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Original Research Article

An observational, prospective and comparative study to assess metabolic abnormality in patients of urolithiasis in paediatric age group in a tertiary care center of Bihar

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ABSTRACT

Introduction: In paediatric age group urolithiasis is less common with overall occurrence rate of only 2-3% of total cases. Children with urolithiasis are related with significant morbidity. Different metabolic parameters either serum or urinary gets deranged in urolithiasis. Evaluation of these parameters help in identification and diagnosis of children who are at increased risk for recurrent stone formation and can be prevented by treating these abnormalities. In this study serum and urinary metabolic risk factors for urolithiasis in children were evaluated, observed and compared.

Materials and Methods: This was an observational, prospective and comparative study on fifty (n=50) children with confirmed diagnosis of urolithiasis below 12 years of either sex. Dietary history, water intake and results of laboratory findings (Serum, urinary parameters and stone analysis) were recorded, evaluated, tabulated and analysed using GraphPad Instat Software. All urine samples were obtained from patients without dietary restrictions.

Results: Out of 50 children, 35 (70%) and 15 (30%) were male and female respectively. Twenty-three participants were below five years of age. On dietary habits low calcium intake and high calcium intake was seen in 60% (n=30) and 14% (n=7) respectively. 64% (n=32) children had low 24-hour urine volume due to low water intake. 64% (n=32) children had metabolic abnormality and out of them serum abnormality was found in 21 and 24-hour urinary metabolic abnormality seen in 11 children. Hypocalcaemia with normal PTH and secondary hyperparathyroidism was seen in 85.71% (n=18) and 14.29% (n=3) of children respectively. Out of 11 children with urinary metabolic abnormality, hypocitruria (n=6) was the most common followed by hypercalciuria (n=3). Stone analysis was done in 20 patients, out of which majority (n=11, 55%) of the children had calcium oxalate stone.

Conclusions: Predominant finding from this study was low urine volume seen due to low water intake. Major metabolic abnormality was hypocalcaemia. Improved fluid ingestion and keeping blood calcium level at ideal level may be beneficial to avert urolithiasis in children.

1. Introduction

Urolithiasis is most common in adults and the occurrence is lees in paediatric age group.[1] Overall occurrence rate of urolithiasis in children is only 2-3% of total cases.[2]

The prevalence, composition of stone, position of stone and clinical characteristics of urolithiasis immensely varies in different geographical area. It contrasts significantly from one country to another.[3,4] Climatic condition, dietary behaviour and socioeconomic factors plays vital role in extensive geographic variation of urolithiasis. Genetic inheritance, environmental factors, nutrition, metabolic abnormalities, anatomical characteristics and calculus-inducing drugs are predisposing risk factors for urolithiasis in children.[1]

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Children have significant morbidity who are suffering from urolithiasis. Different metabolic parameters either serum or urinary gets deranged in urolithiasis. Evaluation of these parameters help in identification and diagnosis of risk factors involved in recurrent stone formation and early diagnosis helps in prevention and treatment of stone disease and related comorbidities.[5,6] Different studies showed range of prevalence of metabolic risk factors from < 20% to >50%.[6–9] In one-third of the stone-formers hypercalciuria and hypocitraturia are seen as the common metabolic abnormalities.[7,9,10] Approximately 20% of cases has reported hyperuricosuria and hyperoxaluria.[7,11]

Global incidence of urolithiasis in paediatric patients has been increased in the last few decades.[12–14] The pattern of urolithiasis has also changed, showing increase in kidney stones secondary to calcium oxalate or calcium phosphate and decrease in bladder stones composed of ammonium and urate.[15]

Change or variation in incidence and pattern of paediatric urolithiasis may be connected to the dietary practices in the different region.[16] That's gives evidence of marked regional variations in the stone prevalence recognised as "Stone Belts". Local climatic conditions also play an important role in stone pathogenesis. It is evident that stone occurrence increases in warmer and sunnier regions. Also, risk of stone disease depends on familial predisposition and genetic susceptibility.[1]

Prevention of stone formation can be done by early diagnosis and treatment of these metabolic risk factors. At present very few studies have been conducted on metabolic assessment of urinary stones in patients of paediatric age group in India.

2. Aims and Objectives

Aim of this study was to evaluate and observe the different metabolic risk factors (serum and urinary metabolic abnormalities) for urolithiasis in children. We had assessed, observed and compared serum metabolic parameters (like calcium, phosphorus, creatinine, uric acid, electrolytes, Parathyroid hormone and albumin) and 24 hours urinary metabolic parameters (like urinary pH, volume, uric acid, calcium, oxalate, creatinine, citrate).

3. Materials and Methods

3.1. Study site

This study was conducted in the Department of General Surgery and Urology, Narayan Medical College and Hospital, Jamuhar, Rohtas, Bihar, India.

3.2. Study duration

One and half year (Eighteen months) from January 2019 to July 2020.

3.3. Study design

This was an observational and prospective study on fifty (n=50) children with confirmed diagnosis of urolithiasis below 12 years of either sex. This study was approved from Institutional Ethical Committee of Narayan Medical College and Hospital, Jamuhar. Informed consent from the parents/guardian of children were taken.

3.4. Inclusion criteria

1. Children with both gender and age $\leq$12 years were included.
2. Children with confirm diagnosis of urolithiasis were included.
3. Children with clear urinalysis and culture report were included.

3.5. Exclusion criteria

1. Children with UTI on urine analysis were excluded.
2. Children had previously diagnosed metabolic, endocrine, gastrointestinal disorder were excluded.
3. Children had Protein Energy Malnutrition were excluded.
4. Children on Calcium, Vitamin D, and Vitamin C supplementation were excluded.

History of disease from study participants were taken carefully and they were thoroughly examined clinically. Various laboratory tests were performed like complete blood count, routine urine and urine culture and sensitivity (to diagnose Urinary Tract Infections, UTI). Diagnosis of Urolithiasis and urinary tract abnormalities were confirmed by

1. Ultrasonography,
2. Intravenous pyelogram and
3. Computed Tomography (CT scan) in selected cases.

During study period those children who had been diagnosed with UTI were treated beforehand, so that, their urinalysis and urine culture report become clear or normal and then their metabolic evaluation was performed.

From all study participants, dietary practice and water consumption per day over previous 3 months was inquired and documented.

All urine samples were taken without any dietary restrictions. Random urine sample was taken in cases of infants and non- toilet-trained children and 24-hour urine was collected in toilet-trained children. Following laboratory investigations were performed and results were recorded.

3.5.1. Urinalysis- Normal level of 24-hour urinary parameter in paediatric age group.[17]

1. Routine urine

2. Urine culture
3. 24 hours urinary pH- 4-9
4. Volume- > 1ml/kg/hr
5. Calcium- < 4 mg/kg/day
6. Oxalate- < 0.57 mg/kg/day
7. Citrate- > 6 mg/kg/day
8. Uric acid- < 10 mg/kg/day
9. Creatinine- 0.5 to 1.0 mg/dL for children ages 3 to 18 years, 0.3 to 0.7 mg/dL for children under age 3

3.5.2. Biochemical investigations included

1. Serum calcium
2. Serum phosphorus
3. Serum creatinine
4. Serum uric acid
5. Serum electrolytes
6. Serum Parathyroid hormone
7. Serum albumin

3.6. Statistical analysis

Data collected from this study had been presented in tabular form. Statistical analysis was performed with the help of Microsoft Excel Software and GraphPad Instat Software.

4. Results

Out of 50 children in this study, 35 (70%) were male and 15 (30%) were female. Twenty-three participants were below five years of age.

According to dietary habits 60% (n=30) and 14% (n=7) of children had low Calcium intake and high calcium intake respectively. 64% (n=32) children showed low 24-hour urine volume due to low water intake.

64% (n=32) children showed metabolic abnormality, out of them serum abnormality and 24-hour urinary metabolic abnormality was found in 21 and 11 children respectively.

Table 1: Serum abnormality in children with urolithiasis

Serum abnormality	No of patient (n=21)
Hypocalcaemia	18(85.71%)
Hypocalcaemia+ Hyperphosphataemia	02 (9.52%)
Hypercalcaemia	00 (00%)
Hyperuricaemia	01 (4.76%)

85.71% (n=18) children had hypocalcaemia with normal PTH and 14.29% (n=3) had secondary hyperparathyroidism (Table 1).

Out of 11 children, hypocitruria was the most common urinary irregularity and seen in 06 patients followed by hypercalciuria in 03 patients (Table 2).

On stone analysis it was found that majority (n=11, 55%) of the children had calcium oxalate stone. Stone analysis was done in 20 patients.

Table 2: Urinary metabolic abnormality in children with urolithiasis

Urinary metabolic abnormality	No of patients (n=11)
Hypercalciuria	03(27.27%)
Hyperoxaluria	01 (9.09%)
Hypocitruria	06 (54.55%)
Hyperuricosuria	01 (9.09%)

Table 3: Analysis of urinary stone in children with urolithiasis

Type of stone	No of patients (20)
Calcium oxalate	11(55%)
Calcium phosphate	02(10%)
Uric acid	03(15%)
Cystine	01(5%)
Struvite	03(15%)

5. Discussion

Urolithiasis in paediatric age group had metabolic and genitourinary anomalies co-exists as a risk factor. Morbidity of urolithiasis is very high.

Urolithiasis can lead to urinary tract infection (UTI), hypertension, scarring of kidney, obstruction and progressive worsening of renal function. UTI is approximately seen in 8-45.9% of children having urolithiasis.[18,19] Also, it is evident from some studies that 62% of patients under five years of age, UTI leads to urolithiasis.[20,21] Hence screening of metabolic risk factors should be essential in all children with stone disease.[22]

In this study low calcium intake was seen in majority of patients (60%) which suggested that low calcium consumption is linked with higher occurrence of urolithiasis and it might have two mechanisms.

1) Low calcium consumption possibly leads to rise in existing intestinal oxalate and this later on increases oxalate absorption, thus raising the super saturation of calcium oxalate. But in this study only one patient had low calcium intake and associated hyperoxaluria.

2) Low calcium consumption excites calcitriol production which causes hypercalcaemia which prevents PTH production and thus causes hypercalciuria.[23–25] In this study, hypercalciuria was seen only in three children and none of them had hypercalcaemia.

In 33 patients, low urine volume was contributory finding. In an earlier study it was perceived that occurrence of nephrolithiasis was decreased in those subjects who had increased levels of dietary calcium. Low water consumption and low urine volume was main finding and result was comparable to earlier works.[26] Stone risk factor in nephrolithiasis was urine volume and for prevention of stone repetitions, large intake of water is preliminary therapy.[27]

Hence for the initial treatment of urinary stones it is highly recommended to take oral fluid by children. Also, mothers should be instructed to give adequate water.

Hypocalcaemia related to diet occurs due to low intake of calcium, high intake of phosphates, low magnesium are common reasons of hypocalcaemia associated with diet. In this study low calcium consumption was the chief cause of hypocalcaemia. Finding correlation between hypocalcaemia and urolithiasis was very difficult in this study because majority of the patient was associated with low water intake and less urine volume.

24-hour urinary abnormality was found only in 22% (n=11) patients, though hypocitruria (n=6, 54.55%) was the most common urinary abnormality and this result was comparable with previous literature. 54% patients had urinary metabolic irregularity seen by Naseri et al.[28]

90% of patients had urinary metabolic abnormality with hypocitruria was most common abnormality seen by Erbagci et al.[29] This opposing result may be due to normal reference level of 24-hour urinary metabolic parameters were taken according to western literature and deficiency of Indian literature on normal reference level of 24-hour urinary metabolic parameters.

Findings of stone analysis does not correlate with urinary findings in this study. Stone analysis done on 20 patients, out of which only five had 24-hour urinary metabolic abnormality. Calcium oxalate stone was found in 11 patients and only three had hypercalciuria. The reason for this contradiction was unknown which may be again 24-hour reference value which is causing the problem in correlation.

6. Conclusion

Predominant finding from this study was low urine volume secondary to low water intake. Hypocalcaemia is major metabolic abnormality in contradiction to western literature. There were no nomograms for urinary excretion of Calcium, uric acid, oxalate and citrate in Indian children. Increased fluid intake and keeping blood calcium level at optimal level may be useful to prevent urolithiasis in children. Reference range for 24-hour urinary parameters must be further studied and established for paediatric population.

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8. Conflict of Interest

The authors declare they have no conflict of interest.

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