Section: Paediatrics

Original Research Article

STUDY OF PREVALENCE OF MICROVASCULAR COMPLICATIONS IN CHILDREN WITH TYPE 1 DIABETES MELLITUS ON MORE THAN THREE YEARS OF TREATMENT IN A TERTIARY CARE CENTRE

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Abstract

Background: Type 1 Diabetes Mellitus (T1DM) is children's most common chronic disease. This study aims to explore the prevalence of hypertension, microalbuminuria, retinopathy, and neuropathy with the duration of diabetes and levels of metabolic control. **Materials and Methods:** A retrospective analysis was conducted on 40 paediatric patients diagnosed with diabetes. Demographic data, including gender distribution, were recorded. Clinical parameters, such as DKA presentation and number of admissions, were assessed. Biochemical parameters were measured, including HbA1c, blood sugar at diagnosis, fasting blood glucose, total cholesterol, triglycerides, creatinine, urea, and urine ACR. **Results:** The study included 40 patients, with 43% being male and 57% female. DKA presentations varied, with Nodka, Mild, Moderate, and Severe categories accounting for 7.5%, 20%, 47.5%, and 25% of cases, respectively. Most patients (67.5%) had one admission, while 15%, 12.5%, and 5% had two, three, and four admissions, respectively. Analysis of biochemical parameters revealed the mean HbA1c level to be 8.61 ± 1.63, ranging from 6 to 12.8. The prevalence of Diabetic Nephropathy among 40 children studied was 15% (n=6). The prevalence of diabetic neuropathy was 5% (n=2). The prevalence of diabetic retinopathy was the least at 2% (n=1) and was statistically insignificant among other microvascular complications. **Conclusion:** Children with T1DM often develop microvascular complications, particularly Diabetic Nephropathy. Risk factors include duration of illness, severe Diabetic Ketoacidosis, poor glycemic control, hypertension, and dyslipidemia. Early identification through routine screening, including microalbuminuria and NCV tests, is essential to prevent long-term morbidity.

INTRODUCTION

T1DM is the most prevalent chronic disease affecting children, highlighting the importance of maintaining optimal metabolic control during childhood and adolescence for these patients' well-being and quality of life. The long-term consequences of poorly managed T1DM encompass challenging health issues, encompassing both microvascular and macrovascular complications that significantly impact the quality of life and life expectancy.[1] Numerous studies have demonstrated that, particularly in adolescents, microvascular complications arise more frequently than expected within 2-5 years following the diagnosis of T1DM. The International Society for Paediatric and Adolescent Diabetes (ISPAD) and the International Diabetes Foundation (IDF) released a global consensus report in 2011, recommending the initiation of annual screening for microvascular complications at 11 and for individuals with a diabetes duration exceeding two years.[2]

The primary pathogenic mechanisms underlying these complications involve oxidative stress, increased sorbitol accumulation, and the formation of advanced glycation end products. The major mechanisms involved in their pathogenesis are increased sorbitol accumulation and elevated levels of diacylglycerol, which activate protein kinase C.[3] The primary pathogenetic mechanism of T1DM lies in the autoimmune response against the body's beta cells in genetically susceptible individuals. Microvascular complications associated with T1DM encompass diabetic nephropathy, retinopathy, and neuropathy. The prevention of these complications

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relies heavily on maintaining adequate metabolic control.[4]

The primary goals of diabetes management in children include maintaining asymptomatic status, avoiding hypoglycemia and episodes of diabetic ketoacidosis, ensuring a regular and happy childhood, promoting normal growth and development, providing diabetes self-management education to the child and family, monitoring blood glucose and HbA1C levels within target ranges, and preventing both microvascular and macrovascular complications.[5] In this study, we aim to investigate the prevalence of hypertension, microalbuminuria, retinopathy, and neuropathy with metabolic control levels and the duration of diabetes.

MATERIALS AND METHODS

This hospital-based cross-sectional study was conducted in the general pediatric wards and pediatric Diabetology Outpatient Departments at the Institute of Child Health and Hospital for Children in Egmore, Chennai, for 11 months, from November 2021 to November 2022. The study population comprised 40 children who met the criteria were selected. The study was commenced after the ethical committee clearance, and informed consent was obtained from the Parent/guardian.

Inclusion Criteria

Children diagnosed with Type 1 Diabetes receiving treatment and having a diabetes duration of over three years were included.

Exclusion Criteria

Type 2 Diabetes Mellitus, Maturity-Onset Diabetes of the Young (MODY), and syndromic diabetes such as Down or Wolfram were excluded.

Data was collected from Children attending diabetic OPD regarding the initial clinical presentation, insulin requirement and glycemic control. In screening for diabetic nephropathy, urine microalbumin level and renal ultrasonography were done. A urinary albumin excretion of 30-300 mg/L in at least two urine samples in 24 hours was evaluated as microalbuminuria, and an albumin level over 300 mg/L in the urine was defined as macroalbuminuria. An ophthalmologist performed a fundus examination after mydriatic application to detect retinopathy. A neurological examination and nerve conduction study was performed for neuropathy evaluation in suspected cases.

Statistical Analysis

The collected data were entered into an Excel sheet, and statistical analysis of data was performed by statistical software SPSS 21.0. Strict confidentiality was maintained while analysing and presenting the data.

RESULTS

The mean age of the children was 10.17 years, with a minimum age of 8 years and maximum age of 12.5 years. The mean age of onset of diabetes was 4.7 years, with a minimum age of 2.5 years and a maximum age of 7.5 years. The observed mean duration of illness was 5.5 years, the minimum duration was four years, and the maximum was eight years. The mean body mass index (BMI) observed in the cases was 17.68, the minimum was 14.3, and the maximum was 23.4 (Table 1).

Table 1: Clinical Parameters in Pediatric Diabetes Patients

Parameter	Mean	Minimum Value	Maximum Value	Confidence Interval- 95%
Age (years)	10.17±1.30	8	12.5	0.41
Age of onset (years)	4.7±1.31	2.5	7.5	0.42
Duration of illness (years)	5.5±0.98	4	8	0.31
BMI (kg/m2)	17.68±1.95	14.3	23.4	0.62

Of the cases, 43% were male, while 57% were female. The diabetic ketoacidosis (DKA) presentations varied, with 7.5% classified as Nodka, 20% as Mild, 47.5% as Moderate, and 25% as Severe. Most patients were admitted once (67.5%), followed by 15% admitted twice, 12.5% admitted thrice, and 5% admitted four times. Most had no family history of diabetes (80%), and hypertension was present in 10% of cases. Hypothyroidism was observed in 5% of cases. The urine analysis showed that 70% had no albumin, 20% had trace amounts, and the remaining cases had varying albumin levels (Table 2).

Table 2: Distribution and characteristics of pediatric diabetes patients

Parameter		Number of cases	Percentage
Gender	Male	17	43
	Female	23	57
Dkaat presentation	Nodka	3	7.5
	Mild	8	20
	Moderate	19	47.5
	Severe	10	25
No. of admissions	1	27	67.5%
	2	6	15%
	3	5	12.5%

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	4	2	5%
Family history	T1 DM	3	7.5%
	T2 DM	5	12.5%
	No	32	80%
Hypertension	Yes	4	10%
	No	36	90%
Hypothyroidism	Yes	2	5%
	No	38	95%
Albumin	Nil	28	70%
	Trace	8	20%
	1+	1	2.5%
	2+	2	5%
	3+	1	2.5%
Renal ultrasound	Normal	37	92.5%
	Grade 1 RPD	2	5%
	Grade 2 RPD	1	2.5%
Vision abnormalities	Nil	39	97.5%
	Refractory error	1	2.5%
Fundus changes	Normal	39	97.5%
	Macular edema	1	2.5%

The renal ultrasound was normal in 92.5% of cases, with the rest showing different grades of renal parenchymal disease. Vision abnormalities were rare, with only one case having a refractory error. Fundus changes were minimal, with 97.5% having a normal fundus and one case showing macular edema. These findings provide valuable insights into the characteristics and associated conditions of the studied diabetes cases (Table 2).

Table 3: Biochemical parameters in pediatric diabetes patients

Parameter	Mean	Minimum-Maximum value	Confidence Interval- 95%
HbA1c	8.61±1.63	6-12.8	0.52
Blood sugar at diagnosis(mg/dl)	469±56.7	386-610	18.14
Fasting blood glucose (mg/dl)	151.8±33.5	110-246	10.73
S. Total cholesterol (mg/dl)	164±25.92	124-214	8.29
S. Triglycerides (mg/dl)	121±23.07	86-180	7.38
S. Creatinine (mg/dl)	0.4±0.10	0.3-0.8	0.03
S. Urea (mg/dl)	23.8±6.46	14-48	2.06
Urine ACR (mcg/mg)	21±28.47	1-112	9.1

The mean HbA1c level was 8.61 ± 1.63, ranging between 6 and 12.8. The average blood sugar at diagnosis was 469 ± 56.7 mg/dl, ranging from 386 to 610 mg/dl. Fasting blood glucose had a mean value of 151.8 ± 33.5 mg/dl, ranging from 110 to 246 mg/dl. The total cholesterol level averaged 164 ± 25.92 mg/dl, with a minimum and maximum value of 124 and 214 mg/dl, respectively. Triglycerides showed a mean value of 121 ± 23.07 mg/dl, ranging from 86 to 180 mg/dl. The mean creatinine level was 0.4 ± 0.10 mg/dl, ranging from 0.3 to 0.8 mg/dl. Urea had a mean value of 23.8 ± 6.46 mg/dl, ranging from 14 to 48 mg/dl. Urine ACR exhibited a mean value of 21 ± 28.47 mcg/mg, ranging from 1 to 112 mcg/mg. These findings provide insights into the average levels and variability of these parameters within the studied dataset, aiding in understanding the individuals' overall health status (Table 3).

Table 4: Descriptive statistics of nerve conduction study among Type 1 DM cases

Parameters		Cases (n=40)			
		Mean ± SD	Min	Max	CI-95%
Right Median Motor	NCV	57.89±4.81	49.3	68.8	1.54
	Amplitude	8.45±2.45	4.3	14.4	0.78
Left Median Motor	NCV	56.63±3.49	50.6	66.7	1.11
	Amplitude	8.61±2.51	4.8	14.1	0.80
Right Median Sensory	NCV	54.47±4.75	44.6	64	1.51
	Amplitude	15.16±6.61	4.1	34.1	2.11
Left Median Sensory	NCV	54.92±5.06	44.6	67.3	1.62
	Amplitude	14.86±6.37	3.6	27.5	2.03
Right Peroneal Motor	NCV	49.29±3.75	42.6	62.3	1.20
	Amplitude	5.34±2.01	2.2	12.5	0.64
Left Peroneal Motor	NCV	48.26±4.009	42.1	60.2	1.28
	Amplitude	5.41±1.40	2.2	8.6	0.44
Right Tibial Motor	NCV	49.40±4.99	39.2	64.2	1.59
	Amplitude	9.53±3.5	4.5	15.9	1.11
Left Tibial Motor	NCV	48.5±4.79	38.9	59.3	1.53

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	Amplitude	9.74±3.89	2.8	20.5	1.24
Right Tibial Sensory	NCV	44.93±4.17	36.3	54.3	1.33
	Amplitude	6.10±3.30	2	17.1	1.05
Left Tibial Sensory	NCV	45.17±5.72	34.8	68.1	1.83
	Amplitude	5.83±2.71	1.7	14.1	0.86

The mean nerve conduction velocity in the right median motor nerve is 57.89±4.81m/s. Amplitude in the right median motor nerve is 8.45±2.45 microV. The mean nerve conduction velocity in the left median motor nerve is 56.63±3.49 m/s with a minimum NCV of 50.6 m/s and maximum NCV of 66.7 m/s. The mean observed amplitude in the left median motor nerve is 8.61±2.51 microV with a minimum of 4.8 microV and a maximum of 14.1 microV. The observed mean nerve conduction velocity in the right median sensory nerve is 54.47±4.75 m/s with a minimum NCV of 44.6 m/s and maximum NCV of 64 m/s. The mean observed amplitude in the right median sensory nerve is 15.16±6.61 microV with a minimum of 4.1 microV and a maximum of 34.1 microV.

The observed mean nerve conduction velocity in the left median sensory nerve is 54.9±5.06 m/s with a minimum NCV of 44.6 m/s and maximum NCV of 67.3 m/s. The mean observed amplitude in the left median sensory nerve is 14.86±6.37 microV with a minimum of 3.6 microV and a maximum of 27.5 microV. The observed mean nerve conduction velocity in the right peroneal motor nerve is 49.29±3.75 m/s with a minimum NCV of 42.6 m/s and maximum NCV of 62.3 m/s.

The mean observed amplitude in the right tibial sensory nerve is 6.10±3.30 microV with a minimum of 2.0 microV and a maximum of 17.1 microV. The observed mean nerve conduction velocity in the left tibial sensory nerve is 45.17±5.72 m/s with a minimum NCV of 34.8 m/s and maximum NCV of 68.1 m/s. The mean observed amplitude in the left tibial sensory nerve is 5.83±2.71 microV with a minimum of 1.7 microV and a maximum of 14.1 microV (Table 4).

Table 5: Risk factors for diabetic neuropathy among the type 1 DM cases

Parameters		**Diabetic neuropathy (n=40)**		**Univariate analysis**		
		Yes	**No**	**Odds Ratio**	**P-value**	**CI95%**
Age at Diagnosis	1-5 years	-	28	0.178	0.178	0.0146
	5-12 years	2	10	5.6	0.178	0.456
Gender	Male	1	22	0.72	0.82	0.042
	Female	1	16	1.37	0.82	0.079
Duration of illness	<5yrs	0	23	0.326	0.377	0.027
	>5yrs	2	15	3.066	0.372	1.74
Fasting blood glucose	Normal	0	17	0.326	0.377	0.027
	Hyperglycemic	2	21	1.61	0.351	0.135
HbA1c	5-10	0	34	0.05	0.01	0.004
	10-12.5	1	3	11.66	0.05	0.57
	>12.5	1	1	37	0.01	1.223
DKA at Presentation	Severe	1	9	2.88	0.23	0.163
	Moderate	1	18	1.11	0.47	0.065
	Mild	0	8	-	-	-
	No DKA	0	3	-	-	-
S. Cholesterol (mg/dl)	<200	0	36	0.02	0.005	0.002
	>200	2	2	36	0.005	2.20
S. Triglycerides (mg/dl)	<150	0	34	0.05	0.01	0.004
	>150	2	4	17	0.016	1.264

The risk factors in association with diabetic neuropathy were discussed. The p-value of age at diagnosis of Type 1 DM between 1-5 years is 0.178, and between 5-12 years is 0.178, which were statistically insignificant. The p-value for gender distribution is 0.82 for both males and females. The p-value for illness >5 years duration is 0.372, which was statistically insignificant. The p-value for the association of hyperglycemia with diabetic neuropathy is 0.351, which is statistically insignificant. The association between HbA1C and diabetic neuropathy were statistically significant. The p-value for values 5-10 is 0.01, 10-12.5 is 0.05 and for HbA1C >12.5 is 0.01. The relationship between the severity of diabetic ketoacidosis at presentation is statistically insignificant. The p-value for severe DKA is 0.23, and for moderate DKA is 0.47. The association between diabetic neuropathy and serum lipid profile is statistically significant. The p-value for serum cholesterol is 0.005, and for serum triglycerides is 0.01.

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Table 6: Distribution of microvascular complications

Microvascular complication	Frequency (n=40)	Percentage
Diabetic nephropathy	6	15%
Diabetic neuropathy	2	5%
Diabetic retinopathy	1	2%

DISCUSSION

Studying microvascular complications in children with T1DM is important due to its potential impact on their quality of life and long-term outcomes. Microvascular complications, such as diabetic nephropathy, retinopathy, and neuropathy, can cause substantial morbidity and mortality in individuals with Type 1 DM. Our study included 40 Type 1 DM children on Insulin therapy for over three years. We have studied microvascular complications like diabetic nephropathy, diabetic retinopathy and diabetic neuropathy. In screening for diabetic nephropathy, urine microalbumin level and renal ultrasonography were done. A urinary albumin excretion of 30-300 mg/L in at least two urine samples in 24 hours was considered microalbuminuria, and an albumin level of more than 300 mg/L in the urine was considered macroalbuminuria.6 For the detection of retinopathy, a fundus examination was done. A neurological examination was performed to diagnose neuropathy, and a nerve conduction study was performed in suspected cases.[7]

In our study, the prevalence of diabetic nephropathy among 40 children studied was 15% (n=6). Supporting our findings, a study by Khalid Al-Rubeaan et al. reported an overall prevalence of diabetic nephropathy of 10.8%. Within this prevalence, 1.2% of cases were identified as microalbuminuria, 8.1% as macroalbuminuria, and 1.5% as end-stage renal disease (ESRD).[8] Previous studies have shown that blood sugar levels are positively associated with neuropathy in patients with diabetes mellitus.[9-11]

In our study, the prevalence of diabetic neuropathy was 5% (n=2). However, Walter-Höliner reported a 32.1% prevalence of diabetic neuropathy.[12] The prevalence of diabetic retinopathy was the least at 2% (n=1) and was statistically insignificant among other microvascular complications. The significant risk factors associated with diabetic nephropathy include age of onset at illness, HbA1C, duration of illness, dyslipidemia, change in renal function test and hypertension, and duration of illness > 5 years, which was statistically significant. In the univariate analysis, the factors like poor glycemic control, HbA1C and serum lipid profile were significantly associated with the causation of diabetic neuropathy. In a study conducted by Kamaleldeen et al.[13] and also the children with microvascular complications had significantly higher mean HbA1C levels (9.99±1.61 vs 8.51±1.5, p=0.000) and serum cholesterol levels (174.98 ± 48.12 vs 166.26 ± 43.28, p=0.05) compared to the patients without microvascular complications. Poor metabolic control and dyslipidemia were the risk factors associated with microvascular complications. They also found that the prevalence of microalbuminuria was 20.5%, and macroalbuminuria was 7.8%. The prevalence of diabetic retinopathy was 1.1%, and diabetic neuropathy was 5.5%. Children with microvascular complications had significantly increased Frequency of DKA (39.2% vs 10.6%, p=0.000) and hypoglycaemic attacks (47.1% vs 29.5%, p=0.001) compared to those without microvascular complications.

In a study conducted by Missambou et al.[14] among Congolese children, adolescents, and young adults with T1DM, the prevalence of microalbuminuria was found to be 21% (n=13), with an additional 14.5% (n=9) being at risk of developing microalbuminuria. The relationship between the levels of HbA1C (a marker of long-term glycemic control) and microalbuminuria was statistically significant ($p<0.05$). Furthermore, the prevalence of retinopathy was 6.4% (n=4) in individuals with a disease duration of > 5 years, while the prevalence of diabetic neuropathy was 1.6% (n=1). The main identified risk factor associated with these complications was poor glycemic control, characterised by high HbA1C levels. Similarly, another study conducted by Narang et al.[15] reported that 45% of patients had diabetic retinopathy, while both microalbuminuria and retinopathy were present in 32% of patients. Among patients aged above 50 years, a higher prevalence of microalbuminuria (51.61%) and retinopathy (56.45%) was observed. Patients with a diabetes duration of > 6 years had an increased likelihood of experiencing microalbuminuria (52.45%) and retinopathy (57.37%).

CONCLUSION

Children with T1DM experience significant microvascular complications, with Diabetic Nephropathy being more common than Diabetic Retinopathy and Diabetic Neuropathy. Predictive risk factors include duration of illness, severity of Diabetic Ketoacidosis, poor glycemic control, hypertension, and dyslipidemia. Routine screening and follow-up are crucial in early identification and prevention of long-term morbidity. Clinical examination alone is insufficient; microalbuminuria and NCV tests are essential for the early detection of complications.

Limitations

This study is limited by its smaller sample size, shorter duration, and lack of long-term follow-up.

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Since it was a cross-sectional study, the sensitivity in identifying the microvascular complications has been limited.

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