Is CKD Screening Program Necessary in Developing Countries?

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Introduction. The prevalence of congenital anomaly of kidney and urinary tract (CAKUT) and related chronic kidney disease (CKD) may be increased in countries with higher rate of consanguineous marriage. Therefore, we evaluated the prevalence of CKD by biochemical and kidney ultrasound measurements in the first-grade pupils.

Methods. This cross -sectional study was carried on children aged 6 to 7 years. Urine analysis, serum creatinine, urine microalbumin to creatinine ratio and kidney ultrasound have been evaluated for participants.

Results. 653 children were recruited to the study. Stage 1 and stage 2 systolic hypertension have been found in 6.5 and 1%, respectively. The percentage of stage 1 and stage 2 diastolic hypertension were 1.3 and 0.3%, respectively. Both weight Z-score and waist Z-score had positive correlation with systolic and diastolic blood pressure. Microalbuminuria (in 2.5%) did not have any correlation with the following factors: hypertension, body mass index, microscopic hematuria, glomerular filtration rate, kidney sonographic abnormalities or kidney parenchymal thickness and family history of kidney transplantation. GFR less than 90 mL/min /1.73 m^2 has been detected in 1.8% of the students. Only 1.7% had urine RBC more than 5 in each high-power field (hpf). Approximately 1.5% had anatomical abnormality of kidney and urinary tract (hydronephrosis or hydroureter).

Conclusion. Considering the higher prevalence of elevated blood pressure and microalbuminuria in Iranian children, a CKD screening program based on evaluating microalbuminuria and blood pressure measurement is needed. However, irrespective of high prevalence of consanguineous marriage in Iran, using kidney ultrasound as a screening tool has not been recommended.

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INTRODUCTION

CKD is not only devastating but also a cost-consuming illness with considerable morbidity and mortality.[1] Regardless of the lower incidence of CKD in the pediatric age group compared with adults, still the unhealthiness makes significant problems in health systems.[2] In our previous cross-sectional study, we found that the annual incidences of advanced stages of CKD were 5.52 per million population (pmp) and 16.8 per million *children* respectively. Furthermore, its prevalence was 5.06 per million population.[3] While most studies have focused on the prevalence of advanced stages of CKD worldwide, the true prevalence of CKD in children remains to be determined.

Considering the epidemiology, congenital anomalies of the kidney and urinary tract (CAKUT) followed by glomerular diseases are the top causes of CKD.[3,4] Some structural abnormalities in CAKUT have an autosomal dominant and or less frequently autosomal recessive genetic basis.[5] Furthermore, autosomal and multifactorial patterns of genetic abnormalities are more frequently observed in children born from consanguinity marriages, which are common in Iran.[6,7] The total rate of consanguineous marriage was estimated at about 38.6%, of which 27.9% was between first cousins.[6]

Therefore, CAKUT and other genetic-based kidney diseases may be more common in Iran and countries with a higher rate of consanguineous marriages.

Mass screening of children to detect early stages of CKD has been set up in many Asian countries, whereas urine analysis or any other tests as screening tools have not been accepted by European countries and recently by the USA.[8-10] In our country, still, no CKD screening has been established.

Regarding differences in social behaviors, various ethnicities, higher consanguineous marriages, and lack of data in our country, we planned to evaluate children at the mid-growth spurt (aged 5 to 7 years) to find the prevalence of urinalysis abnormalities, microalbuminuria, as well as kidney and urinary tract abnormalities.

MATERIALS AND METHODS

Sample Size Estimation and Recruiting Participants

This cross-sectional population-based study was conducted from January 2018 until June 2019 on first-degree primary school students from 10 different areas of Isfahan city, the third large city in Iran. To estimate the sample size, a 95% confidence interval (1.98), probability of CKD prevalence of 2%,[2] and assumed precision of 0.008 were considered, moreover Cochran correction formula for limited sizes was applied.

As a final point, the intended number of participants was 1000 pupils. However, due to the summer holidays followed by the COVID-19 pandemic, 653 children were recruited. To generalize the findings, a multi-stage cluster sampling method was used, which means first of all, the sampling framework including a rural area, schools, and student lists was formed, and then eligible samples were randomly selected using a random number table.

Random number tables in both rows and columns have random numbers that usually reach 99 rows and columns, and they are arranged in five-digit blocks next to each other separately to facilitate sampling.

Consent information and oral assent were taken from parents/caregivers and participants respectively.

The study was approved by the ethics committee of Isfahan University of Medical Sciences.

Before starting the survey, one of the executive team members explained the project to parents/caregivers, children, school staff, and managers.

Executive Method

A questionnaire contained was filled out for each participant; it consisted of questions regarding demographic and anthropometric data, questions about family history of known kidney diseases in first-degree relatives, and past medical history.

Then, every participant was asked to come to a silent room to have their blood pressure (BP) checked by two different pediatricians two times in a 30 minute intervals. The mean of two measured BP was recorded. High readings of BP were measured for the third time after a 30 to 60 minutes interval.

To measure BP, a hand-held cuff-mounted sphygmomanometer MDF Instruments Aneroid with appropriate size for children was used.

Different categories of BP were defined according to the last updated American Academy of Pediatrics (AAP) hypertension guideline.[11] Height and weight were measured by standard protocols and calibrated instruments.

Para-Clinic Evaluation

All selected participants were referred to the university-affiliated children's hospital (Emam Hossein Children Hospital, Isfahan University of

Medical Sciences) for the following paraclinical investigations: urinalysis, urine culture, blood urea nitrogen (BUN) and creatinine, fasting urine microalbumin to creatinine ratio as well as kidney and urinary tract ultrasound.

Urine microalbumin was measured by ELISA method (Stat fax machine). Blood and urine biochemical markers (BUN, serum and urine creatinine) were measured by DIURI/CS400 machine. Urine analysis and sediment were evaluated by fix laboratory technician.

To calculate urine microalbumin to urine creatinine ratio (ACR mg/gm), the following equation was used:[12]

$$\text{ACR}\,(mg/gm) = \frac{urine\ microalbumin\left(\frac{mg}{dl}\right)}{urine\ creatinine\left(\frac{mg}{dl}\right)} \times 1000$$

We also converted ACR (mg/gm) into mg/mmol to have SI units.

The glomerular filtration rate (GFR) was calculated according to the following equations:

- Schwartz Equations: eGFR mL/min /1.73 m^2 = k × (height in cm) ÷ serum Cr mg/dL; k = 0.55[13]
- Counahan-Barratt Equation: eGFR mL/min /1.73 m^2 = (0.43 × height in cm) ÷ serum Cr mg/dL[14]
- Leger Equation: eGFR (mL/min) = [56.7 × Body weight (kg) + 0.142 × Length^2 (cm)]/serum Cr (µmol /L)[15]

Kidney and urinary tract ultrasounds were performed by an expert pediatric radiologist. A GE ultrasound machine model E8 with 3.5, 5 10 MHz probes were used to scan the kidneys and urinary tract.

Before the examination, the child was well hydrated (full bladder wherever possible).

The bladder was examined both before and after urination.

Statistics

Descriptive statistics including absolute number, percentage, mean and standard deviation were used to present the findings.

We also used an independent t-test to compare quantitative data and qualitative data from Chi-square. To estimate the risk, logistic regression and odds ratio with confidence interval were calculated. SPSS 20 software was used for the analysis.

RESULTS

Demographic Findings

As presented in Table 1, from 653 pupils who were recruited to the study, 358 (54.8%) were girls and 295 (45.2%) were boys The male/female ratio was 0.82.

The mean (SD) ages of females and males were 6.52 ± 0.53 years and 6.49 ± 0.55 years respectively without significant difference in terms of gender (P = .4).

Considering BMI tables for boys and girls aged 2 to 18 years (3^{rd} to 97^{th} percentiles), 48.8% had normal BMI. Underweight (BMI less than 10^{th} percentile for age and sex) and overweight (BMI more than 95^{th} for age and sex) were found in 28.8% and 22.3% of the participants respectively.

Blood Pressure Findings

The mean of systolic (SBP) and diastolic BP(DBP) and frequency of normal, elevated, stage 1, and stage 2 hypertension are presented in Table 2. We had 16 participants with high readings of blood pressure. However, these high values did not

Table 1. Demographic Characteristics of the Participants

Gender	Age ± SD, y	Height ± SD, cm	Height Z Score ± SD	Weight, kg	Weight Z score ± SD	Waist ± SD	Waist Z score ± SD	BMI ± SD
Female	6.52 ± 0.53	123.01 ± 8.16	-0.02 ± 0.99	24.89 ± 6.64	-.01 ± 1.05	54.87 ± 6.55	-.017 ± 0.94	16.35 ± 3.13
Male	6.49 ± 0.55	123.47 ± 8.23	0.033 ± 1.0	25.15 ± 5.87	0.02 ± 0.99	55.14 ± 7.37	0.02 ± 1.06	16.45 ± 3.45

Table 2. Mean of SBP and DBP and Frequency of Hypertension in the Participants

Blood Pressure, mmHg	Mean ± SD	Normal Range BP (%)	Elevated BP (%)	Stage 1 Hypertension (%)	Stage 2 Hypertension (%)
Systolic BP	103.42 ± 11.93	60.1	32.4	6.5	1
Diastolic BP	65.69 ± 8.31	82.3	16.1	1.3	0.3
Mean Arterial blood Pressure	78.27 ± 8.32				

approve after the third measurement.

Hypertension is defined based on the AAP guideline.[21]

There was no significant correlation between hypertension in the participants and positive family history of hypertension or kidney disease.

Weight Z-score had a positive weak correlation with systolic (P = .03, r = 0.125) and diastolic BP (P = .03, r = 0.0126).

A significant positive weak correlation was found between waist Z-score and systolic (P = .049, r = .114) and diastolic BP (P = .007, r = 0.156). There was no correlation between height Z -score and systolic and diastolic BP.

Urinary Biomarker Findings

The mean values of ACR in males and females were 27.36 ± 42.21 mg/gm and 28.03 ± 42.21 mg/gm, respectively (P = .94). Calculating the values based on mg/mmol showed 3.09 ± 0.28 in males and 3.17 ± 0.25 in females (P = .83).

After excluding high values of microalbumin / Cr (more than 300 mg/gm), the calculated *reference value* of microalbumin / Cr was 23.81 ± 37.82 mg/gm (mean ± 1.96 SD) (Table 3).

Means ± SE of microalbuminuria Z-score was -0.009 ± 0.059 and 0.006 ± 0.053 in males and females, respectively (P = .93).

Neither microalbuminuria nor microscopic hematuria had a correlation with a positive family history of kidney transplantation and proteinuria (P > .05). In addition, we did not find any correlation between microalbuminuria and the following factors: systolic and diastolic BP, body mass index (BMI), urine RBC more than 5, glomerular filtration rate (GFR), and sonographic kidney parenchymal and cortical thickness.

Microalbuminuria did not have any correlation with a positive family history of hearing loss or kidney disease. However, a family history of hearing loss was correlated with a family history of kidney transplantation and proteinuria in affected families (P = .0001, P = 0.001; respectively).

Nonetheless, no significant correlation was determined between microalbuminuria Z-score and the following variables: systolic or diastolic BP, height Z- score, weight Z- score, and waist Z-score.

Table 3. Frequency of Microalbuminuria in the Participants

Microalbuminuria Values (mg/mmol)	Percent of the Participants	Definition
< 2.2	44.8	Normal*
≥ 2.2 to < 22.6	54.3	Microalbuminuria*
≥ 22.6	0.9	Macroalbuminuria*
< 3.5	79.8	Normal**
≥3.5 to < 10	17.3	Equivocal**
≥ 10 to 47	2.5	Microalbuminuria**
> 47	0.4	Macroalbuminuria**

*Reference 24
**Reference 25

GFR Results

Results of GFR (Schwartz formula, Counahan-Barratt Equation, and Leger Equation) (Reference number) are summarized in Table 4. Based on all 3 equations, the mean of GFRs between males and females was not significantly different. According to Schwartz's equation, 1.8% of the pupils had GFR less than 90 mL/min /1.73 m^2. All these participants had GFR between 67 to 89 mL/min /1.73 m^2. GFR based on Schwartz's formula and Counahan-Barratt Equation had a weakly positive correlation with sonographic left kidney cortical thickness (P = .041, r = 0.086) and right kidney cortical thickness (P = .049, r = 0.078).

Urinalysis Findings

Fasting urine analysis and urine culture were performed for all participants. Significant bacteriuria was reported in 5 participants. Positive urine culture and positive nitrite test were found in 4 participants (female). The Leukocyte esterase test was positive in only one of 4 participants. Trace protein by dipstick was found in 9 participants (1%). A positive urinary bilirubin test was demonstrated in 2 participants. Trace and one plus urine protein test was found in 56 and 8 participants, respectively. Urine protein results by dipstick had a significant positive correlation with ACR (P = .0001, r = 0.143) but not with specific gravity. No participant showed glycosuria.

Table 4. Means of GFRs of the Participants (Results of 3 Different Equations)

eGFR	Gender	Mean ± SD
Schwartz Formula, mL/min /1.73 m^2	Female	132.45 ± 23.94
	Male	133.52 ± 25.17
Counahan-Barratt Equation, mL/min /1.73 m^2	Female	103.55 ± 18.71
	Male	104.38 ± 19.67
Leger Equation, mL / min	Female	78.99 ± 18.07
	Male	79.94 ± 18.61

Approximately 98.3% of the participants had urine RBC equal to or less than 5 in each high-power field (hpf). Five students had urine RBS equal to or more than 10 in hpf. Urine RBC did not have any significant correlation with the following variables: hypercalciuria, hyperuricosuria, and microalbuminuria. Compound hematuria and proteinuria were seen in none of the students. The mean of urine WBC and urine RBC were 2.28 ± 4.34 and 1.66 ± 2.41.

Kidney Ultrasound Measurements

Kidney and urinary tract ultrasounds were performed for every participant to demonstrate kidney size and thickness. Table 5 shows the measurements of the left and right kidneys.

The kidney stone was reported in two participants in the left kidney. Kidney scars or focal decrease of parenchymal thickness and kidney cysts were not reported in any of the participants. Right, and left kidney hydronephrosis were detected in 5 and 4 participants, respectively. A bilateral hydroureter was found in a boy. Approximately 1.5% of the pupils had either hydronephrosis or hydroureter (a total of 10 participants). No participant showed bilateral hydronephrosis.

DISCUSSION

According to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, CKD is a clinical syndrome that has been defined as "abnormalities of kidney structure or function present for more than 3 months".[16]

Various reports from different countries that are mostly derived from patients undergoing renal replacement therapy declare the growing incidence of CKD worldwide.[17]

Increasing the incidence and devastating and progressive nature of CKD face health systems to the profound consequences of morbidity and mortality and to an increased burden of cost, which is barely manageable for many countries.[17] In addition, the obscure and asymptomatic trend of the disease would motivate health systems to find a biochemical or a tool for screening and early detection of people at risk.

Table 5. Right and Left Kidney Ultrasound Measurements

Kidney Parameter, cm	Mean ± SD	Reference Value
LK Length	81.11 ± 7.59	81.11 ± 14.87
RK Length	78.77 ± 6.63	78.77 ± 12.99
LK Parenchymal Thickness	12.75 ± 2.24	12.75 ± 4.4
RK Parenchymal Thickness	11.77 ± 2.16	11.77 ± 4.23
LK Cortical Thickness	6.72 ± 2.87	6.72 ± 5.64
RK cortical Thickness	6.00 ± 1.24	6.0 ± 2.43

Reference value* = mean ± 1.96 SD

Although the Consensus Workshop on Prevention of Progression of Renal Disease 2004, recommended a CKD screening program for adults, the U.S. Preventive Services Task Force (USPSTF) did not recommend CKD screening in normal populations without any risk factor for developing CKD.[18,19]

Considering the limitation of the data registry in children, the estimation of the incidence and prevalence of pediatric CKD is difficult. However, according to published reports during the last three decades, the incidence of CKD has increased gradually.[20]

The asymptomatic nature of the early stages of many kidney diseases arises the tendency to screen for kidney diseases in children. Nevertheless, there is no consensus regarding the benefits and cost-effectiveness of early detection of CKD in children worldwide and a national epidemiologic study has been recommended.[21]

In this study, we assessed 653 students. Since CKD is more common in children older than 6 years in comparison to children less than this age, we recruited children at the age of entering primary school (6 to 7 years old) to evaluate whether CKD is more prevalent in our country with a relatively high rate of consanguineous marriage.

The importance of microalbuminuria in detecting the early stages of CKD has been discussed widely. KDIGO guideline defined CKD not only based on GFR but also according to microalbuminuria.[16] Therefore, screening and detecting the progression of CKD based on measuring the microalbumin to creatinine ratio in spot urine in health and disease has attracted a lot of attention.

In some Asian countries, pediatric CKD screening has been accepted at the national level.[22] In Japan, pediatric CKD screening has been started since 1973. Data from 13 years of urine specimen collection in Japan revealed proteinuria in 0.62% of elementary school children and 0.94% of junior high school children.[21] Nonetheless, persistent proteinuria was reported in 0.08% and 0.37% of elementary school and junior high schools respectively.[21]

The reports from mandatory annual urinalysis in Korea showed that the prevalence of hematuria in 0.64, 0.61, and 0.48% of elementary, junior, and senior high school students respectively. In the same school groups, the prevalence of proteinuria was 0.17, 0.34, and 0.39%.[23]

Kwak *et al* found a significant correlation among anthropometric data (age, height, height z-score, weight, weight z-score, GFR, BMI, and body surface area) with spot urine microalbumin/creatinine ratio.[24]

Shajari *et al* screened 1601 Iranian students aged 6 to 7 years for proteinuria and hematuria in the first-morning urine by examining the urine analysis specimen. Hematuria and proteinuria were found in 1% and 3.6% of children, respectively.[25]

Data analysis from the Third National Health and Nutrition Examination Survey (NHANES III) on American children and adolescents aged 8 to 18 years showed that microalbuminuria existed in 12% of the participants.[26]

A large-scale study on 1986 healthy Chinese children (1078 males, 908 females) aged 6 to 19 years old showed the normal upper limit of ACR equaled 14.7 mg/g for male children and 19.8 mg/g for female children. The authors could find a positive significant correlation between ACR and BMI, SBP, and smoking.[27]

In a study in Argentina, 1564 students aged 9.35 ± 2.00 years old were recruited from 9 elementary schools. The results revealed an inverse correlation between obesity and ACR.[280]

However, results from a study on 200 obese and normal-weight Iranian children indicated significantly higher amounts of ACR among obese children.[29]

Regardless of a few published papers in favor of higher ACR values in hypertensive children in comparison with normotensive children,[30,31] there is no consensus on whether microalbuminuria has a correlation with hypertension or not.[32]

Disagreement between the results of different studies may be due to diversity in participants' ages, method of measuring microalbumin, cut points of microalbuminuria, and method of blood pressure measurement.

In our study based on a different definition, diverse cut points and units of measurement with dissimilar percentages of microalbuminuria were achieved. The percentages of microalbuminuria in our patients were 21.7, 19.8, and 54.3% based on different cut points of ACR (ACR > 30 mg/gm, ACR > 3.5 mg/mmol, ACR > 2.2 mg/mmol), respectively. Macroalbuminuria has been demonstrated in 7 patients.

Applying bivariate analysis could not show any significant correlation between ACR and positive family history of kidney transplantation, kidney diseases, and family history of hearing loss.

In addition, we could not find a correlation between ACR with the following variables: systolic and diastolic BP, MAP, BMI, waist, height, weight, Z scores of weights and waists and heights, urine RBC more than 5, urine WBC, GFR, and sonographic kidney's size and parenchymal and cortical thickness. Nonetheless, no significant correlation was found between microalbuminuria-Z- score and the following variables: systolic or diastolic BP, height Z- score, weight Z- score and waist Z-score.

Although twenty out of 653 participants (3%) had trace or one plus positive protein dipstick, microalbuminuria (ACR > 30 mg/gm) were defined in over 21% of them. Even so, we found a statistically significant positive correlation between urinary protein by dipstick and ACR.

Regardless of the fact that congenital anomaly of the kidney and urinary tract is the leading cause of CKD in children worldwide, kidney ultrasound has not been established as a screening tool to estimate the prevalence of CKD.[33] However, during the last decades, kidney ultrasound of fetuses in the last trimester has found its position in pregnant women.

A study on Chinese children showed CAKUT in 489 out of 26989 (1.67%) with a dominancy of hydronephrosis. More than one-third of these groups needed a surgery during the follow-up.[34]

Evaluating CAKUT in infants in Italy for a period of 18 years proposed an incidence of 0.96% among infants, while vesicoureteral reflux (VUR) was the most common etiology.[35]

Considering the relatively high prevalence of consanguineous marriage in Iran (approximately 38%) and the increasing rate of monogenic CAKUT among children born from consanguineous marriage, we decided to evaluate children at the age of entering primary school to find any structural abnormality which has not been reported during prenatal screening program.[6]

In our study, abnormal ultrasound findings were documented in 10 participants (1.5%). We found hydronephrosis grade 1 and 2a SFU (equal to grade 1 Onen staging) in 9 participants and bilateral hydroureter in one boy.[36,37] During follow-up, only one child had bilateral VUR grades 2 and 3. And two out of 10 with non-resolving hydronephrosis had mild partial ureteropelvic junction obstruction (based on findings of DTPA diuretic scan).

Based on our survey irrespective of the high rate of consanguineous marriage in our country, the incidence of CAKUT was not higher than in the societies with a lower prevalence of consanguineous marriage.

In addition to microalbuminuria as a screening indicator of CKD, the increasing incidence of hypertension among the pediatric group has attracted global attention to screen hypertension as an independent factor of CKD progression.[38]

As stated by Song *et al* in a recent meta-analysis, the prevalence of hypertension and prehypertension in children less than 20 years old were 4% and 9.67% respectively.[39]

According to the pooled data derived from a systematic review and meta-analysis of Iranian children, hypertension was reported in 8.9%. The results of this study attested that the prevalence of hypertension in Iranian children is higher in comparison with the Western countries.[40]

The estimation of the prevalence of hypertension based on the last update of the AAP guideline has been altered.[11,41]

Using an aneroid sphygmomanometer, we found elevated BP in a considerable percentage of the participants (32.4% systolic and 16.1% diastolic hypertension). Approximately 12% of the students had both systolic and diastolic hypertension. In addition, elevated BMI in approximately one-fifth of the students had a positive significant correlation with high BP. There are a growing bulk of data supporting the correlation between increased BMI and a higher level of BP in children.[39]

The shocking increase in the global prevalence of obesity in children and its future consequences such as hypertension, diabetes, and coronary heart disease are heralding signs for urgent intervention.[42]

Backing to the screening method of CKD in children, abnormal urine RBC has its importance. The overall incidence of microscopic hematuria in the pediatric population has been estimated as 0.5 to 2%.[43] Nevertheless, the incidence of microscopic hematuria has a wide spectrum based on the method of evaluation (dipstick or complete urine analysis), ethnicity, age, and prevalence of glomerular and non-glomerular kidney diseases.

In a recent study in India, using urine dipsticks showed a prevalence of 2.77%. Nonetheless, the percentage of hematuria decreased to 0.62% when urine analysis specimens were re-evaluated by complete urine analysis.[44]

A high prevalence of urinary abnormality in 15% of primary school children in Egypt. The prevalence of hematuria by dipstick examination has been found in 9.7%.[45]

In a similar study, the prevalence of abnormal urinary findings in Chinese children was 11.11% at the age of 7 years old. Hematuria was reported in 0.35% of them.[46]

We documented hematuria in 10.1% of the students. Complete urine analysis could find urine RBC of more than 5 /hpf in 1.7%. No correlation was found between hematuria and the following variables: hyperuricosuria, hypercalciuria, microalbuminuria(mg/gm), and family history of hearing loss or kidney transplantation.

While the most available data on CKD is achieved from surveillance of stage 3 to 5 CKD, the true incidence of CKD stage 1 in children is still unclear.

To assess GFR in the participants, three different equations have been used: the Schwartz formula, Counahan-Barratt Equation, and Leger Equation (reference numbers).

Based on the most used formula (Schwartz formula), 1.8% of the pupils had GFR less than 90 mL/min /1.73 m^2. We ascertained that these pupils had GFR between 67.1 to 89 mL/min /1.73 m^2 (stage 1 CKD). None of the participants had CKD stage 2 or more.

We found a weak positive correlation between GFR and kidney cortical thickness. However, we did not recognize any cortical scar or local decreased thickness of parenchyma in both kidneys.

Summarizing our study, we documented a higher prevalence of hypertension, microalbuminuria, and microscopic hematuria in comparison with Western countries. GFR less than 90 mL/min /m^2 based on the Schwartz formula has been detected in 1.8% of the pupils. The prevalence of CAKUT irrespective of the higher rate of consanguineous marriage was not significantly greater than in countries with a low rate of consanguineous marriage.

Urine dipstick as a screening tool for CKD in children is inexpensive but not sensitive.[47] According to the AAP, using urine analysis to screen CKD has been modified during the last decades setting from 4 courses in childhood to doing nothing in the last updated 2007.[48] A systematic review of adult CKD screening programs demonstrated that screening based on either urine analysis or eGFR is cost-effective in adult patients with diabetes or hypertension.[49] In Asian countries with established annual urinary screening programs, such as Japan, fewer ESRD in adolescents has been observed since launching screening programs.[48]

Regardless of controversies in applying for CKD screening programs in children, approaching programs to find preventable and treatable risk factors of CKD in the pediatric population are being considered.[50] In accordance with increasing preventable risk factors of CKD in children and neonates such as prematurity, obesity, hypertension, and low GFR; a national database for children with CKD based on serum creatinine, urine microalbumin, systematic follow-up of high-risk children and finding more sensitive and specific biomarkers of CKD is advised.[50]

Adding to the inadequate standard methods in sample recruiting, problems in measuring serum creatinine in estimating eGFR is another profound step in estimating CKD prevalence in children.

CONCLUSION

Considering the higher prevalence of elevated blood pressure and microalbuminuria in Iranian children, a CKD screening program based on evaluating microalbuminuria and blood pressure measurement is needed. However, irrespective of the high prevalence of consanguineous marriage in Iran, using kidney ultrasound as a screening tool has not been recommended.

CONFLICT OF INTEREST

We certify that none of the authors had a conflict of interest.

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We certify that Gheissari A. designed and conceived of the presented idea, wrote the manuscript, and performed the analysis. Riahinezhad M, Mehrkash M, Merrikhi A, Madihi Y, and Farajzadegan Z had the same contribution to the study, carried out the experiments, and contributed to sample preparation. Esteki B, Amini N, Saeidi M, Vard B, Kermani R, Kelishadi R, Pourmirzaiee MA, Azin N, and Ghanei A carried out the study and implemented the research. All authors discussed the results and commented on the manuscript. We thank the Education Bureau and laboratory and imaging departments staffs of Emam Hossein Children's Hospital for all their efforts to facilitate the study.

Summary at a glance

We evaluated if kidney ultrasound in conjunction with blood pressure control, urine analysis, urine microalbuminuria and glomerular filtration estimation (GFR) are useful in screening chronic kidney disease in children. However, we could not find a significant correlation between microalbuminuria with kidney ultrasound findings.

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