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PEDIATRIC UROLITHIASIS;

EVALUATING BIOCHEMISTRY OF PEDIATRIC UROLITHIASIS

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ABSTRACT… Objectives: To determine the biochemical composition and biochemical types of childhood urolithiasis. **Study Design:** Cross sectional study. **Place and Duration:** Pediatric Surgery Department, Liaquat University of Medical and Health Sciences, and University of Sindh, Jamshoro over one year. **Subjects & Methods:** 30 pediatric cases urinary bladder urolithiasis were selected. Children of age few of ten years were selected. Any contamination form bladder stone was removed by washing them in distilled deionized water. Stones were dried for an overnight in an oven at temperature of 100 ^{0}C. Dried stones were smashed into pieces. Biochemical analysis was performed by the FTIR spectroscopy (Nicolet Avatar 330 FTIR spectrophotometer). Results were analyzed on the software SPSS 22.0 (95% confidence interval). **Results:** Mean age was 4.83 years (SD 2.81 years). Of 30 children, 80% (n=24) were male and 20% (n=6) were female children. Male to female ratio of 4:1 was noted. 16.6% (n=5) were pure stone and 83.3% (n=25) were mixed stones. (P=0.0001). Biochemical analysis showed the calcium oxalate monohydrate (COM)-ammonium hydrogen urate (AHU) was the most common urinary bladder stone. **Conclusions:** The pediatric urolithiasis shows the most common type of urinary bladder stone was the calcium oxalate monohydrate–ammonium hydrogen urate.

Key words: Pediatric Urolithiasis, Biochemical Composition, Fourier Transforms Infrared Spectroscopy.

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INTRODUCTION

Pediatric urolithiasis has increased enormously over the recent decades. Both incidence and prevalence has been on rising.[1,2] Pediatric urolithiasis accounts for considerable morbidity and surgery related mortality due to young age and recurrence rate is very high.[3] Cause of pediatric urolithiasis remains vague and its epidemiology reveals increasing incidence. The vitamin deficiency, dietary factors, genetic factors and environmental factors play role, hence the etiology of pediatric urolithiasis is multifactorial similar to urinary stone of adults.[4] One of etiological factor of the pediatric urolithiasis is the metabolic abnormalities particularly for the idiopathic cases. Hence the metabolic problems must be addressed by proper biochemical evaluation and analysis of pediatric urolithiasis. Metabolic factors must be searched by the biochemical analysis of recovered stones.[5] Knowing of the biochemical composition directs towards the underlying metabolic abnormalities; hence this will help to plan dietary guidelines for prevention of pediatric urolithiasis. Both pharmacological and non-pharmacological factors may intervene to prevent recurrence of pediatric urolithiasis.[6] A previous study reported metabolic abnormality as a cause of lithogenesis in the Pediatric population.[7] A better understanding of metabolic factors may help to inhibit the lithogenesis for both preventive and therapeutic purposes. Urinary bladder stones are composed of organic matrix with embedded mineral crystals within it.[8] In developing countries, there are many casues of increased incidence and prevalence of pediatric urolithiasis. Multiple factors interact altogether resulting in the urolithiasis. Nutritional deficiencies, environmental and genetic factors facilitate the mineralization of organic matrix.[9] Lithogenic promoters of crystallization combined with metabolic defects account for increasing incidence and prevalence of pediatric urolithiasis.[9] Many techniques such as the thermal analysis, chemical analysis, crystallography, and infrared (IR) analysis are used to determine the biochemical composition of bladder stones. Fourier transforms IR (FT-IR) and Raman spectroscopies are reliable methods of determining the biochemical compositions of stones.[10,11] The FT-IR is a validated technique of accurate biochemical analysis of urolithiasis.[10,11] The present study was designed to analyze and study the biochemical composition of pediatric urolithiasis so that the information may be used for therapeutic and preventive purpose in future.

SUBJECTS AND METHODS

The present study cross sectional study took place at the Pediatric Surgery Department, Liaquat University of Medical and Health Sciences in collaboration with University of Sindh, Jamshoro over one year. A sample of 30 pediatric cases urinary bladder urolithiasis was selected. Children of age few of ten years were selected. Children having congenital malformations of urinary tract were excluded.

Pediatric uroliths were collected after ethical permission of the institute. Any contamination form bladder stone was removed by washing them in distilled deionized water. Stones were dried for an overnight in an oven at temperature of 100 ^{0}C. Dried stones were smashed into pieces. Pediatric uroliths were examined grossly. Pediatric uroliths were smashed into fine powder by mechanical method in a pestle and mortar. Powder was used for the Fourier transformation infra red spectroscopy. Biochemical analysis was performed by the FTIR spectroscopy (Nicolet Avatar 330 FTIR spectrophotometer, Thermo Electron Corporation). The range of Nicolet Avatar 330 FT-IR spectro-photometer is varies from 600-4000 cm^{-1}. 32 scans were obtained for each of uroliths. Scans were got by obtaining high signal/noise ratio. Standards of uroliths biochemical composition were purchased from the “Sigma-Aldrich (Chemie GmbH)” USA. Standards for Ca++ oxalate monohydrate (COM), Mg++ ammonium phosphate (MAP), Uric acid (UA), Calcium carbonate (CC) and NH_4^+- hydrogen urate (AHU) were purchased. FT-IR spectra were recorded. Calculation of FT-IR spectra was interpreted by plotting of transmittance versus wave numbers (per cm). Written informed consent was mandatory to be signed by the legal heirs of the pediatric study population. Ethical issues were approved by the ethics committee of the institutes. All of the data collection procedures were in accordance to the Helsinki`s declaration for human research. Data was noted on a pre-designed proforma. Confidentiality of record was maintained strictly. Research variables were analyzed on the software SPSS 22.0 (IBM, Incorporation, USA) using Student t-test (for continuous variables) and Chi square test (for categorical variables). The- level of significance was defined at 95% confidence interval ($P \leq 0.05$) as statistically significant.

RESULTS

Mean age was 4.83 years (SD 2.81 years). Age categories summary is shown in Table-I (Figure-1 and 2). 6-7 years was the most frequent age category (P=0.0001). Of 30 children, 80% (n=24) were male and 20% (n=6) were female children. Male to female ratio of 4:1 was noted. (P=0.0001). Biochemical analysis showed the calcium oxalate monohydrate (COM)- ammonium hydrogen urate (AHU) was the most common urinary bladder stone. Biochemical composition of Pediatric urolithiasis is shown in Table-II. 16.6% (n=5) were pure stone and 83.3% (n=25) were mixed stones (P=0.0001). Of 5 pure pediatric uroliths, frequency of pure uric acid was one and two for each Mg-ammonium phosphate (MAP) and calcium carbonate (CC). Biochemistry of 25 mixed uroliths showed frequency of COM + AHU in 19 cases, COM + AHU + Urate in 3 cases and AHU+ Urate in 3 cases (Table-II, Figure-3).

	Male Pediatric Uroliths	Female Pediatric Uroliths	P-value
0.6 - 2.9 years	7	2	0.046
3 - 4.9 years	8	1	
5 - 5.9 years	3	2	
6 - 7 years	6	1	

Table 1. Age distribution of Pediatric Urolithiasis (n=30)

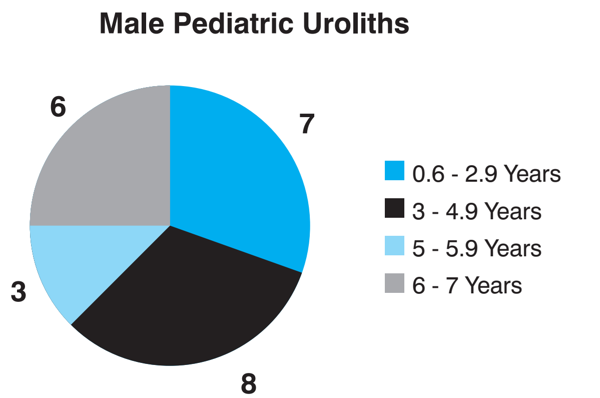

Figure-1. Age distribtion in male pediatirc uroliths

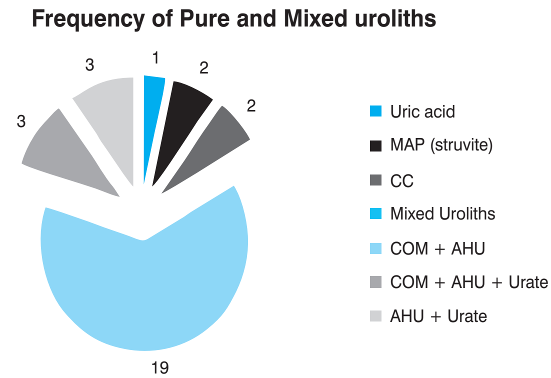

Figure-3. Frequency of Pure and Mixed uroliths

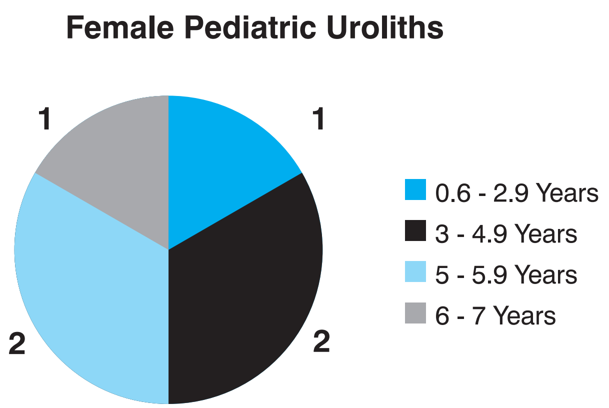

Figure-2. Age distribtion in female pediatirc uroliths

	No.	%	P-vale
Pure Uroliths			
Uric acid	01	3.3	0.04
MAP (struvite)	02	6.6	
CC	02	6.6	
Mixed Uroliths			
COM + AHU	19	63.3	0.0001
COM + AHU + Urate	03	10.0	
AHU + Urate	03	10.0	

MAP -Magnesium ammonium phosphate, CC- Calcium carbonate, COM-Calcium oxalate monohydrate, AHU- Ammonium hydrogen urate

Table-II. Pure and Mixed Pediatric Uroliths (n=30)

DISCUSSION

The present study is the first research on the analysis of biochemical composition and types of Pediatric urolithiasis being reported form our tertiary care hospital. We studied urolithiasis in children of under 10 years of age.

As the pediatric urolithiasis causes considerable morbidity and mortality because of surgery related consequences and recurrence rat,[3,4] the problem need to be understood fully, in particular the biochemical composition of uroliths for future prevention. In present study, of 30 children, 80% (n=24) were male and 20% (n=6) were female children. Male to female ratio of 4:1 was noted. (P=0.0001). Our findings are consistent with previous reports.[11,12] The mean age was 4.83 years (SD 2.81 years) and 6-7 years was the most frequent age category (P=0.0001). The age distribution of present study is supported by previous studies.[13,14] As regards biochemical composition, pure and mixed uroliths were found in 16.6% (n=5) and 83.3% respectively (P=0.0001). Of 5 pure pediatric uroliths, frequency of pure uric acid was one and two for each Mg-ammonium phosphate (MAP) and calcium carbonate (CC). Of 25 mixed uroliths, composition of 19 uroliths revealed COM + AHU, 3 were of COM + AHU + Urate and remaining 3 uroliths were of AHU+ Urate type. The finding of calcium containing stones as predominant found in present study is supported by previous studies.[15,16] We are the first to report on the pure calcium carbonate uroliths from our tertiary care hospital.

In present study, 45.3% uroliths proved of calcium oxalate monohydrate–ammonium hydrogen urate type. This findings is in full agreement with previous,[17,18] which have reported similar biochemical type of uroliths from endemic areas. The urolithogenesis in endemic areas like Pakistan needs biochemical analysis of each recovered renal stone for future preventive strategies to be implemented. The AHU was found in the central nucleus of the uroliths, that is supported by previous studies.[19,20] We found MAP in 2 (6.6%) cases, the finding is supported by a previous study.[21] MAP type of uroliths are produced by the urinary tract infections;[22] hence in future antimicrobial intervention may help to prevent and minimize the risk of lithogenesis in the local pediatric population. Urease producing bacteria initiate the Mg_4+ammonium phosphate (struvite) lithogenesis.[23] In present study, the MAP (struvite) was found in 2 (6.6%) cases, the finding is in agreement with previous studies,[23,24] which had reported an incidence of 10%. The Calcium oxalate uroliths are produced in urinary environment of low citrate and high oxalate.[23,24] The COM + AHU+ urate mixed uroliths were found in 73% of cases (Table-II), the finding is in keeping with previous studies.[25,26] The COM uroliths were the most common type observed in the present study. This type of uroliths shows the presence of urinary tract urease producing bacterial infections, low urinary citrate and hyperoxaluria,[25,26] this supports the findings present study.

Evidence based findings of biochemical composition and type of uroliths of present study shows the underlying metabolic disorders, urinary tract infection and decrease in anti-lithogenic mechanisms in our pediatric study population. The findings of present study show the eradication of urinary tract infections and metabolic disorders may help to reduce the pediatric uroliths in the future. The only limitation of present study is a small sample size. Large scale studies should be conducted to make proper guidelines for the anti-lithogenic mechanisms to be implemented properly.

CONCLUSION

The present study shows the calcium oxalate monohydrate–ammonium hydrogen urate was the most common type of stones in pediatric population. Both pure (16.6%) and mixed (83.3%) uroliths were found in the pediatric population of present study.

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2	Fouzia Shaikh	Materials handling, manuscript write up, Biochemical analysis and laboratory testing, Proof reading.	
3	Shazia Murtaza	Concept, Manuscript write up, Proof Reading, Biochemical analysis, Complilation of resutls.	