Original Research Article

Observational study to assess demographic, clinical profile and outcome of acute kidney injury due to acute gastroenteritis during monsoon season

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ABSTRACT

Background: Worldwide incidence and causes of acute kidney injury (AKI) are variable and even more in developed and developing countries. At least 80% of AKI in tropics is community acquired. Acute gastroenteritis (AGE) is a common problem in developing countries. Present study concentrates on AGE as cause of AKI during monsoon period. It presents in epidemic proportion during monsoon and is preventable with timely intervention.
Methods: The study was carried out prospectively in tertiary care hospital in Mumbai during monsoon season of 2012 and 2013. AKI was staged as per AKIN criteria. Patients were treated for primary disease and AKI, initially conservatively and dialysis if indicated. Patients were followed during the hospital stay.
Results: Two hundred and thirty patients had AKI due to infectious disease during monsoon. Incidence of AKI due to diarrhea was 23%, and affecting males predominantly in 4th decade. Diarrhea and vomiting were the most common presenting complaints. 32% patients required dialysis. Mortality rate was 3.8%.
Conclusions: AKI secondary to AGE is common in tropics. Treatment of primary disease and hemodynamic optimization at the earliest helps to prevent AKI. Presents with less severe AKI and has better outcome. Multiorgan involvement and need for supportive lifesaving therapies were risk factors for AKI.

Keywords: Acute Kidney Injury, Acute Kidney Injury Network criteria, Monsoon, Acute gastroenteritis, Infection, Community acquired Acute kidney injury

INTRODUCTION

In tropical countries the epidemiological pattern of Acute Kidney Injury (AKI) during monsoon reflects infectious disease as most prominent cause.[1] Clinical profile of AKI in tropics is modified by number of factors like severe systemic infection or intoxication, severe toxemia, shock, dehydration, disemminated intravascular coagulation (DIC), multiorgan dysfunction.[1] The catabolic effect of infection with uremic state results in considerable negative nitrogen balance in presence of underlying malnutrition which has a major impact on outcome. There is inadequate affordable healthcare with delayed referral and lack of adequate expertise in primary care units with rising cost of medical treatment and poorly equipped transfer ambulances that contribute to increase in morbidity and mortality from these infections.[1]

Severe Acute Gastroenteritis (AGE) may lead to oliguria due to fluid loss and AKI.[2] Azotemia, and hyperkalemia

due to supervening catabolic state and lactic acidosis due to tissue hypoxia. This may progress to renal shutdown with oligoanuria and its functional consequences with or without significant structural damage. Most effective intervention is prevention. Awareness that AGE typically causes AKI should raise the index of suspicion and impose specific alertness to change in urine volume and blood chemistry when response to adequate hydration is poor.

Awareness of potential renal complications and their treatment is single most cost effective measure. Present study helps to estimate the burden of disease in the city to counter it in future. Studies that have addressed AKI due to AGE that present in epidemic proportions during monsoon are sparse. Present study evaluates diarrhea as cause of AKI diagnosed by Acute Kidney Injury Network criteria.

METHODS

It is an Observational study carried out prospectively. Objectives to study incidence and clinical demography of patients with AKI due to AGE. To study severity of AKI using AKIN criteria and requirement of renal replacement therapy. To study risk factors and mortality in AKI due to AGE.

Inclusion criteria

Patients fulfilling all the following criteria were included.

- Acute Kidney Injury is defined as an absolute increase in creatinine concentration of 0.3 mg/dl or greater as per Acute Kidney Injury Network consensus definition.[3]
- All patients ≥ 18 years age hospitalized with AGE, in Medicine or Nephrology wards/ICU with acute febrile illness (AFI), suspected of infectious etiology and AKI.
- During the monsoon period of 2012 and 2013 each. Monsoon period in Mumbai extends from the month of June to September each year.
- Consenting to be part of study.

Exclusion criteria

Patients with any one of the following were excluded.

- Mentally challenged individuals and pregnant females.
- All known chronic kidney disease patients confirmed by Ultrasound studies or blood or urine abnormalities of renal function of 3 months.
- Patients admitted with AFI suspected of causes not included as part of study but also found during monsoon.

Study methodology

Patients hospitalized with AGE during monsoon seasons of 2012-13 in T.N. Medical College and B.Y.L. Nair Charitable Hospital, Mumbai, with AKI, fulfilling inclusion criteria. Study population predominantly from South, Central and North Mumbai

Consent and Patient Information Sheet

Patients were explained the study, given Patient Information sheet and enrolled in study if willing and after obtaining informed written consent. Patients included in the study were prospectively analyzed.

History and Clinical Examination

Detailed history and clinical examination was performed. Laboratory investigations were noted at admission, during hospital stay and on discharge. Biochemical investigations were carried on Olympus 400 Full Autoanalyser. All patients were evaluated with CBC, Renal function test, electrolytes, liver function test, urine examination, stool examination, hanging drop for cholera, blood and urine culture, ECG, X ray chest, USG Abdomen & KUB.

Severity of AKI was defined by AKIN staging criteria[3]

- Stage I, Serum creatinine increase to 1.5 – 2 fold of baseline.
- Stage II, Serum creatinine increase to 2 - 3 fold of baseline.
- Stage III, Serum creatinine increase to >3 fold of baseline or an absolute increase to >4 mg/dl.
- All patients requiring dialysis were categorized in stage III.
- Patients with baseline serum creatinine were classified in AKIN stages depending upon serum creatinine at admission.

Patients were followed up regularly during the period of hospitalization. Recovery or progression of illness with involvement of other organ systems mainly Pulmonary, Cardiovascular, Hematology and Central Nervous System was noted. Patients were assessed for the requirement of Renal Replacement Therapy.

Standard definitions for hypotension, sepsis, ARDS, MODS, anemia, thrombocytopenia, leucocytosis were followed.[4-7] Patients received assisted ventilation for standard indications.[6]

Treatment

Conservative treatment included

- Optimizing hemodynamic stability by maintaining hydration and blood pressure.

- Vasopressor support to maintain Mean Arterial Pressure ≥65mmHg or Systolic blood pressure more than 100mmHg if conservative management failed to maintain blood pressure.
- Treatment of underlying AGE with cephalosporins/ fluroquinolones/ nitroimidazole as per hospital policy considering common causes of diarrhea.
- Nutritional support.
- Transfusion of blood and blood products as per clinical assessment and patient requirements.
- Assisted Ventilation whenever indicated.
- Avoidance of nephrotoxic drugs.

Renal Replacement Therapy as Intermittent Hemodialysis/ SLED was initiated for appropriate indications like.

- Metabolic Acidosis.
- Pulmonary edema/ fluid overload.
- Hyperkalemia.
- Azotemia.
- Oliguria/ anuria

Statistical data analysis

- Categorical variables were summarized as frequency and Percentage.
- Continuous variables were represented using mean, standard deviation and Median.
- Association between categorical independent and dependant variables was performed using Chi-Square test and Fisher's Exact test for all 2 X 2 tables where p-value of Chi-Square test was not valid due to small counts.
- All tests of significance were two-sided, with a p-value of <0.05 indicating statistical significance.
- The data were analyzed using the Statistical Package for the Social Sciences version 17.0.

RESULTS

There were 230 admissions during study period of AKI suspected of monsoon related illness. Out of these 53 patients (23%) had AGE. Study population comprised 41 males (77.4%) and 12 females (22.6%). Mean age of study population was 42.09 years. Twenty eight patients (52.8%) were in age group of 18-40 years, 16 patients (30.2%) were in age group more than 40 years to 60 years and 9 patients (17%) more than 60 years age. Predominant presenting features were diarrhea 53 patients (100%), vomiting 50 patients (94.3%), Oliguria 45 patients (84.9%), fever 31 patients (58.5%), high coloured urine 24 patients (45.3%), and breathlessness 13 patients (24.9%). On examination 15 patients (28.3%) had pallor, 4 patients (7.5%) had icterus and 2 patients (3.8%) had pedal edema. Thirty two patients (60.4%) had hypotension, 28 patients (52.8%) had tachycardia, and 12 patients (22.6%) had tachypnea. Two patients each (3.8%) had hepatomegaly, and splenomegaly, 3 patients

had ascites. Three patients had ARDS and one patient (1.9%) had pleural effusion. Four patients (7.5%) had altered sensorium on admission. Hematological involvement was seen in 52 patients (98.1%) in form of anemia, 20 patients (49.1%), leucocytosis, 38 patients (71.7%) and thrombocytopenia, 18 patients (34%). Nine patients (6.9%) had multiorgan affection. Proteinuria was present in 26 patients (49%). Two patients (3.8%) and one patient (1.9%) were incidentally detected HIV and HBV positive. Six patients (11.3%) were diabetic and five patients (9.4%) had hypertension. Vasopressor support after optimizing fluid status was required in ten patients (18.9%). Four patients (7.5%) required transfusion of blood and blood products. For respiratory distress 6 patients (11.3%) required CPAP support and 2 patients needed mechanical ventilation. Twenty nine patients (54.7%) were managed for sepsis. Total 24 patients (45.3%) were classified in AKIN stage I, 10 patients (18.9%) in AKIN stage II and 19 patients (35.8%) in AKIN stage III. Total 27 patients (50.9%) recovered within 7 days of treatment initiation and 24 patients (45.3%) required more than 7 days for recovery. Out of 53 patients, 17 patients (32.1%) required renal replacement therapy. In all out of 53 patients, 51 patients recovered and 2 patients (3.8%) succumbed to their illness. Mortality rate in present study was 3.8%. Analysis revealed delay in initiation of definitive therapy lead to increased requirement of supportive therapy in form of Vasopressor support, renal replacement therapy and it was statistically significant with p -0.007.(Table 1).

Table 1: Risk factors for AKI.

Risk factor	Chi square value	P value
Gender	1.82	0.402
Hypotension	1.006	0.605
Vasopressor support	6.994	0.030
Blood product support	7.742	0.021
Mechanical ventilation	3.719	0.156
Delay in treatment >2days	6.995	0.031
Multiorgan failure	6.778	0.034

DISCUSSION

AGE is common problem in developing countries. Non availability of clean drinking water, adulteration of food and beverages, poor sanitation, lack of public awareness about personal hygiene predispose to AGE. In developing countries AGE still remains one of the common causes of communicable disease that lead to AKI.[8] AGE leads to hypovolemia. Failure to correct volume depletion leads prerenal AKI which if persist may progress to ATN which may require RRT

Old age and delay in treatment initiation are causes that predispose to AKI.[9] Acute tubular necrosis (ATN) and Acute Tubulointerstitial nephritis (ATIN) develops following hypotension and decrease in renal blood flow

causes secondary renal ischemia.[10] Most significant factor for high mortality is time interval from onset of acute diarrheal disease to diagnosis of AKI. Unique features of tropical AKI include endemic malnutrition, relative state of hypovolemia due to increase sweating and peripheral vasodilatation due to hot humid climate.

Incidence of AKI is unclear due to varying definition of AKI and overestimated due to referral bias in tertiary care centre.[11,12] Diarrheal diseases are a major public health concern in India.

Incidence of AKI in AGE in present study is 23%. Incidence due to diarrhea has gradually decreased over decades from 23% in 1965-74 to 7.3% in 2001-6.[13] In present study it is 23% likely due to referral bias in tertiary care unit and massive surge in AGE cases during monsoon in recent years. Out of 53 patients, 41 patients (77.4%) were male and 12 patients (22.6%) were female. Reason for gender difference is not clear but likely related to work activities. Similar gender difference were also observed in other studies of community acquired acute kidney injury (CAAKI) in India.[14-16]

Mean age of study population was 42.09 years. About 28 patients (52.8%) were in age group ≤40 years. This implies occurrence of CAAKI more in younger age group also observed in other studies.[14,15] This is mostly related to factors encountered in the environment and exposed due to work related activities.[1]

Diarrhea (100%), vomiting (94.3%), Oliguria (84.9%), fever (58.5%), dyspnea (24.5%) were the common presenting complaints in our study also seen similarly in study by J Inbanathan et al.[17] Derangement of CBC in form of anemia 26 patients (49.1%), leukocytosis 38 patients (71.7%), and thrombocytopenia 18 patients (34%) was seen commonly along with azotemia. Common occurrence of leukocytosis/ thrombocytopenia reflects infection as a cause with underlying malnutrition predisposing to anemia in presence of infection/inflammation.

Major complications noted were hypotension 32 patients (60.4%), sepsis 29 patients (54.7%), and multiorgan failure 9 patients (16.9%) encephalopathy 4 patients (7.5%) and ARDS 3 patents (5.66%). J Inbanathan et al recorded hypovolemic shock (61%), anemia (19%), pulmonary edema (14%) metabolic encephalopathy (7%) as complications.[17] Hypotension and sepsis being most common complications suggest gastrointestinal fluid loss due to infectious diarrhea with suboptimal rehydration and delayed initiation of definitive treatment.

In our study majority of patients 24 (45.3%) presented in AKIN stage I followed by 19 patients (35.8%) in stage III and 10 patients (18.9%) in stage II. Majority of patients presented in lesser stages of AKI stage I and II as health care services have widespread availability in metro cities. Treatment is initiated at such centers but due to rising

cost of treatment or worsening disease process patient is shifted to government hospitals. In study by Yang F et al 52% patients were in AKIN stage III, 16.2% in stage II and 33.7% in stage I AKI.[18] Majority patients had severe AKI probably as study considered all causes of AKI. Severity of AKI also depends on underlying cause of AKI. Prerenal and renal causes were significantly associated with AKIN stage I and II AKI. Prerenal AKI can induce compensatory regulation in body and hence it can be mild.[18]

In present study 67.9% patients recovered with conservative and supportive therapy whereas 32.1% patients required renal replacement therapy. Rate of dialysis requirement was 36%. In the present study mortality rate was 3.8% which was almost equal to 4% in study by J. Inbanathan et al.[17]

In 27 patients (50.9%) AKI recovered within 7 days of initiation of definitive treatment. Remaining patients required more than 7 days for recovery. Patients recovered early as majority presented early in illness with lesser stage of AKI and responded to conservative treatment. In study by Swarna Gupta et al 25% patients were discharge within 7 days. Rest required more than 7 days for recovery. All patients in this study received dialysis. Thus prolonged duration of recovery reflects underlying severe AKI.[19]

More severe the stage of AKI longer is the duration of recovery which was statistically significant with P <0.001. Delay in seeking medical attention and initiation of definitive treatment leads to progression of illness, worsening AKI, Multiorgan failure and requirement of supportive care like vasopressor, assisted ventilation and RRT and it was statistically significant with p value 0.007.[9] Need of Vasopressor support, Multiorgan failure, transfusion of blood products and delay in treatment were significant risk factors for severe AKI.

People with poor socioeconomic status in urban slums are predisposed to infections and communicable diseases. Due to rising cost of health care people opt for either traditional medicine or inadequate treatment once patient achieves symptomatic benefit thus predisposing to drug resistance and further delay in appropriate adequate treatment worsens underlying disease.

Shock refractory to fluid resuscitation needs Vasopressor support. Consequent hypotension and hypoperfusion leads to cellular injury and multiorgan failure.[20] Anemia leads to hypoxia induced cellular injury and multiorgan failure. Oxygen is vital for maintenance of all organs. Kidneys have rich blood supply. They are sensitive to ischemia, hypoxia and susceptible to damage in patients with respiratory injury. Respiratory failure can lead to multiple organ failure due to hypoxia with increased mortality. Multiorgan failure occurs in critical illness with Systemic Inflammatory Response Syndrome, sepsis and worsening of underlying disease.[20]

CONCLUSION

Tropical infection causing diarrhea contributes to significant proportion of AKI during monsoon. Seen mostly in adults in 3rd and 4th decade and commonly in males. Educating people regarding personal hygiene, sanitation will reduce incidence of AGE, creating awareness among physicians about diarrheal illness contributing to AKI. Early and appropriate rehydration, hemodynamic optimization will help to prevent AKI. Early detection and referral will reduce morbidity and mortality. Majority patients present in less severe stage of AKI and recover within a week of initiating treatment. Delay in initiation of definitive treatment with need of vasopressor support and multiorgan failure are risk factors predisposing to severe AKI and prolonged hospital stay.

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