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Original Article

Investigating Renal Dysfunction and Dyslipidemia in Obese and Overweight Children

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ABSTRACT

Background and Aim: Childhood obesity and chronic kidney disease (CKD) are both substantial public health concerns. Obesity is known to contribute directly and indirectly to the development of CKD. This study evaluates kidney damage related to obesity and metabolic comorbidities in overweight and obese children.

Methods: A prospective cross-sectional study was conducted in the Obesity Clinic of a Children's Hospital in Iran from 2017 to 2020 on obese and overweight children aged 2 to 18 years. Biochemical parameters, such as total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TG), creatinine, estimated glomerular filtration rate and fasting glucose were measured. A binary logistic regression was used to assess the association between body mass index (BMI) Z-score and biochemical parameters. Two-sided $P<0.05$ was considered significant.

Results: The participants exhibited a mean BMI Z-score of 2.39±0.70. The prevalence of obesity was 78.6% among boys and 52.9% among girls. Additionally, 78.9% of them had an estimated glomerular filtration rate of less than 90 mL/min/1.73 m^2. Impaired fasting glucose was present in 15.6% of the participants, while hypercholesterolemia was noted in 66.7% of them.

Conclusion: Significant percentages of overweight and obese children have decreased estimated glomerular filtration rate. In addition, dyslipidemia, in the forms of high cholesterol, high TG, and low HDL is found in these children.

Keywords: Child, Obesity, Dyslipidemia, Glomerular filtration rate, Chronic kidney disease (CKD)

Introduction

Obesity is one of the important health problems in children that can increase the morbidity and mortality of people throughout their life [1]. The prevalence of childhood obesity among 2 to 17-year-olds in the United States has risen from 14.6% in 1999–2000 to 17.4% in 2013–2014 [2]. In a review study published in 2014, the prevalence of obesity was 5.1% and overweight was 10.8% in Iranian children and adolescents [3]; however, the prevalence of obesity in 2- to 15-year-olds, has increased to 11.4% in Iran in 2021 [4].

Obesity has many physical and psychosocial consequences in childhood. Children who are obese are prone to high blood pressure, impaired glucose tolerance, and type 2 diabetes [5]. Non-alcoholic fatty liver disease, dyslipidemia [6, 7] and renal injury are important comorbidities of obesity in children [8, 9].

Beyond problems in childhood, obesity in children is an independent risk factor for obesity in adulthood, which has socioeconomic and health consequences for the individual and the society [10]. Children classified with severe obesity encounter greater cardiovascular and metabolic risks than their overweight or moderately obese peers. Additionally, early signs of vascular dysfunction have been observed in these children with severe obesity [11]. Moreover, obesity-related kidney injury may manifest through glomerular hyperfiltration, increased activity of the renin-angiotensin-aldosterone system, and insulin resistance [12, 13].

Due to the high burden of these comorbidities, it is necessary to determine the obesity-related comorbidities in overweight and obese children, for timely intervention. Accordingly, this study assesses obesity-related kidney function and metabolic morbidities in overweight and obese children.

Materials and Methods

A prospective cross-sectional study was conducted on obese and overweight children aged 2 to 18 years old who visited the Obesity Clinic of Children's Hospital between October 2017 and February 2020 in Iran. The participants with chronic diseases were excluded from the study.

The information on these patients was extracted from the clinic files. If the file was incomplete, the information was obtained from the parents. Time of visit, date of birth, sex, height, weight, underlying disease, and medications used were recorded.

The height and weight of all participants were measured. Then, their body mass index (BMI) was calculated and BMI Z-score was determined concerning age and gender. Based on the World Health Organization (WHO) criteria, obesity in children under 5 years of age was defined as Z-Score +3 and above, and overweight as Z-Score between +2 and +3. Obesity in children aged 5 to 18 years was defined as a Z-Score of +2 and above, and overweight as a Z-Score between +1 and +2 [14]. A blood sample was taken to measure serum levels of fasting glucose, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (TG) and creatinine. The revised Schwartz formula was used to calculate the estimated glomerular filtration rate (eGFR) [8].

Glomerular filtration rate (GFR) less than 90 mL/min/1.73 m^2 for children was considered impaired kidney function. Also, fasting glucose ≥100 mg/dL, cholesterol ≥170 mg/dL, HDL≤45 mg/dL, LDL≥110 mg/dL [15] and TG greater than 75 mg/dL for the age under 9 years and greater than 90 mg/dL for the age 9 to 18 years were considered metabolic risk factors in children. Regarding liver enzymes, elevated alanine aminotransferase (ALT) levels exceeding 22 U/L in girls and 26 U/L in boys were considered indicative of a risk factor for non-alcoholic fatty liver disease in obese children [16, 17].

Statistical analysis

For the qualitative variable, the percentage-frequency and for the quantitative variable the Mean±SD was calculated. The SPSS software, version 25, was used to analyze the data.

The difference between the means of biochemical parameters in boys and girls was measured by the Mann-Whitney test, and the difference between cut-off points of biochemical parameters was determined by the Fisher exact test. A binary logistic regression was used to investigate the association and odds ratio between biochemical parameters and BMI Z-score. Meanwhile, two-sided $P<0.05$ was considered significant.

Results

In this study, the total number of people visiting the clinic was 183 between October 2017 and February 2020. Five people under two years old, two people over 18 years old, 13 people with chronic diseases, and four

Table 1. Baseline anthropometric parameters and laboratory measurements of the participants

Variables	Mean±SD/No. (%)			P# (Boys vs Girls)
	All Participants (n=90)	Boys (n=56)	Girls (n=34)	
Age (y)	9.19±3.58	9.31±3.57	8.99±3.63	0.65
BMI (kg/m²)	26.62±4.29	27.18±4.48	25.68±3.84	0.08
BMI Z-score	2.39±0.70	2.49±0.75	2.22±0.59	0.13
Fasting glucose (mg/dL)	92.20±10.11	92.93±7.58	90.99±13.33	0.14
Cholesterol (mg/dL)	174.64±27.90	176.86±28.79	171±26.38	0.3
LDL (mg/dL)	107.12±22.20	109.56±21.31	103.09±23.35	0.41
HDL (mg/dL)	45.47±7.31	44.49±5.99	47.06±8.93	0.66
TG (mg/dL)	130.57±55.92	134.48±60.39	124.12±47.82	0.24
GFR (mL/min/1.73 m²)	83.48±18.47	81.67±16.22	86.46±21.61	0.44
ALT (U/L)	29.67±11.09	31.09±10.37	27.34±11.97	0.06
BMI Z-score (obese)	62(68.9)	44(78.6)	18(52.9)	0.02*
Fasting glucose ≥100 (mg/dL)	14(15.6)	8(14.3)	6(17.6)	0.77
Total cholesterol ≥170 (mg/dL)	60(66.7)	39(69.6)	21(61.8)	0.49
LDL≥110 (mg/dL)	25(27.8)	16(28.6)	9(26.5)	1
HDL≤45 (mg/dL)	18(20)	10(17.9)	8(23.5)	0.59
TGs ≥90 mg/dL**	76(84.4)	47(83.9)	29(85.3)	1
GFR≤90 (mL/min/1.73 m²)	71(78.9)	46(82.1)	25(73.5)	0.43
ALT>26 (U/L**)	56(62.2)	37(66.1)	19(55.9)	0.37

Abbreviations: GFR: Glomerular filtration rate; LDL-c: Low-density lipoprotein cholesterol; HDL-c: High-density lipoprotein cholesterol; ALT: Alanine transaminase; BMI: Body mass index.

#Calculated by the Mann-Whitney test or Fisher exact test,* P<0.05 significant, **Triglycerides ≥75 for the age under 9 years and ≥90 for the age greater than 9 to 18 years and ALT>22 in girls and >26 in boys were significant.

people due to lack of recorded height or weight were excluded from the study. Out of 159 eligible participants for the study, 69 individuals did not consent to undergo blood testing. Consequently, a total of 90 participants were included in the statistical analysis.

Table 1 demonstrates the anthropometric characteristics and biochemical parameters of the participants. The mean age of the patients was 9.19±3.58 years, with a mean BMI Z-score of 2.39±0.70. Overall, 68.9% of the participants were classified as obese, with boys exhibiting a significantly higher prevalence of obesity compared to girls (P=0.02).

The mean cholesterol level in all participants was 174.64±27.90 mg/dL, with 66.7% of them exhibiting hypercholesterolemia. Moreover, 27.8% of these children had elevated LDL levels, while 20% had reduced HDL levels. Analysis of TG levels revealed that 73.7% of children aged 2-5 years, 84.6% of children aged 6-11 years and 94.7% of children aged 12-18 years had hypertriglyceridemia, with prevalence increasing with age.

The mean fasting blood glucose level was 92.20±10.11. Impaired fasting glucose was seen in 15.6% of the participants. Among these people, 62.2% had abnormal alanine transaminase levels.

Table 2. Binary logistic regression analyses for the association of BMI Z-score and biochemical parameters

Dependent Variables	Odds Ratio	95% CI	P
Fasting glucose ≥100 (mg/dL)	0.81	0.35-1.89	0.62
Total cholesterol ≥170 (mg/dL)	1.35	0.69-2.60	0.38
LDL ≥110 (mg/dL)	0.91	0.46-1.77	0.77
HDL ≤45 (mg/dL)	0.65	0.29-1.48	0.30
TGs ≥90 (mg/dL)**	0.7	0.33-1.51	0.37
GFR ≤90 (mL/min/1.73 m²)	4.79	1.59-14.47	0.005*
ALT >26 (U/L)**	0.96	0.52-1.76	0.89

Abbreviations: GFR: Glomerular filtration rate; LDL-c: Low-density lipoprotein cholesterol; HDL-c: High-density lipoprotein cholesterol; ALT: Alanine transaminase.

*P<0.05 significant, **Triglycerides ≥75 for the age under 9 years and ≥90 for the age greater than 9 to 18 years and ALT>22 in girls and >26 in boys is considered significant.

In addition, eGFR was compared between overweight and obese boys and girls. The average GFR of girls was 86.46±21.61 mL/min/1.73 m^2 and for boys was 81.67±16.22 mL/min/1.73 m^2, which has no significant difference with P=0.44. In addition, 78% of individuals had a GFR of less than 90 mL/min/1.73 m^2.

Table 2 presents binary logistic regression analyses examining the relationship between BMI Z-score as an independent variable and biochemical parameters as dependent variables among participants. The findings indicate a notable association between higher BMI Z-scores and increased odds of kidney failure, with an odds ratio of 4.79 (95% CI, 1.59%, 14.47%, P=0.005) for eGFR less than 90 mL/min/1.73 m^2.

Discussion

The prevalence of childhood obesity has reached alarming levels globally, with significant implications for health, including renal function. According to recent estimates, approximately 38.2 million children under the age of 5 were classified as overweight or obese in 2019, marking a concerning trend that continues to rise. Among older children and adolescents aged 5-19 years, the prevalence of overweight and obesity has surged from 4% in 1975 to over 18% in 2016 [18].

Obesity exerts a profound negative influence on renal function, assessing eGFR a critical measure in this population [19]. Dyslipidemia, a common metabolic abnormality in obesity, further complicates renal health by promoting the reabsorption of fatty acids and cholesterol within renal tubular cells. This process can trigger tubulointerstitial inflammation, leading to foam cell formation and tissue damage. Additionally, dyslipidemia can adversely affect mesangial and glomerular capillary endothelial cells, including podocytes [19].

In our investigation, we examined biochemical abnormalities among overweight and obese children attending an obesity clinic at a tertiary children's hospital. The study included 90 children referred between October 2017 and February 2020. Our findings revealed a substantial prevalence of dyslipidemia among these children, with 66.7% exhibiting high cholesterol levels, 84.4% high TGs, 27.8% high LDL cholesterol, and 20% low HDL cholesterol. In addition, the average GFR was 83.48±18.47 mL/min/1.73 m^2 and 78% of individuals had a GFR less than 90 mL/min/1.73 m^2. These results align with recent studies highlighting the high prevalence of dyslipidemia and reduced eGFR in obese and overweight children and adolescents [20, 21].

Correia-Costa et al. compared renal function using creatinine and cystatin C in 313 children aged 8 to 9 years with obesity or overweight against non-obese children, revealing a positive correlation between BMI z-score and both creatinine and cystatin C. This correlation suggests that as BMI Z-score increases, eGFR tends to decrease [8]. Similarly, Santucci's study, involving 165 overweight and obese children indicated that elevated uric acid levels, older age and puberty were associated with reduced GFR values in these individuals [22]. Van Dam's study, involving 600 overweight and obese children indicated that while serum creatinine levels were within the normal range, eGFR declined with age, high-

J Ped Nephrol
Journal of Pediatric Nephrology

lighting the progressive nature of renal impairment in this population [23].

Di Sessa's study on 396 obese children underscored the clinical implications of renal impairment, with 20% of participants demonstrating eGFR less than 90 mL/min/1.73 m^2. These children also exhibited higher BMI, insulin resistance, and non-alcoholic fatty liver compared to those without renal impairment, with an odds ratio of 1.92 for kidney injury in metabolically unhealthy obese children, reinforcing the association between metabolic abnormalities and renal dysfunction [24]. The present study confirms these findings, revealing a significant association between increasing BMI z-score and the likelihood of kidney failure, with an odds ratio of 4.79 (95% CI, 1.59%, 14.47%, P=0.005) for eGFR less than 90 mL/min/1.73 m^2.

Conclusion

This study supports existing studies indicating a significant prevalence of dyslipidemia, characterized by elevated cholesterol, TGs and low HDL, among overweight and obese children. It emphasizes the importance of conducting lipid profile tests to address these issues and reduce the risk of cardiovascular disease in adulthood. Furthermore, abnormal ALT and impaired fasting glucose are common in such children, and monitoring for renal failure using eGFR should be more frequent to assess kidney function in obese children.

Study limitations

While this study provides valuable insights, it is important to note several limitations. These include small sample size, absence of blood pressure measurements, lack of urine tests for proteinuria, and undocumented duration of obesity. Our findings revealed a mean BMI z-score of 2.39, with 78% of individuals showing eGFR below 90 mL/min/1.73 m^2. This percentage is notably higher than in comparable studies, possibly due to prolonged obesity duration and progression through hyperfiltration stages before referral to pediatric tertiary care for treatment.

Given these findings, interventions to address childhood obesity and managing abnormalities in biochemical parameters among children can play a crucial role in preventing the development of dyslipidemia and kidney disease. Such interventions may ultimately enhance the quality of life for these children as they transition into adulthood.

Ethical Considerations

Compliance with ethical guidelines

This article is taken from disease registry, titled "registry system for evaluation of childhood obesity in Iran" and project with code number "IR.SBMU.MSP.REC.1400.017" from Ethic Committee, that was supported by Deputy of Research and Technology in Shahid Beheshti University of Medical Sciences.

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Authors' contributions

Beheshteh Olang and Shiva Fatollahierad had substantial contributions to the conception and design of the work; they had substantial contributions to acquisition, analysis, interpretation of data and drafting the work and revising it critically for important intellectual content. They had also contributed for final approval of the version to be submitted and they have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Aliakbar Sayyari and Amirhossein Hosseini had substantial contributions to the conception and design of the work; and revising it critically for important intellectual content. They had also contributed for final approval of the version to be submitted.

Mahmoud Hajipour had substantial contributions to the analysis, statistical analysis, interpretation of data, and contributed to final approval of the version to be submitted. Zahra Fazeli Farsani had substantial contributions to Acquisition of data, and contributed to final approval of the version to be submitted. All authors have read and approved the manuscript.

Conflict of interest

The authors declared no conflict of interest.

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