Problems and Prospects of Neglected Renal Calculi in Pakistan

Can This Tragedy be Averted?

Manzoor Hussain, Altaf H. Hashmi, Syed Adeebul Hassan Rizvi

Sindh Institute of Urology and Transplantation (SIUT), Civil Hospital, Karachi, Pakistan

Corresponding Author:

Manzoor Hussain, MBBS; MS
Department of Urology, Sindh Institute of Urology and Transplantation, Civil Hospital, Karachi, 74200, Pakistan

Tel: +92 219 498 9172
Fax: +92 213 272 6165
E-mail: info@siut.org

Received May 2012
Accepted November 2012

Purpose: To report our recent experience of treating patients with stones associated with renal failure, some of the factors underlying this problem, and few suggestions to avert this tragedy.

Materials and Methods: From January 2010 to December 2010, a total of 2838 new patients with stone disease were treated at a tertiary care center. The medical files of 278 patients presenting with stone disease and renal failure were reviewed and compared with a cohort of 878 patients with normal renal functions. Their demographic and clinicopathological parameters were noted and analyzed.

Results: Of 2838 patients, 278 presented with acute and chronic renal failure, 40 (1.4%) with unilateral non-functioning kidneys, and 25 (0.8%) with pyonephrosis and perinephric abscess. Management in 278 (9.7%) subjects was divided into initial relief of obstruction by percutaneous nephrolithotomy and double-J stents followed by definitive management in the form of open surgery, percutaneous nephrolithotomy, extracorporeal shockwave lithotripsy, and ureterorenoscopy to make these patients stone-free. Results of treatment showed that 72% of patients either recovered their renal functions or became dialysis-free at the end of the follow-up period.

Conclusion: Complications of renal calculi in the era of modern treatment can be prevented by public education and organizing courses for family physicians as well as opening new stone clinics in the rural areas of the country equipped with modern treatment facilities and strategies for prevention of renal calculi.

Keywords: kidney calculi, renal failure, anuria, Pakistan

INTRODUCTION

Stone disease is one of the common causes of obstructive uropathy and nephropathy in Pakistan, which affects all age groups, including children, adults, and elderly.[1] The impact of the obstruction due to stone is influenced by degree of obstruction, its duration, the baseline condition of the kidneys, the potential for recovery, and the presence of infection.[2]

Stone disease is not only the cause of pain and infection, but carries a significant morbidity and mortality.[3] Renal failure (RF) due to stone disease could be caused by long standing obstruction, infection, and irritation due to crystals in the renal tubules, or associated medical conditions like diabetes and hypertension, or previous procedures done on the kidney for removal of stones.[4]

Neglected renal calculi is a different entity in Pakistan, because on one hand, there is increasing incidence of stone disease and on the other hand, the inadequate facilities for treatment result in very late presentation with large and multiple calculi with RF or any other complication.

In the last 30 years, advances in the management of stone disease in the form of extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PCNL), ureterorenoscopy (URS), retrograde intrarenal surgery (RIRS), and laparoscopy have diminished the role of open stone surgery all over the world.[5] Unfortunately, in spite of advances, the number of patients with stone presenting with complications is on rise in the public sector hospitals in Pakistan.[6]

The reported life-threatening complication rate due to stone disease is about 12%.[7] The management of this group of the patients is a challenge and multi-disciplinary. Although various endourologic methods can be applied to make these patients stone-free,[8] open surgery remains cost-effective.[3]

Previous report from our institute showed that the frequency of RF in patients with renal calculi was about 8% and frequency of end-stage renal disease due to stone disease was 7.3 %.[1] Similarly, 5.3% of acute RF was due to ureteral and renal calculi.[6] Other investigators have also reported the problems of both acute and chronic RF due to stone disease from other parts of the country.[9,10] Literature review shows that the problem of RF due to stone disease also exists in other developing countries, such as India[8] and China,[11] but rarely in Western countries.[12]

Herein, we report our recent experience of treating patients with stones associated with RF, some of the factors underlying this problem, and few suggestions to avert this tragedy.

MATERIALS AND METHODS

A total of 2838 new patients with stone (age ≥14 years) were registered for treatment at this institute from January 2010 to December 2010. This descriptive study was carried out on 278 patients who presented with RF and were admitted in the ward for treatment. A group of 878 patients with stone with normal renal functions, who were admitted in the ward for management, was taken as control group to study co-morbidities and site of stones in these groups. Rest of the patients (1682) were managed as outpatients in the stone clinic and lithotripsy departments.

At the time of admission, full history taking, physical examination, ultrasonography of the kidneys, and the kidney, ureter, and bladder (KUB) x-ray were performed in every subject. Blood chemistry, complete hemogram, and serum urea, creatinine, and electrolytes were evaluated. Urine analysis and culture/sensitivity were done if patients were not anuric.

After investigations, the patients were evaluated jointly by a nephrologist, urologist, and radiologist. If urea and creatinine were >200 mg/dL and >10 mg/dL, respectively, serum potassium would be >5.5 mEq/L and HCO_3 <15 mEq/L or if acidosis was present on arterial blood gas analysis, then hemodialysis would be done as an initial treatment. If renal functions were within acceptable level for anesthesia and patients were afebrile, then double-J (DJ) stents with or without URS were used to relieve the obstruction.

If ultrasonography showed hydronephrosis with fine echoes, PCNL would be done under local anesthesia to relieve the obstruction and to drain the infection. In some patients, bilateral PCNL was done. Once patients were stabilized with improvement in renal functions, definitive procedures were done in the form of ESWL, URS, PCNL, and open surgery depending on the indications.

Complications were noted after definitive surgery. Patients

Table 1. Comparison of site of stones in the study and the control groups.

Site of stones	Study group (n = 278)	Control group (n = 878)	*P*
	Number (%)	Number (%)	
Bilateral renal	108 (38.8)	152 (17.3)	.0001
Bilateral ureteral	33 (11.8)	39 (4.4)	.0001
Bilateral renal + Bilateral ureteral	8 (2.8)	1 (0.1)	.0001
Bilateral renal + Unilateral ureteral	9 (3.2)	5 (0.56)	.001
Unilateral ureteral	29 (10.4)	153 (17.4)	.005
Unilateral renal	49 (17.6)	437 (49.7)	.0001
Uniteral renal + Ureteral	31 (11.1)	45 (5.1)	.0001
Unilateral renal + Bladder	5 (1.8)	8 (0.9)	.22
Ureteral + Vesical	-	6 (0.6)	.16
Bilateral renal + Bladder	1 (0.3)	24 (2.7)	.18

were followed up in stone clinic with ultrasonography, renal function tests, urine for culture/sensitivity, and KUB x-ray after discharge from the ward. Pre- and postoperative serum levels of creatinine (at 3 months after definitive treatment) were compared to study the effect of relief of obstruction. If patients' renal function deteriorates after definitive surgery, they would be prepared for live-related renal transplantation. During hospitalization in the ward, these patients were managed jointly by nephrologists, urologists, infectious disease team, and anesthetists.

Neglected renal calculi were defined as patients with stone who present very late with complications, such as RF, pyonephrosis, and perinephric abscess. We hypothesized that the laterality, site, size, and co-morbidities influence the development of RF in patients with stone.

RESULTS

Two hundred and seventy-eight (9.7%) patients presented with RF (serum creatinine ≥1.5 mg/dL), including 25 (0.8%) with pyonephrosis or perinephric abscess and 40 (1.4%) with unilateral non-functioning kidneys, while remaining 2560 (90.2%) had normal renal functions (serum creatinine <1.5 mg/dL). Of 278 patients with RF, 200 (72.3%) were from rural areas, while 78 (27.7%) were from urban areas of the country. Two hundred and fourteen (77.6%) subjects belonged to poor socioeconomic class. There were 193 (69.4%) men and 85 (30.5%) women with male-to-female ratio of 2.2:1.

Similarly, 878 patients with renal stones with normal renal functions (control group) were evaluated for male-to-female ratio, which was found to be 1.4:1. The duration of symptoms of renal calculi and RF ranged from <1 month to >4 years. Ninety patients presented early with duration of <1 month; these patients had symptoms of acute RF with duration of anuria ranging from 2 to 8 days.

The causes of delay in diagnosis and neglect were analyzed in 278 patients. It showed that 12% of patients had silent renal calculi and their first presentation was with RF. Other causes included family physicians (19%), hakims, homeopaths and quacks (24%), and dentists (45%). The site of stones in 278 patients with RF was bilateral renal or ureteral in 158 (55.6%) patients. Similarly, of 878 control patients, 197 (21.6%) had bilateral disease (Table 1).

Analysis of co-morbid conditions in 278 patients with RF showed that 35 (12.5%) were diabetics, 55 (21%) were hypertensive, and 4 (1.4%) were both diabetic and hypertensive. Seventeen (6.1%) had radiolucent stones. Comparison of co-morbidities in the patient and control groups is shown in Table 2.

Management in 278 patients with stone with RF was divided into initial resuscitation and definitive treatment. In 113 (40.6%) subjects, PCNL was done to relieve obstruc-

Table 2. Comparison of co-morbids, congenital anomalies, and radiolucency in the study and the control groups.

Co-morbids	Study group (n = 278)	Control group (n = 878)	*P*
	Number (%)	Number (%)	
DM	35 (12.5)	19 (2.1)	.0001
Hypertension	22 (7.9)	16 (1.8)	.0001
DM + Hypertension	4 (1.4)	3 (0.3)	.04
Adult polycystic kidneys	2 (0.7)	-	.012
Crossed fused ectopia	-	2 (0.2)	.42
Horseshoe kidney	1 (0.3)	3 (0.3)	.96
Stones with UPJO	-	7 (0.7)	.44
Radiolucent stones	17 (6.1)	21 (2.3)	.002
Pelvic kidney with stones	-	2 (0.2)	.42

DM, indicates diabetes mellitus; and UPJO, ureteropelvic junction obstruction.

tion and in 19 (6.8%), URS and DJ stent were successful, but 103 (37%) patients presented with severe uremic symptoms; therefore, hemodialysis was needed, while in 43 (15.4%), conservative medical treatment consisting of hydration, antibiotics, and correction of electrolyte imbalance was done.

After initial management, definitive procedures were done in 278 patients. In 158 (56.8%) subjects, open surgery was performed while PCNL was done in 18 (6.4%) and ESWL with stent in 13 (4.6%) patients. Definitive stone surgery in ureteral calculi included URS in 33 and URS + DJ stent + ESWL in 15 patients; the rest were treated by open surgery (Table 3).

Pre- and postoperative serum creatinine levels were available in 220 patients; remaining patients either died or underwent renal transplantation. Pre-operative serum creatinine ranged from 1.6 to 28 mg/dL with mean serum creatinine of 10.7 mg/dL, while at 3 months postoperative follow-up, serum creatinine ranged from 0.6 to 8.0 mg/dL with mean value of 2.76 mg/dL. The overall results of surgery in 278 patients showed that 72.3% of patients were dialysis-free at the end of the follow-up, 14% received renal transplantation, and 10.4% died till 2010 (Table 4).

Stone analysis in 207 samples analyzed by infrared spectroscopy showed that 62.5% stones contained calcium oxalate or calcium phosphate either in pure (16%) or mixed (43.5%) form. Similarly, uric acid stones were seen in 11.1% in pure form and in 17.3% in mixed with other compounds constituting 28.3% of samples. Struvite stones were present in 5.6% samples with ammonium hydrogen urate in 3.3% and 2,8-dihydroxyadenine in 0.4% patients (Table 5).

DISCUSSION

Renal stones presenting very late with complications are quite common in Pakistan and have been very well reported in the past[13] and present literature.[14] There are many reasons for this tragedy; one is the silent stones not causing any pain, presenting very late with RF or pyonephrosis. Other is treatment of renal calculi by hakims, homeopaths, and alternative medicines leading to delay in the diagnosis and treatment, and family physicians, who deliberately treat these patients with pain killer drugs and do not try to investigate the cause of the flank pain. The real reason of this neglect is the poverty and poor health facilities in rural areas of the country. There are 24 urology centers in public and private sectors with 24 lithotripters, but they are functional only in few centers.

The incidence of renal calculi is increasing worldwide and Pakistan is not an execption, but treatment modalities are not increasing in parallel resulting in delay and neglect in the treatment of renal calculi in this country. At Sindh Institute of Urology and Transplantation, a tertiary care center

Table 3. Management of stones with renal failure in 278 patients.

Initial Management	Number (%)
Percutaneous nephrostomy	113 (40.6)
DJ stents	19 (6.8)
Hemodialysis	103 (37)
Conservative	43 (15.4)
Definitive Management	
Extended pyelolithotomy	65 (23.3)
Pyelolithotomy + DJ + ESWL	9 (3.2)
Pyelolithotomy + URS + DJ	20 (7.1)
Anatrophic nephrolithotomy	21 (7.2)
Anatrophic nephrolithotomy + URS + DJ	2 (0.7)
Pyeloureterolithotomy	4 (1.4)
Nephrectomy	31 (11.1)
PCNL	26 (9.3)
PCNL + URS	2 (0.7)
ESWL + DJ	13 (4.6)
URS + DJ	33 (11.8)
URS + DJ + ESWL	15 (5.3)
Ureterolithotomy	25 (8.9)
Ureterolithotomy + DJ + ESWL	2 (0.7)
Cystolithotomy	6 (2.1)
Cystolithoclast	2 (0.7)
ESWL bladder stone	2 (0.7)

DJ indicates double-J; ESWL, extracorporeal shockwave lithotripsy; URS, ureterorenoscopy; and PCNL, percutaneous nephrolithotomy.

for renal and urologic diseases, about 9.8% of all patients with stone present with RF, which is probably the highest number ever reported in the world literature.[8,15] Obviously, the referral nature of the center influences this rate. This shows that in spite of minimally-invasive and non-invasive methods, this complication has not reduced in our recent practice. We can avert this tragedy by opening more comprehensive stone centers in the country equipped with lithotripsy machines, facilities for PCNL, ureteroscopy, and facilities for open and laparoscopic surgery, as has happened in developed countries.

Comparison of site of stones in RF and control groups showed that RF was more common in patients with bilateral stone disease and stones in solitary kidney. It means that patients with bilateral renal calculi need thorough investigations to prevent this tragedy and should be treated on priority basis before they go into complications. In 6 patients, large bladder calculi presented with RF; stones were occupying almost all the capacity of the bladder. Neglected bladder calculus presenting with RF has also been reported from China.[16]

Co-morbidities, such as diabetes mellitus, hypertension, and congenital anomalies, were compared between the study and control groups. Patients with RF had slightly higher numbers in co-morbidities, which shows that a minor contributing factor may be a co-morbidity leading to RF. Associated obstruction and stasis caused by congenital anomalies were not a contributing factor in RF.

Radiolucent stones were more commonly seen in patients with RF compared to the control group, which shows that uric acid nephropathy may be a contributing factor in this population. This was supported by the stone analysis reports in this group of patients. Computed tomography scan played a vital role in diagnosis of these patients.

Management of patients with stone and RF is different from the patients with stone and normal renal function. They were initially treated by PCNL to establish urine flow and to drain the infection, but in 19 (6.8%) patients, the ureteroscopy was directly performed, stones were fragmented, and DJ stents were passed without doing PCNL and hemodialysis. This group of patients was selected carefully due to possibility of septicemia. Careful selection included afebrile patients, normal or near normal electrolytes, and preferably a negative urine culture. Acute renal failure due to ureteral calculi can be treated directly by ureteroscopy, lithoclast fragmentation, and DJ stents, as has been recently reported from China.[11] In 37% of our patients, hemodialysis was done as an initial treatment, which showed severe fluid and electrolyte disturbance, and very late presentation leading to uremia.

Initial mode of drainage of obstructed kidneys with RF is controversial; there are advantages and disadvantages of PCNL and DJ stents. Double-J stenting obviates the need for external collection device, but is associated with bothersome lower tract symptoms and a higher incidence of urinary tract infection, and requires general anesthesia in many cases. However, if the patient has uncorrectable coagulopathy or platelet abnormality, ureteral stenting is in-

Table 4. Results of treatment (n = 278 patients).

Outcomes	Number (%)
Complete recovery (serum creatinine 0.6 to 1.5 mg/100 mL)	64 (23)
Improvement of renal functions (serum creatinine 1.6 to 3 mg/100 mL)	96 (34.5)
Renal functions remained stable (dialysis-free) (serum creatinine 3 to 6 mg/100 mL)	41 (14.7)
No recovery (Dialysis dependent)	9 (3.2)
Renal transplantation	39 (14)
Mortality	29 (10.4)

Table 5. Stone analysis in the study group (n = 207).

	Number (%)
CaOx (M) + CaP	84 (40.5)
CaOx (M)	28 (13.5)
CaP	5 (2.4)
CaP + Fat + Proteins	2 (0.9)
CaOx (D) + CaOx (M)	4 (1.9)
CoD + CaP	7 (3.3)
UA	23 (11.1)
UA + CaOx (M) + CaP	16 (7.7)
UA + CoM + AHU	1 (0.4)
UA + CaOx (M)	15 (7.2)
UA + NaH-Urate	2 (0.9)
UA + CoD	2 (0.9)
Struvite + CaP	16 (4.7)
Struvite	2 (0.9)
AHU	2 (0.9)
AHU + UA	5 (2.4)
2, 8-Dihydroxyadenine	1 (0.4)

CaOx indicates calcium oxalate; M, monohydrate; CaP, calcium phosphate; D, dihydrate; CoD, calcium oxalate dehydrate; UA, uric acid; CoM, calcium oxalate monohydrate; AHU, ammonium hydrogen urate; and NaH, sodium hydrogen.

dicated. Internal stenting requires x-ray exposure; hence, should be avoided in pregnancy. On the other hand, PCNL should be strongly considered in pyonephrosis and in case of DJ stenting failure.[2]

Definitive management in stones with RF requires multi model therapy ranging from open surgery to endourology (PCNL, URS, or ESWL). Because of multiple and very large staghorn calculi, these patients are best treated with open surgery due to the following reasons. Open surgery provides higher chances of making these patients stone-free in one sitting, and also drainage of pus with excellent stone-free rates like in our patients.

Recently, many studies from India have shown PCNL as the best method of definitive treatment in this group of patients.[17,18] We have done PCNL in 18 subjects with renal calculi. In our experience, the rate of redo PCNL was high in cases of multiple renal calculi, which needs multiple general anesthesia and multiple admissions, and is not cost-effective. Multiple anesthesia and procedures can affect the recovery of renal functions. Furthermore, many patients do not prefer to undergo multiple procedures. The aim of surgery in these patients is to make them stone- and dialysis-free if possible and to get maximum mileage from these chronically obstructed kidneys to save the cost of dialysis. In our experience, open surgery provides the best chance in experienced hands as compared to PCNL. Overall stone clearance rate after ESWL in these patients was observed to be poor in our study and others.[19]

An analysis of the outcome of management at the end of the follow-up showed that 57% of patients either had complete recovery of or improvement in renal functions after definitive treatment. Another group of 41 (14.7%) remained dialysis-free after management with overall 72% of the patients benefiting from surgery and becoming dialysis-free. This is a good achievement in a developing country like Pakistan to save the cost of dialysis in these patients and give them better life with joint management by urologists, nephrologists, and anesthetists at our center.

Recovery of renal functions after relief of obstruction provides human model for study of recovery potential as most of the studies reported in the literature are animal-based.[2] Since our center is a public sector renal transplant center in the country, 39 (14%) of the patients received renal transplantation in this group, which is an achievement to rehabilitate these patients back to normal life. Recovery of renal

functions after removal of stones with open surgery has also been reported by other researchers.[20]

The mortality in neglected renal stones with RF was seen in 29 (10.4%) of the patients, which reflects the delayed and irreversible damage due to renal stones. The common causes of mortality in these patients are sepsis and other complications of dialysis and end-stage renal disease.[3] All subjects who recovered their renal functions were regularly followed up in stone clinic with advice on hydration, diet, and treatment of urinary tract infection and hypertension. This strategy helps in stabilizing renal functions and prevention of future recurrence.[5]

CONCLUSION

Our recent data show the increasing number of neglected renal calculi presenting very late for management, which on one hand, is a challenge and on the other hand, a tragedy, which should have been averted in the modern era of shockwave therapy and endourology. Unfortunately, we have not yet succeeded in averting this tragedy.

This tragedy can be avoided by organizing public awareness programs in print and electronic media to educate the patients to seek early consultation. Furthermore, education programs should be organized for family physicians for early diagnosis, treatment, and referral to tertiary care urologic centers. As most of the patients are coming from rural areas and belong to poor socioeconomic class, there is a need to open new stone clinics in these areas equipped with qualified urologists, lithotripter machines, PCNL, and ureteroscopy facilities.

ACKNOWLEDGEMENTS

We acknowledge with gratitude the efforts of Professor Dr. Muhammed Mubarak, Associate professor, Department of Pathology, SIUT, for his critical review of the manuscript and help in the preparation of this paper for publication.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Rizvi SA, Manzoor K. Causes of chronic renal failure in pakistan: a single large center experience. Saudi J Kidney Dis Transpl. 2002;13:376-9.
2. Wilson DR. Pathophysiology of obstructive nephropathy. Kidney Int. 1980;18:281-92.
3. Hussain M, Lal M, Ali B, et al. Management of urinary calculi associated with renal failure. J Pak Med Assoc. 1995;45:205-8.
4. Worcester E, Parks JH, Josephson MA, Thisted RA, Coe FL. Causes and consequences of kidney loss in patients with nephrolithiasis. Kidney Int. 2003;64:2204-13.
5. Alivizatos G, Skolarikos A. Is there still a role for open surgery in the management of renal stones? Curr Opin Urol. 2006;16:106-11.
6. Naqvi R, Ahmed E, Akhtar F, Yazdani I, Naqvi NZ, Rizvi A. Analysis of factors causing acute renal failure. J Pak Med Assoc. 1996;46:29-30.
7. Hussain M, Rizvi SA, Askari H, et al. Management of stone disease: 17 years experience of a stone clinic in a developing country. J Pak Med Assoc. 2009;59:843-6.
8. Gopalakrishnan G, Prasad GS. Management of urolithiasis with chronic renal failure. Curr Opin Urol. 2007;17:132-5.
9. Amanullah GK, Lal S, Soomro MI, Jalbani MH. Calculus anuria and its remedy. J Ayub Med Coll Abbottabad. 2010;22:112-4.
10. Khan FA. Calculous anuria. J Pak Med Assoc. 1979;29:256-62.
11. Yang S, Qian H, Song C, Xia Y, Cheng F, Zhang C. Emergency ureteroscopic treatment for upper urinary tract calculi obstruction associated with acute renal failure: feasible or not? J Endourol. 2010;24:1721-4.
12. Rule AD, Bergstralh EJ, Melton LJ, 3rd, Li X, Weaver AL, Lieske JC. Kidney stones and the risk for chronic kidney disease. Clin J Am Soc Nephrol. 2009;4:804-11.
13. Khan FA. *Calculus renal failure*. Lahore New Fine Printing Press; 1981.
14. Rizvi SA, Naqvi SA, Hussain Z, et al. The management of stone disease. BJU Int. 2002;89 Suppl 1:62-8.
15. Kukreja R, Desai M, Patel SH, Desai MR. Nephrolithiasis associated with renal insufficiency: factors predicting outcome. J Endourol. 2003;17:875-9.
16. Wei W, Wang J. A huge bladder calculus causing acute renal failure. Urol Res. 2010;38:231-2.

17. Kumar S, Ganesamoni R, Mandal A. Efficacy and outcome of percutaneous nephrolithotomy in patients with calculus nephropathy. Urol Res. 2011;39:111-5.

18. Agrawal MS, Aron M, Asopa HS. Endourological renal salvage in patients with calculus nephropathy and advanced uraemia. BJU Int. 1999;84:252-6.

19. Hung SF, Chung SD, Wang SM, Yu HJ, Huang HS. Chronic kidney disease affects the stone-free rate after extracorporeal shock wave lithotripsy for proximal ureteric stones. BJU Int. 2010;105:1162-7.

20. Singh I, Gupta NP, Hemal AK, Aron M, Dogra PN, Seth A. Efficacy and outcome of surgical intervention in patients with nephrolithiasis and chronic renal failure. Int Urol Nephrol. 2001;33:293-8.