METABOLIC RISK FACTORS OF URINARY STONE DISEASE IN CHILDREN

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ABSTRAK

Tujuan Penelitian: *Mengetahui hubungan faktor risiko metabolik dengan terjadinya batu saluran kemih pada anak.* ***Bahan & Cara:*** *Pada periode penelitian dikumpulkan semua pasien anak dengan batu saluran kemih yang berobat ke Rumah Sakit Hasan Sadikin. Data mengenai umur, riwayat keluarga, indeks massa tubuh (IMT) dikumpulkan. Pada kelompok kontrol dilibatkan pasien anak yang dirawat karena penyakit yang lain, dengan umur dan IMT yang dicocokkan dengan kelompok kasus. Pemeriksaan darah (asam urat, kalsium, dan fosfat) dan analisis urine 24 jam (Kalsium, fosfat, natrium, magnesium, asam urat, pH dan volume) dilakukan sebelum tindakan pembedahan. Pasca pembedahan dilakukan analisis batu. Data dari kedua kelompok dibandingkan dengan uji statisik Kruskal Wallis.* ***Hasil Penelitian:*** *Pada penelitian preliminary ini terkumpul 16 subjek, 8 subjek dengan batu saluran kemih dan 8 subjek sebagai kontrol. Tidak didapatkan perbedaan bermakna kadar kalsium, fosfat, dan asam urat darah. Perbedaan bermakna ditemukan pada kadar kalsium urine 24 jam antar kedua kelompok (40,8 mg vs 10,6 mg; p = 0,027). Setelah dilakukan penyesuaian kadar elektrolit dan asam urat urine 24 jam terhadap kadar kreatinin urine 24 jam, ditemukan perbedaan bermakna rasio kalsium/mg kreatinin antara kelompok dengan dan tanpa batu (0,23 vs 0,02 mg/mg kreatinin, p = 0,002). Tidak ditemukan perbedaan bermakna rasio elektrolit lainnya (fosfat, magnesium, natrium) dan asam urat urine 24 jam per mg kreatinin.* ***Simpulan:*** *Kadar kalsium urine 24 jam pada anak dengan batu saluran kemih lebih tinggi dibandingkan anak tanpa batu.*

Kata Kunci: *Batu saluran kemih, anak, faktor risiko metabolik.*

ABSTRACT

Objective: *To evaluate metabolic risk factor of urinary stone disease in children.* ***Material & method:*** *In this hospital-based preliminary study, children with urinary stone disease who underwent stone removal in Hasan Sadikin Hospital were included. Control group consisted children with other diseases, matched for age and BMI. Blood evaluation (uric acid, calcium and phosphate) and 24-hour urine evaluation (calcium, phosphate, sodium, magnesium, uric acid, acidity, and urine volume) were measured before the stone removal. Stone analysis was performed later. Data was analyzed using Kruskal Wallis and Spearman correlation test.* ***Results:*** *Eight subjects with urinary tract stone and 8 normal subjects were included to the study. This study included 4 (50%) subjects with renal stone, 3 (37,5%) subjects with bladder stone, and 1 (12,5%) subject with distal urethral stone. Stone analysis revealed 6 (75%) calcium oxalate, 1 (12,5%) calcium phosphate, and 1 (12,5%) struvite stone. There was no significant difference in blood calcium, phosphate, and uric acid between groups. 24 hours urinary calcium level was higher in subjects with stone disease (40,8 mg vs 10,6 mg, p=0,027). Urinary calcium-to-creatinine ratio was also higher in stone disease (0,23 vs 0,02 mg/mg creatinine, p=0,002). There was no significant difference of other urinary electrolites and uric acid level between groups.* ***Conclusion:*** *Twenty four hours urinary calcium level and urinary calcium-to-creatinine ratio is higher in children with urinary stone disease.*

Keywords: *Urinary stone disease, children, metabolic risk factors.*

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BACKGROUND

Urinary stone disease in children is rare, especially in developed countries. Prevalence in Argentina reached 2-2,7%. Prevalence in Turkey is higher (17%). Diet, race/genetic, climate, fluid intake, and metabolic factors influences its prevalence.[1,2,4-9]

Despite its low prevalence, urinary stone disease in children may cause significant morbidity, mortality, and high recurrence rate (65%). Metabolic abnormalities were found in many cases. Complications occured due to stone disease, such as chronic kidney failure and infection, may lead to

chronic hemodialysis or kidney transplantation. Therefore, adequate preventive measures should be an integral part of its management.[3-5]

Recent studies showed that metabolic factors were the most signifcant factor in stone formation in children. Spivacow et al studied 90 children in Buinos Aires within 1994-2000. Metabolic abnormalities were found in 84,4% cases, 52,2 % cases with single metabolic abnormality and 31,1% with multiple abnormalities. Idiopathic hypercalciuria is the most common abnormality (40%). Stapleton et al also found similar result (42%). Basaklar and Kale in Europe found higher result (54%). Hypocitraturia is also common abnormality found (37,8%). Tefekli et al reported that hypocitraturia is the most common abnormality found in children with stone disease (60,6%). Prevention measures should be done based on metabolic abnormalities found in each case.[6-8]

Other factors, such as climate, diet, socioeconomic, and lifestyle, also contribute to stone formation. These factors cause significant variation in stone disease prevalence among countries. Data in Indonesia is still limited.

OBJECTIVE

This study aim to evaluate metabolic risk factors of urinary stone disease in children, which will determinate preventive measures.

MATERIAL & METHOD

This hospital-based preliminary cross sectional study was held within 2009-2010 in Hasan Sadikin Hospital, Bandung. Sixteen children were included based on consecutive sampling and matched for BMI and age. They were classified into stone former (8 children) and non-stone former (8 children). All children were younger than 18 years old. Non-stone former group consisted children who were admitted due to other diseases. Exclusion criteria included urinary tract anatomy disorder, dehydration, inadequate urine collection, and stone-inducing drugs.

Blood tests (uric acid, calcium and phosphate) and 24-hour urine evaluation (calcium, phosphate, sodium, magnesium, uric acid, acidity, and urine volume) were measured before the stone removal. Stone analysis was performed later. Urinary electrolytes and uric acid level (mg) were adjusted for urinary creatinine content (mg), in order to reduce bias. Stone composition was determined by two or more dominant element in removed stone. Data was analyzed using Kruskal Wallis and Spearman correlation test.

RESULTS

Table 1 shows subject characteristics including age, weight, height, and BMI. It is seen that no significant difference in those parameters between groups. The age mean is 6,25 years old. BMI between groups was not significantly difference (16,62 vs 16,61, p = 0,793).

Table 2 shows the distribution of stone location and composition. There were 4 (50%) subjects with kidney stone, 3 (37,5%) subjects with bladder stone, and 1 (12,5%) subject with ureteral stone. Calcium Oxalate was the most common stone found. Stone analysis revealed 6 (75%) calcium oxalate, 1 (12,5%) calcium phosphate, and 1 (12,5%) struvite stone.

Table 1. Subject characteristics.

Variable	Group		p value
	Stone former (n = 8)	Non stone former (n = 8)	
Age			
Mean (years)	6,25	6,25	
Range (years)	2; 12	2; 12	
Weight			
Mean (kg)	15,6	16,1	0,83
Range (kg)	8; 25	8; 25	
Height			
Mean (m)	1,02	1,03	0,958
Range (m)	0,55; 1,55	0,55; 1,44	
BMI			
Mean	16,62	16,63	0,793

Table 2. Stone location and composition.

Variable	n	Percentage
Location		
Kidney	4	50%
Distal ureter	1	12,50%
Bladder	3	37,50%
Stone composition		
Calcium Oxalate	6	75%
Calcium Phosphate	1	12,50%
Magnesium Ammonium phosphate	1	12,50%

There was no significant difference in blood calcium, phosphate, and uric acid between groups. Twenty four hours urinary calcium level was higher in subjects with stone disease (40,8 mg vs 10,6 mg, p=0,027). Table 3 shows further details. After adjustment for urinary creatinine, urinary calcium-to-creatinine ratio was also higher in stone disease (0,23 vs 0,02 mg/mg creatinine, p = 0,002) (table 5). There was no significant difference of other urinary electrolites and uric acid level between groups, even after adjustment to urinary creatinine level. We found no correlation between urinary sodium and calcium level (R = 0,29, p = 0,27).

Table 3. Blood creatinine, uric acid, and electrolytes between groups

Variable	Group		p value
	Stone former (n = 8)	Non stone former (n = 8)	
Blood creatinine			0,916
Mean (mg/dl)	3,7	0,5	
Range (mg/dl)	0,3; 18,6	0,4; 0,7	
Blood calcium			0,834
Mean (mg/dl)	4,5	4,6	
Range (mg/dl)	3,6; 5,2	4,3; 5,0	
Blood phosphate			0,126
Mean (mg/dl)	6.6	5	
Range (mg/dl)	5; 12	4,0; 6,2	
Blood uric acid			0,636
Mean (mg/dl)	6,1	4,4	
Range (mg/dl)	2,3; 11,8	3,4; 5,3	

Table 4. Urinary electrolytes and uric acid in 24 hours specimen.

Variable	Groups		p value
	Stone former (n = 8)	Non stone former (n = 8)	
Urinary volume			0,599
Mean (ml)	769,7	845	
Range (ml)	150; 1150	350; 1000	
Urinary calcium			0,027
Mean (mg)	40,8	10,6	
Range (mg)	7,0; 72	3,5; 20,0	
Urinary phosphate			0,009
Mean (mg)	0,11	0,2	
Range (mg)	0,04; 0,19	0,10; 0,26	
Urinary magnesium			0,528
Mean (mg)	1,96	2,25	
Range (mg)	0,4; 3,2	1,0; 4,1	
Urinary uric acid			0,141
Mean (mg)	240	316	
Range (mg)	104; 439	173; 491	
Urinary sodium			0,37
Mean (mg)	85,4	61,6	
Range (mg)	50; 170	52; 72	

Table 5. Ratio of urinary uric acid and electrolytes per mg urinary creatinine.

Variable	Group		p value
	Stone former (n = 8)	Non stone former (n = 8)	
Urinary calcium/mg creatinine			
Mean (mg/mg creatinine)	0,23	0,02	0,002
Range (mg/mg creatinine)	0,03; 0,63	0,01; 0,05	
Urinary phosphate/mg creatinine			
Mean (10^{-4} mg/mg creatinine)	5	4,6	0,401
Range (10^{-4} mg/mg creatinine)	2,1; 9,7	2,3; 8,7	
Urinary magnesium/mg creatinine			
Mean (10^{-3} mg/mg creatinine)	9,3	4,7	0,401
Range (10^{-3} mg/mg creatinine)	3; 24	3; 6	
Urinary uric acid/mg creatinine			
Mean (mg/mg creatinine)	1,05	0,7	0,115
Range (mg/mg creatinine)	0,5; 2,1	0,5; 1	
Urinary sodium/mg creatinine			
Mean (mg/mg creatinine)	0,58	0,15	0,093
Range (mg/mg creatinin)	0,07; 1,28	0,08; 0,24	

DISCUSSION

Age and BMI were matched between groups, because kidney function was affected by them. We found that kidney is the most common stone site in children, similar result was found in Pakistan and Tunis (64% and 76%).[1-20]

Blood calcium and phosphate were tested to detect any hormonal abnormality and may determine the type of hypercalcuria. Hyperthyroidism may show hypercalcemia and hypophosphatemia. Hypercalciuria with hypercalcemia can be found in resorptive hypercalciuria. High uric acid level may represent uric acid metabolism abnormality, which may cause uric acid stone formation. We did not found significant difference in blood calcium, phosphate, and uric acid between group. Tefekli et al also found similar result. This showed that hypercalciuria in our patients did not associated with resorptive hypercalciuria.[19]

Urinary calcium level in stone former group is higher than non-stone former group (40,8 mg vs 10,6 mg, p = 0,027). The difference was also seen after adjustment for urinary creatinine level (0,23 vs 0,02 mg/mg creatinine, p = 0,002). Although urinary calcium level in stone former group is higher, only one subject fulfill the criteria for hypercalciuria (more than 4 mg/kg BW). It showed that other factors, such as age, race, and climate, may interfere the hypercalciuria-induced stone formation. Idiopathic hypercalciuria is the most common abnormality (40%) found in children with stone disease. Stapleton et al also found similar result (42%). Basaklar and Kale in Europe found higher result (54%). Hypocitraturia is also common abnormality found (37,8%).[8-19,22]

Calcium oxalate was the most common stone in this study (75%). Alaya et al in Tunis found same result, also in Saudi Arabia (37,8%) and Turkey. In three patients with endemic stones, calcium oxalate was the dominant elements. This may be caused by high cereal and vegetables diet, but low in animal protein, calcium, and phosphate. High cereal and low animal protein diet may cause urinary ammonium and urate level increase, and high oxalate (vegetables) intake may induce calcium oxalate formation.[1-20,23]

After adjustment for urinary creatinine level, significant difference was only found in calcium-creatinine ratio between groups (0,23 vs 0,02 mg/mg creatinin, p = 0,002). Similar results was also found by DeFoor et al (0,214 vs 0,168 mg/mg creatinin, p < 0,05). They found that calcium-creatinine ratio is more accurate than 24 hours urinary calcium level for evaluation of stone disease in children.

CONCLUSION

Twenty four hours urinary calcium level and urinary calcium-to-creatinine ratio is higher in children with urinary stone disease.

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