Estimated glomerular filtration rate and blood pressure in a sample of obese Egyptian adolescents

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Background/aim
Obesity is a major risk factor for some comorbid conditions. Our goal was to study the relationship between obesity and kidney function in adolescents using estimated glomerular filtration rate (eGFR) as well as to study blood pressure (BP) in obese adolescents.
Patients and methods
This study included 45 male and female adolescents who visited the Child Health Clinic at the NRC, Egypt, with BMI more than or equal to 85th centile and aged 10–18 years old, and 45 age-matched and sex-matched healthy controls with BMI less than 85th centile. Serum creatinine as determined by the spectrophotometric method, the estimated glomerular filtration calculated using the revised Schwartz formula, and BP were compared between the studied groups.
Results
The results indicated that serum creatinine and BP were significantly higher in obese patients than healthy control group ($P<0.05$). In contrast, the eGFR was lower in the obese patients than in the control group ($P<0.05$). In obese adolescents, there were negative correlations between eGFR and systolic BP, diastolic BP, creatinine, and BMI ($P\leq0.05$). In addition, there were positive correlations between BMI and each of systolic and diastolic BP ($P<0.01$).
Conclusions
Obese adolescents exhibited lower eGFR estimations, slightly increased serum creatinine, and elevated BP results, being compatible with some degree of renal impairment. Therefore, BP and renal function should be routinely checked in obese adolescents.

Keywords:
blood pressure, creatinine, estimated glomerular filtration rate, obesity

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Introduction

Obesity and chronic kidney disease (CKD) are two public health problems that have been increasing worldwide. In the United States, it is estimated that one-third of adults are overweight and one-third are obese [1]. In Egypt, the percentage of overweight children aged 5–19 years old was 35% in males and 36.4% in females, whereas that of obesity was 10.5 and 9.5%, respectively, according to the Egypt Demographic and Health Survey in 2014 [2].

It has been pointed out that obesity may be a potential cause or even a risk factor for the development of renal disease in elderly as well as pediatric age group [3].

Obesity-induced derangements that are nephrotoxic may be an explanation in trying to link these two health problems. One of these derangements is adipose tissue producing some adipokines such as leptin, adiponectin, tumor necrosis factor-α, angiotensin-II, transforming growth factor-β, and monocyte chemoattractant protein-1 [4].

Furthermore, obesity can promote renal dysfunction and end-stage renal disease by triggering processes such as insulin resistance, glucose intolerance, hyperlipidemia, atherosclerosis, and hypertension [5].

CKD is an increasing global public health problem that may affect people's quality of life negatively, especially in their early productive years [6]. Studies in general pediatrics and findings regarding differences in glomerular filtration rate (GFR) in normal weight and obese children have been somewhat

contradictory, where some found high GFR in obese caused by hyperfiltration whereas other studies reported opposite results or no differences at all [7,8].

It is difficult to assess kidney function in children in general and to what degree the kidneys contribute in the metabolic group of disorders that arise with the advent of obesity at these young ages. On the contrary, as external, precise, but invasive, methods cannot be applied to healthy children, we can count on estimated glomerular filtration rate (eGFR) formulas. This study aimed to compare kidney function, assessed by serum creatinine and eGFR, and blood pressure (BP) between the studied obese and control groups.

Patients and methods

Patients and study design

The present study enrolled 45 adolescents who visited the Child Health Clinic at Medical Research Center of Excellence (MRCE), National Research Center, Dokki, Cairo, Egypt. All cases had BMI above or equal to 85th centile (obese group). In addition, 45 adolescents, age and sex matched, with BMI below 85th centile, served as the control group (nonobese group). Inclusion criteria were adolescents of both sexes aged 10–18 years old. The exclusion criteria were chronic illnesses and endocrine problems to avoid secondary causes of hypertension and obesity.

Ethical considerations

The present study was conducted with the Code of Ethics of the World Medical Association, according to the principles expressed in the Declaration of Helsinki. This study was approved by the local Medical Ethical Committee of the National Research Center with approval number 16/130. A written informed consent was provided by all children and their parents before their inclusion in the study.

Methods

An anonymous self-administered questionnaire meeting the objective of the study was used to collect the data. After the questionnaire was completed, sociodemographic characteristics, height, weight, and BP were assessed by a trained medical professional. Height and weight were taken to the nearest 0.1 cm and 100 g using the Holtain portable measuring device and a digital Seca scale while the participants were barefooted and wearing minimal clothing. Before the examination, the scale was calibrated. At least two physicians conducted each of these measurements; one took the measurements and the other documented the results. It was decided to take the average of the two measurements. BMI calculation was done using the following formula: weight (kg)/height $(m)^2$, and values were compared with the WHO growth charts through the software AnthroCalc v1.66 Home, where normal represented 5–84th percentile and overweight and obese represented more than or equal to 95th percentile [9].

The studied groups were classified with the same cutoff point used by Mahfouz Nermine *et al*. [10] in their study about body weight concern into a case group with a BMI more than or equal to 85th centile and a control group with a BMI less than 85th centile.

BPs were taken using a mercury sphygmomanometer of Diamond Mercurial BP apparatus. The BPs were taken at a regular state of health after excluding factors that may affect the readings, such as fear and anxiety, by giving a 10-min rest while talking with the child. BP was measured on the right arm with support at heart level for consistency and compared with standard tables with the child in sitting posture with back supported chair and foot touching the ground. An appropriately sized bladder cuff was used, with a width of 10 cm and a length of 24 cm for adolescents with an arm circumference less than or equal to 26 cm, whereas 13-cm width and 30-cm length for adolescents over 26 cm in arm circumference. The cuff should span two-thirds of the arm's circumference, with the lower edge 2.5 cm above the cubital fossa, as per the WHO guidelines, and according to Flynn *et al*. [11].

Laboratory procedures

Venous blood samples were collected, and serum was separated and kept at −20°C till analyzed. The compensated Jaffé calibrated to an isotope dilution mass spectrometry technique was used to determine serum creatinine levels using an Olympus AU 5400 analyzer (Beckman-Coulter, Brea, California, USA) [12]. The following formulae were used to calculate eGFR:

eGFR [ml/min/1.73 m^2=k×height (cm)÷serum creatinine (mg/dl)], with a k constant of 0.413 in the revised Schwartz formula (Schwartz-R) [13].

Statistical analysis

The Statistical Package for the Social Sciences (SPSS Statistics for Windows, Version 21, Chicago: SPSS Inc.), version 21.0 was used. The normally distributed data were represented as mean and SD, and variables were subjected to the independent *t* test. Pearson

correlation was used for exhibited the different correlation between the estimated parameters. Statistical significance was defined at *P* value less than 0.05.

Results

Detailed anthropometric data are shown as mean and SD in Table 1. The average age of the participants was 13.05±2.61 and 12.62±2.6 years for obese and nonobese groups, respectively. Obese children showed a significant increase in weight (73.41±18.26 vs. 37.39±10.68), weight centile (96.26±4.80 vs. 27.43 ±25.05), height centile (51.50±28.89 vs. 32.60±28.74), BMI (30.55±5.61 vs. 17.22±2.71), and BMI centile (98.30±2.68 vs. 34.40±28.16) as compared with their control counterparts, whereas no difference in height was observed.

BP levels were significantly higher in the obese group, where systolic BP was 107.56±11.13 in cases versus 97.63±7.84 in controls, with *P* value of 0.001, and diastolic was 68.66±9.88 in cases versus 62.88±5.98 in controls, with *P* value of 0.002, as shown in Table 2.

The data shown in Table 3 reported a significant increase in serum creatinine levels in obese adolescents (0.94±0.23) than control healthy group (0.79±0.21), with *P* value of 0.007, whereas a significant decrease in eGFR was reported when estimated by the Schwartz-R formula (73.10±22.33 vs. 85.30±32.25, with *P*=0.048).

The present study showed statistically significant negative correlations between eGFR and each of systolic BP, diastolic BP, creatinine, and BMI, where r=−0.317, −0.378, −0.127, and −0.868, respectively, at *P* value less than 0.05 in obese adolescents, as shown in Table 4.

The data reported in Table 5 showed highly significant positive correlations between BMI and each of systolic BP and diastolic BP (r=0.45 and 0.41, respectively, at $P<0.01$) in obese adolescents.

Discussion

Obesity-related renal impairment in children and adolescents is still a controversial topic, and contradictory results continue to emerge. Some researchers discovered that hyperfiltration develops as a result of the kidneys' physiological adaptation to increased body mass [14].

Table 1. Anthropometric data of obese and nonobese groups of adolescents

Parameters	Obese group BMI ≥85th percentile	Nonobese group BMI <85th percentile	*P* value
Age (years)	13.05±2.61	12.62±2.60	0.100
Weight (kg)	73.41±18.26	37.39±10.68	0.001*
Weight centile	96.26±4.80	27.43±25.05	0.0001*
Height (cm)	154.16±10.65	146.05±13.04	0.160
Height centile	51.50±28.89	32.60±28.74	0.001*
BMI	30.55±5.61	17.22±2.71	0.01*
BMI centile	98.30±2.68	34.40±28.16	0.002*

All data are expressed as mean±SD.
*Significant difference between two groups at *P* value less than 0.05 using *t* test.

Table 2. Comparisons of blood pressure in obese and nonobese groups of adolescents

	Obese group	Nonobese group	*P* value
Systolic BP (mmHg)	107.56±11.13	97.63±7.84	0.001*
Diastolic BP (mmHg)	68.66±9.88	62.88±5.98	0.002*

All data are expressed as mean±SD.
BP, blood pressure.
*Significant difference between two groups at *P* value less than 0.05 using *t* test.

Table 3. Comparison between renal function markers in obese and nonobese groups of adolescents

	Obese group	Nonobese group	*P* value
Serum creatinine (mg/dl)	0.94±0.23	0.79±0.21	0.007*
eGFR Schwartz-R (ml/min/1.73 m^2)	73.10 ±22.33	85.30±32.25	0.048*

All data are expressed as Mean±SD.
eGFR, estimated glomerular filtration rate.
*Significant difference between two groups at *P* value less than 0.05 using *t* test.

Table 4. Correlation coefficient between estimated glomerular filtration rate and different parameters in obese and nonobese groups

	Obese group		Nonobese group	
	r	*P*	*r*	*P*
Systolic BP (mmHg)	−0.317*	0.043	−0.132	503
Diastolic BP (mmHg)	−0.378*	0.015	−0.103	602
Serum creatinine(mg/dl)	−0.127	0.447	0.439*	0.012
BMI	−0.868**	0.000	−0.191	0.295

BP, blood pressure.
*Significant correlation at *P* value less than 0.05.
**Highly significant correlation at *P* value less than 0.01.

Table 5. Correlation coefficient between BMI and different parameters in obese and nonobese groups

	Obese group		Nonobese group	
	r	*P*	*r*	*P*
Systolic BP (mmHg)	0.456**	0.003	0.229	0.166
Diastolic BP (mmHg)	0.415**	0.007	0.053	0.752
Serum creatinine (mg/dl)	–0.047	0.78	0.302	0.093
eGFR Schwartz-R (ml/min/ 1.73 m2)	–0.868**	0.000	–0.191	0.295

BP, blood pressure; eGFR, estimated glomerular filtration rate.
**Highly significant correlation at *P* value less than 0.01.

Significant positive correlations were found in this study between kidney function presented by serum creatinine and BMI, where obese adolescents showed significantly higher values of serum creatinine and lower levels of eGFR.

Some authors have reported that pre-pubertal children who are overweight or obese do indeed show a significant decrease in eGFR [15].

Some researchers consistently found substantial positive associations between obesity measurements and renal eGFR [16]. On the contrary, others found no significant differences in variations in levels of GFR between obese and nonobese children [17].

In this study, we found that obesity was associated with decreased kidney function presented by serum creatinine. Likewise, in some studies, authors have found decreased renal function in obese children [18]. In a study done in the United States, although levels of eGFR were found to be significantly lower in obese group, they concluded that obesity had no significant role in altering the eGFR [19].

In this study, we found a statistically significant inverse relationship between eGFR and BMI, implying that those with a high BMI had renal affection. This goes along with two studies reported by He *et al.* [20] and Dada *et al.* [21]. On the contrary, other studies demonstrated a lack of association between BMI and GFR [22].

Several studies in the pediatric age have demonstrated that eGFR formulas are trustworthy methods for assessing renal function, but the accuracy of creatinine clearance is rarely reported and also due to the lengthy and inaccuracy of the 24-h urine collection method that may affect creatinine clearance together with tubular secretion of creatinine, which may rise eGFR. A valid alternative is the revised Schwartz formula (Schwartz-R) using serum creatinine to estimate eGFR in nonoverweight and overweight/ obese adolescents [23].

There are various possible mechanisms through which obesity can lead to kidney injury in pediatric age, one of which is that obesity leads to a series of structural, dynamic, and biochemical changes that contribute to kidney injury and which is believed to start with a state of excessive filtration, which later strengthens the progressive damage, with increased protein loss and final stage of glomerular hyperplasia and fibrous scarring [24].

Obesity is also associated with low-grade chronic inflammation, which is typically different in the presentation from normal inflammation but is much the same in that it shares disruptions resulting from typical inflammatory mediators [25]. In inflammatory conditions associated with obesity, the increased size of adipocytes plays a crucial role, because the more adipose tissue increases, the adipocyte production increases, and this leads to a spectrum of pathophysiological processes associated with inflammation [26].

Adipose tissue is more than just a fat reservoir; it is also a dynamic tissue that contributes in the production of 'adipokines' such as adiponectin, leptin, angiotensin-II, and tumor necrosis factor-α, which is also called inflammatory cytokines [4].

Obesity also triggers a cascade of events that include insulin resistance, glucose intolerance, hyperlipidemia, and atherosclerosis and high BP, all of which are associated with an increased risk of developing cardiovascular disease. The relationship between CKD and dyslipidemia may be due to insulin resistance to action which reduces the activity of lipoprotein lipase [5].

In our study, we reported that BP is higher in the obese group and that both systolic and diastolic values were elevated which is consistent with some studies such as Koebnick *et al.* [27] who found 2.1% higher prevalence of hypertension in overweight adolescents than those with normal body weight aged 12–19 years. Other studies also showed that the chances of developing high BP are lower in overweight adolescents compared with obese adolescents and significantly much higher when compared with normal-weight individuals [28–31].

It is worth to say that the attribution of high BP caused by excess weight is greater during adolescence than in childhood as a study reported overweight and obesity account for only 5 and 9% of hypertension, respectively, in females and males children aged 5–6 years of age [32]. Chiolero *et al.* [33] reported that the attributable fraction of hypertension for both overweight and obesity was highest among adolescents aged 12–13 years (attributable fraction=39%).

It is estimated that BP increases by 10 mmHg in systole and by 3 mmHg in diastole with every decimal point increase in BMI. These fundamental differences would have a significant effect on CVD risk if it persisted into adulthood [34].

In the past few decades, the prevalence of systemic hypertension among adolescents has been well documented at ~3.5%. Obese adolescent males had a prevalence of more than 30%, whereas obese adolescent females had a prevalence of 23–30% [35].

In a study done on 1618 children aged 12–16 years, systolic hypertension and diastolic hypertension were found to be prevalent in 12 and 13.7%, respectively, with a higher prevalence of obesity (45.5%) among them than the estimated prevalence among all of the studied children (18%) [36].

In children and adolescents with normal body weight, there is a consistent positive relationship of weight with BP during children's growth and development [37]. Studies showed that elevated BMI is associated with higher BP in the future and the risk increased with severity of obesity where severe obesity (BMI >99th percentile) is associated with a fourfold rise in the prevalence of elevated BP, compared with merely a twofold increase in individuals with obesity (BMI 95th–98th percentiles) [38].

Obesity results in increased renal tubular sodium absorption, which impairs internal pressure and leads to volume expansion as a result of sympathetic nervous system and renin–angiotensin–aldosterone system activation [39].

A crucial event in the development of systemic hypertension in obesity is an increase in sodium reabsorption and the resulting rise in extracellular volume. Furthermore, if glomerular hyperfiltration, insulin resistance, diabetes mellitus, and systemic hypertension coexist, there is an increase in renal blood flow and GFR, which eventually lead to renal damage and a decrease in GFR [40]. Sympathetic nervous system activation in obesity may be caused by different factors such as increased levels of fatty acid, increased levels of angiotensin-II, hyperinsulinemia, and hyperleptinemia. This sympathetic nervous system activation together with increase in leptin levels increases systemic BP through nitric oxide synthesis inhibition (potent vasodilator) [41].

Visceral obesity with increased visceral fat and accumulation of visceral adipose tissue leads to renal compression that increases the hydrostatic pressure of the interstitial fluid and increases intrarenal pressure. Increased intrarenal pressure compresses loop of Henle reducing fluids flow through renal tubules, which consequently leads to sodium reabsorption [42].

In cases of 'overnutrition,' the supply of fatty acid to the tissues exceeds the metabolic demands resulting in a compensatory increase in oxidation. Increased fatty acid metabolism results in the production of harmful substances such as lipid peroxidation products, which promote apoptosis and fibrosis in nonadipose tissues such as myocardium, pancreatic islets, skeletal muscle, and the kidneys, and this is called 'lipotoxicity' [40].

There is evidence that the type of glomerulonephritis associated with obesity is focal and segmental glomerulosclerosis, presenting firstly with increase in albumin excretion, which gradually increases with the severity of obesity and can lead to nephrotic syndrome and progressive loss of kidney function [43].

Conclusion

To sum up, we reported that overweight and obese adolescents at the age of 12–18 years already present significantly higher values of serum creatinine and lower levels of eGFR, indicating a certain degree of renal involvement in the complex network of obesity-related adverse effects. Our results also showed that BP was higher in obese group and that both systolic and diastolic values were elevated. This means that the association of obesity with renal involvement presented by lower eGFR levels and increased kidney function together with cardiovascular risk factors showed by hypertension warns us that overweight and obese youngsters are more likely to develop cardiovascular and chronic renal diseases.

Recommendation

We recommend follow-up of overweight and/or obese children to understand the effect of obesity on renal function as well as BP monitoring at every clinical visit, and secondarily, we recommend initiation of weight

loss prevention programs through combined regimens of dietary caloric restriction and/or increased physical activity.

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Conflicts of interest

There are no conflicts of interest.

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