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Research Article

Clinical profile and factors associated with microalbuminuria in type 1 diabetes mellitus in children and adolescents

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ABSTRACT

Background: The aim of this study was to determine the pattern of clinical presentation and factor associated with microalbuminuria.
Methods: Urinary albumin excretion of children and adolescents diagnosed with type 1 diabetes mellitus attending diabetic clinic of Katihar medical college hospital over a period of one year. Collected blood and urine samples were analysed for glycated haemoglobin, cholesterol, triglycerides, and for 12 hour urinary albumin concentration. Blood pressures were recorded and clinical data collected.
Results: During the study period 215 patients were diagnosed with type1 DM. Out of 215, fourty-three patients (20%) had persistent microalbuminuria. Factor associated with microalbuminuria in diabetic patients include duration of diabetes mellitus, higher blood pressure, higher cholesterol and triglyceride levels.
Conclusion: Type 1 DM is treatable and testing is acceptable and accessible to the patients. As microalbuminuria is an early microvascular complications, it is highly recommended to screen all diabetic patients for the incidence of microalbuminuria and modifiable risk factors like dyslipidemia at the onset and then yearly assessment. Efforts need to be intensified in education of health workers and population at large for quick presentation and prompt diagnosis in order to predict overt diabetic nephropathy and also to prevent its progression.

Keywords: Microalbuminuria, Cholesterol, Diabetes mellitus

INTRODUCTION

It is estimated that more than 346 million people worldwide have diabetes mellitus. By the year 2030, it is predicted that diabetes will become the seventh leading cause of death in the world.[1] Worldwide, from 1990 to 2008, the incidence of type 1 diabetes has been increasing by 2.8% to 4.0% per year.[2] Type 1 Diabetes Mellitus (DM) is characterized by deficient insulin production. Symptoms include excessive urination, thirst, constant hunger, weight loss, vision changes and fatigue.[3] Complications associated with diabetes such as nephropathy, neuropathy, cardiovascular disease, stroke and death, can be prevented or delayed with appropriate treatment.[4]

Microalbuminuria is predictive of future diabetic nephropathy in adults with diabetes.[5] Several studies suggest that at these early stages progression of diabetic nephropathy can be prevented.[6,7]

Prevalence of DM is increasing globally specially in Asian countries and more so in India.[8]

Despite of available information, till now no research work had been published from Katihar, which is located

in eastern zone of Bihar. Knowledge about prevalence, pattern of clinical presentation and factor associated with microalbuminuria is important for development of screening practices and might have implication in disease control.

METHODS

A review of all children and adolescents attending diabetic clinic of Katihar medical college and hospital between January 2014 and December 2014 was carried out. This study was approved by ethical committee of Katihar Medical College, Katihar.

Inclusion and exclusion criteria

Patients with diagnosis of type 1 diabetes mellitus with age between 5 and 19 years were included. Patient being treated for medical condition such as rheumatoid arthritis, taking nephrotoxic chemotherapy or having renal disease other than that caused by diabetes, febrile disease and urinary tract infection were excluded.

Diabetes type 1 was diagnosed by typical symptoms, random blood glucose (RBG) >200 mg/dl or fasting blood glucose (FBG) ≥126 mg/dl. Diabetic ketoacidosis (DKA) was diagnosed by significant hyperglycemia (>250 mg/dl), Ketonuria or ketonemia, serum bicarbonate ≤15mg/dl and DKA associated chemical signs (e.g. dehydration, Kassmaul respiration, etc.). Serum cholesterol, serum triglycerides, HbA_{1C}, blood pressure was recorded.

Urine albumin execration was considered to be raised if it was 30-300 mg/24 hour on atleast three consecutive occasions. Children and adolescents were considered to have normal albuminuria if it remained <30 mg/24 hour. Normal range for HbA_{1C} in a non-diabetic subject was considered 3.9-6.4%.

In order to exclude patient with overt disorders of lipid metabolism (e.g. familial hypercholesterolemia), the following cut-off levels for serum lipids were defined:

a) Total cholesterol <300 mg/dl b) LDL cholesterol <200 mg/dl c) HDL cholesterol >20 mg/dl.

On the basis of records two groups were formed, a group with normoalbuminuric patients and a second group of microalbuminuric patients. Factors (age of onset of diabetes, diabetes duration, age at completion of study, insulin dose, HbA_{1C}, cholesterol, triglyceride, systolic blood pressure, diastolic blood pressure) affecting both groups will be compared.

Chi-square test will be applied and P values will be calculated. Difference will considered significant when P <0.005.

RESULTS

During the study period 215 patients were diagnosed with type1 DM. All children presented with the polyuria and the polydipsia. Other presenting features are shown in Table 1.

Out of 215 study cases, 43 patients (12 boys, 31 girls; 20%) had microalbuminuria (MA) in the three consecutive occasions over a period of one year.Table 2 shows that 1 out of 2 toddlers had microalbuminuria (50%), 5 out of 18 school age diabetic children had microalbuminuria (27.8%) whereas, in adolescents, 5 out of 23 had microalbuminuria (21.73%). However the difference was not statistically significant. Four boys (18.91%) and seven girls (33.33%) were found to be microalbuminuric but the difference was not statistically significant (P = 0.298).

Table 2 also shows that microalbuminuria was found in (11.11%) of children with a duration of diabetes mellitus less than 5 years but the highest proportion was found when the duration was more than 10 years (33.33%). However, the difference was not statistically significant.

Table 2 also shows that poor glycaemic control was associated with higher proportion of microalbuminuria.8 out of 19 cases with poor glycaemic control (42.10%) while only an 3 out of 24 (12.5%) among those with accepted glycaemic control had microalbuminuria. The difference was only statistically significant among the adolescent group (13-19 years). There was significant difference in systolic and diastolic blood pressure among diabetic children with or without MA (P = 0.033 and P = 0.024 respectively).

Table 3 the mean cholesterol (177.9 ± 3.1 mg/dl) and TG (219.2 ± 91.9 mg/dl) were significantly higher (P <0.001) in group with microalbuminuria than the group with normal albuminuria [cholesterol, (142.4 ± 37.1 mg/dl) and TG, (138.1 ± 3 mg/dl)]. The dose of insulin in group with microalbuminuria was significantly higher (1.4 ± 0.71 U/kg) than the group without microalbuminuria (1.5 ± 0.137 U/kg) (P <0.001).

Table 1: Clinical features at presentation.

Clinical feature	Frequency
Polyuria	43 (100%)
Polydipsia	43 (100%)
Polyphagia	33 (76.74%)
Weight loss	26 (60.46%)
Vomiting	25 (58.13%)
Shock	15 (34.88%)
Acidotic breath	10 (23.25%)
Abdominal pain	10 (23.25%)
Altered consciousness	10 (23.25%)

Table 2: Clinical data for normoalbuminuric and microalbuminuric patients with type 1 diabetes mellitus.

Factors	Normo-albuminuric	Micro-albuminuric	Total	P value
1) Age				
Toddler <6	1	1	2	0.654
School age	13	5	18	
Adolescent	18	5	23	
2) Sex				
Male	8	4	12	0.298
Female	30	7	37	
3) Duration of diabetes mellitus				
3 to <5 years	8	1	9	0.509
5-10 years	18	7	25	
>10 years	6	3	9	
4) Control of diabetes mellitus				
4a) Toddler <6 years				
Good control (HbA_{1C} <8.5)	0	1	1	0.157
Poor control (HbA_{1C} >8.5)	1	0	1	
4b) School age 6-12				
Good control (HbA_{1C} <8)	3	2	5	0.473
Poor control (HbA_{1C} >8)	10	3	13	
4c) Adolescent (13-19 years)				
Good control (HbA_{1C} <7.5)	17	1	18	0.000
Poor control (HbA_{1C} >7.5)	1	4	5	
5) Systolic blood pressure				
<90th percentile	9	7	16	P
90-95 percentile	17	1	18	
>95th percentile	6	3	9	
6) Diastolic blood pressure				
<90th percentile	9	6	15	P
90-95 percentile	18	1	19	
>95th percentile	5	4	9	

Table 3: Clinical data for normoalbuminuric and microalbuminuric patients with type 1 diabetes mellitus.

Feature	Normo-albuminuria	Micro-albuminuria
Cholesterol (mg/dl)	142.4 ± 37.1	177.9 ± 3.1*
Triglyceride (mg/dl)	138.1 ± 3	219.2 ± 91.9*
Insulin dose (U/kg)	1.4 ± 0.71	1.5 ± 0.136*

*P <0.001 was considered statistically significant by t test

DISCUSSION

Diabetes has an asymptomatic stage that may be present for upto seven years before diagnosis.[4] From this information it is obvious that we have emerging challenge in our hands.

We describe our observation in a population of 43 patients. Clinical features at presentation in our subjects were similar to those reported by Ibekwe et al.[9] except that all our subjects had polyuria and polydipsia, while polyphagia was less seen frequently. The clinical picture differed from those of Omoshalewa Ugege et al.,[10] who reported polydipsia in 75% and polyphagia in only 62.5% of their subjects. A cumulative prevalence of 25.58% with microalbuminuria has been identified in participating subjects. In a study by Chaturvedi N et al. MA occurred in 41.4% of patients.[11] Groups from Australia reported prevalence rate of 6-18%.[12] The variation is wide and may be related to the degree of diabetes control as it is affected by education, socioeconomic status and influence of race/ethnicity. Improper collection and storage of urine samples may affect measured levels of microalbuminuria, as urine proteins are significantly but variably underestimated after storage at -20 degree C.[13]

We found 3.1:1 ratio of girls to boys with microalbuminuria in this study was similar to Moore TH et al.,[14] showing that development of microalbuminuria is accelerated in girls. But this finding is in contrast to the finding to the finding of Patel et al.[15] whose study showed that microalbuminuria was more common among males. While Zahare Razavi et al. also reported that there was no sex predelication in their study.[16]

Microalbuminuria occurring in older children is found to be clinically significant, while the same in younger children may reflect functional, reversible renal changes.[17] Chae et al.[18] observed that the duration of diabetes was significantly higher in the microalbuminuria group while Basiratnia et al.[19] observed no significant correlation between the duration and microalbuminuria. Currently, IPSAD (International society of Pediatric and Adolescent Diabetes) 2009[20] recommends screening from 11 years with 2 years diabetes duration and from 9 years with 5 years duration to capture most evolving microalbuminuria in children and adolescents. Based on the above criteria 9 children would not have been diagnosed with microalbuminuria in this group. These suggest that children with diabetes are at risk of developing increased albumin excretion and this would warrant regular screening.

Development and progression of microalbuminuria is closely linked to hypertension as reported by Gross et al.[21] and Zahara et al.,[16] which is similar to finding in our study. An increase in blood pressure is associated with increase in urinary albumin excretion in both adults and children.[22] There is controversy as to whether an increase

in blood pressure precedes or is as a result of the development of microalbuminuria.[23] Angiotensin Converting Enzyme (ACE) inhibitors delay in progression of diabetic nephropathy by normalizing glomerular capillary pressure independent of their antihypertensive effects in hypertensive and normotensive adults with diabetes had been reported.[24] Such trials in childhood and adolescence are now urgently needed.

Diabetic Nephropathy (DN) is associated with cardiovascular disease[25] and dyslipidemia is considered as a risk factor for both condition.[26] In addition, cholesterol level increases as DN progresses and also correlate positively with the rate of fall in the glomerular filtration rate.[27] Patient with microalbuminuria had significantly higher mean cholesterol and TG levels and received higher dose of insulin as compared to patient with normal albuminuria. The above finding shows poorer glycemic control in patients with microalbuminuria suggesting that the most obvious first line treatment option is to improve glycemic control. Nonetheless, today it is well established that the process of developing atherosclerosis begins in childhood and the extent of atherosclerotic lesions in adulthood is associated with levels of traditional cardiovascular risk factors such as dyslipidemia and hypertension in early life.[28,29] Evidence from DCCT/EDIC study demonstrates that progression of carotid intima media thickness is associated with serum lipoprotein status in type 1 DM.[30]

CONCLUSION

Type 1 DM is treatable, and testing is acceptable and accessible to the patients. As microalbuminuria is an early microvascular complication, it is highly recommended to screen all diabetic patients for the incidence of microalbuminuria and modifiable risk factors like dyslipidemia at the onset and then yearly assessment. Efforts need to be intensified in education of health workers and population at large for quick presentation and prompt diagnosis in order to predict overt diabetic nephropathy and also to prevent its progression.

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