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Chemical Composition Of Pediatric Urolithiasis In District Khairpur Mir's

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ABSTRACT

Urolithiasis represents a substantial global health concern, with a particularly high incidence observed in the Afro-Asian stone belt, including Pakistan. While its multifactorial etiology remains under investigation, epidemiological studies consistently highlight age, sex, socioeconomic status, diet, climate, and geography as key risk factors. Urinary stone disease contributes significantly to urological caseloads, accounting for 40-50% of admissions in some hospitals, affecting all age groups. Notably, developing nations frequently exhibit two peaks in incidence: one in children, predominantly involving bladder stones, and another in adults with a higher prevalence of kidney stones. This prospective study investigated 40 pediatric urolithiasis patients in Khairpur, Pakistan, to characterize the local incidence and stone composition. Our findings revealed a strong male predominance (77.5% males vs. 22.5% females) and a peak incidence within the 3-4 year age group. Anatomical distribution showed that lower urinary tract stones were more common, present in 57.5% of patients, while upper urinary tract stones accounted for 42.5%. Chemical analysis identified calcium oxalate and phosphate (70%) as the predominant stone components, followed by uric acid (22.5%) and magnesium ammonium phosphate (7.5%). The persistent high burden of childhood urolithiasis in this region, particularly the endemic nature of bladder stones in rural and socioeconomically disadvantaged areas, underscores the urgent need for further comprehensive, long-term research. Such investigations are crucial to elucidate specific etiologies and inform targeted public health interventions to mitigate this significant pediatric health issue.

INTRODUCTION

Urolithiasis, characterized by the formation of solid calculi in the urinary tract, is a prevalent global health concern, ranking as the third most common urological disorder. Its incidence can reach up to 15% in Western populations, with a notable elevated occurrence in the Afro-Asian "stone belt," encompassing tropical and subtropical regions (Pak & Resnick, 2014; Scales et al., 2012). These calculi, varying in shape and chemical composition, can deposit throughout the upper and lower urinary tracts (Borghi et al., 2007). Despite its high prevalence, the precise mechanisms of urinary stone formation remain incompletely understood, influenced by a complex interplay of genetic, environmental, and metabolic factors (Coe et al., 2000).

Epidemiological studies indicate a diverse range of risk factors for urolithiasis. While stone disease can affect individuals of all ages, its age-specific prevalence varies geographically (Soucie et al., 1994; Akman et al., 2003; Dizdar et al., 2009; Al-Hosani et al., 2013). In developing countries, including Pakistan, bladder stones are more frequently observed in children, particularly those aged 1-5 years, whereas renal stones are more common in adults, typically between 21-30 years (Rizvi et al., 2011). A male predominance in urolithiasis incidence is widely reported across various populations (Türk et al., 2016). Furthermore, a sedentary lifestyle is associated with a higher risk of stone formation compared to physically active individuals (Johnson et al., 2012). The underlying etiology of urinary stones involves intricate physicochemical processes, primarily supersaturation of urine with lithogenic salts, imbalances in inhibitors, and aberrant crystallization (Evan, 2007; Lieske et al., 2014). Global trends reveal significant variations in urolithiasis patterns between developed and developing nations. Nephrolithiasis, often termed a "modern disease," is increasingly observed in adolescents from developed countries and urbanized regions of industrialized states, correlating with higher socioeconomic strata (Curhan, 2007). Conversely, bladder stones remain a significant burden in economically disadvantaged regions, including Pakistan. Studies highlight a higher incidence of pediatric urolithiasis in rural and less prosperous areas compared to more affluent parts of such countries (Ali & Khan, 2015; Khan & Zafar, 2016).

Although not immediately life-threatening, urinary stones can cause significant morbidity, leading to pain, obstruction, and potential renal impairment (Preminger, 2011; Lotan & Pearle, 2007). The management of urolithiasis involves both medical and surgical approaches, necessitating comprehensive diagnostic evaluation to identify the specific stone composition, underlying metabolic abnormalities, and contributing systemic diseases (Goldfarb & Coe, 2015). Radiological and laboratory investigations are critical for accurate diagnosis and guiding appropriate therapeutic strategies, including stone removal and management of complications (Assimos, 2009). Due to the high recurrence rate of urolithiasis (70-80%), meticulous stone analysis and patient counseling are essential to prevent future stone formation, though stone analysis is sometimes overlooked in clinical practice (Moe, 2006). Contemporary treatment emphasizes minimally invasive procedures, though open surgery retains a vital role for complex cases.

This study aims to determine the chemical composition of urinary stones in Khairpur Mir's, Pakistan, through wet chemical analysis. The research will investigate incidence rates based on age, sex, stone location, clinical presentation, and stone constituents among patients admitted to the Department of Surgery at Ghulam Muhammad Mahar Medical College, Khairpur Mir's, during the study period. Such localized efforts are crucial for enhancing clinical understanding and informing future diagnostic and therapeutic approaches to stone disease.

Literature Review

Urolithiasis, the formation of solid calculi within the urinary tract, is a significant global health concern and a leading urological disorder (Scales et al., 2012; Turk et al., 2016). These calculi, varying in chemical composition, can occur throughout the urinary system (Borghi et al., 2007). While widely prevalent, incidence is notably higher in tropical and subtropical regions, often referred to as the Afro-Asian "stone belt" (Scales et al., 2012).

The urinary system, including the kidneys, ureters, bladder, and urethra, is essential for urine formation, transport, storage, and excretion (Moore et al., 2018). Kidneys maintain fluid, electrolyte, and acid-base balance, excrete waste, and produce vital hormones (Guyton & Hall, 2016). Urine is formed in nephrons through glomerular filtration, followed by selective tubular reabsorption of beneficial substances (e.g., water, sodium, calcium) and secretion of waste (Sherwood, 2012). The precise regulation of urinary pH, influenced by buffering systems, significantly affects the solubility of stone-forming salts (Weiner & Wingo, 2004).

The pathophysiology of stone formation is multifactorial, typically beginning with the supersaturation of urine with lithogenic salts (Coe et al., 2000). This supersaturation drives nucleation—the initial formation of a solid crystal phase—which can be homogeneous or heterogeneous (Tiselius & Alken, 2001). Subsequent crystal growth and rapid aggregation lead to larger particles, with crystal retention within renal tubules being crucial for clinical stone formation (Pak, 1988; Khan & Hackett, 1993).

An individual's susceptibility to urolithiasis is determined by the balance between stone promoters and inhibitors (Kok, 2000). Promoters include low urine volume, acidic urine pH, and elevated concentrations of calcium, oxalate, urate, and cystine (Goldfarb, 2013). Conversely, endogenous inhibitors such as citrate, magnesium, osteopontin, and Tamm-Horsfall protein, among others, mitigate stone formation (Pak, 1994; Lieske et al., 2017). Hypocitraturia is a common finding in stone formers, and alkaline citrate supplementation is an effective therapeutic strategy (Trinchieri et al., 2004).

Epidemiological data reveal evolving patterns, with nephrolithiasis increasingly associated with developed nations. However, bladder stones remain prevalent in children from developing countries like Pakistan (Curhan, 2007; Rizvi et al., 2011). Studies in regions like Southeast Iran and Pakistan show diverse age distributions in pediatric cases, often peaking in toddlers (1-5 years) (Sadeghi et al., 2015; Ali & Khan, 2015). A consistent male predominance and higher prevalence in rural areas are also observed in pediatric populations (Ali & Khan, 2015; Al-Hosani et al., 2013). Factors like sedentary lifestyles and dehydration, particularly in hot climates like Khairpur, contribute to risk.

The etiology of urinary stone disease is complex, involving:

- **Anatomical Aspects:** Structural irregularities such as pelvi-ureteric junction obstruction, horseshoe kidney, and caliceal diverticula can cause urine stasis and increase stone risk (Walsh et al., 2007).
- **Infection:** Urinary tract infections, especially those caused by urease-producing bacteria (e.g., *Proteus*), are strongly linked to the formation of infection (struvite) stones (Assimos, 2009).
- **Metabolic Aspects:** Underlying metabolic abnormalities are crucial. Hypercalciuria (excess urinary calcium) is the most common, categorized as absorptive, renal, or resorptive (Pak, 1994). Hyperoxaluria (excess urinary oxalate), hypomagnesuria, cystinuria, and rare conditions like xanthinuria also contribute to stone formation (Lieske et al., 2017; Goldfarb, 2013).

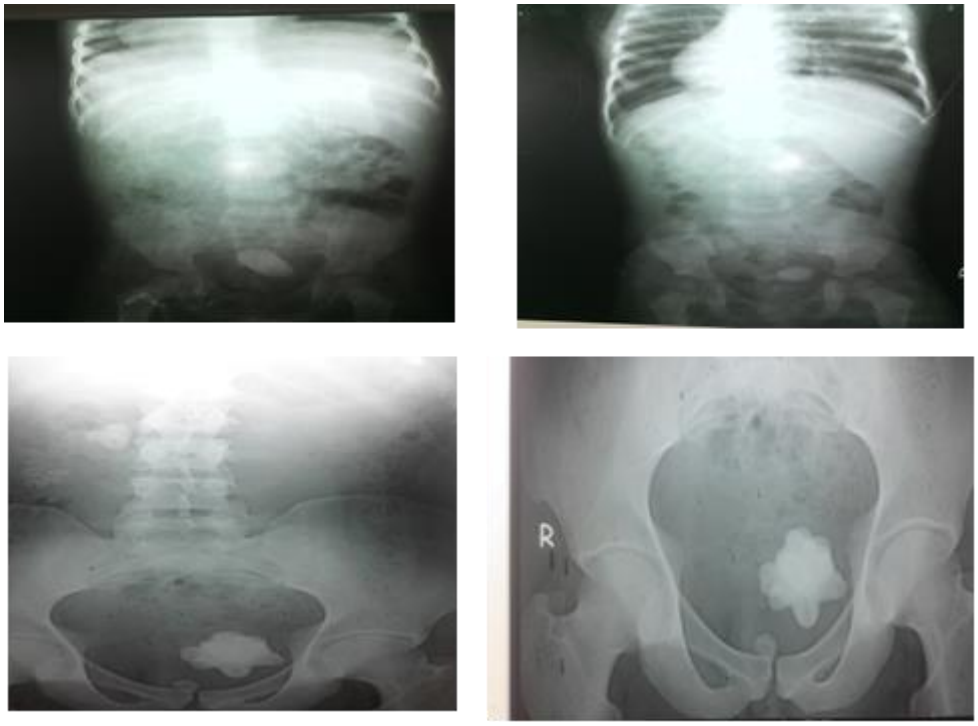
Urinary stones are broadly classified by their chemical composition:

- **Calcium Stones:** The most common, comprising calcium oxalate (monohydrate and dihydrate) and calcium phosphate (apatite, brushite).
- **Non-Calcium Calculi:** Include struvite (infection-related), uric acid (associated with acidic urine), rare cystine, and very rare xanthine stones (Assimos, 2009; Weiner & Wingo, 2004).

Clinical presentations vary, but acute, severe renal colic and flank pain are common (Preminger, 2011). Hematuria and urinary tract infections (with fever and systemic symptoms) are frequent complications. While some stones may be asymptomatic, severe obstruction can lead to calculous anuria and renal dysfunction (Moe, 2006).

Material and Methods

This study included 40 of 120 urolithiasis patients who underwent open stone surgery at Ghulam Muhammad Mahar Medical College / Civil Hospital Khairpur Mir's. Patients, selected based on medical records and relevant investigations, were under 14 years old, with single or multiple stones and functional



renal units.

Diagnosis typically involved plain abdominal X-rays, as shown in **Figure 1**, which illustrates both a large bladder stone in a 6-year-old male and another in a 3-year-old female due to outlet obstruction. CT scans were used for specific cases. Pre-operative assessments, including blood and urine tests, and informed consent were obtained. Following general anesthesia, appropriate open surgical procedures (e.g., pyelolithotomy, cystolithotomy) were performed. The 40 surgically removed stone samples were washed, dried at 60°C, and ground into powder for chemical analysis.

Wet chemical analysis of the 40 stone samples was conducted at the Department of Biochemistry, Shah Abdul Latif University Khairpur Mir's. This manual method relied on color changes and precipitate formation using prepared reagents. Stone powder (50 mg) was first treated with HCl to detect carbonates and then centrifuged to separate supernatant and sediment for further tests. Specific tests were performed to identify the presence of calcium (white precipitate with ammonium oxalate), magnesium (blue/purple precipitate with NaOH and 2,4-dinitrodiphenylamine), ammonium (semisolid layer with NaOH and HgI4), oxalate (CO_2 gas with MnO_4 upon heating), phosphate (blue sediment with ammonium molybdate and halogen salts), uric acid (deep blue color with Na_2CO_3 and sodium tungstate), and cystine (purple-red color with ammonium hydroxide, buffer, sodium sulfite, and sodium nitroprusside).
Statistical analysis was performed using SPSS version 18.0, with chemical constituents, stone location, and age presented as frequencies and percentages.

Results and Discussions

Age and Sex distribution revealed that out of 40 patients (77.5%) were male and (22.5%) female. The minimum age was 1 year and maximum age was 12 years and mean age 4.7 years.

Figure 1. Radiological Imaging of Urinary Calculi. (A) Plain film of abdomen and pelvis showing a large vesical stone in a 6-year-old male. (B) Plain film of urinary calculi in a 3-year-old female due to bladder outlet obstruction. (C) General plain film of abdomen.

Table 1. Age and Sex distribution

Years	Male	Female	Total
1-3	11 27.5%	6 15.0%	17 42.5%
4-6	13 32.5%	3 7.5%	16 40.0%
7-9	3 7.5%	0 0.0%	3 7.5%
10-12	4 10.0%	0 0.0%	4 10.0%
Total	31 (77.5%)	9 (22.5%)	40 (100%)

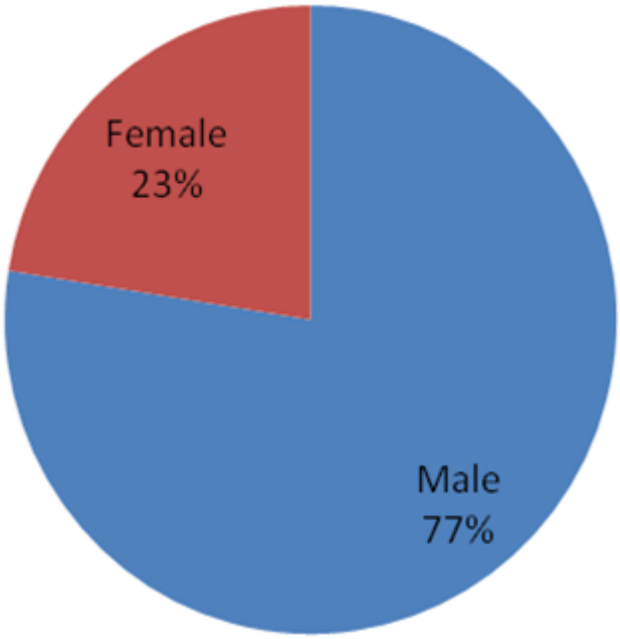


Figure 2. Gender Distribution Graph

Table.2. Showing Anatomical location of urinary calculi out of (n=40) out of total renal 36 (30.0%), vesical 60 (50.0%) , ureteral 15 (12.5%) , uretheral 9 (7.5%).

Table 2. Anatomical location of Stones

Anatomical site	Male	Female	Total
Renal	11 (27.5%)	1 (2.5%)	12 (30.0%)
Vesical	13 (32.5%)	7 (17.5%)	20 (50.0%)
Ureteral	4 (10.0%)	1 (2.5%)	5 (12.5%)
Uretheral	9 (7.5%)	00 (0.0%)	09 (7.5%)

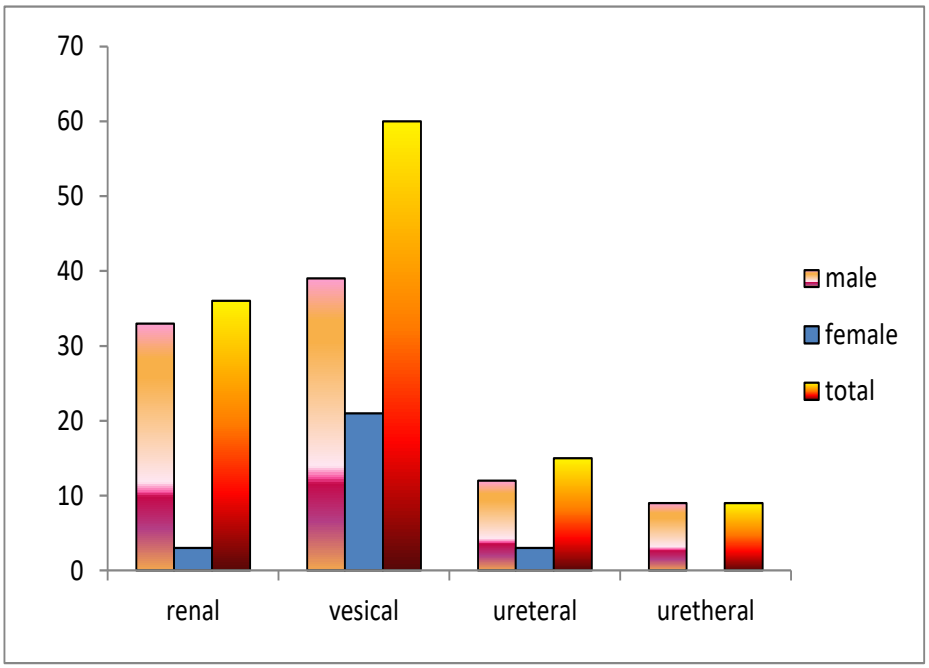


Figure 3. Anatomical location of Stones (Gender Wise)

Table.3 highlights the **clinical presentations of urolithiasis** across 40 pediatric patients, categorized by sex. **Pain** and **dysuria** were the most frequently reported symptoms overall, affecting 77.5% and 75.0% of patients, respectively. Males generally exhibited a higher prevalence of most symptoms, with the notable exception of bladder outlet obstruction, which was slightly more common in females. Calculus anuria was observed exclusively in males (10.0% of total cases).

Table 3. frequency of Symptoms in Patients

Symptoms	Male	Female	Total
Pain	(55.0 %)	(22.5 %)	(77.5 %)
Hematuria	(35.5 %)	(10.0 %)	(45.0 %)
Swelling in the loin	(17.5 %)	(12.5 %)	(30 %)
Dysuria	(60.0 %)	(15.0 %)	(75.0 %)
Bladder outlet obstruction	(12.5 %)	(15.0 %)	(27.5 %)
Calculus anuria	(10.0 %)	(0.0 %)	(10.0 %)
Total	(190 %)	(75 %)	(265 %)

Table.4. Wet chemical analysis of urinary calculi (n=40) and showed calcium 40%, calcium oxalate and uric acid 30% magnesium ammonium phosphate 7.5%, and uric acid 22.5%.

Table 4. Chemical composition of different constituents of childhood Uroliths.

Chemical Composition of Uroliths	Number of Patients	Percentage %
Calcium oxalate	03	7.5%
Calcium phosphate	04	10%
Calcium oxalate phosphate	03	7.5%
Magnesium ammonium phosphate	03	7.5%
Calcium oxalate+Calcium phosphate	06	15%
Calcium oxalate+Uric acid	12	30%
Uric acid	09	22.5%
Total	40	100%

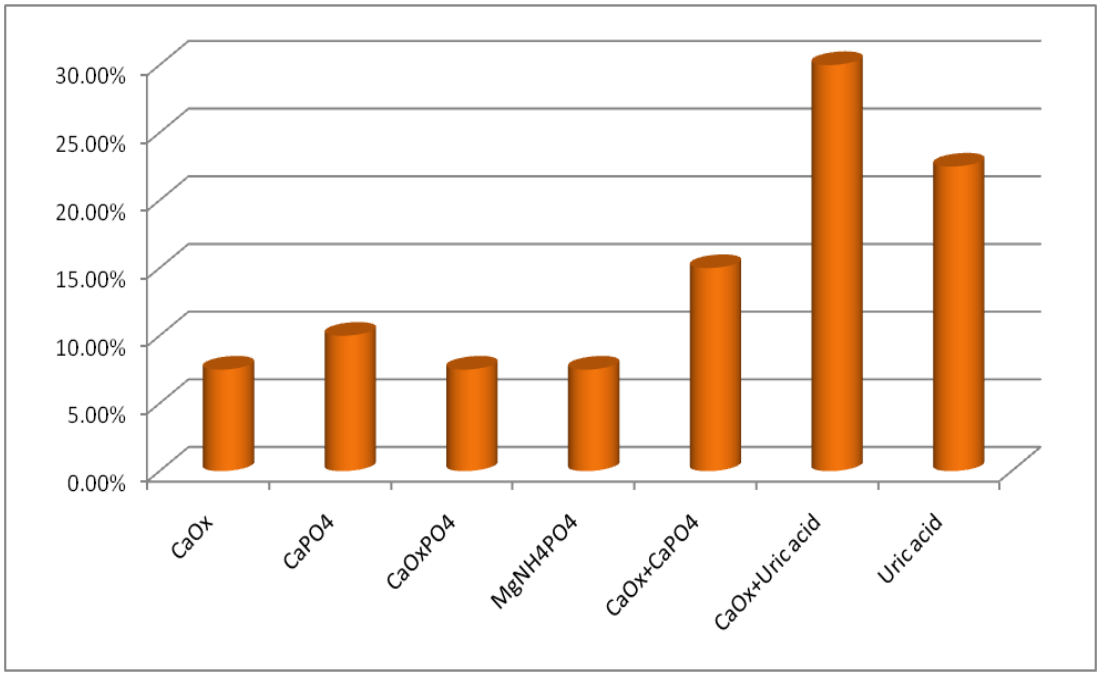


Figure 4. Chemical composition of different constituents of childhood Uroliths.

Discussion: Urolithiasis in children poses a significant burden, with its etiology, presentation, and incidence varying widely based on geographic and economic factors (Rizvi et al., 2011; Turk et al., 2016). In regions like Pakistan, urinary stones remain endemic, particularly in impoverished areas such as Northern Sindh, representing a notable percentage of pediatric urological admissions (Rizvi et al., 2011).

This study, involving 40 pediatric patients, found a marked male predominance (77.5% males, 22.5% females; 3.4:1 ratio), consistent with global trends, although some studies report closer male-to-female ratios (Rizvi et al., 2011; Akman et al., 2003). Patient ages ranged from 1 to 14 years, with a mean of 4.7 years, which is lower than the mean age of 10.16 years reported in some developed regions (Dizdar et al., 2009).

Anatomical locations varied; this study observed a higher prevalence of vesical (bladder) stones (50%), followed by renal (30%), ureteral (12.5%), and urethral (7.5%) calculi. This contrasts with some studies reporting higher upper urinary tract involvement in children (Assimos, 2009). Clinically, pain (77.5%) and dysuria (75%) were the most frequent symptoms, with bladder outlet obstruction and hematuria also common, reflecting the foreign body effect of stones.

Chemical analysis is critical for guiding management and preventing recurrence, given the high recurrence rates (70-80%) (Moe, 2006). This study's analysis of stone composition revealed calcium oxalate (40%) and mixed calcium oxalate + uric acid (30%) as the most common types, aligning with findings from the global "stone belt" (Scales et al., 2012). Magnesium ammonium phosphate (7.5%) and pure uric acid (22.5%) stones were also detected. While calcium and oxalate are common, preventing recurrence emphasizes high fluid intake, reduced intake of oxalate-rich foods, salt, and proteins, and increased citrus juice consumption. Open surgery remains a viable, cost-effective option in resource-limited settings.

Conclusion:

Pediatric urolithiasis remains a significant health challenge in regions like Khairpur Mir's, Pakistan, characterized by a notable male predominance and high incidence of bladder stones. Our findings underscore the critical role of chemical analysis, revealing **calcium oxalate** and **mixed calcium oxalate with uric acid** as the most prevalent stone compositions, consistent with global patterns in stone-prone areas. These results emphasize the need for targeted preventative strategies focusing on dietary modifications and increased fluid intake. Ultimately, understanding the unique epidemiological and compositional profile of pediatric stones in specific geographical contexts is crucial for developing effective diagnostic and therapeutic approaches and reducing recurrence in this vulnerable population.

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