ORIGINAL ARTICLE

Association Between Microalbuminuria and Demographic Profile with Diabetes Mellitus in Children and Adolescents

*ST Huq[1], S Hossain[2], M Parveen[3], T Ayub[4]

Abstract

Introduction: Diabetic nephropathy is the leading cause of morbidity and mortality in diabetes mellitus. Microalbuminuria is the first clinical sign of nephropathy. **Methods:** This was a cross-sectional study conducted on 512 children and adolescents with diabetes mellitus (DM) attending CDiC Clinic in BIRDEM-2 hospital over a one-year period, to determine the association of microalbuminuria with demographic variables. Clinical data were recorded including age of onset of diabetes, age at registration, duration of diabetes, hypertension and family history. Then the results were compared between patients without microalbuminuria and those with microalbuminuria. **Results:** In this study, we observed that the prevalence of microalbuminuria was 88.7% and normoalbuminuria was 7.7% in children and adolescents with diabetes mellitus. The study also revealed a higher mean age at diagnosis in microalbuminuria compared to normoalbuminuria (15.6 ± 2.2 vs 16.2 ± 2.2) which was statistically significant. The participants also had a higher mean at visit, shorter duration of diabetes in microalbuminuric subjects compared with normoalbuminuric subjects which was statistically significant (p<0.001). We also found statistical significance of hypertension in the microalbuminuric group (52.7% vs 40.9%). The study showed a positive family history in normoalbuminuric patients. **Conclusion:** We found a high prevalence of microalbuminuria which was associated with higher age, short duration of diabetes, hypertension and family history of diabetes.

Keywords: Diabetes mellitus, Children and adolescents, Microalbuminuria.

Introduction

Elevated urinary albumin excretion is an early sign of diabetic kidney disease. The American Diabetes Association (ADA) recommends screening for microalbuminuria annually in people with diabetes after 10 years of age and 5 years duration of diabetes, with a diagnosis of microalbuminuria requiring two of three tests to be abnormal.[1] In people with childhood onset type 1 diabetes the cumulative prevalence of microalbuminuria is around 12-25% after 5to 10years of diabetes.[2] Type 2 diabetes (T2DM) is increasing in children and adolescents and their increased risk for vascular disease is similar to that seen in adults with T2DM.[3] In concurrence with the reports from the developed countries, obesity, female sex, parental history of T2DM and pubertal age appeared to be strongly associated with the disease in Asian children. In a study done in CDiC of BIRDEM-2 General Hospital, in children the prevalence of newly diagnosed with type 2 diabetes mellitus was 8%.[4] Persistent microalbuminuria is highly predictive of progression to overt proteinuria and risk for CVD. The rate of progression of microalbuminuria to macroalbuminuria appears to be similar between adults & children with diabetes, but in children macroalbuminuria occurs at an earlier age.[5] Established risk factors for microalbuminuria in adolescents and children with diabetes include duration of diabetes, positive family history, poor glycemic control and hypertension.[6,7] Limited studies were done on the association of demographic profile and microalbuminuria in children and adolescents with diabetes in Bangladesh. So, the aim of this study is to find out the association of microalbuminuria at its earlier stage in children and adolescents so that early detection can arrest the progression of microalbuminuria. The study may reflect a picture of early detection of microalbuminuria

1. Dr. Sultana Tahmina Huq, Associate Professor, Department of Biochemistry, Prime Medical College, Rangpur, Bangladesh. Email: farihalipon@gmail.com.
    ORCID: https://orcid.org/0009-0005-9557-772X
2. Dr. Sahadat Hossain, Lecturer, Department of Biochemistry, Chandpur Medical College, Chandpur, Bangladesh.
3. Dr. Mukta Parveen, Associate Professor, Department of Biochemistry, Gazi Medical College, Khulna, Bangladesh.
4. Dr. Tohfa-E-Ayub, Assistant Professor, Department of Biochemistry, Ibrahim Medical College, Dhaka, Bangladesh.

in children and adolescents with diabetes in our country and this may be helpful for the clinicians to prevent further progression of renal diseases with the diabetic children and adolescent patients.

Materials and Methods

Children and adolescents with diabetes who were regularly attending the outpatient department of Changing Diabetes in Children (CDiC) clinic a pediatric diabetes multidisciplinary clinic in BIRDEM-2 Hospital over a 1-year period from July 2018 to June 2019 were included in this descriptive cross-sectional study (n=512). "Child" or "children" was used for individuals of 0 to 18 years of age and the term "adolescent" for those between 13 to 18 years of age.[8] Diabetes mellitus was diagnosed according to WHO, ISPAD and Mohan's criteria.[9-11]

The patients who had other illness, thyroid disorder or taking any other medications were excluded from this study. Patients were classified clinically as T1D with abrupt onset of typical symptoms of diabetes, usually who were non-obese, absence of signs of insulin resistance (hyperlipidemia, hypertension, acanthosis nigricans, ovarian hyperandrogenism, nonalcoholic fatty liver disease), severe diabetes with markedly elevated HbA1c, presenting with diabetic ketoacidosis, requiring insulin from the time of onset. Pancreatic autoantibodies are were not available in our clinic. Patients presented with overweight or obesity at pubertal age, with signs of insulin resistance, acanthosis nigricans, hypertension, dyslipidemia, polycystic ovaries and positive family history in 1st or 2nd degree relatives were classified as T2D. Children and adolescents were included in this study if albumin concentration had been measured two or more times within 6 months.

Spot early morning urinary albumin concentration was measured by DCA analyzer Normoalbuminuria was defined as urinary albumin concentration <30 mg/L in all urine samples collected. Microalbuminuria was defined as urinary albumin concentration 30-300mg/L on at least two of three samples Macroalbuminuria was defined if it was >300mg/L in at least two samples. HbA1c was assessed by Clover A1c using photoelectric method. Informed written consent were taken from patients and their families. Statistical analysis was performed with the help of software SPSS for Windows (statistical package for social science, version 20). Association between the two groups were evaluated by using Students chi square test. P value less than 0.001 (p<0.001) considered as highly significant result.

Results

Among 512 participants, T1D were 61.9% and T2D were 38.1%. The relative frequency of microalbuminuria in diabetic children and adolescents are shown in the Table 01. We observed that microalbuminuria was 88.7% and normoalbuminuria was 7.7% in children and adolescents with diabetes mellitus. The study revealed higher mean age at diagnosis in microalbuminuria compared to normoalbuminuria 16.2±2.2 vs 15.6 ± 2.2, p<0.001 which was statistically significant (Table 02).

Compared with the patients with normoalbuminuria, microalbuminuric patients had significantly higher mean age at diagnosis (12.2 ± 2.5 vs 11.0 ± 3.4; p<0.001). The mean duration of diabetes was longer in patients with normoalbuminuria compared to patients with microalbuminuria which was also statistically significant (5.2 ± 2.8 vs 3.6 ± 2.1, p<0.001). The shortest duration of development of microalbuminuria was 7 months. Hypertension was significantly higher in microalbuminuric group than compared with normoalbuminuric group (52.7% vs 40.9%, p<0.001). The study also revealed a higher positive family history of diabetes mellitus in normoalbuminuric group than microalbuminuric group and it was statistically significant (51.4%% vs 46.3%, p<0.001).

Table 01: Frequency of Microalbuminuria with diabetes mellitus in the study population

	Type 1 DM		Type 2 DM	
ACR	Frequency	Percentage	Frequency	Percentage
<30	278	87.7	15	7.7
30-299.9	37	11.7	173	88.7
≥ 300	2	0.6	7	3.6

Table 02: Association between Microalbuminuria and Demographic variables

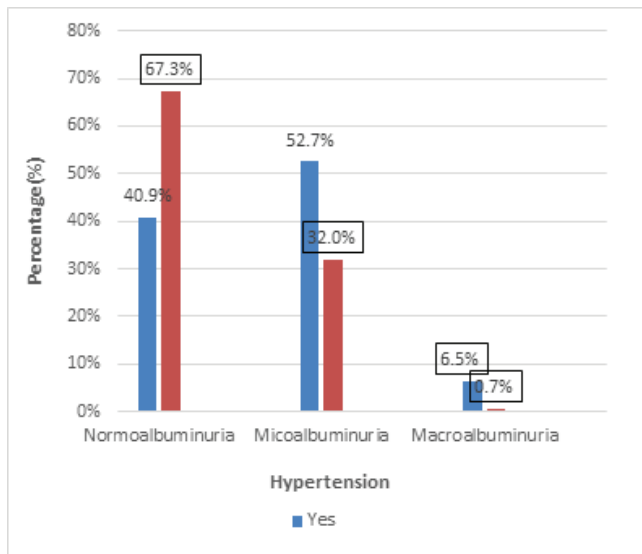| Variables	ACR (mg/g)			p-value
	<30 (n=293)	30-300 (n=210)	≥ 300 (n=9)	
Age at visit(yrs)	16.2 ± 2.2	15.6 ± 2.2	16.6 ± 2.2	<0.001
Age at diagnosis(yrs)	11.0 ± 3.4	12.2 ± 2.5	12.5 ± 3.6	<0.001
Duration of diabetes(years)	5.2 ± 2.8	3.6 ± 2.1	4.1 ±3.1	<0.001

*ANOVA test was done to measure the level of significance

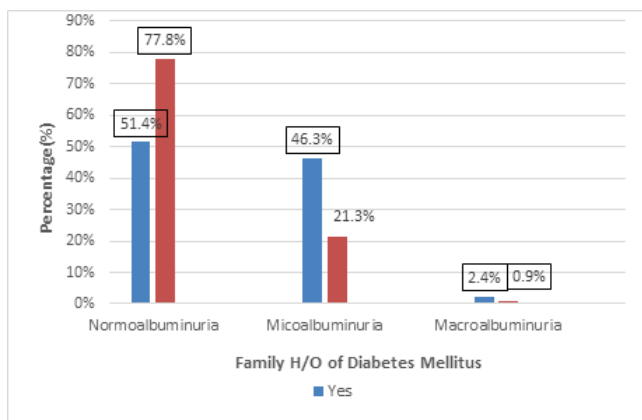**Figure 01: Association of HTN with microalbuminuria**

Figure 02: Association of Family history of diabetes with microalbuminuria

Discussion

A total of 512 subjects were taken in our study. Among them 317 were type 1 and 195 were type 2 diabetic children and adolescents. The prevalence of microalbuminuria in children with T1D varies between 3-30%.[12-15] The wide range of prevalence in various studies may be due to multiple genetic factors in different ethnic groups. Diabetic nephropathy is the major life-threatening complication of diabetes mellitus. Therefore, detection of microalbuminuria is of crucial importance to define strategies and carry out interventions for the prevention of decline in kidney function.[16] The prevalence of microalbuminuria was highest 88.7% in T2D in our population. Higher prevalence was found in adolescents with T2D in comparison with T1D in different reports.[17] Microalbuminuria was observed in 18% of Korean patients with type 2 diabetes compared with 11% with type 1 diabetes.[18] This difference can be explained by

other studies that measured the frequency of persistent microalbuminuria, while in our study we measured the microalbuminuria in spot urine sample. In our study, we found age at visit was higher in normoalbuminuria compared with microalbuminuria which was statistically significant. Our study was in consistent with other studies.[2]

Increasing age increased the risk of microalbuminuria. In our study we found age at diagnosis was higher in microalbuminuria than normoalbuminuria. This is in agreement with other studies.[19,20] Our study reveals that duration of diabetes is higher in normoalbuminuria than microalbuminuria and that was statistically significant. Although longer duration of diabetes was determined as risk factors for complications in previous reports.[21-23] In this present study seven patients developed microalbuminuria within 2 years of diagnosis of diabetes. Among them, two developed earliest within 1 year. One study done in India has demonstrated microalbuminuria in five children with <2 years duration of diabetes.[24] Screening from age 11 years with 2 years duration of diabetes and from 9 years with 5 years duration are recommended according to ISPAD 200 guideline.[25]

Hypertension was found higher in microalbuminuric patients than normoalbuminuria patients (52.7% vs 40.9%) which was statistically significant. Our results agree with the SEARCH for Diabetes in Youth study in which they reported hypertension in one quarter of young affected people in US.[26,27] Family history was positive in normoalbuminuric patients than microalbuminuric patients which was also statistically significant (51.4% vs 46.3%). The American Academy of Diabetes recommends for screening overweight in children aged 10 years or more with a family history of diabetes and or signs of insulin resistance for diabetes.[28] As we could not follow up patients, we could not confirm that whether microalbuminuria is transient or persistent. Another limitation of this study is history of fever, exercise, infections and menstrual bleeding cannot be taken properly.

Conclusion

Although the study was done in a single center of Bangladesh and microalbuminuria was diagnosed by only by spot urine sample, we found the prevalence of microalbuminuria was 88.7%. We also found some associated risk factors like higher age, less duration of diabetes, hypertension and positive family history. So, early screening for microvascular complications in children and adolescents with diabetes can assist in preventive strategies.

References

1. Daniels M, Stephanie N, Maahs DM, Lori M et al. Factors associated with microalbuminuria in 7,549 children and adolescents with type 1 diabetes in the T1D exchange clinic registry. Diabetes Care, Volume 36, 2013.

2. Zabeen B, Nahar J, Islam N, Azad K, Donaghue K. Risk factors associated with microalbuminuria in children and adolescents with diabetes in Bangladesh. Indian Journal of Endocrinology and Metabolism; Vol 22, Issue 1, 2018

3. Amutha A, Pradeepa R, Chella KS, Anjana RM, Unnikrishnan R, Mohan V. Lipid profile in childhood and youth onset type 2 diabetes and their association with microvascular complications. Journal of the association of physicians, 2017; 63:42.

4. Zabeen B, Nahar J, Tayyeb S, Mohsin F, Nahar N, Azad K. Characteristics of children and adolescents at onset of type 2 diabetes in a tertiary hospital in Bangladesh. Indian Journal of Endocrinology and Metabolism, 2016; 20:18-22.

5. Marcovecchio M.L, Tossavainen P.H and Dunger DB. Prevention and treatment of micro vascular disease in childhood type1 diabetes, British Medical Bulletin 2012, vol. 94; 145-164.

6. Schultz CJ, Konopelska-Bahu T, Dalton RN, Carrroll TA et al. Microalbuminuria prevalence varies with age, sex and puberty in children with type 1 diabetes followed from diagnosis in a longitudinal study. Oxford regional prospective study group. Diabetes Care 1999; 22: 495-502.

7. Donaghue KC, Fairchild JM, Craige ME et al. Do all prepubertal years of diabetes duration contribute equally to diabetes complications? Diabetes Care 2003; 26: 1224-9.

8. Wgerrett DK, Hout C, Legault L, Nakhla M, Rosolowsky E. Type 1 diabetes in children and adolescents. Can J Diabetes 2018; 42: S234-246.

9. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabet Care 1999;20 (Supp 11): ASS.

10. ISPAD Clinical Practice Consensus Guidelines 2014 Compendium. Definition, epidemiology and classification of diabetes in children and adolescents. Pediatric Diabetes 2014; 15 (Supple. 20):4-17

11. Mohan V, Nagalotimath SJ, Yajnik CS, Tripathy BB. Fibrocalculous pancreatic diabetes. Diabetes Metab Rev 1998; 14:153-70.

12. Schultz CJ, Neil HA, Dalton RN et al. Blood . pressure does not rise before the onset of microalbuminuria in children followed from diagnosis of type 1 diabetes. Oxford Regional Prospective Study Group. Diabetes Care 2001; 24:555-60.

13. Moayeri H, Dalili H. Prevalence of microalbuminuria in children and adolescents with diabetes mellitusType 1. Acta Med Iran 2006; 44: 105-10.

14. Viswanathen V, Snehalatha C, Shina K, Ramachandaran A. Persistent microalbuminuria in type 1 diabetic subjects in South India. J Assoc Physicians India 2002; 50: 1259-61.

15. Downie E, Craig ME, Hing S, Cusumano J et al. Continued reduction in the prevalence of retinopathy in adolescents with type 1 diabetes: Role of insulin therapy and glycemic control. Diabetes Care 2011; 34: 2368-73.

16. Chiarelli F, Verrotti A, Mohn A et al. The importance of microalbuminuria as an indicator of incipient diabetic nephropathy: therapeutic implications. Ann Med. 1997; 29 (5): 439-445.

17. Eppens MC, Craig ME, Cusumano J, Hing S et al. Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes. Diabetes Care 2006; 29: 1300-6.

18. Yoo EG, Choi IK, Kim DH. Prevalence of microalbuminuria in young patients with type 1 and type 2 diabetes mellitus. J Pediatr Endocrinol Metab 2004; 17: 1423-7.

19. Jawad KA, Mea'ad KH, Lamia M. Microalbuminuria in children and adolescents with type 1 diabetes mellitus. The Medical Journal of Basrah University, 2007; 25:2.

20. Al-Eisa A, Al-Hajri A, Al-Shuaib et al. Early onset microalbuminuria in children with type 1 diabetes in Kuwait. Curr Pediatr Res; 2017:21(2):254-259.

21. Olsen BS, Johannesen J, Sjolie AK, Borch-Johnsen K et al. Metabolic control and prevalence of microvascular complications in young Danish patients with type 1 diabetes mellitus. Danish Study Group of Diabetes in Childhood. Diabet Med 1999; 16:79-85.

22. Salgado PP, Silva IN, Vieira EC, Simoes e Silva AC. Risk factors for early onset of diabetic nephropathy in pediartic type 1 diabetes. J Pediatr Endocrinol Metab 2010; 23:1311-20.

23. Raile K, Galler A, Hofer S, Herbst A et al. Diabetic nephropathy in 27,805 children, adolescents and adults with type 1 diabetes: Effect of diabetes duration, A1C, hypertension, dyslipidemia, diabetes onset and sex. Diabetes Care 2007; 30: 2523-8.

24. Poovazhagi V, Senguttuvan P, Padmaraj R. Prevalence of microalbuminuria in children with type 1 diabetes mellitus. Diabet Clin 2012; 9.

25. Donaghue KC, Charelli F, Trotta D et al. Microvascular and macrovascular complications associated with diabetes in children and adolescents. Paediatr Diabet 2014: 15(Suppl 20): 257-69.

26. Bell RA, Mayer-Davis EJ, Beyer JW. SEARCH for Diabetes in Youth Study Group. Diabetes in non-Hispanic white youth: prevalence, incidence and clinical characteristics 2009; Diabetes Care: 32(suppl.2):S102-S111

27. Eppens MC, Craig ME, Cusumano J, Hing S. Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes 2006; Diabetes Care: vol.29;6:1300-1306.

28. American Diabetes Association Type 2 Diabetes in children and adolescents. Pediatrics 2000; 105: 671-80.