



Urinary Abnormalities in Asymptomatic Children of Ho Chi Minh City: A Population-Based Study

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Authors' contributions

Author LNND participated in the design, performed the statistical analysis and drafted the manuscript. Author TKAP helped in data collection and report. Author TLBD managed the literature searches. Authors AR, FJ and MHTT are head of the project, provided advice for the study design and supervised the manuscript redaction.

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ABSTRACT

Aims: To estimate the prevalence of urinary abnormalities in asymptomatic children aged 3 to 5 and to estimate the prevalence of urological anomalies detected by renal ultrasound among children with abnormal urine findings in an urban district of Ho Chi Minh City.

Study Design: cross-sectional population-based study.

Place and Duration of Study: Twelve kindergartens in Binh Thanh district, Ho Chi Minh City, Vietnam from March to June 2012.

Methodology: There were 11,093 children aged 3 to 5 attending 25 public and 17 private kindergartens including 2,657 in wealthy wards and 8,436 in non-wealthy wards. A total sample size of 2,402 children was required. Using a probability proportional-to

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size method, 8 kindergartens in public area and 4 kindergartens in private area were randomly selected. Overall, 2,433 children were enrolled including 1,244 boys. The children were screened by dipstick. Those with abnormal results were confirmed by a second dipstick. Children with two positive dipsticks were retested 3 months later and underwent renal ultrasound for urological anomalies.

Results: Abnormalities were detected in 7.8% of the subjects. Prevalence of proteinuria, hematuria, nitrituria, leucocyturia, and combined nitrituria and leucocyturia were 0%, 0.3%, 0%, 5.6%, and 0.2%, respectively. Girls had more abnormal results than boys (14.1% vs 1.8%, $p < 0.001$). After a three-month period, the number of children with persistent abnormalities was 37. The renal ultrasound detected 5 (13.5%) hydronephrosis cases. No significant difference was found when comparing public to private kindergartens and wealthy to non-wealthy region.

Conclusion: In such a region with high population density, the high prevalence of nitrituria and/or leucocyturia in girls calls for a good education for parents and caregivers in order to prevent urinary tract infection, and the low prevalence of proteinuria and hematuria suggests that the appropriate age for urinary screening in Vietnam might be over 6 years.

Keywords: Binh Thanh; Can Gio; chronic kidney disease; dipstick; Ho Chi Minh City; urinary abnormalities.

ABBREVIATIONS

ABU : Asymptomatic bacteriuria, CKD : Chronic kidney disease, CH2 : Children's Hospital 2 HCMC : Ho Chi Minh City, UTI : Urinary tract infection, VCUG : Voiding cystourethrogram, VUR : Vesicoureteral reflux.

1. INTRODUCTION

Chronic kidney disease (CKD) is a public health problem worldwide. Its incidence is steadily increasing among children [1,2]. Vietnam is a country of 88,772,884 inhabitants with 34.6% of the population under the age of 15 years [3]. Vietnam is similar to other developing countries where there is no current national epidemiologic data on pediatric renal failure. Detection and management of renal problems in Vietnamese children are not conducted early enough to prevent complications [4-6]. It is clear that there is no global consensus on the usefulness of screening for CKD in children. Many well-established mass screening in Japan, Korea, and Taiwan showed the benefits of conducting such program. Dipstick remains the simplest and least expensive method for urinary screening among healthy children.

An epidemiological study carried out in Can Gio - a rural district of Ho Chi Minh city (HCMC) - Vietnam in 2011 showed that the prevalence of nitrituria and leucocyturia was 2% and 1%, respectively, and a hygiene education campaign for parents was necessary [7]. Abnormal findings were higher in communes with very low population density. Such data were not available in urban area. Binh Thanh is an urban district of HCMC with a population of 470,054 inhabitants over an area of 20.76 km² corresponding to a density of 22,642 persons/km². Some general data of Binh Thanh and Can Gio are presented in Table 1.

Table 1. General data of the district of Binh Thanh as compared with the district of Can Gio and with Ho Chi Minh City (HCMC)

Indicators	Binh Thanh (Urban)	Can Gio (Rural)	HCMC
Area (km ²)	21	704	2,095
Population (persons)	470,054	68,846	7,396,446
Population density (persons/km ²)	22,642	98	3,531
Number of communes and towns	20	7	322
Number of general hospitals/total hospitals	3/4	1/1	59/93
Number of doctors per 10,000 inhabitants	NA	NA	13.4
Yearly average income per capita (USD)	1588	965	1475

Source: Statistical office in Ho Chi Minh City

The aims of our study were to estimate the prevalence of urinary abnormalities in asymptomatic children aged 3 to 5 in Binh Thanh district together with the prevalence of urological anomalies detected by renal ultrasound among children with abnormal urine findings. The results were then compared with published data in Can Gio to obtain a good view of urinary abnormalities among asymptomatic children in HCMC and to contribute education campaign for children's caregivers.

2. MATERIALS AND METHODS

2.1 Sample Size and Sampling Method

This cross-sectional population-based study was conducted in 2012 among healthy children aged 3 to 5 in Binh Thanh district, HCMC, Vietnam. It is estimated that about 90% of children aged 3 to 5 living in Binh Thanh are going to kindergartens. According to criteria of Ministry of labour, invalids and social affairs taking into account the average income of each ward, the People's committee of Binh Thanh district divided the district into 2 regions, 4 wealthy wards and 16 non-wealthy wards. In each region, there are both public and private kindergartens.

According to data provided by the District Office of Education, there were 11,093 children aged 3 to 5 attending 25 public and 17 private kindergartens in Binh Thanh in 2011 with 2,657 children in wealthy wards and 8,436 children in non-wealthy wards.

For a multistage sampling method, a sample size of 1,537 children was required to have a precision of 0.05 in estimating a prevalence of 0.5 with a correction for cluster effect of 4. With an expected missing data rate at 20% and a refusal rate at 20%, 2,402 children need to be enrolled in the study. Using a probability proportional-to-size method, we randomly selected 12 kindergartens, 8 out of 25 kindergartens in public area and 4 out of 17 kindergartens in private area. The final sample size was 2,744 children but parents of 2,433 agree to participate.

2.2 Data Collection

In each selected kindergarten, all children were invited to participate. Their parents were informed about the study and signed an informed consent form. Before the screening day, the parents received a clean urine container and were instructed on how to obtain the

specimen. The first morning midstream urine sample was collected at home in the supplied container and the signed consent form was brought to school in the early morning by parents. Results were read in the same morning by a pediatrician and a technician from the Children's Hospital 2 (CH2), with the help from the health stations' staff of the ward where the kindergarten locates. Children with a positive result were proposed for screening by a second dipstick for confirmation. Those who were still positive after the second dipstick were proposed for a third followed-up dipstick at CH2 after three months. Children with a third positive dipstick underwent urine culture and renal ultrasound at CH2.

Ten reagent dipsticks (under product name "Cromatest") and dipstick readers (DARA trademark) were supplied by Linear Chemicals (Spain). Dipsticks were considered abnormal if at least one of the following findings were detected: 1) Positive nitrite, 2) ≥ 25 white blood cells/ μL , 3) ≥ 10 red blood cells/ μL , 4) proteinuria ≥ 150 mg/dL was detected.

2.3 Data Analysis

Data were analyzed using SPSS 20. Data are reported as number and percentage or as mean and standard deviation. Proportions were compared using Chi square tests. A p-value less than 0.05 was considered as statistically significant.

3. RESULTS

Among 11,093 children aged 3 to 5 in the district, 2,744 children from 12 kindergartens were invited to participate. 88.7% of parents gave their consent for the first dipstick, leading to a sample size of 2,433 children. Of the 2,433 children, 813 (33.4%) were from private kindergartens and 1,620 (66.4%) were from public kindergartens. Positive dipsticks were found in 350 children (14.4%). Twenty two of them were not confirmed by a second dipstick. The remaining number of fully screened children was 2,411 (Fig. 1). The mean age was 4.2 ± 0.6 years and the boy/girl ratio was 1244/1167.

There were 188 (7.8%) children with two positive dipsticks out of the 2,411 screened children. This final percentage varied from 3.3% to 12.8% across kindergartens. One hundred and sixty five (87.8%) were girls. When comparing public kindergartens to private kindergartens, wealthy to non-wealthy regions, and area with population density $\leq 40,000$ persons/ km^2 to area with population density $>40,000$ persons/ km^2 , no significant difference was found (Table 2).

Table 2. Percentage of children with urinary abnormalities after two dipsticks according to the type of kindergarten, the economic status and the population density

	Number of children	Positive	%	p-value
Type of kindergarten				0.63
Public kindergartens	1603	122	7.6	
Private kindergartens	808	66	8.2	
Economic status				0.13
Wealthy wards	1193	103	8.6	
Non wealthy wards	1218	85	7.0	
Population density				0.93
≤ 40.000 persons/ km^2	827	65	7.9	
>40.000 persons/ km^2	1584	123	7.8	

Fig. 2 pointed out that girls had more often abnormal results than boys with 14.1% versus 1.8% (165/1167 and 23/1244, $p < 0.001$).

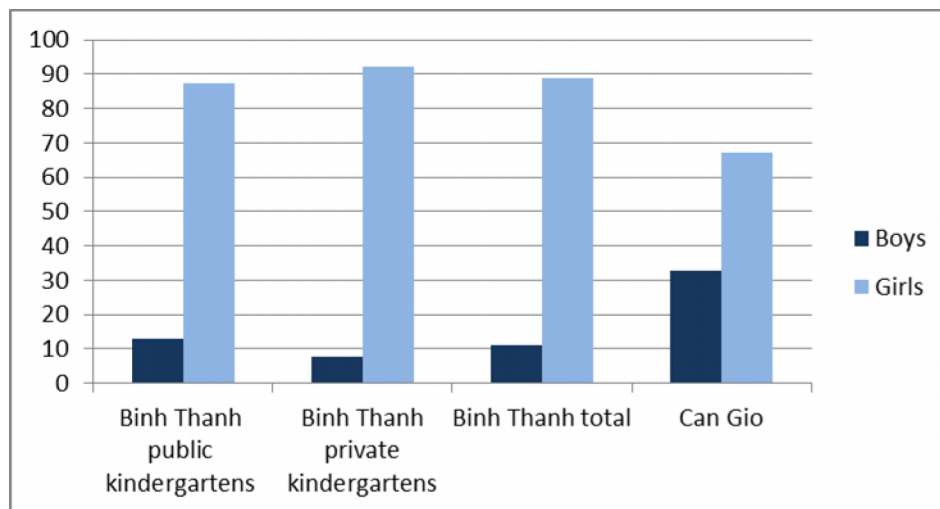


Fig. 2. Positive nitrituria and/or leucocyturia in girls and boys at kindergartens of Binh Thanh, an urban district as compared with Can Gio, a rural district of Ho Chi Minh City

Among the 188 children with two positive findings, there were 149 children who had two similar results with both dipsticks including 7 for hematuria, 136 for isolated leucocyturia and 6 for combined nitrituria and leucocyturia, accounting for a prevalence of 0.3%, 5.6% and 0.2%, respectively. Table 3 presents a comparison of these results of Binh Thanh district with results of Can Gio district [7].

Table 3. Comparison of the results after two dipsticks in Binh Thanh and in Can Gio districts

	Binh Thanh urban district	Can Gio rural district	p-value
Proteinuria	0/2411 (0%)	2/1957 (0.1%)	0.39
Hematuria	7/2411 (0.3%)	2/1957 (0.1%)	0.30
Nitrituria without leucocyturia	0/2411 (0%)	39/1957 (2%)	<0.001
Both nitrituria and leucocyturia	6/2411 (0.2%)	5/1957 (0.3%)	0.79
Leucocyturia without nitrituria	136/2411 (5.6%)	19/1957 (1%)	<0.001
Positive urine culture	1/2411 (0.04%)	5/1957 (0.3%)	0.13
Hydronephrosis	5/2411 (0.2%)	4/1957 (0.2%)	0.75

After 3-month follow-up, a third dipstick was examined at CH2 and revealed that the number of persistent nitrituria and/or leucocyturia was 37. Among them, 35 had isolated leucocyturia, 1 had combined nitrituria and leucocyturia, and 1 had hematuria. Out of 36 samples of urine that were cultured, one sample grew more than 10^5 CFUs of *Staphylococcus aureus* - the bacterial pathogen that are responsible to cause urinary tract infection. The renal ultrasound was performed at CH2, detecting 5/37 cases with hydronephrosis (code N13.30 in ICD-10).

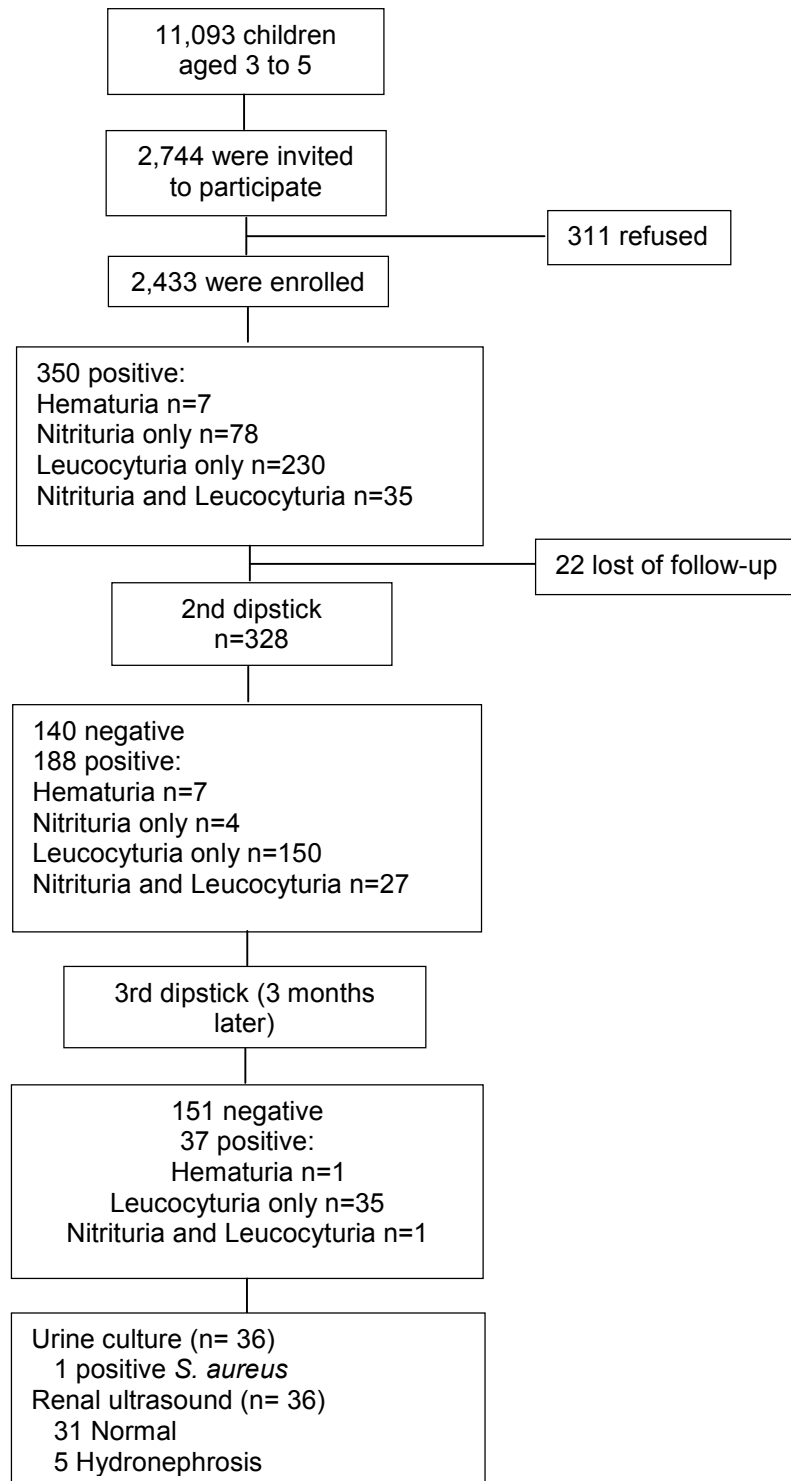


Fig. 1. Number of children with urinary abnormalities among asymptomatic children in Binh Thanh district of Ho Chi Minh City, Vietnam

4. DISCUSSION

Binh Thanh is located in the center of HCMC and is not far from Children's Hospital 2. The district has one district hospital, and two public general hospitals, all of which have department of pediatrics. Data on child healthcare are managed by Center for Disease Control and Prevention of Binh Thanh district. The healthcare system is controlled in the same manner with all other districts. The population density is extremely higher than the average density of the city (22,642 persons/km² vs 3,531 persons/km²) and is 230 times higher than the density in Can Gio district (98 persons/km²). In Binh Thanh district that has a very high population density, the positive rates of UTIs suggestive parameters were higher than in Can Gio (nitrituria and/or leucocyturia, 5.8% vs 3.3%) [7]. In a study conducted in USA, authors have shown that a high population density was associated with higher prevalence of water-associated infectious diseases, and it was also associated with a higher probability of outbreak occurrence [8]. In Can Gio, although there was a lower population density, hygiene conditions were not good because of a lack of fresh water. Whereas in Binh Thanh, there is a good system to supply clean water but the extremely high population density may worsen hygiene conditions.

Isolated leucocyturia was the most common abnormality compared to nitrituria in the population of the rural district-Can Gio [7]. After undergoing follow-up, it remains the highest positive parameter with 35/36 children having leucocyturia. The proportion is indicative of asymptomatic urinary tract infections (UTIs) and this is the reason why urine culture was done. Asymptomatic bacteriuria (ABU) is defined by a bacterial count $\geq 10^5$ colony forming units per mL urine in asymptomatic individuals. Basing on the definition, this study found a low prevalence (0.04%) of ABU with only one case. The ABU prevalences in Nepal, Nigeria were at 1.39% and 4%, respectively [9,10]. Some other authors reported a prevalence that varies from 0.026% to 14% depending on age and gender [11-14]. In Vietnam, antibiotics are easily prescribed without any evidence of presence of bacteria. The irrational use of antibiotics is one of the factors that can affect the result of urine culture in both symptomatic and asymptomatic children. Another factor that can be taken into account is the microbiology laboratory techniques. Another study among children with unexplained fever consulting at Binh Thanh district hospital was conducted to obtain a relevant response and to estimate the UTIs prevalence in febrile children with nitrituria and/or leucocyturia. ABU was also observed in children with neurogenic bladder. Patients with neurogenic bladder often have an increased number of white blood cells in their urine, which makes UTIs diagnosis difficult [15]. Because our population was made up of healthy children at toilet trained age, neurogenic bladder is not a concern and may not be responsible for the high proportion of leucocyturia in this study.

The percentage of children with isolated nitrituria in Can Gio was significantly higher than in Binh Thanh (2% vs 0%), whilst the ABU prevalence was low in both districts. A possible explanation is a greater number of false-positive results in Can Gio. Beside the possibility of prolonged specimen storage at room temperature due to large area of Can Gio, vaginal contamination may be the main cause of false-positive nitrituria because fresh water is problematic in the district. Vaillancourt et al. [16] proved that the contamination rates are within limits if the obtained urethral area is cleaned with soap and water. With improper cleaning, the incidence of contamination increases by three folds. As one can see, the prevalence of UTIs is higher in girls than in boys [15,17]. Therefore, the hygiene education campaign for girls in kindergartens and primary schools is necessary not only in rural areas but also in urban districts. In addition, according to a survey of knowledge, attitude and practice on urinary tract infection of children's caregivers in Can Gio district - Ho Chi Minh

City (HCMC) - Vietnam, only 3% had proper knowledge about UTIs symptoms, 25% had appropriate knowledge about the care for prevention of UTIs and 23% had good attitudes towards prevention of UTIs [18]. We have therefore conducted a study in Can Gio to provide the knowledge and the correct practice guidance for children's caregivers to prevent UTIs. The proportion of children with isolated leucocyturia in Binh Thanh was significantly higher than in Can Gio (5.6% vs 1%). As previously discussed, this may be the result of false-positive leucocyturia which due to the use of some antibiotics (imipenem, meropenem, clavulanic acid), other sources of esterase (eosinophils, trichomonas, epithelial cells), or high urine pH. In this study, we didn't evaluate urine pH. Therefore, we could not find the exact reason of the high proportion of isolated leucocyturia in Binh Thanh. However, there is an investigable reason that in urban districts of Vietnam, antibiotics are much easier to find than in rural districts.

In this study which carried out among asymptomatic children, renal ultrasound is the noninvasive modality for screening abnormalities of urinary tract. Furthermore, ultrasound is free from radiation exposition. From the population of 37 children with three positive dipsticks, five subjects had hydronephrosis. The proportion of children with positive dipstick presenting hydronephrosis in Binh Thanh was similar to the results in Can Gio (0.2%). [7] This data suggests a proportion of vesicoureteral reflux (VUR) in asymptomatic children. A renal ultrasound was suggestive VUR if "dilatation of the pelvi-calyces" and/or "dilatation of the ureters" and/or "dilatation of the collecting system" of one or both kidneys were detected. Most of VUR cases are diagnosed after UTIs [19,20]. In diagnosing and managing of uncomplicated UTIs in children, ultrasound itself has little value because voiding cystourethrogram (VCUG) is the gold standard procedure for diagnosis of VUR [21]. Our data suggests that the real prevalence of VUR among asymptomatic subjects may be higher. The exact incidence of VUR is not known because it is not feasible to do VCUG in a large cohort of healthy children. Of the patients diagnosed with VUR following a UTIs, 65% were less than 7 years old [22].

Study in adults who were diagnosed with VUR in childhood revealed a high proportion of abnormal glomerular filtration rate among patients with bilateral reflux nephropathy [23]. The two most important factors that are believed to influence the probability of renal injury in patients with VUR are the severity of the VUR and the patient's age at the onset of UTIs. Other factors affecting the probability of renal scarring in children with VUR and UTIs include delayed treatment of UTIs, recurrent UTIs, and bacterial virulence [20]. Hence, after the screening, we distributed the leaflets and posters to provide the parents and health stations' staff with knowledge about UTIs and UTIs prevention in children. Parents should be educated about healthy voiding and stooling habit as means of preventing UTIs. Parents should be made aware of the possibility of UTIs recurring once their child is diagnosed with VUR.

In Vietnam, the principal cause of pediatric end-stage renal disease was from glomerular origin [5,6]. That's the relevance for conducting the screening. Nevertheless, the proportion of 0% of proteinuria in our study was lower than data in any other regions or countries such as Tokyo, Malaysia, Lebanon, and Egypt [24-27]. On the other hand, the 0.3% prevalence of hematuria is lower than the prevalence from previous studies [25,28] and higher than what was reported in Nepal, Malaysia, and Japan [24,26,29]. Only persistent hematuria reveals the presence of kidney disease, therefore, a follow-up after three months was performed. The number of children with hematuria decreased to 1 case. The difference among countries can be explained by the age of screened children and by different etiologies among regions. From these results, we suggest that the appropriate age for urinary screening in Vietnam

should be older than 6 years in urban area with high population density. In Binh Thanh, the low prevalence of proteinuria and hematuria suggests that it is necessary to conduct a cost-effective evaluation before setting up any urinary screening for children. In the previous study in the remote district of Can Gio, the training for dipstick usage for all medical staff at health stations and in places with very low population density was proved necessary and routine urinalysis can be set up if close controls are conducted. Close controls included well-prepared training of dipstick usage, right method of collecting urine sample, good preservation of dipstick, and good maintaining dipstick readers. Furthermore, in Can Gio, a rural district with low socioeconomic status, with difficult access to healthcare services and with a very low population density, it is important to provide knowledge about the usefulness of dipsticks in district hospitals where there is no pediatrician.

5. CONCLUSION

The high prevalence of nitrituria and/or leucocyturia among asymptomatic children found in the district of Can Gio and in Binh Thanh requires hygiene education and UTI prevention program for parents in remote areas and in region with extremely high population density. Because of a high prevalence of nitrituria and/or leucocyturia in girls, there is an urgent need of hygiene education for girls at pre-school age. The low prevalence of proteinuria and hematuria suggest that the appropriate age for urinary screening in Vietnam should be older than 6 years in areas with high population density. A cost-effective evaluation is also necessary before setting up any urinary screening for children.

ETHICAL CONSIDERATION

Standards of ethics for studies conducted in Vietnam were respected. The study protocol was approved by the Ethical Committee of the HCMC Health Administration and by the Ethical Committee of Children's Hospital 2 in HCMC. The study was a collaboration between Children's Hospital 2 and Université catholique de Louvain (Brussels, Belgium). The protocol was approved by the University. Informed consent form was obtained from parents of all children involved in the study, with standard assurances of confidentiality.

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The corresponding author has full access to all data of the study and has final responsibility for the decision to submit for publication.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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