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ORIGINAL ARTICLE

Effect of Diabetes Control on the Prevalence of Subtle Urinary Tract Infection in Type-1 Diabetic Children

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ABSTRACT

Keyword: T1DM, UTIs, Glycemic Control, Controlled, Uncontrolled.

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Background: It is important to highlight that opinions on how blood sugar regulation affects UTIs vary. There is much debate regarding the connection between blood sugar regulation and UTIs. This study aimed to explore the role of diabetic control among T1DM children in the occurrence of UTI. **Methodology:** this observational case_control study was carried out in the Pediatrics Department, Aswan University Hospital on 106 children (53 controlled and 53 uncontrolled T1DM). **Results:** cases with uncontrolled T1DM were younger in age and had lower BMI. Additionally, the younger age at onset was correlated with uncontrol of disease and those patients had higher prevalence of DKA. Further, the levels of CRP and HbA1c were significantly lower in controlled T1DM vs. uncontrolled T1DM group. Also, pus cells, ketones, casts and leucocytes were significantly increased in uncontrolled T1DM group than uncontrolled T1DM group. **Conclusion:** glycemic control in T1DM children with UTIs.

INTRODUCTION

Diabetes can lead to severe complications or death in children **(1)**. Diabetic patients are more prone to bacterial infections, elevated risk of hospitalization, and increased mortality related to infections. Among diabetics, the most prevalent infection is the urinary tract infection (UTI). UTIs contribute to overall medical expenses and are a primary cause of end-stage renal disease **(2)**. In 1 diabetes mellitus (T1DM), glycemic fluctuation and chronic hyperglycemia impair endothelial function through various mechanisms that contribute to the onset of different levels of diabetic microangiopathy, including retinopathy, nephropathy, and peripheral neuropathy **(3)**.

Since the advent of intensive insulin therapy protocols for managing T1DM, it is now uncommon for children and teenagers to have clinically detectable microangiopathy. Nonetheless, vascular dysfunction might show subclinical symptoms which contribute to higher rates of morbidity and mortality and are linked to poor quality of life **(4)**.

Despite extensive research, infections' function as a catalyst for the autoimmune process that results in the clinical development of T1DM, there is limited data on the risk of infections in individuals with de novo or old T1DM. There is a bidirectional relationship between infections and T1DM: inadequate glycemic management heightens the odds of infections, while for both recently diagnosed and chronic patients, infection might serve as a trigger for metabolic dysfunction, which may result in diabetic ketoacidosis **(5)**.

There were multiple reasons that caused the incidence of UTIs in diabetic patients i.e., increased glucose levels in renal parenchyma foster proliferation of microorganisms (this is a contributing factor to pyelonephritis and other renal issues, such as emphysematous pyelonephritis). Various immune system disorders, affecting humoral, cellular, and innate immunity, can contribute to the development of UTIs in individuals with diabetes. Diabetic patients with UTI exhibited reduced levels of interleukin-6 and interleukin-8 in the lower urinary tract **(6)**.

The current study aimed to explore the role of diabetic control among T1DM children in the occurrence of UTI.

PATIENTS AND METHODS

From May 2023 to April 2024, this observational case_control study was carried out on 106 children with subtle UTIs at the Pediatric Department of Aswan University Hospital in Egypt. According to G*Power software v. 3.1.9.7 (Faul, et al., 2007), the minimum required sample utilizing two population means formula with an independent t-test, the following assumptions were taken into account: $\alpha = 95\%$; Power $(1 - \beta)$: 99 percent; Effect size is equal to 0.5; Two-tailed test was 106 cases. children which further subdivided into two groups: **Group-I** (n=53): including children with controlled T1DM, **Group-II** (n=53): including children with uncontrolled T1DM. Both groups were on regular follow up at Pediatric Endocrinology outpatient's clinic.

Children aged 1 to 15 years, diagnosed with T1DM (regardless of their diabetic control status), were recruited for the current work. Conversely, those with symptomatic UTI during the study, a history of urologic disease, other autoimmune diseases, or chronic diseases were excluded.

Procedure

All eligible cases under study underwent complete history taking (demographic data, diabetes-focused history, history indicative of UTI, history suggestive of chronic diabetic complications and a record of other medications used (e.g., antibiotics). Clinical examination (anthropometric measurements, general/systemic examination. Laboratory investigation (complete blood count (CBC), Renal function test and urine analysis.

Statistical analysis

IBM-SPSS version 26 **(7)** was applied for data processing. For data summarization: Means, standard deviations, medians, inter-quartile range (IQR) and frequency was presented. Test of significances: Chi-square and Fisher Exact tests were applied to analyze the differences in frequency distributions among groups. Shapiro-Wilk test and histogram was used to test for data normality. For continuous variables with two categories; independent sample t-test analysis was be carried out to compare the means of normally distributed data, while Mann-Whitney U test was be calculated to test the median differences of the data that don't follow normal distribution. A two-tailed p-value < 0.05 indicated significance.

Ethical considerations

All ethical committee regulations from the faculty of medicine were adhered to. Each patient had a private file governed by a non-disclosure policy during data presentation, ensuring that all presented information did not reveal any personal details identifying any of the patients. Guardians of all participants had to sign a written consent after reviewing the patient information sheet or having it read to them. The research conformed to the Declaration of Helsinki regarding ethical guidelines for human and animal research (8) and followed the STROBE guidelines for observational studies (9). Additionally, no incentives or rewards were given to participants or their caregivers.

RESULTS

The current study, conducted in the pediatrics department of Aswan University Hospital, included 106 pediatric cases with T1DM.

As shown in **table 1**

Table 1: Disease characteristics of the diabetic patients.

		Group I (n=106)
Age during disease onset (years)	• **Mean ± SD**	8.64 ± 2.24
	• **Range**	2 - 12
Duration of disease (years)	• **Mean ± SD**	1.99 ± 2.03
	• **Range**	0 – 6
Type of presentation	• **DKA**	76 (71.7%)
	• **Hyperglycemia**	30 (28.3%)
Insulin dosage (IU)	• **Mean ± SD**	0.92 ± 0.2
	• **Range**	0.6 - 1.2

Table 2: Demographic data Differences Between groups

		Controlled T1DM (n=53)	Uncontrolled T1DM (n=53)	P-value
Age/years	• **Mean ± SD**	11.28 ± 2.9	9.94 ± 3.4	< **0.001***
	• **Range**	5 – 15	3 - 15	
Sex	• **Male**	28 (52.83%)	30 (56.6%)	= 0.284**
	• **Female**	25 (47.17%)	23 (43.4%)	
Weight (kg)	• **Mean ± SD**	37.66 ± 10.2	30.28 ± 9.4	< **0.001***
	• **Range**	21 – 55	13 - 52	
Height (cm)	• **Mean ± SD**	136.68 ± 14.6	127.36 ± 17.9	= 0.097**

	• **Range**	102 – 153	94 - 157	
BMI (kg/m^2)	• **Mean ± SD**	19.75 ± 2.3	18.21 ± 2.1	**= 0.041***
	• **Range**	16.52 - 24.06	13.46 - 23.49	

***Independent Sample T test was used to compare mean between the two groups**
****Chi-square test was used to compare frequency between the two groups**
T1DM: type 1 diabetes mellitus, BMI: body mass index

Table 3: Comparison of Disease characteristics among studied groups.

		Controlled (n=53)	Uncontrolled (n=53)	P-value
Age during disease onset (years)	• **Mean ± SD**	9.32 ± 1.74	7.96 ± 2.48	**< 0.001***
	• **Range**	5 - 12	2 – 11	
Disease Duration /years	• **Mean ± SD**	3.35 ± 1.07	3.69 ± 1.64	= 0.421*
	• **Range**	1 - 5	1 – 6	
Type of presentation	• **DKA**	31 (58.49%)	45 (84.91%)	**< 0.001****
	• **Hyperglycemia**	22 (41.51%)	8 (15.09%)	
Insulin dosage (IU)	• **Mean ± SD**	0.94 ± 0.2	0.9 ± 0.21	= 0.494*
	• **Range**	0.7 - 1.2	0.6 - 1.2	

***Independent Sample t-test compare mean between two groups**
****Chi square test was used to compare proportions between groups**
T1DM: type 1 diabetes mellitus, DKA: diabetic ketoacidosis

Regarding the laboratory data **(table 4),**

Table 4: Difference in Laboratory investigations between studied groups

		Controlled T1DM (n=53)	Uncontrolled T1DM (n=53)	P value
Hb (g/dl)	• **Mean ± SD**	11.54 ± 0.97	11.39 ± 0.96	= 0.147*
	• **Range**	9.3 - 13.2	9.3 - 12.5	
Platelets ($x10^9$/L)	• **Mean ± SD**	249.06 ± 69.36	271.53 ± 104.13	= 0.372*
	• **Range**	135 - 367	143 – 433	
TLC ($x10^9$/L)	• **Mean ± SD**	12.07 ± 3.22	13.99 ± 4.71	= 0.077*
	• **Range**	7.3 - 17.9	6.3 – 22	
Urea (mg/dl)	• **Mean ± SD**	53.57 ± 10.63	57.75 ± 16.13	= 0.171*
	• **Range**	36 - 75	21 - 87	
Creatinine (mg/dl)	• **Mean ± SD**	1.1 ± 0.17	1.2 ± 0.23	= 0.076*
	• **Range**	0.8 - 1.4	0.6 - 1.6	
CRP (mg/dl)	• **Median**	18	32	**<0.001****
	• **IQR**	12 - 20	11.5 - 50	
HbA1c (%)	• **Mean ± SD**	7.87 ± 0.31	12.25 ± 1.55	**<0.001***
	• **Range**	6.8 - 8.2	9.2 - 14.5	

***Independent Sample t-test compare mean between two groups**

****Mann Whitney U test compare median between two groups**

T1DM: type 1 diabetes mellitus, Hb: hemoglobin, TLC: total leucocyte count, CRP: c reactive protein, HbA1c: glycated hemoglobin, *: significant as P value ≤ 0.05, P1: P value between controlled and uncontrolled T1DM, P2: P value between controlled T1DM and group II, P3: P value between uncontrolled T1DM and group II

The differences in urinalysis findings were depicted in **table 5**.

Table 5: Difference in Urinalysis Findings between studied groups

		Controlled T1DM (n=53)	Uncontrolled T1DM (n=53)	P value
pH	• **Mean ± SD**	5.88 ± 0.24	5.83 ± 0.19	= 0.234*
	• **Range**	4.8 - 6	4.9 - 6	
Pus cells	• **0-5**	12 (22.64%)	5 (9.43%)	**= 0.046****
	• **>5**	41 (77.36%)	48 (90.57%)	
RBCs	• **0-4**	48 (90.57%)	46 (86.79%)	= 0.263**

	• **>4**	5 (9.43%)	7 (13.21%)	
Crystals	• **Nil**	14 (26.42%)	2 (3.77%)	
	• **Uric acid**	24 (45.28%)	31 (58.49%)	**= 0.005****
	• **Amorphous urate**	15 (28.3%)	20 (37.74%)	
Casts	• **Nil**	40 (75.47%)	29 (54.72%)	
	• **Granular**	11 (20.75%)	14 (26.42%)	**= 0.024****
	• **Hyaline**	2 (3.77%)	10 (18.87%)	
Protein	• **Nil**	53 (100%)	44 (83.02%)	
	• +	0 (0%)	5 (9.43%)	**= 0.007****
	• ++	0 (0%)	4 (7.55%)	
Leucocytes	• **Nil**	33 (62.26%)	19 (35.85%)	
	• +	18 (33.96%)	20 (37.74%)	
	• ++	2 (3.77%)	14 (26.42%)	**= 0.002****
	• +++	0 (0%)	0 (0%)	
	• ++++	0 (0%)	0 (0%)	

***Independent Sample t-test compare mean between two groups**
****Chi square test was used to compare proportions between groups**
T1DM: type 1 diabetes mellitus, RBCs: red blood cells, *: significant as P value ≤ 0.05, P1: P value between controlled and uncontrolled T1DM, P2: P value between controlled T1DM and group II, P3: P value between uncontrolled T1DM and group II

DISCUSSION

The connection between infections and diabetes mellitus is a topic of great interest in the medical literature. Proper glycemic control in diabetics has been shown to improve immune function and reduce morbidity and mortality from serious infections **(10)**. The β-cells of the pancreas, which make and secrete insulin, are the target of an autoimmune process that causes T1DM. Insulin deficiency and hyperglycemia are the results of this process, which kills the cells **(11)**.

UTIs are more common in people with DM and can have dangerous repercussions. UTI risk factors include a compromised immune response, insufficient bladder emptying, and altered metabolic control **(12)**. T1DM cases that have poor glycemic control are more likely to experience UTI. This association implies that factors directly related to glycemic control may affect the risk of lower UTI and are independent of other well-established predictors of UTI **(13)**.

It is important to highlight that opinions on how blood sugar regulation affects UTIs vary. There is much debate regarding the connection between blood sugar regulation and UTIs. It works well for UTIs, but in Greeling's study, blood sugar control had no effect on the presence of UTIs. **(14)**. According to Chiţă et al. 2017, when using a multivariate logistic regression model, glycemic control—which is determined by HbA1c levels—appeared as a significant risk factor for UTIs, but in univariate analysis, it had no discernible impact **(12)**. The presence of UTIs and metabolic control have not been linked in other reports **(15-16)**.

The current study aimed to determine the effect of glycemic control on the presence of UTI in children with T1DM. A total of 106 children with T1DM were recruited for in this study. Cases were

categorized into two equal groups: Group I consisted of 53 controlled T1DM patients and Group II: 53 uncontrolled T1DM patients.

In this study, cases with controlled T1DM were older than those with uncontrolled diseases. In contrast, the duration of disease was similar between the two groups. Regarding the type of presentation, a higher proportion of patients in the uncontrolled T1DM group presented with diabetic ketoacidosis and hyperglycemia compared to the controlled T1DM group.

Agreed with the current results, Janifer et al., found that age and the length of diabetes were found to have a substantial impact on **(17)**. Also, insulin medication was found to be one of the risk factors for recurrent UTIs in women, according to Gorter et al., 2010 **(18)**. Similarly, according to Wilke et al., 2015, insulin therapy did not raise the risk of recurring UTIs **(19)**. Further, the percentage of patients with UTI and the length of diabetes were correlated in another study with 1157 Indian patients (42% aged less than 10 years) **(20)**.

Likewise, we found that cases with controlled T1DM had higher mean BMI than those with uncontrolled disease. In disagreement, Al-Rubeaan et al. 2013 found no connection between diabetic patients' age and their increased risk of UTI. On the other hand, both sexes are more susceptible to UTIs as they age, but females are more susceptible than males i.e., according to the Carrondo study, the UTI rate for those between the ages of 18 and 64 was 9%, while the incidence for those over 85 was 27.5% **(16)**. According to previous studies, women experienced UTIs at a higher rate than men did. This seems to be connected to bladder neurological dysfunction, physiological bladder changes brought on by aging or dyspnea, and women's closeness to the anus **(21)**.

Furthermore, in this study, CRP and HbA1c were significantly lower in controlled than uncontrolled T1DM groups. These results are consistent with earlier studies that found a link between the occurrence of UTIs and higher CRP and HbA1c levels **(21)**. Based on Ribera et al. (2006), symptomatic UTIs in DM patients were linked to elevated inflammatory biomarkers and a HbA1c level more than 7% **(22)**.

The finding of this study was that pus cells, ketones, Casts, protein and leucocytes were significantly increased in uncontrolled T1DM group than controlled group. This was supported by the findings of different studies that claimed that inadequate glycemic control may both directly and indirectly raise the risk of UTIs having pathophysiological backing. First, increased urine glucose levels may serve as a culture medium, encourage bacterial adhesion to the urinary tract, and encourage the growth of harmful bacteria **(23-24)**. In accordance, pyuria was found to be detectable by the dipstick leukocyte esterase test (which has a sensitivity of 75% examination) or by microscopic examination (defined as ≥10 leukocytes/mm3) **(25)**. Similar results were detected in other studies that examined the relationship between glycemic control and incidence of UTIs **(26-27)**.

Conclusion and Recommendation

In conclusion, cases with uncontrolled T1DM were younger in age and had lower BMI. Additionally, younger age at onset was correlated with uncontrol of disease and those patients had higher prevalence of DKA. Further, levels of CRP and HbA1c was significantly lower in controlled T1DM vs. uncontrolled T1DM group. Also, pus cells, ketones, casts and leucocytes were significantly increased in uncontrolled T1DM group than uncontrolled T1DM group.

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