Frequency of Diabetic Retinopathy and Its Association with HbA1c in Children and Adolescents with Type-I Diabetes Mellitus

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ABSTRACT

Objective: To determine the frequency of diabetic retinopathy and its association with HbA1c in children and adolescents having Type-I Diabetes Mellitus (T1DM).

Study Design: Analytical, cross-sectional study.

Place and Duration of the Study: Department of Paediatric Endocrinology and Diabetes, National Institute of Child Health, Karachi, Pakistan, from October 2023 to March 2024.

Methodology: Children aged between 5-18 years having known T1DM were analysed. Children who had record of HbA1c for the last one year (4 HbA1c readings, three months apart) were enrolled. HbA1c was categorised as good (<7%), fine (7-10%), and poor (>10%). Patients were referred to ophthalmologists with more than five years of disease screening experience for diabetic retinopathy.

Results: In 137 patients, 79 (57.7%) were females. The mean age and age at the time of diagnosis were 13.42 ± 2.48 years and 7.42 ± 3.60 years. The mean of last one-year HbA1c (4 separate readings, three months apart) was 10.44 ± 2.50%. The glycaemic control was found to be good, fine, and poor based on the mean of the last one-year in 6 (4.4%), 63 (46.0%), and 68 (49.6%) patients, respectively. Diabetic retinopathy was diagnosed among 30 (21.9%) patients. The comparison of mean HbA1c levels between various diabetic retinopathy classifications showed the statistically significant relationship of higher HbA1c levels with diabetic retinopathy ($p = 0.011$).

Conclusion: The frequency of diabetic retinopathy was high (21.9%) among children and adolescents with T1DM. Higher HbA1c levels were significantly associated with diabetic retinopathy, highlighting the critical role of glycaemic management in preventing retinal complications.

Key Words: *Children, Adolescents, Diabetic retinopathy, HbA1c, Type-I diabetes mellitus*.

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INTRODUCTION

Diabetic retinopathy (DR) is a frequent cause of preventable blindness among diabetic patients. About one-third of diabetic patients develop diabetes retinopathy.[1,2] University of Wisconsin-Medison conducted an epidemiologic study of diabetic retinopathy (WESDR) study and found that 3.6% of Type-I diabetes mellitus (T1DM) and 1.6% of Type-II diabetes mellitus (T2DM) were legally blind.[3] In T1DM, 86% of blindness was attributable to DR.[3] Glycaemic control, disease duration, hypertension, and micro-albuminuria are some of the major risk factors for DR.[4-9]

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Very few studies are available to identify the prevalence of DR in children with T1DM, especially in Pakistan. Even the international data vary widely regarding the prevalence of DR in T1DM.[10-14] The reported burden of DR was found to be as low as 3.8% to as high as 29%.[10-14] The findings of this study may help in estimating the local burden of DR, thereby, enabling in devising of strategies and allocation of resources, and screening of children preventing further complications such as blindness. Furthermore, this study can help in generating local data as no such study has been conducted to determine the association of HbA1c level with DR in T1DM children and adolescents in Pakistan.

This research aimed to determine the frequency of DR and its association with HbA1c in children and adolescents having T1DM.

METHODOLOGY

This analytical, cross-sectional study was conducted at the Department of Paediatric Endocrinology and Diabetes, National Institute of Child Health, Karachi, Pakistan, from October 2023 to

March 2024. Approval from the Institutional Ethical Review Board was obtained. A sample size of 137 was calculated taking the anticipated proportion of DR in T1DM as 15%,[15] with 95% confidence level and 6% margin of error. Inclusion criteria were children aged between 5-18 years having known T1DM for more than five years of duration. Children were included if they had records of HbA1c for the last one year (4 HbA1c separate readings, three months apart). Patients with immunosuppressive disorders such as HIV, chemotherapy, transplantation or neoplastic disorders, or those using medicines that could increase blood glucose levels, such as corticosteroid, beta-glucose, and thyroid hormones, were excluded. Written and informed consents and assents were acquired from parents/guardians of all patients, and those who refused to participate were excluded from this research.

Patients meeting the eligibility criteria were enrolled. A detailed history was obtained. Demographic characteristics such as age, gender, age at the time of onset of T1DM, weight, height, body mass index (BMI), residence, educational status of mother and father, total monthly household income, and family history of diabetes were noted. HbA1c level of the patients was recorded for the past year (4 readings, three months apart), and categorised as good (<7%), fine (7-10%), and poor (>10%).

Patients were referred to ophthalmologist having more than five years of disease screening experience for DR. Patients were classified as Grade 1, no apparent retinopathy when fundus examination was normal, Grade 2, mild non-proliferative retinopathy (NPDR), characterised by the presence of a few microaneurysms, Grade 3, moderate NPDR, characterised by the presence of microaneurysms, intraretinal haemorrhages or venous beading, Grade 4, severe NPDR, characterised by haemorrhages and venous beading (VB) of greater severity requiring laser treatment, or Grade 5, proliferative DR (PDR), characterised by neovascularisation of the disc, neovascularisation of the retina, neovascularisation of the iris, neovascularisation of the angle, vitreous haemorrhage or tractional retinal detachment.[10]

Data were analysed using IBM-SPSS statistics, version 26.0. Mean and standard deviation or median and interquartile range (IQR) were computed for quantitative variables. Normality distribution of the data was confirmed using the Shapiro-Wilk's test. Frequency and percentages were computed for qualitative variables. Chi-square / Fisher's exact test was applied to see the association of qualitative variables with respect to DR. Analysis of variance (ANOVA) was applied to compare mean HbA1c levels between various DR classifications. A p-value of ≤0.05 was considered as significant.

RESULTS

In a total of 137 patients, 79 (57.7%) were females. The mean age, weight, height, and BMI were 13.42 ± 2.48 years (ranging between 6 and 18 years), 36.15 ± 8.88 kg (ranging between 18-60 kgs), 142.86 ± 11.58 cm (ranging between 115 and 166 cm), and 19.70 ± 4.48 kg/m^2 (ranging between 10 and 32 kg/m^2), respectively. The mean age at the time of diagnosis of T1DM was 7.42 ± 3.60 years (ranging between 5-18 years). The mean HbA1c (%) at three months, six months, nine months, and 12 months were 10.51 ± 3.03, 10.16 ± 3.07, 10.05 ± 2.95, and 10.57 ± 2.94, respectively. The mean of last one-year HbA1c (4 separate readings, three months apart) was 10.44 ± 2.50%. The HbA1c was found to be good, fine, and poor on the basis of mean of the last 1 year (4 readings apart) as 6 (4.4%), 63 (46.0%), and 68 (49.6%) patients, respectively (Table I).

The DR was diagnosed among 30 (21.9%) patients. Further distribution revealed that 21 patients had Grade 2 retinopathy, 8 patients had Grade 3, and 1 patient had Grade 5, whereas the remaining 107 patients had no apparent retinopathy. Comparing the characteristics of T1DM with the presence of DR was significantly associated with the educational status of the mother as illiterate (63.3% *vs*. 52.3%, p = 0.025). All other study variables did not show any significant association with DR (p >0.05) and the details are shown in Table II.

The comparison of mean HbA1c levels between various DR classifications showed that statistically significant relationship of higher HbA1c levels was found with DR (p = 0.011), and the details are shown in Figure 1.

Table I: Characteristics of study participants.

Characteristics		Frequency (%)
Gender	Male	58 (42.3%)
	Female	79 (57.7%)
Age (years)	5-12	49 (35.8%)
	13-18	88 (64.2%)
Age at the time of diagnosis (years)	≤5	40 (29.2%)
	>5	97 (70.8%)
Residence	Rural	45 (32.8%)
	Urban	92 (67.2%)
Educational status of mothers	Illiterate	75 (54.7%)
	Literate	62 (45.3%)
Educational status of fathers	Illiterate	53 (38.7%)
	Literate	84 (61.3%)
Monthly household income (PKR)	≤25,000	76 (55.5%)
	>25,000	59 (44.5%)
Family history of diabetes		63 (46.0%)
Weight loss		40 (29.2%)
Polyuria		33 (24.1%)
Polydipsia		32 (23.4%)
Mean HbA1c (%) of last one year (4 readings apart)	Fine	63 (46.0%)
	Good	6 (4.4%)
	Poor	68 (49.6%)

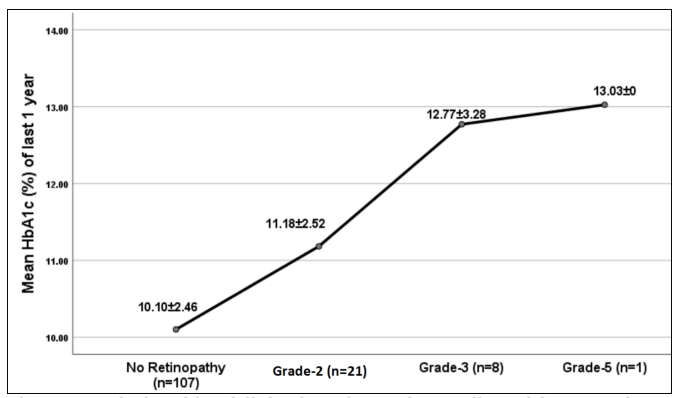

Figure 1: Relationship of diabetic retinopathy grading with mean HbA1c of last one year

Table II: Comparison of characteristics of Type-I DM patients with the presence of diabetic retinopathy (n = 137).

Characteristics		Diabetic retinopathy		p-value
		Yes (n = 30)	No (n = 107)	
Gender	Males	13 (43.3%)	45 (42.1%)	0.900
	Females	17 (56.7%)	62 (57.9%)	
Age (years)	5-12	7 (23.3%)	42 (39.3%)	0.108
	13-18	23 (76.7%)	65 (60.7%)	
Age at the time of diagnosis (years)	≤5	10 (33.3%)	31 (29.0%)	0.645
	>5	20 (66.7%)	76 (71.0%)	
Residence	Rural	8 (26.7%)	37 (34.6%)	0.415
	Urban	22 (73.3%)	70 (65.4%)	
Educational status of mothers	Illiterate	19 (63.3%)	56 (52.3%)	0.025
	Literate	11 (36.7%)	81 (47.7%)	
Educational status of fathers	Illiterate	8 (26.7%)	45 (42.1%)	0.126
	Literate	22 (73.3%)	62 (57.9%)	
Monthly household income (PKR)	≤25,000	11 (36.7%)	65 (60.7%)	0.019
	>25,000	19 (63.3%)	42 (39.3%)	
Family history of diabetes		16 (53.3%)	47 (43.9%)	0.361
Weight loss		12 (40.0%)	28 (26.2%)	0.141
Polyuria		10 (33.3%)	23 (21.5%)	0.180
Polydipsia		9 (30.9%)	23 (21.5%)	0.331
Mean HbA1c (%) of last 1 year (4 readings apart)	Good	-	6 (5.6%)	0.145
	Fine	11 (36.7%)	52 (48.6%)	
	Poor	19 (63.3%)	49 (45.8%)	

DISCUSSION

This study revealed that 21.9% children and adolescents with T1DM exhibited DR. Compared to the findings of this study, a recent study from Morocco showed a relatively higher proportion of DR (30%) among patients with T1DM.[16] The IMDIAB 25 years follow-up study revealed the incidence of DR as 17.3% which is somewhat closer to what the authors found in the present research.[17] Of particular significance was the relationship between HbA1c levels and DR. The analysis indicated a significant linkage of higher HbA1c levels and DR, underscoring the importance of glycaemic control in preventing retinal complications in T1DM patients. This finding aligns with existing literature emphasising the pivotal role of glycaemic management in reducing the risk of DR.[18] A study from Iran found that patients with DR had significantly higher levels of HbA1c ($p = 0.001$) and these findings are similar to what was noted in this research.[19] Some other studies have also demonstrated that increased levels of HbA1c and fasting blood sugar are linked with DR.[20-22] A large multicentral survey analysing 35,891 patients of T1DM revealed that variability in HbA1c added to the risk of DR ($p < 0.001$).[23] It has also been postulated that with every 1% increase in HbA1c, the risk of DR increases by 20-30% in T1DM.[24] Comparison with others corroborates the observed association between elevated HbA1c levels and DR, supporting the notion that optimising glycaemic control is a paramount in mitigating retinal complications in T1DM patients.[19]

A significant association was observed between the educational status of mothers and the presence of DR, highlighting a potential socio-economic influence on disease manifestation. The identification of socio-economic factors, such as maternal education, as potential determinants of DR underscores the multifactorial nature of the disease and emphasises the need for holistic approaches to its management. A study by Al-Odayani *et al*. from Saudi Arabia exhibited that enhancing glycaemic control and reducing short and long-term complications in children with diabetes, necessitates the involvement of mothers with adequate knowledge and education regarding the condition.[25] Overall, this study contributes valuable insights into the epidemiology of DR in children and adolescents with T1DM. This study underscores the critical importance of glycaemic control in preventing retinal complications. Future research should further explore the interplay between socio-economic factors, glycaemic management, and DR to inform targeted interventions aimed at reducing the burden of this sight-threatening complication in vulnerable populations.

Being a single-centre study conducted on a relatively modest sample size were some of the inherent limitations of this research which warrants further exploration. This study did not analyse correlation of treatment strategies and medicines with the presence of DR.

CONCLUSION

The frequency of diabetic retinopathy was high (21.9%) among children and adolescents with T1DM. Higher HbA1c levels were significantly associated with diabetic retinopathy, highlighting the critical role of glycaemic management in preventing retinal complications.

ETHICAL APPROVAL:

Approval for the study was obtained from the Institutional Ethical Review Board of the National Institute of Child Health Karachi, Pakistan (Reference Number: IERB-29/2022, Dated: 24-06-2024). The study was conducted in accordance with the Declaration of Helsinki.

PATIENTS' CONSENT:

Informed and written consent were obtained from the parents of the patients.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
ZK: Conception, design, manuscript drafting, and accountability for the data integrity.
MNI: Data acquisition, manuscript revision, ensuring data accuracy, proofreading, and critical revision.
VRR: Statistical analysis, manuscript revision, proofreading, critical revision, and ensuring statistical integrity.
MR: Data interpretation, proofreading, critical revision, and ensuring data accuracy.
TML, IA: Conception, design, literature review, proofreading, and critical revision.
All authors approved the final version of the manuscript to be published.

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