Association of Glomerular Filtration Rate With Cardiometabolic Risk Factors in Iranian Adolescents

CASPIAN III Study

Ramin Tajbakhsh,[1] Ramin Heshmat,[2] Saeid Safiri,[3] Mahya Vafaeenia,[2] Mohammad Esmaeil Motlagh,[4] Morteza Mansourian,[5] Shaghayegh Beshtar,[6] Omid Safari,[1] Hamid Asayesh,[7] Hossein Ansari,[8] Mostafa Qorbani,[1,9] Roya Kelishadi[10]

[1]Non-communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, Iran
[2]Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[3]Managerial Epidemiology Research Center, Department of Public Health, School of Nursing and Midwifery, Maragheh University of Medical Sciences, Maragheh, Iran
[4]Department of Pediatrics, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[5]Health Management and Economics Research Center; Department of Health Education and Promotion, School of health; Iran University of Medical Sciences, Tehran, Iran
[6]School of Allied Medical Science, Iran University of Medical Sciences, Tehran, Iran
[7]Department of Medical Emergencies, Qom University of Medical Sciences, Qom, Iran
[8]Health Promotion Research Center, Department of Epidemiology and Biostatistics, Zahedan University of Medical Sciences, Zahedan, Iran
[9]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[10]Department of Pediatrics, Child Growth and Development Research Center, Research Institute for Primordial Prevention of Noncommunicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction. This study aimed to assess the association of glomerular filtration rate (GFR) with cardiometabolic risk factors in Iranian adolescents.

Materials and Methods. Data of the 3rd round of a school-based surveillance system entitled "Childhood and Adolescence Surveillance and PreventIon of Adult Non-communicable Disease (CASPIAN III)" study was used for this study. A sample of 367 adolescents aged between 10 and 18 years was randomly selected. Glomerular filtration rate was estimated using the original and the updated Schwartz equations. The association of GFR with anthropometric data, blood pressure, lipid profile, and blood glucose was assessed in boys and girls by age group.

Results. Of the participants, 50.4% were boys and 26.2% were from rural regions. In the age group of 14 to 18 years, the ratio of low- to high-density lipoprotein cholesterol was significantly lower in the girls than the boys ($P < .001$), and the girls had significantly higher triglyceride and FBG levels. Significant correlations were found between GFR and waist circumference (r = 0.150 and $P = .009$ with the original Schwartz; r = 0.190 and $P < .001$ with the updated Schwartz) and body mass index (r = 0.115 and $P = .03$ with the original Schwartz; r = 0.121 and $P = .02$ with the updated Schwartz).

Conclusions. The above findings showed that obese and overweight Iranian adolescents were more likely to have lower kidney function. Strategies to decline impaired kidney function may include prevention of obesity and central obesity in this population.

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Original Paper

INTRODUCTION

Recently, cardiovascular disease (CVD) is recognized as a leading risk factor of mortality worldwide in developed and developing countries.[1] Data showed that approximately 17.5 million people died from CVD in 2012, and over three quarters of CVD deaths happened in low- and middle-income countries.[2] According to the report of previous studies, the prevalence of predictors of CVD were high among Iranian children and adolescents,[3,4] and it has been

indicated that most of obese children experienced one of the cardiovascular risk factor.[5] Data showed the prevalence of hyperlipidemia, high systolic pressure, high diastolic pressure, systolic or diastolic hypertension, overweight, and obesity were 45.7%, 4.2%, 5.4%, 7.7%, 18.1%, and 4.8%, respectively.[3,4]

Cardiovascular diseases are one of the main causes of death in patients with chronic kidney disease.[6] The findings of previous prospective clinical trials have presented that a low level of glomerular filtration rate (GFR) is associated with CVD risk factors including hypertension, diabetes mellitus, and dyslipidemia.[7,8] Also, it was observed that serum uric acid level was high in adolescents with metabolic syndrome, and it was suggested that serum uric acid might be an additional component of metabolic syndrome even during adolescence.[9,10] Obesity has been mentioned as a risk factor for chronic kidney disease and end-stage renal disease.[11] In the past 20 years, incidence of obesity-related glomerulopathy has increased 10-fold.[12] In 3 decades, the prevalence of chronic kidney disease and end-stage renal disease have increased by increasing in prevalence of obesity in pediatric population.[13] Data suggested hypertension is maybe a main cause of kidney disease in the pediatric population with chronic kidney disease.[14] Finding of a study in Italy showed that children with prehypertension had low levels of GFR.[15]

Nonetheless, at the present time, limited data are available about the relationship between CVD risk factors and GFR in the general pediatric population in Iran. The aim of this study was to assess the association of GFR with cardiometabolic risk factors in Iranian adolescents.

MATERIALS AND METHODS

Study

The present study was a side project of the 3rd round of a school-based surveillance system entitled "Childhood and Adolescence Surveillance and PreventIon of Adult Noncommunicable Disease III (CASPIAN III)" study that was done on a subsample of 367 adolescents aged between 10 years and 18 years selected by random sampling from 5625 students. The CASPIAN III study was planned as a cross-sectional study in 2009-2010. The details of methodology have been described previously.[16] The participants of this study were 5625 students, aged 10 to 18 years, who were selected from urban and rural areas of 27 provinces in Iran by multistage random cluster sampling method.

Measurement

Weight, height, and blood pressure of the participants were measured through standard methods. Body weight was measured with light clothing and without shoes to the nearest 0.1 unit of measure, and height was measured under the same circumstance. Waist circumference (WC) was measured at the umbilicus level to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing weight by squared height (kg/m^2). Blood pressure was measured twice, while participants were in a seated position after at least 5 minutes using a standard mercury sphygmomanometer, and average systolic and diastolic measures were used for the statistical analysis.

After an overnight fast, fasting blood glucose (FBG), serum levels of triglyceride, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were tested using the relevant kits by an enzymatically by auto-analyzers. Uric acid was measured on a standard auto-analyzer with Uricase and Reagent (Parsazmun Co, Tehran, Iran). Serum creatinine was determined using the enzymatic methods on a Hitachi 917 auto-analyzer. Glomerular filtration rate was estimated by 2 different formulas using serum creatinine. The original Schwartz equation[17] and the updated Schwartz equation[18] were calculated as follows:

GFR (original) = k × height (cm)/serum creatinine (mg/dl) × 88.4

GFR (updated) = 0.413 × height (cm)/ serum creatinine (mg/dL)

where k is 61.9 for males aged greater than 13 years old and 48.6 for all the others.

Ethics Considerations

The study protocol was approved by the Ethics Committee of Tehran and Isfahan University of Medical Sciences. After explaining the study objectives, oral consent from students and written consent from their parents were collected. Each patient's information was given a code and saved as confidential.

Statistical Analysis

Data analysis was done using the SPSS software (Statistical Package for the Social Sciences, version

16.0, SPSS Inc, Chicago, IL, USA). Normality of the distribution of continuous variables was assessed using the Kolmogrov-Smirnov test. Continuous variables were presented as mean ± standard deviation. The *t* test was used to compare continuous variables between sexes. Association of independent variables and cardiometabolic risk factors was assessed using the Pearson correlation test. The significant level was set at a *P* value less than .05.

RESULTS

The mean age of the participants was 15.21 ± 2.35 years. Of the participants, 185 (50.4%) were boys and 182 (49.6%) were girls. In terms of living area, 96 (26.2%) of the students lived in rural and 271 (73.8%) lived in urban areas. The results of physical measurements are presented in Table 1. On average, the girls had significantly greater height ($P < .001$), WC ($P = .002$), BMI ($P = .006$), systolic blood pressure ($P = .004$), and diastolic blood pressure ($P = .005$) than the boys. While there was no significant differences between the sexes in the younger age group, the girls aged 14 to 18 years had significantly greater body weight ($P < .001$), height ($P = .01$), WC ($P = .001$), waist-height ratio ($P = .02$), and BMI ($P < .001$) than the boys with the same age range.

Table 2 is showed the results of biochemical parameters among the participants. In the age group of 14 to 18 years, the ratio of low- to high-density lipoprotein cholesterol was significantly lower in the girls than the boys ($P < .001$), and the girls had significantly higher triglyceride and FBG levels. No significant differences were found in the younger age group.

The findings of correlations are shown in Table 3 between cardiometabolic risk factors and GFR, based on the updated and original Schwartz equations.

Table 1. Mean Values of Anthropometric and Blood Pressure Indexes According to Sex and Age Groups of Studied Population

Measurement	Age Group 10 to 14 Years			Age Group 10 to 14 Years			All		
	Male	Female	*P*	Male	Female	*P*	Male	Female	*P*
Age, y	12.6 ± 1.3	12.5 ± 1.2	.23	16.6 ± 1.1	16.8 ± 1.0	.004	15.08 ± 2.3	15.3 ± 2.3	.38
Body weight, kg	43.9 ± 15.8	39.7 ± 13.4	.44	54.1 ± 10.4	65.6 ± 18.7	< .001	50.15 ± 13.7	56.30 ± 21.0	.31
Height, m	146.2 ± 10.1	144.5 ± 11.4	.29	158.4 ± 7.0	168.7 ± 9.1	.01	153.6 ± 10.3	160.0 ± 15.3	< .001
Waist circumference, cm	68.8 ± 12.0	67.8 ± 11.7	.83	73.3 ± 10.0	80.7 ± 14.1	< .001	71.6 ± 11.0	76.1 ± 14.6	.002
Waist-height ratio	0.47 ± 0.06	0.46 ± 0.07	.79	0.46 ± 0.06	0.47 ± 0.07	.02	0.46 ± 0.06	0.47 ± 0.07	.36
Body mass index, kg/m^2	20.0 ± 5.4	18.8 ± 4.1	.10	21.5 ± 4.0	22.9 ± 5.1	< .001	20.9 ± 4.6	21.5 ± 5.2	.006
Systolic blood pressure, mm Hg	103.1 ± 19.1	103.5 ± 15.7	.90	105.8 ± 16.3	113.5 ± 15.4	.85	104.7 ± 17.4	109.9 ± 16.2	.004
Diastolic blood pressure, mmHg	64.0 ± 11.7	66.4 ± 11.5	.87	66.8 ± 10.0	72.1 ± 11.2	.62	65.7 ± 10.7	70.0 ± 11.6	.005

Table 2. Mean Values of Biochemical Variables According to Sex and Age Groups of Studied Population*

Measurement	Age Group 10 to 14 Years			Age Group 10 to 14 Years			All		
	Male	Female	*P*	Male	Female	*P*	Male	Female	*P*
Total cholesterol, mg/dL	18.6 ± 29.5	148.1 ± 31.5	.80	151.3 ± 32.6	147.2 ± 35.5	.95	150.3 ± 31.4	147.5 ± 34.0	.43
LDLC, mg/dL	77.5 ± 23.7	82.0 ± 27.8	.68	86.3 ± 27.1	83.3 ± 25.3	.11	83.2 ± 26.2	82.8 ± 26.1	.89
HDLC, mg/dL	45.9 ± 14.4	44.9 ± 14.4	.77	43.0 ± 11.3	40.4 ± 11.7	.48	44.18 ± 12.6	42.06 ± 12.9	.12
Triglyceride, mg/dL	126.7 ± 79.5	105.1 ± 73.2	.51	104.5 ± 48.4	117.8 ± 64.0	.001	113.25 ± 63.1	113.26 ± 67.5	> .99
Fasting blood glucose, mg/dL	86.8 ± 14.7	88.8 ± 11.2	.76	86.1 ± 11.1	89.0 ± 14.7	.03	86.4 ± 12.6	86.01 ± 13.5	.07
Serum creatinine, mg/dL	0.66 ± 0.18	0.67 ± 0.20	.12	0.63 ± 0.2	0.66 ± 0.21	.49	0.64 ± 0.19	0.67 ± 0.21	.14
Serum uric acid, mg/dL	5.2 ± 1.6	4.9 ± 1.59	.91	5.0 ± 1.5	5.0 ± 1.4	.18	5.1 ± 1.5	5.1 ± 1.5	.27
LDLC/HDLC ratio	1.8 ± 0.9	2.0 ± 1.2	.25	2.2 ± 1.1	2.1 ± 0.85	< .001	2.0 ± 1.1	2.1 ± 1.0	.10
GFR based on updated Schwartz	0.66 ± 36.5	99.2 ± 40.5	.22	115.6 ± 43.2	119.6 ± 50.9	.20	109.3 ± 41.3	112.2 ± 48.3	.07
GFR based on original Schwartz	154.5 ± 67.1	132.0 ± 53.8	.35	196.1 ± 73.2	159.2 ± 67.8	.28	179.8 ± 73.5	149.4 ± 64.3	.12

*LDLC indicates low-density lipoprotein cholesterol; HDLC, High-density lipoprotein cholesterol; and GFR, glomerular filtration rate.

Table 3. Corrections Between Cardiometabolic Risk Factors and Glomerular Filtration Rate*

parameter	GFR Estimated With Original Schwartz Formula						GFR Filtration Estimated With Updated Schwartz Formula					
	10 to 14 Years		14 to 18 Years		All		10 to 14 Years		14 to 18 Years		All	
	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
Waist circumference	0.182	.03	0.035	.60	0.151	.004	0.144	.09	0.128	.05	0.190	< .001
Waist- height ratio	0.071	.41	0.028	.67	0.050	.34	0.059	.49	0.068	.31	0.070	.18
Body mass index	0.161	.06	0.002	.98	0.115	.03	0.095	.27	0.056	.40	0.121	.02
Systolic blood pressure	0.035	.69	-0.080	.23	0.005	.92	-0.016	.86	-0.001	.99	0.033	.54
Diastolic blood pressure	-0.006	.94	-0.053	.43	0.008	.88	-0.013	.88	0.023	.73	0.048	.36
Total cholesterol	0.158	.07	-0.040	.55	0.022	.67	0.159	.06	-0.048	.47	0.015	.77
LDLC	0.100	.30	0.004	.96	0.051	.37	0.123	.20	-0.013	.85	0.043	.45
HDLC	0.038	.66	0.011	.87	-0.013	.81	0.027	.75	-0.018	.79	-0.030	.57
Triglyceride	0.022	.80	0.018	.79	-0.008	.88	0.010	.91	0.029	.66	0.018	.73
Fasting blood glucose	0.031	.72	0.026	.70	0.001	.99	0.059	.49	0.026	.69	0.035	.51
LDL/HDL ratio	0.057	.55	0.046	.51	0.075	.18	0.068	.48	0.034	.63	0.067	.24
Uric acid	-0.070	.18	-0.101	.24	-0.051	.44	-0.087	.10	-0.129	.13	-0.065	.33

*GFR indicates glomerular filtration rate; LDLC, low-density lipoprotein cholesterol; and HDLC, high-density lipoprotein cholesterol.

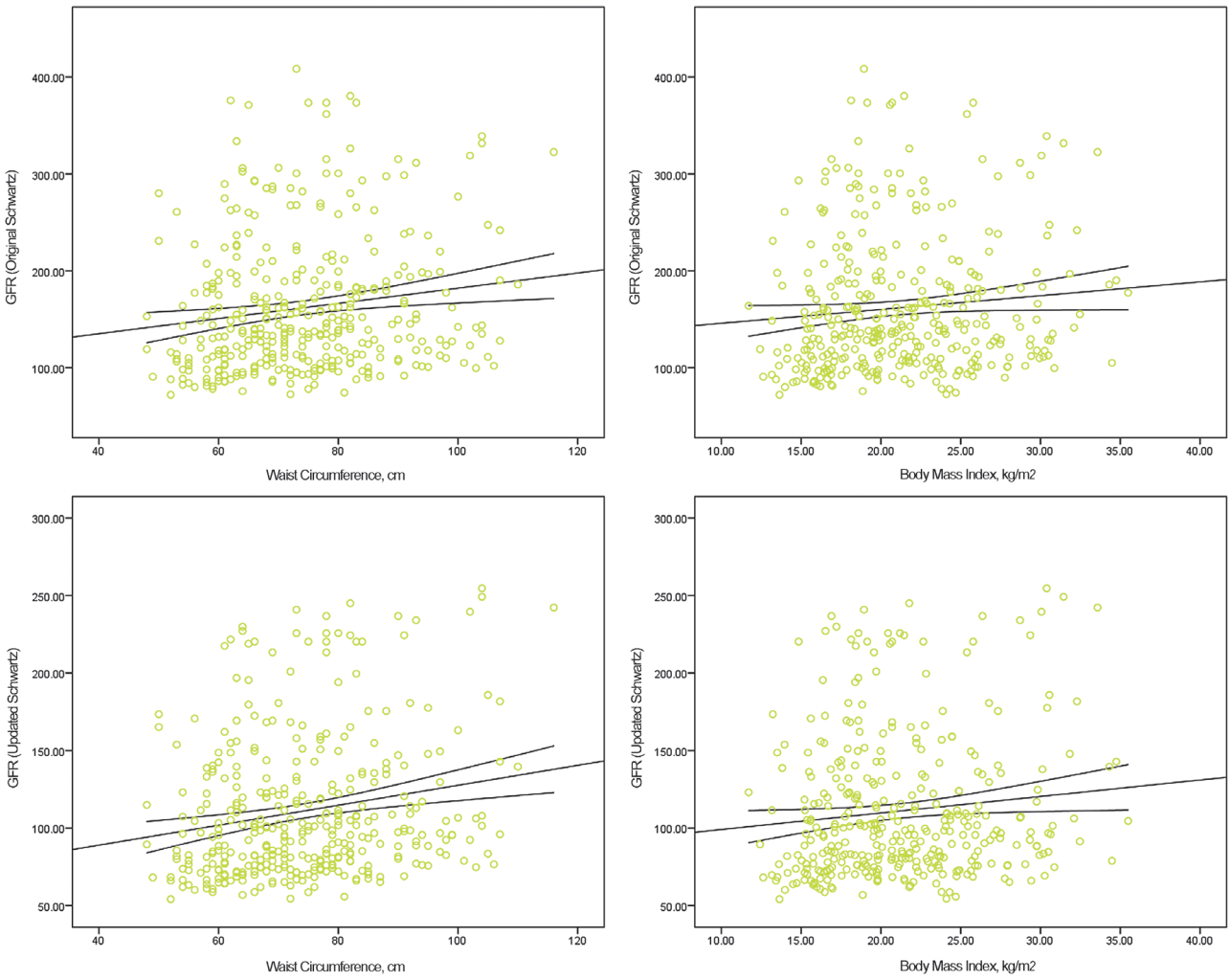
Overall, positive correlations were found between GFR and WC (r = 0.150 and *P* = .009 with the original Schwartz; r = 0.190 and *P* < .001 with the updated Schwartz) and BMI (r = 0.115 and *P* = .03 with the original Schwartz; r = 0.121 and *P* = .02 with the updated Schwartz). Correlations of GFR with WC and BMI are plotted in the Figure.

DISCUSSION

In the present study, the association between cardiometabolic risk factors and GFR were assessed among Iranian children and adolescents. The results of correlation of anthropometric and biochemical indexes with GFR showed that WC and BMI had positive correlations with GFR that were in agreement with previous studies.[19,20] Data suggested that people with obesity and central obesity have a greater risk for impaired kidney function. Results of Pinto-Sietsma and colleagues' study indicated that obese participants had a high risk for increased filtration and micro-albuminuria, and that central fat distribution was significantly related to kidney function loss.[20] Robust evidence suggested that central obesity make subjects more prone to dysfunction of kidney through insulin resistance,[21,22] which may affect GFR by renal hemodynamics influence.[23] Previous studies showed that the central obesity fat distribution was related to reduced kidney plasma and blood flow and increased filtration fraction and albuminuria, while these findings were not seen in individuals with peripheral fat distribution.[20] Findings of a cohort study among healthy men showed that after approximately 14 years of follow-up, a high BMI was significantly associated with the risk of chronic kidney disease, and those participants who had weight gain more than 10% of their baseline BMI had a significant 30% increase the risk of chronic kidney disease.[24] Data from De Boer and colleagues' study[25] indicated that high BMI and WC were each associated with loss of estimated GFR during 7 years of follow-up and the odds ratios were 1.10 per 5 kg/m^2 for BMI and 1.14 per 12 cm for WC. The mechanism that associates obesity with kidney damage remains not well understood. Data suggested that obesity may cause kidney dysfunction through impaired glucose metabolism, blood pressure, inflammation,[25] and hemodynamic as well as hormonal effects.[26,27]

Findings of our study exhibited that overall girls had higher averages of WC, BMI, systolic blood pressure, and diastolic blood pressure. Results of biochemical variables presented no striking difference between the boys and girls, overall. There was no significant difference in serum levels of creatinine and uric acid or GFR between boys and girls, and these results does not agree with the previous study that showed higher uric acid and GFR levels in boys than girls. It was suggested that sex applies a positive correction with GFR in favor of boys.[19]

The results of our study showed that FBG and lipid profile were not significantly associated with GFR that were not in agreement with



Correlation of body mass index and waist circumference with estimated glomerular filtration rate (GFR) based on the original and updated Schwartz equations

previous studies.[19,28] Koulouridis and coworkers presented that fasting glucose, total cholesterol, and low-density lipoprotein cholesterol had negative correlations with estimated GFR among children and adolescents, and when these variables were included in multiple regression analysis model, only the correlation of fasting glucose remained significant.[19] The mechanism that hyperfiltration happened among those with primary stages of diabetes mellitus was different from the hyperfiltration among individuals with obesity and central obesity.[19] The findings of previous studies showed that the prevalence of cardiometabolic risk factors, including low high-density lipoprotein cholesterol, high triglycerides, lipoprotein A, hemocyteine,[29] hypertension, and lipid abnormalities,[30] were high among patients with chronic kidney disease. Evidence suggested that the cardiovascular risk factors seemed to carry different weights in patients with kidney diseases compared to the general population[31,32] and showed that more than 90% of patients with chronic kidney disease experienced hypertension.[33]

Our study had some limitations. The study design was cross-sectional that did not allow conclusion about causation. Despite this limitation, the present study was extracted from a large nationwide population-based survey which could improve generalizability of results.

CONCLUSIONS

The findings of present study showed that BMI and WC were correlated with GFR among Iranian adolescents. Strategies to alleviate impaired kidney

function may include prevention of obesity and central obesity. Further longitudinal studies are necessary to investigate the causal association between cardiometabolic risk factors and GFR, as well as their clinical implications.

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CONFLICT OF INTEREST

None declared.

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Correspondence to:
Mostafa Qorbani, MD
Non-communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj, Iran
E-mail: mqorbani1379@yahoo.com

Roya Kelishadi, MD
Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences, Shariati Hospital, Tehran, Iran, Iran
E-mail: royakelishadi@gmail.com

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