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Association of Urinary Albumin with Selected Cardiovascular Disease Risk Factors in Obese Adolescents

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ABSTRACT

Background: Childhood obesity has become a growing health problem in Egypt and other countries in the world. The prevalence of albuminuria is higher in obesity, and could represent an early indicator for cardiovascular diseases (CVD) in obese adolescents. Whether there is a real association between albuminuria and other CVD risk factors remains a matter of debate.

Purpose: In an attempt to answer this debate question, this study aims to assess the association of urinary albumin with central obesity, blood pressure, fasting lipid profile, and insulin resistance in obese adolescents.

Methods: Forty obese adolescents aged 10-18 years, diagnosed with simple obesity were recruited from the National Nutrition Institute in Egypt. Exclusion criteria were adolescents with diabetes, kidney or liver prob-lems, and/or hormonal abnormalities. Measurements included anthropometric assess-ment, blood pressure measurement; and lab analysis for urinary albumin, fasting blood glucose, fasting insulin, and fasting lipid profile. The Spearman correlation coefficient was used for statistical analysis.

Results: Statistically significant positive correlations have been found only between albuminuria and each of: duration of obesity (r=0.93, p= 0.00), waist/height ratio (r=0.65, p=0.00), and/or systolic blood pressure (r=0.33, p= 0.041).

Conclusions: Urinary albumin has been significantly associated with the long-term exposure to excess body weight, central fatness, and systolic blood pressure, but not with diastolic blood pressure, dyslipidemia or insulin resistance in obese adolescents. Early detection of al-buminuria can have a protective role against future hypertension and related target organ damage in this young population. The observations of our study may aid efforts directed to planning better health care system for obese children and/or adolescents in Egypt.

Keywords: Urinary albumin–CVD risk factors–obese adolescents

1 INTRODUCTION

Obesity in childhood and/or adolescence life has become one of the most common health problems worldwide, and has been associated with metabolic syndrome in this younger population [1, 2] . A number of chronic medical problems such as type 2 diabetes, dyslipidemia, cardiovascular disease (CVD), and hypertension in children and adolescents could be attributed to obesity [3]. In adult obesity, evidence shows a significant association between albuminuria and other car-diovascular risk factors [4]. In childhood/adolescence obesity, there are conflicting results; while some research work found a signif-icant correlation between albuminuria and CVD risk fac-

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tors [5–8] , other studies did not [9–11] .

Therefore, this study was conducted to re-investigate the association between urinary albumin and selected CVD risk factors in obese adolescents in Egypt, in an attempt to resolve this controversy. The results of this study may help recent interests about the addition of microalbuminuria screening to the routine assessment of cardiovascular risk factors in obese children and adolescents, for early detection and prevention of future cardiovascular and metabolic problems in this population.

2 METHODS

2.1. Ethical consideration

This study was approved by the ethical committee of Al-Azhar University. Informed consents were obtained from subjects or from their parents before getting them involved in the study.

2.2. Subjects

Forty obese adolescents (25 boys, and 15 girls) were included in this study; they were selected from the National Nutritional Institute in Egypt. The inclusion criteria included both boys and girls, aged 10-18 year, and/or diagnosed with simple obesity, according to the BMI percentile for age and sex [12] . Full medical history taking was done, and accordingly, the exclusion criteria were secondary obesity due to hormonal abnormalities, diabetes, and liver or kidney problems. The anthropometric and clinical characteristics of the subjects are presented in Table 1.

2.3. Measurements

2.3.1. Anthropometric measurements

Anthropometric data were interpreted and presented by using the z-score classification system which is recognized as the best method for anthropometric data analysis compared to other methods [10]. This system uses the following formula for calculating the Z-score: Z-score = (observed value - median value of the reference population) / standard deviation value of reference population [13].

2.3.1.1. Body weight (BW)

All our participants were asked to take off shoes, all outerwear clothing, such as jackets, sweaters or sweatshirts. The participants stood on the weight scale with both feet in the center of the platform, with the body upright and arms hanging at their sides naturally.

2.3.1.2. Height

First, the participants were asked to remove shoes and to stand straight, looking forward with heels close together, shoulders relaxed, and hands at sides. Then the height was measured from the right side of the participant by using a wall-mounted stadiometer. The calculated height was adjusted for age and sex, according to WHO references [12], to determine height z-score.

2.3.1.3. Body mass index (BMI)

Body mass index was calculated for each participant by the following formula: BMI = weight (in kg) / height (in meters)^2. Then, according to WHO charts of BMI z-score for boys and girls, the calculated BMI was plotted against the age and BMI-Z score was determined [12].

2.3.1.4. Waist circumference (WC)

Each participant was asked to remove his/her clothes, to stand with their feet fairly close together, and to breathe normally. WC was measured using a flexible, non-stretchable tape around the waist in a horizontal position to the nearest 0.5 after normal expiration [14] .

2.3.1.5. Waist to height ratio (W/HtR)

W/HtR is a reliable method used to identify central fatness and related cardio-metabolic risks in children and adolescents. Waist circumference of each participant (in Cm) was divided by his/her height (in Cm) and waist/height ratio was then calculated [15, 16].

2.3.2. Blood pressure measurement

Systolic and diastolic blood pressure were measured in the sitting position using a standardized mercury sphygmomanometer with an appropriate blood pressure cuff. The data of the systolic and diastolic blood pressure were compared to the Blood pressure tables for adolescents of "the fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents" [17].

2.3.3. Lab analysis

2.3.3.1. Urinary microalbumin

Morning spot urine samples were collected and assessed by ELIZA kits, Micro-albumin ORG5MA(ORGENTEC Diagnostika, Germany),. Immunometric Enzyme Immunoassay for the quantitative determination of Micro-Albumin in urine was done by using an immunoassay device (State fax, USA).

2.3.3.2. Fasting blood glucose (FBG)

FBG was measured by colorimetric enzymatic method GOD-POD using a fully automated biochemistry device BT 1500 (Biotecnica instruments, Italy).

2.3.3.3. Fasting insulin

Fasting insulin levels were measured by ELISA kits (Monobind, USA) using an immunoassay device (State fax, USA). After measurement of fasting insulin, homeostatic model assessment (HOMA) score was calculated for assessment of insulin resistance, according to the following formula: HOMA-IR = Fasting blood glucose (mg/dL) × fasting insulin (μIU/ mL) /405 [18].

2.3.3.4. Fasting lipid profile

Total cholesterol, serum triglyceride and high-density lipoprotein (HDL) were measured by colorimetric enzymatic method CHOD- PAP by using a fully automated biochemistry device BT 1500 (Biotecnica instruments, Italy). While low-density lipoprotein (LDL) was calculated by this equation: [total cholesterol – HDL – (triglyceride/5)] [19].

2.4. Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The Spearman correlation coefficient was used for statistical analysis. P values of less than 0.05 were considered as statistically significant. Data were presented as means ± standard deviations.

3 RESULTS

As shown in table 1, the mean values of urinary albumin, fasting insulin, and insulin resistance (HOMA-IR) are higher than normal. The mean values of cholesterol, triglycerides, and LDL are above the acceptable reference range (I.e. at the border lines). As shown in Table 2 , a statistically significant positive correlation did exist between microalbuminuria and each of duration of obesity, waist/height ratio and systolic blood pressure.

Table 1. Anthropometric and clinical characteristics of the subjects

Characteristics	Study group (n=40)
Age (Years)	12.48 ± 1.99
Height Z-score	0.32±1.02
Body mass index Z-score	3.21±0.44
Waist circumference Z-score	0.87±0.88
Waist/height ratio z-score	0.94±0.95
Urinary microalbumin (μg/ml)	88.35±85.21
Systolic blood pressure Z-score	0.62±1.21
Diastolic blood pressure Z-score	0.55±1.02
Fasting blood glucose (mg/dL)	95.59 ± 15.81
Fasting insulin (μIU/ mL)	44.25±34.92
Insulin resistance (HOMA-IR)	10.5±8.42
Cholesterol (mg/dL)	177.90 ± 32.79
Triglyceride (mg/dL)	114.98 ± 56.00
HDL (mg/dL)	46.90 ± 8.26
LDL (mg/dL)	107.93 ± 33.04
Creatinine (mg/dL)	0.70 0.13

Data are presented as means ± standard±deviations Normal reference values: Albuminuria ≤ 25 µg/ml; FBG = 70- 115 mg/dl; Fasting insulin = 0.7- 25 µIU/ml; HOMA < 3; Cholesterol < 170 mg/dL; Triglyceride (10- 19 years) < 90 mg/dL; HDL > 45 mg/dl; LDL < 100 mg/dL; Creatinine = 0.6-1.1 mg/dL

Table 2. Correlation between albuminuria and each of the anthropometric and the clinical parameters

Variables	Study group (n=40) Albuminuria	
	r	p value
Duration of obesity (years)	0.933	0.000*
Body mass index (kg/m2)	0.293	0.067
Waist/height ratio	0.646	0.000*
Systolic blood pressure (mmHg)	0.325	0.041*
Diastolic blood pressure (mmHg)	0.274	0.087
Insulin resistance (HOMA-IR)	0.146	0.368
Cholesterol (mg/dL)	0.071	0.665
Triglyceride (mg/dL)	0.070	0.668
HDL (mg/dL)	-0.094	0.562
LDL (mg/dL)	0.069	0.671

* significant p value (i.e.< 0.05)

4 DISCUSSION

Obesity in children and adolescents has become a major health concern worldwide in both developed and developing societies. Childhood obesity is now considered as an independent risk factor for the development of future metabolic and cardiovascular diseases [3]. High level of urinary albumin is quite common in obese children and adolescents [20]. Whether this condition is related to other risk factors co-existing with obesity remains a matter of debate. Some studies [5–8], have found an association between albumin-uria and the traditional cardiovascular risk factors. The pur-pose of this study was to re-explore this association in a sample of Egyptian children and adolescents in an attempt to solve this debate.

The main findings of the present study were: (a) urinary albumin in the obese adolescents was above the normally referenced range. (b) Urinary albumin in obese children and adolescents did have a significantly positive correlation with the duration of obe-sity (i.e. the long-term exposure to excess weight), and with the central fat distribution pattern of obesity measured by waist/height ratio. (c) Furthermore, urinary albumin was sig-nificantly positively associated with systolic but not diastolic blood pressure. (d) Moreover, In regard with blood lipids and insulin resistance, urinary albumin showed non-significant associations with either of them.

In accordance with these findings, Csernus et al. [21], have Our study has shown that, urinary albumin in obese adolescents was above the normal range, and has also reported a significantly positive association between albuminuria and central obesity status. significantly higher levels of albuminuria in obese children compared to normal weight peers, suggesting early renal dysfunction as a consequence of obesity. Prior research work has also reported that higher incidence of microalbu-minuria was significantly related to central obesity, both in obese adolescents [22], and obese adults [23], suggesting weight loss as an essential goal in cardiovascular risk man-agement. Contrary to this finding, a negative associ-ation between albuminuria and childhood obesity in some studies [24, 25]. However, there is an additional evidence supporting this finding, as central obesity has been shown to be an important risk factor for renal function abnormalities, including albuminuria [26]. Variable degrees of albuminuria have been also found to be positively correlated with the severity of obesity [27]. Furthermore, Filler et al. [28] reported a significant increase in BMI z-score in pediatric Nephrology population, with an overall BMI z-score higher than the comparable normal USA young population in the same time span. Moreover, overweight subjects have shown an increased GFR compared with lean subjects, suggesting a significant positive relation to BMI [29]. The higher preva-lence of albuminuria in obese children and adolescents could be explained by the pathophysiological changes that occur in renal hemodynamics including hyperfiltration together with hyperperfusion, both of which play an important role in renal injury [30].

Our study has also shown that urinary albumin has been significantly associated with the systolic but not the diastolic blood pressure in obese adolescents. In line with these results, three studies have found that mi-croalbuminuria was associated with hypertension in obese children and adolescents [6, 7, 31, 32]. In a Chinese study by Wu et al [31], systolic but not diastolic BP was positively correlated with urinary albumin excretion in children, and those with systolic BP of 110- 130 mm Hg had significantly higher microalbuminuria than those with systolic BP≤90 mm Hg. Furthermore, in a Korean study, Cho and Kim [32], have found that microalbuminuria was associated with sys-temic hypertension in obese adolescents.

Moreover, Naughty et al [6] , have also reported an association between mi-croalbuminuria and hypertension in obese adolescents. To add , in obese adults, it was found that albuminuria has a positive correlation with blood pressure particularly with systolic BP [33] . This association could be explained by the fact that elevation in systemic blood pressure leads to endothelial damage which increases vascular permeability resulting in the development of microalbuminuria [34] .

The routine evaluation of urinary albumin was previously proposed by the European Society of Hypertension guidelines is one of the laboratory tests, for assessing target organ damage in hypertensive adult subjects [35]. In paediatric population, the European Society of Hypertension pediatric guidelines recommended the assessment of microalbuminuria to be included in clinical practice [36] . In addition, the more recent pediatric guidelines of the Canadian Hypertension Education Program also recommend the detection of urinary albumin to assess for the existence of target organ damage in children with confirmed hypertension [37].

Our study has also shown that, urinary albumin, insulin resistance, cholesterol, triglycerides, and LDL were above the normal range in obese adolescents. However, we did not find a n a ssociation b etween a lbuminuria a nd e ither o f insulin resistance or blood lipids. These findings a re i n accordance with Rademacher et al. [38], who have reported that the urinary excretion of Albumin is not related to insulin resistance in adolescents. Furthermore, Radhakishun et al. [10] have reported no association of microalbumiuria with impaired glucose tolerance or serum blood lipids in overweight and obese children. Moreover, Gurecká et al. [11] has reported no association between microalbuminuria and serum blood lipids in older adolescents.

5 CONCLUSION

A significant association between albuminuria and some cardiovascular risk factors, namely systolic hypertension and central obesity has been established , with no association with other cardio-metabolic risk factors, in particular, insulin resistance and dyslipidemia. Accordingly screening for microalbumiuria in obese children and adolescents may be a useful tool for early detection of subjects at risk of future systolic hypertension with anticipated target organ damage affecting the renal and the cardiovascular systems. Nevertheless, longitudinal observation studies with large sample size are needed to confirm our results.

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