

Original Article

The Correlation of Opium Addiction with the Occurrence of Staghorn Renal Stones

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HIGHLIGHTS

- Evaluation of the effect of opiate addiction on the occurrence of staghorn renal stones.
- Higher proportions of men and uneducated persons with staghorn renal stones.
- Nonmedical Opiate addiction could be considered a risk factor for staghorn kidney stones.

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ABSTRACT

Introduction

To evaluate the effect of opiate addiction on the occurrence of the staghorn renal stones.

Methods

In a case-control study from January 2020 to April 2020, sixty-three patients with staghorn renal stones enrolled in our study and compared with the 60 healthy patients. The exclusion criteria were age <18 years, single kidney, renal anomalies, and previous history of malignancy. The primary demographic data, including age, sex, educational status, smoking history, and nonmedical opium utilization, were compared between the two groups.

Results

The incidence of staghorn kidney stones was significantly higher in males than females (45; 71.4 % male vs. 27; 45.0 % P-value=0.003) respectively. There was no significant difference regarding smoking status between the patients with a staghorn kidney stone and the control group (14; 22.2 % vs. 15; 25.0 % P-value=0.717). The prevalence of addiction in patients with staghorn kidney stones was significantly higher than in the control group (30 patients; 46.2% vs. 7 patients; 11.7 %, P-value<0.001). In the case group, fifty patients (79.4%) were undergraduates compared to 28 patients (46.7%) in the control group (P-value<0.001).

Conclusions

Our study represents higher proportions of men and uneducated persons with staghorn renal stones. Nonmedical Opiate addiction could be considered a risk factor for staghorn kidney stones.

Keywords: Urolithiasis; Staghorn Stone; Struvite Stone; Opium Addiction

Introduction

STAGHORN CALCULI FORMED 10-20 % OF ALL RENAL STONES. THEY WERE CATEGORIZED INTO TWO DIFFERENT ENTITIES: PARTIAL STAGHORN, WHICH IS DEFINED AS STONES OCCUPYING THE RENAL PELVIS AND AT LEAST TWO CALYCES, AND COMPLETE STAGHORN WHICH OCCUPIES THE RENAL PELVIS AND ALL CALYCES. THE PRIMARY TYPE OF STAGHORN STONES IS STRUVITE (INFECTIOUS STONE), BUT STONES LIKE URIC ACID AND CYSTEINE COULD RESULT IN STAGHORN STONES (1, 2). STAGHORN RENAL STONES ARE MORE COMMON IN WOMEN THAN THE OTHER RENAL STONES THAT ARE MORE COMMON IN MALE PATIENTS. THE MAIN RISK FACTORS FOR THESE STONES ARE URINARY TRACT INFECTION, STASIS, FEMALE SEX, NEUROGENIC BLADDER DUE TO THE SPINAL CORD INJURY, LONG-TERM URINARY CATHETER, AND RENAL ANOMALIES (3-6). ANECDOTAL REPORTS REGARDING THE FATE OF UNTREATED STRUVITE STONES SHOWED THAT THE STAGHORN STONE COULD RESULT IN SIGNIFICANT MORBIDITY AND MORTALITY (7-10). THE RECENT GUIDELINES ADVOCATED COMPLETE METABOLIC EVALUATION AND PROMPTED STEPWISE MANAGEMENT OF STAGHORN RENAL STONES WITH MINIMALLY INVASIVE SURGERIES LIKE PERCUTANEOUS RENAL SURGERIES (11-13).

ON THE OTHER HAND, RENAL STONES ARE ASSOCIATED WITH PAIN, SO DIFFERENT MEDICATIONS SUCH AS OPIATES ARE PRESCRIBED FOR PAIN CONTROL IN ACUTE STONE EPISODES OR A PERIOPERATIVE SETTING. SUCH MEDICATIONS COULD RESULT IN OPIATE DEPENDENCE. HOWEVER, ONE ASPECT OF CARE THAT HAS NOT BEEN WELL-UNDERSTOOD IS WHAT HAPPENS TO PATIENTS FOLLOWING A STONE EVENT REQUIRING MEDICAL NARCOTIC PRESCRIPTIONS AND EVEN NONMEDICAL OPIUM UTILIZATION (14, 15). OPIATE ADDICTION COULD AFFECT THE RENAL ENVIRONMENT AS IN HEROIN SUBSTANCE USERS, HEROIN NEPHROPATHY WAS REPORTED DUE TO ITS EFFECT ON GLOMERULAR FUNCTION (16, 17). THIS STUDY AIMS TO EVALUATE THE RELATIONSHIP BETWEEN OPIUM ADDICTION AND THE OCCURRENCE OF STAGHORN KIDNEY STONES.

Methods

In a case-control study from January 2020 to April 2020, sixty-three patients with staghorn renal stones enrolled in our study after obtaining written informed consent.

Table 1. Comparing the demographic information between case and control groups

Variable	Groups		P-value
	Case	Control	
Age, mean (SD)	43.7 (14.0)	58.6 (17.3)	< 0.001
Sex (male), number (%)	45 (71.4 %)	27 (45.0 %)	0.003
Education, number (%)			
Under diploma	52 (80.0 %)	28 (46.7 %)	< 0.001
Diploma and higher	13 (20.0 %)	32 (53.3 %)	
Smoker (yes), number (%)	14 (22.2 %)	15 (25.0 %)	0.717
Opium user (yes), number (%)	30 (46.2 %)	7 (11.7 %)	< 0.001

SD: standard deviation

This study was approved by the Tehran University of Medical Sciences ethics committee (IR.TUMS.VCR.REC.1398.1032). A non-contrast abdominopelvic spiral computed scan (CT) was obtained to diagnose staghorn renal stones. The exclusion criteria were age <18 years, single kidney, renal anomalies, previous history of malignancy, and opium dependence before renal stones occurrence. The control group (sixty patients) was selected from the patients referred to ultrasonographic imaging for other causes than renal stones. In the control group, any history of previous renal stones and detection of new renal stones in ultrasound resulted in exclusion from the study. The primary demographic data, including age, sex, educational status, smoking history, and nonmedical opium utilization, were compared between the two groups. The discrete and continuous variables are reported as numbers (percent) and mean (standard deviation). The Chi-Squared test and T-test were used to compare the discrete and continuous variables between the two groups. The logistic regression models were fitted to measure the impact of opium usage on being afflicted by a kidney stone, yielding odds ratios (ORs). The P-value < 0.05 was considered significant.

Results

The case and control groups contained 63 and 60 patients, respectively. The variables are compared between two groups in Table 1. The P-values were obtained through a T-test and Chi-square test for continuous and discrete variables, respectively. Accordingly, there were higher proportions of male, uneducated, and opium-user patients in the case group (staghorn renal stone), while a higher mean age for the control group (58.6 years vs. 43.7 years). The incidence of staghorn kidney stones was significantly higher in males than females (45; 71.4 % male vs. 27; 45.0 % P-value=0.003). There was no significant difference regarding smoking status between the patients with a staghorn kidney stone and the control group (14; 22.2 % vs. 15; 25.0 % P-value=0.717).

The prevalence of addiction in patients with staghorn

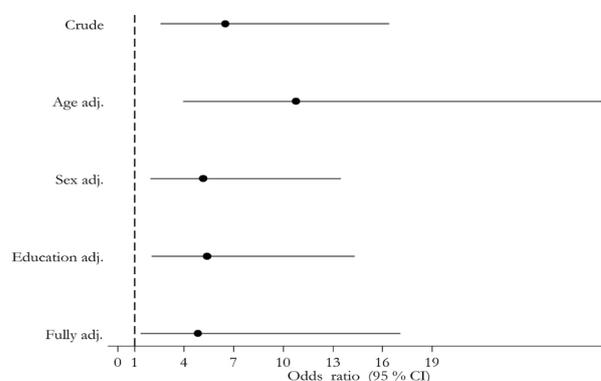


Figure 1. The adjusted logistic regression models

Table 2. Opium usage in strata of sex and education

Variable	Groups		P-value	P-value for comparing strata	
	Control	Case			
Sex, N (%)	Female	1 (3.03 %)	5 (27.8 %)	0.017	0.372
	Male	6 (22.2 %)	25 (53.2 %)	0.009	
Education, N (%)	Under diploma	5 (17.9 %)	26 (50.0 %)	0.008	0.736
	Diploma and higher	2 (6.2 %)	4 (30.8 %)	0.049	

kidney stones was significantly higher than in the control group (30 patients;46.2% vs. 7 patients;11.7 %, P-value<0.001). As presented in Table 1, in the case group fifty-two patients (80%) were undergraduates compared to 28 patients (46.7%) in the control group(P-value<0.001). Moreover, Opium usage was assessed in the strata of sex and education. The findings are presented in Table 2. Both for sex and education, the groups showed significantly different opium usage inside the strata, though there were no differences.

The logistic regression models crudely fitted on opium usage and adjusted for the age, sex, and education covariates. The findings are presented in Figure 1 in ORs (95% confidence intervals).

Discussion

The staghorn renal stone comprised about 10-20 percent of all nephrolithiasis. This type of stone merits special consideration due to the significant morbidity (renal failure) and mortality resulting from sepsis (18-20). A study by Blandy et al., evaluated the overall risk of mortality in sixty patients with staghorn renal stones that were managed conservatively compared to the 125 cases treated with surgery. During ten years of follow-up, the mortality rate was 28 % vs. 7.2% in the non-operatively managed group compared to the interventional group by surgery, respectively (7). The most common staghorn stone is struvite stone which is mainly related to urinary tract infections resulting from urease-producing bacteria such as *Proteus*, *Klebsiella*, and *Pseudomonas* species (21). As we know, staghorn renal stones are more common in the female sex due to the higher incidence of urinary tract infections in this group. At the same time, our study demonstrated a different finding, as the male patients were dominant in the staghorn renal stones group (22, 23). The other risk factors for staghorn stones are urinary tract obstruction, renal anomalies, indwelling urinary catheters, and neurogenic bladder (22, 24). Due to the recurrent episodes of stone formation, patients who have utilized the medical opiate for acute pain control are susceptible to opium dependency. In an interesting study by Ketabchi et al., they compared 450 urolithiasis patients with 340 healthy patients and discovered that opium addiction was more common in urolithiasis patients (34.88% vs.

4.70%; P-value<0.001) (25). Tamadon et al. evaluated the relationship between cigarette smoking and urolithiasis. They compared 102 urolithiasis patients with 121 healthy persons and found that cigarette smoking is a risk factor for nephrolithiasis (26.5% vs. 14.9%; OR=2.06, 95% CI: 1.06-4.01, P-value=0.034) (26). Whereas, in our study, we did not find any difference regarding smoking between the two groups. Nonmedical opioid utilization is a common problem among the different communities; the average rate of opioid abuse is estimated at 5 percent (27). In a study by Novick et al., they assessed 2286 healthy persons regarding opiate and cocaine use .they found that opiate and cocaine use is significantly associated with a decline in renal function and albuminuria (28). Opioid utilization may affect renal function in different ways. The exact mechanism of Renal function impairment is not well-known, but acute and chronic renal damage was reported. The heroin-associated nephropathy is a well-described entity recognized many years ago as focal-segmental glomerular sclerosis (29, 30). The proposed mechanisms that the opioid users may also be susceptible to renal damage are the effect of opium on the renin-angiotensin-aldosterone axis and anti-diuretic hormone that could decline renal blood flow and dehydration. These changes may predispose opiate users to renal stone formation (31). To the best of our knowledge, this study is the first one that evaluated the relationship between nonmedical opiate usage and the occurrence of the staghorn renal stone. According to the obtained statistical data, opioid addiction could be considered a risk factor for staghorn kidney stones. In a study by Saint-Elie et al., regarding the relationship between socioeconomic and educational levels and stone formation, they assessed 99 patients with renal stones. They revealed that most patients had high education levels (62 patients with high vs. 37 patients with low education levels) (32). Although no study examined the relationship between staghorn kidney stones and the level of education, our study revealed lower education levels in this category of stones. We suggest that further studies with a larger sample size should be conducted to strengthen this hypothesis and probably investigate the impact of genetic mutation in the occurrence of staghorn renal stones.

Our study has some limitations, such as the small

sample size and lack of data regarding the effect of cigarette smoking on other types of stones, as we only evaluated the effect of smoking and opiate on staghorn renal stones.

Conclusions

Our study represents higher proportions of male and uneducated persons with staghorn renal stones. Nonmedical Opiate addiction could be considered a risk factor for staghorn kidney stones.

Authors' contributions

All authors contributed equally.

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Conflict of interest

All authors declare that there is no potential competing or conflict of interest.

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Ethics statement

This study was approved by the Tehran University of Medical Sciences ethics committee (IR.TUMS.VCR.REC.1398.1032).

Data availability

Data will be provided on request.

Abbreviations

CT Computed scan
Ors Odds ratios

References

1. Diri A, Diri B. Management of staghorn renal stones. *Renal failure*. 2018;40(1):357-62.
2. Torricelli F, Monga M. Staghorn renal stones: what the urologist needs to know. *International braz j urol*. 2020;46:927-33.
3. Parkhomenko E, De Fazio A, Tran T, Thai J, Blum K, Gupta M. A multi-institutional study of struvite stones: patterns of infection and colonization. *Journal of endourology*. 2017;31(5):533-7.
4. Healy KA, Ogan K. Pathophysiology and management of infectious staghorn calculi. *Urologic Clinics of North America*. 2007;34(3):363-74.
5. Karki N, Leslie SW. Struvite And Triple Phosphate Renal Calculi. 2021.
6. Ebrahimi M, Fakhr Yasseri A, zareian L, Zahmatkesh P, Keshavarz Pakseresht B, Khoshchehreh M, et al. Exciting Impact of Potassium Citrate in The Treatment of Kidney Stones in Rat. *Translational Research in Urology*. 2021:176-81.
7. Blandy JP, Singh M. The case for a more aggressive approach to staghorn stones. *The Journal of urology*. 1976;115(5):505-6.
8. Vargas AD, Bragin SD, Mendez R. Staghorn calculus: its clinical presentation, complications and management. *The Journal of urology*. 1982;127(5):860-2.
9. Teichman JM, Long RD, Hulbert JC. Long-term renal fate and prognosis after staghorn calculus management. *The Journal of urology*. 1995;153(5):1403-7.
10. Jafari Shahdani MR, Fattahi B, Mohseni MG, Aghamir SMK. Comparison of Mini-perc and Retrograde Intrarenal Surgery in Residual Stone Fragments with Hounsfield Unit after Percutaneous Nephrolithotomy. *Translational Research in Urology*. 2021;3(2):40-4.
11. Tzelvel L, Türk C, Skolarikos A. European Association of Urology Urolithiasis Guidelines: Where Are We Going? *European Urology Focus*. 2021;7(1):34-8.
12. Assimos D, Krambeck A, Miller NL, Monga M, Murad MH, Nelson CP, et al. Surgical management of stones: American urological association/endourological society guideline, PART I. *The Journal of urology*. 2016;196(4):1153-60.
13. Aghamir SMK, Salavati A, Hamidi M, FallahNejad A. Primary Report of Totally Tubeless Percutaneous Nephrolithotomy Despite Pelvi-calyceal Perforations. *Urology journal*. 2017;14(4):4020-3.
14. Lightfoot M, Ng C, Engebretsen S, Wallner C, Huang G, Li R, et al. Analgesic use and complications following upper pole access for percutaneous nephrolithotomy. *Journal of endourology*. 2014;28(8):909-14.
15. Mirzaei A, Zendehtdel K, Rashidian H, Aghaii M, Ghahestani SM, Roudgari H. The Impact of OPIUM and Its Derivatives on Cell Apoptosis and Angiogenesis. *Translational Research in Urology*. 2020;2(4):110-7.
16. Mallappallil M, Sabu J, Friedman EA, Salifu M. What do we know about opioids and the kidney? *International journal of molecular sciences*. 2017;18(1):223.
17. Mohseni M, Khazaeli MH, Aghamir SMK, BINIAZ A. Changes in intrarenal resistive index following electromagnetic extracorporeal shock wave lithotripsy. 2007.
18. Rous SN, Turner WR. Retrospective study of 95 patients with staghorn calculus disease. *The Journal of urology*. 1977;118(6):902-4.
19. SINGH M, Chapman R, Tresidder G, BLANDY J. The fate of the unoperated staghorn calculus. *British journal of urology*. 1973;45(6):581-5.
20. Silverman DE, Stamey TA. Management of infection stones: the Stanford experience. *Medicine*. 1983;62(1):44-51.
21. Shafi H, Shahandeh Z, Heidari B, Sedigiani F, Ramaji AA, Pasha YRY, et al. Bacteriological study and structural composition of staghorn stones removed by the anatrohic nephrolithotomic procedure. *Saudi Journal of Kidney Diseases and Transplantation*. 2013;24(2):418.
22. Wall I, Heggren E, Larsson L, Tiselius H-G. Biochemical risk factors in patients with renal staghorn stone disease. *Urology*. 1986;28(5):377-80.
23. Mohammadi A, Nikoobakht MR, Hosseini SR. Urolithiasis in Renal Transplantation Patients: An Update of the Literature. *Transla-*

- tional Research in Urology. 2021;3(4):149-53.
24. Viprakasit DP, Sawyer MD, Herrell SD, Miller NL. Changing composition of staghorn calculi. *The Journal of urology*. 2011;186(6):2285-90.
 25. Ketabchi AA, Ebad-Zadeh MR, Parvaresh S, Moshtaghi-Kashanian GR. Opium dependency in recurrent painful renal lithiasis colic. *Addiction & health*. 2012;4(1-2):73.
 26. Tamadon MR, Nassaji M, Ghorbani R. Cigarette smoking and nephrolithiasis in adult individuals. *Nephro-urology monthly*. 2013;5(1):702.
 27. Wu L-T, Woody GE, Yang C, Blazer DG. Subtypes of nonmedical opioid users: results from the national epidemiologic survey on alcohol and related conditions. *Drug and alcohol dependence*. 2010;112(1-2):69-80.
 28. Novick T, Liu Y, Alvanzo A, Zonderman AB, Evans MK, Crews DC. Lifetime cocaine and opiate use and chronic kidney disease. *American journal of nephrology*. 2016;44(6):447-53.
 29. Dettmeyer RB, Preuß J, Wollersen H, Madea B. Heroin-associated nephropathy. *Expert opinion on drug safety*. 2005;4(1):19-28.
 30. Fakhr Yasseri A, Saatchi M, Abedi Yarandi V. Optimal Time of Ureteral Catheter Removal after Retrograde Intrarenal Surgery. *Translational Research in Urology*. 2021;3(2):54-8.
 31. Ikononov OC, Stoynev AG, Kurtev IV. Effect of morphine withdrawal on food and water intake, urine output and electrolyte excretion in the rat: participation of the renin-aldosterone-system in renal excretory changes. *Acta physiologica Hungarica*. 1984;63(2):137-46.
 32. Saint-Elie DT, Patel PV, Healy KA, Solomon T, Pattaras JG, Qian J, et al. The Impact of Income and Education on Dietary Habits in Stone Formers. *Urology*. 2010;76(2):307-13.

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