

# Symptoms and signs of kidney diseases in children during COVID-19 pandemic in Slovenia

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*Aim: The purpose of the study was to determine the prevalence of symptoms and signs of kidney diseases in children in Slovenia and to gain insight into the burden of kidney diseases in children at the primary care level at the time of the COVID-19 pandemic.*

*Methods: The study methodology was cross-sectional. Data were obtained via an anonymous online questionnaire sent to all primary care paediatricians in Slovenia via e-mail. An exact binomial test was used for each symptom case in order to determine whether the proportion of symptoms and/or signs in the sample deviates from the "theoretical" prevalence reported in the literature.*

*Results: Data were obtained from 65 paediatricians and 9829 evaluated children were included in the study. The proportion of children with some symptoms and signs of kidney diseases, mostly found incidentally, such as haematuria, proteinuria and hypertension were lower than previously described in the literature. There was no statistically significant difference in the prevalence of symptoms and signs suggesting serious kidney diseases, such as oedema or persistent proteinuria. The most common cause of children's visit to the outpatient clinics at the primary care level due to symptoms and signs of kidney diseases was urinary tract infection.*

*Conclusions: Children with serious kidney diseases were identified as commonly as described in the literature, despite the COVID-19 pandemic. The latter influenced negatively the discovery rate of symptoms and signs of kidney diseases that are found incidentally, such as haematuria, proteinuria and hypertension.*

**Key words:** COVID-19; KIDNEY DISEASES; CHILDREN; SIGNS AND SYMPTOMS; URINALYSIS

## INTRODUCTION

In 2020, in outpatient healthcare at primary level in Slovenia, a total of 1,243,012 visits were carried out in the age group 0-18 years, which included preventive visits, curative visits, home visits and telephone consultations. The proportion of children and adolescents diagnosed with urinary tract disease at the first visit was 4.52% (ICD-10: all diagnoses from N00–N99 – the chapter of diagnoses in ICD-10 relating to urinary tract diseases) (8).

The study investigated the frequencies of symptoms and/or signs of urinary tract disease occurring in paediatric outpatient clinics at primary care level. The questionnaire aimed to capture the most frequent symptoms and/or signs of urinary tract diseases and thus to evaluate the proportion of these conditions in the work of the primary paediatrician. The results were compared with published data on their incidence

worldwide. It was taken into account that the study was conducted during the COVID-19 pandemic, which could have had an impact on the frequency of the studied symptoms and/or signs due to different work patterns, more difficult access to the doctor or delayed visits to the doctor.

## PATIENTS AND METHODS

Data were collected between September 28<sup>th</sup>, 2021, and February 17<sup>th</sup>, 2022, via an anonymous online structured

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TABLE 1. Prevalence of symptoms and signs of kidney diseases compared with those in the peer-reviewed literature.

	Number of patients	Prevalence in the study (%) (CI – confidence interval)	Prevalence reported in the literature (%)	p-value
Children with any symptoms and/or signs of kidney diseases	548	5.57 % [95 % CI 5.13-6.05 %]	23.89 % † (8)	(p < 0.001)
UTI	102	1.04 % [95 % CI 0.85-1.26 %]	6-8 % (3,13,14)	(p < 0.001)
CAKUT	54	0.55 % [95 % CI 0.41-0.72 %]	3.26 % (15,16)	(p < 0.01)
CAKUT + anomaly of another organ system	10/54	18.5 % [95 % CI 9.5 – 31 %]	30 % (6)	(p = 0.871)
Oedema due to kidney disease	1	0.01 % [95 % CI 0.002-0.005 %]	4.7/100 000 children (17)	(p = 0.370)
Nocturnal enuresis	96	0.98 % [95 % CI 0.79-1.19 %]	5-10 % (18)	(p < 0.001)
Haematuria	66	0.67 % [95 % CI 0.52-0.85 %]	1.5-2 % (4,19)	(p < 0.001)
Proteinuria	67	0.68 % [95 % CI 0.53-0.86 %]	10 % (12,20)	(p < 0.001)
Persistent proteinuria	13	0.13 % [95% CI 0.07-0.23 %]	0,10 % (9,20)	(p = 0.334)
SRP ‡	17/67	25.4 % [95% CI 15,5-37,5 %]	18 – 100 % (20)	(p > 0.05)
Hypertension	70	0.71 % [95% CI 0.56-0.90 %]	4 % (11)	(p < 0.001)
Other abnormalities in urinalysis (glucosuria,...)	18	0.18 %	/	/
At least 2 symptoms and signs of kidney disease	34	0.34 %	/	/

## Legend:

† Proportion of children and adolescents who were diagnosed with urinary tract diseases (N0-N99), congenital malformations, deformities and chromosomal abnormalities (Q00-Q99) or diagnosed under symptoms, signs and abnormal findings at the first visit, not elsewhere classified (R00-R99).

‡ SRP – sport related proteinuria in active athletes (members of a sports club or other organised form of regular exercise)

CAKUT - congenital anomalies of the kidney and urinary tract

UTI – urinary tract infection

questionnaire sent by e-mail to all primary care paediatricians in Slovenia.

The survey methodology was cross-sectional, as it covered a specific time interval in the recent past, namely the last week before the questionnaire was answered. The time frame of last week was chosen since this enabled us to get a representative sample of children in need of medical evaluation and, at the same time, prevented from doubling data from same children that might have happened with a longer time frame, where some children might have come to follow-up (due to urine abnormality, high blood pressure or other incidental finding). In these cases, children usually do not come to follow-up examination in the same week in clinical practice.

The sample studied consisted of children aged up to 18 years who had symptoms and signs of kidney diseases and had been treated in paediatric outpatient clinics at primary level during the aforementioned period. A condition for inclusion in the study was a fully completed questionnaire, filled in by a cooperating doctor, practising paediatrics at primary level in Slovenia. The study included 9829 evaluated children from 65 paediatric outpatient primary care clinics in Slovenia. An exact binomial test was used for each symptom case in order to determine whether the proportion of symptoms and/or signs in the sample deviates from the “theoretical” prevalence reported in the literature. The analysis was conducted using the R language (version 4.1.2) and its “binom.test ()” command was applied. Using this, the

following parameters were determined: the number of “events” equals the number of persons with the symptom and the size of the total sample equals the number of all patients. The proportional share to be assessed by the statistical test was also established.

## RESULTS

The study included 9,829 children and adolescents under the age of 18 from 65 paediatric outpatient clinics in Slovenia. In all cases, a binomial test was performed to test whether the proportion of symptoms and/or signs in the sample deviated from the expected prevalence reported in the literature. Results are presented in Table 1.

## DISCUSSION

The study was conducted during the COVID-19 pandemic, which had an impact on the frequency of detected symptoms and signs of kidney diseases due to different work patterns, temporarily more difficult access to medical services, or delays in seeing a doctor. We have examined how often certain symptoms and signs of kidney diseases appeared in one week period by a primary care paediatrician and gained an insight into the proportion of children who required medical evaluation for kidney diseases. Among these, urinary tract infections (UTI) were the most common, whereas oedema due to kidney disease was the least common. Although the prevalence of UTIs in our sample is lower in

comparison to literature data, not all medically examined children could be included in our sample due to the different organisation of outpatient clinics. The UTIs are an acute condition and are often treated in emergency centres and not necessarily in the primary paediatric outpatient clinic. We observed a lower proportion of children with congenital anomalies of the kidney and urinary tract (CAKUT) who were evaluated in the outpatient clinic at the time of the study, maybe due to their regular follow-ups at a nephrology or urology outpatient clinic or department instead of at a primary care paediatrician. The prevalence of nocturnal enuresis (NE), involuntary emptying of the bladder at night, respectively bed-wetting, in children over 5 years of age, was lower than in the literature, as it is not as threatening, as it is unpleasant for the child and his/her parents and represents a psychological distress and may affect the self-image (9). Most cases resolve spontaneously (9), which is why many children with NE were not included in our study. Nevertheless, NE was the second most frequent symptom in our study, indicating a high prevalence of this condition in the population of Slovenian children.

Compared to previous descriptions in the literature, there was no statistically significant difference in the prevalence of symptoms and signs indicating serious kidney diseases, such as oedema due to nephrotic syndrome, persistent proteinuria and CAKUT with associated congenital abnormality of another organ system, suggesting that these children have been identified and managed, which is very crucial for the prognosis of these diseases. Similar findings were also observed in the prevalence of sport related proteinuria (SRP). In child athletes the proteinuria itself is in most cases an incidental finding, but when detected it should be further evaluated. If it is orthostatic, it most likely does not cause further problems. Therefore, these children do not present acutely to the outpatient clinic for this reason. Better screening could be achieved if the study was conducted as part of a systematic screening of all children in the generation, both healthy and symptomatic.

The prevalence of haematuria and proteinuria in our study was lower than that in comparable studies, probably because it is very often an incidental finding in routine curative examinations (5, 10). However, the prevalence of these signs was reduced significantly at the time of the study due to COVID-19 pandemic. Similar result was found in case of elevated blood pressure, as arterial hypertension is often asymptomatic in children and is therefore most often detected incidentally (11).

In 34 children included in the study, two or more symptoms and signs, indicating a kidney disease with greater certainty, were present (12). The overall proportion of all children with

any of the symptoms and/or signs of kidney diseases was 5.57%.

## CONCLUSION

Epidemiological studies such as ours have highlighted the diversity of work with children at primary care level, as well as the prevalence of symptoms and/or signs of kidney diseases and the consequent burden they place on paediatricians. Children with serious kidney diseases, mostly presenting as oedema, persistent proteinuria or CAKUT with associated congenital abnormality of another organ system, were identified as commonly as described in the literature, despite the COVID-19 pandemic. The latter influenced negatively the discovery rate of symptoms and signs of kidney diseases that are found incidentally, such as haematuria, proteinuria and hypertension. Future research on the subject could be focused more on specific symptoms and/or signs or the study could be conducted as part of a systematic screening of all children in the generation, both healthy and symptomatic to achieve better screening.

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## SAŽETAK

## Simptomi i znakovi bubrežnih bolesti u djece tijekom pandemije COVID-19 u Sloveniji

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*Cilj: Svrha istraživanja bila je utvrditi prevalenciju simptoma i znakova bubrežnih bolesti kod djece u Sloveniji i dobiti uvid u teret bubrežnih bolesti kod djece na razini primarne zdravstvene zaštite u vrijeme pandemije COVID-19.*

*Metode: Metodologija istraživanja bila je presječna. Podaci su dobiveni putem anonimnog „online“ upitnika koji je poslan svim pedijatrima primarne zdravstvene zaštite u Sloveniji putem e-pošte. Za svaki slučaj simptoma korišten je točan binomni test kako bi se utvrdilo odstupa li udio simptoma i/ili znakova u uzorku od „teorijske“ prevalencije objavljene u literaturi.*

*Rezultati: Podaci su dobiveni od 65 pedijatara, a u studiju je uključeno 9829 ispitanice djece. Udio djece s nekim simptomima i znakovima bubrežnih bolesti, većinom slučajno otkrivenih, kao što su hematurija, proteinurija i hipertenzija, bio je manji nego što je dosad opisano u literaturi. Nije bilo statistički značajne razlike u prevalenciji simptoma i znakova koji upućuju na ozbiljne bolesti bubrega, poput edema ili trajne proteinurije. Najčešći uzrok odlaska djece u ambulante primarne zdravstvene zaštite zbog simptoma i znakova bubrežnih bolesti bila je infekcija mokraćnog sustava.*

*Zaključci: Djeca s ozbiljnim bolestima bubrega identificirana su jednako često kao što je opisano u literaturi, unatoč pandemiji COVID-19. Potonje je negativno utjecalo na stopu otkrivanja simptoma i znakova bubrežnih bolesti koje se nalaze slučajno, kao što su hematurija, proteinurija i hipertenzija.*

**Ključne riječi:** COVID-19; BOLESTI BUBREGA; DJECA; ZNAKOVI I SIMPTOMI; ANALIZA URINA