



A clinical study on outcome of kidney function tests among ARF patients treated at tertiary care hospital

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Abstract

Serum creatinine provides the most accurate and consistent estimation of GFR. However other biomarkers are now under study. Correct interpretation of serum creatinine extends beyond just knowing normal values for the specific laboratory. Serum creatinine must always be interpreted with respect to patient's weight, age and sex. The patients included in the study were from both ICU and wards. Final sample size came to be 104 subjects of Acute Kidney Injury of varied etiology. In our study, the total number of patients in the Risk, Injury and Failure groups were- 28(26.9%), 32 (30.8%) and 44 (42.3%) patients respectively. Out of these, 23 (22.1%), 32 (30.8) and 35 (33.7%) of patients of the groups Risk, Injury and Failure had complete recovery. 5 patient each of risk and (4.8% each) and 9 patients (8.7%) of failure groups expired.

Keywords: kidney function tests, ARF, serum creatinine

Introduction

Changes in urine output generally are poorly correlated with changes in GFR. Approximately 50-60% of all causes are ARF are nonoliguric. However, categories of anuria, oliguria and non- oliguria may be useful in differential diagnosis of AKI [1]. Anuria (<100ml/d)-It is seen in urinary tract obstruction, renal artery obstruction, rapidly progressive glomerulonephritis, bilateral diffuse renal cortical necrosis.

Oliguria (100-400ml/d) – Can accompany any cause of renal failure. Non-oliguria (>400ml/d) – Acute interstitial nephritis, acute glomerulonephritis, partial obstructive nephropathy, and ischemic ATN, radio contrast induced ARF, and rhabdomyolysis [2].

Microscopic examination of urine is essential in establishing differential diagnosis.

Normal urinary sediment without hemoglobin, protein, cells or casts is generally consistent with pre-renal and post-renal failure, HUS/thrombotic thrombocytopenic purpura (TTP), preglomerular vasculitis, or atheroembolism.

Granular casts suggest ATN, glomerulonephritis, interstitial nephritis. RBC casts suggest glomerulonephritis, malignant hypertension. Dysmorphic RBCs suggest glomerulonephritis injury [3].

WBC casts indicates acute interstitial nephritis, pyelonephritis. Eosinophiluria is an indicator of acute allergic interstitial nephritis, atheroembolism.

Crystalluria should warn about the presence of acyclovir, sulfonamides, methotrexate, ethylene glycol toxicity, radio contrast agent.

The urea concentration correlates poorly with the GFR. Because urea is highly permeable to renal tubules, urea clearance varies with urine flow rate [4].

Urea is filtered freely, but reabsorption along the tubule is a function of urine flow rate. During antidiuretics, urine flow rate less than 30mL/h, urea clearance is as low as an estimated

30% of GFR. Under conditions of diuresis, urine outputs greater than 100mL/h, urea clearance can increase to 70-100% of GFR.

This information can be used clinically to help differentiate pre-renal failure from other etiologies of ARF.

In pre-renal conditions, low urine flow rates favor BUN reabsorption out of proportion to decrease in GFR, resulting in disproportionate rise of BUN relative to creatinine, creating a serum BUN-creatinine ratio > in pre-renal failure [5].

BUN concentration is dependent on nitrogen balance and renal function. BUN concentration can rise significantly with no decrement in GFR by increase in urea production with steroids, trauma or GI bleeding. Tetracycline increases BUN by decreasing tissue anabolic rates. Basal BUN concentration can be depressed severely by malnutrition or advanced liver disease.

Always first estimate basal BUN concentration when attempting to correlate changes in BUN with GFR.

Serum creatinine provides the most accurate and consistent estimation of GFR. However other biomarkers are now under study. Correct interpretation of serum creatinine extends beyond just knowing normal values for the specific laboratory. Serum creatinine must always be interpreted with respect to patient's weight, age and sex. The GFR can be estimated by the following formula:

Cockcroft - Gault equation: $GFR \text{ mL/min} = (140 - \text{age in years}) (\text{weight in kg}) (0.85 \text{ if female} / (72 \times \text{serum creatinine mmol/L}))$

As suggested by these data, knowledge of a patient's baseline creatinine becomes very important. Small changes with low baseline levels of creatinine are important clinically much more than large changes with high basal creatinine. Significant decrements in GFR can occur in the normal range of creatinine [6].

Certain diseases and medications can interfere with the

correlation of serum creatinine with GFR. Acute glomerulonephritis causes increased tubular secretion of creatinine, falsely depressing the rise in serum creatinine when ARF occurs in acute glomerulonephritis.

Methodology

Universal Sampling Technique was used for selection of study subjects. All the patients coming to medicine department during the study period and fulfilling the inclusion and exclusion criteria were taken for study after taking prior informed consent. The patients included in the study were from both ICU and wards. Final sample size came to be 104 subjects of Acute Kidney Injury of varied etiology.

All the study subjects were followed up on daily basis, till discharge, death or return of their renal function to baseline. Socio-Demographic, biochemical and clinical profiles of all patients were recorded.

Variables assessed were: age, sex, type of primary disease (medical or surgical), type of AKI (pre-renal/renal/post-renal), risk factors, indications and type of dialysis and outcomes (recovery/death/discharge on dialysis).

Inclusion Criteria

- Age >18 year
- Patients who fulfill the RIFLE criteria for Acute kidney disease (Risk, injury, failure).
- Minimum of 24 hours of admission

Exclusion Criteria

- Patients of established Chronic Kidney Disease and end stage renal disease.
- Pre-renal factors like volume depletion which is correctable within 48 hours.
- Discharge against medical advice.
- Deaths within one day of admission.

Results

Out of total patients, 28(26.9%) had stage of risk, while 32 (30.8%) had stage of injury and 44(42.3%) had stage of failure according to RIFLE criteria.

Table 1: Distribution based on RIFLE Staging

	No. of cases	Percent
Failure	44	42.3
Injury	32	30.8
Risk	28	26.9
Total	104	100.0

A total of 8 (7.7%) patients were on dialysis while 96(92.3%) were treated conservatively.

Table 2: Distribution based on Dialysis

	No. of cases	Percent
No	96	92.3
Yes	8	7.7
Total	104	100.0

A total of 14(13.5%) patients died during the study, many of which were due to sepsis and MODS.

Table 3: Distribution based on Outcome

	No. of cases	Percent
Dead	14	13.5
Recovered	90	86.5
Total	104	100.0

Out of total, 19(18.3%) females and 25(24.0%) males had failure with 8(7.7%) females and 24(23.1%) males had injury while 7(6.7%) females and 21(20.2%) males fall into risk according to rifle criteria. No gender difference was observed in the distribution of patients according to rifle criteria.

Table 4: Sex Distribution based on RIFLE staging

		Failure	Injury	Risk	Total	
Sex	Female	No. of cases	19	8	7	34
		% of Total	18.3%	7.7%	6.7%	32.7%
	Male	No. of cases	25	24	21	70
		% of Total	24.0%	23.1%	20.2%	67.3%
Total		No. of cases	44	32	28	104
		% of Total	42.3%	30.8%	26.9%	100.0%

Table 5: Age Distribution based on RIFLE Grading

			Rifle Criteria			Total	
			Failure	Injury	Risk		
AGE	<=20	No. of cases	2	0	2	4	
		% within AGE	50.0%	.0%	50.0%	100.0%	
	21-30	No. of cases	7	7	2	16	
		% within AGE	43.8%	43.8%	12.5%	100.0%	
	31-40	No. of cases	8	7	6	21	
		% within AGE	38.1%	33.3%	28.6%	100.0%	
	41-50	No. of cases	5	11	5	21	
		% within AGE	23.8%	52.4%	23.8%	100.0%	
	51-60	No. of cases	14	5	2	21	
		% within AGE	66.7%	23.8%	9.5%	100.0%	
	>60	No. of cases	8	2	11	21	
		% within AGE	38.1%	9.5%	52.4%	100.0%	
	Total		No. of cases	44	32	28	104
			% within AGE	42.3%	30.8%	26.9%	100.0%

No age difference was observed in the distribution of patients according to rifle stage.

Out of the total of patients enrolled, 90(86.5%) had complete recovery, and 14(13.5%) patients expired.

In our study, the total number of patients in the Risk, Injury and Failure groups were- 28(26.9%), 32 (30.8%) and 44 (42.3%) patients respectively. Out of these, 23 (22.1%), 32 (30.8) and 35 (33.7%) of patients of the groups Risk, Injury and Failure had complete recovery. 5 patient each of risk and (4.8% each) and 9 patients (8.7%) of failure groups expired.

Table 6: Outcome based on RIFLE staging

			Rifle Criteria			Total
			Failure	Injury	Risk	
Outcome	Dead	No. of cases	9	0	5	14
		% of Total	8.7%	0.0%	4.8%	13.5%
	Recovered	No. of cases	35	32	23	90
		% of Total	33.7%	30.8%	22.1%	86.5%
Total		No. of cases	44	32	28	104
		% of Total	42.3%	30.8%	26.9%	100.0%

Discussion

In this study, there were 96(92.3%) patients due to medical causes, Out of these medical cases CCF had highest mortality with 5 patients followed by gastroenteritis 3 patients, UTI 2, pneumonia 2, and snake bite 1 patient.

There were 8(7.7%) patients due to medico surgical causes, out of these 1 patient died due to post lscs perforation, patients with cellulitis and obstructive uropathy had complete recovery.

The overall mortality was 13.5%. The mortality in the medical group was high compared to medico-surgical causes.

In our study, the total number of patients in the Risk, Injury and Failure groups were- 28 (26.9%), 32 (30.8%) and 44 (42.3%) patients respectively. Out of these, 23 (82%), 32 (100%) and 35 (79.5%) of patients of the groups Risk, Injury and Failure had complete recovery. 5(17.86%) patient with risk and 9 patients (20.5%) of failure groups expired.

According to the study done by Marlies Ostermann *et al* [7], 17% patients were in the risk group, 11% had injury and 7.6% had failure. Mortality in respective groups was 20.9%, 45.6% and 56.8% respectively.

A total of 8 (7.7%) patients were on dialysis while 92.3% were not on dialysis.

A total of 14 patients died (mortality rate – 13.5) during the study.

The first description of ARF, then termed ‘ischuria renalis’, was by William Heberden in 1802 [8]. ARF, then named Acute Bright’s Disease, was described in William Osler’s Textbook for Medicine (1909), as a consequence of toxic agents, pregnancy, burns, trauma, or operations on the kidneys [9].

During the First World War the syndrome was named “war nephritis”. The first detailed report of fatal acute renal failure is accredited to Hackradt, a German pathologist in 1917 and was based on soldiers who sustained severe traumatic injury. His description was neglected until the Second World War, when the crush kidney syndrome in victims of London Blitz was described [10]. A landmark article was first published in 1941 by Bywaters and Beall during World War II. They reported 4 cases of crush injury followed by impaired renal function [11].

Homer W. Smith introduced the term “acute renal failure”, in a chapter on “Acute renal failure related to traumatic injuries” in his textbook, the kidney-structure and function in health and disease (1951) [12].

During 1950s, the knowledge of ARF was greatly increased by three physicians, William J. Kolff who invented artificial kidney [13], John P. Merrill who illustrated the clinical course and management of ARF [14], and George E. Schreiner, who described and encouraged the treatment of ARF [15].

Before 2004 there was no definite literature on the diagnostic criteria or clinical definition of ARF which resulted in at least 35 different definitions in medical literature. This gave rise to a wide range of incidence estimates for ARF from 1 to 25% of ICU patients and has led to mortality rate estimates of 15 to 60%.

To establish a uniform definition for AKI, in 2002 the Acute Dialysis Quality Initiative (ADQI) Group formulated the first consensus definition of AKI which was five tiered (RIFLE)-Risk to the renal function, Injury to the kidney and its

function, and Failure of kidney to function, as well as the two outcome stages, Loss of kidney function and End-stage kidney disease. Since then many studies and research works have been done on acute renal failure using the RIFLE criteria.

In 2004, the Acute Dialysis Quality Initiative (ADQI) group developed the RIFLE system through a broad consensus of the experts.

The Acronym RIFLE stands for the increasing severity classes of AKI R-Risk, I- Injury and F-Failure, and the two outcome classes L-Loss and E-End stage kidney disease. The first three severity grades are defined on the basis of the changes in serum creatinine or urine output where the worst of each criterion is used. And last of the two outcome criteria (loss and end stage kidney disease), are defined by the duration of loss of kidney function, 4 weeks and 3 months, respectively.

This definition was intended to establish the presence or absence of clinical AKI in a given patient or situation, and to describe the severity of this syndrome. It did not aim to predict mortality or adverse outcomes or to trigger standardized therapeutic interventions.

In 2008, a systematic review of 24 studies which described the epidemiology of AKI by means of the RIFLE criteria, and attempted to associate the severity of AKI with clinical outcome [16]. The majority of the studies were done at hospitalized patients in general or in intensive care unit (ICU) settings. The analysis showed that a stepwise increase in the relative risk of death occurred with each successive AKI category (at Risk, 2.40; Injury 4.15; Failure 6.37 versus non-AKI patients).

The RIFLE criteria are also currently being used in trials of therapies for AKI and in studies on AKI pathophysiology. Where a uniform and standardized definition of the disease is mandatory. The RIFLE criteria have also been modified for use in the pediatric setting.

However, after more than 6 years of clinical utilization, several limitations of the RIFLE criteria have emerged.

First, any clinical sign of AKI appear only after a notable decline in GFR. Second, the use of 6 hour and 12 hour urine output measurements is unsuitable for retrospective studies, since such data are not collected as part of routine clinical practice. Not only is urine output affected by diuretic use, but this parameter can only be accurately assessed in patients with a urinary catheter. A third limitation of the RIFLE criteria is that the serum creatinine and GFR measurements are based on changes from a baseline value, which are not always available. Fourth, investigators might be tempted to use the change in estimated GFR rather than changes in measured GFR to assess the severity of AKI—an approach that should be considered inherently incorrect, since the MDRD equation (as with all GFR or creatinine clearance equations) is valid only in steady-state conditions, and is certainly invalid in situations where renal function is rapidly changing, as is the case in AKI. Fifth, a study published in 2004 demonstrated that even small increase in serum creatinine levels, such as an absolute increase of 26.5 $\mu\text{mol/l}$ (0.3 mg/dl)—below those specified for the RIFLE class ‘at Risk’—are associated with poor outcomes. Finally, the RIFLE criteria do not consider the nature or site of the precipitating injury, although the same could be said of consensus definitions used for other diseases.

Conclusion

- A total of 8 (7.7%) patients underwent dialysis while 96(92.3%) were treated conservatively.
- A total of 14 patients died during the study which constitutes 13.5% of total patients.
- No age and gender difference was observed in the distribution of patients according to rifle staging.
- 9 out of 44 patients in failure and 5 patient out of 28 belonging to risk stage died in the study.

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