Role of Zinc and Advanced Glycation End Products in Children with Type 1 Diabetes Mellitus: Relation to Microvascular Complications

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Abstract

Background: Zinc's role in enzymatic activities against oxidative stress may influence microvascular complications in young T1DM patients. Conversely, elevated AGE levels in pediatric T1DM correlate with oxidative stress, contributing to complications like retinopathy and nephropathy. Understanding the intricate interplay between zinc and AGEs holds promise for targeted interventions in disease management.

Objectives: To assess the relationship between zinc, advanced glycation end products (AGEs), and microvascular complications in children with type 1 diabetes mellitus.

Patients and methods: The study included 60 pediatric diabetic patients categorized into two groups based on microvascular complications into group A whom are diabetic patients with albuminuria either macro or micro albuminuria, group B whom are diabetic without albuminuria. A control group comprised 30 healthy children. Clinical examinations, BMI calculations, and biochemical analyses, including HbA1c, RBS, urine albumin/creatinine ratios, and serum zinc levels, were conducted. ELISA assays and colorimetric methods were employed for pentosidine and zinc assessments.

Results: The study found significantly elevated Serum Pentosidine (4.94 ± 6.35 pg/ml) and decreased serum Zinc levels (23.25 ± 8.4 µg/dl) in cases compared to controls, with p-values of 0.0005 and <0.0001, respectively. Negative correlation ($r = -0.718$, $p < 0.0001$) existed between serum Zinc and Pentosidine. Diabetes duration, insulin dose, hospital admissions, and PICU admissions positively correlated with both Pentosidine and Zinc levels. Hb showed a significant negative correlation with Pentosidine ($r = -0.734$, $p < 0.0001$) and positive correlations with Zinc ($r = 0.716$, $p < 0.0001$). WBCs and RBS positively correlated with Pentosidine ($r = 0.526$, $p = 0.0028$; $r = 0.848$, $p < 0.0001$), while Plt and HbA1c showed no significant correlation. In Kidney Function Tests, serum urea correlated positively with Pentosidine ($r = 0.387$, $p = 0.0344$), and serum zinc showed a negative correlation with serum urea ($r = -0.414$, $p = 0.023$). The study highlighted intricate correlations between clinical and biochemical parameters, emphasizing the complex interplay in diabetic cases.

Conclusion: In T1DM patients, weight and BMI trends reveal linkages to microvascular problems and changed body composition. T1DM without comorbidities had lower HbA1c and decreased kidney function, with macro and microalbuminuria indicating renal involvement. The complex relationship between serum pentosidine, zinc, and clinical indicators suggested T1DM microvascular problems. The results stress the need for rigorous surveillance and individualized treatment to understand the disease's complexity.

Keywords: AGEs; Pentosidine; Type 1 DM ; Zinc ; Microvascular complications.

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Introduction

The onset or exacerbation of complications, potentially through its involvement in essential enzymatic activities combatting oxidative stress. Delving into the intricate interconnections between zinc and microvascular complications promises valuable insights, offering targeted interventions for enhanced disease management in young T1DM patients **(Bjørklund et al., 2020).**

Conversely, advanced glycation end products (AGEs) are molecules resulting from nonenzymatic reactions between sugars and proteins or lipids **(Twarda-Clapa et al., 2022).** In the realm of T1DM in children, AGEs assume significance in the realm of microvascular complications. Elevated AGE levels correlate with oxidative stress and vascular damage, contributing to the progression of complications like retinopathy and nephropathy. A nuanced understanding of the impact of AGEs on microvascular complications provides a foundation for developing strategies to alleviate their effects, ultimately enhancing health outcomes in children with T1DM **(Du et al., 2022).**

The intricate interplay between zinc and AGEs introduces an additional layer of complexity to the comprehension of microvascular complications in pediatric T1DM. Plausibly, zinc, with its antioxidant properties, may influence the formation or accumulation of AGEs, thereby modulating their impact on vascular health. Investigating the dynamic relationship between these two elements holds promise for uncovering therapeutic avenues aimed at preventing or mitigating microvascular complications in children with T1DM **(Álvarez-Almazán et al., 2020; Al-Taie et al., 2021).**

The main aim of the study was to assess the relationship between zinc, advanced glycation end products (AGEs), and microvascular complications in children with type 1 diabetes mellitus.

Patients and Methods

This study employed a comparative design and was conducted at Qena University Hospital. A total of 60 pediatric diabetic patients were enrolled from the Pediatric Intensive Care Unit (PICU), outpatient pediatric endocrinology clinic, and the pediatric department. Additionally, 30 age and sex-matched healthy controls were included in the study. The diabetic patients were categorized into three groups: Group (A) comprised 30 children with diabetes and microvascular complications (specifically albuminuria), Group (B) consisted of 30 children with diabetes but without microvascular complications, and Group (C) included 30 unrelated healthy children as the control group.

Inclusion criteria involved all diabetic pediatric patients enrolled in the Pediatric Department of Qena University Hospital suspected to have microvascular complications. Exclusion criteria excluded non-pediatric cases of type 1 diabetes mellitus and patients who refused to participate

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Ethical Approval

The study obtained approval from the scientific and ethical committees at the Faculty of Medicine, South Valley University. Informed consent was obtained from the parents of the pediatric patients (code SVU_MED_PED025_1_22_3_366)

Methodology

Patients admitted to the pediatric general department, PICU, or seen at the endocrinology outpatient clinic were included. The following data were collected:

Patient data was collected comprehensively in the research. Their medical history, including name, age, and sex, was thoroughly examined. Diabetes duration, insulin dose, and diabetic hospitalizations were included in the current history. Past, prenatal, natal, postnatal, developmental, and familial diabetes histories were also evaluated.

Patients were examined clinically to determine their health. This included a general assessment, vital signs, and BMI calculation. To fully assess the patients' health, chest, abdomen, and heart exams were done.

Detailed biochemical analysis was also included. Affinity chromatography, Liquizyme, and Immuno turbidimetry were used to quantify HbA1c, RBS, and urine albumin/creatinine ratios. Renal function testing included serum urea and creatinine.

The BZEK1837-50 ELISA Kit was utilized for human pentosidine biochemical assay. Supplied by Chongqing Biospes Co., Ltd, China

Serum Zinc assay using colorimetric method with 5 Brom-PAPS, Catalog No. : 225 01 050 supplied by (Spectrum For Diagnostic Industries - Free Zone Ismailia Free Zone co. , Egypt).

Statistical Analysis

IBM SPSS version 22.0 was used to analyses computer-generated data. To express quantitative data, percentages and numbers were employed. Before utilizing the median in nonparametric analysis or the interquartile range in parametric analysis, it was required to perform Kolmogorov-Smirnov tests to ensure that the data were normal. We used the (0.05) significance threshold to establish the significance of the findings. The Chi-Square test is used to compare two or more groups. The Monte Carlo test may be used to adjust for any number of cells with a count less than 5. Fischer Chi-Square adjustment was applied to tables demonstrating non continuous data.

Results

Groups A, B, and C had mean ages of 11.53 ± 0.94, 11.63 ± 1.19, and 11.3 ± 1.21 years, respectively (p=0.5069). Gender distribution varied slightly among groups, with no significant difference (p=0.4291). Residence distribution also showed no significant difference (p=0.7308). Weight, length, and BMI differed significantly among groups (p<0.0001), with pairwise comparisons showing significant differences. (**Table .1** and **Fig.1**).

Table 1. Demographic data and basal characteristics of included subjects in all groups.

Variables	Group A (Diabetic cases with Albuminuria) (N = 30)	Group B (Diabetic Cases Without Albuminuria) (N = 30)	Group C (Controls) (N = 30)	P. Value
Age (Years)	11.53 ± 0.94	11.63 ± 1.19	11.3 ± 1.21	0.5069
Sex (N (%))				
Male	13 (43.33%)	18 (60%)	16 (53.33%)	0.4291
Female	17 (56.67%)	12 (40%)	14 (46.67%)	
Residence (N (%))				
Urban	15 (50%)	12 (40%)	14 (46.67%)	0.7308
Rural	15 (50%)	18 (60%)	16 (53.33%)	
Anthropometric measurements				
Weight (Kg)	34.2 ± 2.3	35.8 ± 3.44	48.13 ± 12.11	>0.0001
	P(A/B) =0.0385, P(A/C) =0.0001, P(B/C) =0.0001			
Length (Cm)	151.67 ± 5.94	154.7 ± 7.56	152.17 ± 14.57	0.4619
BMI (Kg/m^2)	14.93 ± 1.54	15.07 ± 2.11	20.38 ± 1.32	>0.0001
	P(A/B) =0.7702, P(A/C) =0.0001, P(B/C) =0.0001			

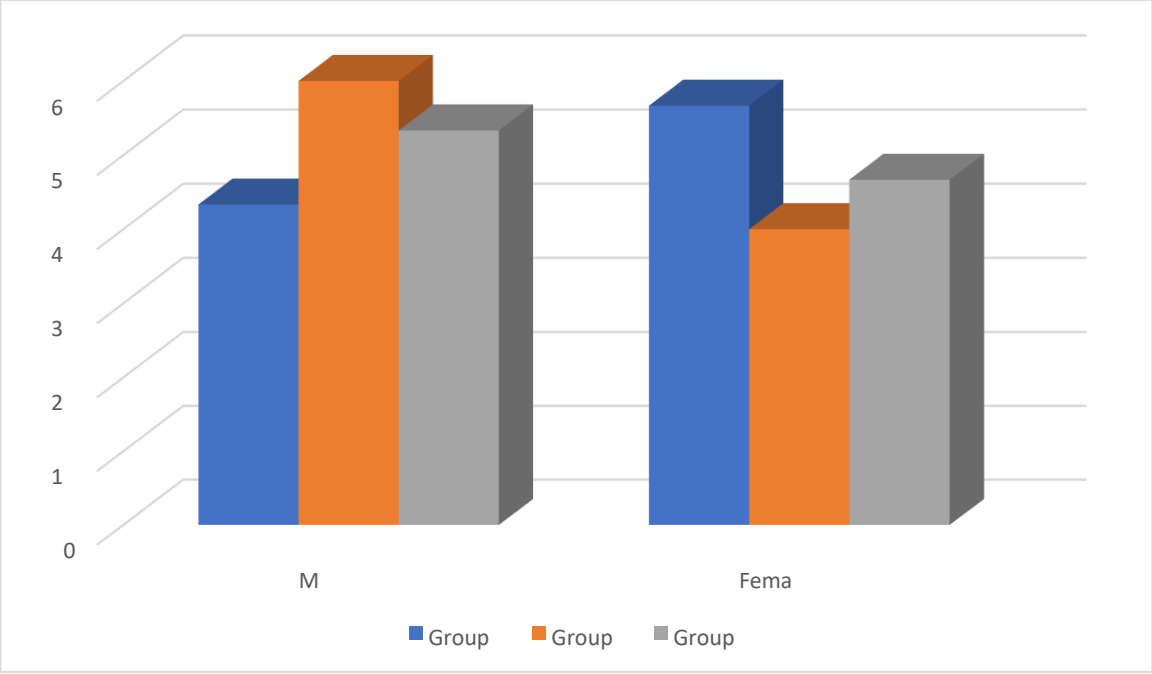

Fig.1. Gender distribution among included subjects in all groups

Table 2. Laboratory investigations among included subjects in all groups

Variables	Group A (N = 30)	Group B (N = 30)	Group C (N = 30)	P. Value
CBC				
Hb (g/dl)	11.96 ± 0.45	12.57 ± 0.26	12.02 ± 0.6	<0.0001
	P(A/B) <0.0001, P(A/C) =0.874, P(B/C) =0.875			
WBCs (Cells/mm^3)	7709 ± 1336.46	5333.87 ± 1126.5	7173.67 ± 1669.43	<0.0001
	P(A/B) <0.0001, P(A/C) <0.0001, P(B/C) =0.004			
Plt (Cells/mm^3)	232100 ± 68144.04	217733.33 ± 62094.44	249933.33 ± 64294.01	0.1628
HbA1c (%)	9.13 ± 1.46	9.03 ± 1.35	4.77 ± 0.48	<0.0001
	P(A/B) =0.7840, P(A/C) =0.0001, P(B/C) =0.0001			
KFT				
Serum urea (mg/dL)	33.43 ± 2.9	22.47 ± 4.65	22.57 ± 3.87	<0.0001
	P(A/B) <0.0001, P(A/C) <0.0001, P(B/C) =0. 9282			
Serum creatinine (mg/dL)	0.71 ± 0.14	0.44 ± 0.13	0.48 ± 0.13	<0.0001
	P(A/B) <0.0001, P(A/C) <0.0001, P(B/C) =0.2382			
Urinary albumin/creatinine ratio	1316.47 ± 1731.97	17.67 ± 5.02	14.4 ± 4.87	<0.0001
	P(A/B) =0.0001, P(A/C) =0.0001, P(B/C) =0.0131			

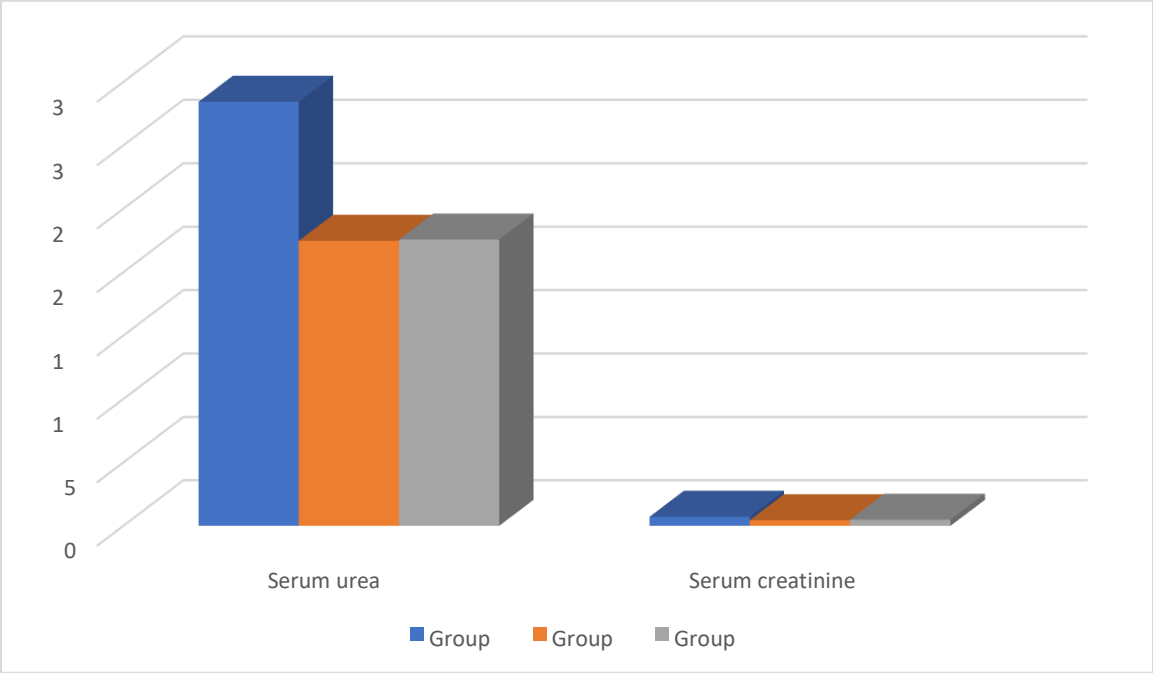

Fig.2. KFT among included subjects

Group A had lower hemoglobin levels (11.96 ± 0.45 g/dl) compared to Group B (12.57 ± 0.26 g/dl) and Group C (12.02 ± 0.6 g/dl) with p<0.0001. White blood cell counts and hemoglobin A1c values also differed significantly among the groups. In kidney function tests, Group A exhibited higher serum urea (33.43 ± 2.9 mg/dL) and serum creatinine levels (0.71 ± 0.14 mg/dL) compared to Group B and Group C, with highly significant differences. The urinary albumin/creatinine ratio varied significantly among the groups, being highest in Group A (**Table2, Fig.2**)

Table 3. Comparison between cases and controls regarding serum pentosidine Concentration and serum zinc level

Measured Biochemical parameters	Cases (N = 60)	Controls (N = 30)	P. Value
Serum Pentosidine Concentration (pg/ml)	4.94 ± 6.35	0.67 ± 0.46	0.0005*
	2.635 (1.459 - 5.739)	21.65 (17.165 - 29.65)	
Serum Zinc level (µg/ dl)	23.25 ± 8.4	51.27 ± 6.16	<0.0001*
	0.531 (0.285 - 0.94975)	50.435 (46.9 - 53.605)	

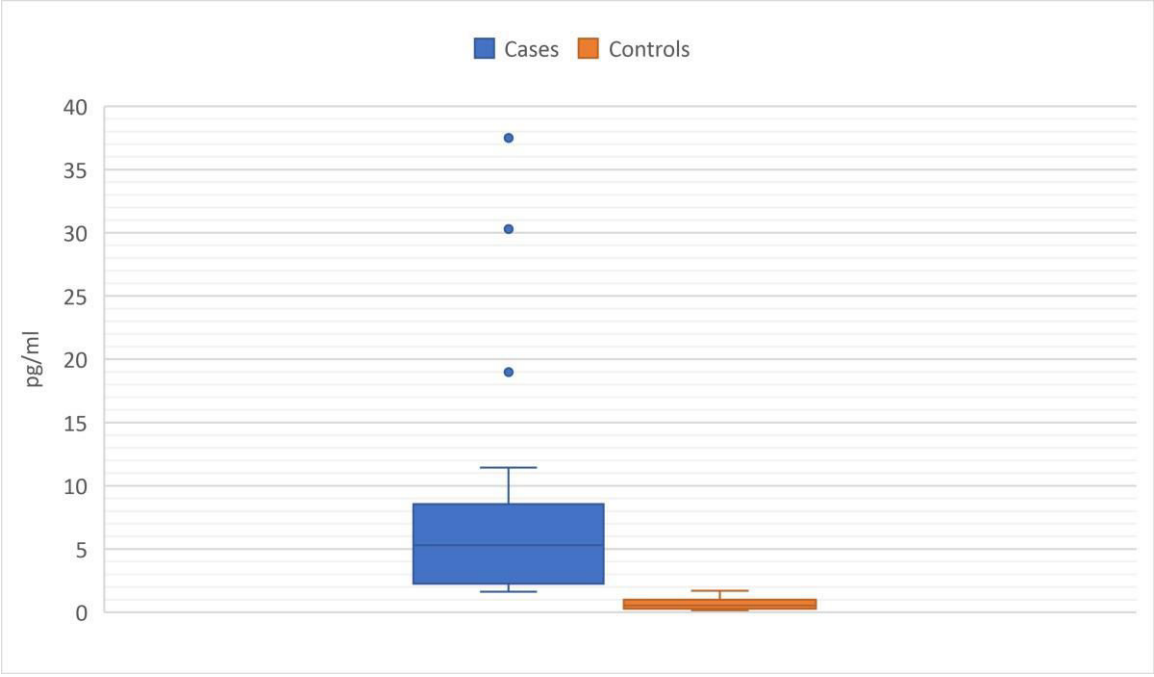

Fig.3. Comparison between cases and controls regarding serum pentosidine concentration

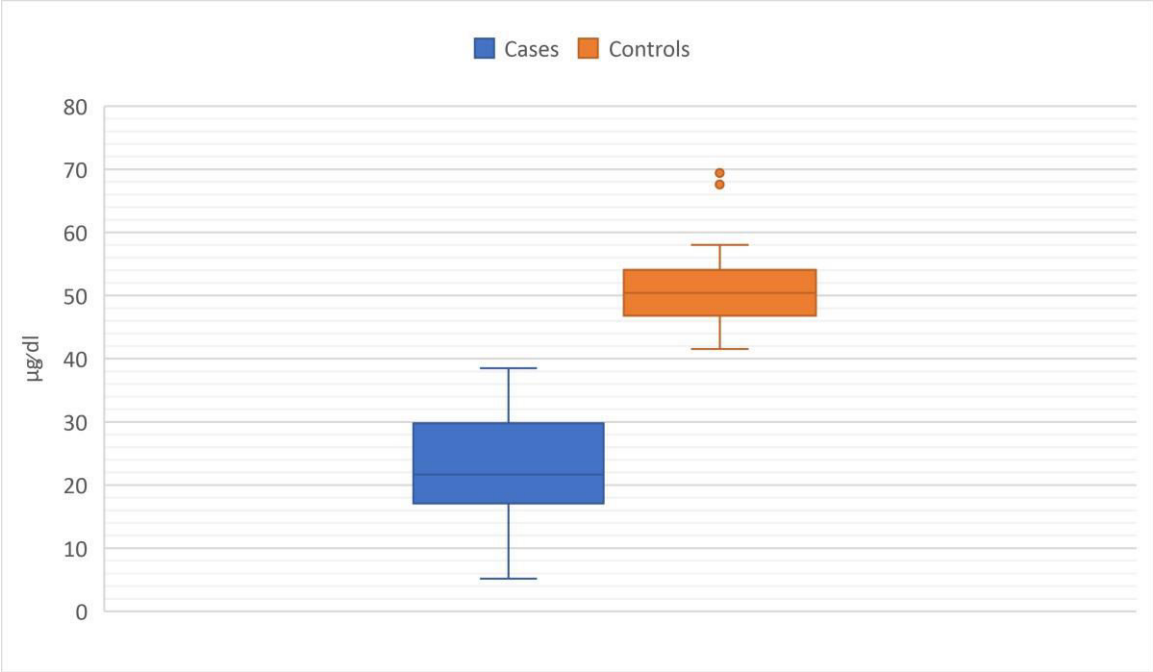

Fig.4. Comparison between cases and controls regarding serum zinc level

The results revealed a significant increase in Serum Pentosidine Concentration among cases (4.94 ± 6.35 pg/ml) as compared to controls (0.67 ± 0.46 pg /ml), with a P-value of 0.0005, signifying a notable elevation in Pentosidine levels in the cases group . Additionally, Serum Zinc levels exhibited a substantial decrease in cases (23.25 ± 8.4 µg/dl) in contrast to controls (51.27 ± 6.16 µg/dl), with a P-value of <0.0001, indicating a significant reduction in Zinc levels in the cases group. (**Table.3, Fig.3 &4**)

Table 4. Serum pentosidine concentration and serum zinc level among included subjects in all groups

Measured Biochemical parameters	Group A (N = 30)	Group B (N = 30)	Group C (N = 30)	P. Value
Serum Pentosidine Concentration (pg/ml)	7.56 ± 8.15	2.33 ± 1.65	0.67 ± 0.47	<0.0001
	5.29 (2.2885 - 8.403)	1.446 (1.20275 - 3.51875)	0.531 (0.285 - 0.94975)	
	P(A/B) =0.0011, P(A/C) =0.0001, P(B/C) =0.0131			
Serum Zinc level (µg/dl)	16.2 ± 4.43	30.29 ± 4.87	51.27 ± 6.27	<0.0001
	17.13 (15.0875 - 18.275)	29.7 (27.725 - 34.425)	50.435 (46.9 - 53.605)	
	P(A/B) =0.0001, P(A/C) =0.0001, P(B/C) =0.0131			

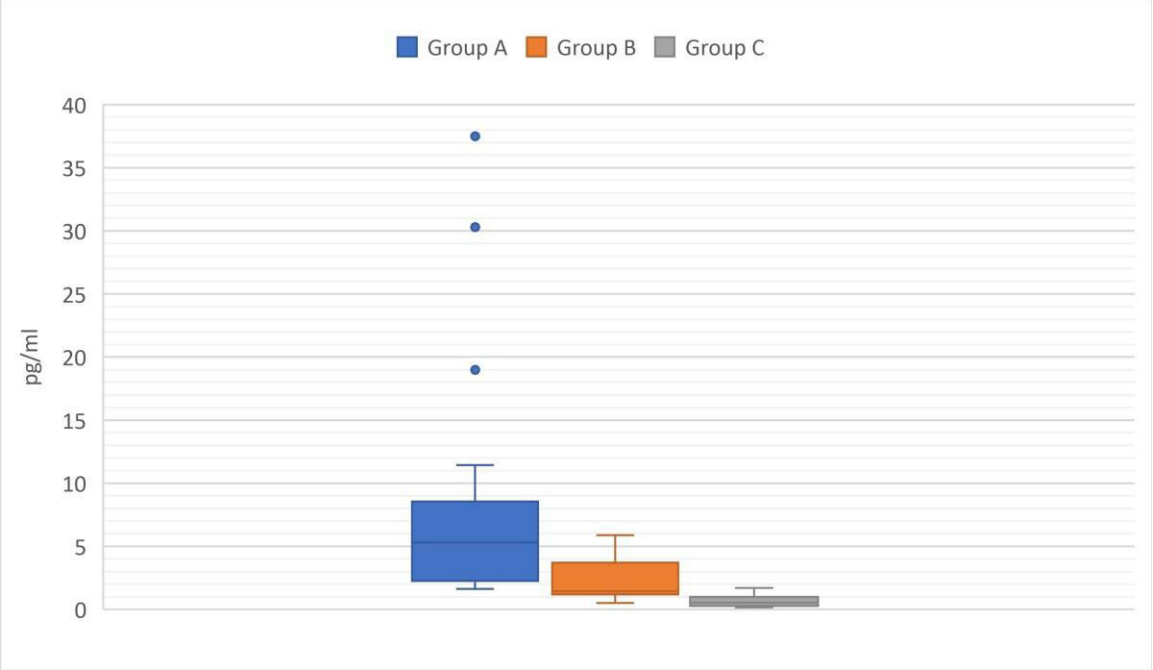

Fig.5.Serum pentosidine concertation among included subjects in all groups

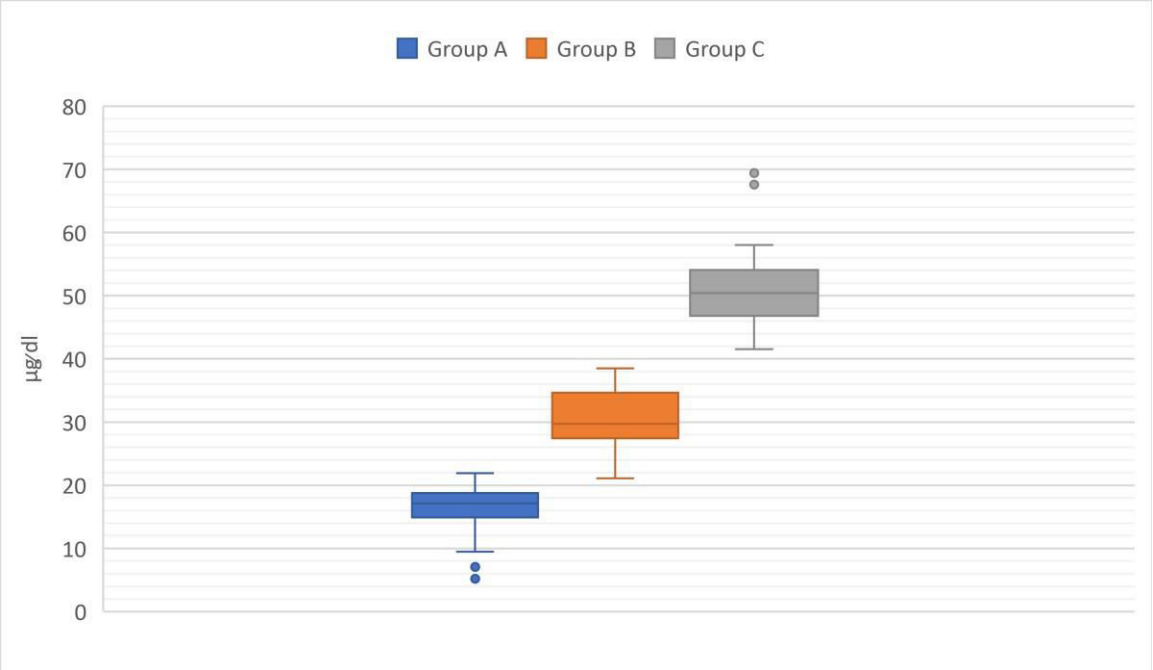

Fig.6.Serum zinc level among included subjects in all groups

Serum pentosidine concentration in Group A was 7.56 ± 8.15 pg/ml, significantly higher than Group B (2.33 ± 1.65 pg/ml) and Group C (0.67 ± 0.47 pg/ml) with $p<0.0001$. Conversely, serum zinc levels showed a contrasting trend, with Group A at 16.2 ± 4.43 µg/dL, Group B at 30.29 ± 4.87 µg/dL,

and Group C at 51.27 ± 6.27 µg/dL, demonstrating highly significant differences (p<0.0001). Pairwise comparisons emphasized the substantial variations in both pentosidine concentration and zinc levels between Group A and the other two groups. (**Table. 4, Fig.5 & 6**)

Table 5. Correlation between different parameter with serum pentosidine concentration and serum zinc level among Group A subjects

Variables	Serum Pentosidine concentration		Serum Zinc level	
	r	P. Value	r	P. Value
Serum Pentosidine Concentration			-.718**	<0.0001*
Serum Zinc level	-.718**	<0.0001*		
Age	-0.17727	0.3487	0.1426	0.4522
duration of diabetes	0.418*	0.0271	-0.573**	0.0009*
Insulin Dose	0.671**	<0.0001*	-0.64**	0.0001*
Times of previous hospital admission due to diabetic complications	0.704**	<0.0001*	-0.703**	<0.0001*
Previous admission in PICU	0.667**	0.0001*	-0.624*	0.0002*
Gestational Age at Delivery	0.026062	0.8913	0.067507	0.723
General examination				
Blood Pressure				
SBP	0.203981	0.2796	-0.32644	0.0783
DBP	-0.11469	0.5462	0.13526	0.4761
RR	0.179977	0.3413	0.015935	0.9334
HR	0.16612	0.3803	-0.05439	0.7753
Weight	-0.23948	0.2024	0.297494	0.1104
Length	0.055316	0.7716	0.021837	0.9088
BMI	-0.2174	0.2485	0.198508	0.293
Capillary refill time	-0.14271	0.4519	0.219552	0.2437
lab investigations				
CBC				
Hb	-0.734**	<0.0001*	0.716**	<0.0001*
WBCs	0.526*	0.0028	-0.517**	0.0034*
Plt	-0.15814	0.4039	.421*	0.0206*
HbA1c	0.206781	0.2729	-0.17266	0.3616
RBS	0.848**	<0.0001*	-0.754**	<0.0001*
KFT				
Serum urea	.387*	0.0344*	-.414*	0.023*
Serum creatinine	0.136864	0.4708	-0.26452	0.1578
Urinary albumin/creatinine ratio	.369*	0.0445*	-0.25263	0.178

A significant negative correlation (r = -0.718, p<0.0001) was found between Serum Zinc levels and Serum Pentosidine concentration, suggesting an unfavorable association.

Age had no significant correlate with serum pentosidine levels (r = -0.17727, p = 0.3487). However, substantial positive relationships were seen with diabetes duration (r = 0.418, p = 0.0271) and insulin dosage (r = 0.671, p<0.0001). The study found significant positive correlations between Serum Pentosidine concentration and previous hospital admissions for diabetic complications (r = 0.704, p<0.0001), PICU admissions (r = 0.667, p<0.0001), and urinary albumin/creatinine ratio (r = 0.369, p = 0.0445). Gestational age at delivery was uncorrelated (r = 0.026062, p = 0.8913) .

SBP, DBP, RR, HR, Weight, Length, BMI, and Capillary refill time did not correlate with Serum Pentosidine concentration.

In lab studies, Hb has a significant negative correlation with Serum Pentosidine concentration (r = -0.734, p<0.0001), WBCs have a positive correlation (r = 0.526, p = 0.0028), and RBS has a positive correlation (r = 0.848, p<0.0001). There were no significant connections between Serum Pentosidine concentration and Plt (r = 0.15814, p = 0.4039) or HbA1c (r = 0.206781, p = 0.2729) . In the Kidney Function Test (KFT), blood urea correlated positively with serum pentosidine concentration (r = 0.387, p = 0.0344), whereas serum creatinine did not (r = 0.136864, p = 0.4708). Urinary albumin/creatinine ratio and serum pentosidine concentration correlated positively (r = 0.369, p = 0.0445) .

No significant link was identified between age and serum zinc levels (r = 0.1426, p = 0.4522). There was a substantial negative association between Serum Zinc levels and diabetes duration (r = -0.573, p = 0.0009) and insulin dosage (r = -0.64, p<0.0001). Significant negative relationships were seen between Serum Zinc levels and past hospital admissions for diabetes complications (r = -0.703, p<0.0001) and PICU admissions (r = -0.624, p<0.0002). The link between gestational age at delivery was not significant (r = 0.067507, p = 0.723) .

SBP, DBP, RR, HR, Weight, Length, BMI, and Capillary refill time did not correlate with Serum Zinc level.

Laboratory studies found significant correlations between CBC parameters and serum zinc levels: Hb (r = 0.716, p<0.0001), WBCs (r = -0.517, p = 0.0034), and Plt (r = 0.421, p = 0.0206). The connection between HbA1c and serum zinc was not significant (r = -0.17266, p = 0.3616). There was a substantial negative connection between RBS and Serum Zinc levels (r = -0.754, p<0.0001).

The Kidney Function Test (KFT) showed a negative connection between serum urea and zinc (r = -0.414, p = 0.023). Serum creatinine and urine albumin/creatinine ratio did not correlate with serum zinc (r = -0.26452, p = 0.1578 and r = -0.25263, p = 0.178), (**Table.5**).

Table 6. Correlation between different parameter with serum pentosidine concentration and serum zinc level among diabetic cases

Variables	Serum Pentosidine concentration		Serum Zinc level	
	r	P. Value	r	P. Value
Serum Pentosidine concentration			-.533	<0.0001*
Serum Zinc level	-.533	<0.0001*		
Age	-0.09897	0.4518	0.060557	0.6458
Duration of diabetes	0.543**	<0.0001*	-0.502	<0.0001*
Insulin Dose	0.704	<0.0001*	-0.614	<0.0001*
Times of previous hospital admission due to diabetic complications (DKA,hyperglycemia,hypoglycemia)	0.705	<0.0001*	-0.64	<0.0001*
Previous admission in PICU	0.698	<0.0001*	-0.609	<0.0001*
Gestational Age at Delivery	-0.06218	0.6369	0.065051	0.6214
SBP	0.103289	0.4323	0.050608	0.701
DBP	-0.06232	0.6362	0.118796	0.366
RR	0.142832	0.2763	-0.23497	0.0707
HR	0.001201	0.9927	0.129572	0.3238
Weight	-0.20439	0.1172	.272	0.0356*
Length	-0.06341	0.6303	0.215369	0.0984
BMI	-0.11458	0.3834	0.043292	0.7426
Capillary refill time	.298	0.0209*	-.666	<0.0001*
Hb	-0.756	<0.0001*	0.622	<0.0001*
WBCs	0.625	<0.0001*	-0.566	<0.0001*
Plt	-0.04399	0.7386	0.072681	0.581
HbA1c	0.120515	0.359	-0.14485	0.2695
RBS	0.665**	<0.0001*	-0.537	<0.0001*
Serum urea	.467	0.0002*	-.719	<0.0001*
Serum creatinine	.352	0.0058*	-.611	<0.0001*
Urinary albumin/creatinine ratio	.486	0.0001*	-.480	0.0001*

A significant negative correlation (r= -0.533, p=0.0001) was found between Serum Zinc levels and Serum Pentosidine concentration, indicating an inverse relationship.

Examining correlations with Serum Pentosidine concentration, no significant correlation was found with age (r = -0.09897, p=0.4518). However, significant positive correlations were

established with the duration of diabetes (r = 0.543, p=0.0001), insulin dose (r = 0.704, p=0.0001), times of previous hospital admission due to diabetic complications (r = 0.705, p=0.0001), and previous admission in PICU (r = 0.698, p=0.0001). No significant correlation was found with gestational age at delivery (r = -0.06218, p=0.6369).

In general examination, Blood Pressure parameters showed no significant correlation with Serum Pentosidine concentration, except for a positive correlation with capillary refill time (r = 0.298, p=0.0209).

In laboratory investigations, CBC parameters exhibited significant negative correlations between Hb and Serum Pentosidine concentration (r = -0.756, p=0.0001), positive correlations between WBCs and Serum Pentosidine concentration (r = 0.625, p=0.0001), and no significant correlations with Plt (r = 0.04399, p=0.7386) and HbA1c (r = 0.120515, p=0.359). In the Kidney Function

Test (KFT), significant positive correlations were identified with serum urea (r = 0.467, p=0.0002), serum creatinine (r = 0.352, p=0.0058), and urinary albumin/creatinine ratio (r = 0.486, p=0.0001).

Regarding correlations with Serum Zinc levels, no significant correlation was found with age (r = 0.060557, p=0.6458). However, significant negative correlations were identified with the duration of diabetes (r = -0.502, p=0.0001), insulin dose (r = 0.614, p=0.0001), times of previous hospital admission due to diabetic complications (r = -0.64, p=0.0001), and previous admission in PICU (r = -0.609, p=0.0001). No significant correlation was found with gestational age at delivery (r = 0.065051, p=0.6214).

In general examination, Blood Pressure parameters showed no significant correlation with Serum Zinc level, except for a positive correlation with weight (r = 0.272, p=0.0356) and a negative correlation with capillary refill time (r = -0.666, p=0.0001).

In laboratory investigations, CBC parameters exhibited significant positive correlations between Hb and Serum Zinc level (r = 0.622, p=0.0001), negative correlations between WBCs and Serum Zinc level (r = -0.566, p=0.0001), and no significant correlations with Plt (r = 0.072681, p=0.581) and HbA1c (r = -0.14485, p=0.2695). In the Kidney Function Test (KFT), significant negative correlations were identified with serum urea (r = -0.719, p=0.0001), serum creatinine (r = -0.611, p=0.0001), and urinary albumin/creatinine ratio (r = -0.48, p=0.0001), (**Table.6**)

Discussion

In our study, there is no significant variation in age, sex distribution, or residency between the three groups (p > 0.05). Statisticians found no significant sex distribution differences amongst diabetes subgroups (p = 0.4291).

In our study, there is no significant variation in age, sex distribution, or residency between the three groups (p > 0.05). Men led Group B (60%), whereas women dominated Group A (56.67%). Sex distribution was not significantly different (p = 0.4291). We agree with **Ramaphane et al. (2021)** that female microalbuminuria prevalence has increased. Omar et al. (2015) reported no gender differences in microalbuminuria prevalence. 50% of

Group A lived in cities, whereas 60% of Group B lived in rural regions. No meaningful change was seen. Environmental variables may explain why metropolitan areas have more Type 1 Diabetes Mellitus, according to **Alotaibi et al. (2017).**

Group A had lower weight and BMI than controls (Group C). Although T1D patients had lower BMIs, **Kaminski et al. (2013)** found that 21% were obese upon diagnosis. Weight increase after diagnosis was impacted by insulin and calorie consumption, according to **Fröhlich-Reiterer et al. (2014).** According to **Verbeeten et al. (2011),** childhood obesity increases T1D risk. **Rosenstock et al. (2018)** found that diabetics had more proteinuria and albuminuria but had similar BMIs.

Individuals with macro albuminuria in our study exhibited prolonged diabetes duration, increased insulin requirements, and higher frequencies of hospital admissions. Biomarkers indicated compromised kidney function and metabolic control, including lower hemoglobin and white blood cell counts, elevated random blood sugar levels, higher serum urea and creatinine concentrations, increased urinary albumin/creatinine ratio, high serum pentosidine concentration, and lower serum zinc levels. Regular monitoring of these biomarkers in diabetic patients is crucial. **Garofolo et al. (2018)** investigated a type 1 diabetes cohort of 774 patients, noting numerical differences in daily insulin dose across subgroups, though not statistically significant (p=0.094). **Majaliwa et al. (2007)** found in a Tanzania study involving 99 individuals with type 1 diabetes mellitus that missing insulin doses were associated with CKD development.

Our study show that diabetic patients with albuminuria (Group A) in our study **(Abdel-Moneim et al., 2020)** exhibited significant abnormalities in CBC parameters in the form of elevated leukocytic counts and low hemoglobin levels, higher HbA1c levels, and impaired kidney function compared to those without albuminuria (Group B) and the control group (Group C). **Abdel-Moneim et al. (2020)** found distinct hematological and biochemical differences in 70 children with T1DM, including increased leukocyte and neutrophil counts and significant depletion in hemoglobin values compared to healthy controls. **Thomas (2004)** reported that over half of T1DM patients with macroalbuminuria had WHO-defined anemia (52%). Our results align with **Hidayati et al. (2021),** showing significantly elevated HbA1c levels in T1DM cases with Albuminuria ($p = 0.03$).

In our study, DM patients with macro and micro albuminuria exhibited higher RBS than those without microvascular complications and controls, emphasizing the importance of strict RBS monitoring in diabetes as also mentioned by (Pak J Med Sci, 2013). **Eric S. Kilpatrick (2006)** found no additional role of blood glucose variability in microvascular complications.

DM patients had higher serum pentosidine (p=0.0005*) and lower Serum Zinc level (p=<0.0001*) compared to controls. **Jaisson et al. (2016)** found elevated serum

AGEs in three T1DM groups compared to controls

van Eupen et al. (2013) observed higher AGEs levels in individuals with T1DM. **Mamilly et al. (2021)** reported significantly elevated pentosidine levels

in pediatric T1DM patients. **Samadi et al. (2020)** noted approximately 3- and 2-fold lower plasma zinc levels in T1DM patients compared to controls. **Sobczak et al. (2019)** found no significant difference in plasma zinc concentrations between T1DM groups and controls with a smaller sample size. **Yuan et al. (2018)** reported a mean zinc level of 169.6 ± 142.4 µg/dL in diabetic subjects and 156.1 ± 126.5 µg/dL in controls, with an odds ratio for DM at 1.09 (95% CI: 0.81–1.48) in a 4.6-year follow-up

In our study, DM patients with Albuminuria showed impaired kidney function (higher kidney test parameters) compared to T1DM without Albuminuria and controls. **Mirijello et al. (2018)** observed higher serum creatinine levels in T1DM patients with macro albuminuria. **David B. Dunger (2018)** reported a higher cumulative incidence of microalbuminuria in diabetic adolescents with a high-ACR group. **Coca et al. (2017**) found no significant UACR difference in DKD cases. Cardiovascular implications were indicated in T1DM with severe kidney involvement (macro albuminuria), supported by **Shim et al. (2008). Liu et al. (2003)** reported lower cardiac function in DM patients with albuminuria, aligning with our findings.

Albuminuria-afflicted DM patients had greater serum pentosidine and lower serum zinc levels than controls.T1DM patients had higher pentosidine and lower zinc levels than controls, suggesting a role in microvascular problems. The macro group had greater pentosidine and lower zinc levels than the micro group, indicating a link to T1DM albuminuria severity.

Hamid et al. (2021) found elevated pentosidine levels in diabetic nephropathy patients, indicating a correlation with kidney diseases. **Mohammed et al. (2022)** observed increased pentosidine, creatinine, and urea levels in diabetic nephropathy patients. **Nishad et al. (2021)** demonstrated a significant association between AGEs and impaired kidney function using the AGE index in a study with 130 subjects with albuminuria. **Koska et al. (2022)** conducted a large-scale cohort study showing a strong correlation between AGEs and renal outcomes of macro albuminuria in participants from ACCORD and VADT trials. **Dhia J. Al-Timimi (2014)** reported low serum zinc levels ($p < 0.01$) in DM subjects and microalbuminuria association with low zinc levels. **Luo et al. (2015)** observed significantly lower serum zinc levels in patients with microvascular complications ($P = 0.002$) compared to those without complications.

In diabetic individuals with albuminuria, a substantial negative correlation appears between serum pentosidine and zinc ($r = -0.718$, $p < 0.0001$). Duration of diabetes, insulin dosage, and hospital admissions correlate favorably with pentosidine concentration (p=0,0271 r=0,418 , $p < 0.0001$ r=0,671 , $p < 0.0001$ r=0,704 respectively) and adversely with zinc (p=0,0009 r=-0,573 , p=0,0001 r=-0,64 , $p < 0.0001$ r=-0,703 respectively). Random blood sugar is substantially favorably connected with pentosidine ($p < 0.0001$, r=0,848) and strongly adversely correlated with zinc ($p < 0.0001$, r=-0,754). Serum urea interacts favorably with pentosidine ($r = 0.387$, P. Value = 0.0344) and adversely with zinc level ($r = -0.414$, P. Value = 0.023), indicating the interrelationship of glycemic management, oxidative

stress, and zinc status in diabetic patients with albuminuria.

Butt et al. (2021) found serum AGEs and zinc significantly contributed to diabetic microvascular complications, with an 82.8% impact on severity (R2=0.828). **Hamid et al. (2021)** observed positive correlations between pentosidine and urea (r=0.54, p=0.005) and creatinine (r=0.71, p=0.00) in micro and macroalbuminuria patient groups. **Kerkeni et al. (2013)** identified a positive association between serum AGEs, sRAGE, pentosidine, and microvascular complications in DM, with pentosidine independently influencing complications (p = 0.004). **Indyk et al. (2021)** confirmed a positive relationship between serum glycated hemoglobin and pentosidine (r = 0.3941, p = 0.0098).

In overall diabetic patients, a substantial negative link develops between serum pentosidine and zinc (r = -0.533, p < 0.0001). Duration of diabetes, insulin dose, and hospital admissions favorably interact with pentosidine (r = 0.543, P. Value = 0.0001), (r = 0.704, P. Value = 0.0001), (r = 0.705, P. Value = 0.0001) respectively, and adversely with zinc level (r = -0.502, P. Value = 0.0001), (r = -0.614, P. Value = 0.0001), (r = -0.64, P. Value = 0.0001) respectively.

Weight suggests a weak negative link with pentosidine and a weak positive association with zinc. Capillary refill time is positively related with pentosidine and considerably negatively with zinc. kidney function tests (urea, creatinine) and urinary albumin/creatinine ratio are strongly positive correlated with pentosidine (r = 0.467, P. Value = 0.0002), (r = 0.352, P. Value = 0.0058), (r = 0.486, P. Value = 0.0001) respectively , and negatively with serum zinc level (r = -0.719, P. Value = 0.0001) (r = -0.611, P. Value = 0.0001), (r = -0.48, P. Value = 0.0001) respectively.

Tupe et al. (2015) observed that zinc administration reduced in vitro glycation of albumin with diabetic glucose, lowering AGEs. Consistent with **Dhia J. Al-Timimi (2014),** serum zinc in DM inversely correlated with creatinine (r = −0.331, p < 0.001) and microalbuminuria (r = −0.587, p < 0.001). **Mohtashamian et al. (2023)** found a significant negative correlation (r = -0.304, p = 0.004) between serum zinc levels and creatinine, suggesting a potential association between zinc status and renal function.

Conclusion

In individuals with T1DM, our study revealed distinct patterns in weight and BMI, where BMI was lower in diabetic patients with albuminuria compared to patients without albuminuria indicating potential associations with microvascular complications and altered body composition. Poorer glycemic control (HbA1c) was noted in T1DM with albuminuria more with macro albuminuria than microalbuminuria. Impaired kidney function was evident in T1DM with albuminuria, with diverse renal involvement in macro and microalbuminuria cases. Albuminuria-afflicted DM patients had greater serum pentosidine and lower serum zinc levels than controls.T1DM patients had higher pentosidine and lower zinc levels than controls, suggesting a role in microvascular problems. The macro group had greater pentosidine and lower zinc levels than the micro group, indicating a link to T1DM albuminuria severity.

The intricate interplay between serum pentosidine, serum zinc, and clinical and biochemical parameters highlighted potential links to microvascular complications in T1DM. Comprehensive monitoring and tailored management strategies are crucial for understanding the multifaceted nature of the disease.

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