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# Pediatric acute renal failure in southwestern Nigeria

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**Pediatric acute renal failure in southwestern Nigeria.**

*Background.* Acute renal failure (ARF) was investigated to determine the prevalence of ARF clinical types, etiology, comorbidities, and outcome in Nigerian children.

*Methods.* Consecutive cases of ARF admitted from March, 1994 through February, 2003 were prospectively studied. Information were obtained concerning the following: age, gender, body surface area, early (within 48 hours of onset of ARF) or late (>48 hours of onset of ARF) presentation, admission duration, etiology, comorbidities, urine volume/day, dialysis need, reasons for considering dialysis, laboratory investigations, and outcome in each patient. Histopathologic reports of percutaneous renal and surgical biopsies, as well as autopsy specimens, were reviewed.

*Results.* There were 78 boys and 45 girls (M:F, 1.73:1); mean age was 6.28 ± 4.0 years. A portion of patients presented early (46.3%), while 53.7% presented late. Oliguric (63.41%), anuric (20.33%), and nonoliguric (16.26%) ARF were the clinical types seen. Dialysis requirement was significantly higher in oliguric ($P < 0.005$) and anuric ($P < 0.005$) than nonoliguric ARF. Primary and secondary etiologies accounted for 29% and 71% of ARF cases, respectively. Renal Burkitt's lymphoma (47.2%), glomerulonephritis (27.8%), nephrotic syndrome (16.7%), hemolytic uremic syndrome (5.5%), and acute tubulointerstitial nephritis (2.8%) were primary etiologies. Plasmodium falciparum malaria (42.53%), septicemia (28.73%), hypovolemia (11.49%), and obstructive uropathy (8.05%) were major secondary etiologies. Financial constraints on the part of parents of patients, as well as inadequate and/or lack of dialysis equipment, were major inhibitions to effective management of the patients; in fact, 6 patients took voluntary discharge due to inability to afford the cost of treatment. Mortality risk factors were late presentation [odds ratio (OR) 3.5, $P < 0.001$], dialysis eligibility (OR 3.8, $P < 0.001$), nondialysis (OR 23.1, $P = 0.00004$), primary etiology (OR 2.6, $P < 0.025$), and presence of ≥2 comorbidities (OR 2.9, $P < 0.025$); overall mortality rate was 46.2%.

*Conclusion.* These results show that many of the causes of ARF in our patients are preventable; it should be possible to reduce morbidity due to ARF through purposive preventive measures.

**Key words:** children, etiology, comorbidities, dialysis, Outcome Africa, prevention.

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Acute renal failure (ARF) is a serious disorder of kidney functions with significant morbidity and mortality in children. Morbidities such as electrolytes derangement, fluid overload, sepsis, neurologic abnormalities, hypertension, metabolic acidosis, disordered coagulation, and endocrine dysfunction are common [1–3]. Mortality rate in some series ranged from 16% to 63.3% [4–6]. Data on ARF from the West African (WA) subregion to which Nigeria belongs are rather few [7–10] and infrequent compared to other parts of the world [1–6, 11–14].

ARF in WA presents unique features that are peculiar to developing countries where cultural practices, religious beliefs, poverty, and unstable health policies due to political instability significantly influence clinical presentation and outcome of diseases; causes of ARF are largely due to preventable diseases like gastroenteritis, malaria, and typhoid septicemia [7–10]. ARF is a common pediatric problem in WA but largely under-reported due to paucity of pediatric nephrologists. This study was an attempt at reporting our data on ARF in Nigerian children. The objectives were to determine the prevalence of ARF clinical types, etiology, comorbidities, and outcome in a Nigerian pediatric nephrology unit with ARF incidence of 10 new cases per million children population per year [15].

## METHODS

Consecutive cases of ARF admitted from March, 1994 through February, 2003 were prospectively studied. Information obtained were those contained in a programmed data form; these included age, gender, body surface area, early or late presentation to the hospital, admission duration, etiology of ARF, associated comorbidities, urine volume per day, dialysis need, indications for considering dialysis, hematology, plasma and urinary biochemical investigations, as well as eventual clinical outcome in each patient. Histopathologic reports of percutaneous renal and surgical biopsies and autopsy specimens were reviewed.

### Early presentation

This category comprises patients who presented to the hospital within 48 hours of onset of acute renal insufficiency.

### Late presentation

This category comprises patients who presented more than 48 hours after onset of renal insufficiency.

### Classification of ARF

*Oluguric acute renal failure (OARF).* Defined as urinary output less than 300 mL/m$^2$ /day in addition to sudden onset of progressive plasma accumulation of nitrogenous wastes and electrolytes imbalance in a previously healthy child.

*Nonoliguric ARF (NOARF).* Defined as sudden onset of deteriorating plasma biochemical status in spite of a urinary output that is greater than 300 mL/m$^2$/day without the use of diuretics.

*Anuric ARF (ANARF).* Defined as acute deterioration of plasma biochemical status, as well as production of a urine volume that is less than 1 mL/kg/day in the absence of urinary tract obstruction.

### Investigations

The following investigations were carried out to determine etiology of ARF in the patients:

*Hematology/oncology.* Blood film appearance; full blood counts; platelets counts; glucose-6-phosphate dehydrogenase enzyme assay; direct and indirect Coombs tests; bleeding time; clotting time; prothrombin time; partial thromboplastin time et kaolin; tumor aspirate (in suspected Burkitt's lymphoma cases) for cytology; bone marrow aspirate and cerebrospinal fluid were obtained for cytology to either confirm or exclude presence of Burkitt's cells.

*Microbiology.* Thin and thick blood films for malaria parasites; blood culture for aerobic and anaerobic bacteria; urine microscopy, culture and sensitivity (midstream or suprapubic specimen); stool microscopy, culture and sensitivity.

*Biochemistry.* Urinalysis for proteinuria, reducing substances, pH, specific gravity, hemoglobinuria, and bilirubin; plasma for electrolytes, urea, uric acid, creatinine, phosphate, calcium, proteins, cholesterol and bilirubin; urinary sodium, potassium, phosphate, calcium, protein and creatinine.

*Histopathology.* Renal biopsy, surgical biopsy, autopsy specimens.

*Radiology.* Renal ultrasound for bipolar diameter, transverse diameter and cortical thickness; urinary bladder (including ureters) ultrasound; micturating cystourethrogram in patients with obstructive uropathy.

### Conservative management of oligoanuria

Fluid intake was restricted to 300 to 400 mL/m$^2$/day (insensible loss) plus urine volume the previous 24 hours. Salt intake (sodium) was restricted to 0.5 to 1.0 mmol/kg/day usually not exceeding 10 to 20 mmol/day irrespective of age. Occasionally, salt-free diet was prescribed in very bad patients. Protein intake was usually 0.5 to 1.0 g/kg/day. Carbohydrate was liberalized; where oral intake was not feasible, 10% dextrose water infusion was prescribed. Fats/oils were taken as palm oil in the cooked food. Hyperkalemia was conservatively treated with 10% calcium gluconate intravenously (IV) at 0.3 mL/kg/dose, followed by IV salbutamol, 125 to 250 μg stat, repeated 6 hourly, and 8.4% sodium bicarbonate, 2 to 3 mL/kg IV bolus. These were then followed by IV soluble insulin 0.25 U/kg 6 hourly (until satisfactory potassium level was achieved) in addition to glucose infusion, 4 g/kg over a 24-hour period. Plasma potassium was monitored 2 to 4 hourly in patients treated with insulin/glucose infusion. Dialyses were prescribed for patients whose plasma potassium levels were >6.5 mmol/L. Conservative management was maintained, however, in patients who could not afford dialysis or to be dialyzed for some other reasons. Hypertension was treated with IV furosemide, 2 to 4 mg/kg/day, especially in patients with acute glomerulonephritis; in other cases, severe hypertension was treated with IV hydralazine, 0.2 to 0.5 mg/kg repeated 6 hourly until blood pressure dropped to upper limit of normal for age when oral α-methyldopa was introduced at 25 to 50 mg/kg/day. Captopril (0.25 to 0.6 mg/kg/day in 2 divided doses), amilodipine (0.15 to 0.3 mg/kg/day), or lacidipine (0.06 to 0.12 mg/kg/day) were prescribed in a few patients who could afford them.

### Eligibility criteria for dialysis

Clinical criteria for dialysis included pulmonary edema, congestive heart failure, symptomatic severe anemia, severe hypertension not responsive to drugs, uremic symptoms (e.g., bleeding diathesis, pericarditis, seizures, altered sensorium, nausea, vomiting), and fluid overload.

### Biochemical

Biochemical criteria included metabolic acidosis (plasma bicarbonate <15 mmol/L), hyperkalaemia (plasma potassium >6.5 mmol/L), plasma urea >25 mmol/L, plasma creatinine >300 to 500 μmol/L in children <5 years of age, and >500 μmol/L in patients >5 years of age, and hyperphosphatemia (phosphate >1.7 mmol/L).

### Urinary output

Urinary output was monitored by urethral catheterization in: (*1*) all anuric patients; (*2*) patients with obstructive uropathy; (*3*) patients <5 years of age because of bedwetting; and (*4*) unconscious patients. Catheters were changed weekly and discontinued once the patients

developed urinary tract infection (UTI). Those with UTIs were promptly treated with ceftriaxone parenterally.

### Analyzed hematologic and biochemical data

These included haematocrit, sodium, potassium, bicarbonate, calcium, phosphate, urea, uric acid, creatinine, urinary/plasma creatinine ratio ($U_{cr}/P_{cr}$), and fractional excretion of filtered sodium (FeNa,%).

FeNa was determined from $U_{Na}/U_{cr} \times P_{cr}/P_{Na} \times 100$.

$U_{Na}$ and $P_{Na}$ are urinary and plasma concentrations of sodium, respectively; $U_{cr}$ and $P_{cr}$ are urinary and plasma concentrations of creatinine, respectively.

### Statistical analysis

Statistical mean ± SD were compared using Student *t* test; where indicated, chi-square and Fisher exact tests were carried out to compare proportions for statistical significance. Values of $P < 0.05$ was regarded as statistically significant.

Association between a risk factor and mortality from ARF was tested by determining the odds ratio (OR) from the cross-product ratio in a simple 2 × 2 chi-square test table; the 95% confidence interval (CI) was determined from Miettinen's test-based approximation using the chi-square (95% CI = $OR^{(1\pm1.96/X)}$ [16]), 1.96 being the 5% point of the standard normal distribution, $X = \sqrt{\mathbf{X}^2}$.

## RESULTS

Among the 123 patients studied, 78 (63.40%) were boys and 45 (36.60%) were girls; male/female ratio was 1.73:1. 59 (48%) were less than 5 years old while 64 (52%) were over 5 years old. Overall mean age ± SD was 6.28 ± 4.0 (0.05 to 15.0) years. While 57 (46.30%) presented early, 66 (53.70%) presented late to the hospital.

OARF (63.41%), ANARF (20.33%), and NOARF (1626%) were the three clinical types of ARF seen. A breakdown of their clinical characteristics showed that there were 50 boys and 28 girls among the OARF clinical type; their mean age ± SD was 6.8 ± 3.81 (0.05 to 15) years. However, among the ANARF clinical type there were 15 boys and 10 girls; their mean age was 5.8 ± 3.6 (0.5 to 12) years. There were 13 boys and 7 girls among the NOARF; their mean age was 6.13 ± 4 (0.9 to 13) years. Of the 123 patients, 66 required dialysis while 57 did not. Among those who required dialysis, OARF, ANARF, and NOARF accounted for 40, 23, and 3 cases, respectively. Thirty-eight OARF, 2 ANARF, and 17 NOARF cases required no dialysis.

Clinical and laboratory features warranting dialysis in eligible patients are shown in Table 1. The need for dialysis was significantly higher between OARF ($P < 0.005$) and ANARF ($P < 0.005$) compared to NOARF patients; similarly, the need for dialysis was significantly higher in ANARF than OARF (< 0.005) patients.

**Table 1.** Frequency of clinical and laboratory features warranting dialysis in eligible patients ($N = 66$)

| Dialysis indications | Patient number (%) |
|---|---|
| Clinical | $N = 27$ |
| Bleeding diathesis/anemic heart failure (AHF) | 9 (33.33) |
| Severe hypertension (SHTN)/congestive heart failure (CHF)/seizures/coma | 7 (25.93) |
| SHTN not responsive to antihypertensive drugs | 4 (14.81) |
| AHF/uremia/seizures | 3 (11.11) |
| SHTN/pulmonary edema | 2 (7.41) |
| Fluid overload | 2 (7.41) |
| Laboratory | $N = 25$ |
| Hyperkalemia (≥6.5 mmol/L) | 6 (24) |
| Metabolic acidosis (bicarbonate <15 mmol/L) | 5 (20) |
| Metabolic acidosis/hyperkalemia/ hyperphosphatemia | 5 (20) |
| Severe azotemia (urea ≥25 mmol/L) | 4 (16) |
| Hyperphosphatemia (phosphate >1.7 mmol/L) | 3 (12) |
| Severe azotemia/hyperkalemia | 2 (8) |
| Clinicolaboratory | $N = 14$ |
| Severe azotemia/seizures/coma | 5 (35.71) |
| Severe azotemia/bleeding diathesis (BD) | 3 (21.43) |
| Severe azotemia/SHTN/pulmonary edema | 3 (21.43) |
| Metabolic acidosis/uremic pericarditis/BD | 3 (21.43) |

Primary and secondary etiologies of ARF are summarized in Table 2. Primary and secondary etiologies accounted for 36 (29.0%) and 87 (71.0%) cases, respectively. Renal Burkitt's lymphoma (RBL) and P. falciparum malaria (PFM) were, respectively, the leading primary and secondary causes of ARF in the patients.

Plasma and urinary data obtained within 72 hours of admission of the patients are shown in Tables 3 and 4, respectively.

Mean hematocrits for OARF, ANARF, and NOARF were 22.15 ± 6.1%, 17.0 ± 4.2%, and 15.8 ± 7.3%, respectively; all had similar degrees of anemia, $P > 0.50$. Comorbidity patterns are shown in Table 5; anemia was present in all patients. It was the sole comorbidity in 34 of 123 (27.64%) patients and occurred in combination with other comorbid conditions in the remaining 89 (72.36%) patients. Hypertension was present in 30 patients; hypertension was due to RBL ($N = 17$), poststreptococal acute glomerulonephritis ($N = 9$), fluid overload due to faulty fluid giving sets ($N = 2$), and nephrotic syndrome ($N = 2$).

### Outcome of patients

Six patients (5%) discharged against medical advice due to financial constraints; all 6 had OARF, and 5 were <5 years old while 1 was >5 years old. The remaining 117 patients were managed until they were either

**Table 2.** Etiology of acute renal failure in Nigerian children

| Etiology | Patient number (%) |
|---|---|
| Primary | $N = 36$ (29) |
| Renal Burkitt's lymphoma | 17 (47.2) |
| Glomerulonephritis | |
| PSAGN[a] | 9 (25) |
| MPGN[b] | 1 (2.8) |
| Nephrotic syndrome | 6 (16.7) |
| Hemolytic uremic syndrome | 2 (5.5) |
| Acute tubulointerstitial nephritis | 1 (2.8) |
| Secondary | $N = 87$ (71) |
| Plasmodium falciparum malaria | 37 (42.53) |
| Septicemia | 25 (28.73) |
| Hypovolemia | |
| Gastroenteritis | 9 (10.34) |
| Severe hemorrhage | 1 (1.15) |
| Obstructive uropathy | |
| Posterior urethral valves | 5 (5.75) |
| Urinary bladder rhabdomyosarcoma | 2 (2.3) |
| Intravascular hemolysis | |
| G-6-PD deficiency[c] | 4 (4.6) |
| Autoimmune hemolytic anemia | 2 (2.3) |
| CTHD[d] | |
| Purpura fulminans | 1 (1.15) |
| Thrombotic thrombocytopenic purpura | 1 (1.15) |

[a]Post-streptococcal acute glomerulonephritis.
[b]Membranoproliferative glomerulonephritis.
[c]Glucose-6-phosphate dehydrogenase deficiency.
[d]Consumptive thrombohemorrhagic disorder.

regularly discharged or demised. Of the 117 patients, 54 were <5 years old (survivors = 26 and nonsurvivors = 28) and 63 were >5 years old, with 37 survivors and 26 nonsurvivors. The difference was not significant (OR 1.5, 95% CI 1.3–3.0; $P > 0.50$). Fifteen of 51 (29.41%) and 39 of 66 (59.10%) patients who presented early and late, respectively, to the hospital, demised. Late presentation was significantly more than three times a mortality risk factor (OR 3.5, 95% CI 1.6–7.5; $P < 0.001$).

All were admitted for a mean period of $16.02 \pm 8.5$ (0.5 to 44) days. Survivors among OARF spent $21.53 \pm 8.4$ [10 to 43] days on admission, while nonsurvivors spent $10 \pm 10.10$ (0.5 to 44) days. Among NOARF patients, survivors spent $20.5 \pm 7.1$ [10 to 33] days, while nonsurvivors spent $16 \pm 10.2$ [5 to 25] days. The periods spent on admission by survivors and nonsurvivors among ANARF patients were $19.3 \pm 10.1$ [10 to 41] days and $5.13 \pm 2.42$ (1.0 to 9.0) days, respectively. All survivors spent similar number of days on admission, $P > 0.50$.

Sixty-six patients were eligible for dialysis; however, 6 took voluntary discharge (mainly OARF), 10 were dialyzed, and the remaining 50 patients were managed conservatively. Financial constraints, shortage and/or lack of dialysis equipment, inadequate staff, and late presentation precluded dialysis treatment in those not dialyzed. Of the dialyzed patients, 7 were by peritoneal dialysis (PD) and 3 by hemodialysis (HD). Twenty-three (38.3%) dialysis-eligible patients survived, while 37 (61.7%) demised; among noneligible patients, 40 (70.0%) survived while 17 (30%) demised. The difference was significant, with the risk of mortality being almost 4 times higher in dialysis-eligible than noneligible patients (OR 3.8, 95% CI 1.8–8.1, $P < 0.001$). Among dialyzed patients, 9 (90%) survived while 1 (10%) demised; and of the nondialyzed dialysis-eligible patients, 14 (28.0%) survived while 36 (72.0%) demised (OR 23.1, 95% CI 4.4–122; $P = 0.00004$). A comparison of etiology of ARF with outcome revealed that of the 36 patients whose renal failure was of primary origin, there were 13 survivors (12 OARF, 1 ANARF), 22 nonsurvivors (14 OARF, 8 ANARF), and a case (OARF) of voluntary discharge. Among the 13 survivors, etiology in 3 was due to RBL (OARF), 7 (6 OARF, 1 ANARF) to glomerulonephritis (GN), and 1 each to nephrotic syndrome (NS), hemolytic uremic syndrome (HUS), and acute tubulointerstitial nephritis (ATIN); the latter 3 cases presented as OARF. However, of the 22 nonsurvivors, etiology in 14 was due to RBL (10 OARF, 4 ANARF), 3 to GN (1 OARF, 2 ANARF), 4 to NS (3 OARF, 1 ANARF), and 1 to HUS (ANARF). On the other hand, there were 51 survivors (26 OARF, 17 NOARF, 9 ANARF) and 31 nonsurvivors (21 OARF, 3 NOARF, 7 ANARF) among the 87 patients whose ARF was of secondary etiology. The remaining 5 patients (OARF) took voluntary discharge. Of the 51 survivors, etiology in 25 (13 OARF, 9 NOARF, 3 ANARF) was due to P. falciparum malaria (PFM), 14 to septicemia (4 OARF, 5 NOARF, 5 ANARF), 3 to gastroenteritis (2 OARF, 1 ANARF), 1 to severe hemorrhage (OARF), and 1 each (NOARF) to posterior urethral valves (PUV) and urinary bladder rhabdomyosarcoma (UBR). Furthermore, of the remaining 6 survivors' etiology in 3 (OARF) was due to glucose-6-phosphate dehydrogenase deficiency (G-6-PD-), 2 to autoimmune hemolytic anemia (1 OARF, 1 NOARF), and 1 to purpura fulminans (OARF). Of the 31 nonsurvivors, etiology in 9 (7 OARF, 2 ANARF) was due to PFM, 10 to septicemia (7 OARF, 3 ANARF), 5 to gastroenteritis (3 OARF, 2 ANARF), 4 to PUV (2 OARF, 2 NOARF), and 1 each to UBR (NOARF), G-6-PD- (OARF), and thrombotic thrombocytopaenic purpura (OARF).

Of the 35 patients with primary ARF, 13 (37.0%) survived while 22 (63.0%) demised; however, 50 of 82 (61.0%) cases of secondary ARF survived while 32 (39.0%) demised. The difference was significant (OR 2.6, 95% CI 1.2–5.7; $P < 0.025$).

Table 6 compares the outcome of 1 comorbidity with ≥2 comorbidities in each of the three ARF types. However, pooled data of 117 patients managed until regularly discharged or demised, showed that patients with ≥2 comorbidities had significantly higher mortality than those with 1 comorbidity (OR 2.9, 95% CI 1.2–6.9; $P < 0.025$).

Among OARF patients, 36 of 78 (46.0%) survived, 6 took voluntary discharge (8.0%), and 36 (46.0%) demised. Ten of 25 (40.0%) ANARF patients survived

**Table 3.** Plasma biochemical comparisons of clinical types of acute renal failure

| Plasma biochemistry | NOARF[a] Mean (SD) | *P* value for NOARF versus OARF | OARF[b] Mean (SD) | *P* value for OARF versus *P*ANARF | ANARF[c] Mean (SD) | *P* value for A ANARF versus NOARF |
|---|---|---|---|---|---|---|
| Sodium *mmol/L* | 134.2 (4.6) $N = 20$ | <0.001 | 129.37 (6.0) $N = 78$ | <0.005 | 124.4 (7.15) $N = 25$ | <0.001 |
| Potassium *mmol/L* | 3.85 (1.0) $N = 20$ | <0.05 | 4.38 (0.98) $N = 78$ | <0.001 | 5.7 (1.5) $N = 25$ | <0.001 |
| Bicarbonate *mmol/L* | 19.2 (1.14) $N = 20$ | <0.02 | 18.45 (1.46) $N = 78$ | <0.001 | 17.3 (1.2) $N = 25$ | <0.001 |
| Calcium *mmol/L* | 1.39 (0.21) $N = 16$ | <0.02 | 1.25 (0.18) $N = 54$ | <0.01 | 1.07 (0.28) $N = 21$ | <0.001 |
| Phosphate *mmol/L* | 1.28 (0.23) $N = 17$ | <0.001 | 1.65 (0.44) $N = 50$ | <0.001 | 2.43 (0.80) $N = 23$ | <0.001 |
| Uric acid *mmol/L* | 0.36 (0.13) $N = 15$ | <0.001 | 0.52 (0.18) $N = 65$ | <0.001 | 0.90 (0.18) $N = 23$ | <0.001 |
| Urea *mmol/L* | 23.0 (12.0) $N = 20$ | >0.5 | 23.31 (10.25) $N = 78$ | >0.2 | 25.48 (12.12) $N = 25$ | >0.2 |
| Creatinine μ*mol/L* | 435 (249) $N = 20$ | <0.001 | 674.2 (311) $N = 78$ | <0.001 | 940.38 (314) $N = 25$ | <0.001 |

[a]Nonoliguric acute renal failure.
[b]Oliguric acute renal failure.
[c]Anuric acute renal failure.

**Table 4.** Urinalysis data of anuric (ANARF), oliguric (OARF), and nonoliguric (NOARF) acute renal failure patients

| Urinary data | ANARF[a] Mean ± (SD) $N = 25$ | *P* value for ANARF versus OARF | OARF[b] Mean± (SD) $N = 78$ | *P* value for OARF versus NOARF | N0ARF[b] Mean ± (SD) $N = 20$ | *P* value for ANARF versus NOARF |
|---|---|---|---|---|---|---|
| Urine volume | 0.78 ± 0.07 | – | 173.1 ± 58.3 | <0.001 | 432.3 ± 101.3 | – |
| Sodium *mmol/L* | 114.7 ± 26.1 | <0.001 | 86.0 ± 38 | <0.001 | 61.0 ± 21.2 | <0.001 |
| Creatinine μ*mol/L* | 3418.3 ± 1654.6 | >0.1 | 2905.4 ± 920 | <0.001 | 2133.1 ± 382 | <0.001 |
| $U_{cr}/P_{cr}$ | 3.7 ± 2.0 | >0.5 | 3.5 ± 3.2 | <0.05 | 5.3 ± 3.0 | <0.05 |
| FeNa % | 26.1 ± 9 | <0.001 | 15.7 ± 4.0 | <0.001 | 8.6 ± 1.8 | <0.001 |

[a]Urine volume expressed as mL/kg/day; volume not compared with OARF/NOARF due to non-uniformity of units.
[b]Urine volume expressed as $mL/m^2$/day.

while 15 (60%) demised; 17 of 20 (85.0%) NOARF patients survived while 3 (15.0%) demised. There were significantly more deaths between OARF ($P < 0.005$) and ANARF ($P < 0.005$) compared to NOARF patients; mortality was, however, similar in both OARF and ANARF patients, $P > 0.50$. Survivors between OARF and ANARF were oliguric and anuric for 9.8 ± 4.7 (4.0 to 20.0) days and 9.5 ± 3.4 (4.0 to 15.0) days, respectively. Plasma creatinine normalized, 13 ± 3.1 (9.0 to 18.0) days, 10.92 ± 4.2 (5.0 to 18.0) days, and 5.71 ± 2.1 (3.0 to 9.0) days postdiuresis in ANARF, OARF, and NOARF, respectively. Diuresis duration before normalization of plasma creatinine levels was significantly shorter in NOARF compared to either OARF, $P < 0.001$, or ANARF, $P < 0.001$; it was similar in both OARF and ANARF, $P > 0.20$. Mean plasma creatinine levels at discharge for OARF, ANARF, and NOARF were 68.55 ± 12.3 (50.0 to 98.0), 68.80 ± 16.10 (45.0 to 96.00), and 64.5 ± 16.23 (36.0 to 100.0) μmol/L, respectively. All values were similar, $P > 0.50$.

The overall mortality ($N = 54$) and survival ($N = 63$) rates among the 117 patients managed until regularly discharged or demised were 46.2% and 53.8%, respectively. Twenty-one of 63 survivors were lost to follow-up, while 42 were regularly followed-up for 1.0 to 16.0 (3.6 ± 2.93) months.

## DISCUSSION

There is a general preponderance of boys over girls with respect to ARF in some studies [4, 5, 17]. In our series, ARF was almost two times as common in boys than girls. The mean age of occurrence of ARF in this study, 6.28 ± 4.0 years was found to be similar to that reported in other studies [5, 12, 18], thus showing that infants and young children are the most vulnerable to ARF. Mortality has been particularly found to be much higher in this age group [5, 19]. In this study, age below 5 years was not a significant mortality risk factor (OR 1.5, $P > 0.50$) compared to earlier studies [5, 19] because all cases of RBL were found in patients whose ages were over 5 years; RBL alone, known to be associated with poor prognosis [20], accounted for 54% of deaths in that age group.

The majority of our patients (53.7%) presented late to the hospital. This is similar to 48% found among Indian

**Table 5.** Comorbid conditions in acute renal failure (ARF)

| Comorbidity patterns[a] | OARF[b] | NOARF[c] | ANARF[d] | Total (%) |
|---|---|---|---|---|
| Two comorbidities ($N = 40$) | | | | |
| Anemia plus: | | | | |
| Urinary tract infection (UTI) | 6 | 8 | 0 | 14 (35) |
| Congestive heart failure (CHF) | 6 | 2 | 2 | 10 (25) |
| Septicemia (SCM) | 3 | 0 | 2 | 5 (12.5) |
| Hypertension (HTN) | 1 | 1 | 3 | 5 (12.5) |
| Cerebral malaria | 2 | 1 | 0 | 3 (7.5) |
| Aspiration pneumonitis | 2 | 0 | 0 | 2 (5) |
| Lobar pneumonia | 1 | 0 | 0 | 1 (2.5) |
| Three comorbidities ($N = 29$) | | | | |
| Anemia plus: | | | | |
| Tumor lysis syndrome (TLS), HTN | 9 | 0 | 0 | 9 (31.03) |
| Bleeding diathesis (BD), SCM | 3 | 2 | 1 | 6 (20.69) |
| Pulmonary edema, HTN | 3 | 0 | 1 | 4 (13.80) |
| Paralytic ileus (PLI), SCM | 3 | 1 | 0 | 4 (13.80) |
| Seizures, coma | 2 | 0 | 1 | 3 (10.34) |
| Uremic pericarditis, CHF | 2 | 0 | 1 | 3 (10.34) |
| Four comorbidities ($N = 20$) | | | | |
| Anemia plus: | | | | |
| TLS, HTN, seizures | 4 | 0 | 4 | 8 (40) |
| Seizures, coma, HTN | 3 | 0 | 1 | 4 (20) |
| Uremic pericarditis, BD, CHF | 2 | 0 | 2 | 4 (20) |
| Xerophthalmia (in kwashiorkor patients), SCM, PLI | 2 | 0 | 0 | 2 (10) |
| Peritonitis, BD, CHF | 2 | 0 | 0 | 2 (10) |

[a]Only septicemic conditions that developed while on admission are tabulated; etiologic data are excluded.
[b]Oliguric ARF.
[c]Nonoliguric ARF.
[d]Anuric ARF.

patients [5]. Most patients in this country would initially try spiritualists, herbalists/diviners, and self-medication on account of beliefs and poverty before seeking medical opinion, usually when clinical status would have become precarious. Like in the Indian study, late presentation was found to be a risk factor for mortality in our series (OR 3.5, $P < 0.001$).

OARF (63.41%), ANARF (20.33%), and NOARF (16.26%), as seen in this study, presented, respectively, with variable severity of clinical and laboratory features with significant impact on therapeutic intervention and outcome. This prevalence pattern is at variance with those of other studies. In one series, ANARF and OARF, respectively, accounted for 53.6% and 46.4% [21]; in another series, NOARF (60%) and OARF (40%) were found [1]. Yet in another series, a different combination of OARF (65%) and NOARF (35%) was reported [22]. These variations have significant impact on dialysis requirement. Units with preponderance of NOARF patients have little need for dialysis because of the mild nature of the disease [1, 22]. Conversely, demand for dialysis treatment was higher in the unit with large number of ANARF and OARF patients [21]. In this study, OARF and ANARF accounted for 95.45% of all dialysis-eligible patients; the need for dialysis treatment was therefore significantly higher, $P < 0.005$, in either OARF or ANARF compared to NOARF.

Heart failure (due to either severe anemia or hypertension), hyperkalemia, metabolic acidosis, and severe azotemia occurring either solely or in combination with other clinical entities, were major indications for dialysis treatment in our patients. However, in Ghana [10] and Morocco [4], deteriorating clinical status, fluid overload, rapidly rising urea or plasma level ≥33 mmol/L, severe hyperkalemia, and hypernatremia were major indications for dialysis treatment. Only 10 of 60 (17%) dialysis-eligible patients received dialysis treatment. This is disturbingly low when compared with dialysis access rate of 62% [10] and 100% [4, 12] reported in other countries. In Nigeria, poor access to dialysis treatment is quite a formidable problem [8, 15]. Financial constraints on the parts of parents, shortage and/or lack of dialysis equipment, inadequate staff, and late presentation, which had earlier been reported from this center [15], continue to be major reasons for nondialysis of eligible patients. Dialysis eligibility (OR 3.8, $P < 0.001$) and nondialysis of eligible patients (OR 23.1, $P = 0.00004$) were mortality risk factors in this study. Early dialysis treatment has been associated with better prognosis in ARF patients [4, 11, 12].

All over the world, prevalences of primary and secondary etiologies of ARF vary from center to center. In some centers, primary etiology predominates, accounting for 57% to 93% of cases [4, 12, 21, 23, 24]. In others, secondary etiology predominates, accounting for 66% to 100% of cases [7, 10, 25]. In our series, secondary etiology predominates, accounting for 71% of cases. These are largely due to preventable diseases as in other West African studies [7, 10]. In most of those centers where ARF was mostly of primary origin, hemolytic uremic syndrome (HUS) and acute glomerulonephritis (AGN) lead [4, 12, 21]. HUS, largely reported to be the leading cause of ARF in children in developed countries and South America [11, 12, 14, 26], is a rare etiologic entity in Africa [4, 7–10], except in South Africa, where it occurs in epidemic proportions [27]. This study further confirms the rarity of HUS in Africa. Nigeria falls within latitude 15° North and South of the equator, where both Burkitt's lymphoma and malaria are endemic [28, 29]. It is, therefore, not surprising that RBL and PFM were, respectively, the leading primary and secondary causes of ARF in our series. It has been postulated that chronic malaria infection causes immunosuppression, thereby causing malignant transformation of Epstein-Barr virus–infected

**Table 6.** Relation between number of comorbidities and outcome of acute renal failure ($N = 117$)

| | Number of comorbidities | | Outcome of 1 comorbidity | | Outcome of ≥2 comorbidities | | |
|---|---|---|---|---|---|---|---|
| ARF types | 1 | ≥2 | Survivors | Nonsurvivors | Survivors | Nonsurvivors | *P* value |
| OARF[a] $N = 78$ | 22 | 56 | 15 | 5 | 21 | 31 | <0.01 |
| ANARF[b] $N = 25$ | 7 | 18 | 4 | 3 | 6 | 12 | 0.1987 |
| NOARF[c] $N = 20$ | 5 | 15 | 4 | 1 | 13 | 2 | 0.4605 |

[a]Oliguric acute renal failure; 6 of 78 patients discharged against medical advice. Therefore, their eventual outcome was not known.
[b]Anuric acute renal failure.
[c]Nonoliguric acute renal failure.

lymphocytes to Burkitt's lymphoma [30]. A confirmation of this hypothesis could explain why RBL and PFM were, respectively, the leading primary and secondary etiologies of ARF in this study; it could also mean that preventive measures against malaria would significantly reduce the frequency of ARF cases due to Burkitt's lymphoma. In this study, primary etiology was associated with higher risk of mortality (OR 2.6, $P < 0.025$) than secondary etiology largely because of the high number of deaths recorded among the RBL patients (Table 3). This contrasts sharply with findings elsewhere, where secondary etiologies were associated with significant mortality [24, 31]. Etiology rather than ARF and its attendant biochemical disorders, which are amenable to correction, has been recognized as being more an important mortality risk factor [13, 22]. It is instructive to note that gastroenteritis, which was the most common cause of ARF in some series in this country [8], ranks a distant third (10.34%) behind PFM (42.53%) in our series (Table 3). Aggressive health education in the last 15 years, improved management of gastroenteritis by health workers, and better understanding of the use and ready acceptability of salt-sugar solution and oral rehydration salts by mothers of patients in our catchment areas could have accounted for this remarkable drop in incidence of gastroenteritis-associated ARF.

Nephrotoxins, burns, and trauma that are commonly associated with NOARF [1, 32] in children and adults were not seen in this study; instead, malaria, septicemia, posterior urethral valves, urinary bladder rhabdomyosarcoma, and severe intravascular hemolysis were observed, thus suggesting that causes other than nephrotoxins, burns and trauma may cause NOARF.

Severity of biochemical disorders that normally occur in ARF is dependent on the degree of renal damage. Hyponatremia, metabolic acidosis, hypocalcemia, hyperphosphatemia, hyperuricemia, and hypercreatinemia were found to be significantly more severe in OARF and ANARF than NOARF (Table 4). This is in consonance with findings from other studies [1, 21]. Urinary sodium losses (sodium concentration and FeNa, Table 5) were found to be significantly heavier in both ANARF and OARF than NOARF. This is again similar to findings from an earlier study [1]. Similarly, ANARF and OARF patients exhibited poorer ability to concentrate urine ($U_{cr}/P_{cr}$ ratio <20) compared to NOARF.

Comorbidities are common features of childhood ARF [1, 3] with significant contribution to mortality. The comorbid pattern in this study is of serious and frightening kind; ARF coexisted with equally serious and sometimes fatal morbidities like cerebral malaria, kwashiorkor, aspiration pneumonitis, severe hypertension, heart failure, peritonitis, paralytic ileus, and tumor lysis syndrome. The comorbidities significantly influenced mortality in the patients ($P < 0.025$), with the mortality risk being almost three times higher in those with 2 or more comorbidities. This confirms earlier assertion that comorbidities, like etiology, influence outcome more than ARF itself [13, 22]. This strongly suggests early detection and aggressive management of comorbidities. NOARF had the lowest comorbidity rate (17%) in this study compared to either ANARF (20%) or OARF (63%). This is similar to the findings of other workers [1]. While it is clear that comorbidities are inarguably associated with increased risk of mortality in this and other studies, ARF in Southwestern Nigeria and other parts of the world (especially the developed world) differ significantly in certain areas. For example, ARF in Southwestern Nigeria presents an etiologic pattern that is at variance with what is seen elsewhere; HUS remains the dominant cause of ARF in developed countries and South America [11, 12, 14, 26]. Unlike in developed countries, ready access to dialysis treatment is uncommon in Nigeria; in this series, majority (83%) of our dialysis-eligible patients were not dialyzed due to a number of factors earlier discussed. Furthermore, early treatment is still not possible in a good number of our patients due to late presentation in hospital.

Unlike in OARF and ANARF, recovery in NOARF was significantly faster, $P < 0.001$, as plasma creatinine concentration normalized within $5.71 \pm 2.1$ days of onset

of diuresis. Survival was equally better in NOARF, $P < 0.005$, than either OARF or ANARF. The overall mortality rate of 46.2% was comparable to 41.5% [5], 46.9% [13], and 50% [25] mortality rates recorded in other centers. It certainly could be reduced through (*1*) close monitoring of all OARF and ANARF patients and prompt accessibility to dialysis, (*2*) early detection and management of comorbidities, (*3*) close monitoring of dialysis-eligible patients, and (*4*) careful and slow induction of remission with low-dose cytotoxic drugs in RBL patients with dialysis back-ups. Early presentation in hospital is also expected to improve outcome. Given the fact that the major causes of ARF in this series are preventable, it should be possible to reduce morbidity due to ARF through purposive preventive measures.

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## REFERENCES

1. Anderson RJ, Linas SL, Berns AS, *et al*: Nonoliguric acute renal failure. *New Engl J Med* 296:1134–1138, 1977
2. Anderson RJ, Schrier RW: Clinical spectrum of oliguric and nonliguric acute renal failure, in *Acute Renal Failure: Contemporary Issue in Nephrology*, edited by Brenner BM, Stein JH, New York, Churchill Livingstone, 1980, pp 1–6
3. Ahsan N, Cronin RE: Dialysis considerations in the patient with acute renal failure, in *Principles and Practice of Dialysis*, edited by Henrich WL, Baltimore, Williams and Wilkins, 1994, pp 426–436
4. Bourgia A, Zaid D: Acute renal insufficiency in children: Retrospective study of 89 cases. *Annales de Pediatrie* 40:603–608, 1993
5. Kandoth PW, Agarwal GJ, Dharnidharka VR: Acute renal failure in children requiring dialysis therapy. *Indian Pediatr* 31:305–309, 1994
6. Marotto MS, Marotto PC, Sztajnbok J, Seguro AC: Outcome of acute renal failure in meningococcemia. *Ren Fail* 19:807–810, 1997
7. Seriki O: Acute uraemia in Nigerian children. *West Afr Med J* 23:120–125, 1975
8. Abdurrahman MB, Onuora CU, Babaoye FA, Narayana PT: Renal failure in children in Northern Nigeria. *East Afr Med J* 60: 472–473, 1983
9. Adu D, Anim-Addo Y, Foli AK, *et al*: Acute renal failure and typhoid fever. *Ghana Med J* 4: 172–174, 1975
10. Adu D, Anim-Addo Y, Yeboah ED, *et al*: Acute renal failure in Ghanaian children. *J Trop Paediatr* 30:36–39, 1984
11. Latta K, Offner G, Brodehl J: Continuous peritoneal dialysis in children. *Adv Perit Dial* 8:406–409, 1992
12. Yoshiya K, Iijima K, Yoshikawa N: A clinico-pathological study of 90 children with acute renal failure. *Nippon Jinzo Gakkai Shi Japanese J Nephrol* 39:483–489, 1997
13. Werner HA, Wensley DF, Lirenman DS, LeBlanc JG: Peritoneal dialysis in children after cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 113:64–70, 1997
14. Morghal NE, Brocklebank JT, Meadow SR: A review of acute renal failure in children: Incidence, aetiology and outcome. *Clin Nephrol* 49:91–95, 1998
15. Olowu WA: Renal failure in Nigerian children: Factors limiting access to dialysis. *Pediatr Nephrol* 18:1249–1254, 2003
16. Kirkwood BR: *Essentials of Medical Statistics*, Oxford, Blackwell Scientific Publications, 1988
17. Srivastava RN, Bagga A, Moudgil A: Acute renal failure in north Indian children. *Indian J Med Res* 92:404–408, 1990
18. Arora P, Kohli HS, Kher V, *et al*: Prolonged peritoneal dialysis in ARF using Tenckhoff catheter. *Indian Pediatr* 30:981–985, 1993
19. Gallego N, Gallego A, Pascual J, *et al*: Prognosis of children with acute renal failure: A study of 138 cases. *Nephron* 64:399–404, 1993
20. Olowu WA: Hypertension and acute renal failure in Nigerian children with Burkitt's lymphoma: Report of three cases and review. *Ann Trop Pediatr* 17:169–174, 1997
21. Arora P, Kher V, Gupta A, *et al*: Pattern of acute renal failure at a referral hospital. *Indian Pediatr* 31:1047–1053, 1994
22. Gordillo-Paniagua G, Hernandez-Rodriquez O: Physiology, diagnosis and treatment of acute renal insufficiency. *Boletin Medico dell Hospital Infantil de Mexico* 48:656–662, 1991
23. Espinel CH, Gregory AW: Differential diagnosis of acute renal failure. *Clin Nephrol* 13:73–77, 1980
24. Hodson EM, Kjellstrand CM, Mauer SM: Acute renal failure in infants and children: Outcome of 53 patients requiring haemodialysis treatment. *J Pediatr* 93:756–761, 1978
25. Mendoza SA: Peritoneal dialysis for acute renal failure in children. *Pediatr Nephrol* 5:715–717, 1991
26. Spizzirri FD, Rahman RL, Bibiloni N, *et al*: Childhood haemolytic uraemic syndrome in Argentina: Long-term follow-up and prognostic features. *Pediatr Nephrol* 11:156–160, 1997
27. Bhimma R, Coovadia HM, Adhikari M, Connolly CA: Re-evaluating criteria for peritoneal dialysis in "classical" ($D^+$) haemolytic uraemic syndrome. *Clin Nephrol* 55:133–142, 2001
28. Burkitt DP: Aetiology of Burkitt's lymphoma—An alternative hypothesis to a vectored virus. *J Natl Cancer Inst* 42:19–28, 1969
29. Olweny CLM: Lymphoma and leukaemia. I. Tropical Africa, in *Haematology in Tropical Areas*, edited by Luzzatto L, London, WB Saunders Co Ltd, 1981, pp 873–893
30. Malaria and immunology. *Lancet* 2:1974–1975, 1978
31. Fargason CA, Langman CB: Limitations of the paediatric risk of mortality score in assessing children with acute renal failure. *Pediatr Nephrol* 7:703–707, 1993
32. Odutola TA, Ositelu SB, D'Almeida EA, Mabadeje AFB: Five years experience of haemodialysis at the Lagos University Teaching Hospital—November 1981 to November 1986. *Afr J Med Sci* 18:193–201, 1989