Original Article

Urinary screening of elementary school students in Taicang, China

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Abstract

Background: Chronic kidney disease in children is a severe progressive disease that influences the growth, development, and life quality of patients. This study aimed to explore the detection rate of proteinuria and hematuria in elementary school students in Taicang, China.

Materials and methods: From 2015 to 2019, urine specimens were selected from 11,753 pupils in Taicang. The samples were tested for proteinuria and hematuria by applying single urine tests and urine sediment microscopic examinations. The observation results were divided into three groups: hematuria, proteinuria, and co-existing hematuria and proteinuria. In addition, kidney biopsies were carried out.

Results: The positive rate of urinary abnormalities was 0.842% (99 cases), of which there were 51 cases (0.433%) of proteinuria, 42 cases (0.357%) of hematuria, and six cases (0.051%) of co-existing proteinuria and hematuria. In terms of gender, of the 99 cases, 63 were female students (1.142%) and 36 were male students (0.577%). Additionally, the age distribution results indicated that the prevalence of urine abnormalities in each age group from age 7 to age 13 were 11.11%, 12.12%, 12.12%, 16.16%, 29.29%, 18.18% and 3.03%, respectively. Furthermore, one immunoglobin A nephropathy case was certified by renal biopsy assay in the follow-up at six months.

Conclusions: The urine screening revealed that abnormal proteinuria was the main form of urinary abnormalities in elementary school students from Taicang. Urine screening is necessary for early detection and intervention of kidney disease. [*Ethiop. J. Health Dev.* 2020; 35(2):000-000]

Key words: Urine screening, Taicang, elementary school student, proteinuria, hematuria

Introduction

Chronic kidney disease (CKD) in children is a chronic progressive ailment that seriously affects the normal growth and development of children (1). CKD is generally asymptomatic until it progresses to severe renal insufficiency, and some patients eventually develop end-stage renal disease (ESRD) (2). Data from China and overseas indicate that the prevalence of CKD has increased in recent years. Moreover, the proportion of patients with ESRD is rapidly increasing at a rate of 5%-8% per year in countries in Europe and the USA (3,4). Research scholars believe CKD is caused by multiple factors, the most common of which is renal dysplasia, which accounts for about 70% of cases (5). Urinary system infection, cystic kidney disease and nephrotic syndrome are also etiologies of child CKD (6,7). From studies of supportive clinical diagnostics and long-term research findings, the role of proteinuria in progressive renal damage has been well established. The three-layer structure of the glomerular filtration barrier (endothelium layer, the glomerular basement membrane, and the podocytes) acts as the checkpoint for protein infiltration. Inflammation in the fluid-filled space of this structural barrier of interstitium may lead to infiltration of protein molecules through the activation of various tubular cell-derived chemokines and complements . Glomerular changes are common in chronic nephropathies, including the irreversible damage of nephrons. This damage can decrease the function of the entire renal mass by upregulation of capillary hydraulic pressure on the glomerular wall. This capillary pressure disrupts the size-selective barrier for blood and filtrate of the glomerular barrier, causing ultrafiltration of protein to take place. The healthy functioning of kidneys is therefore considered under the lowering of proteinuria. Early detection of heavy proteinuria may reduce the chance of glomerular nephritis (GN). GN is characterized by the damage of glomeruli, thus causing inactivity of the kidneys, with less waste filtering and extra fluid disposal from the body. Early detection is important to delay and reduce the incidence of kidney disease in children. Thus, the nephrology community has shifted its focus from chronic renal failure (CRF) and alternative therapies to the early diagnosis of CKD.

Urine screening has become an effective and simple technique for early diagnosis of CKD in children (8). What's more, urine screening can decrease the number of ESRD cases and defer the development of CKD (9). In countries at different levels of development, such as Japan, South Korea and Nigeria, urine screening schemes for children and adolescents have been implemented (10,11). Routine urine examination is simple and can indirectly reflect the situation of kidney involvement, which is a valid screening index (12). Several researchers have demonstrated that 50%-90% of diagnosed CKD patients are discovered by urine

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screening, hinting at the necessity and effectiveness of urine screening for children (13,14).

Every day, we excrete 40-80 mg of protein through urine. Usually, excretion of more than 150mg of protein is generally referred as the proteinuria, although a universal generalized value for proteinuria is not available. Accordingly, correlation with other factors is integrated to draw the line of hyper-proteinuria. It is worth noting that the results of urine screening are affected by diverse factors, and the correct retention of urine samples is a necessary condition to ensure the accuracy of the analysis results. At present, although the diagnosis rate of CKD in children has been improved due to urine screening, the specific prevalence rate has not been determined. Through the epidemiological investigation of CKD, some domestic scholars have found that the prevalence of CKD in China is high and the detection rate is low (15).

In total, 11,753 primary and secondary school students in Taicang participated in this research, and several cases were followed up for six months to explore the patterns and strategies of urine screening in Taicang.

Materials and methods

Screening of research subjects and management: From 2015 to 2019, 11,753 elementary school students (7-13 years old) in Taicang (Jiangsu, China) were selected for urinalysis. The pupils who participated in the experiment signed an informed consent form and received instructions to urinate at home by themselves. Prior to urination, the participants were required to empty their bladders. The morning urination samples were collected the next day and stored under dark conditions for detection within four hours.

Typically, to detect the presence of protein in urine samples, the dipstick color change method, and protein-precipitation, electrophoresis methods are commonly used. High-performance liquid chromatography (HPLC) and species-specific albumin enzyme-linked immunosorbent assays (ELISA) are employed for the detection of albumin. Patients suffering from diabetes are more prone to kidney damage for the malfunctioning of enzymes; therefore, assessment of albuminuria is more effective for them.

Urinalysis experiments in the present study were carried out using urine test paper (DIRUI, Changchun, China). The method mainly tested urinary occult blood and protein in urine. In the second urinalysis experiment, the reagent strips were applied to separate positive hematuria specimens. Meanwhile, the urine sediment was examined microscopically. The results were divided into three groups: proteinuria group, hematuria group, and co-existing proteinuria and hematuria group. In this research, the privacy of all participants was protected, and the aberrant participants (proteinuria, hematuria, and both abnormalities) were registered and sent to the designated hospital for further follow-up treatment.

Data processing and statistical methods: The results from the urine tests were input into a computer and carefully checked by the specialist. The positive rates between different groups were detected with chi-squared tests utilizing SPSS 11.5 software (Chicago, Il, *USA*).

Results

The positive cases of urinalysis: In 11,753 enrolled children, the samples of proteinuria, hematuria and both abnormalities were examined. The second urinalysis disclosed that 99 cases were abnormal samples, which accounted for about 0.842% of the total detected samples. In total, 51 cases were certified as proteinuria (0.433%), 42 cases were diagnosed as hematuria (0.357%), and six cases were testified as co-existing proteinuria and hematuria (0.051%) (see Table 1). Figure 1 shows the incidence rates of proteinuria and hematuria by sex. The 99 abnormal samples were from 63 female students and 36 male students. Of these, the incidence of proteinuria in female students (57 cases) was significantly higher than that in male students (14 cases). There was no obvious difference in the proportions of hematuria and co-existing proteinuria and hematuria cases in female students and male students.

Figure 1: **Prevalence of positive (proteinuria, hematuria and co-existing proteinuria and hematuria) cases in different genders**

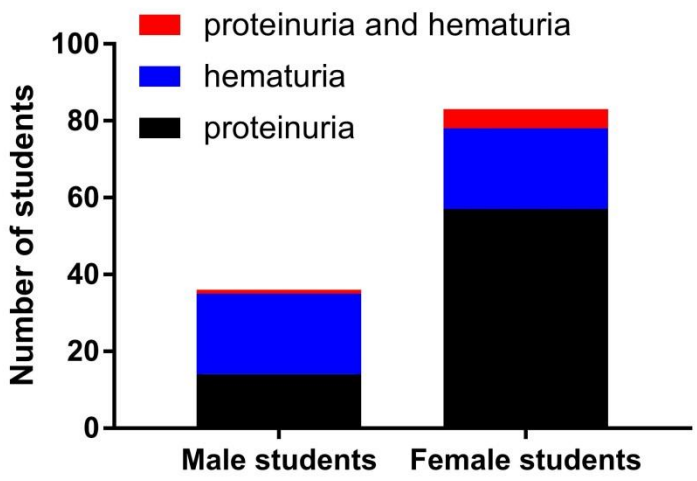
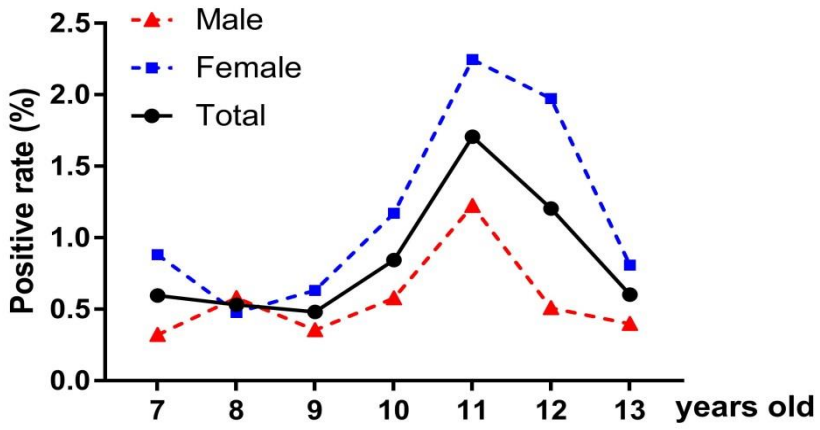


Table 1: **Prevalence of positive (proteinuria, hematuria and co-existing proteinuria and hematuria) cases in pupils**

Groups	Positive number	Positive rate
Proteinuria	51	0.433%
Hematuria	42	0.357%
Co-existing proteinuria and hematuria	6	0.051%
Total	99	0.842%

Age distribution of the prevalence of proteinuria and hematuria: Of the 99 abnormal cases, the proportion of female students was 1.142% (63 cases), and the proportion of male students was 0.577% (36 cases). The ages of these abnormal sample were concentrated between 7 and 13 years old. The prevalence of urine abnormalities by each age year – 7, 8, 9, 10, 11, 12 and 13 – were 11.11% (11 cases), 12.12% (12 cases), 12.12% (12 cases), 16.16% (16 cases), 29.29% (29 cases), 18.18% (18 cases) and 3.03% (three cases), respectively. The positive detection rates presented an increased trend with the increased age until a peak at 11 years old (see Figure 2). Therefore, the findings demonstrated that urinary abnormalities (proteinuria, hematuria, and both abnormalities) were more common in children at 10-12 years old.

Figure 2: **Prevalence of proteinuria and hematuria age from 7 to 13 years old**
The 99 abnormal cases were distributed from 7 to 13 years old. Of these age groups, urine abnormalities were most common at age 11.



Renal puncture diagnosis: Of the 99 abnormal cases, 32 proteinuria cases and 10 hematuria cases were followed up after six months. Re-examination results disclosed that eight patients still had small amounts of proteinuria, and 24 cases were normal. Of the 10 hematuria cases, one case was still diagnosed with proteinuria. Renal biopsy revealed that this case was compatible with a diagnosis of immunoglobin A (IgA) nephropathy. This patient with IgA nephropathy received oral mycophenolate mofetil (twice daily: morning 0.5mg; evening 0.25mg) and benazepril (10mg once daily) treatment for one week, and the follow-up was continued.

Discussion

Hematuria is the main indicator of serious renal dysfunction, and CKD has a high mortality rate once it develops into ESRD. ESRD is a significant worldwide public health problem, and renal replacement therapy is expensive. Hematuria may be classified as 'gross' or 'microscopic'. Under a microscope, if any red blood cells are observed in urine samples, complete urological investigation is the only way to intervene. If the dysmorphic red blood cells in a urine sample are positively detected at an early stage, this patient may survive for a long time (16). Urine screening has been performed for people of different genders, ages and occupations in several developed countries, and is regarded as an important strategy for early detection and intervention of CKD (17,18). Urine screening could discover early asymptomatic kidney patients in elementary school students, and provide opportunities for early intervention, thereby alleviating the severity of CKD and reducing the occurrence of ESRD (19-21). In this research, urine screening was implemented in 11,753 children from Taicang, and uncovered the present status of children with CKD in Taicang.

Urine analysis is the preferred method for urine screening due to its simplicity, low cost and rapid detection of disease (22). Proteinuria often indicates kidney damage, which is linked to IgA nephropathy, diabetic nephropathy, and hypertensive kidney damage (23). Hematuria refers to the increase of red blood cells (RBCs) in urine, which is closely related to glomerulonephritis, urinary tract infection, renal neoplasm, and polycystic kidney disease (24). Therefore, proteinuria and hematuria have become the important indicators for urine screening. Previous research indicates that partial proteinuria and hematuria

cases can emerge in healthy children. In Japan, the positive rates of hematuria and/or proteinuria in primary and secondary school students were 0.65% and 1.39%, respectively, from 1974 to 1986 (25). Additionally, the urine screening in Japan and Finland revealed that the detection rate of asymptomatic hematuria was about 0.4%-4% (26,27). We carried out urine screening in Taicang to uncover the conditions of proteinuria and hematuria in elementary school students in Taicang. The screening results indicated that 99 children were diagnosed with a urinary abnormality. Of these, proteinuria cases, hematuria cases and co-existing proteinuria and hematuria cases accounted for 0.433%, 0.357% and 0.051%, respectively.

Recently, proteinuria has been generally discovered in children, and the prevalence is approximately 1%-10% (28). In like manner, we also discovered that proteinuria was the main urinary screening result for elementary school students in Taicang. Our results were similar to those in a study by Nodoshan *et al.*, whose research disclosed that proteinuria was the most common abnormality in Yazd, Iran (29). The prevalence of proteinuria in Taicang was much lower than that in other areas, such as Iran (1.79%) (29) and Nigeria (3.5%) (30). Geographical area, racial group, socio-economic and genetical differences may account for different risks of developing proteinuria, although no studies have been carried out to investigate such risk factors. The difference may be due to the disparate number of samples screened and the local environment. The interesting discovery in the current study in Taicang was that proteinuria cases in female students were significantly higher than in male students. This conclusion is similar to the results of urine screening in Taiwan. From 1990 to 1992, the prevalence of proteinuria among girls was clearly higher than that among boys (31). Further, the prevalence of proteinuria and/or hematuria is likely to be associated with diverse age groups. Data from Taiwan indicated that the age of 12 and 13 were the peak years for the detection of proteinuria in students (20). In Shanghai, Rao *et al.* showed that the prevalence of urinary abnormality in students increased with age, and the peak was observed among 12-years-old (32). Our screening results uncovered those pupils in Taicang diagnosed with proteinuria and/or hematuria were concentrated in years 7 to 11. The detection rate of abnormal urine increased with age before the age of 11, and there was a significant peak at the age of 11 years old. The age at high risk of proteinuria and/or hematuria revealed in this study was similar to those above-mentioned reports. The proteinuria and/or hematuria may be related to the incidence of some cryptic kidney diseases at a certain age.

In the past, various kidney diseases were found by early urine screening in schools, among which IgA nephropathy was the most common (33,34). Clinical trials suggested that the primary glomerulonephritis followed by ESRD is characterized by IgA nephropathy. Histopathological studies have confirmed the predominant deposition of IgA in the glomerular mesangium (38). Research from Japan reports that of 49 children with asymptomatic proteinuria and hematuria, 34 were diagnosed with various kidney diseases by kidney biopsy, of which 21 were IgA nephropathy (26). In Korea, IgA nephropathy was discovered in 34 of 51 children with proteinuria and hematuria (35). Among 67 children with proteinuria and/or hematuria in Shanghai, two cases were diagnosed with IgA nephropathy (32).

In the current study, the follow-up results showed that one case was certified as IgA nephropathy via kidney biopsy from 40 proteinuria cases. Due to the small number of samples tested, fewer cases of IgA nephropathy were discovered than in other research studies. More studies are needed to confirm the results of the current study. Mycophenolate mofetil and benazepril were used to treat the IgA nephropathy patient for one week in our research, and the follow-up will continue. It is worth noting that kidney biopsy is the crucial standard for the diagnosis of CKD, but it is invasive, and is hard to perform dynamical detection during the disease progression (36,37). CKD is progressive, so kidney biopsy cannot be utilized as an indicator for routine monitoring of disease changes in clinical practice.

In the current study, proteinuria was found to be the most prevalent urine abnormality in elementary school students in Taicang. This abnormality may have a high risk of developing IgA nephropathy. Therefore, urine screening and regular follow-up are effective methods for early detection of kidney disease and provide the direction of early intervention. Accordingly, it is worth extending testing to primary schools. In addition, the establishment of the multi-center cooperation model is needed, which may lay a certain foundation for the construction of the health network of urine screening in schools.

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Conflicts of interest: The authors declare that they have no conflict of interests.

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