

## Nephrolithiasis induced end stage renal disease in patients on hemodialysis in Baghdad (A Multicenter study)

Ali J. Hashim Al Saedi<sup>1\*</sup>, Abdul Hakeem A. Karim<sup>2</sup> and Mortadha Mohammad Hadi<sup>3</sup>

<sup>1</sup>Department of Medicine, College of Medicine Baghdad, University of Baghdad, Medical City, Baghdad, Iraq, <sup>2</sup>Department of Science, College of Basic Education, Al Mustansiriyah University, Baghdad, Iraq and <sup>3</sup>Physician Department of Medicine Baghdad Teaching Hospital, Baghdad, Iraq

**Abstract:** *Background:* Kidney stones are the third most common disease of the urinary system. Nephrolithiasis still remains underappreciated cause of end stage renal disease. Clinical presentation varies from asymptomatic small stones to large obstructing staghorn calculi leading to chronic kidney disease. *Objective:* The study aims to evaluate prevalence of nephrolithiasis induced end stage renal disease among patients on maintenance Hemodialysis therapy. *Patients and Methods:* An analytic cross sectional multicenter study that involved 996 patients on maintenance Hemodialysis that was performed from August 2014 to February 2015 in the dialysis units in Baghdad. The patients were grouped into 49 patients who had nephrolithiasis and 947 as a control group, 29 were females and 20 were males. The age ranged between (38-71) years. All patients with nephrolithiasis were evaluated using abdominal ultrasonography and abdominal computed tomography scan. *Results:* Total number of nephrolithiasis incident ESRD cases was 4.91 % (49 of 996 patients). The mean age of the patients with nephrolithiasis induced ESRD was  $56.41 \pm 8.26$  years, 28 patients (57.14%) distributed between ages 40 to 59 years old, 19 patients (38.77%) within age 60 years old and more, while only 2 patients (4.08%) seen between ages 20 to 39 years old and no patients reported below age of 20 years. *Conclusion:* Nephrolithiasis remains the cause of potentially avoidable end stage renal disease in too many patients despite recent major advances in the diagnosis and management of patients forming stones.

**Keywords:** Nephrolithiasis, End stage renal disease, Hemodialysis.

### Introduction

Kidney stones are common, the life time incidence has increased to nearly 10% in the United States [1] and they are the third most common disease of the urinary system [2-3]. It is an increasingly prevalent systemic disorder with substantial health and economic consequences [4]. An initial kidney stone was most commonly seen in patients in their 30s and 40s; however, epidemiologic data now suggest that there has been an increase in nephrolithiasis in younger patients, which may coincide with the increase in metabolic syndrome such as diabetes, hypertension, and obesity in younger people [5-6].

Risk factors for stone formation include crystaluria, socioeconomic factors, hot climate, family history and medications (e.g triamterine and calcium containing antacids) [7]. Kidney stones may be associated with complications such as infection, acute renal failure (due to

obstructive uropathy), and chronic kidney disease [3]. The contribution of nephrolithiasis related to end stage renal disease (ESRD) in patients requiring renal replacement therapy (RRT) has never been specifically evaluated [8].

Nephrolithiasis still remains underappreciated cause of ESRD and this is all the most unfortunate since such prognosis is now preventable in most cases [8]. There are four main types of kidney stones Calcium salts, uric acid, cysteine, and struvite are the constituents of most kidney stones [9]. Calcium oxalate and calcium phosphate stones make up 75–85% of the total and those constituents may be admixed in the same stone [1]. Risk factors for calcium stones are primary hyperparathyroidism, hypercalciuria, hyperoxaluria, and hypocitraturia [10]. Uric acid stones constitute 5-1% of all kidney stones and may be due gout, dehydration or metabolic syndrome [11]. Cysteine stones

constitute 1% and usually hereditary [12]. Lastly struvite stones which constitute 5-10 % of all kidney stones and caused by infections with urease-splitting organisms such as *Proteus* and *Klebsiella* species that hydrolyze urea to ammonium, which alkalinizes the urine and leads to precipitation of phosphate ion complexes [2].

*Aim of study:* The aim of the study is:

1. Evaluating prevalence of nephrolithiasis induced ESRD among patients who develop ESRD from any other cause who are on maintenance dialysis therapy.
2. Evaluating the prevalence of nephrolithiasis induced ESRD among age groups and evaluating whether age is a risk factor for nephrolithiasis induced ESRD compared with patients who had ESRD from other causes.
3. Evaluating the prevalence of nephrolithiasis induced ESRD according to gender and evaluating whether gender is a risk factor for nephrolithiasis induced ESRD compared with patients who had ESRD from other causes.

### Material and Methods

An analytic cross sectional study performed in the period between August 2014 and February 2015 in the dialysis units in Baghdad hospitals (multicenter study) which include:

1. Baghdad teaching hospital.
2. AL Imamain AL\_Kadhimain teaching hospital.
3. AL\_kindy teaching hospital.
4. AL\_Karama teaching hospital.
5. AL\_Imam Ali general hospital.
6. Kidney transplant center/ Medical city.

Two groups were involved in the study, the study group and control group. The study group (49 patients) are the patients who have urinary stone disease as exclusive or preponderant cause of ESRD who start maintenance dialysis therapy and they were assessed by means of detailed history including presenting clinical features at time of diagnosis (most common clinical presentations of the 49 patients who had nephrolithiasis induced ESRD were loin pain most commonly bilateral, anuria, hematuria and irritable symptoms of frequency and urgency). Also the history focused on the ways of confirming diagnosis and all the patients were evaluated using general urine examination (GUE), abdominal ultrasonography

and abdominal CT scan. The control group (947 patients) are those who have ESRD from causes other than nephrolithiasis and start maintenance dialysis therapy in the hospitals involved in this study. Data collection was focused on detecting patients start maintenance dialysis therapy because of nephrolithiasis as exclusive or preponderant cause of ESRD depending on the history of first clinical presentation and the investigations that performed at time of presentation to confirm the diagnosis and recording the age and gender of all patients independent on the cause of their ESRD. The analysis of these data had been done and the results were concluded and tabulated in tables and figures, to be compared with the results of other studies. All patients were informed on research purposes, and all patients records data is kept completely confidential.

Patients who developed renal stones after starting maintenance dialysis therapy are not involved in this study as well as there are three patients had history of unilateral nephrectomy due to nephrolithiasis many years ago and in the recent times they developed ESRD and start maintenance hemodialysis are not involved. patients with unilateral stones and those with renal stones and diabetes mellitus, hypertension, adult polycystic kidney disease or other possible cause for renal failure are also excluded from the study.

*Statistical methods:* Anderson darling test was done to test the normality of age and found that age follow normal distribution so mean and standard deviation (SD) was chosen to present the age, this considering continuous variable.

*Discrete variable:* Age groups (ordinal presentation of age as increment by 20 years) and gender were presented using number and percentage. Two sample chi square tests were used to analysis the possible association between discrete variable with nephrolithiasis and ESRD, P value where chosen to be significant when less than 0.05. All data were analyzed using SPSS 20 soft package.

**Results**

The overall proposition of nephrolithiasis related ESRD among the total number of incident ESRD cases was 4.91% (i.e, 49 of 996 patients) as seen in table 1.

Variable	Nephrolithiasis		ESRD		Total
	No	%	No	%	
	49	4.92	947	95.08	

Table 2 and figure 1 show that the mean age of the patients with nephrolithiasis induced ESRD was 56.41 ± 8.26 years (range of 38-71 years old), 28 patients (57.14%) distributed between ages 40 to 59 years old, 19 patients (38.77%) within age 60 years old and more, while only 2 patients (4.08%) seen between ages 20 to 39 years old and no patients reported below age of 20 years old. Regarding patients with ESRD from causes other than nephrolithiasis, 427 patients (45.08%) distributed between ages 40 to 59 years old, 323 patients (34.10%) within age 60 years old and more, 139 patients (14.67%) seen between ages 20 to 39 years old and 58 patients (6.12%) reported below age of 20 years old. P value for age is 0.006.

Age group	Nephrolithiasis		ESRD		P value
	No	%	No	%	
< 20	0	0	58	6.12	0.006
20 – 39	2	4.08	139	14.67	
40 – 59	28	57.14	427	45.08	
≥ 60	19	38.77	323	34.10	
<b>Mean ± SD</b>					
Age group	56.41 ± 8.26				
P value significant when less than 0.05					

**Fig-1:** Prevalence of nephrolithiasis induced ESRD according to age

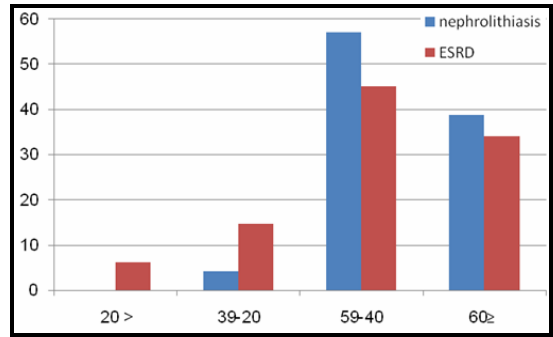


Table 3 figure 2 show that of the 49 patients, there were 20 men (40.81%) and 29 women(59.18%) with a gender ratio of 0.73 while patients with ESRD from causes other than nephrolithiasis show the reverse, 607 (64.09%) patients are men and 340 (35.90%) patients are women. P value for the sex is 0.001.

Gender	Nephrolithiasis		ESRD		P value
	No	%	No	%	
Female	29	59.18	340	35.90	0.001
Male	20	40.81	607	64.09	
P value significant when less than 0.05					

**Fig-2:** Prevalence of nephrolithiasis induced ESRD according to gender

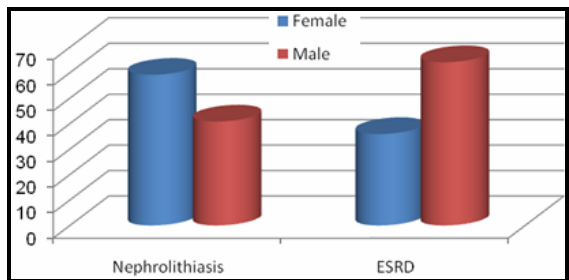


Table 4 shows the clinical and demographic characteristics, duration of symptoms as well as duration of Hemodialysis patients underwent.

<b>Table-4: Clinical and demographic characteristics</b>		
<b>Variable</b>	<b>Number</b>	<b>Percentage</b>
<b>Symptoms = 49</b>		
Renal colic	21	42.9
Accidental discovery	8	16.3
UTI	6	12.2
Macroscopic hematuria	6	12.2
Kidney failure	5	10.2
Anuria	3	6.1
<b>Duration of symptoms = 49</b>		
< 1 months	3	6.1
1 – 6 months	3	6.1
0.5 – 1 years	10	20.4
1 – 2 years	14	28.6
2 – 3 years	8	16.3
3 – 4 years	5	10.2
4 – 5 years	4	8.2
5 – 6 years	1	2.0
> 6 years	1	2.0
<b>Duration of dialysis = 49</b>		
< 6 months	10	20.4
6 – 12 months	13	26.5
12 – 18 months	8	16.3
18 – 24 months	7	14.3
24 – 30 months	6	12.2
30 – 36 months	4	8.2
>36 months	1	2.0

**Discussion**

In our study, nephrolithiasis related ESRD contributed 4.91% (49 patients out of total 996 patients) of the total series of patients who started maintenance dialysis therapy in departments of dialysis in the hospitals mentioned during a

period of 6 months. These results are agreement and non-agreement with those extracted from recent studies done in the foreign countries where they show lower and higher rates of nephrolithiasis induced ESRD table 5.

<b>Table-5: Reported nephrolithiasis prevalence in foreign countries</b>								
<b>No</b>	<b>Study</b>	<b>Country</b>	<b>Patients</b>	<b>Time</b>	<b>Prevalence</b>	<b>Time</b>	<b>Prevalence</b>	<b>Agreement</b>
1	Paul et al [13]	USA	1391	1989	4.7%	2000	3.2%	No
2	Nowfar et al [14]	Us	181092957	1998	0.52%	2003	0.47%	No
3	Ounissi et al [8]	Indian	7128	1992	-	2006	0.63%	No
4	Scales et al [15]	Us	12110	2007	-	2010	8.8%	yes

In our study, of the 49 patients with nephrolithiasis induced ESRD 20 patients were men and 29 patients were women. This is different with Phillip and Franco & Stefano [16-17] showed that men are at greatest risk of developing nephrolithiasis with incidence and prevalence rates between two and four times that of women and in agreement with Stamatiou et al, Taylor et al and Pearle et al [18-20] suggested that nephrolithiasis prevalence is more common in women compared with men to have stones.

Historically, kidney stones have occurred more commonly in men than in women. However, by any number of metrics, the gender gap in stone disease is closing [18, 21-22]. Administrative data from the Nationwide Inpatient Sample showed a decline in the male-to-female ratio among hospital discharges with a primary diagnosis of kidney or ureteral stone from 1.7:1 in 1997 to 1.3:1 in 2002 [22]. The change in the male-to-female ratio is thought to reflect a disproportionate increase in stone disease among women, rather than a decline among men [18]. The reasons for the observed rise in stone disease among women are not certain, but the impact of obesity, a known risk factor for kidney stones, was found to be greater in women than in men [19-20]. Also, the increased prevalence of nephrolithiasis induced ESRD in this study compared to other studies may be attributed to many factors. Irreversible renal impairment was observed essentially in patients with a delayed diagnosis, suboptimal urological and medical management, or intrinsically severe forms of stone disease.

Severe forms of nephrolithiasis, remain an underestimated cause of potentially avoidable ESRD and the need RRT. Those patients had first presentation as CKD and they were mainly having staghorn stones, so this must be kept in mind in view of the disastrous consequences that may result from delayed or improper diagnosis and treatment. Other factors were mainly related

to the low patients education about their symptoms and the future risks, because many patients ignored their symptoms until presentation with more advanced complications. Adequate analysis of stones and/or crystalluria together with proper metabolic evaluation are of crucial diagnostic value. They should never be neglected, especially in patients with the onset of nephrolithiasis in childhood, severely recurrent stones, nephrocalcinosis or incipient renal insufficiency.

*Limitations:* This study is limited by the fact that people with kidney stones were identified by their presentation to health services, meaning that our findings do not apply to those who did not seek medical care for a stone episode. Consequently we cannot comment perfectly on the association between asymptomatic kidney stones and adverse renal outcomes. We were not able to determine the composition of the kidney stones and thus cannot assess the specific risk associated with different stone types. Finally, since the dataset we used did not include genetic information, we cannot assess how many of the patients in our study had a monogenic disorder predisposing to stones.

### Conclusion

Nephrolithiasis remains the cause of potentially avoidable ESRD in too many patients despite recent major advances in the diagnosis and management of patients forming stones. These findings highlight the crucial importance of accurate stone analysis and metabolic evaluation to provide early diagnosis and proper therapy for a condition that may lead to ESRD through recurrent stone formation and/or crystal infiltration. ESRD and RRT should be prevented in the future in most patients with renal stone disease.

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\*All correspondences to: Dr. Ali J. Hashim Al Saedi, Department of Medicine, College of Medicine Baghdad, University of Baghdad, Medical City, Baghdad, Iraq. E-mail: dralijasm.hashim@yahoo.com / alsaedinephrology@gmail.com