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URINARY BLADDER STONE;

BIOCHEMICAL COMPOSITION OF URINARY BLADDER STONE IN CHILDREN

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ABSTRACT… Objective: To analyze the biochemical composition and biochemical types of urinary bladder stones in children. **Study design and setting:** Observational study, Department of Pediatric Surgery, Liaquat University of Medical and Health Sciences, Jamshoro/Hyderabad. **Place and Duration:** One year duration from January to December 2006. **Materials & Methods**: A sample of 30 children was selected according to criteria of inclusion of age <10 years of urinary bladder stones without any anomaly. Urinary bladder stones were washed in distilled H_2O deionized to remove contaminations. Urinary bladder stones were dried at 100 ^{0}C for overnight in an oven. The urinary bladder stones cut into pieces were used for the FTIR spectroscopy analysis, carried out on "Nicolet Avatar 330 FTIR spectrophotometer". Data was analyzed on SPSS 22.0 at 95% confidence interval. **Results**: Of 30, 6 (20%) were female and 24 (80%) were male. The male dominancy was noted with male to female ratio of 4:1. Mean± SD age was noted as 4.839 $\pm$ 2.819 years. Urinary stones of pure and mixed biochemistry were noted in 5 (16.6%) and 25 (83.3%) respectively (P=0.0001). Most frequent urinary bladder stone found was the calcium oxalate monohydrate - ammonium hydrogen urate. **Conclusions**: Most frequent type of urinary bladder stones was the calcium oxalate monohydrate–ammonium hydrogen urate type in the children.

Key words: Biochemical composition, Urinary bladder stones, Fourier transforms infrared spectroscopy, Children.

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INTRODUCTION

Childhood urinary bladder stones have been increasing and recent decades have shown an increased incidence and prevalence.[1,2] This urinary bladder stones now account for considerable morbidity due to high recurrence rates.[3,4] Causative agents and epidemiological factors remain unknown for the increased incidence of urinary bladder stones. However, environmental, genetic, vitamin deficiencies, and dietary factors have been suggested.[5,6] Metabolic abnormalities have been reported as underlying process for the idiopathic urinary bladder stones in the children, hence metabolic problems must be evaluated once the diagnosis of kidney stones is confirmed.[7] Knowing the metabolic factors may guide towards general dietary, pharmacological and non-pharmacological interventions at least for the prevention of recurrence of urinary bladder stones.[8,9] Previous studies have reported increased rate of metabolic abnormalities in the children with urinary bladder stones.[10] In this context, metabolic factor combined with inflammatory features of lithogenesis may help for better therapeutic and preventive measures of urinary bladder stones. Biochemically, the urinary bladder stones comprise of organic matrix embedded in which are the mineral crystals.[10,11] Developing countries show increased incidence and prevalence of urinary bladder stones due to nutritional, genetic and environmental factors which play role in the pathogenesis of mineral crystallization of niche of organic matrix.[10-12] Metabolic defects combined with stone promoters and promoters of crystallization all account for the lithogenesis.[12] Risk factors of multiple origins have been reported in association to metabolic defects in previous studies.[13,14] Biochemical compositions of urinary bladder stones may be determined by various techniques such as the thermal and wet chemical analyses, crystallography and infrared (IR) analysis such as the Fourier transform IR

(FT-IR) or Raman spectroscopy.[15,16] The FT-IR spectroscopy is a validated methods reported to be the most accurate for the analysis of biochemical composition of urinary bladder stones with minimal time factor. The FT-IR spectroscopy is valuable technique for detecting the relative proportion of each constituent without using any solvent.[15,16] As the biochemical composition of urinary bladder stones is helpful for therapeutic and preventive purpose, hence it is worth to analyze for effective patient management. Also it is reported that the composition of urinary bladder stones vary according to geographical area [16] making it mandatory to analyze the biochemical composition for clinical management. The present prospective study was conducted to study the biochemical composition of childhood urinary bladder stones as this will be helpful for the doctors, patients and community as proper therapeutic options may then be advised. The present study will be helpful for community as regards the current trends of biochemistry of urinary bladder stones for stopping the lithogenesis and prevention of recurrence.

MATERIALS AND METHODS

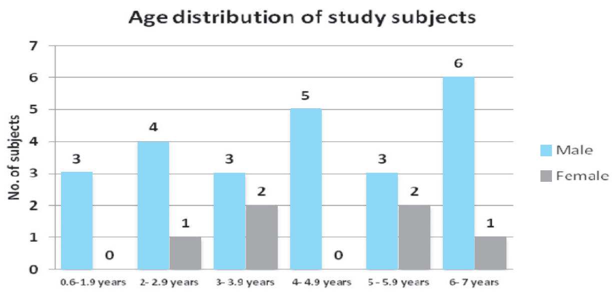
A sample of 30 children, presenting at the Department of Pediatric surgical ward of Liaquat University Hospitals, were selected over year duration. The study subjects were selected according to criteria of inclusion of age <10 years of urinary bladder stones without any anomaly. Urinary bladder stones removed by surgical procedure were collected by the researcher. They were washed in distilled H_2O deionized to remove contaminations. Urinary bladder stones were dried at 100 ^{0}C for overnight in an oven. Dried urinary bladder stones were examined and cut into 2 pieces with fine jewelers saw. The urinary bladder stones cut into pieces were used for the FTIR spectroscopy analysis, carried out on "Nicolet Avatar 330 FTIR spectrophotometer" (Thermo Electron Corporation). "Nicolet Avatar 330 FTIR spectrophotometer" has a range of 600-4000 cm^{-1}. For each urinary stone, 32 scans were obtained evaluate by obtaining high signal/noise ratio. Pure standard sample of anhydrous uric acid, Ca++ oxalate monohydrate; Mg++ ammonium phosphate, Ca++ carbonate, and NH_4^+- hydrogen urate were purchased from the "Sigma-Aldrich (Chemie GmbH)" USA. Records of FT-IR spectra were obtained and recorded. Stone pieces were obtained and examined from different parts of urinary bladder stones. Smashed stone pieces were homogenized into fine powder in a pestle and mortar before analysis on the FTIR spectrometer. Fourier transformation calculation was performed on computer, and infra red spectrum was read which plots transmittance vs. wave numbers (per cm). Written informed consent from parents was mandatory. Approval was taken from Ethical committee. A pre designed proforma was used for the data entry. Data was analyzed on SPSS 22.0 using Student t-test (continuous variables) and Chi square test (categorical variables) at 95% confidence interval.

RESULTS

The present study analyzed the biochemical composition of urinary bladder stones from 30 children. Of 30, 6 (20%) were female and 24 (80%) were male. The male dominancy was noted with male to female ratio of 4:1. Mean± SD age was noted as 4.839 $\pm$ 2.819 years. Age categories are shown in the table I. Most frequent age group belonged to the 6-7 years (P=0.0001). Bar graph 1 shows the frequency of age distribution. Biochemical composition of urinary bladder stones is shown in the table II and graph 2. Urinary stones of pure and mixed biochemistry were noted in 5 (16.6%) and 25 (83.3%) respectively (P=0.0001). Of 5 pure urinary stones; one was pure uric acid stone, 2 were Mg-ammonium phosphate and 2 were calcium carbonate. Of 25 mixed urinary stones, 19 were calcium oxalate monohydrate + ammonium hydrogen urate, 3 were calcium oxalate monohydrate+ ammonium hydrogen urate + urate and 3 were ammonium hydrogen urate + urate as shown in table II.

	Male	Female	P-value
0.6-1.9 years	3	0	0.0001
2- 2.9 years	4	1	0.0003
3- 3.9 years	3	2	0.046
4- 4.9 years	5	0	0.0001
5 - 5.9 years	3	2	0.046
6- 7 years	6	1	0.0001
Total	24	06	-

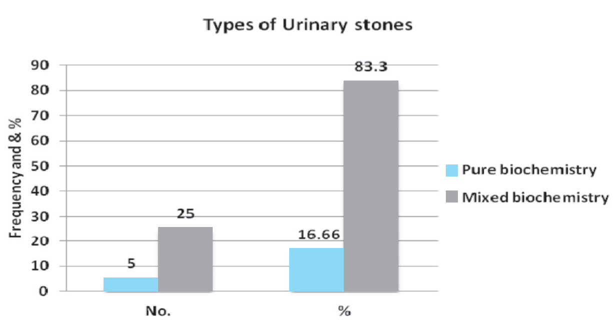
Table-I. Age wise gender distribution of study subjects (n=30)



Graph-I. Bar graph showing frequency of age distribtion of male and female

	No.	%
Pure biochemistry		
Uric acid	01	3.33
Magnesium ammonium phosphate (struvite)	02	6.66
Calcium carbonate	02	6.66
Mixed biochemistry		
Calcium oxalate monohydrate+ Ammonium hydrogen urate	19	63.33
Calcium oxalate monohydrate+ Ammonium hydrogen urate+ Urate	03	10.0
Urate+ Ammonium hydrogen urate	03	10.0
Total	30	100

Table II. Frequency of urinary stone by biochemical composition (n=30)



Graph 2. Frequency of urinary stone by biochemical composition

DISCUSSION

The present is the first research report on the biochemical analysis of urinary bladder stones in children of under 10 years of age from our tertiary care hospital. Of 30, 6 (20%) were female and 24 (80%) were male.

The male dominancy was noted with male to female ratio of 4:1. The findings are in agreement with previous studies.[17,18] The mean± SD age was noted as 4.839 $\pm$ 2.819 years (P=0.0001). The findings are in agreement with previous studies[19,20] Urinary stones of pure and mixed biochemistry were noted in 5 (16.6%) and 25 (83.3%) respectively (P=0.0001). Of 5 pure urinary stones; one was pure uric acid stone, 2 were Mg-ammonium phosphate and 2 were calcium carbonate. Of 25 mixed urinary stones, 19 were calcium oxalate monohydrate + ammonium hydrogen urate, 3 were calcium oxalate monohydrate+ ammonium hydrogen urate + urate and 3 were ammonium hydrogen urate + urate. The above findings show the predominantly calcium stones and this is consistent with previous studies.[21-23] Pure calcium carbonate urinary stones are first time being reported by the present study. Approximately 45.3% of the urinary bladder stones proved of calcium oxalate monohydrate–ammonium hydrogen urate biochemical nature. The finding is in keeping with previous studies[24,25] from endemic areas, but contrary to a study from Pakistan.[15] This points towards the common risk factor involved in the lithogenesis from endemic areas. In present study, the NH_4+ hydrogen urate was present in the nucleus and surrounding inner part of periphery of stones, this finding is in keeping with previous studies.[26,27] The Mg++ ammonium phosphate (struvite) stone was noted in 6.66%, this is in agreement with previous study[29] and this type of urinary stone is produced by the urinary tract infections; hence antimicrobial intervention is necessary.[21] A previous study[30] proposed the theory that the urease producing bacteria are associated with Mg_4+ammonium phosphate (struvite) stones and incidence of 10% has been reported among all stones. In present study 6.66% proved to be the Mg_4+ammonium phosphate (struvite) stones which is in agreement with previous studies.[30,31] Citrate is a recognized inhibitor of urinary lithogenesis, and is present in large quantities in the oranges, grapes, and vegetables. Citrate interferes with the nucleation of stone formation. Hypocitraturia is a risk factor for the urinary lithogenesis of calcium oxalate monohydrate type.[31,32]

The Ca++ oxalate monohydrate–ammonium hydrogen urate was most frequent type of urinary stone found in the present study and these points to the urinary tract infection and hyperoxaluria.

Similar findings have been reported by the previous studies[31-33] as they found hyperuricosuria to be the most common metabolic risk factor in their study which is in contrast to present and previous studies.[25-27] This shows the majority of children with urinary bladder stones are suffering from metabolic disorders and urinary tract infections which is necessary for pharmacological intervention at early stage for effective prevention of urinary bladder stones. The present study suggests prospective large scale studies at our tertiary care hospitals to reach to a proper destination for the effective strategy of preventing the urinary bladder stones.

CONCLUSION

In the present study, the Biochemical composition of urinary bladder stones reveals both pure and mixed biochemical composition noted in 5 (16.6%) and 25 (83.3%) respectively. Most common type of urinary bladder stone was the calcium oxalate monohydrate–ammonium hydrogen urate stone.

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2	Shazia Murtaza	Literature review, Materials handling, Manuscript write up, Proof Reading, Biochemical analysis.	
3	Rafique Ahmed Jalbani	Concept, manuscript write up, Biochemical analysis and laboratory testing, compilation of results, Proof reading.	