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THE RELATIONSHIP BETWEEN MICROALBUMINURIA AND GLOMERULAR FILTRATION RATE IN TYPE 1 DIABETIC CHILDREN: HOSPITAL BASED STUDY

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ABSTRACT

Background: Diabetics' first indicator of nephropathy is microalbuminuria. Early identification of microalbuminuria in diabetics is essential for preventing and treating diabetic nephropathy. The aim of this study was to examine the relationship between glomerular filtration rate (GFR) and urine albumin excretion in children with type 1 diabetes (T1DM) and its importance in detection of diabetic nephropathy. **Method:** This cross-sectional study was conducted at the emergency and diabetes clinics of Children Welfare Teaching Hospital-Medical City/Baghdad from February 1 to August 31, 2023. In a study of 123 children with T1DM, 75 were female and 48 were male. They ranged in age from 5-13.5, with a duration of diabetes from 2-11 years. Patients were admitted with RBS >300 mg/dl and had blood samples taken for serum creatinine and RBS testing. GFR was estimated using Schwartz formula in all patients. Urine from the first morning was tested for albumin: creatinine ratio. A paired sample T test and 0.05 statistical significance were used to analyses data. **Results:** In this study, 26 (21.1%) patients with DM more than five years had positive urine spots (17 females and 9 male), two (7.6%) had macro albuminuria, and 90 (73.1%) had negative results. Microalbuminuria was associated with poor glycemic control (p: 0.009), but not with diabetes duration (p: 0.182), urine spot, age (P: 0.278), sex (P: 0.860), or S. creatinine (P: 0.095). Microalbuminuria was associated with glomerular hyper filtration (p: 0.013). **Conclusion:** Urine albumin-to-creatinine ratio increases with glomerular hyper filtration. Poor glycemic management may cause early diabetic nephropathy regardless of duration.

KEYWORDS: Microalbuminuria, glomerular filtration rate, type 1 diabetic, Children.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder defined by persistent hyperglycemia accompanied by impaired metabolism of carbohydrates, lipids, and proteins.[1] The etiology of DM involves defects in insulin secretion, insulin action, or both, which vary significantly among patients and disease types.[2] The disease is broadly classified into Type 1 diabetes mellitus (T1DM), Type 2 diabetes mellitus (T2DM), and other specific types such as neonatal diabetes. T1DM, also known as juvenile diabetes, results from autoimmune destruction of pancreatic beta cells, leading to an absolute insulin deficiency. This autoimmune process is often identified by the presence of specific antibodies, including anti-glutamic acid decarboxylase and islet cell antibodies.[3] A smaller subset of T1DM cases is idiopathic.[4] On the other hand, T2DM is predominantly characterized by insulin resistance and a relative deficiency in insulin secretion, with a growing prevalence among pediatric populations over the past two decades.[5] T1DM represents approximately 10% of global diabetes cases and is a significant chronic condition in children, with peak incidences occurring between 5 to 7 years of age and during puberty.[6] Although autoimmune diseases predominantly affect females, T1DM affects males and females almost equally, with ongoing debates about sex-specific differences in early autoimmune markers.[7] The disease develops through a multi-stage process, starting with the presence of pancreatic autoantibodies and progressing to clinical hyperglycemia with significant metabolic dysregulation.[8] In addition to T1DM and T2DM, neonatal diabetes is an uncommon form of the disease, typically manifesting as hyperglycemia within the first six months of life. It is often caused by mutations in genes critical for pancreatic beta-cell function, with cases

classified as transient or permanent depending on the course of the disease.[9] The pathogenesis of T1DM involves genetic predisposition and environmental triggers leading to beta-cell destruction via an autoimmune process. The main genetic risk factors include polymorphic alleles within the Human Leucocyte Antigen (HLA) complex, which accounts for 40–50% of the genetic susceptibility.[10] Clinically, T1DM presents with symptoms such as polyuria, polydipsia, polyphagia, and weight loss, often accompanied by fatigue and weakness.[5] Effective management requires a combination of insulin therapy, nutrition planning, and regular exercise to achieve glycemic control and prevent complications, such as diabetic ketoacidosis and hypoglycemia.[11] Despite advances in treatment, DM continues to impose substantial medical and economic burdens, with long-term complications including diabetic nephropathy, retinopathy, and neuropathy.[12] Understanding the pathogenesis, risk factors, and progression of DM is crucial for improving management strategies and patient outcomes. The aim of this study was to examine the relationship between glomerular filtration rate (GFR) and urine albumin excretion in children with type 1 diabetes (T1DM) and its importance in detection of diabetic nephropathy.

METHOD

This cross-sectional study was conducted at the emergency and diabetic clinic of Children Welfare Teaching Hospital, Baghdad, from February 1 to August 31, 2023. A total of 123 patients with type 1 diabetes mellitus (T1DM) were included and divided into two groups: Group 1 comprised 82 patients (49 females, 33 males), aged 5–13 years, with a diabetes duration of 5–11 years. Group 2 included 41 patients (26 females, 15 males), aged 10.5–13.5 years, with a diabetes duration of 2–4 years. All participants were diagnosed with T1DM per American Diabetes Association criteria and on insulin treatment. Oral consent was obtained from parents. Inclusion criteria were all diabetic patients with hyperglycemia managed with insulin. Exclusion criteria included newly diagnosed diabetics, patients with neonatal diabetes, diabetic ketoacidosis (DKA), diabetic nephropathy, urinary tract infection (UTI), incomplete investigations, or diabetes duration less than two years. Data were collected using a questionnaire for variables like age, sex, diabetes duration, HbA1c, height, and weight. Blood and urine samples were analyzed for serum creatinine, random blood sugar, and albumin-to-creatinine ratio (ACR). Normoalbuminuria was defined as ACR <30 mg/g, microalbuminuria as >30 mg/g in males and ≥42 mg/g in females, and macroalbuminuria as >300 mg/g. Glomerular filtration rate (GFR) was estimated using the Schwartz formula. Serum creatinine and GFR were measured twice: at admission (hyperglycemia, RBS ≥300 mg/dL) and discharge (RBS <200 mg/dL) following IV fluids and insulin management. Statistical analysis using SPSS version 26 employed paired sample t-tests and Wilcoxon signed ranks tests, with significance set at $P \leq 0.05$. Data were expressed as mean/standard deviation or frequency/percent depending on variable type.

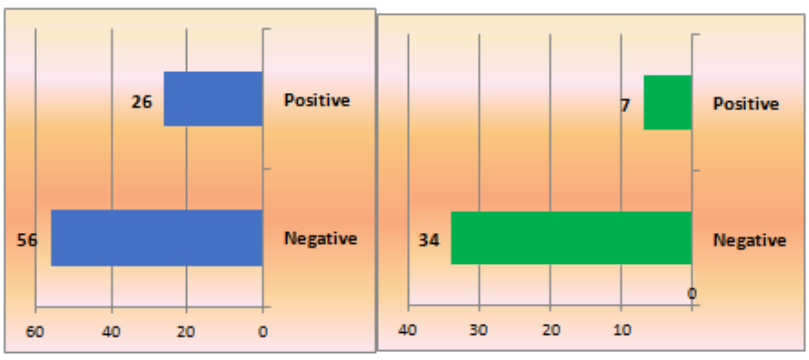
RESULTS

The total number of patients with T1DM included in this study was 123, 75 (61 %) of them females and 48 (39 %) were male with M: F ratio of 1:1.6. their age group was ranging from (5- 13.5) years with a mean of 11.3±1.7 and duration of diabetes between 2 - 11 years. (Table 1).

Table 1: Distribution of patients according to sex, mean age and duration of diabetes.

Duration of diabetes	Female 75	Male 48	Mean age (years) Mean ± SD
≥5 years	59.8%	40.2%	11±1.9
<5 years	63.4%	36.6%	11.9±1
Total	61.0%	39.0%	11.3±1.7

Out of 123 patients included in this study 33 (26.9%) patient had positive urine spot for albumin, 26 (21.1%) had T1DM for > 5 years and 7(5.8%) had T1DM for< 5 years. (Figure 1). Retinal exam results were available for most of patients and only one female had evidence of diabetic retinopathy.



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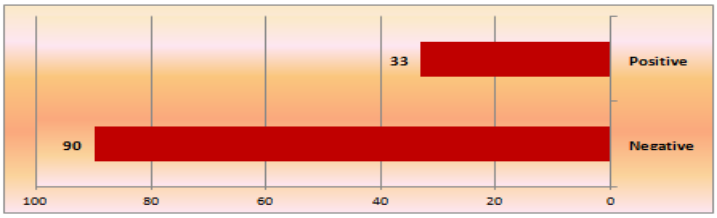

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Figure 1: Distribution of patients according to the result of urine spot for albumin (A) ≥5 years (B) <5 years (C) Total.

A significant association was found between microalbuminuria and poor control (increased HbA1c) (p value 0.009) and there was no significant correlation between the duration of diabetes and microalbuminuria (p value 0.182). (Table 2).

Table 2: Comparison of urine spot of patients with duration of disease, and HbA1C.

Variable	Urine spot						P value
	Macroalbuminuria		Microalbuminuria		Negative		
	N=2	%	N=31	%	N=90	%	
Duration							
≥5 years	2	100	24	77.4	56	62.2	0.182[1]
<5 years	0	0	7	22.6	34	37.8	
HBA1C							
<8	0	0	0	0	9	10.1	0.009[1]
8-9	0	0	2	6.4	13	14.4	
>9	2	100	29	91.6	68	75.5	

Chi- square test

There was no significant association between urine spot and age of patients (P: 0.278) and between urine spot and sex (P: 0.860) and S. creatinine (P: 0.095) (Table 3).

Table 3: Comparison of urine spot of patients with age, sex and serum creatinine.

Variable	Urine spot						P value
	Macroalbuminuria		Microalbuminuria		Negative		
	N=2	%	N=31	%	N=90	%	
Age group							
5-10 y	1	50	5	16.1	26	28.9	0.278[1]
>10 y	1	50	26	83.9	64	71.1	
Sex							
Male	1	50	11	35.5	36	40	0.860[1]
Female	1	50	20	64.5	54	60	
S. Creatinine							
Mean±SD	0.8±0.2		0.5±0.2		1±5.1		0.095[2]

*Significant result, Chi-square test, Kruskal-Wallis test.

There was a significant association between glomerular hyper filtration and positive urine spot (P: 0.013), there is increase positive urine spot in patients with GFR more than 140. (Table 4). We found two patients had macro albuminuria ACR> 300 mg/ g, one of them male, the other was female and by retinal examination she had retinopathy, both of them had normal GFR, and normal blood pressure.

Table 4: Comparison of urine spot with GFR.

GFR	Urine spot						P value
	Macroalbuminuria		Microalbuminuria		Negative		
	N=2	%	N=31	%	N=90	%	
<90-70	1	50	1	3.2	1	1.1	0.013*[1]
140-90	1	50	2	6.5	2	2.2	
>140	0	0	28	90.3	87	96.7	

Chi-square test

There was a significant decrease in S. creatinine from admission (0.9) to (0.4) at discharge, GFR increased on average from admission (159 ml/ min) to discharge (183 ml/min) and RBS reduced from(326mg/dl) on admission to (161mg/dl) at discharge, with statistical significance (p value 0.0001) (Table 5).

Table 5: Comparison of lab characteristics of the patients between admission and discharge times.

Variable	At admission Mean ± SD	At discharge Mean ± SD	P value
S. creatinine	0.9±4.4	0.4±0.1	0.000*[1]
GFR	159.3±45.5	183.3±45.6	0.000*[2]
RBS	326.5±59	161.5±27.8	0.000*[2]

[1]Wilcoxon signed ranks test, [2]Paired t test.

DISCUSSION

This study evaluated the association between hyperglycemia, microalbuminuria, and renal function in type 1 diabetes mellitus (T1DM) patients. A total of 123 patients were included, categorized based on diabetes duration. Microalbuminuria was identified in 26 patients (21.1%) with diabetes duration >5 years and 7 patients (5.8%) with duration <5 years. However, no significant relationship between diabetes duration and microalbuminuria was observed (P: 0.182), aligning with a study from the University of Port Harcourt Teaching Hospital[13] but contrasting with Downie et al.[14], who found a link between prolonged hyperglycemia and renal injury. Early microalbuminuria in some patients was attributed to poor glycemic control and other risk factors.

A significant association between microalbuminuria and poor glycemic control was noted, consistent with several studies.[15] Higher HbA1c levels in albuminuric patients supported the relationship between poor glycemic control and microalbuminuria. However, this finding contrasted with studies like those from Sub-Saharan Africa and Pedro Ernesto University Hospital, which did not find HbA1c predictive of microalbuminuria.[16] No correlation between microalbuminuria and sex was found (P: 0.860), consistent with studies from Basrah Maternity and Children Hospital.[17] However, other studies reported sex differences, with female sex linked to microalbuminuria[18,19], while some, including German and Swiss studies, indicated male predominance.[20,21] These discrepancies might be due to the study's short duration and smaller sample size. No significant association was found between microalbuminuria and age, similar to findings by Donaghue et al.[22] and Olsen et al.[23], though other studies reported age as a risk factor.[24] Similarly, no significant correlation between microalbuminuria and abnormal serum creatinine was observed, consistent with findings from an Indian nephrology study.[25] A significant correlation between hyperfiltration (GFR >140 mL/min/1.73 m²) and microalbuminuria was observed (P: 0.013), supporting Rudberg et al.'s[26] findings and other studies[27] However, the role of hyperfiltration in diabetic nephropathy remains controversial, with some studies finding it predictive while others, like Steinke et al., did not.[28] Two patients exhibited macroalbuminuria (ACR >300 mg/g), both with high HbA1c levels and retinopathy, yet normal GFR. Blood glucose levels significantly influenced GFR, with glycemic control causing variations. While other studies reported decreased GFR with glycemic control[29], this study found an increase, attributed to methodological differences and sample size. Limitations included reliance on estimated GFR, incomplete investigations, and the study's short duration.

CONCLUSION

Urine albumin-to-creatinine ratio increases with glomerular hyper filtration. Poor glycemic management may cause early diabetic nephropathy regardless of duration. Early intervention, effective glucose control, and urine spot albumin creatinine ratio screening are the greatest non-invasive predictors of diabetic nephropathy risk and should be frequently tested to detect early kidney impairment.

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