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Acute kidney injury profile of COVID-19 patients and associated risk factors a rural hospital-based retrospective study from Vadodara, Gujarat

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***Abstract*---**Background: Clinical outcome of patients hospitalized with COVID-19 and acute kidney injury (AKI) are not well understood. The clinical significance of abnormal electrolytes and renal outcome in COVID-19 patients have been poorly documented. We aim to exhibit the electrolyte abnormalities, renal outcome and associated risk factors in hospitalized COVID-19 patients in rural tertiary care hospital in Vadodara district, Western India. Method: A hospital record based retrospective study was conducted. Total 994 patients hospitalized with COVID-19 between 1st April 2021 to 30th June 2021 and those meeting inclusion criteria were included for the analysis. The laboratory data of interest included electrolytes reports like Na+, K+, CL-, creatinine and blood urea. Result: Of the total

hospitalized COVID-19 patients, 324 patients were eligible. For the criteria for suspected AKI - 279 (86.11%) and no AKI - 45 (13.88%) patients were found. Suspected AKI patients were classified into four conditions: 1) HYPERNATREMIA (14.33%); HYPERKALEMIA (2.15%); BCR ratio >20 (65.59%); HIGH Cl- (17.92%). Out of total AKI patients, (36.91%) died whereas (13.3%) patients died in no AKI group. All patients were provided antibiotics, steroids and anti-viral therapies irrespective of AKI status, which we presume might have contributed in high mortality among suspected AKI. Conclusion: Electrolyte and derangements in AKI among COVID-19 patients are dominant and found to be associated with increased mortality.

***Keywords*---**acute kidney injury, COVID-19, mortality, gujarat.

Introduction

Since late 2019, severe acute respiratory coronavirus disease 2019 [COVID-19] resulting in acute respiratory syndrome in has become a worldwide pandemic (1). Morbidity and mortality from COVID-19 have been primarily attributed to the respiratory failure and acute respiratory distress syndrome, often in the setting of multiorgan failure. Acute kidney injury (AKI) is one of the linked symptoms in COVID-19 patients. The menial outcomes among COVDI-19 patients are also not clear given their association with relative immune dysregulation and inflated inflammatory responses (2,3). Acute kidney injury (AKI) is a common obstacle observed among hospitalised patients, mainly in the intensive care unit (ICU) (4,5). In initial reports, AKI frequency in people with COVID-19 has ranged from 5% to 29% with basic variation between centres, possibly due to alterations in population demographics and risk factors for AKI (4,6–11). Acute kidney injury (AKI) is a syndrome perceive by a rapid (hours to days) deterioration of kidney function. It is often diagnosed in the context of other acute illnesses. The clinical concerns of AKI include the accumulation of waste products, electrolytes, and fluid, but also indistinct effects, including reduced immunity and dysfunction of non-renal organs (organ cross-talk)(12). Outcomes among hospitalized patients with COVID-19 and AKI are incompletely understood. However, the characteristics of AKI and its link of morbidity and mortality among COVID-19 patients is not clear. The present study aims to asses AKI profile and its association to mortality among COVID-19 patients admitted in Parul Sevashram hospital (PSH).

Methodology

Study design

A single-centre record based retrospective study was conducted at tertiary care hospital –PSH, Vadodara, Gujarat State, India.

Inclusion criteria

- All patients who tested positive by Polymerase Chain Reaction test for COVID-19
- COVID-19 positive patients admitted at PSH from April to June 2021
- COVID-19 patients who had electrolytes reports within 48 hours of hospital admission.

Exclusion criteria

- COVID-19 patients who died within 24 hours
- COVID-19 patients with other than AKI comorbid conditions

Data collection

Data for this study was obtained from the Medical Records division. Of total 994 COVID-19 patients, 324 patients' data meeting inclusion and exclusion criteria were selected for the review. Details of records retrieval is schematically presented in Fig 1.

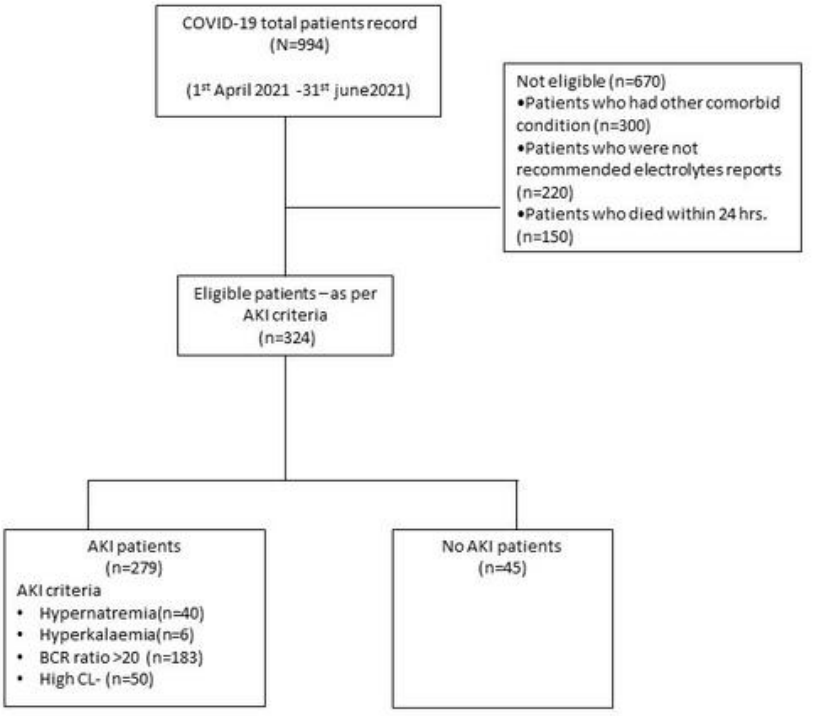

Fig 1. Details of records retrieval are schematically presented

Data extraction

Demographic information (Age and Gender), clinical characteristics (medications antibiotics, anti-viral and steroid; mortality) and laboratory findings (NA^+, K^+, Cl^-

creatinine, and blood urea) were extracted from the selected medical records. We extracted details of hospital admission such as intensive care unit (ICU) stay, need of oxygen therapy in terms of types of mechanical ventilation provided.

Operational definitions

Electrolyte abnormalities: When the level of electrolytes in the body is too low or too high, the resulting condition is called an electrolyte abnormalities. The reference range of serum sodium(NA^+) 135-140 mEq/ml, potassium(K^+) 3.5-5.6 mEq/ml, chloride(Cl^-) 8.5-10.5 mg/dl, creatinine 0.5-1.5 mg/dl, blood urea 25-45 mg/dl .

- Hypoelectrolytemia: Value less than the lower range
- Hyperelectrolytemia: Value greater than the upper range Acute kidney injury (AKI): Abrupt abnormalities in following criteria:
  - Hypernetrimia**:** NA^+ >140 mEq/ml & K^+<3.5 mEq/ml (Satirapoj *et al.*, 2016)
  - Hyperkalaemia: NA^+<135 mEq/ml & K^+>5.6 mEq/ml (Satirapoj *et al.*, 2016)
  - BUN/Creatinine ratio (BCR): >20 (Uchino *et al.*, 2012)
  - High chloride: Cl^- >10.5 mg/dl (Zang *et al.*, 2013)
- Suspected AKI: Patients with abnormal four electrolytes conditions
- No AKI: Patients with normal four electrolytes conditions

Plan of statistical analysis

Demographic and clinical data were compared between AKI and No AKI patients. Data were expressed as mean ± SD, median and its high to low range, and p value was calculated using chi-square test for categorical variables was used. Descriptive variables presented as number (n) and percentage (%). All analysis were performed using Microsoft Excel 2019 spread sheet.

Results

From 1st April, 2021 to 30th June 2021, 994 patients were admitted to PSH with a diagnosis of COVID-19. Of these, total of 324 patients' data were retrieved. Demographic, clinical and laboratory findings. Of the total 324 patients, 63% were males and 37% were females. Similar gender distribution was noted in patients with and without AKI (males=63%; females=37% in patients with suspected AKI; and males=60% and females=40% in patients with no AKI).

Suspected AKI & No AKI

Of the 324 patient records, 279 (28.06%) patients were classified as suspected AKI and 45 patients had no AKI. Suspected AKI were further categorized into four conditions: 1) Hypernatremia (14.33%); 2) Hyperkalemia (2.15%); (3) High BCR ratio (65.59%); and 4) high Cl^- ratio (17.92%). Table-1 provides demographic details of patients' records.

Table 1
Demographic characteristics of the study population

VARIABLES	TOTAL	AKI	NO AKI	(P-value)
	(N=324)	(N=279)	(N=45)	
AGE				
<18	0	0	0	
19-35	39	34 (31.03 ± 3.96)	5(32.6 ± 2.72)	
36-65	214	186 (52.84 ± 8.14)	28(51.53 ± 9.15)	N/A
>65	102	59 (72.88 ± 5.16)	12(72.75 ± 5.47)	
GENDER				
MALE	203	176 (63.5%)	27(60%)	
FEMALE	121	103 (36.91%)	18(40%)	0.043*
COMORBID CONDITIONS				
HYPERTENSION	16	12(4.30%)	4 (8.8%)	
DIABETES MELLITUS	25	9(3.2%)	0	
CARDIOVASCULAR DISEASE	10	10(3.58%)	0	N/A
ADMISSION TYPE				
ICU	234	203(72.7%)	31(68.8%)	
WARD	90	76(27.24%)	14(31%)	0.104
MECHANICAL VENTILATION				
NC	53	39 (13.9%)	14(31.1%)	
MASK	133	112(40.14%)	21 (46.6%)	
NRBM	86	76 (27.24%)	10(22.2%)	0.023*
LENGTH OF STAY				
48 HRS	9	8(2.86%)	1(0.35%)	
3-15 DAYS	264	224(80.2%)	40 (14.33%)	
16-30 DAYS	37	34(12.18%)	3(1.07%)	N/A
>30 DAYS		9(3.22%)	0	
DISCHARGED	215	176 (63.08%)	39 (86.6%)	
DIED	109	103 (36.91%)	6(13.3%)	0.0499*

Comorbid conditions

Patients who developed AKI had a higher proportion with comorbid conditions (11.11%) including diabetes mellitus, hypertension, cardiovascular disease compared to patients with no AKI (8.88%) (Table-1).

Mortality

Out of 279 suspected AKI patients, 103 (36.91%) had died within 72 hours to 30 days while among patients with no AKI, 6 deaths (13.3%) were recorded (Table-2)(Table-3). The difference was statistically significant ($p = 0.00001$; <0.05).

Table 2
Characteristics of patients who develop AKI

VARIABLES	CONDITION 1 (TOTAL NO= 40)	CONDITION 2 (TOTAL NO= 6)	CONDITION 3 (TOTAL NO= 183)	CONDITION 4 (TOTAL NO= 50)	P-value
	HYPERNATREMIA	HYPERKALEMIA	(BCR RATIO >20)	(HIGH Cl^-)	
GENDER					
MALE	25 (62.5%)	6 (100%)	115 (62.8%)	30 (60%)	0.74
FEMALE	15 (37.5%)	0 (0.0%)	68 (37.15%)	20 (40%)	
SEVERITY OF ILLNESS					
ICU	29 (72.5%)	4 (66.6%)	136 (74.31%)	34 (68%)	0.82
WARD	11 (27.5%)	2 (33.3%)	47 (25.68%)	16 (32%)	
MECHANICAL VENTILATION					
NRBM	13 (32.5%)	1 (16.6%)	49 (26.77%)	13 (26%)	0.65
NC	15 (37.5%)	1 (16.6%)	56 (30.60%)	18 (36%)	
MASK	12 (30%)	4 (66.6%)	77 (42.07%)	19 (38%)	
SURVIVED	31 (77.5%)	4 (66.6%)	111 (60.65%)	30 (60%)	0.23
DIED	9 (22.5%)	2 (33.3%)	72 (39.34%)	20 (40%)	

Medication

We observed that all COVID-19 patients were provided atibiotics, antiviral and steroid therapies irrespective of suspected AKI or no AKI conditions (Table-5). About 72.75% with suspected AKI were admitted to an ICU, 27.14% were admitted to COVID-19 ward. We noted that 99% patients with suspected AKI required mechanical ventilation; 27.24%, patients required NRBM ventilation; 32.25% patients required NC ventilation, and 40.14% patients required MASK ventilation (Table-3).

Table 3
Mortality among patients with suspected AKI and No AKI

TOTAL NO=324	SURVIVE	DIED	(P-value)
AKI (N=279)	176 (63%)	103 (36%)	.00001*
NO-AKI (N=45)	39 (86.6%)	6 (13.3%)	

Table 4
Overall Characteristics of patients with suspected AKI and No AKI

Variables	No AKI TOTAL N=45 (%)	AKI TOTAL N=279 (%)	(P-value)
AGE	52(28 - 84)	52 (32-90)	
GENDER			
MALE	27(60%)	176(63.5%)	
FEMALE	18 (40%)	103(36.91%)	0.043*

SEVERITY OF ILLNESS			
ICU	31(68.8%)	203(72.7%)	
WARD	14 (31%)	76 (27.24%)	0.104
MECHANICAL VENTILATION			
NRBM	10(22.2%)	76(27.24%)	
NC	14(31.1%)	39(13.9%)	
MASK	21(46.6%)	112(40.14%)	0.023*
SURVIVED	39(86.6%)	176(63.08%)	
DIED	6(13.3%)	103(36.91%)	0.0499*

Table 5
Comparative Treatment protocol profiling of Suspected AKI patients and No AKI patients

COVID-19 Treatment Prescription	Suspected AKI				No AKI
	Hypernatremia	Hyperkalemia	BCR >20	High Cl^-	
Antibiotics	40	6	183	50	45
Steroid therapy	40	6	183	50	45
Antiviral therapy	40	6	183	50	45

Proportion of patients who were admitted to ICU were higher in suspected AKI than no AKI (72.7% AKI & 68.8% no AKI). 99% of suspected and 100% no AKI patients required mechanical ventilation; 27.24 % patients with suspected AKI and 22.1% with no AKI required NRBM ventilation; 32.25% patients with suspected AKI and 31.1% with no AKI required NC ventilation, and 40.14% patients with suspected AKI and 46.6% with no AKI required MASK ventilation. These differences were statistically significant (p=0.023; <0.05). Fig.2 and Fig.3 shows COVID-19 patients' profiling for AKI across four conditions. Of all conditions, BCR ratio >20 condition was higher (66.6%) than hypernatremia (14.3%), hyperkalaemia (2.2%) and high Cl^- (17.9%). In hyperkalaemia, all patients were male. Higher mortality (69.9%) was observed in patients with BCR ratio condition. In terms of mortality across all four conditions, male patients had higher proportion.

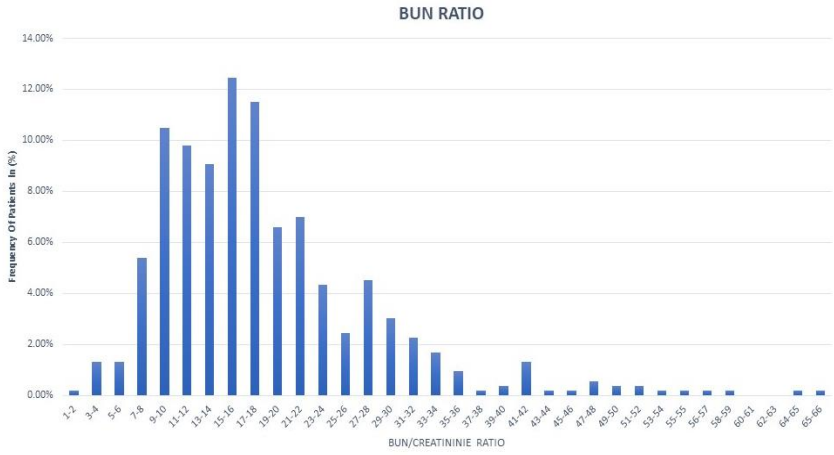

Fig 2. Distribution for BUN/Creatinine ratio

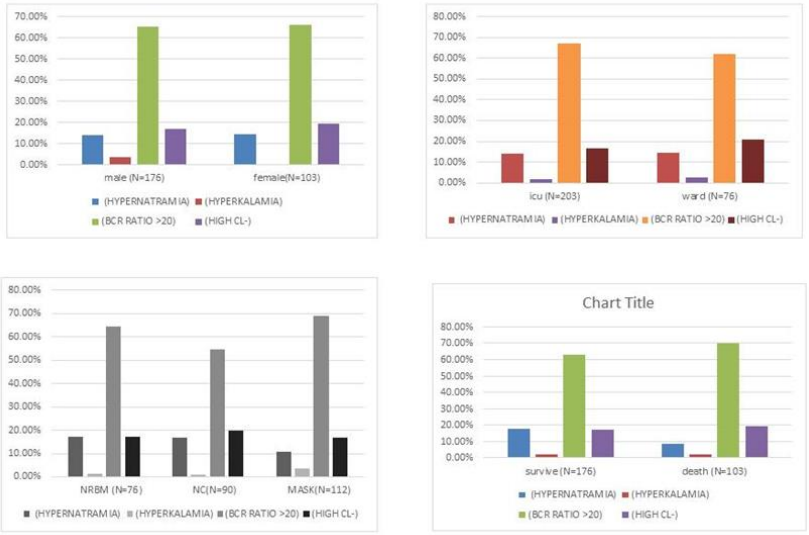

Fig 3. Patient admission status with COVID-19 and suspected AKI

Discussion

We conducted a single-centre retrospective study of COVID-19 patients admitted at rural tertiary care hospital in Vadodara, Gujarat. The increase in the cumulative incidence of AKI in our sample was likely associated with clinical deterioration and higher mortality (13). Currently, a number of published studies describe hospitalized patients with COVID-19 and AKI. The incidence of AKI in these studies varies widely due to differences in criteria for hospital admission, definition of AKI, ethnicities, and other variables. The studies also had considerable heterogeneity among demographic characteristics, severity, risk factors, morbidities, and mortalities (14). Previous studies have suggested that COVID-19 in people with chronic comorbidities have more likelihood of becoming a critically ill, requiring hospitalization or cause death (15).

We identified various risk factors for AKI in our study. Risk factors for the development of AKI were indicators of severe COVID-19, specifically the need for ventilator support or anti-viral, antibiotic and steroid treatment. Reported risk factors for generally poor outcomes of COVID-19 were suspected AKI, increased age, male gender (1). Similar to previous reports, our patients with AKI were more likely to be male, have a history of electrolyte imbalance, and have severe respiratory failure requiring mechanical ventilation. The fact that COVID-19 patients required ICU admission within the first week of hospitalization, also points out the contribution of AKI to disease severity. The other studies conducted to asses kidney outcomes have generally taken eighter one or two parameters, for example; hyper chloride, and urinary sodium despite reporting of other parameters. Based on synthesis of existing evidence, we have taken four parameters for defining potential AKI and no AKI. Prospective studies should validate these four parameters for suspecting potential AKI. Higher mortality was noted in COVID-19 patients with AKI. It was also observed that antibiotics, anti-viral and steroid medications were prescribed irrespective of AKI conditions which may be the cause of increased incidences of deaths. This needs further investigation. However, judicious use of antibiotics, anti-viral and steroids among COVID-19 patients with AKI can be considered before establishing the treatment protocol.

Conclusion

Serum Electrolyte derangements including hypernatremia, hyperkalemia, high BCR ratio (>20), high Cl^- are dominant in patients with AKI and COVID-19. Suspected AKI condition was associated with increased mortality.

Abbreviation

AKI= acute kidney injury, BUN= blood urea nitrogen. BCR= BUN/creatinine Ratio, ICU= intensive care unit. NC=Nasal cannula, NRBM=Non rebreather mask.

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Conflicts of Interest: Authors declare no conflict of interest.

Ethics approval

The study was approved by Institutional Ethics Committee of Parul Institute of Medical Sciences and Research, Parul University, Vadodara, Gujarat.

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