Acute renal failure in Nigerian children: Port Harcourt experience

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Abstract Acute renal failure (ARF) is a significant cause of morbidity and mortality in children. It may be pre-renal, intrinsic, or post-renal (obstructive) in aetiology. ARF was investigated in children in the south-southern part of Nigeria to determine the prevalence, aetiology, management and outcome of ARF. A retrospective review of data from all children from birth to 16 years of age admitted into the Department of Paediatrics, University of Port Harcourt Teaching Hospital (UPTH), with the diagnosis of ARF over an 18 year period (January 1985 to December 2003) was performed. Information was obtained about the age, sex, clinical features, blood pressure, laboratory and radiological investigations, aetiology, and treatment received including dialysis. Information on the outcome, factors influencing outcome, and possible causes of death were reviewed. There were 211 patients, 138 (65.4%) males and 73 (34.6%) females (M:F, 1.9:1), with a hospital prevalence of 11.7 cases/year. The patients were aged 5 days to 16 years (mean 5.6±4.7 years). Oliguria was the most common clinical presentation in 184 (87.2%) patients. Hypertension was seen in only 39 (18.5%) patients. The causes were age-related. The neonates had ARF from severe birth asphyxia 27 (35.5%), septicaemia 17 (22.4%), with tetanus 4 (5.3%) and congenital malformations 11 (14.5%). Sixty-one (28.9%) and 29 (13.7%) patients had ARF from gastroenteritis and malaria respectively. The patients with leukaemia were all more than 10 years old and had acute lymphoblastic leukaemia. Two patients (1.9%) had Burkitts lymphoma involving the abdomen and 3 patients had HIVAN. 112 (53%) patients had anaemia with a mean haematocrit of 20.25±6.9%. Dialysis was indicated in 108 patients, but only 24 patients (22.2%) had peritoneal dialysis (PD), because of financial constraints and lack of dialysis equipment. Mortality rate was 40.5%. The causes of death were uraemia 60 (70.6%), overwhelming infection 5 (5.9%), and recurrent anaemia 20 (23.5%). Hypertension ($X^2$ 15.7, $P<0.001$) and lack of dialysis ($X^2$ 7.96, $P<0.01$) significantly affected outcome. Other factors associated with demise were delayed presentation (58.8%), use of herbal treatment (35%), and unaffordability of treatment (40%). ARF is a significant cause of mortality in Nigerian children. The patients are not adequately managed because of poverty and lack of facilities for dialysis. The causes of ARF in our environment are preventable, and should be expected.

Keywords Acute renal failure · Aetiology · Outcome · Nigerian children

Introduction

Acute renal failure (ARF) is a life-threatening condition causing significant morbidity and mortality in children [1]. It accounts for 2–10% of paediatrics admissions in developed countries [2]. The causes may be pre-renal, intrinsic, or post-renal (obstructive), and they differ between neonates and older children [1, 2]. It ranges from congenital to acquired disorders [1], including drugs [3, 4, 5], bee stings [6], snake venom [7], malarial infections [8], mucocutaneous diseases [9], and hereditary disorders [10].

Current data on the aetiology, management and outcome of ARF in children are limited in developing countries. The outcome is worsened by poverty and unavailability of facilities for dialysis. We therefore performed retrospective analysis investigating the prevalence, causes, management and outcome of ARF in a south-southern part of Nigeria. Limitations in the management of the cases are also discussed.

Patients and methods

A retrospective review of data for all children admitted into the Department of Paediatrics, University of Port Harcourt Teaching Hospital (UPTH), with the diagnosis of ARF over an 18-year period
The chi-square test was performed to compare proportions for statistical significance.

**Results**

During the study period, out of a total admission of 21,020 children ARF had been diagnosed in 211 (1.0%). This gave a hospital prevalence of 11.7 cases of ARF/year. They comprised of 138 (65.4%) males and 73 (34.6%) females, male-to-female ratio 19:1. The patients were aged 5 days to 16 years (mean 5.6±4.7 years). Seventy-six (36.0%) were infants and 54 (25.6%) were over 10 years old.

Oliguria was the most common clinical presentation, by 184 (87.2%) patients (Table 1). Hypertension was seen in only 39 (18.5%) patients. The various causes of ARF are shown in Table 2. The causes were age-related. The neonates had ARF as a result of severe birth asphyxia 27 (35.5%), septicaemia 17 (22.4%), tetanus 4 (5.3%), and congenital malformations 11 (14.5%). One patient had septicaemia from peritonsillar abscess. Haemolytic uraemic syndrome was diagnosed in 7 (3.3%) children with a history of dysentery preceding ARF. Sixty-one (28.9%) and 29 (13.7%) patients had ARF from gastroenteritis and malaria, respectively. Diagnosis of acute glomerulonephritis (AGN) was made clinically by the presence of haematuria, oliguria, proteinuria, and cast, with or without hypertension. The patients with leukaemia were all above 10 years, and had acute lymphoblastic leukaemia confirmed by bone marrow aspirate. Two patients (1.9%) had Burkitt’s lymphoma involving the abdomen.

One-hundred and twelve (53%) patients had anaemia with a mean haematocrit of 20.2±6.9%. However, 50 (23.7%) of the patients received blood transfusions. These were patients with malignancy (6, 12%), malaria (29, 58%) and septicaemia (17, 34%). HIV screening was made a routine investigation for all patients with renal disorder from year 2000. Three (1.4%) patients were positive for both HIV 1 and 2. Hepatitis B surface antigen (HBsAg) estimation was not requested when ARF resulted from pre-renal conditions. However, patients with AGN were all requested to have HBsAg estimation. Only 2 patients were HBsAg positive. They had received blood transfusions previously, one being a sickle cell anaemia patient. Renal biopsy was only performed for one patient with HIVAN at post mortem, and the specimen was sent to Europe because there is no facility for immunofluorescence (IF) and electron microscopy (EM) in Nigeria.

Mean serum urea and creatinine levels were 25.9±14.3 mmol L⁻¹ and 540±363 μmol L⁻¹ respectively. Abnormal urinalysis consisting of haematuria with or without proteinuria was observed in all the patients with AGN, malaria nephropathy, and HUS.

Dialysis was indicated in 108 (51.2%) patients. However, only 24 patients (22.2%) had peritoneal dialysis (PD), because of financial constraints and lack of dialysis facility. None of the patients had haemodialysis, because there was no functional haemodialysis machine in the hospital. Conservative treatments used were fluid re-
stricture to 400 mL m\(^{-2}\) day\(^{-1}\) added to previous day urine output, antihypertensives, and intravenous 8.4% sodium bicarbonate, 2 mL kg\(^{-1}\) bolus, and 50% glucose solution 1–2 mL kg\(^{-1}\) with regular insulin 0.1 U kg\(^{-1}\) over 1 h to manage hyperkalaemia. Conservative management was maintained for those patients who could not be dialysed.

Fluid challenge using 20 mL kg\(^{-1}\) normal saline and IV frusemide 2–4 mg kg\(^{-1}\) day\(^{-1}\) was used for the 61 patients with pre-renal failure from gastroenteritis. Other treatments included intravenous antibiotics, Cytotoxic drugs comprising cyclophosphamide 30 mg kg\(^{-1}\), vincristine 1.5 mg m\(^{-2}\) and, actinomycin D 15 mg kg\(^{-1}\), and allopurinol 50–100 mg three times daily for patients with malignancy. Six (2.8%) patients with posterior urethral valve had bladder catheterization for urinary drainage, and four subsequently had surgical valve ablation.

Eighty-five (40.5%) patients died in the hospital. They comprised of 80 (93.8%) on conservative management and 5 (6.3%) dialysed patients. Mortality was significantly higher in those patients who had hypertension (X\(^2\) 15.7, P<0.001) and also in those for whom dialysis was not used despite being indicated (X\(^2\) 7.96, P<0.01). The causes of death were uraemia 60 (70.6%), overwhelming infection 5 (5.9%), and recurrent anaemia 20 (23.5%). Other factors associated with demise include delayed presentation (>48 hours after the onset of oliguria) (58.8%), use of herbal treatment (35%), and unaffordability of treatment (40%). Six-month and one-year follow up periods were achieved for 80% and 32.3% of patients, respectively.

**Discussion**

This study recorded a high hospital prevalence of ARF of 11.7 cases/year. The true incidence of ARF may be higher, however, because renal failure in newborns is often missed and not reported to the nephrology unit. In the United States of America the annual incidence of community-acquired ARF is approximately 100 cases per 1 million population, and it is diagnosed in only 1% of hospital admissions at presentation. On the other hand, hospital-acquired ARF occurs in as many as 4% of hospital admissions and 20% of critical care admissions [11]. All our cases were community-acquired ARF.

The greater proportion of patients with ARF in this study were infants, supporting the vulnerability of infants to ARF [3, 4, 5, 12]. The mean age of occurrence of ARF was 5.6±4.7 years. This is similar to that reported by Olowu et al. [12] and other studies [12, 13, 14]. The male preponderance noted in this study is comparable with previous studies within and outside Nigeria [12, 14, 15]. Increased urological abnormalities observed in males may account for gender difference in renal disorders as seen in this study, although cultural factors leading to male gender preference in our country may lead to parents bringing their male children to hospital more frequently than the female.

ARF is characterized by a rapid decline in renal functions, usually accompanied by oliguria (<1 mL kg\(^{-1}\) h\(^{-1}\)), but occasionally patients may be nonoliguric or polyuric [1, 2, 11, 12]. Oliguric ARF (OARF) was the commonest presentation in this study, 87.2%. This is higher than, but comparable with 63.4% OARF reported in a Nigerian study [12]. Anaemia was seen in 53.1% of the patients, necessitating blood transfusion in 50 (23.7%) patients. The anaemia could be caused in part by high *Plasmodium falciparum* malaria infection in Nigeria, a malaria-endemic area. Anaemia has been reported as a common medical problem in Nigeria, occurring in approximately 40% of medical patients [16]. This finding, therefore, shows that the presence of anaemia does not always suggest chronic renal failure in the tropics. Hypertension was found in patients with glomerulonephritis and in some with severe malaria.

The aetiology of ARF may be pre-renal, intrinsic, or post-renal (obstructive), and the causes differ between neonates and older children [1, 2, 4, 11, 17]. Pre-renal was the most common type of ARF found in this study. This was predominantly because of birth asphyxia in the neonates and gastroenteritis in the older children. This contrasts with the aetiologies of ARF in developed countries, where most are intrinsic renal diseases from nephrotoxins [1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 17]. The high incidence of birth asphyxia in our environment is mainly because ignorance and cultural factors cause pregnant mothers to use traditional birth attendants, only to present with their asphyxiated babies late to hospitals. Olowu et al. reported that 71% of ARF in their study was of secondary aetiology, but none was from birth asphyxia [12]. The authors did not, however, indicate whether neonates were included in their study.

HUS has been reported as the most common cause of acute renal failure in children in developed countries [1, 11, 17]. This study noted HUS in 3.3% of the ARF cases, confirming the low incidence of HUS in Nigeria and other African countries [12, 18], although under-reporting and under-diagnosis may have contributed to the very low incidence in our series.

*Plasmodium falciparum* malaria was implicated in 13.7% of all cases of ARF seen in this study. This was lower than that reported in a previous Nigerian study [12]. Similarly, Burkitt’s lymphoma (BL) was a rare cause of ARF in this study, in contrast with the report by Olowu et al. [12]. However, Nigeria falls between 10° north and south of equator (lymphoma belt), where lymphoma and malaria are endemic, the incidence of BL varies from 0 to 7.6% per 100,000 population within the lymphoma belt [19, 20, 21]. This probably accounts for the aetiological differences noted in the two Nigerian studies. This study supports the rarity of primary renal lymphoma (PRL) [22, 23]. Renal involvement invariable secondary type occurs in about 3% to 7.6% of patients with lymphoma.

That acute renal failure because of leukaemic infiltration into the kidney is rare in childhood acute lymphoblastic leukaemia (ALL) [24] was confirmed in this
study. ARF-complicating urinary tract obstruction found in 2.8% of patients has been reported in previous studies [14, 25, 26]. Human immunodeficiency virus (HIV) infection has achieved epidemic proportions in Nigeria [27]. HIV-associated nephropathy (HIVAN) is the most commonly encountered cause of both acute and chronic RF in seropositive HIV patients [28, 29]. The prevalence rates vary from 1% to 10% in the HIV-infected population [29]. The course of the disease can be rapid or chronic and the histopathologic features vary substantially depending on the age of the patient and the stage of the disease [30]. Renal biopsy shows several glomerular and tubular lesions, the most prevalent of which is HIV-associated focal segmental glomerulosclerosis (FSGS) [29, 30, 31, 32]. HIV-associated FSGS has a striking predilection for patients of African descent [29, 32]. Because of financial difficulties only 1 of our HIV seropositive patients had renal biopsy at post mortem. His clinical course progressed rapidly within 3 weeks and he died despite his receiving PD. None of the patients had CD4 lymphocyte count and anti retroviral treatment.

Mortality rates for ARF have changed in developed countries since the advent of dialysis [1, 2, 11]. The indications for and timing of renal replacement therapy (RRT) are important and remain controversial [1, 11, 13]. PD has usually been the preferred therapy for isolated failure of the kidney in children and is universally available in developed countries. Dialysis materials are not, unfortunately, readily available in our hospital, and most of the patients are poor. As a result of these problems dialysis access was only 22.2%. Uraemia with seizures and heart failure were major clinical indications for dialysis in the patients.

The hospital mortality rate of 40.5% noted in this study is comparable with 46.2% reported by Olowu et al. [12], but higher than 25% in a USA study [11]. Mortality was significantly higher in patients who had hypertension ($X^2=15.7, P<0.001$) and also in those where dialysis was not used despite being indicated ($X^2=7.96, P<0.01$). Although OARF was associated with higher dialysis requirement, it did not significantly effect outcome ($P>0.05$). Recovery from ARF is primarily dependent on restoration of RBF. Early RBF normalization results in better prognosis for recovery of renal function [1, 11]. Delayed presentation to the hospital and use of herbs were mortality risk factors in this study, as has been previously reported [12, 20]. This practice is common in African culture where illnesses are thought to be of spiritual cause and parents would visit traditional healers and use herbal preparations before visiting orthodox hospitals.

In conclusion, ARF is a common cause of morbidity and mortality in Nigerian children. The causes are mainly pre-renal and are therefore preventable. Furthermore, because of poverty, late presentation, and lack of facilities for dialysis, the patients are not adequately managed. We advise efforts aimed at preventing gastroenteritis, birth asphyxia, and sepsis, to control the incidence of ARF in our environment.

References
