JOURNAL OF RADIOGRAPHY AND
RADIATION SCIENCES

PATTERNS AND PREVALENCE OF MICROBIAL AGENTS IN KIDNEY STONE PATIENTS IN A TERTIARY HOSPITAL

[1,2]Amisu M*, [1]Adegboyega O, [1]Sotubo S, [1]Odeyemi A, [3]Okundia K.A
[1]Department of Medicine, Lagos State University College of Medicine, Ikeja, Lagos, Nigeria.
[2]Division of Nephrology Unit, Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria.
[3]University of Lagos.
**Correspondence:* m.amisu06@gmail.com
https://doi.org/10.48153/jrrs/2024/XZBK6083

Article info
First Submission
24th July 2024

Revised
31st July 2024

Accepted
16th October 2024

ABSTRACT

Background: Most often, kidney stones symptoms remain unnoticed until the event of recurrent urosepsis which may inadvertently progress to chronic pyelonephritis which is quite burdensome to manage. The prevalence of infective nephrolithiasis is 7 to 79%. It is not clear whether the relationship between kidney stone formers and uropathogen accounts for this scourge, reciprocally causal or just mutually coincidence. This research thus aims to determine the prevalence of urinary tract infection (UTI) in patients with kidney stones

Methodology: This is a retrospective cross-sectional study of 110 patients referred from the urology and family medicine department of LASUTH conducted between October 2021 to September 2023. Inclusion criteria include all adult patients with abdominal-pelvic ultrasound or CT abdomen evidence of kidney stones who also had positive urine culture results weeks after kidney stone diagnosis. Demographic data, documentation of previous history of kidney stones and UTIs were also inferred. Data collected were analyzed using SPSS 23.0. Risk of UTI is predicted by logistic regression. Power of significance was set at 0.05

Result: One hundred and ten stone formers were screened for data analysis**.** The mean age was 45.6±12.8 with a range of 19 – 78 years, there were more male 58(52.7%) than female 52(47.3%). The commonest stones were calcium oxalate 70.0%, calcium phosphate 15.5% and uric acid 10% respectively. The patterns of microbial infection were *Proteus* 44.4%, *Haemolyticus* 18.5%, *E Coli* 14.8%, *Klebsiella* 14.8% and *Corynebacteria* 7.5%. *Proteus* was significantly associated with uric acid and calcium oxalate stones with P value at 0,01 and 0.03 respectively while uric acid had 37 odds of developing UTI.

Conclusion: This study submitted that calcium oxalate and uric acid stone formers have very high predilection for the event of urinary tract infections. Early detection of the UTI and treatments have direct implication in preventing recurrent UTI which could progress to chronic pyelonephritis.

Keywords: Microbial agent, kidney stone, UTI, infective nephrolithiasis, LASUTH

Introduction

Kidney stones often remain unnoticed until urinary symptoms, such as kidney colicky pains, dysuria, hematuria, or urosepsis. There is a complex clinicopathological relationship between renal stone formers and the occurrence of bacteria urinary infection, a case of proverbial “chicken and egg”. [1] The event of kidney stones and UTIs can co-occur or can be a notable etiology of one another. It is well documented in research how recurrent urosepsis, especially of the upper UTI, promotes and propagates kidney stones. [1,2] However, studies regarding the prevalence of infective nephrolithiasis vary due to the heterogeneity of the stone types that form a nidus for the uropathogens. The prevalence of kidney stones is rising globally likewise its morbid impact is equally on the increase. [2,3] Several factors have been reported to be responsible for the establishment of stones within the kidney cells, among these factors is microbial growth in the urinary tract, a condition commonly referred to as urinary tract infections (UTIs). The development of UTI in patients with kidney stones is an unending paradox and if not properly treated can progress from acute pyelonephritis to chronic pyelonephritis, a more fatal complication form of advanced kidney disease. [4,5] Specifically, urease-forming bacteria such as Staphylococcus, Providencia, Pseudomonas, Klebsiella, and Proteus domiciles in the urinary tract infection have been implicated in adding to the evolution of less common struvite stones(magnesium-ammonium-phosphate). Some other mechanisms have been hypothesized as the possible pathogenesis of UTIs in patients with kidney stones. Uropathogens have been studied to adhere to calculi thereby promoting crystal aggregation, similarly, bacterial colonies may also increase the incorporation of protein into the stone matrix with the subsequent formation of infective nephrolithiasis. Invariably, renal stones usually act as a nidus for bacteria colonies and infection. Other factors documented as part of the pathogenetic mechanism of infected kidney stones include urease-forming bacteria such as Staphylococcus, Providencia, and Pseudomonas. Klebsiella and Proteus domiciles have been implicated in the evolution of less common struvite stones (magnesium-ammonium-phosphate) via a urea-splitting mechanism in which urease released from bacteria metabolize urea into carbon iv oxide and ammonia which then combines with water to form ammonium and hydroxide ions. The resulting ammonium reacts with magnesium, and phosphate under alkaline conditions to form magnesium-ammonium-phosphate stones. [6,7] Another study also reported that bacteria produce an enzyme called citrate lyase which decreases the level of citrate leading to supersaturated urine and the formation of crystals, despite some studies that attempted to establish a link between bacteria and the formation of calcium oxalate and calcium phosphate stones, this unending fraternity remain nebulous. Evidence from some studies showed a positive culture in stones isolated from patients who passed kidney stones. Specifically, a study found 13% to 44% of cultures positive for calcium oxalate stone alone with E. coli while Pseudomonas spp was the most common bacteria isolated from stone cultures followed by the urease splitting bacteria which is implicated in the formation of struvite stones. [8-10] Similarly, a previous study established the isolation and sequencing of similar bacteria from both the bladder urine and stones culture from the same patients, however, the proportion of isolated bacteria varies relatively. [11,12] In an observational study conducted by Holmgren et al at Swedish cottage hospitals, he found out 28% of patients admitted with kidney stones had microscopic urine culture and sensitivity-positive results, in comparison with the general population without kidney stones. He further noted that proper treatment of kidney stones prevents the occurrence of UTI. However, a meta-analysis of the prevalence of UTIs among stone formers ranges between 7% - 79% in studies done in Japan and Pakistan respectively. The prevalence of kidney stones is increasing likewise the development of superimposed UTIs. There have been few cohort studies that show relationships between patients with renal calculi at risk of UTIs. This research therefore seeks to investigate the prevalence and bacterial pattern of subjects presenting with kidney stones.

Methods:

This is a retrospective cross-sectional study of 110 patients sorted by a simple random technique referred from the urology and family medicine department of Lagos State University Teaching Hospital (LASUTH) The approval for the research was granted by the Health Research and Ethical Clearance (HREC). Inclusion criteria include all adult patients with abdominal-pelvic ultrasound and CT abdomen evidence of renal calculi who had urinary microscopic culture and sensitivity-positive results weeks after kidney stone diagnosis. The patient's medical records for stone chemistry results of 24-hour urinary calcium, phosphates oxalates, uric acid, and serum parathyroid hormones were retrieved consecutively. The urine microscopy culture and sensitivity results of positive bacteria growth were documented. A previous history of kidney stones and urosepsis was also inferred. Exclusion criteria comprising patients with DM and UTI. All data collected were entered in MS Excel 2016 and analyzed using SPSS 23.0. 3 The descriptive analysis entailed the calculation of percentages and ratios including tabular and graphical presentations. The inferential statistics was used to determine the chi-square test and draw the relationship between the dependent and independent variables. values <0.05 were considered statistically significant. Logistic regression to determine the odds of urine culture growth.

Results:
A total of one hundred and ten subjects presenting at the Nephrology clinic was used in this study

Table 1: Demographic characteristics of subjects

Variable	Frequency(N=110)	Percentage (%)
	Age group (Years)	
≤40	45	40.9
41 - 60	49	44.6
>60	16	14.5
Range	19 - 78	
Mean SD	45.6±12.8	
	Gender	
Female	52	47.3
Male	58	52.7

The majority of the subjects 49(44.6%) were within the age of 41 to 60 years. The mean age was 45.6±12.8 with a range of 19 – 78 years, there were more male 58(52.7%) than female 52(47.3%).

Table 2: Characteristics of chemistry associated with kidney stone

Variable	Frequency (N=110))	Percentage (%)
	Calcium Oxalate (μmol)	
Normal	33	30.0
High	77	70.0
	Calcium Phosphate (μmol)	
Normal	93	84.5
High	17	15.5
	Uric acid (μmol)	
Normal	99	99.0
High	11	10.0
	Calcium Citrate	
Normal	105	95.5
Abnormal	5	4.5
	Parathyroid Hormone ($Pmol^{-1}$) n=72	
Normal	49	68.1
High	23	31.9
Mean SD	5.6±1.7	

Seventy-seven (70.0%) subjects had Calcium Oxalate stones; As much seventy-two (65.5%) did the Parathyroid Hormone test, with 23(31.9%) presenting with elevated Parathyroid Hormone.

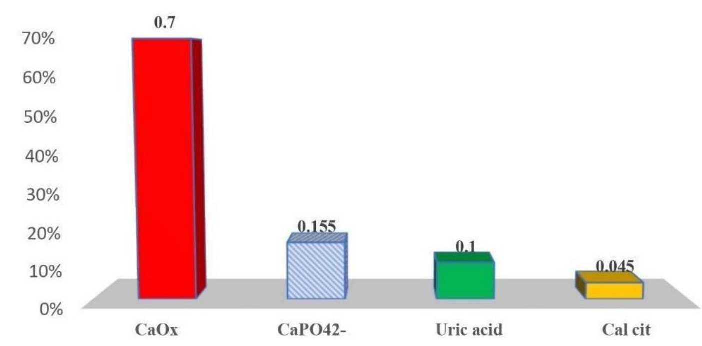

Figure 1: Patterns of kidney stones

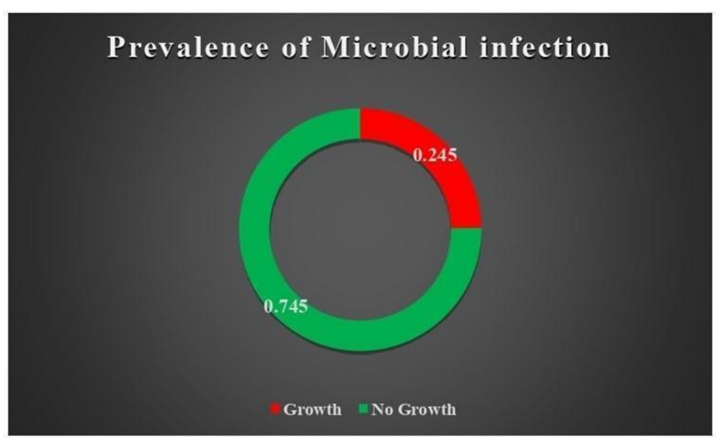

Figure 2: Prevalence of Microbial infection

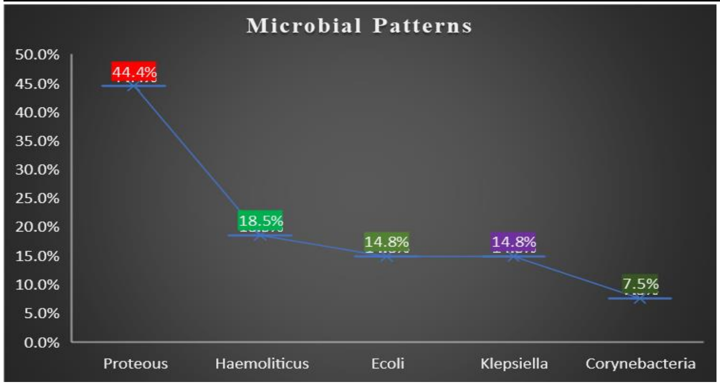

Figure 3: Patterns of Microbial in subjects with Kidney Stone

Table 3: Association between Microbial Patterns and Stone Patterns

Microbial patterns			**X^2**	**P-value**
	Calcium Oxalate		2.513	1.00
	High	**Normal**		
E.coli	1 (100.0)	0 (00.0)		
Haemoliticus	3 (100.0)	0 (00.0)		
Klebsiella	2 (100.0)	0 (00.0)		
Proteus	7 (87.5)	1 (13.5)		
Uric Acid			1.640	.851
	High	**Normal**		
E.coli	0(00.0)	1(100.0)		
Haemoliticus	1(100.0)	0(00.0)		
Klebsiella	1(100.0)	0(00.0)		
Proteus	1(100.0)	0(00.0)		
Calcium Phosphate			5.227	.667
	High	Normal		
E.coli	0(00.0)	1(100.0)		
Haemoliticus	1(100.0)	0(00.)		
Klebsiella	1(100.0)	0(00.0)		
Proteus	2(100.0)	0(00.0)		
	Citrate		2.628	1.00
	High	Normal		
corynebacteria	0(00.0)	1(100.0)		
Ecoli	0(00.0)	1(100.0)		
Proteus	1(100.0)	0(00.0)		

X^2 – Chi square

Table 4: Association between Microbial Infection and Stone Patterns

Microbial status			**X^2**	**P-value**
	Calcium Oxalate		2.513	1.00
	High	Normal		
No growth	64(66.7)	32(33.3)		
Growth	13(92.9)	1(7.1)		
	Uric Acid		1.640	.851
	High	Normal		
No growth	8(7.5)	98(92.5)		
Growth	3(75.0)	1(25.0)		
	Calcium Phosphate		5.227	.667
	High	Normal		
No growth	11(10.6)	93(89.4)		
Growth	6(100.0)	00(00.0)		
	Citrate		2.628	1.00
	High	Normal		
No growth	4(3.7)	103(96.3)		
Growth	1(33.3)	2(66.7)		

X^2= Chi square, *= Statistically significant

Upon adjusting for age as a possible confounder the odds of having no Microbial growth was found to be 83.5(4.266 -1633.3) times significantly higher among subjects with high uric acid stone.

OR=Odd Ratio, AOR=Adjusted Odd Ratio, CI= Confidence Interval, P= P-Value

	Microbial Growth	**P**	**COR (95% C.I)**	**AOR (95% C.I)**	**P**
Uric Acid	Growth	No Growth			
High	3	8	0.03*	36.8(3.418 – 395.2)	83.5(4.266 – 1633.3)
Normal	1	98			

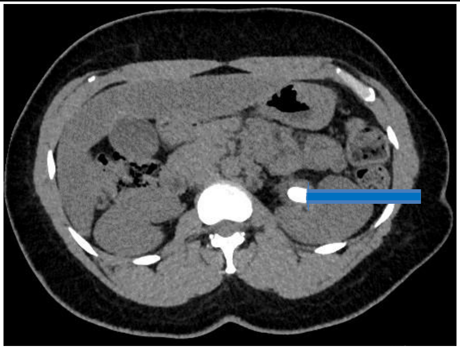

Figure 4: Axial CT scans at the level of 1 L1 & L2 showing an oval dense calculus (HT1020) within the left kidney (see blue arrow). No evidence of obstruction was noted. (Non-Obstructive calculus)

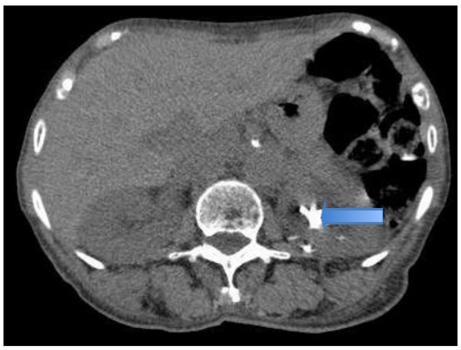

Figure 5: Axial CT of the abdomen at the level of L1/L2 showing irregularly shaped calcific density within the calyceal system of the left kidney. Note the aortic calcific density

Discussion

Our study set out to investigate the microbial patterns and most prevalent bacteria found in patients with renal calculi. Age and gender have a marked influence on the types of stone formed.[13] This epidemiological variation was reported by Lieske 1 JC et al in a study done in the United States of America.[13] In the current study, the majority of the subjects were adults, average age of 45.6±12.8 years this exceeds the mean age submitted by Farshad Kakian, Mohammad Ghasemi Palangi, and Nahal Hadi. Another study done in North West Nigeria reported [14] that the majority of the subjects were in their third decade in age whereas, in the current study most of the subjects were in their fourth decade. [14, 15] As with previous studies, the present research found a male preponderance with a male-to-female ratio of 1.1:1. [5,15, 16] We deduced from our study that the majority of our patients were in the 5th decade and this was thought to be due to late presentations by the studied populations.

Our work showed that calcium oxalate was the most prevalent stone isolated, followed by calcium phosphate and uric acid stones respectively, this is in concordance with another work done in Nepal. [17] Most researchers demonstrated that a significant number of metabolic stones like calcium oxalate, calcium phosphate, or struvite stones were strongly associated with uropathogens which appeared heterogeneous, and this could be related to direct affinity of the bacteria to the renal calculi through different mechanisms. Our study found a significant association between calcium oxalate stones and urinary microbial growth. This finding is similar to research by Barr-Beare E et al where E. coli was noted to selectively aggregate on and around calcium oxalate monohydrate crystals. In the same vein, another study in Iran documented the association between kidney stones and Gram-negative bacilli like E. coli and Klebsiella. [11,14] In the current study, we revealed a statistically significant association between uric acid and subjects with positive urine culture. It was also noted that uric acid stones have about 37-fold affinity for urosepsis when compared to patients with other types of stones. The bacteria cultured on the uric acid stones are proteus, hemolytic, and Klebsiella. Conversely,a study by Ranjilt S et al reported that uric acid stone yielded a culture-positive *Pseudomonas* spp. [17] The literature review attempted to establish a relationship and commonalities between bacterial infections and the development of kidney stones. Although the present study does not find subjects with struvite stones yet urease producing bacteria like *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Morganella* spp, and *Corynebacteria* have been established to be associated with struvite stones, however, the most prevalent bacteria in our research are Proteus spp followed by *Haemoliticus*, E Coli, *Klebsiella* and *Corynebacteria*. In contrast, our finding does not correlate with several studies where E. coli was reported to be the commonest bacteria, [5,14, 15, 17] but, coincidentally, our work is in line with a study conducted in Finland where Proteus species, *Klebsiella*, *Pseudomonas*, and *Corynebacterium* were found to be the commonest bacteria seen in infected kidney stones. [18] Similarly to our study, a comparative study by Holmgren et al [19] among kidney stone formers totaling 1325, the study revealed that urosepsis was seen as most commonly associated with proteus spp but that 7 magnesium ammonium phosphate was the most prevalent stone while oxalate stones were documented among patients without urinary bacteria culture. In the Holmgren et al study, like any other popular work, the study population was larger and the culture media were the expelled urinary stones, unlike the relatively small population size in our study where we cultured the urine. This invariably accounted for the notable differences in outcomes in prevalence and microbial types. This study and previous works have shown that the occurrence of urinary tract infections in patients with kidney stones is quite common and can worsen renal function if not identified early and treated.

Conclusion

The most common stone was calcium oxalate while Proteus mirabilis was the most prevalent bacteria. We demonstrated that there was a significant association between renal stones and urinary tract infections and uric acid was found to be 37 folds significantly high among subjects with positive culture growth.

References

1. Gao H, Lin J, Xiong F, Yu Z, Pan S, Huang Y. Urinary microbial and metabolomic profiles in kidney stone disease. Frontiers in Cellular and Infection Microbiology. 2022:1297. doi: 10.3389/fcimb.2022.953392
2. Geraghty RM, Cook P, Walker V, Somani BK. Evaluation of the economic burden of kidney stone disease in the UK: a retrospective cohort study with a mean follow-up of 19 years. BJU international. 2020 Apr;125(4):586-94. DOI: 10.1111/bju.14991
3. Antonelli JA, Maalouf NM, Pearle MS, Lotan Y. Use of the National Health and Nutrition Examination Survey to calculate the impact of obesity and diabetes on cost and prevalence of urolithiasis in 2030. European urology. 2014 Oct 1;66(4):724-9. DOI: 10.1016/j.eururo.2014.06.036
4. Scales Jr CD, Smith AC, Hanley JM, Saigal CS, Urologic Diseases in America Project. Prevalence of kidney stones in the United States. European urology. 2012 Jul 1;62(1):160-5. DOI: 10.1016/j.eururo.2012.03.052
5. Schwaderer AL, Wolfe AJ. The association between bacteria and urinary stones. Annals of translational medicine. 2017 Jan;5(2). DOI: 10.21037/atm.2016.11.73
6. Flannigan R, Choy WH, Chew B, Lange D. Renal struvite stones—pathogenesis, microbiology, and management strategies. Nature reviews Urology. 2014 Jun;11(6):333-41. DOI: 10.1038/nrurol.2014.99
7. Marien T, Miller NL. Treatment of the infected stone. Urol Clin North Am. 2015;42(4):459–72. DOI: 10.1016/j.ucl.2015.05.009
8. Tavichakorntrakool R, Prasongwattana V, Sungkeeree S, Saisud P, Sribenjalux P, Pimratana C, Bovornpadungkitti S, Sriboonlue P, Thongboonkerd V. Extensive characterizations of bacteria isolated from catheterized urine and stone matrices in patients with nephrolithiasis. Nephrology Dialysis Transplantation. 2012 Nov 1;27(11):4125-30. DOI: 10.1093/ndt/gfs057
9. Thompson RB, Stamey TA. Bacteriology of infected stones. Urology. 1973 Dec 1;2(6):627-33. DOI: 10.1016/0090-4295(73)90323-3
10. Golechha S, Solanki A. Bacteriology and chemical composition of renal calculi accompanying urinary tract infection. Indian Journal of Urology. 2001 Jan 1;17(2):111. DOI:10.4103/0970-1591.21038
11. Barr-Beare E, Saxena V, Hilt EE, et al. The Interaction between Enterobacteriaceae and Calcium Oxalate Deposits. PLoS One 2015;10: e0139575. https://doi.org/10.1371/journal.pone.0139575
12. De Ferrari ME, Macaluso M, Brunati C, et al. Hypocitraturia and Ureaplasma urealyticum urinary tract infection in patients with idiopathic calcium nephrolithiasis. Nephrol

Dial Transplant 1996; 11:1185. DOI: 10.1093/oxfordjournals.ndt.a027486

13. Lieske JC, Rule AD, Krambeck AE, Williams JC, Bergstralh EJ, Mehta RA, Moyer TP. Stone composition as a function of age and sex. Clinical journal of the American Society of Nephrology: CJASN. 2014 Dec 12;9(12):2141. DOI: 10.2215/CJN.05660614
14. Kakian F, Ghasemi Palangi M, Hadi N. Epidemiology of kidney stone and bacterial strains with antibiotic resistance in Shiraz, southwest of Iran, 2014-2019. International Journal of Epidemiology and Health Sciences. 2021 Mar 1;2(3). http//doi.org/10.51757/IJEHS.2.3.2021.47993
15. Aji SA, Alhassan SU, Mohammad AM, Mashi SA. Urinary Stone Disease in Kano, North Western Nigeria. Nigerian Medical Journal. 2011 Apr 1;52(2).
16. Ekeke ON, Okpani CP. Management of urinary stone disease in a resource limited tertiary hospital. IOSR Journal of Dental and Medical Sciences. 2018; 17:38-45.
17. Ranjit S, Singh AK. Bacteriological profile of urine in patients with different types of kidney stones in a tertiary care hospital: A descriptive cross-sectional study. JNMA: Journal of the Nepal Medical Association. 2020 Nov;58(231):871. DOI: 10.31729/jnma.5226
18. Çiftçioglu N, Björklund M, Kuorikoski K, Bergström K, Kajander EO. Nanobacteria: an infectious cause for kidney stone formation. Kidney international. 1999 Nov 1;56(5):1893-8. DOI: 10.1046/j.1523-1755.1999.00755.x
19. Holmgren K, Danielson BG, Fellström B, Ljunghall S, Niklasson F, Wikström B. The relation between urinary tract infections and stone composition in renal stone formers. Scand J Urol Nephrol. 1989;23(2):131-6. https://doi.org/10.3109/00365598909180827