



METABOLIC AND MORPHOLOGICAL ABNORMALITIES OF UROLITHIASIS AMONG AGE GROUP UNDER 18 YEARS: A LITERATURE REVIEW

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ABSTRACT

Pediatric urolithiasis is an important kidney disorder encountered in clinical practice. There has been considerable regional variability in the reported incidences of urolithiasis. The purpose of this review article is to highlight the various aspects of metabolic and morphological abnormalities related to kidney stones in age group less than 18 years. A Medline search was used to identify manuscripts dealing with metabolic and morphological abnormalities portrayed in urolithiasis; most common among the above said abnormalities are; Obstruction of ureteropelvic junction, Ureteral strictures, Horseshoe kidneys, Malrotated kidneys, Narrow calyx neck, Calyx diverticula, Medullary sponge kidney disease, Invasive surgical procedures leading to scar tissue; Metabolic anomalies such as Hypercalciuria, Hypocitraturia, Hyperoxaluria, Hyperuricosuria, Hyperphosphaturia and Cystinuria. The results revealed varying descriptives of metabolic and morphological abnormalities in minor age groups. The body of available literature reveals the gravity of rarely encountered condition pediatric urolithiasis in various regions with debilitating metabolic and morphological abnormalities with idiopathic etiologies and known etiologies; which spearheads further research.

KEYWORDS : Pediatric urolithiasis; metabolic abnormalities; morphological anomalies; Epidemiology

Introduction

Urolithiasis is considered to be one of the most common urological disorders and has afflicted humans since good old generations of human kind. Incidence of nephrolithiasis is more common in certain areas. In Europe, kidney stones occur in 1-2 children per million populations per year. In underdeveloped countries, children more frequently have endemic bladder stones than renal stones. Endemic bladder calculi are common in developing countries where dietary protein is mostly derived from plant sources rather than meat. These areas include Eastern Europe, Southeast Asia, India, and the Middle East. Upper urinary calculi associated with urease-producing bacterial infection occur in England and Europe.

Numerous dietary items may contribute to renal stone production. A high oxalate intake may contribute to calcium oxalate stone production. Excessive purine intake may contribute to the production of stones containing uric acid and uric acid plus calcium components. A ketogenic diet, prescribed to reduce seizures, places children at risk for both uric acid and calcium stone formation. In general, urinary calcium increases with dietary calcium intake. Urinary calcium increases in patients with high sodium chloride intake. Dietary phosphate restriction, if severe, increases urine calcium excretion. A diet high in protein from animal sources, glucose or sucrose increases urinary calcium and, in some cases, may contribute to stone formation. Vitamins A and D can contribute to calcium urolithiasis when taken in excessive amounts. Fructose consumption is also associated with an increased risk of kidney stones.

A study by Pong et al, that investigated the incidence for pediatric urolithiasis in Taiwan from 1998-2007, reported that the trend of annual newly diagnosed incidences for boys, girls, and all children declined. This also coincided with a decline in medical costs and annual medical care visits for pediatric urolithiasis during this period. Children can present with stones at any age (eg, premature newborn to teenager). In children, calcium stones are most common. The approximate frequency of kidney stone types in the pediatric age group is calcium with phosphate or oxalate (57%), struvite (24%), uric acid (8%), cystine (6%), endemic (2%), mixed (2%), and other types (1%). With children, particularly younger children, the primary cause of stone formation (eg, hypercalciuria, hyperuricosuria) can usually be identified with a thorough evaluation.

Materials and Methods

This review article is intended to highlight the various aspects of

metabolic and morphological abnormalities of urolithiasis related to patient's clinical profile with age under 18 years. A Medline search was used to identify manuscripts dealing with specific and relevant metabolic and morphological abnormalities; most common among the above said abnormalities are Obstruction of ureteropelvic junction, Ureteral strictures, Horseshoe kidneys, Malrotated kidneys, Narrow calyx neck, Calyx diverticula, Medullary sponge kidney disease, Invasive surgical procedures leading to scar tissue; Metabolic anomalies such as Hypercalciuria, Hypocitraturia, Hyperoxaluria, Hyperuricosuria, Hyperphosphaturia and Cystinuria. Various search strategies has adopted to unleash the possible available literature in-order to inculcate. We also share our experience on the subject.

Metabolic and morphological abnormalities of urolithiasis

A retrospective review was performed of the records of 85 children with urinary-tract calculi evaluated and treated during a 12-year period. The study evaluated the patients' age, sex, initial complaints, etiology, relevant pathological factors, stone location, mode of treatment, and stone analysis. There were 68 boys and 17 girls, a ratio of 4:1. Patient age ranged from 10 months to 16 years (average 8.2 years). Hypercalciuria was the most common metabolic disorder. Anatomic anomalies and metabolic disorders are of great importance in the etiology of stone disease.

A retrospective study was conducted among 221 patients (113 girls and 108 boys) with urolithiasis to assess the metabolic causes of urolithiasis. Analysis of stone constituents in 122 patients showed the proportion of calcium oxalate (44.7%), calcium phosphate (23.6%), and cystine (8.1%) stones to be similar in all age-groups. Conditions that predisposed to metabolic urolithiasis were identified in 115 patients (52%). Hypercalciuria was confirmed in 49 of 145 patients (33.8%) and hyperoxaluria in 25 of 124 (20.2%). Eight of 96 patients had hyperuricosuria, and 5 of 54 had hypocitraturia. Of 66 patients with structural anomalies of the genitourinary tract, 24 (36%) had metabolic abnormalities and 26 (39%) had chronic infection. Among patients with chronic infection, 29% had metabolic abnormalities. Of the 221 patients, 148 (67%) had two or more stones during a mean follow-up of 59 months. Among 140 patients with 12 months or more of follow-up, metabolic activity was present in 31 (22.1%) at the time of most recent examination. Overall, 166 of 221 children (75.1%) were found to have factors that predisposed to urolithiasis.

A retrospective study conducted to determine the epidemiology, etiology, dietary and urinary risk factors, and the composition of

calculi in pediatric stone formers in Pakistan among 1,440 children. There were anatomical abnormalities in 96 patients (12%), metabolic abnormalities in 206 (25%), infection stones in 60 (7%) and idiopathic stones in 444 (55%). Urinary analysis in idiopathic stone formers revealed hypercalciuria in 17 (11%), hyperoxaluria in 62 (40%), hyperuricosuria in 41 (27%) and hypocitruuria in 97 (63%). Diet involved a low intake of protein in 60 cases (44%), calcium in 45 (33%), potassium in 105 (77%) and high oxalate in 75 (55%). The composition was calcium oxalate in 362 stones (47%), ammonium hydrogen urate in 210 (27%) and struvite in 49 (6.4%).

Hyperuricosuria with or without hypercalciuria amounted to about 23% of the possible cause of urolithiasis. Approximately three fourth of urolithiasis caused by hyperuricosuria was calcium oxalate stones and the rest was uric acid stones. Uric acid is one of the compositions of urinary stones itself, but it has an activity of calcium oxalate stone formation.

An experimental study conducted to assess whether phosphaturia relates to urinary metabolic abnormalities and recurrent stone formation among 1,068 consecutive stone formers and 106 normal controls. Urine values for phosphaturia that were higher than 95% of the normal control values were defined as indicating hyperphosphaturia, and the effect of phosphaturia on urinary metabolites and stone recurrence was determined. This study demonstrates that hyperphosphaturia is closely associated with urinary metabolic abnormalities.

A systematic literature search was performed using MEDLINE, EMBASE, and Cochrane Database of Systematic Reviews from the databases' inception through November 2016. Studies assessing the incidence and types of kidney stones in patients with horse shoe kidney (HSK) were included. A total of 14 observational studies with 943 patients (522 adults and 421 pediatric) with HSK were enrolled. The estimated pooled incidence of kidney stones was 36% (95% confidence interval [CI], 15%–59%) in adults with the HSK. Within reported studies, 89.2% of kidney stones were calcium-based stones (64.2% calcium oxalate [CaOx], 18.8% calcium phosphate [CaP], and 6.2% mixed CaOx/CaP), followed by struvite stones (4.2%), uric acid stones (3.8%), and others (2.8%). Kidney stones are very common in adult patients with HSK with an estimated incidence of 36%. Calcium-based stones are the most prevalent kidney stones in adults with HSKs. These findings may impact the prevention and clinical management of kidney stones in patients with HSK

Conclusion

The global picture of incidence of urolithiasis among age group under 18 years over the last few decade portrays with varying but significant metabolic and morphological abnormalities. The pattern of occurrence of stone disease has also changed, with an increase in kidney stones secondary to multiple known or idiopathic etiologies are at unleashing path. The body of available literature reveals the gravity of rarely encountered condition pediatric urolithiasis in various regions with debilitating abnormalities in concern with metabolic and morphological aspect of the affected; which spearheads further research.

REFERENCES

- Pediatric Urolithiasis: Background, Pathophysiology, Etiology. 2017 Jun 21 [cited 2018 Mar 5]; Available from: <https://emedicine.medscape.com/article/983884-overview>
- Diagnosis and management of hypercalciuria in children : Current Opinion in Pediatrics [Internet]. [cited 2018 Mar 5]. Available from: https://journals.lww.com/co-pediatrics/Abstract/2009/04000/Diagnosis_and_management_of_hypercalciuria_in_n.9.asp
- Reference values for urinary calcium excretion and screening for hypercalciuria in children and adolescents | Springer for Research & Development [Internet]. [cited 2018 Mar 5]. Available from: <https://rd.springer.com/article/10.1007%2FBF00442743?l=rd>
- Ozokutan BH, Küçükaydin M, Gündüz Z, Kabakioğlu M, Okur H, Turan C. Urolithiasis in childhood. *Pediatr Surg Int*. 2000 Jan 1;16(1–2):60–3.
- Idiopathic hypercalciuria: Association with isolated hematuria and risk for urolithiasis in children - *Kidney International* [Internet]. [cited 2018 Mar 5]. Available from: [http://www.kidney-international.org/article/S0085-2538\(15\)34811-0/abstract](http://www.kidney-international.org/article/S0085-2538(15)34811-0/abstract)
- Alon US, Zimmerman H, Alon M. Evaluation and treatment of pediatric idiopathic urolithiasis—revisited. *Pediatr Nephrol*. 2004 May 1;19(5):516–20.
- Division of Nephrology and Hypertension - Primary Hyperoxaluria [Internet]. Mayo Clinic. [cited 2018 Mar 5]. Available from: <http://www.mayo.edu/research/departments-divisions/department-internal-medicine/division-nephrology-hypertension/primary-hyperoxaluria>
- Genetic testing for Hyperoxaluria [Internet]. Blueprint Genetics. [cited 2018 Mar 5]. Available from: <https://blueprintgenetics.com/tests/panels/nephrology/pr-imary-hyperoxaluria-panel/>
- Monico CG, Rossetti S, Belostotsky R, Cogal AG, Herges RM, Seide BM, et al. Primary Hyperoxaluria Type III Gene HOGA1 (Formerly DHDP5L) as a Possible Risk Factor for Idiopathic Calcium Oxalate Urolithiasis. *CJASN*. 2011 Sep 1;6(9):2289–95.
- Milliner DS, Murphy ME. Urolithiasis in Pediatric Patients. *Mayo Clinic Proceedings*. 1993 Mar 1;68(3):241–8.
- Rizvi SAH, Naqvi SAA, Hussain Z, Hashmi A, Hussain M, Zafar MN, et al. Pediatric Urolithiasis: Developing Nation Perspectives. *The Journal of Urology*. 2002 Oct 1;168(4, Part 1):1522–5.
- Sharma AP, Filler G. Epidemiology of pediatric urolithiasis. *Indian J Urol*. 2010;26(4):516–22.
- Koide T. [Hyperuricosuria and urolithiasis]. *Nihon Rinsho*. 1996 Dec;54(12):3273–6. 41
- Grover PK, Ryall RL, Marshall VR. Effect of Urate on Calcium Oxalate Crystallization in Human Urine: Evidence for a Promotory Role of Hyperuricosuria in Urolithiasis. *Clinical Science*. 1990 Jul 1;79(1):9–15.
- Dursun I, Poyrazoglu HM, Dusunel R, Gunduz Z, Gurgoze MK, Demirci D, et al. Pediatric urolithiasis: an 8-year experience of single centre. *Int Urol Nephrol*. 2008 Mar 1;40(1):3–9.
- Hypocitruuria: Overview of Hypocitruuria, Importance of Citrate, Risk Factors in Hypocitruuria. 2017 Sep 20 [cited 2018 Mar 5]; Available from: <https://emedicine.medscape.com/article/444968-overview>
- Zuckerman JM, Assimos DG. Hypocitruuria: Pathophysiology and Medical Management. *Rev Urol*. 2009;11(3):134–44.
- Tekin A, Tekgul S, Atsu N, Sahin A, Ozen H, Bakkaloglu M. A study of the etiology of idiopathic calcium urolithiasis in children: hypocitruuria is the most important risk factor. *The Journal of Urology*. 2000 Jul 1;164(1):162–5.
- VanDervoort K, Wiesen J, Frank R, Vento S, Crosby V, Chandra M, et al. Urolithiasis in Pediatric Patients: A Single Center Study of Incidence, Clinical Presentation and Outcome. *The Journal of Urology*. 2007 Jun 1;177(6):2300–5.