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Research article

PROGNOSTIC INDICATORS AND PATTERNS OF RENAL RECOVERY IN PATIENTS REQUIRING HEMODIALYSIS FOR ACUTE KIDNEY INJURY

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ABSTRACT

Background: The outcome of patients with acute kidney injury (AKI) is highly variable. Patients who receive renal replacement therapy (RRT) for similar diseases may recover differently. The factors that operate in each patient may alter the prognosis and outcome. **Aims:** Our study aims at identification of prognostic factors influencing recovery in patients who required hemodialysis for AKI. **Material and Methods:** Patients admitted in different ICUs with AKI who underwent hemodialysis in a tertiary care hospital over a three year period were included in the study. Time from day one of disease to first dialysis, hematological and biochemical parameters were noted. Patients were grouped based on the time taken for recovery of renal function following hemodialysis into group A (<2 weeks) and group B (>2 weeks). Studied parameters have been statistically analyzed to find any significant association with recovery time. **Results:** Out of 63 patients, 9 progressed to chronic kidney disease. In the remaining 54, Group A comprised 31 and group B 23. Out of all the factors studied, serum creatinine (7.0±1.3 vs 8.4±3.8; P=0.018), S. bicarbonate (21.7±2.8 vs 19.7±3.8; P=0.03), pH at admission (7.25±0.13 vs 7.1±0.19; P=0.048); number of hemodialysis sessions (3.5 ±1.5 vs 5±2.4; P=0.016) and time lag from day one of disease to first hemodialysis (8.6 ± 3.6 vs 11.5±5.9; P=0.007) showed significant association with recovery time. **Conclusion:** Recovery following AKI is influenced by factors liked delayed presentation, late initiation of hemodialysis, low pH and low bicarbonate which can predict delayed renal recovery following hemodialysis.

Keywords: Acute Kidney Injury, Hemodialysis, Seurm creatinine.

INTRODUCTION

Acute kidney injury (AKI) is defined as a sudden loss of kidney function that results in the retention of urea and other nitrogenous waste products along with dysregulation of extracellular volume, electrolytes and acid base balance.[1] It constitutes up to 20% of critically ill patients and is easily identified by a rise in the serum creatinine.[2]

The quantitative definition of AKI has long been a debate due to gross variations in various methods employed in measuring the glomerular filtration rate (GFR). In view of the need for a simple and uniform definition, RIFLE criteria was proposed and was later modified and presented as AKIN criteria.[3,4] This, along with the recent change in the name of ARF to AKI will represent the entire spectrum of kidney disease and help in early detection of cases. These criteria rely on the baseline serum creatinine and the relative rise is used in the categorization into risk or injury or failure group. Even though serum creatinine is not an ideal marker of renal failure, it is

inexpensive and is readily available making it an invaluable investigation. Novel biomarkers of AKI like cystatin-C, Neutrophil gelatinase-associated lipocalin (NGAL), Kidney injury molecule 1(KIM 1) and many others are available, but their clinical utility is still under validation.[5]

The etiologies of AKI vary, most common being sepsis as reported from many studies globally. Infectious causes dominate the charts all over the world and severe malaria is an important addition to the list of AKI in India. It is known that patients with persistently high serum creatinine are at increased risk of developing chronic kidney disease due to tubular damage and interstitial scarring. The rates of renal recovery in different studies varied from 36-99%, but these studies defined recovery by dialysis independence.[6-8]

Renal replacement therapy is life saving, especially in AKI and the decision to initiate, type and timing of RRT is the choice of the treating physician as per certain indications like anuria, uremic symptoms, refractory hyperkalemia, volume overload and metabolic acidosis. It is prudent to initiate "timely" rather than "early" hemodialysis as too early dialysis is as bad as delayed dialysis as it can result in increase in mortality.[9] Intermittent hemodialysis is the most common method of RRT employed in India with varied outcomes. Renal transplantation is rarely if at all, needed for AKI patients. Following RRT, the decision to wean to conservative management is done based on the recovery of clinical, biochemical and metabolic parameters. These patients who are weaned from RRT generally recover; some early, some late and some may progress to ESRD, the factors operating are unclear.[10] In India, non availability of RRT in many centers, financial constraints and patient unawareness regarding disease are major barriers for measuring the burden of renal disease in the community. The factors that determine the prognosis in these patients are believed to be multiple and our study aims at their identification.

MATERIAL & METHOD

This study was done in a tertiary hospital over a three year period from 2010 March to February 2013. Informed consent was taken from all the patients and Ethical clearance was obtained from Institutional Ethics Committee of the hospital**.**

Inclusion criteria: 1) Patients both male and female aged between 20 to 70 years. 2) Patients admitted for various diseases in different intensive care units (ICU) including medical, surgical, cardiac, obstetric, Cardiothoracic and burns unit who developed AKI or admitted with AKI. 3) Patients who required hemodialysis in our hospital for severe renal disease. A total number of 63 patients formed the study population.

Exclusion criteria: Patients with renal disease who did not receive hemodialysis, Patients with previous history of renal disease, obstructive uropathy or acute on chronic kidney disease and patients who already received hemodialysis outside before admission were excluded from the study.

Their age, sex, place of living and occupation were noted. Physical examination was done and history regarding possible risk factors was taken. All patients have undergone hematological tests including Hb%, total and differential counts, and platelet counts. Their Serum creatinine, urea, random blood sugar, electrolytes and arterial blood gas analysis at admission were noted. Along with the treatment for primary condition, all patients underwent hemodialysis for different indications like uremic encephalopathy, Anuria/oliguria, refractory hyperkalemia, metabolic acidosis, volume overload etc. Standard bicarbonate hemodialysis protocol was given to all the patients which included two hours of dialysis at initiation and then increased to four hours during subsequent sessions. The number of sessions of dialysis required for the recovery of each patient was noted. The decision to wean from dialysis was made after the correction of primary metabolic abnormality or achievement of significant clinical improvement or adequate urine output. These patients were followed up thereafter starting from day one after weaning from dialysis. Serial measurements of S. Creatinine and urea were done after the 1st week, 2nd week, 3rd week and after 3 months. Falling patterns of Serum creatinine in patients who successfully completed the follow up was noted.

Patients were classified based on the time taken for normalization of Serum creatinine (recovery) into two groups: Those who recovered within 2 weeks were placed in **group A (N=31)** and those who recovered after 2 weeks were kept under **Group-B (N=23)**. Various parameters mentioned above were studied between the two groups to identify any significant

differences which are likely to influence the prognosis and outcome.

RESULTS

Out of 64 patients admitted for hemodialysis, 41(65%) were males and 22 (35%) were females. Most of the patients were agricultural laborers (65%). Out of 63 patients who completed three months of follow up, 9 (14.3%) met the definition of CKD at third month and hence these patients were not considered to have recovered. The remaining 54 Patients who recovered following hemodialysis, were grouped into group-A (n=31) and group-B. (n=23). The most common age group involved was between 41-50 years.

Table 1: Patients age groups

Age in years	Group A (%)	Group B (%)
20 or below 20	1	0
21-30	2	2
31-40	6	5
41-50	9	10
51-60	8	4
Above 60	5	2
Total	31 (57 %)	23 (43 %)

Various hematological and biochemical parameters, risk factors, number of dialysis sessions were compared between the two groups to find any association with recovery time, as shown in *Table-2*

Table 2: showing comparison of various parameters between the two groups.

	Group-A (n=31)	**Group-B (n=23)**	
	Mean ± SD	Mean ±SD	***P value***
Age in years	48.4 ± 12.9	45.5±10.6	0.38
Hb%	9.6±2.5	9.5±2.2	0.87
TLC (cells/mm^3)	12890±5602	13626±5974	0.64
RBS (mg/dl)	146±68.6	156.7±123.7	0.68
S.Creatinine (mg/dl)	6.4±1.1	8.6±3.7	**0.01***
B.Urea (mg/dl)	183.3±58.9	210.8±76.1	0.14
Serum.Na^+ (mEq/L)	142±7.94	137±9.8	0.06
Serum.K^+ (mEq/L)	4.98±1.12	5.39±1.34	0.22
P^H	7.25±0.13	7.16±0.19	**0.048***
S.Bicarbonate (meq/L)	21.7±2.86	19.7±3.86	**0.03***
HDS	3.54±1.52	5.04±2.40	**0.01***
T.D (days)	8.6±3.6	11.5±5.9	**0.04***
Recovery duration(weeks)	1.83±0.37	3.57±1.2	-----
HDS- number of hemodialysis sessions required, T.D- time delay between first symptom to hemodialysis. *Significance.			

Table 3: showing Gender, Habits and Other risk factors between two groups

RISK FACTOR		**Group-A** (n=31)	**Group-B** (n=23)	***P* value**
Sex	Male	18	16	0.28
	Female	13	7	0.27
Diabetes		5	10	**0.028***
Hypertenson		8	3	0.21
Smoking		11	9	0.5
Alcoholism		4	3	0.56
NSAID abuse		7	2	0.16
. Group A – Patients who recovered within two weeks; Group B – Patients who recovered after two weeks; (* represents statically significant)				

Table 4: showing different causes of AKI

Etiology of AKI	N=54 (%)
Severe Malaria	17 (27.2%)
Sepsis	9 (14.3%)
Post Gastroenteritis	7 (11.1%)
Leptospirosis	6 (9.6%)
Acute glomerulonephritis	5 (8%).
Unknown	7(11%)
Post cardiac or abdominal surgery	5 (8%)
Acute pyelonephritis	2 (3.2%)
Dengue Hemorrhagic fever	1 (1.61%)
Road traffic accident with Rhabdomyolysis	1 (1.61%)
Snakebite	1 (1.61%)
Contrast Nephropathy	1 (1.61%)
Acute Pancreatitis	1 (1.61%)
Total	54 (100%)

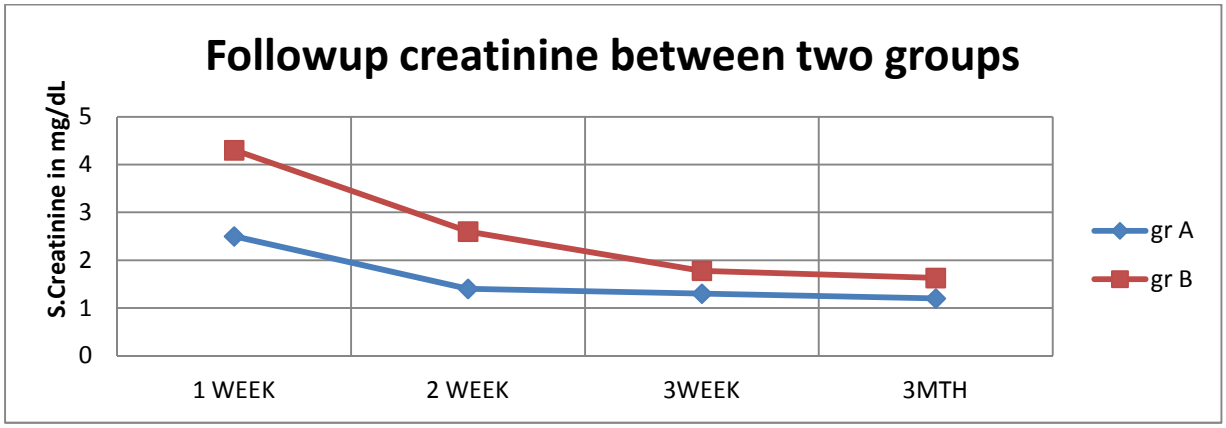

Fig 1: Shows fall of serum creatinine from day-1 after last session of hemodialysis (Note: The curves belonging to both the groups are steep during the first week)

Statistics: All the statistical work was performed by using SPSS trail version 16 and Microsoft Excel 2007. Descriptive statistics were presented in the form of Mean ± Standard Deviation and Percentages. The independent samples T test is used to compare means and a p value < 0.05 is taken as statically significant.

DISCUSSION

Hemodialysis forms an important therapeutic option for severe AKI, but treatment of the primary condition is as important. In our study, all the patients fell into failure stage of RIFLE due to very high serum creatinine at presentation and stage 3 of AKIN criteria as all of them underwent hemodialysis. Males are commonly affected as they mostly work outside, getting exposed to infections, toxins and sustain dehydration.[11] Patients over 40 years of age comprised 75% of the cases. This could be explained by gradually falling renal reserve with age. Our study highlighted the importance of recognizing severe malaria as important cause of AKI in India as it was the most common cause. Overall, infections comprised 75% of all causes of AKI. Nine patients (14.3%) met the definition of CKD after three months but their disease progression was not followed thereafter. Maximum recovery following weaning from hemodialysis was noticed in the immediate first week. There was a gradual fall of serum creatinine during subsequent three months.

Comparison between patients with early (group-A) and late recovery (group-B) was done after the follow up period of three months. Age and hematological parameters showed no difference between the two

groups. Mean random blood sugar, blood urea, serum potassium are higher in group-B but showed no statical significance. Mean serum creatinine (6.4±1.1 vs 8.6±3.7; p <0.05), S. Bicarbonate (21.7±2.8 vs 19.7±3.8; p <0.05) and pH at admission (7.25±0.13 vs 7.1±0.19; p < 0.05), total number of hemodialysis sessions (3.5±1.5 vs 5±2.4; p <0.05), time delay between disease and treatment (8.6±3.6 vs 11.5±5.9; p <0.05), has shown statically significant association with the recovery time. Patients with high serum creatinine at admission (implying higher renal functional loss) took much longer to recover. Studies have shown that higher stages of AKI can result in prolonged hospital stay due to delayed renal recovery.[12] patients with severe metabolic acidosis characterized by low bicarbonate and low pH took much longer time to recover. Metabolic acidosis results due to multiple factors apart from inability of the kidney to excrete metabolic acids. Hepatic involvement, which is commonly seen in Malaria, Leptospirosis, Dengue infections, Sepsis and as a component of multi organ dysfunction syndrome (MODS) along with starvation in these patients can contribute to significant metabolic acidosis.

AKI patients who required more number of hemodialysis sessions had delayed recovery. This is because patients who had severe disease required more number of sessions and the recovery after weaning is also delayed owing to the severity. A very important outcome of this study is that delay in the initiation of hemodialysis in indicated patients resulted in delayed recovery following weaning. This is evidenced by the significantly higher time gap (days) between first symptoms and first hemodialysis in group B patients (A vs B = 8.6 ± 3.6 vs 11.5 ± 5.9; p=0.04). The exact timing of dialysis, duration and withdrawal of dialysis sessions is Physician's discretion, and is subjected to variations.[13] Adding to delayed hospitalization, conservative approach is implemented by some, even when there is clear indication for RRT, which can actually worsen the metabolic complications and there by mitigating the chances of recovery even after subsequent RRT. The term "door to dialysis time" is suggested by some authors to emphasize the importance of timely hemodialysis. [14]

In our study, patients with diabetes had delayed recovery. This could be because of underlying preexisting diabetic nephropathy in these patients. Contrast nephropathy is one condition where unequivocal evidence exists regarding renal damage and poor recovery following RRT in diabetes.[15] whether or not, this can be extrapolated to other causes of AKI is not known. In our study, factors like gender, hypertension, smoking, alcoholism and even NSAID intake have not shown any association with recovery time. This is in contrast to earlier studies documenting NSAID use as a potential cause of renal damage as well as delayed renal recovery.[16] However, we did not collect the data regarding the type, quantity and duration of use of NSAIDS in any patient included in the groups due to unreliability of patient history.

The limitations of our study include small sample size, lack of application of Glomerular filtration rate, lack of long term follow up in recovered patients as some of them could have landed in worsening of renal function following apparent recovery, thus missing the true burden of AKI progressing into CKD.

CONCLUSION

AKI can have varied etiologies, and infections form the bulk of these cases. Along with the correction of primary cause, timely RRT can have significant impact on the recovery of patients. Patients presenting late, patients with high serum creatinine, low Ph and low serum bicarbonate at admission, patients who required more number of hemodialysis sessions and known diabetics irrespective of diabetes control, are prone for delayed recovery following weaning from hemodialysis.

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