

Estimated Glomerular Filtration Rate and Microalbuminuria as Biomarkers for Detection of Chronic Kidney Diseases in Obese and Overweight Egyptian Children

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Abstract:

Background: World Health Organization (WHO) reports that kid obesity is a major problem for international health, particularly in low- and middle-income nations. Also, significant growth retardation in children is often caused by chronic kidney disease (CKD); **Objectives:** This study aimed to evaluate the efficacy of estimated glomerular filtration rate (eGFR) and microalbuminuria in detecting chronic renal disease in overweight and obese Egyptian children. **Patients and Methods:** The participants in this cross-sectional research were 138 children aged 5 – 18 years. According to their BMI, there were 45 clinically healthy children as a control group, 43 overweight children and 50 obese children; **Results:** according to eGFR, there were 14 children (32.6%) with CKD in the overweight group and that there were 24 children (48%) with CKD in the obese group. According to microalbuminuria, there were 8 children (18.6%) with CKD in the overweight group while there were 15 children (30%) with CKD in the obese group. The prevalence of CKD was higher in the obese group, **Conclusion:** It was found that the serum creatinine, serum urea, and albumin in urine levels are all significantly higher in the obese and overweight groups, whereas the eGFR is significantly lower. The eGFR increased with age and height in a statistically meaningful way. The eGFR was also inversely related to body mass index, creatinine, urea, white blood cell count, and creatinine in the urine. Moreover, there was a favorable connection between albumin/creatinine ratio and diastolic blood pressure.

Keyword: Glomerular Filtration Rate; Microalbuminuria; Chronic Kidney Diseases; Obese; Overweight.

Introduction

A serious worldwide health issue, childhood obesity is an epidemic ⁽¹⁾. As an adult, being overweight poses a higher risk for medical complications such renal disease ⁽²⁾. The additional characteristics of the metabolic syndrome include central obesity, dyslipidemia, hypertension, and hyperglycemia ⁽³⁾. The rising rate of obesity is directly causing a rise in the number of people diagnosed with CKD. The occurrence of CKD in young children and teenagers has also been on the rise, and those affected by the condition have a dramatically increased chance of passing away ⁽⁴⁾. Being overweight or obese, having diabetes, or having high blood pressure are all factors that put a person at an increased risk of developing CKD. In 2017, around 700 million individuals throughout the globe were living with CKD at any one moment. Obesity is recognized as a contributor to the development of CKD, and it also seems to play a part in the illness's development and progression. There has been a significant rise in the prevalence of obesity among women of reproductive age, which has been linked to an increase in the likelihood that their children may acquire chronic conditions such as obesity and CKD ⁽⁵⁾. Thus, the field of pediatric nephrology acknowledges obesity as a major health concern ⁽⁶⁾.

When determining whether or not a kid is obese, a doctor will look at the child's BMI and compare it to the acceptable percentiles for their age and gender. Obesity in children is characterized by having a BMI that is greater than the 95th percentile and that is less than or equal to the 85th percentile, whereas childhood overweight is characterized by having a BMI that is greater than the 85th percentile and that is lower than the 95th percentile. BMI of 30 or more is associated with severe obesity, according to the American Heart Association.

Absolute BMI less than 35 kg/m² or 120% of the 95th percentile ⁽¹⁷⁾ Cardiovascular and metabolic diseases are more common in those who were very obese as children and teenagers ⁽⁷⁾

Microalbuminuria (MA) is a term that was first used many years ago to characterize the presence of albumin in urine at levels too low to be detected by conventional "dipstick" procedures ⁽⁸⁾. For adults, new recommendations suggest that MA may be defined as 30-300 mg/d in a timed urine sample ⁽⁹⁾.

Many epidemiological studies have consistently linked microalbuminuria to an elevated risk of general CKD development to later stages or possibly ESRD ⁽¹⁰⁾

The National Health and Nutrition Examination Survey (NHANES), which was conducted in the United States between 1999 and 2004, found that 90 percent of people with stage 1 CKD and 87 percent of people with stage 2 CKD were diagnosed with generic CKD due to MA. MA was defined as a urine albumin creatinine ratio (UACR) of 30-299 mg/g creatinine without gender or age adjustments ⁽¹¹⁾

The purpose of this research was to investigate whether or not determining the GFR and the presence of microalbuminuria in children from Egypt who are overweight or obese is useful for the early diagnosis of chronic renal illness.

Subjects and Methods

Measurements of eGFR and microalbuminuria were used in this comparative cross-sectional investigation to determine their use in identifying CKD in overweight and obese Egyptian children.

Study Settings (Location): Pediatric Department of Benha University Hospital, Benha, Egypt.

Study duration: the period between October 2021 and March 2023.

Patients group: The study included 138 patients aged (5 – 18) years. The patients were included in the study

according to their weight and their BMI according to the following equation ($BMI (kg.m^{-2}) = \text{Body weight (kg)} / [\text{Body height (m)}]^2$) then subdivided into two groups: Group 1a: Forty-three (43) patients with overweight ($BMI > 85^{\text{th}}$ percentile and $< 95^{\text{th}}$ percentile). Group 1b: fifty (50) obese patients ($BMI > 95^{\text{th}}$ percentile). Control group (Group2): Included forty-five (45) newborns and children of similar age and both sexes were chosen from the Benha University Hospital pediatric clinic.

Inclusion criteria: Ages from 5 years up to 18 years, patients diagnosed to have obesity and overweight .

Exclusion criteria: Children with endocrinal reasons of obesity (e.g., Cushing's syndrome, hypothyroidism), children with a history of chronic renal illness, children less than 5 years old, children more than 18 years old, newborns, and children without parental authorization are ineligible.

Patients consent: The parents or legal guardians of all study participants provided written permission after being fully briefed on the purpose of the research and the planned methods.

Ethical consideration: The local ethics committee from the School of Medicine at Benha University gave its approval to the whole research plan. At each stage of the research, participants' anonymity and confidentiality were protected. The participation of guardians was voluntary and may be terminated at any moment without any penalties. No secondary analysis was performed on the data collected. M.S: 13.11.2021

Methods

All the participants were subjected to the following:

Complete history taking including: Demographic data including age, sex and residence, dietetic history with assessment of eating habits, past history of any diseases, family history of similar conditions and maternal obesity during pregnancy.

Clinical examination including General examination including anthropometric measures and vital signs as temperature, heart rate, respiratory rate and blood pressure and system examination for all children.

Laboratory investigations: Serum urea and creatinine and complete blood count (CBC)

Samples collection and analysis: Venipuncture was performed with care and little tourniquet pressure was used to draw blood from the antecubital fossa. In this case, 19–21-gauge needles were utilized. Rather of storing those in a freezer, refrigerator, or water bath, specimens were kept at ambient temperature (20–25 °C). Tubes stored in an upright, capped position, at room temperature, and away from severe vibration, mixing, or agitation. All samples showing signs of coagulation were thrown out. In order to perform a full blood count (CBC), measure serum creatinine using the alkaline picrate technique, and measure serum urea, two samples of 2 ml of venous blood in standard tubes containing Tri-potassium ethylenediamine tetra-acetate (K3-EDTA) anticoagulant are required.

Diagnosis of chronic kidney disease by Measuring the estimated glomerular filtration: For determining the GFR of a patient based on the Schwartz formula prediction equation, the NKF-K/DOQI Guidelines for CKD in Children and Adolescents recommended taking into consideration the patient's height, age, and gender in addition to the blood creatinine concentration. The equation used to determine an individual's eGFR is as follows: $[0.55 \text{ patient's height (cm)}] / [\text{serum creatinine (mg/dl)}]$. The value of this constant shifts to 0.70 when looking at males who are adolescents (instead of 0.55).

The following are the typical eGFR ranges for various ages: 2–12 years (males and females), $133 \pm 27 \text{ ml min}/1.73 \text{ m}^2$, 13–21 years (males), $140 \text{ ml min}/1.73 \text{ m}^2$, and

13-21 years (females), 126 ±22 ml min/1.73 m².

In another study demonstrated that the Iothalamate GFR (IoGFR) and the Schwartz formula had an agreement of around 80%, with a sensitivity of 90% and a specificity of 67% for detecting IoGFR 90 ml/min/1.73 m².

Measuring microalbuminuria: Early in the morning, the youngster was placed in the supine position, and a urine sample was obtained. Urinary albumin concentrations were measured with a solid-phase fluorescent immunoassay, and urinary creatinine levels were measured with the Jaffe rate reaction method, using a CX3 analyzer (Beckman Instruments AU480, Brea CA). The urinary albumin/creatinine ratio was expressed as milligrams of albumin per gram of creatinine. **Calculation and assessment of body mass index:** A Harpenden fixed stadiometer was used to precisely measure the subjects' stature to the closest 0.1 cm.

Statistical analysis and data interpretation: Using SPSS (Statistical Software for the Social Sciences, version 22.0 Armonk, NY), the following statistical analyses of the research's data were carried out: The phrases mean, standard deviation, and range are used whenever it is necessary to characterize quantitative variables. Quantitative and percentage-based descriptions are used to discuss qualitative features. The Chi-square (2) test was employed to compare quantitative data across groups where the standard deviation

(SD) was less than 50% of the mean. The Mann-Whitney U-test was used in situations in which the SD was between 20% and 50% of the mean.

Results

This comparative-cross sectional study included 138 children aged 5 – 18 years. They were divided into three age and sex matched groups, 45 clinically healthy children as a control group, 43 overweight children and 50 obese children.

Table (1) shows that there were no statistically significant differences between the different groups as regards age and sex. Among the children included, there were 22 (48.9%) boys and 23 (51.1%) girls in the control group, 21 (48.8%) boys and 22 (51.2%) girls in the overweight group while there were 26 (52%) boys and 24 (48%) girls in the obese group, with no statistically significant differences between the groups.

Table (2) shows that the mean serum creatinine was statistically significantly higher in the obese group when compared to the control and overweight groups, but that there was no statistically significant difference between the overweight and control groups.

This graph demonstrates that the mean eGFR was significantly higher in the control and overweight groups compared to the obese group, with no statistically significant difference between the control and overweight groups.

Figure (1): Boxplot of eGFR in the cases of the study groups.

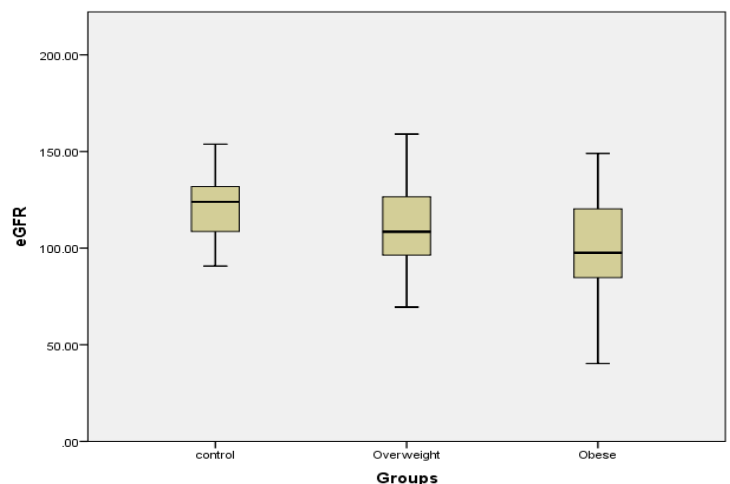


Table (1): Demographic data of the study groups.

Demographic data	Control group N= 45	Overweight group N= 43	Obese group N= 50	Test of sig.
Age (Years)	8.83 ± 2.34	8.85 ± 2.42	8.46 ± 2.23	F= 0.428 P = 0.653
Gender	Boys	22 (48.9%)	21 (48.8%)	$\chi^2 = 0.125$ P = 0.939
	Girls	23 (51.1%)	22 (51.2%)	

Quantitative data are to be regarded as mean ± SD.

Qualitative data are to be regarded as number (Percent)

F: One-way ANOVA test

Table (2): Kidney functions in the study groups .

Kidney functions	Control group N= 45	Overweight group N= 43	Obese group N= 50	Test of sig.
Serum creatinine (mg/dl)	0.61 ± 0.08	0.68 ± 0.14	0.81 ± 0.26	F = 14.751 P < 0.001* P1 = 0.112 P2 < 0.001* P3 = 0.004*
Serum urea (mg/dl)	21.51 ± 6.22	31.11 ± 5.44	28.86 ± 7.54	F = 26.490 P < 0.001* P1 < 0.001* P2 < 0.001* P3 = 0.226
eGFR (ml/min/1.73 m ²)	123.96 (90.75-153.80)	108.51 (69.47-1128.95)	97.63 (40.25-149)	KW = 10.029 P < 0.001* P1 = 0.984 P2 < 0.001* P3 < 0.001*
Albumin in urine	15.60 (3.50-43.50)	11.80 (2.80-130.50)	25.10 (2.11-95.60)	KW = 6.588 P < 0.001* P1 = 0.238 P2 = 0.009* P3 = 0.397
Creatinine in urine	84.60 (16.30-203.40)	130.80 (65.68-302.99)	144.60 (27.82-327.78)	KW = 35.013 P < 0.001* P1 < 0.001* P2 < 0.001* P3 = 0.356
Albumin/creatinine ratio	20.16 (6.25- 33.37)	10.67 (2.80-58.26)	17.97 (2.07-67.90)	KW = 4.969 P = 0.106

F: One-way ANOVA test KW= Kruskal Wallis test

P: General intergroup significance

P1: Significance of the overweight group compared to the control group.

P2: Significance of the obese group compared to the control group.

P3: Significance of the obese group compared to the overweight group.

* Significant (P <0.05)

Table (4) shows that according to eGFR, there were 14 children (32.6%) with CKD in the overweight group while there were 24 children (48%) with CKD in the obese group. Obesity increased the prevalence of CKD; however, it did not reach a statistically significant level (p=0.131).

Table (5) shows that according to microalbuminuria, there were 8 children

(18.6%) with CKD in the overweight group while there were 15 children (30%) with CKD in the obese group. Obesity was associated with a greater rate of CKD, although the difference was not substantial enough to be considered statistically significant. (p=0.204).

Table (3): Correlation between albumin/creatinine ratio and clinical and laboratory data .

Clinical and laboratory data		Albumin/creatinine ratio
eGFR	rs	0.015
	p	0.861
Age	rs	0.050
	p	0.561
height	rs	0.054
	p	0.529
weight	rs	-0.016
	p	0.854
BMI	rs	-0.046
	p	0.592
Creatinine	rs	0.012
	p	0.891
urea	rs	-0.138
	p	0.108
SBP	rs	-0.130
	p	0.130
DBP	rs	-0.286**
	p	0.001
HGB	rs	0.156
	p	0.068
WBCs	rs	-0.095
	p	0.266
Neutrophil	rs	-0.016
	p	0.853
lymphocytes	rs	0.014
	p	0.872
PLATLETS	rs	0.041
	p	0.634

rs : Spearman’s correlation coefficient, *: Statistically significant (p< 0.05)

Table (4) shows that there was a statistically significant positive correlation between albumin/creatinine ratio and DBP.

Table (4): Prevalence of CKD in the obese and overweight groups according to eGFR.

CKD	Overweight group N= 43	Obese group N= 50	Test of sig.
No CKD	29 (67.4%)	26 (52%)	$\chi^2 = 2.281$
CKD	14 (32.6%)	24 (48%)	P = 0.131

χ^2 = Chi-square test

P: intergroup significance

Table (5): Prevalence of CKD in the obese and overweight groups according to microalbuminuria.

CKD	Overweight group N= 43	Obese group N= 50	Test of sig.
No CKD	35 (81.4%)	35 (70%)	$\chi^2 = 1.613$
CKD	8 (18.6%)	15 (30%)	P = 0.204

χ^2 = Chi-square test

P: intergroup significance

Discussion

There is mounting evidence that children who are overweight or obese are at a higher chance of becoming overweight as adults and may be at a higher risk of acquiring chronic diseases⁽¹²⁾.

Around one-third of children with CKD may have severe growth impairment before reaching end-stage renal disease. Children with a complication of CKD called severe development failure have a high risk of death on top of the medical, social, and psychological difficulties they already face⁽¹³⁾.

This comparative-cross sectional study included 138 children aged 5 – 18 years. According to their BMI, there were 45 clinically healthy children as a control group, 43 overweight children and 50 obese children.

This distribution didn't reflect the actual prevalence of overweight or obesity in the included children as the distribution was controlled to achieve equal age and sex distribution.

No significant difference was seen between the sexes; however, the current study did identify a slightly higher percentage of boys in the obese category.

According to the study that utilizes the CDC growth chart, found that 4.6% of boys and 8.9% of girls were overweight or obese; these results were supported by the present research⁽¹⁴⁾. Similar findings were reported by who performed research in Tanzania and found that the prevalence of overweight and obesity among males was 12.1% and 4.9% using the WHO chart, respectively, while among women it was 18.7% and 8.0%.⁽¹⁵⁾

There were large differences in the research groups' dietary histories, and these differences were statistically significant. Compared to the obese group, the control and overweight groups had considerably greater rates of breastfeeding. Overweight mothers were more likely to report breastfeeding than their obese counterparts, according to the study's authors.

According to the study only 6.1% and 3.2% of overweight and obese children, respectively, were breast fed (P value 0.05) (OR = 47.2, 95% CI: 26- 84.1). Overall, 41.1% of overweight children and 33.1% of obese children were provided feeding formula⁽¹⁶⁾.

In addition, found a significant connection (p value 0.001) between lactation nutrition and body mass index (BMI) among children in Port Said, Egypt; whereas 5.7% and 18.1% of breast-fed infants were obese and overweight, respectively, 36.5% of formula-fed children were⁽¹⁷⁾.

A number of earlier researchers also found a strong correlation between breast feeding and a reduced risk of overweight and obesity in children. Reports suggest that breastfeeding may help prevent excess weight growth in children; this is significant since kids who are overweight are more likely to be overweight as adults⁽¹⁸⁾.

Regular exercise was hypothesized to be a moderator affecting the steepness of the weight gain curve, and increased calorie intake was blamed for the pandemic of overweight and obesity in the United States⁽¹⁹⁾. Overweight and obesity are caused by a caloric imbalance, or failure to expend enough energy, and are affected by many different aspects of one's biological, social, and environmental environments⁽²⁰⁾.

In this comparison of athletic abilities, considerable and statistically significant disparities were found across the groups. The prevalence of sports involvement was significantly lower in the obese group compared to the control and overweight groups. Also, a far higher proportion of the overweight than the obese participate in sports on a regular basis⁽¹⁶⁾

Fast food consumption was more common among obese and overweight students than among their leaner counterparts, with 62.5% and 56.8% of those groups doing so, respectively (OR = 6.86, 95% CI: 4.6 - 10.19), supporting the findings, who also discovered a strong correlation between

fast food intake and obesity ($P= 0.001$). (16).

This is in agreement with the research of Salem and colleagues, who discovered that obese children had much higher baseline and resting metabolic rates (BMR and RMR) than their leaner counterparts ($P 0.001$)⁽²¹⁾

Another study showed that teenage risk for overweight and obesity was elevated when individuals engaged in less physical activity and more sedentary behaviors, such as watching too much television or using a computer⁽²²⁾.

Similarly to, another study indicates that higher body mass indexes are linked to more frequent restaurant visits. Similar to what has been observed elsewhere; we discovered a positive correlation between body mass index and the number of times per month that people visited "fast food" establishments⁽²³⁾.

Obesity was shown to be more common in the children who engaged in sedentary activities like watching too much television or using computers for extended periods of time.

According to research which found a statistically significant correlation between parental obesity and their children's obesity or overweight status ($p=0.001$), this was the case ($OR = 134.4$, $95\% CI: 47.06 - 372.6$). Almost all children who were overweight (92.7%) or obese (97.2%) had at least one obese parent⁽¹⁶⁾.

This was in agreement with the results of a cross-sectional research conducted in Menoufia Governorate. Thirty-six students made up the sample (148 boys and 158 girls). Children having a positive family history of obesity (27.4%) were found to be substantially more likely to be obese themselves (14.6%) than those without such a history⁽²¹⁾.

Evidence from the study demonstrated a considerable positive connection ($p < 0.001$) between maternal and paternal BMI and child BMI⁽¹⁷⁾.

The present research found that the mean systolic and diastolic blood pressures of

the overweight and obese groups were considerably higher than those of the control group. There was no discernible difference between the two groups, statistically speaking.

This was consistent with the study performed on a total of 100 kids, split evenly between boys and girls (53 in the control group and 47 in the obesity group), averaging 8.6 and 3.4 years old. There was a statistically significant difference in mean diastolic blood pressure, according to the authors' findings. Diastolic blood pressure was 9.56 mm Hg higher in obese youngsters than in their normal-weight peers. Two of the overweight participants in their research were found to have hypertension⁽²⁴⁾.

The risk of developing hypertension is lower in overweight than in obese teenagers, but substantially greater than in normal-weight people, as shown by other research⁽²⁵⁾.

According to eGFR, 14 children (32.6%) in the overweight group and 24 children (48.2%) in the obese group were diagnosed with CKD over the course of this research. In the obese group, CKD prevalence was greater, although not significantly so ($p=0.131$). Eight children with CKD were found in the overweight group (18.6%), and fifteen were found in the obese group (30%), as measured by microalbuminuria. Prevalence of CKD was higher in the obese group, although the difference was not statistically significant ($p=0.204$).

Similar findings were discovered in their research, which included the examination of 799 young people with median ages of 11.0 years and median GFR values of 49.9 mL/min/1.73 m². Children with glomerular chronic kidney disease who were overweight had an impaired kidney function in 27% of the cases, whereas children who were obese had an impaired kidney function in 18% of the cases (median SDS 0.91; IQR 0.10 to 1.73) 17% of children with glomerular CKD and 29% of children with non-glomerular CKD

were overweight or obese, when height and age were taken into account; however, 16% and 14% of children with non-glomerular CKD were overweight or obese, when height and age were taken into account⁽¹³⁾.

Nearly half of the children and adolescents who had glomerular disease were either overweight (18%) or obese (27%), which is close to the rate that was observed in the general child and adolescent population in the United States⁽²⁶⁾.

In the research published in 2022, there were a total of 247 patients diagnosed with glomerular CK and 600 patients diagnosed with non-glomerular CKD. Among individuals diagnosed with non-glomerular illness, 423 (71%) were classified as having a normal body mass index (BMI), while another 85% (14%), and 92% (15%) were classified as being overweight or obese. One hundred thirty-four (54%) of patients diagnosed with glomerular disease were of normal weight, forty-nine (20%) were overweight, and sixty-four (26%) were obese⁽²⁷⁾.

There was a favorable association between age and height and eGFR in the present research. The eGFR was also inversely related to body mass index, creatinine, urea, white blood cell count, and creatinine in the urine. In addition, there was a favorable association between the albumin/creatinine ratio and diastolic blood pressure.

Found that in obese adolescents, eGFR was negatively correlated with systolic BP, diastolic BP, creatinine, and BMI ($r=0.317$, 0.378 , 0.127 , and 0.868 , respectively, at P value less than 0.05).⁽²⁸⁾

On the contrary, other studies demonstrated a lack of association between BMI and GFR⁽²⁹⁾. The variations could be explained due to variations in the equations used for assessment of eGFR. Yet, there are caveats to the present research. The present findings may be limited by the study's small sample size and the fact that it was conducted at a single site. In addition, the study

understated the incidence of childhood obesity.

Conclusion

We find that the serum creatinine, serum urea, and albumin in urine levels are all significantly higher in the obese and overweight groups, whereas the eGFR is significantly lower. The eGFR increased with age and height in a statistically meaningful way. The eGFR was also inversely related to body mass index, creatinine, urea, white blood cell count, and creatinine in the urine. In addition, there was a favorable association between the albumin/creatinine ratio and diastolic blood pressure.

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