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A Cross-sectional Prospective Study of Asymptomatic Urinary Abnormalities, Blood Pressure, and Body Mass Index in Healthy School Children

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Introduction: Screening school children for urinary abnormalities is an inexpensive task but is not commonly undertaken in India. Although debated in western countries, its utility in early diagnosis of kidney disorders has been proved by studies from Asia. We examined the prevalence of asymptomatic urinary abnormalities (AUA), obesity, and hypertension in school children and analyzed data to identify potential risk factors among those detected with such abnormalities.

Methods: Children and adolescents 8 to 18 years of age of either gender, attending 14 public schools in West Bengal, were screened prospectively from July 2013 to July 2016 for detecting asymptomatic urinary abnormalities by a spot urine test using a dipstick. Sociodemographic profile, medical examination (weight, height, and blood pressure), and questionnaire-based data were recorded.

Results: A total of 11,000 children were screened. Of these, data from 9306 children were available for AUA, obesity, and hypertension. The prevalence rate was 7.44% (95% confidence interval [CI] = 6.91%−7.97%) for at least 1 AUA. Isolated hematuria was present in 5.2% (95% CI 4.75%−5.65%), whereas isolated proteinuria was present in 1.9% (95% CI = 1.62%−2.18%). The prevalence of prehypertension was 13.43% (95% CI = 12.74%−14.12%) and that of hypertension and abnormal body mass index was 4.05% (95% CI = 6.43%−7.47%) and 38.67 (95% CI = 37.68%−39.66%) respectively.

Discussion: The prevalence rates of AUA were comparable with those in some Asian countries but higher than in most developed countries. Of children and adolescents 8 to 18 years of age, those 13 to 18 years had significantly more high risk factors such as AUA, hypertension, and obesity.

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Screening for urinary abnormalities is generally considered important for adults, but there is no clear consensus with respect to children.[1] Asian countries such as Japan, Taiwan, and Korea have already established annual primary school screening programs for children. Published data from Japan have demonstrated a significant impact of population-based screening in children in the form of an increase in the mean age of end-stage renal disease (ESRD) mainly due to glomerulonephritis. However, in Japan, like India, diabetic nephropathy is now emerging as a leading cause of ESRD.[2] In India, population-based data on chronic kidney disease (CKD) is not very robust, but a high overall prevalence of 17.2% has been reported.[3] Among the causes of CKD, diabetic nephropathy (31%) has been reported as the most common, followed by CKD of unknown origin (16%), chronic glomerulonephritis (14%), and hypertensive nephrosclerosis (13%).[4] This is based on data obtained from the adult population. In pediatric and adolescent age groups, detection of early proteinuria, hematuria, proteinuria with hematuria, hypertension, body mass index (BMI) abnormalities, and a composite data analysis may be more helpful in diagnosing renal disease earlier and initiating measures to slow progression to advanced stages of CKD. The mean age at diagnosis of diabetes in India is lower than in developed countries. Obesity

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plays a central role in the insulin resistance syndrome, which includes hyperinsulinemia, hypertension, hyperlipidemia, type 2 diabetes mellitus, and increased risk of atherosclerotic cardiovascular disease.[5,6] The incidence of type 2 diabetes reported in children has increased alarmingly. Screening programs for children in India must be tailored to the epidemiology of CKD in the country. This study is the first to take a multipronged approach to analyze the prevalence of asymptomatic urinary abnormalities, obesity, and hypertension in children as well as to identify the high-risk group among these children.

METHODS

This was prospective, cross-sectional, population-based, observational study conducted from July 2013 to July 2016 at 14 public schools of Kolkata district in the state of West Bengal and was coordinated from the Institute of Post Graduate Medical Education and Research (IPGMER) Kolkata. After obtaining clearance from the institutional ethics committee and the concerned state and individual school authorities, we screened healthy junior and high school children and adolescents 8 to 18 years of age for clinical parameters and asymptomatic urinary abnormalities (AUA). Children already diagnosed with hypertension, diabetes, or any systemic diseases as per their medical records were excluded. We decided to screen about 11,000 children so that we would get a sample of 7000 evaluable participants, assuming a prevalence rate of 2.5% (results of a previous study from India) of isolated hematuria, with a 95% confidence interval [CI] and a 5% margin of error.

Study tools included urine dipsticks (as they have acceptable sensitivity ranging between 91% and 96% and are relatively inexpensive[7]), blood pressure (BP), height, body weight recordings, and questionnaire-based data. The BMI percentiles were recorded as per the growth charts of the Indian Academy of Pediatrics (2015) for 5- to 18-year-old Indian children and adolescents.[8] The categories of hypertension and BMI abnormalities were based on the definitions provided by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (NHBPEP) Classification of Prehypertension and Hypertension in Children and Adolescents[9] and Centers for Disease Control and Prevention (CDC) definitions of childhood obesity,[10] respectively. Further details of methods and statistical analyses used are given as Supplementary Methods.

RESULTS

Figure 1 depicts the study activity flow chart and the number of evaluable subjects. A total of 11,000 children were screened, and complete data of 9306 children were available, of whom 52% (n = 4841) were boys and 48% (n = 4465) were girls. Of the total, 51.4% (n = 4780) were in 8 to 12 years of age (younger age group) and the remaining 48.6% (n = 4526) were 13 to 18 years of age (adolescent age group).

Table 1 summarizes the data for asymptomatic urinary abnormalities in the entire study population as well as the age-stratified subgroups. A total of 692 subjects had at least 1 or more urinary abnormality (blood/protein/leukocytes/nitrite).The point prevalence rate of asymptomatic urinary abnormality in the study population was 7.44% (95% CI = 6.91%−7.97%). Supplementary Table S1 shows the comparison of urinary abnormalities in first screening in children in various studies across different countries and other parts of India. Supplementary Table S2 shows the prevalence of abnormal blood pressure in the study population along with age-group comparison.

Analysis of different types of urinary abnormalities showed that isolated hematuria (IH) was present in 5.2% (n = 483; 95% CI = 4.75%−5.65%, whereas isolated proteinuria (IP) was present in 1.9% (n = 175; 95% CI = 1.62%−2.18%, and proteinuria with hematuria (HP) were present in 0.23% (n = 22) of the study population. Age-stratified analysis showed that isolated proteinuria and leukocytes in urine were significantly higher in the adolescent age group compared to the younger age group and that the difference was statistically significant ($P < 0.05$), whereas isolated hematuria was significantly higher in the younger age group. Proteinuria with hematuria, which may be a signature of glomerular disease or obstructive uropathy, was seen in 0.23% of the study population overall (n = 22).

Tables 2 and 3 depict the blood pressure abnormalities in the study population. In all, 20.38% (n = 1897) participants had some BP abnormality, that is, prehypertension or stage 1 or stage 2 hypertension (as defined in Materials and Methods). A significantly greater number of participants in the adolescent age group had abnormal BP compared with the younger age group, as shown in Table 2. Almost 1 in 4 adolescents and 1 in 5 of the entire study population had abnormal BP. As shown in Supplementary Table S3, BP abnormality of any category, prehypertension, and stage 1 hypertension were significantly more common in boys compared to girls. Asymptomatic urinary abnormalities were more common in the participants with hypertension (n = 1.16%) compared to those with normal BP ($P = 0.00$). Compared to the younger age group, the adolescent age group had a higher prevalence of urinary abnormality with abnormal BP (4.24 vs. 11.82%, $P = 0.00$), as shown in Table 3.

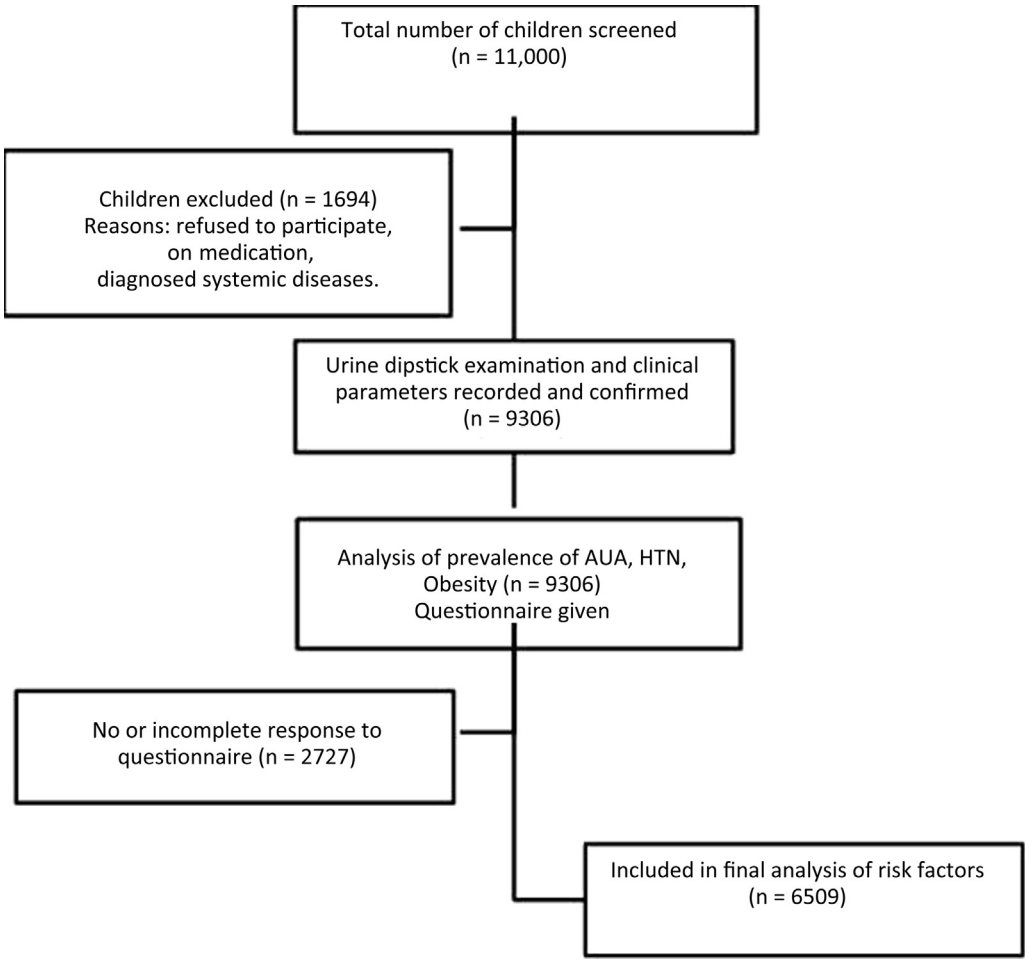

Figure 1. Flowchart of the study participants. AUA, asymptomatic urinary abnormalities; HTN, hypertension.

BMI abnormalities in the 2 age groups and gender distribution are shown in Table 4 and Supplementary Table S4, respectively. High BMI was significantly more prevalent in the younger age group and in girls ($P < 0.05$).

Data collected from the study questionnaire regarding medical and family history were available from 6509 students.

On univariate analysis, a significant association was found between proteinuria and each of the following parameters: low BMI, high BMI, sibling having a history of diabetes, and 13- to 18-year age group (with reference to age group 8−12 years), as shown in Table 5. Multivariate logistic regression found significant association between proteinuria and each of the following parameters: high blood pressure, low BMI, sibling diabetes, and age group 13−18-years (with reference to age group 8−12 years), as shown in Table 6.

DISCUSSION

This is the largest study from India, to our knowledge, in which screening of urinary abnormalities, along with an assessment of BP and BMI, was undertaken; we studied 11,000 school children attending public schools who were 8 to 18 years of age. Screening of urinary

Table 1. Prevalence of asymptomatic urine abnormalities in study population

Urine abnormality	Age groups		Total (N = 9306)	% of Total	*P* value (comparison between 2 age groups)
	8−12 yr (n = 4780)	13−18 yr (n = 4526)			
Blood	273 (5.71%)	210 (4.64%)	483	5.2%	0.02
Protein	55 (1.15%)	120 (2.65%)	175	1.9%	0.00
Leukocytes	19 (0.4%)	40 (0.88%)	59	0.6%	0.004
Nitrite	11 (0.23%)	7 (0.15%)	18	0.2%	0.48
Blood and protein	13 (0.27%)	9 (0.19%)	22	0.23%	0.53
RBCs and leukocytes	8 (0.16%)	0	8	0.08%	0.01
RBCs, leukocytes, and nitrite	0	0	0		
≥1 Abnormality	343 (7.17%)	349 (7.71%)	692 (7.44%)	7.44%	0.34

Table 2. Prevalence of abnormal blood pressure (BP) in the study population, along with age group comparison

BP category	Age groups		Total (N = 9306)	*P* value (comparison between 2 age groups)
	8–12 yr (n = 4780)	13–18 yr (n = 4526)		
BP abnormality	743 (15.54%)	1144 (25.28%)	1897 (20.38%)	0.00
Prehypertension	469 (9.81%)	781 (17.26%)	1250 (13.43%)	0.00
Stage 1 hypertension	137 (2.87%)	240 (5.30%)	377 (4.05%)	0.00
Stage 2 hypertension	137 (2.87%)	133 (2.94%)	270 (2.9%)	0.85

abnormalities in children has not been unanimously accepted as an efficacious measure of decreasing the CKD burden in western countries. However, data from Asian countries such as Japan has shown a significant impact of such screening on CKD burden in terms of increase in mean age of ESRD, especially due to glomerulonephritis. Population-based data from India is not as robust, and screening the whole population of school children may not be cost-effective in a developing country like India. To determine the higher-risk population that would therefore be the most appropriate target age group for screening, the whole study population was divided into 2 age groups, namely, 8 to 12 years and 13 to 18 years.

A comparison of our study with published studies (national and international)[11–21] of urinary abnormality screening in children has been compiled in Supplementary Table S1. In our study, the prevalence of isolated hematuria was 5.71% in the age group 8 to 12 years and 4.64% in the group 13 to 18 years, which was higher than that reported in most studies from developed countries and neighboring Asian countries. The prevalence of isolated proteinuria in our study was comparable to or lower than that of developing countries but higher than that in studies in the United States. The presence of any of the AUA were confirmed with a repeat testing (as specified in Materials and Methods). It is possible that IH may be due to a benign disease or may even resolve on follow-up in apparently healthy children; but it may also be indicative of glomerular or nonglomerular kidney disease with a potential of progression to CKD, lower urinary tract disease, or, rarely, metabolic abnormalities such as hypercalcemia and hyperuricemia.[22] Hence, it warrants follow-up and need for further investigations such as the ultrasonography of the kidneys, ureter, and urinary bladder, renal function tests, and kidney biopsy if a glomerular cause is more probable. Hematuria with positivity of leukocyte esterase/nitrates/nitrites is likely to be due to urinary tract infection. Such children were advised to follow up with their pediatrician or nephrologist. A proportion of these patients may have undetected, asymptomatic, congenital anomalies of the kidney and urinary tract and may require urine culture, treatment of urinary tract infection, as well as additional investigations such as micturating cystourethrography. Early identification of this subgroup will help alter or slow the progression of disease in these children. Despite the lower prevalence of urinary abnormalities in first screening studies from Japan and other Asian countries, these studies found a major long-term favorable impact of such screening on CKD epidemiology.[2] This might be applicable to the Indian population as well, and longitudinal follow-up studies of children with AUA are needed to establish the impact of such screening in India. The prevalence of IH was greater in the younger age group, and isolated proteinuria was significantly higher in the adolescent age group compared to younger age group. The prevalence of proteinuria with hematuria was not different in the 2 age groups. The presence of HP is more indicative of glomerular disease with a potential of progression than IH or IP alone. Together, proteinuria and hematuria may make children eligible for further rigorous screening and, if found to be persistent, imaging and/or biopsy. Another important observation is the prevalence of combined urinary abnormalities and BP abnormalities, which was significantly greater in the adolescent age group, and which may increase the likelihood of glomerular disease or long-term obstructive uropathy in this group.

The prevalence of hypertension was higher than or similar to that of studies from developed countries .[23–25] In our study, the overall prevalence of hypertension,

Table 3. Age group comparison of combined abnormal blood pressure (BP) and urinary abnormalities

Category	8–12 yr (n = 4780)	13–18 yr (n = 4526)	Total (N = 9306)	*P* value (comparison between 2 age groups)
Any urinary abnormality with abnormal BP	46 (4.24%)	96 (11.82%)	142 (7.48%)	0.00
Hematuria with abnormal BP	36 (4.85%)	60 (1.32)	96 (5.01%)	0.01
Proteinuria with abnormal BP	7 (0.94%)	36 (3.14%)	43 (2.21%)	0.00
Hematuria with proteinuria with abnormal BP	1 (0.13%)	5 (0.11%)	6 (0.26%)	0.12

Table 4. Comparison of body mass index (BMI) abnormalities in the 2 age groups

BMI category	Age groups: 8–12 years (n = 4780)	Age groups: 13–18 years (n = 4526)	Total (n = 9306)	*P* value (comparison between 2 age groups)
BMI abnormality	1944 (40.67%)	1655 (36.57%)	3599 (38.67%)	0.00
Underweight	417 (8.72%)	448 (9.90%)	865 (9.3%)	0.05
High BMI (overweight + obese)	1527 (31.94%)	1207 (26.66%)	2734 (29.37%)	0.00
Overweight	855 (17.89%)	783 (17.3%)	1638 (17.6%)	0.46
Obese	672 (14.06%)	424 (9.37%)	1096 (11.78%)	0.00

prehypertension, and stage 1 hypertension were significantly higher in the adolescent age group. Irrespective of age, boys had a higher prevalence of hypertension than girls. Some other studies have also found hypertension to be more common in boys.[26]

Overall BMI abnormality (high and low) and high BMI were significantly more common in the age group of 13 to 18 years. Girls had a higher BMI than boys. The overall prevalence of BMI is higher than those reported in data from developed countries as shown in Supplementary Table S2. However, the prevalence of obesity in children is increasing in both developed and developing countries.[27–33] Studies from other parts of India that have analyzed the subgroups of children from different socioeconomic backgrounds have found a high prevalence of obesity in those from affluent backgrounds, whereas low BMI is more often encountered in the lower socioeconomic groups.

Proteinuria was significantly higher in participants with high BMI. Although the 8- to 12-year age group had significantly higher BMI than the 13-to 18-year age group, the adolescents had higher prevalence of isolated proteinuria, abnormal BP, abnormal BMI, and combined urinary abnormalities and high BP. This implies that the adolescent age group should be the target population to be screened for early detection of kidney disease. Obesity in general is a major emerging risk factor for chronic kidney disease. Childhood obesity in particular is a growing epidemic in India and appears to be a major link with various metabolic complications such as insulin resistance, glucose intolerance, and type 2 diabetes mellitus. Insulin resistance itself may serve as an initiating factor for other metabolic as well as cardiovascular complications as adolescents with obesity grow into adults.[34] As the intention of the study was to use noninvasive screening methods, other risk factors such as dyslipidemia were not looked at in the study; however, data from the Bogalusa Heart Study clearly showed that almost 20% of obese children have adverse levels of at least 1 cardiovascular risk factor (hypercholesterolemia, hyperinsulinemia, hypertriglyceridema, hypertension) and that the presence of multiple risk factors is strongly associated with early stages of atherosclerosis.[35] Herein lies the importance of early screening for obesity and hypertension so that primary prevention can be exercised in this age group. Furthermore, the "nutritional transition" to more western-type food habits, which is becoming increasingly popular, has caused a large part of the population in developing countries to unknowingly become susceptible to the trend toward a rise in obesity. Unless intervention is done, the prevalence of risk factors, especially obesity (and therefore hypertension and diabetes) is likely to increase with time, as has been shown by some Indian studies.[36] It will be cost-effective for government to consider the recommendation of screening the school-going adolescent age group for urinary abnormalities as well as BP and BMI. Identification of obese and overweight individuals as well as those with AUA in the adolescent population, followed by frequent monitoring and life style modification counseling of this high-risk population, as well as detection of the disease proper with definitive treatment, can be the an initial useful preventive measure to practically approach the diabetes- and obesity-related metabolic burden in our adult population. In children and adolescents with additional risk factors such as family history of

Table 5. Univariate analysis of risk factors for proteinuria

Variable	Odds ratio (95% CI)	*P* value
Age group 13–18 yr (ref: 8–12 yr)	2.34 (1.696–3.228)	0.000
Gender (ref: female)	0.81 (0.6–1.093)	0.168
Premature birth	0.76 (0.34–1.64)	0.486
Any positive history in parents	0.921 (0.603–1.407)	0.704
Parental diabetes or hypertension	0.992 (0.641–1.535)	0.97
Parental diabetes	1.218 (0.711–2.085)	0.472
Parental hypertension	0.712 (0.411–1.235)	0.224
Sibling diabetes	2.068 (1.168–3.662)	0.011
Sibling hypertension	1.407 (0.705–2.808)	0.33
Sibling kidney disease	2.182 (0.679–7.107)	0.179
Student h/o hypertension	2.694 (0.360–20.13)	0.315
Student UTI	0.654 (0.265–1.615)	0.354
Student kidney disease	2.443 (0.587–10.17)	0.205
High BMI	1.731 (1.14–2.6)	0.0086
Low BMI	2.749 (1.907–3.964)	0.0001
Hypertension	1.075 (0.607–1.903)	0.764

BMI, body mass index; CI, confidence interval; h/o, history of; ref, reference; UTI, urinary tract infection.

Table 6. Multivariate analysis of risk factors for proteinuria

Variable	Odds ratio (95% CI)	*P* value
Age group 13–18 yr (ref: 8–12 yr)	2.3046 (1.455–3.656)	0.000
Sibling diabetes	2.625 (1.365–5.048)	0.004
Low BMI	3.195 (2.001–5.103)	0.000
Hypertension	2.055 (1.292–3.271)	0.002

BMI, body mass index; CI, confidence interval; ref, reference.

obesity, diabetes mellitus, or cardiovascular disease, or the presence of other risk factors for insulin resistance such as ethnicity, the preventive measures must be intensified.[37] Although adolescents have been found to have significantly more risk factors than younger children it is worthwhile to discourage rapid weight gain during the first years of life as it causes an early adiposity rebound and is in turn associated with the risk for future persistence of obesity.[38] Such a large-scale, multipronged, noninvasive screening approach is likely to result in a long-term beneficial impact on the overall burden of kidney and cardiovascular disease–related morbidity and mortality. Low BMI has been shown in some studies to be a risk factor for albuminuria and/or progression of kidney disease in subjects with as well as without preexisting kidney disease,[39–41] whereas some other studies have not found such an association.[42] The children with low BMI may also have had low birthweight (complete birthweight data were not available), which is a risk factor for albuminuria and progressive kidney disease.[43] We also found a significant association of low BMI with urinary abnormalities, and this group may be at increased risk for CKD.

In this study design, the point prevalence of AUA was recorded and analyzed. Because our study objective was to estimate the point prevalence, longitudinal follow-up data were not collected, and therefore we cannot comment on the prevalence of persistent AUA. The study investigators propose to undertake a longitudinal follow-up project based on the findings of this study. Studies from other parts of the world suggest that subsequent screening may reveal a lower prevalence of urinary abnormalities but that the same trend may not be true for obesity and hypertension, which, on the contrary, may show an increasing trend.

In conclusion, the study results have shown that the point prevalence rate of asymptomatic urinary abnormalities was significantly higher compared to that of several developed countries but comparable to some Asian countries. Despite looking at point prevalence only, the strength of our study lies in identifying a worthwhile screening age group of individuals 13 to 18 years, which had a significantly high incidence of prehypertension, stage 1 hypertension, and obesity along with AUA. The association of high BP with high BMI is well documented; however, interestingly, our study reveals that children and adolescents with low BMI also had significantly higher prevalence of proteinuria. We recommend that screening school children and adolescents for asymptomatic urinary abnormalities and measuring BP and BMI, especially in the high-risk age group of 13 to 18 years, will be a suitable, inexpensive strategy for practicing preventive nephrology in a resource-limited country such as India.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Supplementary Methods.

Table S1. Comparison of urinary abnormalities in first screening in children in various studies across different countries and other parts of India.

Table S2. Comparison of body mass index in various studies across different countries and other parts of India.

Table S3. Gender comparison of blood pressure abnormalities in the study population.

Table S4. Gender distribution of body mass index abnormalities in the study population.

Supplementary material is linked to the online version of the paper at www.kireports.org.

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