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Prevalence of Microalbuminuria and its Association with Cardiometabolic Risk Factors in Children with Obesity and Overweight Attending Obesity Clinic, Kerala, India

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Abstract

Once thought to be a concern of developed nations, low- and middle-income countries are now witnessing a rapid rise in overweight and obesity. Among children of 5-19 years, a huge leap in the prevalence of overweight and obesity was observed during the last 4 decades. Obese children are at increased risk of cardiometabolic morbidities such as hypertension, insulin resistance, diabetes mellitus (DM). Microalbuminuria (MA) denotes endothelial dysfunction and is associated with higher susceptibility to cardiovascular disease in adults

Objective: To assess the prevalence of microalbuminuria and its association with cardiometabolic risk factors in children with obesity and overweight.

Methods: A descriptive cross-sectional study was carried out in children aged 2-15 years with exogenous obesity and overweight. MA was defined as a urinary albumin to urinary creatinine ratio (UACR) of>30 mg/g and <300 mg/g. Weight Hip ratio (WHR), Weight height ratio (WHtR), body mass index (BMI) and blood pressure (BP) were assessed in all children. C reactive protein (CRP), fasting blood sugar, fasting serum levels of insulin and fasting lipid profile and ultrasound (US) abdomen and B- mode US to analyze hepatic steatosis and carotid intima media thickness (cIMT) respectively were done. The degree of insulin resistance was determined by the homeostatic model assessment-insulin resistance (HOMA-IR).

Results: MA was detected in 42 (20.28%) of the obese/overweight children. No association was observed between MA and cardiometabolic risk factors in the current study. Proportion of children with increased right cIMT was significantly higher in the MA group.

Keywords: Obesity; Overweight; Children; microalbuminuria; carotid intima medial thickness; cardiometabolic risk factors

Introduction

Once thought to be a concern of developed nations, low- and middle-income countries are now witnessing a rapid rise in overweight and obesity (ow - ob). Asia was home to nearly 50% of the children with overweight or obesity below 5 years in 2019. Among children of 5-19 years, a leap in the prevalence of overweight and obesity from 4% in 1975 to above 18% in 2016 was observed. Childhood obesity begets adulthood obesity. Children with obesity are at increased risk of cardiometabolic morbidities such as hypertension, insulin resistance, diabetes mellitus (DM) [1]. The Bogalusa Heart Study observed that cardiovascular risk factors that develop during childhood have collective effects rather than add on effects on the severity of cardiovascular disease [2].

Literature data suggest that microalbuminuria denotes endothelial dysfunction and is associated with higher susceptibility to cardiovascular disease in adults [3]. The study reports regarding the association of cardiometabolic risk factors in obese children with albuminuria are contradictory.

We observed a scarcity of studies addressing this issue from South Asia. Hence a cross sectional study was carried out at obesity clinic of department of Pediatrics, Government Medical College, Calicut, Kerala, India to evaluate the prevalence of microalbuminuria and its association with cardiometabolic risk factors in children with ow-ob.

Methods

A descriptive cross-sectional study was carried out in children with ow-ob of age 2-15 years attending the obesity clinic of a tertiary care hospital, Kerala, India. The study was reviewed and approved by institutional ethical board on (IEC number GMCKKD/RP 2017/IEC/189). During the study period of 2 years from 1st January 2016 till 31st December 2017, 207 children with ow-ob (Boys-127; Girls-80) were enrolled after obtaining written informed consent from the guardian of individual study subjects. Children with endogenous obesity (e.g., hypothyroidism or Cushing disease) or any condition known to influence body composition (e.g.: glucocorticoid therapy) those with UACR of>300 mg/g or urinary blood>2+ were excluded from study. Obesity and overweight were defined using BMI percentiles; children >2-year-old with a BMI ≥ 95th percentile met the criterion for obesity, and those with a BMI between the 85th and 95th percentiles fell in the overweight range. A standardized and validated data sheet was prepared to collect the demographic variables and family history of metabolic risk factors such as obesity, hypertension, diabetes, or dyslipidemia. Anthropometric measurements of weight, height and waist circumference were measured by utilizing standard methodology. Weight of the participants was measured to the nearest 0.1 kg using a calibrated electronic scale while on barefoot and wearing

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light clothes. The height was measured to the nearest 0.1 cm. Waist circumference (WC) was measured with a non-stretchable tape at the midpoint of the lowest rib cage and the iliac crest, to the nearest 0.1 cm in a standing position during end-tidal expiration. Hip circumference was measured around the widest portion of the buttocks, with the tape parallel to the floor [4]. Waist/Height ratio (WHt) was computed as the ratio of the waist circumference (cm) and the height (cm). WC cut-offs as proposed by Kuriyan et al (WC>75th centile) were used to identify children with abdominal obesity [5]. Waist/hip ratio (WHR) and WHtR were calculated. 0.9 in boys and 0.8 in girls was taken as a cut-off for WHR and 0.5 as a cut-off for WHtR [6,7]. Pubertal staging was done using Tanner's criteria. Tanner 1 was defined as pre puberty, 11-1V as mid puberty and Tanner V as post puberty [8]. General and systemic examinations were done in all children. Blood pressure (BP) was measured in the right upper limb in sitting position. Hypertension was defined as repeatedly measured systolic BP or diastolic BP exceeding the 90th percentile for the child's age and gender and height [9].

A random 20–30 mL of midstream voided urine was collected in the morning, to measure urine albumin and creatinine. Microalbuminuria (MA) was defined as a urinary albumin to urinary creatinine ratio (UACR) of >30 mg/g and <300 mg/g. A UACR of <30 mg/g was considered normal [10].

CRP, fasting blood sugar, fasting serum levels of insulin and fasting lipid profile were done in all patients. Impaired fasting glucose (IFG) was taken as a fasting plasma glucose level of 100-125 mg/d and hemoglobin A1c (HbA1c) level of 5.7%-6.4% as an indicator of prediabetes [11].

Fasting insulin levels above 15 μU/mL in the prepubertal period, 30 μU/mL in the pubertal period and 20 μU/mL in the post pubertal period, were taken as cut off levels for hyperinsulinism [12]. The degree of insulin resistance was determined by the homeostatic model assessment-insulin resistance (HOMA-IR), calculating the product of fasting plasma insulin concentration (micro units/ml) and the fasting plasma glucose concentration (mill moles/L) divided by 22.5. Risk of insulin resistance was defined for values greater than 2.5(HOMA-IR>2.5) [13].

Serum total cholesterol (TC) levels ≥ 200 mg/dL, triglyceride (TG) levels ≥ 100mg/dl, below 9 year and ≥ 130mg/dl, in 10–19-year, low density lipoprotein (LDL) levels ≥ 130 mg/dL, or high-density lipoprotein (HDL) levels <40 mg/dL were accepted as dyslipidemia [14].

Definition of components of metabolic syndrome (MetS) was made from the criterion proposed by the international diabetes federation [15], with the following modifications: An individual aged 2–15 years has MetS if he or she has central adiposity (≥ 75th waist circumference percentile as proposed by Kuriyan et al) plus at least two of the following criteria: (1) triglycerides levels >95th percentile(0-9 years ≥ 100mg/dl; 10-19 years≥ 130mg/dl), [2] HDL cholesterol level <5th percentile(< 40mg/dl), [3] systolic or diastolic blood pressure ≥ 90th percentile for the age, sex and height [4] fasting plasma glucose ≥ 100 mg/dl or previously diagnosed type 2 diabetes [14,15].

Upper abdominal examination was performed and analyzed by one radiologist for diagnosis of hepatosteatosis. Liver US findings were staged based on the echogenic intensity observed as normal liver appearance (no steatohepatitis) and increased hepatic echogenicity (steatohepatitis) [16].

Carotid intima media thickness (cIMT) was measured by B-mode US using a 10-MHz linear transducer. The subjects were examined supine with the neck extended and the probe in the antero-lateral position. All measurements of IMT were made in the longitudinal plane at the point of maximum thickness on the far wall of the common carotid artery of both sides along a 1 cm section of the artery proximal to the carotid bulb. The IMT was defined as the distance between the intima-blood interface and the adventitia-media junction. The measurement of cIMT higher than the 95th percentile for the age and sex was considered abnormal [17].

Statistics: Statistical analysis was done using the software SPSS 15.0 for Windows (SPSS™ Inc, Chicago, IL, USA). Categorical data was expressed as frequency and percentage and continuous data as mean with 95% confidence interval (CI) for normally distributed parameters. Comparison between groups was done by student's t test for continuous data. All the tests were two sided and a p value <0.05 was considered statistically significant.

Results

207 children including 127 boys and 80 girls who satisfied the inclusion criteria during the study period were included. The mean age of the study participants was 9.87 years (SD=2.72). Among the study population, 168(81.16%) were obese and 39(18.84%) were overweight. Children with obesity included 101 boys (51.69%) and 67(32.37%) girls. Children with overweight comprised 26 (12.56%) boys and 13(6.28%) girls. Out of the 207 enrolled children, 117 (56.52%) were aged between 9-12 years, 54 (26.09%) between 5-8 years, 22 (10.63%) between 13-15 years and 14 (6.76%) between 2-4 years. One-hundred and eighteen (57%) of the study population were prepubertal, 81 (39.13%) were pubertal and 8(3.86%) were post pubertal.

Among the study participants, 42 (20.28%) children with a mean age of 9.7 years (SD=3.3) had microalbuminuria. Of these 32 had obesity (76.19%) and 10 had overweight (23.81%). The remaining 165 children (79.7%) with a mean age of 9.91 years (SD=2.7) presented with no microalbuminuria. Out of the 165 children with no MA, 136 (82.4%) had obesity and 29 (17.6%) had overweight. Clinical and laboratory characteristics of the study population is shown in (**Table1**).

Microalbuminuria was present in 32 out of 168 children with obesity versus 10 out of 39 children with overweight, 23 out of 127 boys versus 19 out of 80 girls, 17 out of 101 boys with obesity versus 15 out of 67 girls with obesity, 6 out of 26 boys with overweight versus 4 out of 13 girls with overweight, though not statistically significant. We also analyzed prevalence of MA among children of different age groups and pubertal staging. MA was found in 5 out of 14 (28.57%) 2-4 years, 11out of 54 (22.22%) 5-8 years, 21 out of 117 (17.95%) 9-12 years and 5 out of 22 (22.73%) 13- 15 years, 22 out of 118 prepubertal (18.64%), 16 out of 81(19.75%) pubertal and 4 out of 8 (50%) post pubertal children. No statistically significant differences were noticed among these groups. Mean UACR was higher in children with overweight compared to children with obesity (20.8 versus 18.6), in girls in comparison to boys (19.6 versus 18.6) and in girls with overweight compared to boys with overweight (25.3 versus 18.5), but not statistically significant. Mean UACR was almost same in girls and boys with obesity and across different age groups. Mean UACR was significantly higher in post pubertal children (36 mg/g) versus 18.7 in pre pubertal and 17.7 in pubertal children.

The patients were compared after categorizing them into those with normal UACR and those with MA. No significant differences were observed between the groups in terms of the demographic and

Table 1: Clinical and laboratory parameters of study subjects.

Clinical and laboratory parameters	Study subjects(n=207)	Percentage (%)
Obese	168	(81.16%)
Overweight	39	(18.84%)
Systolic Blood Pressure above 90th centile	13	(6.28%)
Diastolic Blood Pressure above 90thcentile	11	(5.31%)
High cholesterol	58	(28.02%)
High Triglycerides	83	(40.10%)
High Low density lipoprotein	58	(28.02%)
Low High density lipoprotein	62	(29.95%)
Dyslipidemia	149	(71.98%)
Impaired fasting glucose	22	(10.63%)
Abnormal HbA1c	66	(31.88%)
Abnormal HOMA-IR	111	(53.62%)
Hyperinsulinemia	42	(20.29%)
Metabolic syndrome	51	(24.64%)
Positive C reactive protein	37	(17.87%)
Fatty liver	113	(54.59%)
carotid intima media thickness Right>95th centile	77	(37.19%)
carotid intima media thickness Left>95th centile	73	(35.27%)
carotid intima media thickness both>95th centile	62	(29.95%)
Mean carotid intima media thickness >95th centile	69	(33.33%)
Microalbuminuria	42	(20.29%)
Abbrevations: HOMA-IR- homeostatic model assessment-insulin resistance, HbA1c- Hemoglobin A1c		

Table 2: Demographic/anthropometric factors and cardiometabolic parameters in those with/without Microalbuminuria.

	Normal UACR (n=165)	Microalbuminuria (n=42)	p value
Demographic/anthropometric factors			
Age (years) Mean (95% CI)	9.92 (9.5 – 10.33)	9.68 (8.67 – 10.68)	0.62
Sex % Female (n)	36.97 (61)	45.24 (19)	0.326
BMI (kg/m2) Mean (95% CI)	24.2 (23.7 – 24.7)	24.1 (23.01 – 25.2)	0.835
Waist Hip Ratio Mean (95% CI)	1.01 (1.002 – 1.02)	1.01 (0.998 – 1.02)	0.68
Waist Height R Mean (95% CI)	0.62 (0.61 – 0.623)	0.62 (0.59 – 0.64)	0.964
Pre puberty	96(58.18%)	22(52.38%)	0.498
puberty	65(39.39%)	16(38.10%)	0.878
Post puberty	4(2.42%)	4(9.52%)	0.056
Family History of obesity	112(67.88%)	27(64.29%)	0.658
Family History of Hypertension	106(64.24%)	25(59.52%)	0.571
Family History of dyslipidemia	88(53.33%)	23(54.76%)	0.868
Family History of Diabetes mellitus	112(67.88%)	33(78.57%)	0.177
Family History of heart attacks	68(41.21%)	14(33.33%)	0.351
Cardiometabolic parameters			
High Systolic blood pressure	10(6.06%)	3(7.14%)	0.796
High Diastolic blood pressure	9(5.45%)	2(4.76%)	0.858
High cholesterol	45(27.27%)	13(30.95%)	0.635
Elevated Triglycerides	66(40%)	17(40.48%)	0.955
Elevated Low density lipoprotein	45(27.27%)	13(30.95%)	0.635
Low High density lipoprotein	47(28.48%)	15(35.71%)	0.361
Dyslipidemia	109(66.06%)	30(71.43%)	0.508
Impaired Fasting Glucose	15(9.09%)	7(16.67%)	0.166
High HbA1c	54 (32.7%)	13 (31%)	0.826
Insulin resistance	87(52.72%)	24(57.14%)	0.608
Hyperinsulinemia	30(18.18%)	12(28.57%)	0.135
Metabolic syndrome	37(22.42%)	14(33.33%)	0.169
Positive C reactive protein	31(18.79%)	6(14.29%)	0.497
Fatty liver	89(53.94%)	24(57.14%)	0.71
High cIMT Right	55(33.33%)	22(52.38%)	0.022*
High cIMT Left	54(32.73%)	19(45.24%)	0.129
Mean cIMT	50 (30.3%)	19 (45.2%)	0.067
*Statistically significant at 5% level **Abbrevations:** cIMT- carotid intima media thickness, HbA1c- Hemoglobin A1c			

anthropometric parameters such as age, sex, BMI, WHR, WHtR (see **Table 2**).

Proportion of children with dyslipidemia, IFG insulin resistance and hyperinsulinemia, abnormal left cIMT and mean cIMT were more in MA group compared to normal UACR group (not statistically significant) (**Table 2**). Proportion of children with abnormal right cIMT values, were significantly higher in the MA group.

Study patients with MA and no MA were also compared for mean values of cardiometabolic parameters. Mean values of BP, triglycerides and HDL showed no difference between the 2 groups while that of LDL, Cholesterol, fasting insulin, HOMA-IR and cIMT- right and left were somewhat more elevated (yet not statistically significant) in subjects with MA. Fasting blood glucose

Table 3: Mean values of cardiovascular risk factors in microalbuminuria Vs normoalbuminuria groups.

Cardiovascular/metabolic factors	Normal UACR (n=165)	Microalbuminuria (n-42)	P-value
Systolic BP (mmHg) Mean (95% CI)	101.16 (99.15 – 103.17)	101.86 (97.91 – 105.81)	0.755
Diastolic BP (mmHg) Mean (95% CI)	63.65 (62.25 – 65.05)	63.29 (60.78 – 65.8)	0.801
Triglycerides (mg/dl) Mean (95% CI)	122.07 (110.9 – 133.24)	123.99 (106.59 – 141.39)	0.853
LDL (mg/dl) Mean (95% CI)	112.04 (107.6 – 116.48)	115.78 (104.82 – 126.74)	0.529
HDL (mg/dl) Mean (95% CI)	43.31 (42.08 – 44.54)	43.15 (40.22 – 46.08)	0.917
Cholesterol(mg/dl) Mean (95% CI)	178.19 (173.1 – 183.28)	183.41 (171.81 – 195.01)	0.413
Fasting glucose (mg/dl) Mean (95% CI)	86.54 (84.99 – 88.08)	85.02 (80.68 – 89.36)	0.518
HbA1c Mean (95% CI)	5.36 (5.29 – 5.44)	5.4 (5.24 – 5.56)	0.683
CRP (mg/l) Mean (95% CI)	5.02 (3.87 – 6.17)	4.48 (2.81 – 6.15)	0.597
Fasting insulin (µu/mL) Mean (95% CI)	16.79 (12.32 – 21.26)	18.4 (14.01 – 22.79)	0.609
HOMA-IR Mean (95% CI)	3.33 (2.91 – 3.76)	5.1 (2.66 – 7.54)	0.161
cIMT- Right(mm) Mean (95% CI)	0.41 (0.39 – 0.43)	0.45 (0.41 – 0.5)	0.081
cIMT- Left(mm) Mean (95% CI)	0.4 (0.38 – 0.42)	0.43 (0.39 – 0.47)	0.235
Mean cIMT Mean (95% CI)	0.41 (0.38 – 0.42)	0.44 (0.4 – 0.48)	0.107

Abbrevations: BP- blood pressure, LDL-low density lipoprotein, HDL- High density lipoprotein, HbA1c- Hemoglobin A1c, CRP- C reactive protein, HOMA IR- homeostatic model assessment-insulin resistance, cIMT- carotid intima media thickness.

Table 4: Comparison of Mean UACR in obese and overweight subjects with or without cardiometabolic risk factors.

Parameter	Mean UACR Obese (n=32)	p value	Mean UACR Overweight(n=10)	p value
Normal Systolic blood pressure	(n=29) 46.72 +/- 19.32	0.627	(n-10) 47.50 +/- 20.365	
High Systolic blood pressure	(n=3) **56.33 +/- 30.022**		N=0	
Normal Diastolic blood pressure	(n=28)48.93 +/- 21.147	0.441	(n=9) 48.44 +/- 21.367	0.99
High Diastolic blood pressure	(n=4) 38.50+/- 4.123		(n=1) 39.00	
Normal Cholesterol	(n=24) 47.33 +/- 20.149	0.790	(n=5) 50.20 +/- 26.148	0.674
High cholesterol	(n=8) 48.50 +/- 21.247		(n=5) 44.80 +/- 15.205	
Normal Triglyceridemia	(n=20) 47. 85 +/- 20.543	0.668	(n=5) 40.60 +/- 9.737	0.818
High Triglyceridemia	(n=12) 47.25 +/- 20.191		(n=5) **54.40 +/- 26.820**	
Normal Low density lipoprotein	(n=22) 51.00 +/- 22.318	0.091	(n=7) 49.29 +/- 22.171	0.148
High Low density lipoprotein	(n=10) 40.20 +/- 11.755		(n=3) 43.33 +/- 18.824	
Normal High density lipoprotein	(n=19) 51.26+/- 23.937	0.205	(n=8) 49.75 +/- 22.096	0.511
Low High-density lipoprotein	(n=13) 42.31 +/- 11.448		(n=2) 38.50 +/- 10.607	
No Dyslipidemia	(n=10) 56.70 +/- 26.226	0.099	(n=2) 39.00 +/- 00	0.99
Dyslipidemia	(n=22) 43.50+/- 15.611		(n=8) **49.62 +/- 22.526**	
Normal Fasting glucose	(n=27) 48.07+/-21.064	0.979	(n=8) 49.88 +/- 22.376	0.694
Impaired fasting glucose	(n=5) 45.20 +/- 15.287		(n=2) 38.00 +/- 1.414	
Normal HbA1c	(n=21) 47.76 +/- 21.464	0.781	(n=8) 40.25 +/- 11.145	0.066
Prediabetes	(n=11) 47.36 +/- 18.14		(n=2) **76.50 +/- 27.577**	
Normal Fasting insulin	(n=23) 47.30 +/- 21. 525	0.257	(n=7) 43.29 +/- 13.376	0.491
Hyper insulinemia	(n=9) 48.44 +/- 16.971		(n=3) **57.33 +/- 33.501**	

No insulin resistance	(n=15) 52.13 +/- 24.489	0.195	(n=3) 38.67 +/- 7.506	0.566
Insulin resistance	(n=17) 43.65 +/- 14.866		(n=7) **51.29 +/- 23.400**	
C Reactive Protein within normal range	(n=28) 49.14 +/- 20.997	0.265	(n=8) 43.50 +/- 11.832	0.895
High C Reactive Protein	(n=4) 37 +/- 5.354		(n=2) **63.50 +/- 45.962**	
Normal carotid intima media thickness	(n=14) 48.14 +/- 23.670	0.954	(n=6) 48.00 +/- 24.000	0.991
High carotid intima media thickness Right	(n=18) 47.22 +/- 17.515		(n=4) 46.75 +/- 16.820	
Normal carotid intima media thickness Left	(n=18) 48.06 +/- 21.577	0.761	(n=5) 51.40 +/- 25.165	0.235
High carotid intima media thickness Left	(n=14) 47.07 +/- 18.776		(n=5) 43.60 +/- 16.180	
No fatty liver	(n=13) 48.77 +/- 25.946	0.282	(n=5) 45.20 +/- 11.584	0.763
Fatty Liver	(n=19) 46.84 +/- 15.632		(n=5) 49.80 +/- 28.030	
No Metabolic syndrome	(n=20) 49.50 +/- 20.915	0.395	(n=8) 49.75 +/- 22.096	0.511
Metabolic syndrome	(n=12) 44.50 +/- 19.086		(n=2) 38.50 +/- 10.607	
*Statistically significant at 5% level				

levels and CRP were clearly not associated with the presence of MA. (**Table 3**).

Relationship between Mean UACR and various cardiometabolic risk factors were analyzed in children with overweight and obese group (**Table 4**) and no significant associations were observed.

Discussion

About 1/5th of the study population comprising of 207 children with ow- ob had microalbuminuria. Prevalence of MA was more in girls compared to boys though not statistically significant. Mean UACR was highest for overweight girls. Mean UACR was significantly higher in post pubertal girls in comparison to prepubertal and pubertal girls. No significant differences were found in terms of demographic, anthropometric parameters and cardiometabolic risk factors between those with MA and those with normal UACR. Proportion of children with abnormal right cIMT values, were significantly higher in the MA group. Mean UACR was high in children with obesity having elevated systolic BP and in children with overweight having hypertriglyceridemia, dyslipidemia, prediabetes, hyperinsulinemia, insulin resistance or high CRP, compared to children with ow-ob having no cardiometabolic risk factors, though not significant.

One study from Bangladesh observed microalbuminuria in 14.3% of children with overweight and significant association of hypertension with high urinary microalbumin in these children [18]. Prevalence of MA in the current study was higher than that reported by other studies from Iran (13%) Egypt (14.7%) USA (10.1%) Netherlands (2.7%) and Spain (2.4%) And lower than that reported by from Nigeria (35.4%) and Cairo, Egypt (29%) [3,19-24].

Wide disparity in the prevalence of MA in obese/overweight children from different parts of the world may be due to the ethnic and demographic differences between the population studied as well as to the criteria used to define microalbuminuria. A study from Pakistan observed ethnic variation in proteinuria while no association between MA and ethnicity was seen in study from Netherlands. Glomerular hyperperfusion and hyperfiltration resulting from physiological maladaptation of obesity may cause renal damage resulting in microalbuminuria [25,21]. Literature data suggest faster change in BMI over a short period before kidneys could adapt led to microalbuminuria rather than baseline BMI [26].

Higher prevalence of MA in children with overweight compared to participants with obesity in the current study may be attributed to limited number of overweight children and this was not statistically significant. Similar to current study, study from Spain [22] and from Korea [27] reported no differences between patients with overweight or obesity in regard to prevalence of MA while prevalence of MA in children with obesity compared to those with normal weight was higher in some studies [19,28] and lower in some [29,30]. The reason for varying prevalence rate of MA in children with ow-ob versus children with normal weight is not clear. Some authors opined it may be due to confounding effect of orthostatic proteinuria in children and adolescents with normal weight or due to high blood pressure or insulin resistance induced endothelial dysfunction and glomerular capillary wall dysfunction resulting in albuminuria in individuals with obesity [3,31]. Higher UACR in heathy children with normal weight can also be explained by exercise induced proteinuria, as they are more active compared to their colleagues with ow-ob. Patients should refrain from physical activity for at least 24 hours prior to testing for urine albumin [32].

Conflicting results were given by different studies on comparing children with ow-ob having MA and normal UACR. No significant differences were observed between children with obesity who had normal urine albumin and those with microalbuminuria in regard to anthropometric and cardiovascular risk factors in the US study and Korean study consistent with our observation. Rather than obesity itself, metabolic consequences of obesity such as prediabetes state were proposed to cause albuminuria [27,3]. A study from Spain also pointed out that metabolic derangements had greater effect on MA than hypertension and obesity [22].

Significant association of MA with various cardiovascular or metabolic risk factors were reported by various studies [3,18-20,22-24,28,33]. Californian study reported no association between MA and cardiometabolic risk factors in children with normal weight while in children with overweight, MA was associated with impaired fasting glucose, insulin resistance, hypertension, and diabetes mellitus [30].

Female sex predilection was observed by several other studies consistent with our observation [3,29,23]. Lower prevalence of MA in boys compared to girls may be due to increased muscle mass and hence increased urine creatinine excretion in boys compared to girls resulting in lower urine albumin creatinine ratio [24].

Current study observed that proportion of children with increased right cIMT was significantly higher in group with ow-ob with MA in comparison to those with no MA. Studies from children with type 1 diabetes reported greater cIMT in those with overweight/obesity and MA [34].

Several studies suggested potential role of adipokines mediated inflammation, oxidative stress, dyslipidemia, activation of renin angiotensin aldosterone system and especially hyperinsulinism and insulin resistance in causing hemodynamic disturbances and

endothelial dysfunction leading to widespread organ damage in obesity. Endothelial dysfunction of renal microvasculature leads to hyperfiltration and proteinuria. Endothelial dysfunction is seen in early stages of atherosclerosis. In adolescents with obesity UACR has been speculated as an early indicator of endothelial dysfunction. cIMT has been used as a surrogate marker for atherosclerosis [3,31,22,35-37].

A study from China observed right cIMT correlated better with hemodynamic patterns and left cIMT with biochemical indices. This difference has been thought to be due to the different origins of the left and right common carotid artery (CCA) and hence the different flow intensities they are subjected to such as hydrostatic pressure in case of left CCA versus dynamic pressure in right CCA [38]. South Asians have been reported to demonstrate higher prevalence of coronary artery disease (CAD) manifesting about 10 years earlier than other ethnic population [39].

In contrast to our study, 2 studies from Italy observed prevalence of MA were more in children with obesity who had nonalcoholic fatty liver disease (NAFLD) compared to those without NAFLD [40,41]. Dyslipidemia, alteration in intestinal permeability and disturbance in gut microbiome have been proposed as the possible mechanisms for the association of MA with NAFLD [41].

Major limitation of the current study was absence of control group with normal weight for comparison. Though UACR was determined in the early morning sample, the confounding effect of intense exercise could not be ruled out in our study. Multicentric studies involving larger sample size may provide a better comparison of all parameters between children with normal weight and children with ow-ob and improve the knowledge on the effect of obesity mediated endothelial dysfunction in future cardiometabolic risks.

Conclusion

High Prevalence of microalbuminuria was observed in Indian children with obesity/overweight. MA in the current study showed no association with cardiometabolic risk factors. Our study observed significantly higher proportion of children with increased right cIMT in the MA group compared to those with normal UACR which warrants further studies looking into the association between microalbuminuria and cIMT in children with obesity so that effective management strategies are planned. Premature atherosclerotic lesions observed in children with obesity paves way for increased CAD in adulthood.

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