

**Original Article**

**Patterns of "Severe Acute Renal Failure" in a referral center in Sudan:  
Excluding intensive care and major surgery patients**

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**ABSTRACT.** Acute renal failure (ARF) is a common health problem worldwide. There is limited data on the pattern of ARF in Sudan. Moreover, glomerular diseases, which are a well-known cause of ARF, have not been accurately and adequately diagnosed previously. A retrospective study on the patterns of ARF was carried out in a general nephrology referral center in Sudan during the period from February 2003-February 2004. Patients from intensive care units with ARF and those who developed ARF after massive surgery were excluded from the study. Renal biopsy was performed when indicated and studied with light and immunofluorescent microscopy. Eighty-nine patients (57 (64%) cases were males, and mean age was 39±19.4 years) fulfilled the criteria for the diagnosis of advanced renal failure requiring renal function replacement therapy. Acute tubular necrosis (ATN) was diagnosed in 50 (56%) patients; 33 (66%) ATN patients had renal failure as a complication of volume depletion, fulminant infections (particularly malaria and typhoid fever) or snakebites, and 12 (13.4%) patients ingested paraphenylene-diamine (PPD) (hair/Henna dye) in suicidal attempts. Eight (9%) patients of the total study group had glomerular diseases and 11 (12.3%) had obstructive uropathy associated with ARF; the cause of ARF could not be determined in 17 (19%) patients. Fifty-three (60%) patients recovered their renal function, six (6.7%) patients progressed to chronic kidney disease (CKD), 16 (18%) died and 14 (16%) were lost to follow-up. In conclusion, patients with ARF associated with ATN had a favorable prognosis except when ATN was associated with PPD poisoning.

*Keywords:* acute renal failure, paraphenylene diamine, glomerulonephritis, Sudan

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**Introduction:**

Acute renal failure (ARF) is a common health problem worldwide.<sup>1-5</sup> It is a condition in which a patient, usually with no known

previous renal impairment, develops acutely failing renal function with a rapid increase of blood urea and creatinine, hydrogen ion, potassium and other substances excreted by the kidney over hours or days.<sup>6</sup>

ARF remains a significant cause of morbidity and mortality worldwide. The mortality rates vary from 25% to 90%. The mortality rate is 40-50% in general and 70-80% in intensive care (ICU) settings.<sup>7</sup> Approximately 95% of consultations to nephrologists are related to ARF.<sup>7</sup>

There is limited data on the overall patterns of renal diseases in Sudan.<sup>8-13</sup> It is crucial to know the etiology and clinical features of ARF to promote prevention strategies and to implement adequate resources for the management of this entity.<sup>14</sup> Hair/Henna dye poisoning is a well-recognized cause of ARF and mortality in Sudanese patients.<sup>15-17</sup>

In this study, we report the patterns and outcomes of ARF in Sudanese patients presenting as general nephrology referrals outside the intensive care unit (ICU) settings.

### Patients and Methods

The medical records of 89 patients who had acute deterioration of renal function were retrospectively reviewed. The patients were referred to the Omdurman Military Hospital renal unit for evaluation and management during the period from February 2003-February 2004. Only patients labeled as having 'severe' ARF were included in the study. The term 'severe' was defined as "advanced renal failure requiring renal replacement therapy by dialysis." ARF was considered when there was a sudden rise in serum creatinine concentration to more than 330  $\mu\text{mol/L}$  (3 mg/dL) in patients who had no history of previous renal impairment. Patients with chronic kidney disease (CKD), intensive care and cardiac surgery patients were excluded. The evalua-

tion included relevant demographic and medical data, history of the disease, clinical examination and investigations that included biochemical, hematological, renal ultrasound and renal biopsy when indicated. Renal biopsies were studied by light and immunofluorescence microscopy. Hemodialysis (HD) or peritoneal dialysis (PD) was instituted early in all patients with paraphenylene-diamine (PPD) (hair/Henna dye) poisoning, as there was no known antidote. Patients were followed until recovery, progression to CKD or death. Patients who showed response to conservative management were not dialyzed.

### Results

Eighty-nine (64% males and 36% females) patients with renal insufficiency fulfilled the criteria for the diagnosis of "severe ARF." The mean age of the patients was  $39 \pm 19.4$  years. The most commonly affected age groups were 20-44, 45-65 years and >65 years with a frequency of 46%, 27% and 18%, respectively.

Renal biopsies were performed in 11(12%) patients; eight of them had features indicative of glomerular disease that warranted the procedure. In three patients, biopsies were performed in acutely PPD intoxicated patients and all revealed histological features of acute tubular necrosis (ATN), Figure 1.

ATN was diagnosed in 50 (56.1%) patients; Hair/Henna dye (PPD) intoxication was the cause of ARF in 12 (13.4%) patients who presented with angio-neurotic edema in 100% of the cases, praparesis in 58%, anuria in 57% and muscular tenderness in 33%. The enzyme creatinine kinase (CK) was 10 fold above our laboratory standard in 50% of the patients with the PPD poisoning; T-wave inversion and ventricular ectopic beats were observed in electrocardiographic tracings of 6/12 (50%) patients. Five (40%) of the PPD intoxicated

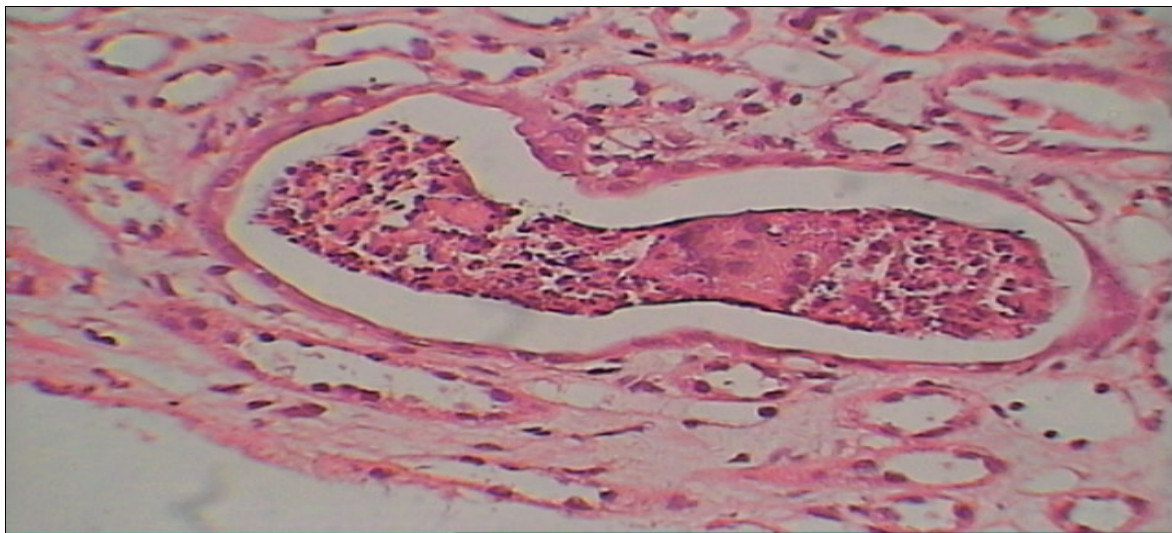


Figure 1. Renal biopsy (H&E stain) showing changes of acute tubular necrosis in a patient with acute PPD poisoning. Note the profound atrophic changes in the tubular lining and the large cast made of shed cells in the tubular lumen

patients died and the rest recovered completely.

Severe volume depletion, malaria, typhoid fever, sepsis, toxemia of pregnancy and snakebites were the causes of ARF in 32 (36%) patients, while drug nephrotoxicity (NSAID, gentamicin or streptomycin) was the cause in five (5.6%) patients, and rhabdomyolysis secondary to crush injury in a road traffic accident was the cause in one (1.1%).

Glomerular disease was the cause of ARF in eight (9%) patients; post-infectious glomerulonephritis in three patients, proliferative type systemic lupus erythematosus nephritis in two, focal segmental glomerulonephritis (FSGN) in two, and IgA nephropathy in one patient.

Eleven (12.3%) patients had obstructive nephropathy associated with ARF; eight (62.5%) patients had nephrolithiasis and three had tumor infiltration.

Multiple myeloma and primary amyloidosis were the causes of ARF in two and one patient, respectively. However, The causes of ARF could not be determined in 17 (19%) patients.

Therapeutic intervention by dialysis was required in 84 (94.4%) patients; acute PD was the modality of therapy in 87(93.3%) patients, and HD in six (6.7%). Five patients (5.6%) responded to conservative management without need for dialysis.

Table 1 summarizes the major causes of

Table 1: Summary of the causes and fate of 89 patients with acute renal failure (ARF) not related to ICU settings.

Causes Of ARF	Males	Females	Recovery (%)	CKD (%)	Death (%)	Loss of follow-up (%)
ATN*	32	18	32 (64)	4 (8)	10 (20)	4(8)
Glomerulopathy	4	4	7 (87.5)	1(12.5)	-	-
Obstructive uropathy	9	2	4 (36)	-	3 (27)	4(36)
Multiple Myeloma	1	1	0	1(50)	1 (50)	-
Amyloidosis	1	0	1 (100)	-	-	-
Unknown	10	7	9 (53)	-	2 (11.7)	6(35.3)
<b>TOTAL</b>	57 (64)	32 (36)	53 (59.6)	6 (6.7)	16 (18)	14 (16)

ATN: acute tubular necrosis, CKD: chronic kidney disease.

Table 2: Causes and outcomes of Patients with Acute Tubular Necrosis (ATN)

Diagnosis	Number of patients (%)	Recovery (%)	Death (%)
Sepsis (malaria, typhoid)	28	15 (54)	05 (18)*
Acute PPD poisoning	12	07 (58)	05 (42)
Nephrotoxic drugs	05	05 (100)	00
Snake bites	05	05 (100)	00
<b>Total</b>	<b>50</b>	<b>32 (64)</b>	<b>10 (20)</b>

\*4 progressed to CKD and 4 were lost to follow-up

ARF and outcome of each group.

The overall mortality rate in the ATN group was 20%. However, the 12 patients who ingested PPD had 42% mortality. Fifty-three (60%) patients had complete recovery, six (7%) progressed to CKD, 16 (18%) died, and 14 (16%) patients were lost to follow-up, Table 2.

There was no immediate mortality among patients with glomerulonephritis. One patient with IgA nephropathy, one with post infectious glomerulonephritis and two with FSGS responded to conservative management and recovered. One patient with post-infectious glomerulonephritis recovered completely after two sessions of PD. Two patients with type IV lupus nephritis recovered from acute renal failure after receiving pulse therapy of methylprednisolone followed by cyclophosphamide. One patient with post-infectious glomerulonephritis progressed to CKD.

One patient with obstruction to a single functioning kidney recovered completely after spontaneous passage of a ureteric stone. Percutaneous nephrostomy was performed in two patients, while another patient was treated with a ureteric catheter. Three patients died because of terminal malignancy and four were lost to follow-up. One patient with multiple myeloma died, whereas the patient with amyloidosis recovered to normal serum creatinine after conservative management.

### Discussion

There is limited data about the patterns of disease in Sudan. Patients with renal disease

are commonly in the age group 20-44, and the majority are males.<sup>2, 4, 20</sup> This is in agreement with our present study in which ARF occurred most frequently in the 20-50 age group, and males were almost twice as frequently affected as females.

The most frequent causes of ARF were those conditions that lead to ATN (56.1%). This finding is in agreement with regional and international data.<sup>2, 19-21</sup> Barsoum<sup>18</sup> reported that malaria and gastroenteritis accounted for the high frequency of cases of ATN leading to ARF. This study showed that patients who ingested PPD in suicidal attempts accounted for 13.4% of ARF. In Sudan, PPD in its pure form (90 - 99% purity) is available in local markets and there are no restrictions for its use or trade.<sup>22</sup> Forty-two percent of the patients who ingested PPD died. Death is usually caused by angio-neurotic edema or fatal arrhythmias due to direct cardio-toxicity of this chemical. The mortality rate in this study is similar to that noted in a previous study from this country.<sup>15</sup> Most of the patients with PPD toxicity showed high levels of CK, which most probably indicates rhabdomyolysis.<sup>16, 23</sup> The neurological and cardiac manifestations reported in this study are similar to previous reports.<sup>15, 16, 23</sup> In this study, three renal biopsies from PPD-intoxicated patients were obtained and studied by light microscopy and immunofluorescence. Biopsies studied showed features of ATN and had neither glomerular nor vascular involvement, a finding confor-



mant with previous reports from this country.<sup>16, 17</sup> To the best of our knowledge, ATN was the only renal patho-logical change reported in patients acutely intoxicated by PPD.<sup>17, 24-26</sup> However, glomerular pathology after chronic PPD intoxication was reported in the majority (94%) of patients.<sup>22</sup> Two cases of chronic renal insufficiency with histopathological changes of vasculitis and crescentic glomerulonephritis after long-term use of hair/Henna dye were reported by Brown et al.<sup>24</sup>

In our study, ARF due to glomerular injury accounted for 8/89 (9%) of all cases, a finding similar to that noted in other countries.<sup>27</sup> There was no immediate mortality among patients with glomerulo-nephritis (GN). Type IV lupus nephritis, confirmed by renal biopsy, recovered completely from ARF following appropriate treatment. Diffuse proliferative lupus nephritis is the most common and severe form of lupus nephritis in which renal insufficiency is frequently seen.<sup>28</sup> To the best of our knowledge, there are no reports on the outcome of lupus nephritis in Sudan. However, the incidence of lupus nephritis was reported to be 14.7%.<sup>29</sup> Aggressive therapy is indicated in all patients with type IV lupus nephritis who are at risk of progressing to renal insufficiency.

Snake bites in this study were not associated with hematological or neurological complications and the associated ARF responded well to dialysis. Similar experiences were reported from India and other areas.<sup>19,30-32</sup>

ARF associated with obstructive nephropathy constitutes 12.3% of this study. Results were similar to regional reports mostly from tropical and desert areas.<sup>4, 21, 33</sup>

Patients who had toxicity to medications, such as antibiotics, had superimposed factors for development of renal disease. Iatrogenic factors are known to contribute to the development of ARF or renal insufficiencies; these factors include decreased renal

perfusion coupled with the use of aminoglycosides, sulfonamides, radio contrast and/or anti-tuberculous treatment.<sup>34</sup>

We conclude that overall prognosis of ARF is not dire once we exclude ARF in the ICU setting. The overall mortality was low and mostly due to PPD poisoning, a largely preventable condition.

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