



### Acute Renal Failure in the Intensive Care Unit: Aetiological and Predisposing Factors and Outcome

*L'insuffisance rénale aiguë (IRA) dans l'unité de soins intensifs : étiologiques et les facteurs predisposants et des resultats*

\*O. O. Okunola, F. A. Arogundade, A. A. Sanusi, A. Akinsola

#### ABSTRACT

**BACKGROUND:** Acute renal failure (ARF) in the intensive care unit (ICU) complicates 20–35% of admissions worldwide. There is no information on the pattern of ARF in our ICU and factors that influence survival.

**OBJECTIVE:** To determine the magnitude of acute renal failure, and outcome among patients at an ICU in Nigeria.

**METHODS:** Adult patients requiring intensive care, and with ARF were recruited. Severity of ARF was assessed using the Liano prognostic scoring system and a modified version of APACHE II prognostic scores. Haemodialysis was offered when indicated. Management outcomes were noted while a relationship was sought between severity of ARF and outcome.

**RESULTS:** Forty (19.6%) of the 204 patients managed during the period had ARF. These included 28 (70%) males and 12 (30%) females. Twelve (30%) of the patients had head injury while eight (20%) had major burns. Surgical sepsis accounted for seven (17.5%), while six (15%) patients had advanced metastatic carcinoma. Multiple fractures accounted for four (10%) while other causes accounted for the remaining 16 (40%). The mean serum creatinine and urea were 863.3±95 μmol/L and 19.45 ± 4.1 mmol/L respectively. The Liano scores ranged from 33% to 99% (mean of 61 ± 4.2%) while modified APACHE II score ranged from 5–19 (mean of 11 ± 3.2). There was a significant correlation between the Liano scores and outcome ( $p < 0.007$ ) while the modified APACHE II score did not influence the outcome ( $P > 0.05$ ). Eighty percent of patients who had two or more organ failure died compared to 20% of the patients with less than two organ failure. Eight (20%) patients survived. Dialysis therapy significantly influenced outcome as 100% of the dialysed patients survived compared to 80% of those who were not.

**CONCLUSION:** Acute renal failure presents a continuing challenge in the ICU setting with attendant of high morbidity and mortality. Dialysis significantly influences survival, hence, the service, should be provided in every, intensive care unit. WAJM 2009; 28(4): 240–245.

#### RÉSUMÉ

**CONTEXTE:** L'insuffisance rénale aiguë (IRA) dans l'unité de soins intensifs [ICU] complique 20–35% des admissions dans le monde. Il n'existe aucune information sur le modèle de l'ARF dans notre unité de soins intensifs et les facteurs qui influencent la survie.

**OBJECTIF:** Déterminer l'ampleur de l'insuffisance rénale aiguë, et les résultats chez des patients à un service de réanimation au Nigeria.

**MÉTHODES:** Les patients adultes nécessitant des soins intensifs, et avec l'ARF ont été recrutés. Gravité de l'ARF a été évaluée en utilisant le système de notation Liano pronostique et une version modifiée des scores pronostiques APACHE II. L'hémodialyse a été offert au moment indiqué. Résultats de la gestion ont été relevés alors qu'une relation a été recherché entre la sévérité de l'IRA et les résultats.

**RÉSULTATS:** Quarante (19,6%) des 204 patients pris en charge pendant la période avait ARF. Il s'agit notamment 28 (70%) hommes et 12 (30%) femmes. Douze (30%) des patients avaient des blessures à la tête tandis que huit (20%) avaient des grands brûlés. Surgical sepsis représentaient sept (17,5%), tandis que six (15%) patients avaient un cancer métastatique avancé. Multiples fractures représentaient quatre (10%), tandis que d'autres causes représentaient les 16 autres (40%). La moyenne de la créatinine sérique et d'urée ont été 863.3 95 μmol / L et 19,45 ± 4,1 mmol/L respectivement. Les scores Liano variait de 33% à 99% (moyenne de 61 ± 4,2%) tandis que modifiée le score APACHE II variait de 5-19 (moyenne de 11 ± 3,2). Il y avait une corrélation significative entre les scores et les résultats Liano ( $p < 0,007$ ), tandis que la modification de score APACHE II n'a pas d'influence sur le résultat ( $P > 0,05$ ). Quarante pour cent des patients qui avaient deux ou plus le dysfonctionnement des organes morts comparativement à 20% de les patients avec moins de deux défaillance d'organe. Huit (20%) patients ont survécu. Dialyse influencé de façon significative les résultats que 100% des patients dialysés ont survécu comparativement à 80% de ceux qui l'étaient pas.

**CONCLUSION:** insuffisance rénale aiguë se présente un défi permanent dans l'unité de soins intensifs qui s'accompagne d'une forte morbidité et de mortalité. Dialyse influence significativement la survie, par conséquent, le service doit être fourni dans chaque unité de soins intensifs. WAJM 2009; 28(4): 240–245.

**Keywords:** Renal failure: acute, haemodialysis: outcome, treatment.

**Mots-clés:** insuffisance rénale aiguë, l'hémodialyse, les résultats, le traitement.

Renal Unit, Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria.

\*Correspondence: O. O. Okunola, Renal Unit, Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, Nigeria.

**Abbreviations:** ARF, Acute renal failure; HRS, Hepato renal syndrome; ICU, Intensive care unit; MOSF, Multiple organ system failure; RIFLE, Rise, injury, failure, loss and end stage;

## INTRODUCTION

The concept of an intensive care unit evolved for various reasons, ranging from the need for close observation of patients with severe metabolic derangements, major burns, post-myocardial infarction, to the life support environment offered especially to neurosurgical patients with multiple injuries.<sup>1</sup> Approximately 5–8% of all hospitalized patients develop acute renal failure [ARF].<sup>2</sup> This figure rises significantly to 20–35% among patients at the intensive care unit.<sup>2–4</sup> Acute Renal Failure in the Intensive Care Setting may present as a complication of the disease condition or as part of the treatment complication itself. It also contributes significantly to morbidity and mortality among intensive care patients.<sup>5–8</sup>

Some factors have been responsible for the increased incidence of ARF in the ICU. These include hypotension due to extensive blood loss,<sup>3–9,12</sup> sepsis from peritonitis<sup>12</sup> crush injuries,<sup>13</sup> myocardial infarction,<sup>14</sup> nephrotoxicity from medications such as aminoglycosides and fluorinated anaesthetic agents like methoxyflurane that are commonly used in the intensive care setting.<sup>17,18</sup> In several instances, ARF could be so severe, thus compromising management outcomes with the mortality ranging from 23% to as high as 90%.<sup>2,3,4</sup>

There have been reports on ARF from different centres in Nigeria<sup>23–25</sup> but no study has been reported on ICU patients. Studies on ARF in the ICU setting in European centres have shown that burns and surgery are the predominant causes<sup>2–4</sup> with, mortality rates of 70–80%.<sup>2,4</sup>

This study was informed by the rather high morbidity and mortality seen in our intensive care unit and the need to find ways of limiting this trend.

## SUBJECTS, MATERIALS, AND METHODS

This was a prospective study of patients admitted into the Intensive care unit of the Obafemi Awolowo University teaching hospital Ile-Ife, a tertiary institution providing specialist health care service to about one million people in south-western Nigeria.

Forty consecutive ICU patients with rapidly rising urea and creatinine and

whose baseline serum urea and creatinine levels were consistently above 8mmol/L and 140µmol respectively were recruited. Other inclusion criteria included a urinary output of <400ml/day. Patients with hypertension and diabetes with clinical features of obstructive uropathy, and those with previous history suggestive of chronic kidney disease were excluded. Their presenting symptoms and the number of days spent at the ICU were recorded. Past medical history to exclude preexisting chronic kidney disease was sought. Other aetiological factors such as sepsis, fluid loss, usage of nephrotoxic drugs/agents, trauma were noted as well as surgical procedures that patients had undergone. Also of relevance were the duration and type of surgery, anaesthetic medications and, problems encountered during surgery particularly hypotension and cardiac arrest.

A modified form of Acute Physiological and Chronic Health Evaluation (APACHE) II score<sup>26,27</sup> was completed for each patient. The LIANO score which is an ARF specific severity of index score that was developed for patients with ARF was also used.<sup>28</sup> A general assessment for presence of organ system failure (using clinicopathological parameters) as defined by Knaus and Wagner<sup>29</sup> with some established clinical criteria was undertaken for all the patients as itemized below:

- a. Cardiovascular failure (*1 or more of the following*); heart rate <54/min; mean arterial pressure <49mmHg; systolic blood pressure <60mmHg.
- b. Respiratory failure (*one or more of the following*); respiratory rate 5/min or ≥50/min, mechanical ventilation for 3 or more days fraction of inspired oxygen (fiO<sub>2</sub>) >0.4, positive end-expiratory pressure >5cmH<sub>2</sub>O, PaO<sub>2</sub> ≤80mmHg, PaCO<sub>2</sub> ≥45mmHg with asterixis, bounding pulse with warm and moist extremities and papilloedema.
- c. Haematological failure (*1 or more of the following*); hematocrit of ≤20%; leucocyte count <1000/ul; platelet count <20,000/ul; disseminated intravascular coagulopathy.
- d. Neurological failure; Glasgow coma scale <6 (in the absence of sedation).

- e. Gastrointestinal failure (*1 or more of the following*); Bleeding from stress ulcer necessitating transfusion of more than 2 units of blood per 24 hours; hemorrhagic pancreatitis, acalculous cholecystitis; necrotising enterocolitis; bowel perforation.
- f. Hepatic failure (*2 or more of the following*); clinical jaundice or total bilirubin level 51µmol/lit (3mg/dl) in the absence of hemolysis; serum glutamic-pyruvic transaminase > twice normal; hepatic encephalopathy.
- g. Sepsis is defined as a microbiological proven focus of infection and deterioration of the clinical state, evidenced by at least one of the following; a) temperature >39°C on two or more occasions; b) leucocytosis >10 x 10<sup>9</sup>/lit; c) positive blood culture.

Multiple organ system failure (MOSF) was defined as the development of abnormalities affecting one or more organs systems in a critically ill patients.<sup>39</sup>

Patients who presented with severe ARF as per the following criteria were offered haemodialysis; symptomatic uraemia, severe hyperkalemia (serum potassium >6.5mmol, uraemic pericarditis, Pulmonary oedema especially in the setting of anuria or oliguria, Intractable acidosis especially with serum bicarbonate <12mmol/l, azotemia with serum creatinine >500mmol/l and serum urea >20mmol/l, hypercatabolic state defined as daily rise in serum urea >10mmol/L, serum creatinine >100µmol/L and elevated potassium .

Access for haemodialysis was through femoral vein cannulation using a single lumen femoral catheter with indwelling life span of 48 hours. Patients requiring dialysis were treated as emergency cases and received three or four sessions of haemo dialysis with one or two days interval. Conventional intermittent haemodialysis with low blood flow rate of 150ml/min, with heparin anticoagulation was used. Great attention was paid to the blood pressure with the use of low ultra filtration and occasional vasopressors support. Mechanical ventilation was given to some critically ill patients who required some forms of assisted respiration.

Conservative management included attempts at reversing the underlying cause and corresponding fluid and electrolyte abnormalities. The fluid intake was restricted to 500ml – 1.0 litre in oliguric patients to match measurable plus insensible losses, the protein intake was restricted to 0.6g/kg/day of high biological value and calories of at least 35kcal/kg were given. For worrisome vomiting, 50% glucose boluses were administered while sepsis was controlled using potent antibiotics in renally adjusted doses [using Cockcroft and Gault equation].<sup>38</sup> Broad spectrum antibiotics were prescribed for infections. A combination of clavulanic-acid/aminopenicillin and metronidazole either in reduced doses or increased dosing intervals was instituted. Cephalosporins were prescribed in reduced doses in severe infections. Nephrotoxic drugs were avoided.

The outcome of this study was based on a reduction of serum urea and creatinine to normal or near normal levels. Data analysis was done using SPSS package (Version 10). Association between categorical variables was tested for using the Chi-square statistics. P value <0.05 was taken as significant.

## RESULTS

Two hundred and four patients [109 males, 95 females] were admitted into the intensive care unit of the hospital during the period of study, which lasted for 21 months. Forty (19.6%) had acute renal failure. There was a male preponderance with a male: female ratio of 2.3:1. This compares with the male to female ratio of 1.1:1 (p>0.05) for admissions to ICU. The ages of the patients ranged from 16 to 75

**Table 1: Distribution of Subject by Age and Sex**

Age Range (Years)	Number (%)		
	Male	Female	Total(%)
11–20	2	1	3(18.8)
21–30	8	2	10(25.0)
31–40	7	3	10(25.0)
41–50	7	3	10(25.0)
51–60	3	1	4(13.3)
61–70	1	1	2(6.6)
≥70	0	1	1(2.5)
<b>Total</b>	<b>28</b>	<b>12</b>	<b>40(100.0)</b>

years with a mean of 39.4 year. Thirty (75%) patients fell within the age bracket of 21–50 (Table 1).

All the patients were in established acute renal failure using the inclusion criteria earlier described. Events leading to the renal failure were pre renal in origin in 12(30%) and renal in 28(70%) of cases(see Table 2). Twenty-three (57.5%) patients presented with non oliguric renal failure (urine volume ranging from 500mls to 2 litres) while 17(42.5%) were oliguric.

Acute renal failure was seen in the

**Table 2: Primary Causes of Acute Renal Failure**

	Male	Female	Total (%)
Head Injury	7	5	12(30.0)
Major Burns	6	2	8(20.0)
Surgical Sepsis	5	2	7(17.5)
Multiple Fractures	3	0	3(7.5)
Advanced Carcinoma	4	2	6(15.0)
Advanced Chronic Liver Disease (With Renal Impairment)	3	0	3(7.5)
Haematological Malignancy	1	0	1(2.5)
<b>Total</b>	<b>29</b>	<b>11</b>	<b>40(100.0)</b>

setting of head injury in 12(30%) cases, major burns eight (20%) cases, surgical sepsis 10%, and in advanced metastasis carcinoma (advanced carcinoma of the stomach, breast and colon) in three (7.5%) of the cases. Multiple fracture was seen in three (7.5%) patients while one patient had multiple myeloma (Table 2).

The pattern of organ failure showed that eight (20%) patients had one organ failure, 19(47.5%) patients had two organs, that failed while 13(32.5%) patients had more than three organs failing.

Serum urea on admission ranged between 7.9 to 31.0mmol/L with a mean value of 15.24mmol/L. Serum creatinine ranged from 363.3µmol/L to 1396µmol/L with a mean value of 863.3mmol/L. Serum potassium ranged between 3.0mmol/L to 7.9mmol/L with a mean value of 4.65mmol/L.

The Liano severity scoring index showed that seven patients had scores less than 50 out of which all survived while, all 11 patients with scores greater

than 50 died (p<0.0001)(Table 3).

All the three patients with advanced chronic liver disease possibly hepatorenal syndrome died, and they could not be dialysed before death.

Thirty-two (80%) of patients died, death was related to the primary diagnosis, the number of organ failures and access to haemodialysis in 29 of the patients. Eight patients survived, out of which five had haemodialysis. Three patients recovered without any renal replacement intervention.

## DISCUSSION

Acute renal failure (ARF) is a common complication in patients admitted to the Intensive Care Unit (ICU).<sup>2,3,4</sup> and often has a multifactorial aetiology in critically ill patients. In various centres, ARF accounts for about 2–5% of patients admitted into the General Medical and Surgical units with mortality ranging from 30 and 51%.<sup>30,31</sup> In the intensive care unit however, ARF constitutes between 23–35% of cases admitted and has a high mortality from 23% to as high as 90%.<sup>3,4</sup> This was also the case as seen in this study with a mortality rate of 80%.

There was a male preponderance amongst the patients in our study, in agreement with studies else-where<sup>6, 7, 19</sup> and this could be due to the general male preponderance that exists in our hospital admissions. However, it is also plausible that males are more easily prone to acute kidney injuries.<sup>23,24</sup> Majority, of our patients had non-oliguric acute renal failure in keeping with experience elsewhere as major burns, traumatic injuries, use of nephrotoxic antibiotics, and increased frequency of the use of

**Table 3: Relationship Between The Number of Organ Failure, the Liano Score, Modified Apache II Score and Haemodialysis with the Outcome/Survival Pattern in the Studied Patients**

Variable	Number			P value
	Alive	Dead	Total	
<b>No of failed organs</b>				
1	3	5	8	P<0.006
2	4	15	19	
>3	-	13	13	
<b>Total</b>	<b>7</b>	<b>33</b>	<b>40</b>	
<b>Liano Score</b>				0.0007
<50%	6	1	7	<b>40</b>
>50%	5	28	33	
<b>Total</b>	<b>11</b>	<b>29</b>	<b>40</b>	
<b>Modified Apache II</b>				Fischers Exact Test [P-1.000]
<10	2	5	7	
>10	11	22	33	
<b>Total</b>	<b>13</b>	<b>29</b>	<b>40</b>	
<b>Dialysis</b>				<b>0.006</b>
Dialysed	5	0	5	
Not Dialysed	3	32	35	
<b>Total</b>	<b>8</b>	<b>32</b>	<b>40</b>	

potent diuretics/mannitol have been associated with non-oliguric acute renal failure.<sup>33</sup>

It is a known fact that multiple organ failure significantly predicts mortality in the ICU with mortality ranging between 30% and 100%.<sup>35</sup> In our study, 80% of our patients who had two or more organ failure died, this is in keeping with reports observed in other centres.<sup>2, 19</sup> This is in contrast to the observation of Knaus and Draper who did not find any correlation between mortality and number of organ failure in a retrospective study.<sup>29</sup> The mortality of ARF in patients on the ventilator is about 80% and mortality dramatically increases with increasing numbers of failed non-respiratory organs.<sup>25</sup> In our study virtually all the patients on artificial respiratory support died.

Sepsis is a major complication of organ failure in most intensive care units<sup>8, 19, 34</sup> but a variety of non-infectious conditions like severe trauma, major surgery and hypovolemic shock may also be responsible. In this study, sepsis accounted for only 17.5% of cases seen while the others played major con-

tributory roles.

Head injury accounted for 30% of the cases seen all of whom died. Head trauma carries a dismal prognosis especially in the setting of acute renal failure.<sup>36, 37</sup> There is some clinical and experimental evidence that the traumatized brain particularly the frontal lobe can very specifically induce haemodynamic changes in the kidney leading to renal cortical ischaemia. Controversy, however, surrounds the contention that there is a specific cerebrorenal failure syndrome as advocated by Skipkins *et al.*<sup>36</sup>

None of the patients with head injury had haemodialysis because of a number of reasons namely, the delay in referring the patients to the nephrologist and non suitability for intermittent haemodialysis which is the only form of haemodialysis available at our centre. However, it is unlikely that intermittent dialysis would have altered prognosis as it worsens cerebral oedema. Sustained low efficiency dialysis or continuous equilibrated peritoneal dialysis would be preferred in this group of patients if they had been dialysed.

Major burns accounted for 20% of the

cases with a mortality of 100%, in agreement with other studies.<sup>37</sup> This is explained by the fact that major degree of burns is often associated with three or more organ failure which confers a poor prognosis. Peritoneal dialysis was not offered as this is a relative contra-indication to its use; also the risk of sepsis in this group of patients is a limiting factor to peritoneal dialysis.

Mortality associated with hepatorenal syndrome (HRS) especially in the ICU is high – as evident in this study, which is comparable to similar work done in Boston by Hou in which mortality was 80%.<sup>31</sup> The few survivors in that study probably had a less severe form of ARF in advanced chronic liver diseases. Dialysis has been reported to be ineffective in the management of HRS as it often increases the risk of severe hypotension, infection and hemorrhage. From our study, Liano score higher than 50% predicts mortality in the ICU and this is in agreement with the observation by other workers.<sup>28</sup> This result also validates the assertion that the Liano score is a useful assessment tool in the ICU population. Contrary to this finding, *modified APACHE II* was not found to predict mortality and survival in agreement with a previous report.<sup>35</sup> This is not surprising as APACHE II has been found to be useful only in risk stratification, as it only measures the severity of physiological impairment in ICU patients while underestimating the risk of mortality in patients with acute renal failure. A major limitation of APACHE II is that the proportion of the score allocated to renal failure is only 4% which deemphasizes the independent mortality risk of acute renal failure. It must be noted that the use of APACHE II score determined at the time of initiation of dialysis for patients with ARF was found to be a statistical predictor of patient's survival and recovery of renal function by Kierdorf *et al.*<sup>35</sup> In the last few years a form of categorisation system for ARF has been used in different settings i.e the Risk, Injury, Failure, Loss, and End stage (RIFLE) criteria,<sup>38</sup> this could not be assessed in our patients because of the need to adhere to the objectives of this work.

Dialysis in ARF patients provides

opportunity for control of fluids and electrolyte derangements particularly hyperkalemia in addition to control of uraemia. However, a randomized trial of HD in the patients could objectively evaluate the pattern of survival. Only 20% of the ICU cases survived and this was majorly because of renal replacement therapy offered and the early recognition and aggressive intervention given by renal physicians in the intensive care unit.

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