20 apparently healthy subjects as a control group. All subjects included in this study were fully informed of the purpose of the study. Prophylactic samples were taken with full commitment, privacy, and confidentiality. Analytical results were used for clinical diagnosis and were provided free of charge to all patients participating in the study. Patients with renal disease were excluded from this study.

### **Inclusion and Exclusion criteria**

Adult patients with type 2 diabetes mellitus were and apparently healthy individuals were included in this study. Subjects with Type 1 DM, T2DM undergoing dialysis, macroalbuminuria, known case of renal failure, nephrotic syndrome, urinary tract infection, haematuria, ketonuria, pregnancy, heart failure, vigorous exercise before collecting the sample and use of systemic steroids in past four weeks were excluded.

### **Sample collection and analysis**

Blood samples were collected using a topical skin antiseptic (70% ethanol). Five ml of venous blood was collected from each diabetic and non-diabetic control male and female using sterile disposable plastic syringes. Blood was collected from the cuboid vein or the back of the hand. Puncture urine samples were collected and refrigerated at -20 °C. Blood and random urine sample were estimated for the level of microalbuminuria and hemoglobin A1C (HbA1C) by using A25 chemistry analyzer and Ichroma immuno-analyzer respectively.

### **Data collection and analysis**

Data was collected by using structured questionnaire and analyzed by using SPSS version 20.

### **Results:**

The analysis shows the baseline characteristics of the study groups between the patient mean and the control group, with significant differences in microalbuminuria between cases and controls ( $26.4 \pm 38.2$  vs  $11.4 \pm 9.2$  mg/l,  $P$  value = 0.001) (**table 1**). We also show the baseline characteristics of hemoglobin A1c between the means of patients and controls, the significant difference in hemoglobin A1c between cases and controls ( $7.38 \pm 2.2$  vs  $5.7 \pm 0.76$  %  $P$  value = 0.001) (**table 1**). The analysis also shows The correlation between Microalbuminuria and (hba1c , year , duration , gender ,type , disease) by use Correlation coefficient(Pearson , spearman's) and probability value ( $P$ -value =0.05) .the correlation between Microalbuminuria and hba1c by used Pearson Correlation coefficient there is no correlation ( $r=0.3$  ,  $p$ -value =0.09) (**table 2**). The correlation between Microalbuminuria and year by used spearman's Correlation coefficient there is significant weak positive correlation ( $r=0.4$   $p$ -value =0.007), and the correlation between Microalbuminuria and (duration , gender, type ,disease) by used spearman's Correlation coefficient there is no correlation ( $r=0.26$ ,  $p$ -value =0.15), ( $r=-0.15$ ,  $p$ -value =0.40), ( $r=-0.02$ ,  $p$ -value =0.88) , ( $r=-0.03$ ,  $p$ -value=0.85 ) respectively (**table 2**).

**(Table 1):** The mean, standard deviation, and probability value (*P-value*) of Microalbuminuria, and HbA1C.

<i>Test</i>	<i>Groups</i>	<i>Mean ± SD</i>	<i>P-value</i>
Microalbuminuria (mg/l)	<i>Case</i>	26.4 ±38.2	0.001
	<i>Control</i>	11.4 ± 9.2	
HbA1c (%)	<i>Case</i>	7.38± 2.2	0.000
	<i>Control</i>	5.7 ± 0.76	

**(Table 2):** The correlation between Microalbuminuria and (hba1c , year , duration , gender)

<i>Variables</i>	<i>Correlation coefficient</i>	<i>P-value</i>	<i>Decision</i>
Microalbuminuria vs hba1c	0.3	0.09	No correlation
Microalbuminuria vs age/years	0.4	0.007	weak correlation
Microalbuminuria vs duration of disease	0.26	0.15	No correlation
Microalbuminuria vs gender	-0.15	0.40	No correlation

- **Discussion:**

Microalbuminuria is an early predictor and sensitive assay for detecting urinary albumin excretion that may precede the development of overt nephropathy in diabetes. Prompt detection and treatment can reduce risk and delay the onset of ESRD. The study was conducted with a test group of 30 diabetic patients and a control group of 20 healthy non-diabetic patients. The frequency results indicated that DM was similar in females and males, with percentages in females (50%) and males (50%). When blood glucose levels rise, glucose binds to proteins, resulting in excessive protein glycosylation and increased glycated end-products. Glomerular deposition of these advanced glycation end-products is increased, leading to renal and glomerular hypertrophy and thickening of the glomerular basement membrane. This allows albumin (a low molecular weight protein) to leak out. This condition is called early nephropathy [microalbuminuria]. In this study, there was a significant increase in microalbuminuria in case studies compared to controls ( $p$  value = 0.000). Similarly, another study found that microalbuminuria was as higher (in terms of higher HbA1c) in patients with uncontrolled type 2 diabetes mellitus [21]. The current study shows a highly significant increase in glycated hemoglobin levels in the test group compared to the control group ( $P$ -value = 0.001). This study is consistent with previous study finding [22]. Elevated levels of urinary FBG, HbA1c, and microalbumin were evident compared to controls. The mean  $\pm$  SD of FBG, HbA1c, and urinary microalbumin were statistically significantly increased in diabetic compared with non-diabetic patients ( $P < 0.0001$ ). Similarly, another study found that glycated hemoglobin and fasting blood glucose levels were significantly increased in the diabetic group compared to healthy subjects ( $p$ -value = 0.001) [23]. Also in this study, there was a significant weak positive correlation between years of diabetes mellitus and microalbuminuria in the test group ( $r = .0392$ ,  $p$ -value 0.03). Based on the results of this study, we recommend the following: Diabetics should be checked for microalbuminuria annually to assess kidney status. All people with diabetes should have their HbA1c

measured at least every 6 months. Further studies are needed to determine other parameters for assessing nephropathy, especially in diabetes.

### **Conclusion:**

The level of microalbuminuria was increased among cases group compared to the control group. HbA1c levels were increased among cases group compared to the control group. In our study group, there was a weak positive correlation between microalbuminuria and patient age. It's recommended that in the future studies to include patients diabetes disease status if its controlled or not to understand the treatment effect on the microalbuminuria and HbA1C.

### **Consent**

Patients undergoing the test were given explanations of the venous blood sample process. All participants were informed about the research objectives and procedures during the interview period. Written valid consent was obtained from all participants. All result was with high privacy and confidentiality.

### **Ethical Approval**

Approval for this study was obtained from the Ethics Committee of the Department of Clinical Laboratory Sciences.

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There was no specific grant for this research from any funding organization in the public, private, or nonprofit sectors.

### **Conflict of Interest:**

The author has affirmed that there are no conflicting interests.

### **References:**

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JCN, Mbanya JC, et al. IDF Diabetes Atlas: Global, regional

- and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract.* 2022; 183:109119.
2. Satchell SC, Tooke JE. What is the mechanism of microalbuminuria in diabetes: a role for the glomerular endothelium? *Diabetologia.* 2008 May;51(5):714-25. doi: 10.1007/s00125-008-0961-8. Epub 2008 Mar 18. PMID: 18347777; PMCID: PMC2292427.
  3. Powers A C. Diabetes Mellitus. In: Jameson JL. (editor) *Harrison's Endocrinology.* 1st ed. New York: McGraw-Hill;2006. p 303-4.
  4. Kareem I, Jaweed SA, Bardapurkar JS, Patil VP. Study of magnesium, glycosylated hemoglobin and lipid profile in diabetic retinopathy. *Indian J Clin Biochem.* 2004; 19(2):124-127. doi:10.1007/BF02894270
  5. Davis RE, Nicol DJ, McCann VJ, Calder JS. Glycosylated haemoglobin levels in patients with diabetes mellitus. *Med J Aust.* 1978;1(10):530-532. doi:10.5694/j.1326-5377.1978.tb141945.x
  6. Gupta DK, Verma LK, Khosla PK, Dash SC. The prevalence of microalbuminuria in diabetes: a study from north India. *Diabetes Res Clin Pract.* 1991;12(2):125-128. doi:10.1016/0168-8227(91)90089-v
  7. Schmitz A, Vaeth M. Microalbuminuria: a major risk factor in non-insulin-dependent diabetes. A 10-year follow-up study of 503 patients. *Diabet Med.* 1988;5(2):126-134. doi:10.1111/j.1464-5491.1988.tb00958.x
  8. Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet.* 2011;378(9785):31-40. doi:10.1016/S0140-6736(11)60679-X

9. Tomic D, Shaw JE, Magliano DJ. The burden and risks of emerging complications of diabetes mellitus. *Nat Rev Endocrinol*. 2022;18(9):525-539. doi:10.1038/s41574-022-00690-7
10. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*. 2006;3(11): e442. doi:10.1371/journal.pmed.0030442
11. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract*. 2019; 157:107843. doi: 10.1016/j.diabres.2019.107843
12. Ramachandran A, Snehalatha C, Latha E, Vijay V, Viswanathan M. Rising prevalence of NIDDM in an urban population in India. *Diabetologia*. 1997;40(2):232-237. doi:10.1007/s001250050668
13. Fotheringham J, Odudu A, McKane W, Ellam T. Modification of the relationship between blood pressure and renal albumin permeability by impaired excretory function and diabetes. *Hypertension*. 2015;65(3):510-516. doi:10.1161/HYPERTENSIONAHA.114.04656.
14. Keen H, Chlouverakis C, Fuller J, Jarrett RJ. The concomitants of raised blood sugar: studies in newly-detected hyperglycaemics: II. Urinary albumin excretion, blood pressure and their relation to blood sugar levels. *Int J Epidemiol*. 2014;43(1):11-15. doi:10.1093/ije/dyt257.
15. Tankeu AT, Kaze FF, Noubiap JJ, Chelo D, Dehayem MY, Sobngwi E. Exercise-induced albuminuria and circadian blood pressure abnormalities in type 2 diabetes. *World J Nephrol*. 2017;6(4):209-216. doi:10.5527/wjn.v6.i4.209.
16. Steppel JH, Horton ES. Exercise in the management of type 1 diabetes mellitus. *Rev Endocr Metab Disord*. 2003;4(4):355-360. doi:10.1023/a:1027302112655.

17. Viberti GC, Hill RD, Jarrett RJ, Argyropoulos A, Mahmud U, Keen H. Microalbuminuria as a predictor of clinical nephropathy in insulin-dependent diabetes mellitus. *Lancet*. 1982;1(8287):1430-1432. doi:10.1016/s0140-6736(82)92450-3
18. Hommel E, Mathiesen E, Edsberg B, Bahnsen M, Parving HH. Acute reduction of arterial blood pressure reduces urinary albumin excretion in type 1 (insulin-dependent) diabetic patients with incipient nephropathy. *Diabetologia*. 1986;29(4):211-215. doi:10.1007/BF00454877.
19. Maahs DM, Snively BM, Bell RA, et al. Higher prevalence of elevated albumin excretion in youth with type 2 than type 1 diabetes: the SEARCH for Diabetes in Youth study. *Diabetes Care*. 2007;30(10):2593-2598. doi:10.2337/dc07-0450
20. Tobe SW, McFarlane PA, Naimark DM. Microalbuminuria in diabetes mellitus. *CMAJ*. 2002;167(5):499-503.
21. Sana MA, Chaudhry M, Malik A, Iqbal N, Zakiuddin A, Abdullah M. Prevalence of Microalbuminuria in Type 2 Diabetes Mellitus. *Cureus*. 2020;12(12):e12318. Published 2020 Dec 27. doi:10.7759/cureus.12318.
22. Rao Deepika PC, Saxena RM. Comparison of glycosylated hemoglobin levels in severe periodontitis patients and healthy controls: a study in an Indian population. *Quintessence Int*. 2013;44(4):319-325. doi:10.3290/j.qi.a29144.
23. Ghazanfari Z, Haghdoost AA, Alizadeh SM, Atapour J, Zolala F. A Comparison of HbA1c and Fasting Blood Sugar Tests in General Population. *Int J Prev Med*. 2010;1(3):187-194.