The Significance of Asymptomatic Kidney Stones as a Predictive Factor for Sepsis in Critically Ill Older Adults

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Objective: The objective of this study was to investigate the impact of kidney stones (KSs) on critically ill older adults (CIOA) staying longer than 24 hours in the ICU. Sepsis is one of the leading causes of mortality for ICU patients. KS disease is a well-known risk factor for bacteriuria and urinary tract infection.

Methods: A total of 256 CIOA were initially evaluated from April 2017 through February 2019. Patients who had urinary ultrasonography and computed tomography within 12 months prior to ICU admission were included. Patients with an additional urological pathology, under the age of 65 years, and with ICU stays of 24 hours or less were excluded. Consequently, 151 patients were eligible and constituted the study group. These patients were divided into 2 subgroups, according to the presence or absence of KSs. These 2 groups were compared with regard to urine culture (UC) results, presence of urosepsis, and septic shock.

Results: The mean age was 80.66 (±7.76) years. There were 18 patients with KSs and 133 without KSs. A total of 71 patients had a positive UC. Repeat UC positivity ($p = 0.002$) and resistant microorganisms ($p = 0.034$) were significantly more frequent in the KS group. The incidences of both urosepsis ($p<0.001$) and septic shock ($p<0.001$) were also significantly higher in patients with KSs.

Conclusion: The presence of KSs in CIOA is frequently associated with urosepsis and septic shock. Large prospective trials are required to evaluate the impact of KSs on the prognosis of patients in the ICU. [*P R Health Sci J 2021;40:33-37*]

Key words: Kidney stones, Urinary tract infection, Critically ill, Older adults, Intensive care unit, Sepsis

Kidney stones (KSs) are one of the most prominent disorders among urinary diseases (1,2). The prevalence and recurrence rates of KSs have been increasing significantly over the last few decades (3). It has been reported that 10 to 12% of the general population have a urinary stone in their lifetime (4,5). Moreover, a recent study reported that the overall prevalence peaked at 19.4% in 60- to 69-year-old adults (6). It was also proposed that the incidence of these stones is rising more quickly in older adults (7,8). Pain is the major symptom in urinary tract stone disease. Whereas many patients with KS have no symptoms. Also, follow-up is a reasonable option for certain patients without symptoms and urinary obstruction (2,4,8). On the other hand, the presence of KSs is a well-known risk for bacteriuria and urinary tract infection (UTI) (9). Moreover, the causative pathogen of sepsis is identified by stone culture but not by urine culture (UC), in certain cases (9). Therefore, the detection of KSs may be a prognostic factor for sepsis for patients in the intensive care unit (ICU).

It is a well-known fact that patients admitted to the ICU already have a tendency to develop infections. Most patients admitted to ICUs require an indwelling urinary catheter to monitor urinary output. Catheter-associated UTIs are among the most common healthcare-associated infections (10). Approximately 16% of critically ill patients experienced urosepsis during their ICU stay (11,12). Older adults (typically defined as individuals 65 years of age and older) are at a higher risk of infection due to age-related changes, and consequently, UTIs are highly prevalent in older adults (13). There is also a significant relationship between nosocomial infections in critically ill older adults (CIOA) and prolonged length of stay (LOS) with increased morbidity and mortality

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(14). However, there are no conclusive data on the significance of KSs as a risk factor for sepsis in CIOA whose LOSs exceed 24 hours.

The objective of this study was to address the impact of KSs on the development of sepsis in CIOA.

Materials and Methods

Study population

A total of 256 patients, hospitalized from April 2017 through February 2019 in a tertiary reference hospital, were initially evaluated in the study; all the patients had ICU stays of 24 hours or longer. The study was performed in accordance with the Helsinki Declaration and approved by the local ethical committee (approved protocol number: 2019/09). The hospital records of all these patients were reviewed retrospectively. Patients who had both urinary ultrasonography (US) and computed tomography (CT) performed in the last 12 months were included in the study. The exclusion criteria excluded patients who had an additional urological pathology (ureter or bladder stone, hydronephrosis, upper urinary tract obstruction, atrophic kidney, known urological malignancy, known neurogenic bladder dysfunction), were under the age of 65 years, and had an ICU stay of 24 hours or less. All the patients included in this study had urinary catheters during their ICU stays.

Each patient's demographics (age, sex), primary diagnosis at ICU admission (acute respiratory failure, acute renal failure, sepsis, acute neurological disorders, trauma), UC results, and repeat positive UC results during his or her ICU stay were recorded; also noted for all the patients were the microorganisms responsible for UTIs (when present), the presence of resistant microorganisms (extended spectrum β-lactamase-producing *Klebsiella pneumoniae* and *E coli*, carbapenem-resistant *Enterobacteriaceae*, multidrug-resistant *Pseudomonas aeruginosa*, and multidrug-resistant *Acinetobacter baumannii*), mortality rates, and ICU LOSs. In addition, US and abdominal CT records of the patients in the year prior to ICU admission or during the ICU stay were re-investigated for the presence of KSs. The date, localization, and size of each patient's KS were also recorded. Sepsis and septic shock were evaluated according to the third international consensus definitions for sepsis and septic shock (sepsis-3) (15). Accordingly, sepsis is defined as a life-threatening organ dysfunction caused by a deregulated host response to infection. Organ dysfunction can be identified as an acute change (≥2 points) in the total sepsis-related organ failure (caused by infection) assessment score and septic shock (defined as hypotension requiring the use of vasopressors to maintain a mean arterial pressure greater than or equal to 65 mm Hg), as well as having serum lactate levels higher than 2 mmol/L, despite adequate volume resuscitation.

The included patients were then divided into 2 groups, according to the presence or absence of KS disease. We analyzed the effect of KSs on the UTIs, urinary tract–originated sepsis, and septic shock in these groups.

Statistical analysis

The statistical analysis was performed using SPSS version 20.0 (SPSS Inc. Chicago, IL, USA). The LOSs in the ICU and the ages of the patients were summarized by means (±SD). Comparisons of the patient groups (defined based on the presence of KS disease) were assessed by the Mann–Whitney U-test. Rates of UC positivity, urinary tract–originated sepsis, septic shock during an ICU stay, and mortality, as well as the sexes of the different patients were summarized using percentages. A chi-square test or Fisher's exact test was used to assess the differences between the rates of these groups. A p value less than 0.05 was considered statistically significant.

Results

In total, 256 individuals were initially evaluated, as they were hospitalized patients in the ICU. However, 54 patients were excluded due to their not having any radiologic imaging for KSs performed during the year prior to their ICU admissions or during their ICU stays. Furthermore, 19 patients with known urological disorders were excluded. Moreover, 17 cases who were younger than 65 years and 15 patients with short (24 hours or less) ICU stays were also omitted. The remaining 151 patients fulfilled the inclusion criteria and constituted the study group. Of these, 73 (48.3%) were male and 78 (51.7%) were female. The mean (±SD) age of the patients was 80.66 (±7.76) years. The primary reasons for ICU admission were acute respiratory failure (35.8%), acute kidney injury (16.6%), and malignancy (12.6%). The primary diagnoses at the ICU admission, radiological imaging methods, and microorganisms in positive UCs of the patients are presented in Table 1.

There were 18 patients in the first group (with KSs) and 133 patients in the second group (without KSs). In the first group, 3 patients had bilateral kidney stones, 9 had right-sided kidney stones and 6 had left-sided kidney stones. The mean size of kidney stones was 5.75 (±4.28) mm (2–15 mm) on the right-side, 6.33 (±4.89) mm (2–18 mm) on the left. Regarding the patients with right-sided KSs, 6 (50%) patients had lower-pole stones, 5 (42%) had middle-pole stones, and 1 (8%) had an upper-pole stone. Regarding the patients with left-sided KSs, 5 (55.5%) patients had lower-pole stones, 2 (22.2%) had middle-pole stones, 1 (11.1%) had an upper-pole stone, and 1 (11.1%) had stones in multiple poles.

A total of 71 patients had positive UC results during their ICU stays. *Candida* was the cause of urinary infections in the majority of the cases (33.8%), followed by *E coli* (29.6%) and *Enterococcus spp*. (12.7%). Subsequently, the most common microorganism found in the urine samples of patients without KS disease was *Candida* (35.6%; n = 21), while *E coli* (33.3%; n = 4) was the most common microorganism found in the urine samples of patients with KS disease.

The comparison of the mean ages of the patients in the first and second groups revealed similar results, those means being 82.67 (±6.99) and 80.38 (±7.85) years, respectively.

Table 1. The primary diagnoses at ICU admission, radiological imaging methods, and microorganisms in positive urine cultures, of all patients

	n (%)
Primary diagnosis	
Acute respiratory failure	54 (35.8)
Acute renal failure	25 (16.6)
Malignancy	19 (12.6)
Sepsis	15 (9.9)
Acute neurologic disorder	14 (9.3)
Trauma	11 (7.3)
Post-operative	4 (2.6)
Gastrointestinal bleeding	4 (2.6)
Acute coronary syndrome	4 (2.6)
Diabetic ketoacidosis	1 (0.7)
Radiological imaging method	
Urinary US	64 (42.4)
Abdominal CT	54 (35.8)
Both (urinary US and abdominal CT)	33 (21.9)
Microorganism in positive urine culture	
Candida spp.	24 (33.8)
Escherichia coli	21 (29.6)
Enterococcus	9 (12.7)
Pseudomonas aeruginosa	7 (9.9)
Klebsiella pneumonia	4 (5.6)
Acinetobacter baumannii	3 (4.2)
Citrobacter freundii	1 (1.4)
Burkholderia cepacia	1 (1.4)
Staphylococcus hominis	1 (1.4)

US: ultrasonography, CT: computed tomography

Just over half of the patients in the second group (without KS disease) were women (54.9% vs. 27.8%; p = 0.031). While the frequency of UC positivity was similar between the 2 groups (p = 0.086), repeat UC positivity (p = 0.002) and resistant pathogen related UTIs (p = 0.034) were significantly more frequent in the group with KSs. Urosepsis (p<0.001) and septic shock (p<0.001) also were significantly more common in patients with KS disease than in those without. Addiotinally, the mean length of ICU stay did not differ between the 2 groups (18.41±23.34 vs. 21.72±21.12 days; p = 0.355). Similarly, the overall ICU mortality rates were also similar between the 2 groups (39.1% vs. 27.8%; p = 0.352) (Table 2).

Discussion

The rates of admission of older patients (≥65 years) to the ICU have increased, with these patients now making up almost half of all ICU admissions (16). There is certainly a need for improved mortality predictions for patients in the ICU, although a different variety of severity scores has been proposed (17). The presence or absence of KSs could provide a new marker for predicting sepsis rates and possibly be included in prediction algorithms for patients in the ICU. KS is a common problem in the general population, and its prevalence has been reported to be as high as 14.8% (4). Moreover, it is shown that the incidence of KS disease has been increasing over the past 50 years, having nearly doubled in the past 15 years in the general population (4,7,18,19). Kittanamongkolchai et al. revealed that the incidence of stones is rising more rapidly in older adults than younger ones (8). In parallel with this, a study by Huang et al. reported a peak prevalence of 34.7% in the 60- to 69 year-old adults who took part in their population-based study (6). A recent cohort study by Cone et al. revealed that older adults (≥65 years) constituted 32% of inpatient care for urinary stone disease (20). In the present study, the incidence of KSs was 11.9% in CIOA. Although past studies suggested that KS was more common in men than in woman, a newer study revealed a decline in the male-to-female ratio (from 3.1 to 1.3) for KSs, which decline took place from 1970 through 2000 (21). Huang et al. found a higher prevalence of nephrolithiasis in men than in women (9.0% vs 5.8%) and more frequent recurrence rates in men than in women (6). Another Asian population–based study reported higher prevalence rates in men than in women (6.0% vs 1.8%) (22). Similar to these eastern population–based studies, in our study, 72.2% of group 2 were male. Nevertheless, all these epidemiological studies suggest that KS disease is a rather common problem for both sexes, and about 10% of older patients in the ICU suffer from KSs.

A potential major clinical consequence of KSs is a UTI. Additionally, chronic bacteriuria has also been reported to be associated with KSs (23). Hugosson et al. also reported that the majority of the stones in their patients were small, with a maximum diameter of 12 mm. They also observed that almost all the patients (20 out of 23 patients) had no infection after stone surgery. In the remaining 3 patients (who did have bacteriuria after stone removal), a residual stone smaller than 3 mm remained. Therefore, small KSs may also be a risk factor for a UTI. In this study, the maximum stone diameter was found to be 18 mm, and the mean stone size was 5.75 (±4.28) mm in the right kidney and 6.33 (±4.89) mm in the left kidney. The current trial also supports the notion that small stones

Table 2. Comparison of the groups according to presence of kidney stone

	Group I: Patients without kidney stones; n = 133 (88.1%)	Group II: Patients with kidney stones; n = 18 (11.9%)	p
Demographics			
Age (years), median (min–max)	80.0 (65–102)	83.5 (68–94)	0.184
Female, n (%)	73 (54.9)	5 (27.8)	0.031*
Urine culture positivity, n (%)	60 (45.1)	12 (66.7)	0.086
Repeat culture positivity, n (%)	12 (9)	7 (38.9)	0.002*
RB in urine culture, n (%)	17 (12.8)	6 (33.3)	0.034*
Urosepsis, n (%)	17 (12.8)	11 (61.1)	<0.001*
Septic shock, n (%)	11 (8.3)	8 (44.4)	<0.001*
ICU LOS (days), median (min–max)	9.0 (1.0–115.0)	18.5 (1.0–82.0)	0.355
Mortality rates, n (%)	52 (39.1)	5 (27.8)	0.352

RB: resistant bacteria; ICU: intensive care unit; LOS: length of stay. *p<0.05

may also be associated with a UTI. Similarly, in a larger study of 120 patients with non-obstructive, asymptomatic KSs and recurrent UTIs, 52% of the patients were reported to have experienced no recurrence of infection after kidney stone removal (24). In the same study, African-American ethnicity, hypertension, and diabetes mellitus (in male patients) have been shown to be associated with recurrent UTI. Similarly, in our study, the male gender (72.2%) was higher in the UTI group. In conclusion all these studies propose that KSs are a risk factor for recurrent UTI.

It is known that UTI is one of the predominant healthcare-associated infections in ICUs (25). In most UTI cases, urethral catheters are what cause this infection. It has also been shown that KSs and increased age are additional, internal risk factors for these catheter-associated UTIs (26). Furthermore, it has been proposed that infection in patients with pre-existing stone disease can lead to life-threatening scenarios, such as sepsis and septic shock (27). It was estimated that these "stone formers" had an infection prevalence of approximately 79% and that the most frequently isolated microorganisms from the urine samples of these patients were gram-negative bacterial species (28). We also documented the fact that gram-negative bacteria species were the most common microorganisms (58.3%; n = 7) in the UCs of patients with KSs in our study. Similarly, Tavichakorntrakool et al. found *E coli* to be the most common microorganism in the UCs of this group's patients with KSs (29). We also observed that recurrent UTI was more common in CIOA with KSs. Additionally, antimicrobial resistance has been frequently observed in bacteria isolated from stone formers with UTIs, in previous studies (29). Similar to these studies, from a total of 9 (excluding 3 *Candida spp*. isolates) bacterial isolates detected in the catheterized urine samples of our study patients with KSs, 6 (66.6%) had antimicrobial resistance (mostly to multiple drugs). Therefore, it may be concluded that multi-drug resistant bacteria led to more frequent (statistically significant) urosepsis and septic shock events in older critically ill KS disease patients in the present study. However, despite the increase of urosepsis and septic shock events in patients with KSs, mortality rates and mean ICU LOSs did not differ between groups. Previously, Chant et al. concluded that when adjustments were made for other prognostic factors in critically ill adults, UTI was not associated with increased mortality; instead, the higher mortality rate appeared to be the result of confounding, unmeasured variables in their systematic meta-analysis (30). However, we suggest that the overall mortality in this cohort study was relatively low and therefore it did not meaningfully influence the results.

This study has some limitations. The first issue is that this was a retrospective trial. Some patients had no abdominal imaging performed at the time of hospitalization in the ICU, because such imaging had not been deemed necessary. Therefore, only those patients with abdominal imaging performed during the 12 months before their ICU admission or during their ICU stay were included. Therefore, the total number of patients in each group remains rather small. In addition, the mortality rate is too small to reach definitive conclusions in terms of mortality risk.

In conclusion, our present study indicates that even small asymptomatic KSs constitute a risk factor for CIOA, since the prevalences of both recurrent UTI and antimicrobial resistance are remarkably high in older critically ill patients with KSs. Consequently, these patients more frequently suffer from urosepsis and/or septic shock events. However, large prospective trials are required to document the exact significance, in terms of mortality rates, of KSs in CIOA.

Resumen

Objetivo: El objetivo de este estudio fue investigar el impacto de la presencia de cálculos renales (CR) en adultos mayores en estado crítico (AMEC) con estadías de más de 24 horas en la unidad de cuidados intensivos (UCI). La sepsis es una de las principales causas de mortalidad para pacientes en la UCI. La presencia de CR es un riesgo bien conocido de bacteriuria e infección del tracto urinario. Métodos: Se evaluaron inicialmente un total de 256 AMEC entre abril de 2017 y febrero de 2019. Se incluyeron pacientes con ecografía urinaria y tomografía computarizada en los últimos doce meses. Se excluyeron los pacientes con patología urológica adicional, menores de 65 años y estadías en la UCI de menos de 24 horas. En consecuencia, 151 pacientes fueron elegibles y constituyeron el grupo de estudio. Estos pacientes se dividieron en dos subgrupos según la presencia o ausencia de CR. Estos dos grupos se compararon con respecto a los resultados del cultivo de orina (CO), la presencia de urosepsis y el choque séptico. Resultados: La edad media fue de 80.66 ± 7.76 años. Hubo 18 pacientes con CR y 133 sin CR. Un total de 71 pacientes tuvieron CO positiva. La positividad recurrente de CO ($p = 0.002$) y los microorganismos resistentes ($p = 0.034$) fueron significativamente más frecuentes en el grupo CR. Las incidencias de urosepsis ($p < 0.001$) y choque séptico ($p < 0.001$) también fueron significativamente mayor en pacientes con los CR. Conclusión: La presencia de CR en AMEC se asocia con urosepsis más frecuente y choque séptico. Se requieren ensayos prospectivos más grandes para evaluar el impacto de CR en el pronóstico de los pacientes en la UCI.

References

1. Nirumand MC, Hajialyani M, Rahimi R, et al. Dietary Plants for the Prevention and Management of Kidney Stones: Preclinical and Clinical Evidence and Molecular Mechanisms. Int J Mol Sci. 2018;19(3):765. Published 2018 Mar 7. doi:10.3390/ijms19030765
2. Moe OW. Kidney stones: pathophysiology and medical management. Lancet. 2006;367(9507):333-344. doi:10.1016/S0140-6736(06)68071-9
3. Johnson CM, Wilson DM, O'Fallon WM, Malek RS, Kurland LT. Renal stone epidemiology: a 25-year study in Rochester, Minnesota. Kidney Int. 1979;16(5):624-631. doi:10.1038/ki.1979.173
4. Romero V, Akpinar H, Assimos DG. Kidney stones: a global picture of prevalence, incidence, and associated risk factors. Rev Urol. 2010;12(2-3):e86-e96.

5. Yasui T, Okada A, Hamamoto S, et al. Pathophysiology-based treatment of urolithiasis. Int J Urol. 2017;24(1):32-38. doi:10.1111/iju.13187
6. Huang WY, Chen YF, Carter S, Chang HC, Lan CF, Huang KH. Epidemiology of upper urinary tract stone disease in a Taiwanese population: a nationwide, population based study. J Urol. 2013;189(6):2158-2163. doi:10.1016/j.juro.2012.12.105
7. Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC. Time trends in reported prevalence of kidney stones in the United States: 1976-1994. Kidney Int. 2003;63(5):1817-1823. doi:10.1046/j.1523-1755.2003.00917.x
8. Kittanamongkolchai W, Vaughan LE, Enders FT, et al. The Changing Incidence and Presentation of Urinary Stones Over 3 Decades. Mayo Clin Proc. 2018;93(3):291-299. doi:10.1016/j.mayocp.2017.11.018
9. Nevo A, Golomb D, Lifshitz D, Yahav D. Predicting the risk of sepsis and causative organisms following urinary stones removal using urinary versus stone and stent cultures. Eur J Clin Microbiol Infect Dis. 2019;38(7):1313-1318. doi:10.1007/s10096-019-03555-6
10. Sampathkumar P. Reducing catheter-associated urinary tract infections in the ICU. Curr Opin Crit Care. 2017;23(5):372-377. doi:10.1097/MCC.0000000000000441
11. Leone M, Garnier F, Avidan M, Martin C. Catheter-associated urinary tract infections in intensive care units. Microbes Infect. 2004;6(11):1026-1032. doi:10.1016/j.micinf.2004.05.016
12. Rosser CJ, Bare RL, Meredith JW. Urinary tract infections in the critically ill patient with a urinary catheter. Am J Surg. 1999;177(4):287-290. doi:10.1016/s0002-9610(99)00048-3
13. Cortes-Penfield NW, Trautner BW, Jump RLP. Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults. Infect Dis Clin North Am. 2017;31(4):673-688. doi:10.1016/j.idc.2017.07.002
14. Kaye KS, Marchaim D, Chen TY, et al. Effect of nosocomial bloodstream infections on mortality, length of stay, and hospital costs in older adults. J Am Geriatr Soc. 2014;62(2):306-311. doi:10.1111/jgs.12634
15. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287
16. Nielsson MS, Christiansen CF, Johansen MB, Rasmussen BS, Tønnesen E, Nørgaard M. Mortality in elderly ICU patients: a cohort study. Acta Anaesthesiol Scand. 2014;58(1):19-26. doi:10.1111/aas.12211
17. Pirracchio R, Petersen ML, Carone M, Rigon MR, Chevret S, van der Laan MJ. Mortality prediction in intensive care units with the Super ICU Learner Algorithm (SICULA): a population-based study. Lancet Respir Med. 2015;3(1):42-52. doi:10.1016/S2213-2600(14)70239-5
18. Akinci M, Esen T, Tellaloğlu S. Urinary stone disease in Turkey: an updated epidemiological study. Eur Urol. 1991;20(3):200-203. doi:10.1159/000471700
19. Scales CD Jr, Smith AC, Hanley JM, Saigal CS; Urologic Diseases in America Project. Prevalence of kidney stones in the United States. Eur Urol. 2012;62(1):160-165. doi:10.1016/j.eururo.2012.03.052
20. Cone EB, Hammill BG, Routh JC, et al. Disproportionate Use of Inpatient Care by Older Adults With Kidney Stones. Urology. 2018;120:103-108. doi:10.1016/j.urology.2018.06.007
21. Lieske JC, Peña de la Vega LS, Slezak JM, et al. Renal stone epidemiology in Rochester, Minnesota: an update. Kidney Int. 2006;69(4):760-764. doi:10.1038/sj.ki.5000150
22. Bae SR, Seong JM, Kim LY, et al. The epidemiology of reno-ureteral stone disease in Koreans: a nationwide population-based study. Urolithiasis. 2014;42(2):109-114. doi:10.1007/s00240-014-0643-6
23. Hugosson J, Grenabo L, Hedelin H, Lincolon K, Pettersson S. Chronic urinary tract infection and renal stones. Scand J Urol Nephrol. 1989;23(1):61-66. doi:10.1080/00365599.1989.11690432
24. Omar M, Abdulwahab-Ahmed A, Chaparala H, Monga M. Does Stone Removal Help Patients With Recurrent Urinary Tract Infections? J Urol. 2015;194(4):997-1001. doi:10.1016/j.juro.2015.04.096
25. Gravel D, Taylor G, Ofner M, et al. Point prevalence survey for healthcare-associated infections within Canadian adult acute-care hospitals. J Hosp Infect. 2007;66(3):243-248. doi:10.1016/j.jhin.2007.04.008
26. Vincitorio D, Barbadoro P, Pennacchietti L, et al. Risk factors for catheter-associated urinary tract infection in Italian elderly. Am J Infect Control. 2014;42(8):898-901. doi:10.1016/j.ajic.2014.05.006
27. Thomas B, Tolley D. Concurrent urinary tract infection and stone disease: pathogenesis, diagnosis and management. Nat Clin Pract Urol. 2008;5(12):668-675. doi:10.1038/ncpuro1254
28. Jan H, Akbar I, Kamran H, Khan J. Frequency of renal stone disease in patients with urinary tract infection. J Ayub Med Coll Abbottabad. 2008;20(1):60-62.
29. Tavichakorntrakool R, Prasongwattana V, Sungkeeree S, et al. Extensive characterizations of bacteria isolated from catheterized urine and stone matrices in patients with nephrolithiasis. Nephrol Dial Transplant. 2012;27(11):4125-4130. doi:10.1093/ndt/gfs057
30. Chant C, Smith OM, Marshall JC, Friedrich JO. Relationship of catheter-associated urinary tract infection to mortality and length of stay in critically ill patients: a systematic review and meta-analysis of observational studies. Crit Care Med. 2011;39(5):1167-1173. doi:10.1097/CCM.0b013e31820a8581