

Incidence and characteristics of kidney stones in patients with horseshoe kidney: A systematic review and meta-analysis

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Abstract

Introduction: The horseshoe kidney (HSK) is the most common type of renal fusion anomaly. The incidence and characteristics of kidney stones in patients with HSK are not well studied. The aim of this meta-analysis was to evaluate the incidence and types of kidney stones in patients with HSK.

Methods: 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 HSK were included. We applied a random-effects model to estimate the incidence of kidney stones. The study protocol was registered with PROSPERO (International Prospective Register of Systematic Reviews; no. CRD42016052037).

Results: 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. Kidney stones were less common in pediatric patients with HSK with an estimated pooled incidence of 3% (95% CI, 2%–5%). The mean age of adult stone formers with HSK was 44.9 ± 6.2 years, and 75% were males. 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%).

Conclusions: 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.

Keywords: Horseshoe kidney, incidence, kidney stones, nephrolithiasis

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INTRODUCTION

Kidney stone disease, also known as nephrolithiasis, is a common problem worldwide,^[1–8] with a prevalence of 7%

in the adults, and $\geq 30\%$ recurrence rate within 10 years.^[1,3,9] The incidence of kidney stones is globally increasing with an estimated prevalence ranging up to 15%.^[10–12] During

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lifetime, approximately 7% of women and 13% of men will develop a kidney stone.^[1,10-12]

Horseshoe kidney (HSK) is the most common abnormality renal fusion anomaly,^[13] estimated to be 1/400–1600 births with the prevalence of 0.25% among the general population.^[14-16] Its developmental abnormalities include the fusion of the lower poles, resulting in abnormal position of the ureter in the renal pelvis, and highly placed ureteropelvic junction.^[17] Impaired drainage of the collecting system and associating ureteropelvic obstruction may predispose the patient to kidney stones.^[14,18-22] Besides, metabolic factors have also been suggested to contribute to stone in patients with HSK.^[15,18,23-25] Nevertheless, unlike the general population, the incidence and characteristics of kidney stones in patients with HSK are not well examined. The objective of this meta-analysis was to evaluate the incidence and types of kidney stones in patients with HSK.

EVIDENCE ACQUISITION

Search strategy

The protocol for this study is registered with PROSPERO (International Prospective Register of Systematic Reviews; no. CRD42016052037). We also followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.^[26] Two investigators (ASP and CI) systematically reviewed the published literature and conference abstracts indexed in MEDLINE, EMBASE, and the Cochrane Databases from database inception through November 2016 without language restrictions, using the terms: “stone” or “nephrolithiasis” combined with “kidney” and “horseshoe”. Other pertinent references were obtained through manual review of these retrieved references.

Inclusion criteria and outcomes

The inclusion criteria were (1) randomized controlled trials (RCTs) or observational studies (case–control, cross-sectional, cohort studies, or case series), (2) both adults and pediatric patient populations with HSK, and (3) data on kidney stones in patients with HSK were provided. Both published studies and conference abstracts were included. Study eligibility was independently determined by the two investigators mentioned earlier. Differing decisions were resolved by joint agreement.

Data extraction

A standardized information collection form was utilized to obtain the resulting data: the first author, study

design, year of publication, country where the study was conveyed, number of patients with HSK kidney studied, number of HSK kidney patients with kidney stones, age and gender of patients with HSK, time of diagnosis of kidney stones, type and location of kidney stones, urine supersaturation profiles, treatment of kidney stones, and outcomes of patients with HSK with kidney stones.

Statistical analysis

MetaXL software (EpiGear International Pty. Ltd., Queensland, Australia)^[27] was utilized for data analysis. The incidence rates and 95% confidence intervals (CIs) of adverse effects were reported using a DerSimonian–Laird random-effects model.^[28] As per our study protocol, a prespecified analysis by adult and pediatric population was performed. A random-effects model was implemented due to the high likelihood of interstudy variances. The Cochran Q-test was completed to appraise statistical heterogeneity. The I^2 statistic was added to evaluate the degree of variation across studies related to heterogeneity instead of chance. An I^2 of 0%–25% represents insignificant heterogeneity, 26%–50% low heterogeneity, 51%–75% moderate heterogeneity, and >75% high heterogeneity.^[29] To assess for publication bias funnel plots were utilized.^[30]

RESULTS

Our search strategy yielded 655 articles. Of these, 607 articles were excluded following the review of their title and abstract based on their relevance and the eligibility criteria. The remaining 48 articles underwent full-length review, and an additional 34 were excluded for failing to meet the criteria (23 articles were excluded because they did not report the outcomes of interest and 11 articles were excluded because they were not observational studies or RCTs).

Fourteen observational studies^[14,15,18-22,24,31-37] with 943 patients (522 adults and 421 pediatric) with HSK met all inclusion criteria and were enrolled for this systematic review and meta-analysis of kidney stones in patients with HSK [Tables 1 and 2]. Figure 1 outlines our search methodology and selection process.

Incidence of kidney stones in patients with horseshoe kidney

Six studies^[14,18-22] evaluated the incidence of kidney stones in patients with HSK as demonstrated in Table 1. The estimated pooled incidence of kidney stones was 36% [95% CI, 15%–59%, $I^2 = 88%$; Figure 2] in adults with HSK. The mean age of adult stone formers with HSK

Table 1: Main characteristics of the observational studies included in the meta-analysis of incidence of stone incidence

	Evans and Resnick ^[18]	Weizer <i>et al.</i> ^[14]	Muttarak and Sriburi ^[19]	Je <i>et al.</i> ^[20]	Yavuz <i>et al.</i> ^[21]	Otay <i>et al.</i> ^[22]
Country	USA	USA	Thailand	USA	Turkey	Saudi Arabia
Year	1981	2003	2012	2015	2015	2016
Total number HSK patients	43	23	14	380	41	144
Number of patients with kidney stones	10	9	11	15	1	25
No of stones	NR	NR	NR	15	NR	NR
Sex of HK patients	NR	16 (69.6%) males, 7 (30.4%) females	12 were men and two were women	198 males, 168 females, and 14 fetuses	22 girls (53.6%) and 19 boys (46.4%)	NR
Sex of HK patients with stone	7/8 patients were men	NR	NR	NR	NR	13 males (62%) and 8 females (38%)
Age of HK patients (years)	NR	42.7 years (range 0-67)	19-74 years (mean age 51.1 years)	Median age, 2.8 years; range, 0-20 years; IQR, 9.7 years	60 (2-192) months	NR
Age of HK patients with stones (years)	38.6 years (range 18-66)		NR	NR	NR	41 years (range 2-78)
Stone location	3 had bilateral diseases	6 kidney; 3 ureter	NR	11 kidney; 4 ureter	NR	52% had stones in the left compartment, whereas 29% had it on the right one and 19% had bilateral renal stones
Stone composition	8 stones analyzed; 3 CaOX, 1 CaP, 2 MgP (infectious), 1 matrix, 1 unknown	5 of 9 CaOX stone composition	NR	NR	NR	NR
Urine supersaturation	6/8 (75%) had metabolic abnormalities; 4 had hypercalciuria	Metabolic abnormality evaluation: 4 (44.4); low urinary volume, 2 hypocitruria, 3 hypercalciuria, 2 hyperuricosuria, 1 hyperoxaluria, 2 calcium oxalate stone composition	NR	NR	NR	NR
Size of stones and treatment	NR	Average stone was 11.2 mm × 14 mm	NR		NR	8 patients with stone size <8 mm (9 patients) were treated expectantly with hydration and alkalization and only one patient required endoscopic intervention; six patients (28.5%) with stone size between 1 cm and <2 cm were treated successfully with SWL with placement of double J stents; 6 patients (28.5%) with stone size of >2 cm were treated successfully with PNL
Outcomes	See below	Obstruction from stones occurred in 7 patients (77.8%). Conservative management was the preferred initial treatment choice for most stone cases in this group, followed by PNL	NR		NR	No significant perioperative complications were encountered after all procedure; indications, method of treatment, and outcome of management of stones associated with HSK are comparable to those with normal kidney morphology. A tailored approach based on stone size is highly recommended

CaOx: Calcium oxalate; CaP: Calcium phosphate; NR: Not reported, SWL: Shock wave lithotripsy, PNL: Percutaneous nephrolithotomy, HSK: Horseshoe kidney, MgP: Matrix gla protein, IQR: Interquartile range

Table 2: Main characteristics of the observational studies with types of kidney stones in patients with horseshoe kidney

	Raj et al. ^[24,31]	Shokeir et al. ^[32]	Miller et al. ^[33]	Ray et al. ^[34]
Country	USA	Egypt	USA	Canada
Year	2004	2004	2008	2010
Total number of patients with HK	37	34	35	41
Number of kidney stones analyzed	24	20	58	31
24 h urine studies	NR	NR	All 16 patients had at least one abnormality (mean 2.94 per patient) with hypercalciuria (81.2%) and low urinary volume (68.8%) being the most commonly identified	NR
Sex of patients with stone	NR	30 were males and 4 were females	29 men and 6 women	25 men/ 16 female
No of stones with each patient single multiple	Multiple mostly (exact number not reported)		NR	
Mean age (years)	49.5 (range 29-76)	41.6±10	55.4 (range 29-84)	52.5±12.1
Stone location	NR		28.6% upper pole; 11.4% interpolar; 74.3% lower pole; 80% renal pelvis	NR
Stone composition	87.5% calcium, 71% CaOx monohydrate stones, 42% CaP, and 33% CaOx dihydrate	50% CaOx, 20% struvite stones, 30% mixed stones	50% CaP (hydroxyl apatite or brushite), 18.2% mixture of CaOx, and 11.4% CaP	26 calcium oxalate monohydrate, 4 calcium dihydrate, 1 CaP
	Skolarikos et al. ^[35]	Wu et al. ^[36]	Ding et al. ^[15]	Blackburne et al. ^[37]
Country	Greece	China	China	USA
Year	2011	2013	2014	2016
Total number of patients with HSK	58	32	16	45
Number of kidney stone analyzed	77	35	16	51
Sex of patients with stone	47 men/11 female	22 male, 10 female	13 male, 3 female	31 male, 14 female
Age of patients with stone	39.9±13.6	38.2 (range 14-72)	42.9±11.6	49.4 (range 23-78)
Stone location	NR	6 staghorn, 9 semi-staghorn, 7 multiple, 6 pelvic, 3 lower pole, 1 interpolar region, 2 upper ureter, 1 semi-staghorn + upper ureter	2 multiple, 9 pelvic, 5 lower pole	NR
Stone composition	63.7% simple stone, 36.2% complex stone, 32.7% staghorn stone	(27/35, 77.1%) CaOx, (4/35, 11.5%) CaP, (2/35, 5.7%) uric acid, (2/35, 5.7%) struvite	9 CaOx monohydrate, 5 CaOx dihydrate, 2 uric acid	27 CaOx stones, 7 apatite, 4 brushite, 3 struvite, 6 uric acid, 3 mixed, 1 dihydroxy adenine

CaOx: Calcium oxalate, CaP: Calcium phosphate, NR: Not reported, HSK: Horseshoe kidney

was 44.9 ± 6.2 years, and 75% were males. Kidney stones were less common in pediatric patients with HSK with an estimated pooled incidence of 3% (95% CI, 2%–5%, $I^2 = 0\%$).

Geographic information was provided in Table 1; 3 studies from the United States and 2 studies from Western Asia and a study from Southeast Asia. Overall, there were no racial preferences. The estimated incidences of kidney stones in adult patients with HSK was 30% (95% CI, 15%–46%; $I^2 = 43\%$) in the United States. Data on the incidence of kidney stones in patients with HSK in other geographical area were limited. The incidence of kidney stones in adult patients with HSK in Asia ranged between 17% and 79%.

Types and locations of kidney stones in patients with horseshoe kidney

Ten studies^[14,15,18,24,31-37] assessed the type of kidney stones in HSK stone formers as shown in Tables 1 and 2. About 89.2% of kidney stones were calcium-based stones (64.2% calcium oxalate [CaOx], 18.8% calcium phosphate [CaP], 6.2% mixed CaOx/CaP), followed by struvite stones (4.2%), uric acid stones (3.8%), and others (2.8%).

Risk factors for kidney stones in patients with horseshoe kidney

This may be owing to ureteropelvic junction obstruction and to the orientation of the calyces, which prevent the passage of the stones.^[15,25,38] Metabolic factors have

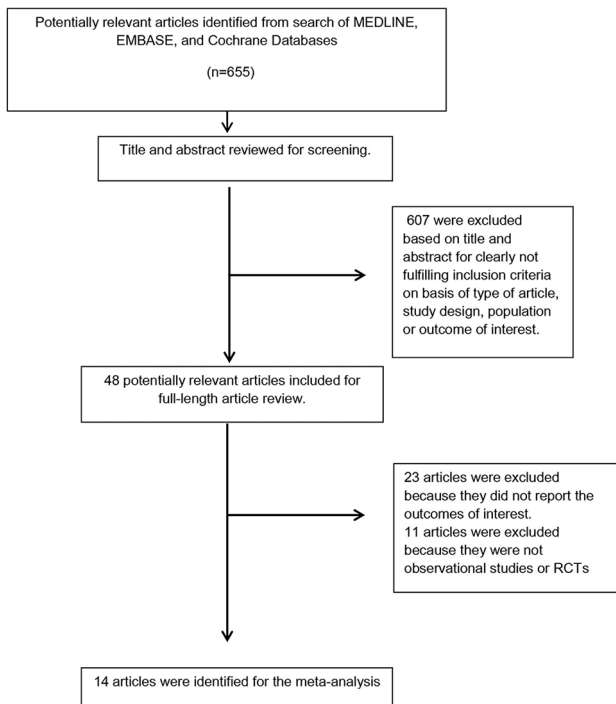


Figure 1: Outline of our search methodology

also been suggested to contribute to stone formation including hyperparathyroidism, low urine volumes, hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia.^[15,18,23-25]

Treatment and outcomes of kidney stones in patients with horseshoe kidney

An HSK is formed by fusion across the midline of two distinct functioning kidneys, connecting at the lower poles by an isthmus, which may prevent the ascent of kidney stones.^[25] Although ureteroscopy (URS) and extracorporeal shock wave lithotripsy (ESWL) are less effective than percutaneous nephrolithotomy (PCNL) for the treatment of kidney stones in patients with HSK, studies have reported successful treatment with URS and/or ESWL, particularly in small (<15–20 mm) calculi.^[15,22] PCNL was used for large stones and required one to four stages to achieve an overall stone clearance rate of >80%.^[25]

Evaluation for publication bias

A funnel plot was not drawn because of the limited number of studies. As a rule of thumb, tests for funnel plot asymmetry should be used only when there are at least ten study groups. Due to limited number of included studies evaluating the incidence of kidney stones in patients with HSK, the power of the test is too low to distinguish chance from real asymmetry.^[39]

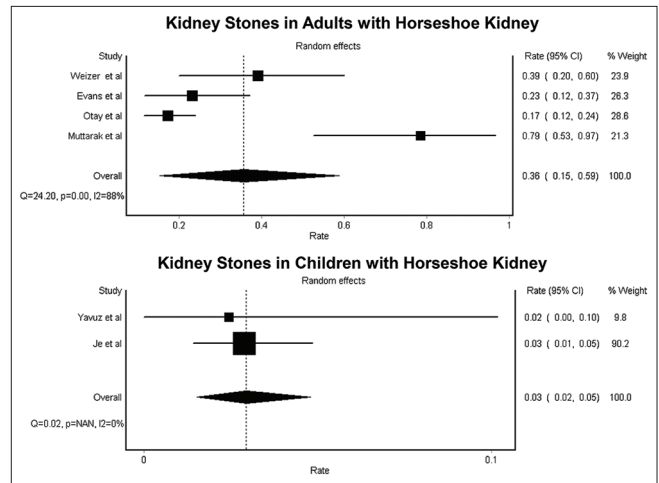


Figure 2: Forest plot of incidence of kidney stones in patients with horseshoe kidney

DISCUSSION

In this study, we showed that an overall incidence of kidney stones in adults with HSK was 36%. Kidney stones were less common in pediatric patients with HSK with an estimated incidence of 3%. The mean age of adult stone formers with HSK was 45 years, and 75% were males. Calcium-based (CaOx and CaP) stones were the most prevalent types of kidney stones in patients with HSK.

The incidence of kidney stones in patients with MSK from our meta-analysis is much higher than reported in the general adult populations.^[10-12] There are several plausible explanations. First, HSK-related abnormal position of the ureter in the renal pelvis and highly placed ureteropelvic junction,^[17] can result in impaired drainage of the collecting system and predispose HSK patient to kidney stones.^[14,18-22] Second, previous studies have demonstrated that metabolic factors including hyperparathyroidism, low urine volumes, hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia^[15,18,23-25] are common in patients with HSK, which may contribute to higher stone formation. Third, the previous reports have demonstrated coexistent HSK with medullary sponge kidney,^[40-42] a known cause of stone disease.^[43]

To date, there have been no available clinical trials comparing the treatment efficacy of URS, ESWL, or PCNL on kidney stones in patients with HSK. PCNL is generally recommended due to anatomical abnormalities and is used for large stones with stone clearance rate of >80%.^[25] However, studies have also shown that URS and ESWL may be effective in small stones.^[15,22]

There are several limitations to our study. First, there were statistical heterogeneities in the analysis of the incidence

of kidney stones in adult HSK patients. The potential sources of this heterogeneity included differences in diagnostic methodology of kidney stones. Second, most included studies were conducted in the United States with the majority of the participants being Caucasian. Therefore, the findings from our study may not represent HSK populations from other parts of the world, and the future studies are required.

CONCLUSIONS

Our meta-analysis demonstrates that kidney stones are common in patients with HSK with estimated incidence of 36%. Kidney stones are prevalent in males with HSK. Calcium-based stones were the most common types of kidney stones in patients with HSK.

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Conflicts of interest

There are no conflicts of interest.

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