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Urolithiasis in patients with normal and high body mass: a single-centre study

Kamica układu moczowego u pacjentów z prawidłową i nadmierną masą ciała – doświadczenie jednego ośrodka

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Abstract

Aim: Assessment of the correlation between high body mass and metabolic causes of urolithiasis in patients treated over a 2-year period in the Department of Paediatrics, Paediatric Nephrology and Allergology at the Military Institute of Medicine in Warsaw. **Material and methods:** A total of 109 children with urolithiasis, aged 9–18 years (mean: 13 years), were enrolled in the study. The patients were divided into two groups: Group I – children with normal body mass (body mass index <85th percentile), and Group II – children with high body mass (body mass index ≥85th percentile). Group I consisted of 74 children (33 girls and 41 boys). Group II comprised 35 children (23 girls and 12 boys). Blood serum and urine samples were collected and tested in the laboratory to determine the causes of urolithiasis. In addition, anthropometric parameters were evaluated, including body mass index, waist circumference, waist-to-hip ratio, body mass, and body height. Also, the lipid profile was examined, and arterial blood pressure was measured in the study subjects. **Results:** Children with high body mass were found to have statistically significantly higher serum uric acid levels [5.4 mg/dL (5.0–6.2) vs. 4.7 mg/dL (4.1–5.4); $p < 0.05$] and statistically significantly higher urinary uric acid excretion (determined on the basis of the uric acid/creatinine ratio in second morning urine) compared to children with normal body mass [0.3 (0.2–0.3) vs. 0.2 (0.2–0.3); $p = 0.01$]. There were no statistically significant differences in the excretion of other crystalloids. In addition, children with high body mass were shown to have significantly higher values of total cholesterol [167.5 (142.0–183.0) vs. 152.0 (136.0–163.0); $p < 0.05$], LDL [103.5 (83.0–117.5) vs. 88.5 (69.0–102.0); $p < 0.05$], and triglycerides [104.0 (89.0–111.0) vs. 64.0 (52.0–106.0); $p < 0.05$] as well as lower mean vitamin D levels (26.6 mg/dL ± 9.25 vs. 22.6 mg/dL ± 6.75; $p = 0.04$), and higher systolic blood pressure (110.2 mm Hg ± 11.0 vs. 115.7 mm Hg ± 11.96; $p = 0.02$) compared to non-overweight children. **Conclusions:** There is a possible correlation between overweight and urolithiasis associated with excessive uric acid excretion. Overweight patients with urolithiasis present disorders in the lipid profile which may have an impact on the formation of calculi. Lower serum vitamin D concentrations in overweight patients do not affect the level of calciuria.

Keywords: urolithiasis, children, body mass index (BMI), obesity, metabolic profile of urolithiasis

Streszczenie

Cel: Ocena korelacji pomiędzy nadmierną masą ciała a metabolicznymi przyczynami kamicy układu moczowego u pacjentów leczonych w okresie 2 lat w Klinice Pediatrii, Nefrologii i Alergologii Dziecięcej Wojskowego Instytutu Medycznego w Warszawie. **Materiał i metody:** Do badania zakwalifikowano 109 dzieci z kamicą układu moczowego w wieku 9–18 (średnio 13) lat. Pacjentów podzielono na dwie grupy: I – dzieci z prawidłową masą ciała (wskaźnik masy ciała <85. centyla) i II – z nadmierną masą ciała (wskaźnik masy ciała ≥85. centyla). Grupę I stanowiło 74 dzieci (33 dziewczynki, 41 chłopców). W grupie II było 35 dzieci (23 dziewczynki i 12 chłopców). U pacjentów zostały wykonane badania laboratoryjne z surowicy oraz moczu w kierunku metabolicznych przyczyn kamicy układu moczowego. Oceniono także parametry antropometryczne: wskaźnik masy ciała, obwód talii, wskaźnik talia–biodra, masę ciała oraz wzrost. Wykonano ponadto ocenę profilu lipidowego oraz pomiar ciśnienia tętniczego. **Wyniki:** W grupie dzieci z nadmierną masą ciała zaobserwowano statystycznie istotnie wyższe stężenia kwasu moczowego w surowicy krwi [5,4 mg/dl (5,0–6,2) *vs* 4,7 mg/dl (4,1–5,4); $p < 0,05$] oraz statystycznie istotnie wyższe wydalanie kwasu moczowego – ocenione współczynnikiem kwas moczowy/kreatynina z drugiej porcji moczu po nocy – w porównaniu z dziećmi o prawidłowej masie ciała [0,3 (0,2–0,3) *vs* 0,2 (0,2–0,3); $p = 0,01$]. Nie zaobserwowano różnic istotnych statystycznie w zakresie wydalania pozostałych krystaloidów. W grupie z nadmierną masą ciała stwierdzono

znamiennie wyższe wartości cholesterolu całkowitego [167,5 (142,0–183,0) *vs* 152,0 (136,0–163,0); $p < 0,05$], frakcji LDL [103,5 (83,0–117,5) *vs* 88,5 (69,0–102,0); $p < 0,05$], trójglicerydów [104,0 (89,0–111,0) *vs* 64,0 (52,0–106,0); $p < 0,05$], niższe średnie stężenie witaminy D (26,6 mg/dl ± 9,25 *vs* 22,6 mg/dl ± 6,75; $p = 0,04$) oraz wyższe wartości ciśnienia skurczowego (110,2 mm Hg ± 11,0 *vs* 115,7 mm Hg ± 11,96; $p = 0,02$) w porównaniu z dziećmi bez nadwagi. **Wnioski:** Możliwa jest zależność między nadwagą a kamicą układu moczowego związaną z nadmiernym wydalaniem kwasu moczowego. Pacjenci z nadwagą i kamicą układu moczowego prezentują zaburzenia w profilu lipidowym, które mogą mieć wpływ na tworzenie złogów. Niższe stężenie witaminy D w surowicy u pacjentów z nadwagą nie wpływa na wielkość kalciurii.

Słowa kluczowe: kamica układu moczowego, dzieci, wskaźnik masy ciała (BMI), otyłość, profil metaboliczny kamicy

INTRODUCTION

Urolithiasis is a condition involving the formation of deposits (calculi) in the kidneys or urinary tract as a result of precipitation of substances that are normal or pathological components of urine. Urolithiasis affects mainly adults, and the prevalence of the disorder is currently estimated to be between 10 and 15% of the general population[1]. In Europe, urolithiasis occurs in approximately 4% of the population (about 5.5% in men, and 4% in women). The disease is also diagnosed in 2% of the paediatric population, but in recent years a steady increase in incidence has been noted[2].
Growing rates of overweight and obesity have become a major public health problem across the world[3–5]. Obesity is prevalent in all age groups, including adults, adolescents and children, leading to a number of disorders. For example, it may contribute to the development of metabolic syndrome, and increase the risk of cardiovascular diseases[6].
One of the measures of overweight and obesity is body mass index (BMI)[7], which is calculated using the following formula:

$$\text{BMI} = \text{body mass [kg]}/(\text{body height [m]})^2$$

In recent years, there has been a growing number of reports showing an association between excessive body mass and an increased risk of urolithiasis in the adult population[8]. In multiple studies, weight gain has been shown to contribute to higher urinary excretion of calcium (Ca) ions, oxalates and uric acid (UA) which are major risk factors for the formation of kidney stones. However, there are considerably fewer reports on the correlation between excessive body mass and urolithiasis in children[9,10].

AIM OF THE STUDY

The aim of the study is to assess the correlation between high body mass and metabolic causes of urolithiasis in patients treated over a 2-year period in the Department of Paediatrics, Paediatric Nephrology and Allergology at the Military Institute of Medicine in Warsaw.

MATERIAL AND METHODS

The study was conducted in 109 children with urolithiasis, aged 9–18 years, treated in the Department of Paediatrics, Paediatric Nephrology and Allergology at the Military Institute of Medicine in Warsaw, in 2016–2017. The study involved a review of the children's medical records. Patients with urolithiasis associated with urinary tract infection, urinary tract defects, severe urinary retention, and rare genetic factors leading to urolithiasis were excluded from the study. The subjects were divided into two study groups. Group I consisted of children with normal body mass (BMI <85th percentile), and Group II – children with high body mass (BMI ≥85th percentile).
Group I comprised a total of 74 children, including 33 girls and 41 boys, aged 9–18 years (mean age: 13 years). Group II comprised 35 children, including 23 girls and 12 boys, aged 9–18 years (mean age: 13 years) (Tab. 1).
Laboratory tests were performed to determine the metabolic causes of urolithiasis in the study subjects. 24-hour urine collection was performed to assess the urinary excretion of crystalloids: Ca, phosphorus (P), UA, magnesium (Mg), oxalates and citrates, and creatinine (Cr). Second morning urine samples collected after overnight fasting were tested for Ca/Cr, P/Cr, Mg/Cr, UA/Cr, and Mg/Ca. Blood serum samples were analysed to determine the levels of sodium (Na), Mg, total Ca, chlorine (Cl), potassium (K), UA, and the hepatic metabolite of vitamin D (25OHD).
In addition, anthropometric parameters were evaluated, including BMI, waist circumference, waist-to-hip ratio, body mass, and body height.
The lipid profile assessed in the study group included total cholesterol, LDL and HDL fractions, and triglycerides. Arterial blood pressure was also measured.

Statistical methods

The results obtained in the study were analysed statistically using STATISTICA software from StatSoft, Inc. (2014). Descriptive analysis was used in each case as the first stage in the assessment of study findings. For the variables whose distribution conformed to the Gaussian distribution, the mean was used as the central measure, and standard deviation (*SD*) was the measure of scatter. The median and quartiles were used for the variables whose distributions deviated significantly from the Gaussian profile. The significance of deviations from the normal distribution was determined using the Kolmogorov–Smirnov test and the Kolmogorov–Smirnov test with the Lilliefors correction. Before proceeding to the analysis of differences between

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	Group I ($n = 74$) (mean ± *SD*)	Group II ($n = 35$) (mean ± *SD*)	*p*
Age	13 (±2.39)	13 (±2.63)	0.7
Gender (F:M)	33:41	23:12	
Body mass [kg]	46.4 (±10.54)	66.9 (±14.99)	<0.05
Body height [cm]	160 (±12.0)	157.5 (±12.41)	0.33
BMI [kg/m^2]	18.4 (±2.29)	25.8 (±3.26)	<0.05
BMI [percentiles]	44 (±25.09)	94.01 (±4.76)	<0.05
Waist-to-hip ratio (WHR)	0.78 (±0.06)	0.81 (±0.05)	<0.05

Tab. 1. Characteristics of children with normal (Group I) and high (Group II) body mass

	Group I, median (q_{25}–q_{75})	Group II, median (q_{25}–q_{75})	*p*
Na [mmol/L]	140.4 (139.0–141.0)	140.0 (139.0–142.0)	0.95
K [mmol/L]	4.5 (4.2–4.7)	4.4 (4.2–4.5)	0.28
Mg [mg/dL]	2.1 (2.0–2.2)	2.1 (2.0–2.2)	0.75
Ca [mg/dL]	10.1 (9.8–10.3)	10.1 (9.9–10.2)	0.58
Cl [mmol/L]	100.6 (100.0–100.2)	100.0 (99.0–101.0)	0.08
UA [mg/dL]	4.7 (4.1–5.4)	5.4 (5.0–6.2)	<0.05*

Tab. 2. Blood serum levels of electrolytes and UA in children with normal and high body mass

	Group I, median (q_{25}–q_{75})	Group II, median (q_{25}–q_{75})	*p*
24-hour urine collection			
Ca [mg/kg/day]	3.1 (1.8–4.6)	2.5 (1.5–3.6)	0.08
P [mg/kg/day]	11.9 (9.0–16.1)	10.6 (8.9–15.0)	0.30
Mg [mg/kg/day]	1.9 (1.4–2.6)	1.6 (1.1–2.3)	0.07
UA [mg/kg/day]	8.2 (6.9–11.0)	8.1 (6.7–9.0)	0.33
Second morning urine			
Ca/Cr	0.1 (0.1–0.2)	0.1 (0.1–0.2)	0.29
P/Cr	0.4 (0.3–0.6)	0.4 (0.3–0.5)	0.64
Mg/Cr	0.1 (0.1–0.1)	0.1 (0.1–0.1)	0.59
Mg/Ca	0.6 (0.4–1.0)	0.7 (0.5–1.1)	0.29
UA/Cr	0.2 (0.2–0.3)	0.3 (0.2–0.3)	0.01*

Tab. 3. Excretion of crystalloids in 24-hour urine collection and second morning urine

	Group I, median (q_{25}–q_{75})	Group II, median (q_{25}–q_{75})	*p*
Cholesterol [mg/dL]	152.0 (136.0–163.0)	167.5 (142.0–183.0)	<0.05*
LDL [mg/dL]	88.5 (69.0–102.0)	103.5 (83.0–117.5)	<0.05*
HDL [mg/dL]	59.0 (52.0–67.0)	53.0 (45.0–67.0)	0.20
Triglycerides [mg/dL]	64.0 (52.0–106.0)	104.0 (89.0–111.0)	<0.05*

Tab. 4. Lipid panel in children with normal and high body mass

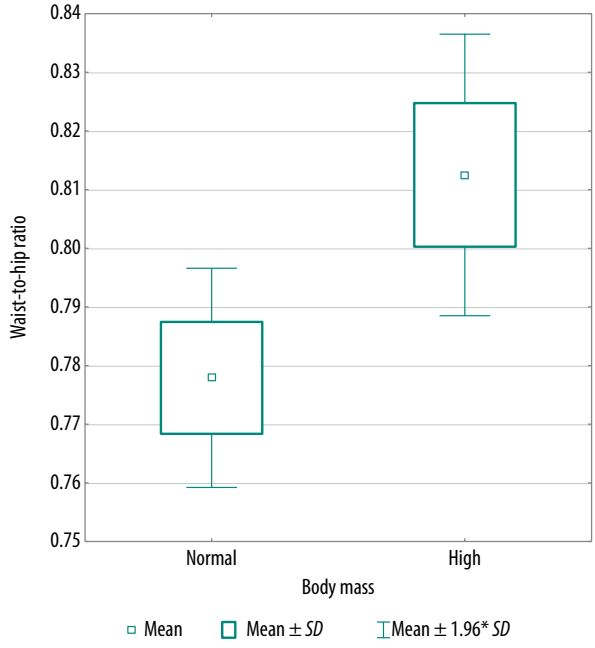

Fig. 1. Waist-to-hip ratio (WHR) in children with normal and high body mass

groups, an appropriate test was selected each time. The selection was based on a prior analysis of the distribution of variables. Parametric tests were used for the variables conforming to the Gaussian distribution (Student's *t*-test), and non-parametric tests were applied for non-Gaussian variables (Mann–Whitney *U* test).

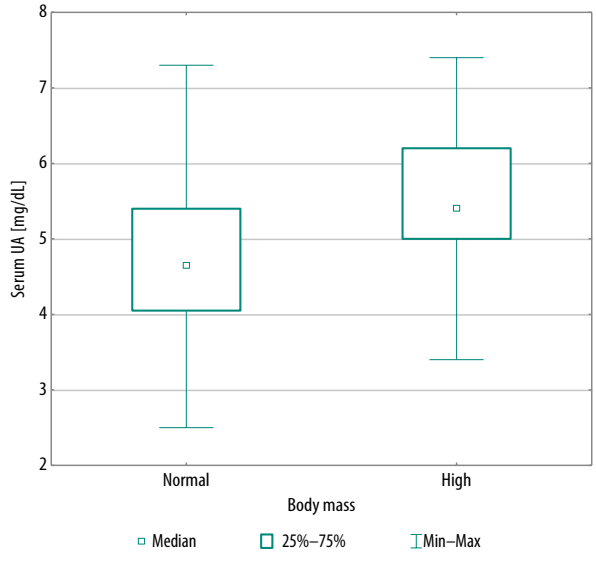

Fig. 2. Blood serum levels of UA in children with normal and high body mass

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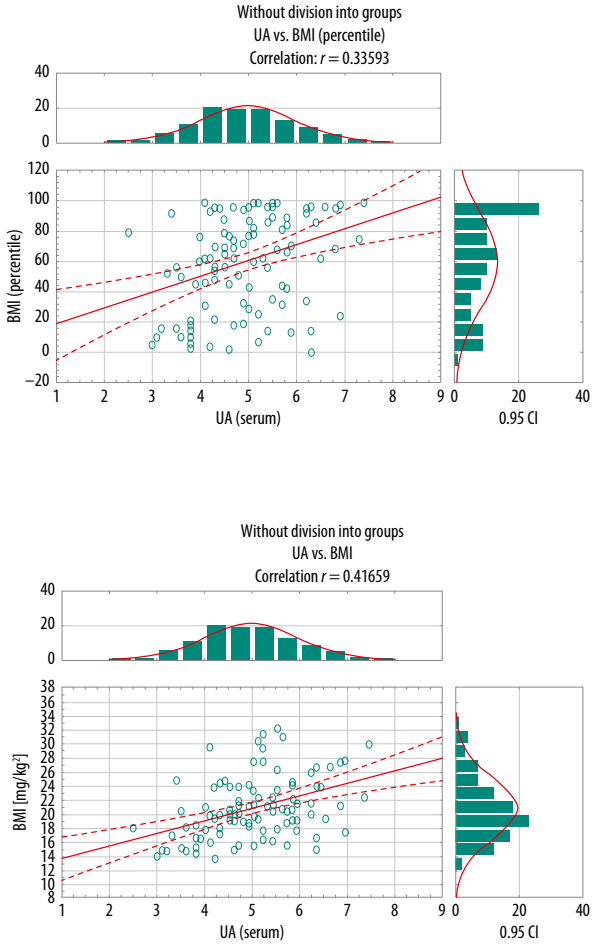

Fig. 3. Correlation between UA and BMI

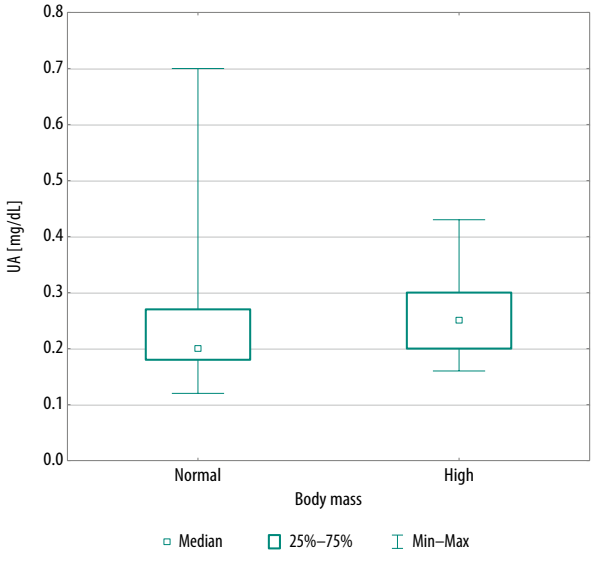

Fig. 4. UA excretion in second morning urine samples in children with normal and high body mass

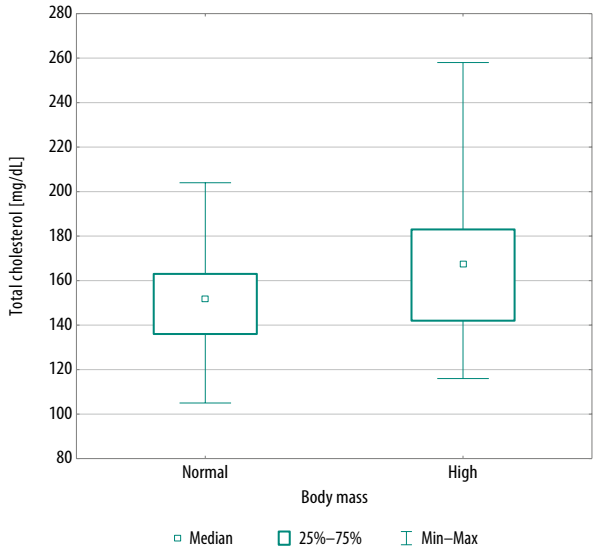

Fig. 5. Total cholesterol in children with normal and high body mass

RESULTS

Characteristics of study groups

The majority (68%) of children with urolithiasis enrolled in the study did not have excessive body mass (Group I, BMI <85th percentile). The mean age of patients in Group I was 13 years (±2.39), and it was the same in Group II (±2.63); the difference was not statistically significant ($p = 0.7$). However, statistically significant differences were noted in the variables of body mass, BMI, and the waist-to-hip ratio (Tab. 1, Fig. 1). The levels of electrolytes and UA in peripheral blood in the study patients are listed in Tab. 2. In Group II (children with high body mass), the mean serum level of UA was 5.4 mg/dL

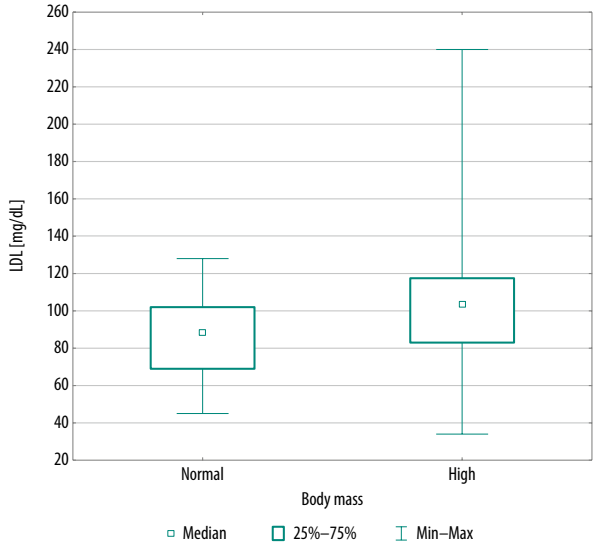

Fig. 6. LDL level in children with normal and high body mass

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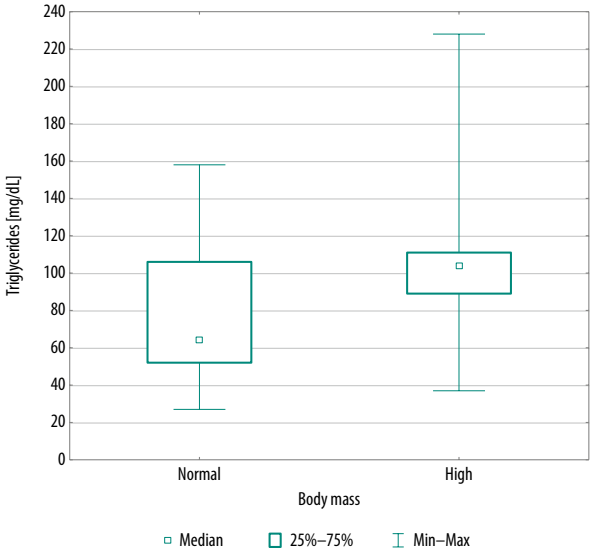

Fig. 7. Triglyceride levels in children with normal and high body mass

(5.0–6.2), while in children with normal body mass it was 4.7 mg/dL (4.1–5.4) ($p < 0.05$) (Fig. 2). No statistically significant differences were found in other study parameters (Tab. 2).

The correlation between serum UA levels and BMI can be described by a linear function ($p < 0.05$), which markedly supports the strength of the association (Fig. 3). The association with BMI was analysed both for the absolute values and percentiles.

The urinary excretion of crystallisation promoters or inhibitors (Mg) was assessed both in the 24-hour urine collection samples and second morning urine samples, after overnight fasting, expressed as urinary Cr excretion (Tab. 3).

In Group II, the excretion of UA in second morning urine was found to be statistically significantly higher than in Group I children. However, there were no statistically significant differences in the excretion of other crystalloids (either in 24-hour urine collection samples or second morning urine samples) (Tab. 3, Fig. 4).

An analysis of lipid fractions found significantly higher levels of total cholesterol, LDL and triglycerides in Group II children compared with Group I children (Tab. 4, Figs. 5–7).

The mean vitamin D level in Group II children was statistically significantly lower than in Group I children (26.6 mg/dL ± 9.25 vs. 22.6 mg/dL ± 6.75; $p = 0.04$) (Fig. 8).

Arterial blood pressure analysis revealed statistically significantly higher systolic blood pressure in Group II compared with Group I (110.2 mm Hg ± 11.0 vs. 115.7 mm Hg ± 11.96; $p = 0.02$). In 7/35 (20%) children with high body mass systolic blood pressure values were shown to be above the 90th percentile. Median percentile value of systolic blood pressure in the group of children with high body mass: 65th percentile.

Median percentile value of diastolic blood pressure in the group of children with high body mass: 66th percentile.

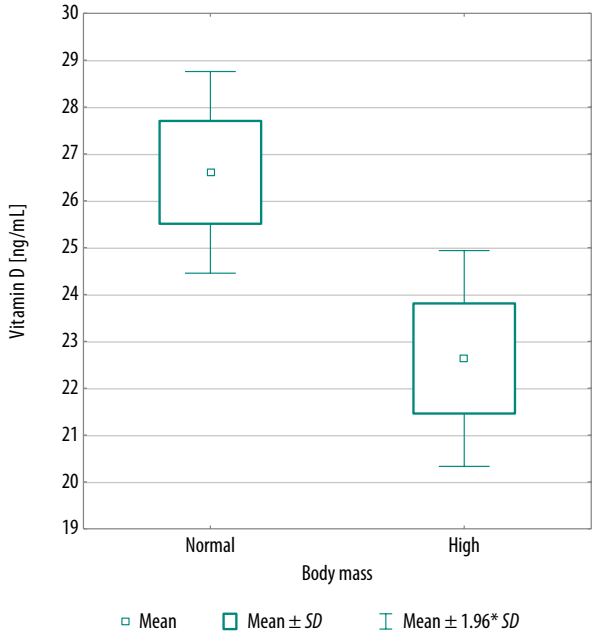

Fig. 8. Mean vitamin D concentration in children with normal and high body mass

DISCUSSION

Urolithiasis affects mainly adults, however in recent years it has been increasingly diagnosed in the paediatric population. Tasian and Copelovitch report an increase in the proportion of children with urolithiasis from 6% to 10% over the past 25 years[11]. Many other authors also point to a significant rise in the incidence of urolithiasis in the paediatric population[12–14]. The trend can be attributed, among other factors, to changing eating habits, lack of physical activity, and the obesity epidemic[15]. Based on studies among a group of adult patients, Taylor et al. showed that high body mass (BMI >85th percentile) increased the risk of urolithiasis. The researchers also suggested that the risk might be higher in women than in men. In addition, an increased risk of formation of kidney calculi was found to be correlated with two different obesity indices: BMI and waist-to-height ratio[10].

Most authors support the view that in children, particularly before the onset of puberty, excessive body mass does not contribute to an increased risk of urolithiasis[8,16,17]. Most patients enrolled in our study were also non-overweight.

The problem of elevated UA levels in overweight and obese individuals has been addressed in the medical literature for many years.

In a study conducted among students, Duan et al. found a relationship between elevated serum UA levels and high body mass[18].

An attempt to evaluate correlations between overweight, urolithiasis and UA metabolism was also made by Kuroczycka-Saniutycz et al., but they found no relationship

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between hyperuricaemia and increased UA excretion in patients with urolithiasis and high body mass. However, their study revealed that increased UA excretion – unlike BMI – was a factor raising the risk of urolithiasis[19].

In our study, children with high body mass and urolithiasis were found to have significantly higher serum UA levels. In addition, statistically significantly higher UA excretion was found in the examined urine samples.

However, there were no statistically significant differences in ionograms or the excretion of other crystalloids.

Published reports have described multiple associations between the body mass of adult individuals and the development of urolithiasis. Taylor and Curhan found that high BMI was associated with elevated excretion of calcium oxalate in women, and Ca in men[20].

Daudon et al. reported a correlation between BMI and an increased risk of urolithiasis, particularly in women with elevated BMI, increased UA excretion, and decreased citrate excretion in urine[21].

Similarly, a multivariate analysis performed by Siener et al. among adult patients showed a positive correlation between BMI and the excretion of Ca and UA, and a negative correlation between BMI and the pH of urine. In another study, Siener et al. observed that an increase in BMI was associated with several risk factors for urolithiasis, including an elevated urine Na level and decreased urine pH in men, and elevated urine UA and Na levels together with a decreased excretion of citrates in women[9,22]. Negri et al. also found higher urinary concentrations of UA and calcium oxalate in obese individuals[23].

However, the study findings in the paediatric population have been inconsistent. In an analysis conducted among 110 patients, Bandari et al. showed that the prevalence of hypercalciuria was higher in overweight and obese children, while the excretion of citrates and phosphates was lower[24]. Contrary observations were made by Dwyer et al., who failed to identify any correlation between obesity and an increased risk of urolithiasis in adolescents[25]. Similarly, Kim et al. found no relationship between high BMI and urolithiasis among evaluated children[8].

However, most cited studies report a correlation between increased BMI and the risk of urolithiasis. Such findings, however, are noted primarily in adults. Consequently, broad-scale observational studies in children with urolithiasis would be warranted. This is particularly important in view of the growing prevalence of obesity in children.

Dyslipidaemia is a common problem in overweight and obese patients[26]. Kang et al. reported that individuals with the propensity for renal calculi are more likely to have high levels of triglycerides and low levels of HDL cholesterol[27]. The view is shared by Masterson et al., who showed a 30-fold higher risk of urolithiasis in patients with low HDL cholesterol levels[28]. Kirejczyk et al. argue that among various lipid disorders which are routinely considered, the development of urolithiasis may be primarily associated with hypercholesterolemia and low HDL levels[26].

Our study also demonstrated lipid disorders in patients with urolithiasis. The levels of total cholesterol, LDL and triglycerides were shown to be statistically significantly higher in children with higher body mass than in non-overweight children with urolithiasis. There was no relationship between low HDL cholesterol levels and the occurrence of urolithiasis.

It is a well-known observation that vitamin D deficiency occurs frequently in overweight individuals. On the other hand, the effect of vitamin D intake on the development of urolithiasis has not been fully elucidated. A number of studies have shown that regardless of age individuals with high BMI have lower concentrations of 25OHD compared to people with normal body mass[29]. Also, some authors claim that elevated levels of vitamin D may increase the urinary excretion of Ca, which predisposes to the formation of kidney calculi[30,31]. In recent years, this view has been increasingly challenged, with a growing number of reports stating that vitamin D is not contraindicated in the majority of patients with urolithiasis. For example, Eisner et al. failed to show any relationship between serum vitamin D levels and 24-hour urinary Ca excretion in individuals who develop urinary calculi. The study was conducted among adult individuals with varying BMI (mean: 27.4; overweight)[32]. In contrast, a meta-analysis conducted by Malihi et al. showed that vitamin D_2 and D_3 supplementation led to changes in Ca metabolism, increasing the risk of hypercalcaemia and hypercalciuria. However, according to the cited authors, the association does not increase the risk of kidney calculi[33].

In our study, it was shown that the mean vitamin D level in the group of overweight patients was statistically significantly lower than in children with normal body mass. However, we found no relationship between the level of vitamin D and calciuria. There were no statistically significant differences in urine Ca excretion and Ca/Cr ratio between overweight and non-overweight children.

The association between excessive body mass and high blood pressure is well-known[16,17]. It has also been reported in the literature that high blood pressure is an independent risk factor for the formation of calculi in the urinary tract.

In our study we found that patients with excessive body mass and urolithiasis had statistically significantly higher values of systolic blood pressure.

Similar observations were made by Sarica et al., showing that children with high body mass and urolithiasis tended to have higher systolic blood pressure[34]. An association between urolithiasis and arterial hypertension was also demonstrated by Shang et al. in a meta-analysis of observational studies[35].

CONCLUSIONS

1. Overweight is not a characteristic feature of most patients with urolithiasis included in the study population.
2. There is a likely correlation between overweight and urolithiasis associated with excessive UA excretion.

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3. Overweight patients with urolithiasis present disorders in the lipid profile which may contribute to the formation of calculi.
4. Lower serum vitamin D concentrations in overweight patients do not affect the level of calciuria.

Conflict of interest

The authors do not declare any financial or personal links with other persons or organisations that might adversely affect the content of the publication or claim any right to the publication.

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