



Association of Neck, Wrist and Hip Circumferences with Kidney Function in Children and Adolescents: The CASPIAN- V Study

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ABSTRACT

Aim: Some evidence exists concerning the relationship between anthropometric measurements and chronic kidney disease. This study aims to investigate the association of neck circumferences (NC), wrist circumferences (WC) and hip (HC) circumferences with kidney function in a pediatric population.

Materials and Methods: In this national study, 4,200 students aged 7-18 years were selected by random cluster sampling from 30 provinces of Iran. NC, WC and HC were measured according to standard protocol and were categorized to either low or high according to their age-sex specific median values. The estimated glomerular filtration rate (eGFR) was calculated based on the "updated" Schwartz equation.

Results: The response rate was 91.5% (n=3,843). The mean standard deviation of eGFR was 96.71 (19.46), 96.49 (21.69), and 96.59 (20.66) mL/minimum/1.73 m² for girls, boys and the total population, respectively. Compared to other participants, those in the high NC group had significantly higher eGFR (102.12±21.31 vs 90.65±18.18, p<0.001) and high creatinine (Cr) (0.66±0.14 vs 0.63±0.11 mg/dL, p<0.001). Individuals categorized as high WC had significantly higher eGFR (102.12±21.31 vs 90.83±18.16, p<0.001) and Cr (0.66±0.15 vs 0.63±0.10) mg/dL, p<0.001). In the multivariate model, high NC, WC and HC were associated with higher eGFR (p<0.001). Moreover, each one-unit (cm) increment in NC, WC and HC increased eGFR by 1.42, 3.24 and 0.46 units, respectively.

Conclusion: The findings of this large population-based study suggest that simple anthropometric measurements, such as WC and NCs, can be used in epidemiological studies to determine those children and adolescents that might be at risk of kidney dysfunction.

Keywords: Kidney function, neck circumference, wrist circumference, children, prevention

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Introduction

Chronic kidney disease (CKD) is an important health problem with complicated associations with other disorders such as cardiovascular diseases (1). Studies conducted in the United States (between 1988-1994 and 1999-2004) have reported that the prevalence of CKD is increasing from 10% to 13.1%. Limited studies exist about CKD in non-Western populations. In Iran, its incidence is reported as 27.8% in females and 14.2% in males (2,3).

CKD will cause a poor quality of life and also a huge economic burden as the patient may need kidney transplantation or dialysis (4). The disease is asymptomatic at the beginning and is not usually detected until the progression and development of complications. This makes the prevention of kidney failure or other outcomes very hard (5). Early detection of the disease can delay the progress to end stage renal disease or other severe complications (6).

Obesity is a growing worldwide problem in both developing and developed countries. It is a major determinant of most chronic disorders including CKD (7,8). Body mass index (BMI) is the most commonly used index for determining weight status. BMI is easy to calculate, but it has some limitations in describing body compositions. Waist circumference is largely used for determining the visceral obesity that is related to complications of obesity (9,10). Measurement of waist circumference differs according to body position and breathing phase, and it is hard to measure it in routine primary care visits and some situations where adequate body exposure are difficult, therefore some other parameters including neck and wrist circumferences (WCs) are described and used in epidemiological studies (11). In the current study, we aim to determine the association of kidney function with neck and WCs in children and adolescents.

Materials and Methods

This multicentric cross-sectional study was conducted as part of the fifth survey of a national school-based surveillance program entitled "Childhood and Adolescence Surveillance and Prevention of Adult non-communicable Disease" study (2015). Detailed methodology has been described previously (12).

Ethical Considerations

The Research and Ethics Committee of Isfahan University of Medical Sciences approved this study (approval number: 194049). Participation in this study was voluntary. After a complete explanation of the study objectives and protocols,

written informed consent and verbal consent were obtained from the parents and students, respectively.

Study Population and Sampling Framework

Participants consisted of students, aged 7-18 years, living in urban and rural areas of 30 provinces of Iran. They were selected by a multistage, stratified cluster sampling method. Using the proportional to size method and with an equal sex ratio, sampling within each of the provinces was conducted according to the student's area of residence (urban or rural) and level of education (primary and secondary). Moreover, the number of samples of different educational grades in urban and rural areas was estimated according to the number of students in each grade. The total sample size was calculated as 480 students in each province (48 clusters of 10 students); in each province, 14 clusters were randomly selected for biochemical testing, i.e. a total of 4,200 students.

Procedure and Measurements

Two sets of questionnaires were developed for students and their parents. The students' questionnaire was derived from the World Health Organization-Global School Student Health Survey. The validity and reliability of the Farsi-translated questionnaire was assessed previously (13,14). During the interviews, not only demographic information, but also complementary information on physical activity (PA), screen time (ST), and socio-economic status, was completed for all participants.

Through the executive process of the survey, all examinations were conducted with calibrated instruments and the recording of information was completed through validated checklists which were designed and conducted under the standard protocol by trained health care professional teams (15,16).

Neck circumference (NC), hip and WC were measured using a non-elastic tape to the nearest 0.1 cm over the skin. NC was measured by a tape underneath the Adam's apple in contact with the patient's skin in a comfortable position (15,17).

WC was measured with subjects in a seated position for both wrists at distal to the prominences of the radial and ulnar and an average was taken (18,19). Neck, wrist and hip were categorized as either low or high according to an age-sex specific median.

Blood Sampling

Eligible students were referred to the laboratory, while one of the parents accompanied him/her. There, 6 mL

venous blood samples were collected after 12-hr overnight fasting. All collection tubes were centrifuged at 2.500-3.000 x g for 10 minutes. Immediately after centrifugation, serum samples were aliquot into 200 microliter tubes and stored at -70 °C. All samples were transferred by cold chain to the Isfahan Mahdieh Laboratory. Serum creatinine (Cr) was measured enzymatically by the Hitachi auto-analyzer (Tokyo, Japan) (20,21).

Definition of Terms

Socio-economic Status

The method, validity and considered variables for calculating the socio-economic status (SES) of Iranian families was approved previously through the Progress in the International Reading Literacy Study (22). Considering that, the principal component analysis of variables including parental education, parents' job, ownership of a private car, school type (public/private), and having a personal computer in the home were summarized in one main component. This component explained 72.0% of variance. This main component was categorized into tertials. The first tertial was defined as a low SES, the second tertial as an intermediate and the third tertial as a high SES.

Screen Time

To assess ST behaviors, the average number of hours per day that participants spent watching TV/VCDs, using personal computers (23), or playing electronic games was asked, then the total cumulative time spent for ST was estimated. Information was recorded separately for weekdays and weekends. The analysis of the correlates of ST was carried out according to the international ST recommendations and ST was categorized into two groups; less than 2 hours per day (low), and 2 hours per day or more (high) (24-26).

Physical Activity

Through a validated questionnaire, information regarding the past week's frequency of leisure time PA outside school was collected (12). PA was considered as at least a 30-minute duration of exercises that led to heavy sweating or a large increase in breathing or heart rate. Based on this, participants described their weekly PA habits via four available responses as follows; none, 1-2 days, 3-6 days, and every day. With the aim of analysis, weekly frequency of PA was categorized into three groups; less than two times per week (mild), two to four times a week (moderate) and more than 4 times a week (vigorous) (27).

Glomerular Filtration Rate

GFR describes the flow rate of filtered fluid through the kidney (28). The estimated eGFR is used to screen for the early detection of kidney damage, to help diagnose CKD, and to monitor kidney status. It is a calculation based on the results of a blood Cr test adjusted for age and sex based on the equation used (28). In the present study, eGFR was calculated based on the "updated" Schwartz equation formula (29):

$$eGFR = \frac{0.413 \times \text{height (cm)}}{\text{serum creatinine} \left(\frac{\text{mg}}{\text{dL}}\right)}$$

Statistical Analysis

Continuous and categorical variables are expressed as mean [standard deviation (SD)] and number (percentage) respectively. The Kolmogorov-Smirnov test was used to examine the normality of continuous variables. Associations of continuous and categorical variables with age groups were compared by ANOVA and the chi-square test, respectively.

The mean of eGFR and Cr across categorized levels of hip, neck, and WCs was compared by t-test. Linear regression analysis was used to examine the association of hip, neck and WCs with eGFR and Cr.

Three models were applied: Model I: the crude model (without adjustment); Model II: was adjusted for age, area of residence (urban or rural), sex, PA, ST and SES; and Model III: was additionally adjusted for BMI. All statistical analyses were performed using a survey analysis method, and were conducted using the statistical program STATA package version 11.0 (stata statistical software: Release 11. College Station, TX: StataCorp LP. Package). P values of less than 0.05 were considered as statistically significant.

Results

The study participants consisted of 3.843 students with a mean age of 12.28±3.15 years, without any significant difference between boys and girls. From them, 50.6% were boys and 71.4% were from urban areas. The characteristics of the participants are presented in Table I. It shows that PA and SES were significantly different between the age groups. Whereas, eGFR and Cr, respectively, with an overall mean ± SD of 96.59±20.66 and 0.65±0.14 (mg/dL), showed significant ascending differences between the age groups (p-trend<0.001). Likewise, BMI, NC, WC and HC, with means of 18.51±4.71 (kg/m²), 29.84±3.99 (cm), 14.72±1.89 (cm), and 79.14±14.64 (cm) followed an ascending trend with increasing age (p-trend<0.001).

Considering the mean \pm SD of eGFR and Cr according to NC, WC and HC; participants in the high NC group had significantly higher eGFR (102.12 ± 21.31 vs 90.65 ± 18.18 , $p < 0.001$) and Cr (high; 0.66 ± 0.14 vs 0.63 ± 0.11 mg/dL, $p < 0.001$). Except for Cr levels in girls, these significant associations were also documented in other groups. Likewise, those participants who were categorized as the high WC group had significantly higher eGFR (102.12 ± 21.31 vs 90.83 ± 18.16 , $p < 0.001$) and Cr [$(0.66 \pm 0.15$ vs $0.63 \pm 0.10)$ mg/dL, $p < 0.001$] than their counterparts. Except for Cr levels of girls, this significant association existed in other groups as well. Regarding the two groups of high and low HC, both boys and girls had higher eGFR in the high HC groups (boys: 103.66 ± 22.38 , girls: 102.10 ± 19.43 mg/dL, $p < 0.001$) (Table II).

Table III shows the association of NC, WC and HC as continuous and categorical variables with eGFR and Cr in linear regression analysis. In a multivariate model, NC, WC and HC, as continuous and categorical variables, were associated with eGFR; participants with high NC, WC and HC, compared with their other counterparts, had significantly higher eGFR ($p < 0.001$). In a multivariate model (Model III), each one unit (cm) increment in NC, WC and HC increased eGFR by 1.42, 3.24 and 0.46 units, respectively.

The multivariate model on the association of NC, WC and HC, as continuous and categorical variables, with Cr, showed that only continuous NC and WC were associated with Cr levels; per each one unit (cm) increment in NC and WC, Cr increased significantly by 0.002 and 0.004 mg/dL, respectively.

Table I. Characteristics of participants by gender and age group: The CASPIAN-V study					
	Age			Total	p value
	7-10 y	11-14 y	15-18 y		
Mean age (year) ¹	8.74 \pm 1.03	12.51 \pm 1.08	16.41 \pm 1.04	12.28 \pm 3.15	<0.001
Sex²					
Boy	2.358 (48.7)	2.826 (50.5)	2.044 (53.2)	7.228 (50.6)	<0.001
Girl	2.485 (51.3)	2.765 (49.5)	1.796 (46.8)	7.046 (49.4)	
Area of residence					
Urban	3.235 (66.8)	3.683 (65.9)	3,276 (85.3)	10.194 (71.4)	<0.001
Rural	1.608 (33.2)	1.908 (34.1)	564 (14.7)	4.080 (28.6)	
BMI (kg/m ²) ¹	16.18 \pm 4.03	18.99 \pm 4.41	21.21 \pm 4.42	18.51 \pm 4.71	<0.001
Physical activity²					
Low	1.470 (32.6)	1.683 (32.3)	1.301 (36.1)	4.454 (33.4)	0.001
Medium	1.482 (32.9)	1.784 (34.3)	1.158 (32.1)	4.424 (33.2)	
High	1.554 (34.5)	1.739 (33.4)	1.147 (31.8)	4.440 (33.3)	
Screen Time²					
Low	4.023 (85.4)	4.553 (84.2)	3.068 (81.5)	11.644 (83.8)	<0.001
High	688 (14.6)	857 (15.8)	698 (18.5)	2.243 (16.2)	
SES²					
Low	1.524 (32.9)	1.830 (34.4)	1.205 (32.8)	4.454 (33.4)	0.06
Medium	1.514 (32.7)	1.723 (32.4)	1.278 (34.8)	4.424 (33.2)	
High	1.595 (34.4)	1.764 (33.2)	1.193 (32.5)	4.440 (33.3)	
Neck circumference ¹	27.25 \pm 3.06	29.97 \pm 3.42	32.93 \pm 3.54	29.84 \pm 3.99	<0.001
Waist circumference ¹	13.44 \pm 1.47	14.92 \pm 1.62	16.03 \pm 1.71	14.72 \pm 1.89	<0.001
Hip circumference ¹	69.08 \pm 10.57	80.32 \pm 12.45	90.18 \pm 13.39	79.14 \pm 14.64	<0.001
eGFR ¹	87.23 \pm 15.72	99.30 \pm 19.76	102.60 \pm 23.20	96.59 \pm 20.66	<0.001
Creatinine (mg/dL) ¹	0.63 \pm 0.10	0.64 \pm 0.11	0.69 \pm 0.16	0.65 \pm 0.14	<0.001

¹Data are presented as mean (standard deviation), ²Data are presented as number (percentage)
CASPIAN-V: BMI: Body mass index, SES: Socio-economic status, eGFR: Estimated glomerular filtration rate, $0.413 \times$ height (cm)/serum creatinine (mg/dL)

Table II. Mean \pm standard deviation of estimated glomerular filtration rate and creatinine according hip, neck and wrist circumference: The CASPIAN-V study

Variable	eGFR			Creatinine (mg/dL)		
	Total	Boy	Girl	Total	Boy	Girl
Neck circumference^a						
Low	90.65 \pm 18.18	90.02 \pm 19.07	91.31 \pm 17.17	0.63 \pm 0.10	0.64 \pm 0.11	0.62 \pm 0.10
High	102.12 \pm 21.31	102.28 \pm 22.34	101.99 \pm 20.08	0.66 \pm 0.14	0.67 \pm 0.14	0.66 \pm 0.15
p value	<0.001	<0.001	<0.001	<0.001	<0.001	0.008
Wrist circumference^b						
Low	90.83 \pm 18.16	89.76 \pm 19.24	91.87 \pm 16.97	0.63 \pm 0.10	0.64 \pm 0.11	0.62 \pm 0.10
High	102.12 \pm 21.33	102.18 \pm 22.07	102.04 \pm 20.39	0.66 \pm 0.15	0.66 \pm 0.16	0.66 \pm 0.14
p value	<0.001	<0.001	<0.001	<0.001	<0.001	0.007
Hip circumference^c						
Low	89.78 \pm 17.98	89.17 \pm 18.3	90.49 \pm 17.53	0.63 \pm 0.11	0.64 \pm 0.11	0.62 \pm 0.10
High	102.89 \pm 20.99	103.66 \pm 22.38	102.10 \pm 19.43	0.66 \pm 0.15	0.66 \pm 0.14	0.66 \pm 0.15
p value	<0.001	<0.001	<0.001	<0.001	0.004	0.005

^aAccording to age-sex specific median, ^bAccording to age-sex specific median, ^cAccording to age-sex specific median, CASPIAN-V: eGFR: estimated glomerular filtration rate

Discussion

As the first study of its kind in a non-Western population, we investigated the association between some anthropometric measurements including hip, neck and WCs with renal function in a large national pediatric population. The results demonstrated that in different age groups of girls and boys, those participants with lower hip, neck and WCs had better kidney function than their counterparts. Adjusted models of logistic regression analysis showed that the association between GFR and the afore mentioned anthropometric measurements was more prominent than that of Cr.

Recently, the evaluation of the associations between anthropometric indices, including neck and WCs, and disease-related biological markers have gained more interest; which is due to its low cost and non-invasive method of measurement (30).

NC is considered as the representative anthropometric parameter of upper-body subcutaneous fat (31). The appropriate inter and intra reliability of NC among 6-16 year-old children and adolescents have been reported on previously (32). Accordingly, multiple measurements are not necessary for this index. In addition, its measurement has a simple method that can be easily performed by health care professionals (32).

Some studies have indicated the association between NC and obesity, cardio metabolic risk factors and insulin

resistance in children (33,34). Moreover, some studies demonstrated that the association between NC and cardiometabolic risk factors is more significant than other anthropometric parameters such as waist circumference or BMI (35).

Although some studies exist regarding the usefulness of measuring NC for predicting renal function in adults, to the best of our knowledge, there is no study in this field based on a pediatric population.

Recently, Yoon et al. (36) in a prospective cohort study (Korean Genome and Epidemiology Study cohort) have evaluated the association between NC and incident CKD. They revealed that NC could be used as an independent predictor for CKD. Their observed association persisted even after adjustment for other anthropometric measurements such as BMI and waist-to-hip ratio, baseline eGFR and traditional risk factors of CKD. They also found that this association would be more prominent in the presence of obesity and elevated BMI.

The findings of the Liu et al. (37) study suggested that NC, as an indicator of upper-body subcutaneous fat, could have a pathogenic role in the occurrence of renal dysfunction. They showed that NC is associated with other indicators of renal function including uric acid, micro albuminuria, 24-hr Cr clearance rate and eGFR based on the Cockcroft and Gault formula as well as cardiovascular risk factors such as serum lipid levels and hs-C-reactive protein.

Table III. Association of hip, neck and wrist circumference with estimated Glomerular Filtration Rate and Creatinine in logistic regression analysis: The CASPIAN-V study

	eGFR			Creatinine (mg/dL)		
	β	SE	p value	β	SE	p value
Neck circumference (cm)						
Model I	1.42	0.08	<0.001	0.004	0.001	<0.001
Model II	0.88	0.10	<0.001	0.001	0.001	0.03
Model III	0.80	0.11	<0.001	0.002	0.001	0.01
Neck circumference, High/Low^a						
Model I	11.47	0.64	<0.001	0.03	0.007	<0.001
Model II	6.73	0.80	<0.001	0.004	0.005	0.45
Model III	6.55	0.86	<0.001	0.004	0.005	0.43
Wrist circumference (cm)						
Model I	3.24	0.17	<0.001	0.01	0.002	<0.001
Model II	2.07	0.22	<0.001	0.003	0.001	0.01
Model II	2.17	0.25	<0.001	0.004	0.001	0.006
Wrist circumference, High/Low^b						
Model I	11.29	0.64	<0.001	0.03	0.007	<0.001
Model II	7.15	0.78	<0.001	0.002	0.005	0.63
Model III	7.07	0.84	<0.001	0.003	0.005	0.62
Hip circumference (cm)						
Model I	0.46	0.02	<0.001	0.001	0.00	<0.001
Model II	0.34	0.02	<0.001	0.00	0.00	0.62
Model II	0.38	0.03	<0.001	0.00	0.00	0.51
Hip circumference, High/Low^c						
Model I	13.11	0.63	<0.001	0.03	0.007	<0.001
Model II	8.93	0.81	<0.001	-0.002	0.005	0.64
Model III	9.18	0.22	<0.001	-0.002	0.006	0.67

^aAccording to age-sex specific median, ^bAccording to age-sex specific median, ^cAccording to age-sex specific median, Model I: Without adjustment, Model II: Adjusted for age, living area, sex, physical activity and screen time, SES, Model III: Additionally adjusted for BMI
eGFR: Estimated glomerular filtration rate, SES: Socio-economic status

To the best of our knowledge, the current findings are the first to show a significant association between NC in children and GFR, which is considered as the most important and earliest indicator of renal dysfunction. It seems that this anthropometric index could be applicable both in epidemiological studies and clinical practice for screening for renal dysfunction in the pediatric population.

The association between obesity and the development of CKD has been documented in some studies (38,39). Moreover, the relationship between obesity and end stage renal disease has a direct correlation irrespective of underlying factors such as hypertension or diabetes (39).

WC is another simple anthropometric measurement, which has a safe and non-invasive method with appropriate intra- and inter-operator reliability (40). In addition, it is related to skeletal frame size, and is not affected by body fat variations (40).

A study in Iranian adults reported that WC, as a novel anthropometric measurement, can be considered as an independent predictor for incident hypertension and cardiovascular disease among non-centrally obese women (41). However, in another study in the same population, WC had significant correlation with lipid profile, but not with metabolic syndrome or cardiovascular diseases (42).

Some other studies indicated that WC is associated with insulin resistance both in children and adults (43), as well as with diabetes in the adult population (44).

A recent study in Italy showed that WC could be used as an indicator of insulin resistance in obese youth (40). A cohort with 30 years of follow up showed that this measurement is an indicator of insulin resistance and BMI in children but not in adults (45).

Thus, considering the association between obesity, insulin resistance and abnormal glucose metabolism with CKD, as well as the current finding on the association between WC and GFR, it is suggested that WC can be used as a predictor of CKD in children.

In this study, although the mean serum Cr level was higher in those participants with higher measurements of hip, neck and WCs, it had no significant correlation with these anthropometric measurements. In addition, these very small differences are of no clinical importance.

This investigation had a cross-sectional design, which is considered as its main limitation. In addition, the results of this study would be more applicable if the association of the afore mentioned anthropometric indices with other markers of kidney function, such as cystatin C, had been investigated.

This study was conducted as a part of a national study with a large sample size and, to the best of our knowledge, this was the first national study in the pediatric population which has evaluated the association of neck and WCs with renal function.

Conclusion

The findings of this large population-based study suggest that both neck and WCs are appropriate, simple, non-invasive and easy to detect anthropometric measurements that can be used in epidemiological and clinical studies for determining those children and adolescents who are at risk of kidney dysfunction.

Ethics

Ethics Committee Approval: The Research and Ethics Committee of Isfahan University of Medical Sciences approved this study (approval number: 194049).

Informed Consent: Written informed consent and verbal consent were obtained from the parents and students, respectively.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.K., M.E.M., Concept: R.H., M.E.M., M.Q., R.K., Design: R.H., M.Q., R.K., Data Collection or Processing: M.T., T.A., G.S., A.M.G., S.Z., Analysis or Interpretation: M.Q., Literature Search: A.M.G., S.D., A.A., Writing: M.M., A.M.G.

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