**Original article:**

**Study of long term outcomes of acute renal failure**

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**Abstract:**

**Introduction:** Acute kidney injury (AKI) is a major public health problem affecting millions of patients worldwide and leading to decreased survival, increased progression to underlying chronic kidney disease (CKD).

**Materials and methods:** This was Prospective follow up study conducted at NRI INSTITUTE OF MEDICAL SCIENCES for two years duration. Study subjects were individuals who are aged above 15 years and diagnosed to have AKI according to AKIN (or) RIFLE criteria.

**Results and Conclusion:** About 97.5% of study population got completely recovered from AKI by the end of 1 year. There was significant drop in serum urea, creatinine levels, electrolyte imbalances. ,eGFR is normalized in majority of patients through-out the study period and also between every follow-up which statistically highly significant. None among the study population had progressed to dialysis dependency.

**Keywords:** Acute kidney injury , RIFLE criteria.

**Introduction:**

Acute kidney injury (AKI) is a major public health problem affecting millions of patients worldwide and leading to decreased survival, increased progression to underlying chronic kidney disease (CKD). AKI is not a single disease but rather a syndrome comprising multiple clinical conditions. Outcomes in AKI are influenced by the underlying disease causing the condition, as well as by the severity and duration of renal impairment and by the baseline condition of the patient. The detrimental effects of AKI are not limited to classical well-known symptoms such as fluid overload and electrolyte abnormalities. AKI can also lead to problems that are not readily appreciated at the bedside and can extend well beyond the ICU stay. This study will is done to look for long-term outcome in survivors of AKI based on definition and classification criteria for AKI given by AKIN and RIFLE systems.[1]

The incidence of acute kidney injury (AKI) is increasing in hospitalized patients. The Acute Dialysis Quality Initiative (ADQI) consensus defines complete renal recovery as return to baseline classification within the RIFLE criteria and partial recovery as a change in RIFLE status in patient free of dialysis. In spite of this, few studies have evaluated renal recovery in the context of this recommendation. [2-8] Ali et al found that 68% of their population had full renal recovery and 5% had partial recovery based on the return of serum creatinine to its baseline value. [9] The factors associated with renal recovery or with progression to ESRD after an episode of AKI are not well established. Despite increasing recognition that renal recovery after AKI is an important outcome, surprisingly little data defining this outcome is available. In our study we included 80 patients who are diagnosed to have acute kidney injury (including both the patients with and without renal replacement therapy) and followed up periodically for about one year from the date of discharge describing the pattern of renal recovery accordingly.

**Materials and methods:**

This was Prospective follow up study conducted at NRI INSTITUTE OF MEDICAL SCIENCES for two years duration. Study subjects were individuals who are aged above 15 years and diagnosed to have AKI according to AKIN (or) RIFLE criteria.

INCLUSION CRITERIA:

Patients who were diagnosed with AKI according to AKIN

EXCLUSION CRITERIA:

1. Patients with acute worsening of chronic kidney disease.
2. Patients who are already diagnosed with chronic kidney disease and on treatment.
3. Patients with co-morbid conditions like diabetes mellitus, essential hypertension and structural kidney diseases like polycystic kidney disease, medullary sponge kidney etc. are excluded.

METHODOLOGY:

This study included follow-up study of 80 survivors of AKI patients with serum urea, serum creatinine, serum electrolytes (low Hco3, hyperkalemia, hyponatremia), Haemogram (abnormal haemoglobin, leukocytosis, thrombocytopenia), Urine routine examination (pyuria, hematuria and proteinuria), Renal biopsy (where-ever indicated), Ultrasonography of abdomen and pelvis (as required), at admission, at discharge, at three months, at six months and at one year from NRI INSTITUTE OF MEDICAL SCIENCES, VISAKHAPATNAM from AUGUST 2018 To JULY 2019.

**Observations and results:**

This is a prospective follow-up study done in NRI INSTITUTE OF MEDICAL SCIENCES, VISAKHAPATNAM. The data was collected as per proforma and analysed. The results of study are depicted below.

**TABLE 1: GENDER DISTRIBUTION**

|  |  |  |
| --- | --- | --- |
| **SEX** | **FREQUENCY** | **PERCENT** |
|  F | 31 | 39 |
|  M | 49 | 61 |
|  TOTAL | 80 | 100 |

**TABLE 2: Incidence of AKI based on etiology**

|  |  |  |
| --- | --- | --- |
| **DIAGNOSIS** | **FREQUENCY** | **PERCENT** |
| ACUTE GASTROENTERITIS | 4 | 5 |
| ACUTE TUBULAR NECROSIS | 3 | 3.75 |
| LEPTOSPIROSIS | 18 | 21.25 |
| LOWER LIMB CELLULITIS | 1 | 1.25 |
| MALARIA | 9 | 11.25 |
| NEPHROTIC SYNDROME  | 2 | 2.5 |
| PANCREATITIS  | 3 | 3.75 |
| SCRUB TYPHUS  | 2 | 2.5 |
| SEPSIS | 34 | 42.5 |
| SNAKE BITE | 5 | 6.25 |
| TOTAL | 80 | 100 |

Based on the above study and data analysis, sepsis contributes as a cause for majority of patients with AKI by different mechanisms (either direct or indirect). Following sepsis, leptospirosis and malaria accounts for second and third major cause of AKI which shows endemicity and increased prevalence of disease .

**TABLE 4: Showing Mean, Standard deviation and Friedman test of S.creatinine during study**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S. Creatinine** | **N** | **Minimum** | **Maximum** | **Mean** | **Std.****Deviation** | **Median** | **Friedman test** | **P value** |
| At admission | 80 | 1.2 | 11.1 | 5.34 | 2.24 | 5.10 | 227.004 | 0.000HS |
| At discharge | 80 | 0.3 | 4.2 | 1.85 | 0.70 | 1.80 |  |
| At 3 months | 80 | 0.4 | 2.5 | 1.25 | 0.33 | 1.20 |  |
| At 6 months | 80 | 0.5 | 1.9 | 1.07 | 0.37 | 1.00 |  |
| At 1 year | 80 | 0.4 | 1.4 | 0.82 | 0.19 | 0.80 |  |

**TABLE 5: Showing pairwise comparisons by Wilcoxon signed rank test**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Mean difference** | **Change** | **P value** | **Significance** |
| S. Creatinine At AdmissionAt DischargeAt 3 MonthsAt 6 MonthsAt 1 Year | 3.4864.0944.2734.520 | 65.2876.6580.0284.74 | 0.0000.0000.0000.000 | HSHSHSHS |
| S. Creatinine At DischargeAt 3 MonthsAt 6 MonthsAt 1 Year | 0.6080.7871.330 | 32.7642.4656.05 | 0.0000.0000.000 | HSHSHS |
| S. Creatinine At 3 Month At 6 MonthsAt 1 Year | 0.1800.430 | 14.4234.63 | 0.0000.000 | HSHS |
| S. Creatinine At 6 MonthsAt 1 Year | 0.250 | 23.62 | 0.000 | HS |

Above tables 4 and 5 represent the change in serum creatinine levels during follow-up period. By Friedman test and pairwise comparison by Wilcoxon signed rank test it is evident that there was significant drop in serum creatinine levels from admission till the end of 1 year (i.e., in every follow-up till end of study period) with P value 0.000 (<0.05).

 **TABLE 6: Showing McNemer test analysis in study population during study period**

|  |  |  |
| --- | --- | --- |
| **Parameter (Serum Creatinine)** | **McNemer Test Value** | **Significance** |
| At Discharge – At Admission | 0.000 | Hs |
| At 3months – At Admission | 0.000 | Hs |
| At 6 Months – At Admission | 0.000 | Hs |
| At 1 Year – At Admission | 0.000 | Hs |
| At 3 Months – At Discharge | 0.000 | Hs |
| At 6 Months – At Discharge | 0.000 | Hs |
| At 1 Year – At Discharge | 0.000 | Hs |
| At 6 Months – At 3months | 0.527 | Ns |
| At 1 Year – At 3months | 0.000 | Hs |
| At 1 Year – At 6 Months | 0.000 | Hs |

**TABLE 7: Showing study population with normal and abnormal creatinine during study period**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Normal** | **Abnormal** | **Total** |
| **Serum Creatinine** | **No. Of Patients** | **%** | **No. Of Patients** | **%** | **No. Of Patients** | **%** |
| At admission | 2 | 2.5 | 78 | 97.5 | 80 | 100 |
| At discharge | 18 | 22.5 | 62 | 77.5 | 80 | 100 |
| At 3 month | 60 | 75 | 20 | 25 | 80 | 100 |
| At 6 months | 62 | 77.5 | 18 | 22.5 | 80 | 100 |
| At 1year | 79 | 98.7 | 1 | 1.3 | 80 | 100 |

From the above tables 6, 7 and figure 5 it is evident that

1. At admission 97.5% of patients had abnormal creatinine and at the end of 1year only 1.3% of patients had abnormal serum creatinine.
2. Improvement of S.creatinine to normal level during follow-up period was significant till end of study period i.e., 1 year (which is evident by P value < 0.000 from McNemer test).

eGFR calculated at the end of 1 year for all study population as per MDRD eGFR formula (according to KDOQI CKD criteria [10] showed that only 2 individuals (2.5%) had eGFR less than 60 ml/min/1.73m2 and are labelled as chronic kidney disease according to KDOQI guidelines. Remaining 78 individuals (97.5%) had eGFR above 60 ml/min/1.73m2.

**TABLE 8: Showing percentage and no. of subjects with CKD at end of 1year.**

|  |  |  |  |
| --- | --- | --- | --- |
| **CKD** | **NO.OF SUBJECTS** | **% PERCENTAGE** | **P VALUE** |
| ABSENT | 78 | 97.5 | 0.000HS |
| PRESENT | 2 | 2.5 |

**TABLE 9: Showing Mean, Standard deviation and Friedman test of Blood urea during study**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Blood Urea** | **N** | **Min** | **Maximum** | **Mean** | **S. Deviation** | **Median** | **Friedman Test** | **P Value** |
| At Admission | 80 | 51 | 319 | 131.54 | 62.60 | 118 | **238.583** | **0.000****Hs** |
| At Discharge | 80 | 14 | 103 | 54.37 | 19.23 | 53 |
| At 3 Months | 80 | 15 | 56 | 31.85 | 8.61 | 30 |
| At 6 Months | 80 | 14 | 49 | 27.35 | 7.78 | 27 |
| At 1 Year | 80 | 14 | 52 | 25.38 | 7.76 | 23 |

**TABLE 10: Showing pairwise comparisons by Wilcoxon signed rank test**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Mean Difference** | **Change** | **P Value** | **Significance** |
| Blood Urea At Admission At DischargeAt 3 MonthsAt 6 MonthsAt 1 Year | 77.17799.696104.190106.165 | 58.6775.7979.2180.71 | 0.0000.0000.0000.000 | HsHsHsHs |
| Blood Urea At Discharge At 3 MonthsAt 6 MonthsAt 1 Year | 22.51927.01328.987 | 41.4249.6953.32 | 0.0000.0000.000 | HsHsHs |
| Blood Urea At 3 Months At 6 MonthsAt 1 Year | 4.4946.468 | 14.1120.31 | 0.0000.000 | HsHs |
| Blood Urea At 6 Months At 1 Year | 1.975 | 7.22 | 0.013 | Sig |

From the above tables 9 and 10, the drop in blood urea levels are analysed during follow-up period by Friedman test and pairwise comparison by Wilcoxon signed rank test .It is evident that there was significant drop in blood urea level from admission to 6 months (about 79.21%) with P value <0.000which is statistically highly significant whereas from 6 months to the end of 1 year, there was slight significant drop in blood urea levels (about 7.22%) with P value of 0.013 (<0.05) which is just statistically significant.

**TABLE 11: Showing McNemer test analysis in study population during study period**

|  |  |  |
| --- | --- | --- |
| **Parameter (Blood Urea)** | **McNemer Test P Value** | **Significance** |
| At Discharge – At Admission | 0.000 | Hs |
| At 3months – At Admission | 0.000 | Hs |
| At 6 Months – At Admission | 0.000 | Hs |
| At 1 Year – At Admission | 0.000 | Hs |
| At 3 Months – At Discharge | 0.000 | Hs |
| At 6 Months – At Discharge | 0.000 | Hs |
| At 1 Year – At Discharge | 0.000 | Hs |
| At 6 Months – At 3months | 0.046 | Sig |
| At 1 Year – At 3months | 0.046 | Sig |
| At 1 Year – At 6 Months | 1.000 | Ns |

**TABLE 12: Showing study population with normal and abnormal Blood Urea during study period**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Normal** | **Abnormal** | **Total** |
| **Blood Urea** | **No. Of Patients** | **%** | **No. Of Patients** | **%** | **No. Of Patients** | **%** |
| At Admission | 0 | 0 | 80 | 100 | 80 | 100 |
| At Discharge | 24 | 30 | 56 | 70 | 80 | 100 |
| At 3 Month | 74 | 92.5 | 6 | 7.5 | 80 | 100 |
| At 6 Months | 78 | 97.5 | 2 | 2.5 | 80 | 100 |
| At 1year | 78 | 97.5 | 2 | 2.5 | 80 | 100 |

From the above tables 11, 12 and figure 8 it is evident that

1. At admission 100% of patients had abnormal blood urea and at the end of 1 year 2.5% of patients had abnormal blood urea.
2. Improvement of blood urea to normal level during follow-up period was significant till 6months (which is evident by P values 0.000 and 0.046 < 0.05 from McNemer test) and after 6months it is statistically insignificant (which is evident by P value 1.000 > 0.05 from McNemer test)

**TABLE 13: Showing study population with normal and abnormal S.electrolytes during study period.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Normal** | **Abnormal** | **Total** |
| **Serum Electrolytes** | **No. Of Patients** | **%** | **No. Of Patients** | **%** | **No. Of Patients** | **%** |
| At Admission | 11 | 13.75 | 69 | 86.25 | 80 | 100 |
| At Discharge | 11 | 13.75 | 69 | 86.25 | 80 | 100 |
| At 3 Month | 78 | 97.5 | 2 | 2.5 | 80 | 100 |
| At 6 Months | 79 | 98.75 | 1 | 1.25 | 80 | 100 |
| At 1year | 78 | 97.5 | 2 | 2.5 | 80 | 100 |

**TABLE 14: Showing McNemer test analysis in study population during study period.**

|  |  |  |
| --- | --- | --- |
| **Parameter (Serum Electrolytes)** | **McNemer Test P Value** | **Significance** |
| At Discharge – At Admission | 1.000 | Ns |
| At 3months – At Admission | 0.000 | Hs |
| At 6 Months – At Admission | 0.004 | Hs |
| At 1 Year – At Admission | 0.000 | Hs |
| At 3 Months – At Discharge | 0.000 | Hs |
| At 6 Months – At Discharge | 0.004 | Hs |
| At 1 Year – At Discharge | 0.000 | Hs |
| At 6 Months – At 3months | 0.000 | Hs |
| At 1 Year – At 3months | 1.000 | Ns |
| At 1 Year – At 6 Months | 0.000 | Hs |

From the above table 13, 14 and figure 9 it is evident that

* About 86.25% of study population had abnormal serum electrolytes at the time of admission and 2.5% abnormal at the end of study period (1year).
* Serum electrolytes took about 3 months duration to get normalised which is statistically significant with P value <0.05.
* After 3 months there was no significant percentage of patients becoming normal which is statistically insignificant with P value >0.05.

**DISCUSSION:**

Acute kidney injury (AKI) [1, 2] is defined as an abrupt decline in renal function resulting in the inability to excrete metabolic wastes and maintain proper fluid and electrolyte balance.. This study was done in survivors of AKI who are defined based on definition and classification criteria for AKI given by AKIN and RIFLE systems to know the long term outcome and sequelae of AKI. The recovery of kidney function following AKI is an important determinant of morbidity and may have long-term implications for the health and well-being of patients. Accordingly, the long-term follow-up study by Schiffl and Fischer is an important addition to our understanding of the natural history of AKI in critical illness. [10,11] They performed a prospective 5-year follow-up study of 425 patients with severe AKI treated with RRT. Notably, no patient had evidence of pre-existing CKD when defined by radiologic signs of CKD, persistent abnormal urinalysis or a decreased estimated glomerular filtration rate (eGFR) or elevated serum creatinine [*>*1.3 mg/dl (115 μmol/L)].

At the time of hospital discharge, only 57% had achieved complete recovery, while the remaining 43% had partial recovery and no patient was receiving chronic dialysis. This study also showed that at end of 1 year, 26% of survivors had evidence of CKD (stages 2–5) and at 5 years, the prevalence of CKD in survivors was only 14%, yet, the apparent improvement with time was largely attributable to deaths for those who had partial recovery. This study had also shown that if patients failed to normalize function by 6–12 months after their episode of AKI, no further recovery occurred. Remarkably, only 2% of survivors progressed to ESRD and required re-initiation of dialysis.

Based on the long-term follow-up study in AKI patients done by Schiffl and Fischer, we had conducted a prospective follow-up study for 1 year on long-term outcome and sequelae of AKI within the survivors of AKI of varied aetiology without any pre-existing evidence of CKD in our hospital setting. In this study, we studied the pattern of recovery and time duration required for recovery of renal function after AKI. We also studied the recovery of other parameters like urine analysis, serum electrolytes and complete haemogram to the normal limits following AKI. This study also analysed the percentage of survivors of AKI progressed into the chronic kidney disease and dialysis dependency.

We studied a total of 80 cases of survivors of episode of AKI of varied aetiology who are admitted in NRI INSTITUTE OF MEDICAL SCIENCES based on purposive sampling technique with both inclusion and exclusion criteria as mentioned above. Patient’s data was collected as per proforma at time of admission, discharge, 3months, 6months and 1year. Collected data was analysed by frequency, percentage, Mean and S.D. Tests such as Friedman test used to compare the change within the group and post hoc analysis by Wilcoxon signed rank test is performed. McNemer test was carried out to compare the change in parameter if any from abnormal to normal in study population during the follow-up period.

 Majority of individuals enrolled in our study are males which was around 61.25%.Majority of the patients with AKI falls between 21 to 30 years. Therefore incidence of AKI is more during 3rd decade of life. Based on the above study and data analysis, sepsis contributes as a cause for majority of patients with AKI by different mechanisms (either direct or indirect). Following sepsis, leptospirosis and malaria accounts for second and third major cause of AKI which shows endemicity and increased prevalence of disease in South-Karnataka region. Based on the recovery of renal function with serum creatinine as a determinant it is evident from the analysis that, at admission 97.5% of patients had abnormal creatinine and at the end of 1 year only 1.3% of patients had abnormal creatinine. Recovery of S.creatinine to normal level during follow-up period was significant till the end of 1 year (which is evident by P value < 0.000 from McNemer test). Significant changes in serum creatinine are assessed by Friedman test and pairwise comparison by Wilcoxon signed rank test and it is evident that there was significant drop in serum creatinine levels from admission till the end of 1 year (i.e., in every follow-up till end of study period) with P value 0.000 (<0.05).

 Progression of AKI to CKD is assessed by calculating the reduced effective glomerular filtration rate (to less than 60 ml/min/1.73m2)according to KDOQI CKD guidelines. eGFR calculated at the end of 1 year for all study population as per MDRD eGFR formula showed that only 2 individuals (2.5%) had eGFR less than 60 ml/min/1.73m2 and are labelled as chronic kidney disease. Remaining 78 individuals (97.5%) had eGFR above 60 ml/min/1.73m2. Data analysis of blood urea levels showed that, at admission 100% of patients had abnormal blood urea and at the end of 1 year 2.5% of patients had abnormal blood urea. Improvement of blood urea to normal level during follow-up period were significant till 6months (which is evident by P values 0.000 and 0.046 < 0.05 from McNemer test) and after 6months drop in blood urea levels were statistically insignificant (which is evident by P value 1.000 > 0.05 from McNemer test) From the end of 3 months to end of 1 year, study population who got normalised are statistically insignificant with McNemer test P value 0.317 (>0.05).

From this study we observed that there was significant drop in serum creatinine levels through-out the study period. It is also observed from the pairwise comparison that drop in creatinine is statistically highly significant in every follow-up.

**Conclusion:**

1. About 97.5% of study population got completely recovered from AKI by the end of 1 year.
2. There was significant drop in serum urea, creatinine levels, electrolyte imbalances. ,eGFR is normalized in majority of patients through-out the study period and also between every follow-up which statistically highly significant.
3. None among the study population had progressed to dialysis dependency.

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