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In-Hospital Outcomes of Patients with Acute Kidney Injury Following Acute Coronary Syndrome in a Tertiary level Hospital.

MSI Tipu Chowdhury[1], Khaled Md. Iqbal[1], Zahidul Mostafa[2], Md. Fakhrul Islam Khaled[1], Sadia Sultana[3], SM Ear-E-Mahbub[1]

[1]Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangaladesh
[2]Department of Cardiology, Cox's Bazar Medical College Hospital, Cox's Bazar, Bangladesh.
[3]MBBS, Chittagong Medical College, Chittagong, Bangladesh.

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ABSTRACT

Background: Acute Kidney Injury (AKI) is a strong predictor of in-hospital adverse outcomes, which is a common complication of acute coronary syndromes (ACS). ACS patients with renal impairment during hospitalization are associated with adverse outcomes like heart failure, cardiogenic shock, arrhythmia, dialysis requirement and mortality. **Objective:** To compare ACS patients with or without AKI has significant risk of in-hospital adverse outcomes. **Methods:** This prospective comparative study was conducted in the Department of Cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period of July 2017 to June 2018. A total of 70 eligible patients were included in this study. Electrocardiography, blood test for serum creatinine (on admission, 12 hours, 48 hours and at the time of discharge), lipid profile, RBS, 2-D echocardiography along with serum troponin, CK MB and electrolytes were done for all patients. **Results:** It was observed that mean age was 58.0±8.5 years in group A (ACS with AKI) and 55.6±12.3 years in group B (ACS without AKI). Male population was predominant in both the groups (85.7% and 74.2%, respectively). Heart failure was more common in group A than in Group B (74.3% vs 34.2% p=0.001 respectively). Arrhythmia was more common in group A than in Group B (100% vs 74.2% respectively). The mean duration of hospital stay was significantly higher in Group A than in the Group B (9.4±2.3 vs 7.2±0.6; p=0.001) days. **Conclusion:** This study showed adverse outcomes including longer duration of hospital stays were more common in the patients with AKI (group A) than in the patients without AKI (group B).

Keywords: Acute Coronary Syndrome, Acute kidney injury, In hospital outcomes.

INTRODUCTION

Cardiovascular disease (CVD) has become the leading cause of death worldwide. In 2013, CVD caused an estimated 17.3 million deaths and led to 330 million disability-adjusted life-years (DALYs) lost about 32% of all deaths and 13% of all DALYs lost that year. As with many high-income countries during the last century, low- and middle-income countries are now experiencing an alarming and accelerating increase in CVD.[1]

In Bangladesh, National data on incidence and mortality of Coronary artery disease (CAD) are few, the incidence of CAD was 0.33%.[2] The prevalence of Ischemic heart disease (IHD) defined by presence of pathological Q on electrocardiogram or current medication for IHD was 3.4% and men was predominant with an important problem even in traditional rural population of Bangladesh.[3] Also, CAD prevalence was between 1.85% and 3.4% in rural and 19.6% in an urban.[4] The most recent data on CAD prevalence was 4.5%.[5]

It is well stated that ACS may be associated to renal dysfunction and significantly increase mortality, morbidity and cost of care. Most studies have found to be associated with greater short- and long-term all-cause and cardiovascular mortality, prolonged duration of hospitalization, increased readmission rates, accelerated progression to CKD stages and higher healthcare costs. In addition, there seems to be a biological gradient between severity of AKI and risk of death. Even small acute changes in sCr (0.3 mg/dL) can modify the risk of death.[6] There is a strong independent graded relationship between severity of AKI and long-term mortality at all time points of follow-up for up to at least 10 years following acute myocardial infarction (AMI).[7,8]

Thus, in this study we tried to evaluate the in-hospital outcomes between patients of ACS with or

Name & Address of Corresponding Author
Dr. MSI Tipu Chowdhury.
Resident,
Department of Cardiology,
Bangabandhu Sheikh Mujib Medical University,
Dhaka, Bangaladesh.

without AKI. It helps to know better about the outcomes and its implication to reduce knowledge gap as well as regular follow up patient before developing any major adverse effect along with chronic renal failure.

MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period of August 2017 to July 2018. A total of 70 eligible patients were included in this study of which 35 patients were included in group A (ACS with AKI) and 35 patients were included in group B (ACS without AKI) with following inclusion and exclusion criteria.

Inclusion Criteria:

- Patients diagnosed as ACS (STEMI/NSTEMI/UA) according to ACC/AHA guideline.
- Patients age ≥ 18 years-old, both sex
- Hospitalization for≥48 hrs.

Exclusion Criteria:

- Patient refused taking part in study.
- Patients with history of any previous MI.
- Patients with history of PCI or CABG.
- Patients with any valvular heart disease, congenital heart disease or primary myocardial or pericardial disease.
- Patients with co-morbidities like CKD, COPD, ESRD, CLD, malignancy

AKI was diagnosed, on the basis of increased serum creatinine level 0.3mg/dL from baseline within 48 hours after hospitalization. They were subjected to electrocardiography, blood test for serum creatinine (on admission, 12 hours, 48 hours and at the time of discharge), lipid profile, RBS, 2-D echocardiography along with serum troponin, CK MB and electrolytes. The study was performed according to the guideline of the Helsinki Declaration and was aprroved by the institutional Review Board (IRB).
Baseline investigations (12 leads ECG, Serum Troponin-I, CK-MB, RBS, Lipid profile, Electrolytes, Urea and Serum Creatinine) were done. On the basis of clinical history, 12 leads ECG and troponin-I, patients diagnosed as a case of ACS. On admission serum creatinine was normal to all selected study population. After admission, all the patients in study group were observed and monitored for 48 hours and further two samples of blood for serum creatinine were taken on 12 hrs and 48 hrs. All the blood reports were collected from patient's clinical record files. The patients whom, serum creatinine 0.3 mg/dL increased from baseline level (on admission) within 48 hrs considered as cut off value to diagnose AKI. The guideline directed medical therapy was given to both groups and follow up was done. The transthoracic echocardiography was performed. The regional wall motion abnormality and left ventricular ejection fraction (LVEF) were measured. Both the groups were evaluated by day to day new change in history and clinical examination till hospitalization. In-hospital outcomes (heart failure, cardiogenic shock, arrhythmia, requirement of dialysis, duration of hospital stay and death) of ACS patients with AKI and without AKI were observed and recorded. The total duration of hospital stay of both the groups was recorded. The last sample of serum creatinine was done on discharge.

Statistical analysis

After compiling the collected data from all patients, statistical analysis was performed using the statistical package for social sciences (SPSS) program, version 23 for windows. Continuous parameters were expressed as mean±SD and categorical parameters as frequency and percentage. Comparisons between groups (continuous parameters) were done by Unpaired student's t test. Categorical parameters were compared by Chi-Square test. Multivariate logistic regression analysis was performed to identify In-hospital mortality risk among patients with AKI. The significance of the results as determined in 95.0% confidence interval and a value of $p < 0.05$ was maintained.

RESULTS

This prospective comparative study was carried out in the Department of Cardiology, University Cardiac Center, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, over a period of one year from July 2017 to June 2018. The main objective of the study was to find out and compare in-hospital outcomes of patients with ACS with or without AKI developed after hospitalization. A total of 70 patients were included in this study of which 35 patients were included in group A (ACS with AKI) and 35 patients were included in group B (ACS without AKI).
It was observed that mean age was 58.0±8.5 years in group A and 55.6±12.3 years in group B. Majority (80%) were >50 years age in group A and majority (68.5%) in group B. The range between the groups were (34-76 & 33-95 years, respectively). The difference was statistically not significant between the groups (P>0.05). [Table 1]

Comparison of study patients by sex 30 (85.7%) patients were male in Group A and 26 (74.2%) group B. 5 (14.3%) female patients were in Group A and 9 (25.8%) in Group B. In both groups male patients were predominant. [Figure 1]

Grouping of study population by serum creatinine. The mean serum creatinine level of group A was 1.92±0.9 and group B was 1.04±0.15. [Table 2]

Table 1: Comparison of study patients by age (N=70)

Age in years	Group A n=35 (%)	Group B n=35 (%)	P value
30 – 40	1(2.9)	4(11.4)	
41 – 50	6(17.1)	7(20.0)	
51-60	14(40.0)	12(34.3)	
≥ 60	14(40.0)	12(34.2)	
Mean±SD	58.0±8.5	55.6±12.3	0.337ns
Range	34-76	33-95	

Data were analyzed using student's t-test and the level of significance was set at <0.05.

Grouping of study population by serum creatinine. The mean serum creatinine level of group A was 1.92±0.9 and group B was 1.04±0.15. [Table 2]

The comparison of serum creatinine raise during in-hospital stay. The first sample was taken on admission (Group A=0.9806 and Group B=0.966), after 12 hours of admission (Group A=1.84 and Group B=1.0283), after 48 hours of admission (Group A=2.9597 and Group B=1.139) and before discharge (Group A=3.3729 and Group B=0.9894). [Figure 2]

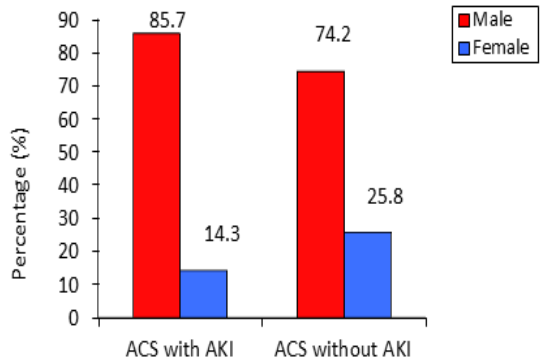

Figure 1: Bar chart showing comparison of study patients by sex

Table 2: Comparison of study patients by Serum Creatinine (N=70)

	Group A (n=35)	Group B (n=35)
Serum Creatinine (mg/dL)	1.92±0.90	1.04±0.15

Data were analyzed using student's t-test and the level of significance was 0.05.

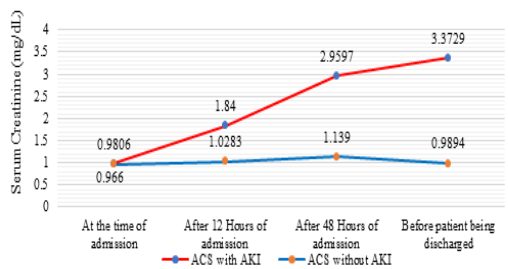

Figure 2: Time graph showing comparison of Serum Creatinine levels in both groups.

Comparison of study patients by risk factors of coronary heart disease (CAD). All the risk factors except smoking were more or equally distributed in both the groups. The predominant risk factor was hypertension (77.1% vs 74.2%) in both groups followed by diabetes mellitus (62.8% vs 48.5%) and dyslipidemia (45.7% vs 42.8%) respectively in both the groups. Family history of IHD was equally present in both the groups. The difference in these risk factor along with family history of IHD were not statistically significant. The smoking was predominant 27 (77%) in group A than 17 (48.5%) group B which was statistically significant between the groups. [Table 3]

Comparison of study patients by haemodynamics. It was observed that the mean systolic blood pressure and diastolic blood pressure was lower in group A than group B (106.4±20.5 vs 131.7±25.9,69.1±12.4 vs 83.1±15.4 respectively=0.001) which was statistically significant. The mean heart rate was higher in group A than group B (92.2±24.3 vs 87.2±15.3 respectively; p=0.314). The difference was not statistically significant. [Table 4]

The base line investigations of the study population was observed that the ECG changes of ST elevation were more common in Group A than Group B (88.6% vs 57.1% respectively) whereas ST depression were more common in Group B than Group A (42.9% vs 11.4% respectively. It was statistically significant between groups (p=0.001). The mean LVEF were significantly lower in the Group A than in the Group B (41.6±7.4 Vs 50.1±8.5 respectively p=0.001) these were statistically significant in between the groups. The mean random blood sugar (RBS) was higher than in group A than group B (12.0±5.4 Vs 9.9±4.2) which was not statistically significant. [Table 5]

It was observe that total 88.5% were STEMI and 11.5% were NSTEMI. Among them, inferior MI(35.5%) were predominant followed by anterior MI (25.8%) and Antero-septal MI (25.8%). [Table 6]

The study patients by in-hospital adverse outcomes, observed that heart failure. It was observed that heart failure was more common in group A than in Group B (74.3% Vs 34.2%; p=0.001 respectively). This was statistically highly significant in between both groups. It was observed that cardiogenic shock was more common in group A than in Group B (51.4% Vs 14.2% p=0.001 respectively). This was statistically highly significant in between both groups. It was observed that arrhythmia was more common in group A than in Group B (100% Vs 0%; p=0.001 respectively). This was statistically highly significant in between both groups. It was observed that 7(20%) patients of group A required urgent dialysis than in the group B. This was statistically highly significant in between the groups. It was also observed that 2(5.7%) patients dead in group A than in group B. [Table 7]

Table 3: Comparison of study patients by risk factors (N=70)

	Group A n=35	Group B n=35	P value
Smoking			
Yes	27(77.1)	17(48.5)	0.013
No	8(22.9)	18(51.5)	
Dyslipidemia			
Yes	16(45.7)	15(42.8)	0.810ns
No	19(54.3)	20(57.2)	
Family history of IHD			
Yes	7(20.0)	7(20)	1.000ns
No	28(80.0)	28(80.0)	
Hypertension			
Yes	27(77.1)	26(74.2)	0.780ns
No	8(22.9)	9(25.8)	
Diabetes Mellitus			
Yes	22(62.8)	17(48.5)	0.229ns
No	13(37.2)	18(51.5)	

Data were analyzed using Chi-square (χ^2)test and the level of significance was 0.05.

Table 4: Comparison of study patients by Haemodynamics (N=70)

	(Group A) (n=35)	(Group B) (n=35)	P value
Systolic BP (mmHg)# (On Admission)	106.4±20.5	131.7±25.9	0.001
Diastolic BP (mmHg)# (On Admission)	69.1±12.4	83.1±15.4	0.001
Heart Rate (bpm)# (On Admission)	92.2±24.3	87.2±15.3	0.314ns

Data were analyzed using student's t-test and the level of significance was 0.05.

* Data were analyzed using Chi-square (χ^2) test & Fisher's Exact Test.

Table 5: Comparison of study patients by investigations (N=70)

ECG*	Group A n=35	Group B n=35	P value
ST Elevation	31(88.6)	20(57.1)	0.012
ST Depression	4(11.4)	13(42.9)	
LVEF# [Mean±SD]	41.6±7.4	50.1±8.5	0.001
RBS (mg/dL) # [Mean±SD]	12.0±5.4	9.9±4.2	0.076ns

Data were analyzed using student's t-test and the level of significance was 0.05.

* Data were analyzed using Chi-square (χ^2) test and the level of significance was 0.05.

The comparison of hospital stay between the groups. The mean duration of hospital stay was significantly higher in the Group A than in the Group B (9.4±2.3 vs 7.2±0.6; p=0.001) days. This was statistically highly significant between the groups. [Table 8]

Table 6: Distribution on clinical diagnosis of ACS with AKI Patients (N=35)

Clinical diagnosis	Frequency	Percentage
STEMI	31	88.5
Anterior MI	8	25.8
Inferior MI	11	35.5
Ext. Anterior MI	4	12.9
Anteroseptal MI	8	25.8
NSTEMI	4	11.5
UA	0	00

Multiple logistic regression analysis of odds ratio for characteristics of the subjects likely affect the outcome of patient between two groups. It revealed that Smoking, Heart failure, Cardiogenic shock, Hospital stay were found to be the independently significant predictors outcome of the patients with AKI Odds ratio being 3.57 (P=0.001), 5.53 (P=.001), 4.353 (P=0.02) and 6.92 (P=.001) respectively. But age (>60), HTN and DM were found no significant predictor outcome of the patient with AKI Odds ratio being 0.78 (P=.621), 0.83 (P=.78) and 0.43 (P=.257) [Table 9]

Table 7: Comparison of study patients by in-hospital adverse outcomes (N=70)

	Group A n=35	Group B n=35	P value
Heart Failure			0.001
Yes	26(74.3)	12(34.2)	
No	9(25.7)	23(65.8)	
Cardiogenic Shock			
Yes	18(51.4)	5(14.2)	0.001
No	17(48.6)	30(85.8)	
Arrhythmia			
Yes	35(100)	26(74.2)	0.001
No	0	9(25.8)	
Requirement of dialysis			
Required	7(20)	0(00)	0.005
Not required	28(80)	35(100)	
Death			
Yes	2(5.7)	0	0.493
No	33(94.3)	35(100)	

Data were analyzed using Chi-square (χ^2) test and Fisher's Exact Test and the level of significance was 0.05.

Table 8: Comparison of study patients by in-hospital stay (N=70)

	Group A (n=35)	Group B (n=35)	P value
Duration of hospital stay (Days)	9.4±2.3	7.2±0.6	0.001

Data were analyzed using student's t-test and the level of significance was 0.05.

Table 9: Multiple Logistic regression analysis of determinants including outcome of patients between two groups (n=70)

	Beta	S.E	P value	OR	95% CI	
					Lower	Upper
Age (>60)	0.24	0.96	0.621	0.783	0.296	2.068
HTN	0.15	0.58	0.781	0.834	0.391	1.247
DM	0.58	0.48	0.257	0.431	0.690	2.365
Smoking	1.27	0.52	0.015	3.574	1.275	10.014
Heart Failure	1.71	0.526	0.001	5.537	1.977	5.516
Cardiogenic Shock	1.84	0.590	0.002	4.353	2.000	8.179
Arrhythmia	0.20	0.127	0.103	1.230	0.959	1.579
Hospital stays (>7 days)	3.39	0.930	0.001	6.922	0.039	1.342

DISCUSSION

This comparative prospective study was carried out to determine in-hospital outcomes (heart failure, cardiogenic shock, arrhythmia, need for requirement of dialysis, total days of hospital stay and death) between patients of ACS with or without AKI.

This study shows the mean age were 58.0±8.5 years in group A and 55.6±12.3 years in group B. Majority (80%) were >50 years age in group A and (68.5%) in group B. The patients with AKI were older, more likely to have co-morbidities. The age distribution of this study was comparatively lower than the study done by Marenzi et al. 2010.[9] The mean age was 69±12 years in group A and 63±10 years in group B. Similarly, the mean age of groups was higher in Fox et al. 2012.[10] It was 68.3±12.37 years in group A and 61.8±12.5 years in group B. Our study groups had lower mean age groups giving impression of early CAD in this region.

Regarding gender distribution in this study population was male predominance in both the groups. 30 (85.7%) patients were male in Group A and 26 (74.2%) group B. 5 (14.3%) female patients were in Group A and 9 (25.8%) in Group B. Therefore, the findings of the study are in well agreement with the findings of the other research works Marenzi et al. 2010.[9] Shacham et al. 2014.[11] also observed the similar male gender predominance in both the study groups (81% vs 66% respectively). So, study supports the evidence of late CAD in female occurring after menopause and less in number.

In this study shows the mean serum creatinine level of group A was 1.92±0.9 and group B was 1.04±0.15. It observed that serum creatine level was higher in group A than group B. Therefore, the findings of the study are in well agreement with the findings of the other research works (Fox et al. 2012).[10] In group A patients had acute massive myocardial injury which resulted in more renal impairment than group B.

This study found risk factors except smoking were significantly higher in group A than group B which was 77% vs 48.5% respectively. The predominant risk factor was hypertension were more in group A than group B (77.1% vs 74.2% respectively). Diabetes mellitus was more in group A than group B which was 62.8% vs 48.5% respectively and dyslipidemia was also more in group A than group B which was 45.7% vs 42.8% respectively. But Family history of IHD was equally present in both the groups. Therefore, the findings of the study are in well agreement with the findings of the other research workers (Marenzi et al. 2010 and Fox et al. 2012).[9,10] Another study Moriyama et al 2017.[12] 2017 reported that smoking, hypertension, diabetes mellitus, dyslipidemias were higher in AKI than without AKI.

Subject of systolic blood pressure in this study shows the mean, on admission, systolic blood pressure and diastolic blood pressure were lower in group A than group B (106.4±20.5 vs 131.7±25.9, 69.1±12.4 vs 83.1±15.4 respectively; p=0.001) which was statistically significant. The mean heart rate was higher in group A than group B (92.2±24.3 Vs 87.2±15.3 respectively; p=0.001). The difference was not statistically significant. Therefore, the findings of the study are in well agreement with the findings of the other research works (Hwang et al. 2011).[13] Hence, it points toward poor haemodynamics parameters in patients with ACS having renal impairment during on admission.

In this study shows the ECG Changes of ST elevation were more in patients with AKI (Group A) than patients with without AKI (Group B) which was 88.6% vs 57.1% respectively. But ST depression were more in patients without AKI (Group B) than patients with AKI (Group A) which was 42.9% vs 11.4% respectively. It was statistically significant between groups (p=0.012). The least common was unstable angina (UA). Similar studies found ECG changes of ST elevation were more in patients with AKI (Marenzi et al. 2012; Bruetto et al. 2012).[9,14] Also, in previous study (Moriyama et al. (2017)[12] found 88% STEMI in with AKI and 82% STEMI in without AKI. So, STEMI patients were in majority and had worse renal impairment than with NSTEMI.

This study shows the mean LVEF was significantly lower in the Group A than in the Group B (41.6±7.4 vs 50.1±8.5 respectively p=0.001) these were statistically significant in between the groups. The mean, on admission, random blood sugar (RBS) was higher than in group A than group B (12.0±5.4 vs 9.9±4.2) which was not statistically significant. These finding were consistent with other studies (Parikh et al. 2008; Marenzi et al. 2010; Marenzi et al. 2013).[7,10,15]

The present study shows that heart failure was more common in group A than in Group B (74.3% vs 34.2%; p=0.001 respectively). This was statistically highly significant in between two groups. Parikh et al. (2008),[7] study found almost similar results (75% vs 42.7% respectively). Another study (Marenzi et al. 2013),[16] noticed that patients with AKI had 61% and without AKI had 8% of in-hospital heart failure.

In this study, Cardiogenic shock was more common in group A than in Group B (51.4% vs 14.2% p=0.001 respectively). This was statistically highly significant in between two groups. Therefore, the findings of the study are in well agreement with the findings of the other research works (Marenzi et al. 2010).[15]

This study shows the arrhythmia was significantly higher in group A than in Group B (100% vs 74.2%; p=0.001 respectively). Sinus tachycardia, AV blocks and VT/VF were higher in group A than group B. It

was observed that 7(20%) of patients required dialysis and 2(5.7%) death in group A. These finding were consistent with other studies (Parikh et al. 2008; Marenzi et al. 2010; Marenzi et al. 2013).[7,15,16]

In this study found mean duration of hospital stays was significantly higher in the Group A than in the Group B (9.4±2.3 vs 7.2±0.6; p=0.001). This was statistically highly significant between two groups. Marenzi et al. (2010),[15] observed that longer hospital stays of patients with AKI. The recovery time for patients with AKI was longer due to more complicated course of disease.

Multiple Logistic regression analysis revealed that Smoking, Heart failure, Cardiogenic shock, Hospital stay were found to be the independently significant predictors outcome of the patients with AKI Odds ratio being 3.57 (P=0.001), 5.53 (P=.001), 4.353 (P=0.02) and 6.92 (P=.001) respectively. But age (>60), HTN and DM were found no significant predictor outcome of the patient with AKI Odds ratio being 0.78 (P=.621), 0.83 (P=.78) and 0.43 (P=.257). Therefore, the findings of the study are in well agreement with the findings of the other research works (Marenzi et al. 2010).[15]

However we have some limitations in our study

- This study recorded only in-hospital (short term) outcomes of heart failure, cardiogenic shock, arrhythmia, dialysis requirement and death. So, complication in the long run could not be determined.
- The study was conducted in a single tertiary level hospital which may not represent the general population.
- The patients with ACS with or without AKI were not included due to different exclusion criteria.

CONCLUSION

This study shows that presence of AKI in patients with ACS is associated with adverse in- hospital outcomes in terms of heart failure, cardiogenic shock, arrhythmia and death. It also shows longer duration of hospital stay. So, the presence of AKI in patients with ACS should alert physicians to an increase risk of morbidity and mortality. These findings give emphasis on our consciousness in management and outcomes for acute coronary syndrome patients with acute kidney injury in CCU.

Recommendation

- ACS patients with AKI should be classified, monitored and interpreted with the help of easily available serum creatinine level meticulously during hospitalization.
- A routine serum creatinine should be done within 48 hours of hospitalization.
- Follow up post MI with renal impairment should be done with serum creatinine after hospital discharge.

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