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Incidence and Prognosis of Acute Kidney Injury with COVID-19 in Hospitalized Egyptian Patients

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ABSTRACT

Background: The recent worldwide pandemic of COVID-19 has been a serious, multidimensional problem that has left a detrimental worldwide impact on individuals of all ages and several organ systems. The typical manifestation of kidney involvement is acute kidney injury (AKI); however, there is a lack of consensus data regarding AKI epidemiology in COVID-19.

Objective: The aim of the current work was to study the incidence and prognosis of acute kidney injury among patients hospitalized with COVID-19.

Subjects and methods: This retrospective, observational cohort study was conducted on 163 COVID19 patients diagnosed by RT-PCR and carried in Inpatient and ICU of Geriatric Isolation Hospital, Ain Shams University hospitals for COVID19.

Results: As regard predictors for AKI; each of presence of chronic kidney disease, mechanical ventilation, CRP > 74, and TLC >13 had high predictive value for occurrence of AKI among hospitalized COVID 19 patients.

Conclusion: It could be concluded that AKI in COVID-19 patients is associated with a high mortality rate in ICU-COVID-19 patients. Our findings suggest that COVID-19 patients, particularly ICU COVID-19 patients, should be closely monitored for the development of AKI. Early identification of AKI, as well as prompt intervention, can improve COVID-19 patient outcomes.

Keywords: Acute kidney injury, COVID-19, Incidence, Mortality, Hemodialysis

INTRODUCTION

Since, severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) was reported in late December 2019, our understanding of coronavirus infection disease (COVID-19) has evolved. COVID-19 affects the respiratory system predominantly, leading to acute respiratory distress syndrome (ARDS) [(1)], but it is increasingly recognized to have systemic involvements such as acute kidney injury (AKI), thrombotic events leading to stroke, acute myocardial infarction, and pulmonary embolism [(2)]. Systemic involvement further adds to the challenges of treating COVID-19 patients with poor outcomes [(3)].

AKI is of particular interest as it is associated with poorer outcomes in general population and COVID-19 [(4)]. The incidence of AKI in COVID-19 patients ranges from 0.5 to 36.6% in different study populations and using different case definitions of AKI. However, few studies have examined risk factors associated with the development of AKI in COVID-19 patients [(5)].

In a meta-analysis of 79 research articles on AKI and COVID-19, only 8 had investigated primarily the risk factors for AKI in COVID-19 patients, whereas most studies confined to describing the incidence and prognosis. The elucidation of risk factors leading to AKI is important for physicians to better manage their patients, given the diverse presentation and clinical course of COVID-19 patients from asymptomatic to ARDS [(6)].

The aim of the study was to study the incidence and prognosis of acute kidney injury among patients hospitalized with COVID-19.

PATIENTS AND METHODS

This retrospective observational cohort study included a total of 163 COVID19 patients diagnosed by RT-PCR by Convenient sample and carried in Inpatient and ICU of Geriatric Isolation Hospital, Ain Shams University hospitals for COVID19. This study was carried out through a period of three months.

Inclusion Criteria:

Adult > 18 years old**,** Evidence of a personally signed and dated informed consent document and COVID-19 confirmed by SARS-CoV-2 PCR.

Exclusion Criteria:

Refusal to sign the informed consent previous SARS-CoV-2 confirmed by PCR, pregnancy and patients transferred to another hospital in another region or discharged by consent

Ethical Considerations:

An approval of the study was obtained from Ain Shams University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All participants were subjected to:

1. Recording of all socio-demographic data (age, gender, occupation).

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2. Full history including COVID-19 symptomatology and severity.
3. Clinical examination including details of vital data (temperature, respiratory rate, blood pressure, and SpO2 on room air).
4. PCR for SARS-CoV-2.
5. Complete blood count with differential.
6. C-reactive protein titre.
7. Serum ferritin.
8. D dimer level, LDH, schistocytes.
9. Liver function tests (Aspartate transaminase and Alanine transaminase).
10. Kidney function tests (creatinine and blood urea nitrogen).
11. Serum electrolytes (sodium and potassium).
12. Urine analysis, protein/creatinine ratio.
13. Chest imaging (High resolution computerized tomography).
14. ECG and echocardiography if required.
15. C3 and C4.

Statistical Analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Table 1 shows that there were non-statistical significant differences between patients with AKI and patients without AKI regarding age, sex, CT findings, and APACHE II while there were high significant difference between two groups regarding duration of admission and smoking.

Table (1): Demographic Data among studied cases

		Pts with no AKI No. = 80	**Pts with AKI No. = 83**	**Test value**	**P-value**	**Sig.**
Age (years)	Mean ± SD Range	63.49 ± 13.36 23 – 84	66.84 ± 11.00 22 – 86	-1.754•	0.081	NS
Gender	Male Female	38 (47.5%) 42 (52.5%)	45 (54.2%) 38 (45.8%)	0.735*	0.391	NS
	Ex-smoker Smoker	11 (13.8%) 0 (0.0%)	33 (39.8%) 0 (0.0%)			
Duration of admission (days)	Median (IQR) Range	11 (8 – 16) 2 – 44	9 (5.5 – 13.5) 1 – 33	-2.773ǂ	**0.006**	**HS**
Smoking	Non-smoker Ex-smoker Smoker	69 (86.3%) 11 (13.8%) 0 (0.0%)	50 (60.2%) 33 (39.8%) 0 (0.0%)	13.983*	**0.000**	**HS**
CT-findings: CO-RADS	Low probability (CO-RADS 1,2) Intermediate (CO-RADS 3) High probability (CO-RADS 4,5)	1 (1.3%) 10 (12.5%) 69 (86.3%)	1 (1.2%) 12 (14.5%) 70 (84.3%)	0.134*	0.935	NS
APACHE II	Mean ± SD	26.47 ± 11.78	34.00 ± 13.45	-1.694•	0.100	NS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test; •: Independent t-test; ‡: Mann Whitney test

Table 2 shows that there were non-statistical significant differences between two groups regarding co morbidities as hypertension, diabetes, obesity, heart disease while there were highly significant differences regarding malaise, chronic kidney diseases and cough.

Table (2): Co-morbidities and symptoms among studied cases

	Patients with no AKI		Patients with AKI		Test value*	P-value	Sig.
	No.=80	%	No.=83	%			
Co-morbidities							
Hypertension	63	78.8%	59	71.1%	1.271	**0.259**	**NS**
DM	47	58.8%	43	51.8%	0.794	**0.373**	**NS**
Obesity	1	1.3%	4	4.8%	1.745	**0.186**	**NS**
Heart disease	16	20.0%	21	25.3%	0.652	**0.419**	**NS**
Asthma	1	1.3%	1	1.2%	0.001	**0.979**	**NS**
Other chronic lung dis	1	1.3%	4	4.8%	1.745	**0.186**	**NS**
Chronic Hematological dis	3	3.8%	3	3.6%	0.002	**0.963**	**NS**
Chronic Kidney dis	4	5.0%	59	71.1%	75.026	**0.000**	**HS**
Chronic Liver dis	6	7.5%	15	18.1%	4.057	**0.044**	**S**
Chronic Neurologic dis	16	20.0%	9	10.8%	2.630	**0.105**	**NS**
Organ bone /marrow transplant recipient	1	1.3%	2	2.4%	0.303	**0.582**	**NS**
Bone marrow Recipient	0	0.0%	1	1.2%	0.970	**0.325**	**NS**
Cancer/malignancy	3	3.8%	6	7.2%	0.945	**0.331**	**NS**
Pregnancy	0	0.0%	0	0.0%	NA	**NA**	**NA**
Surgery	0	0.0%	1	1.2%	0.970	**0.325**	**NS**
Autoimmune disease	0	0.0%	1	1.2%	0.970	**0.325**	**NS**
Symptoms							
Fever	47	58.8%	53	63.9%	0.448	**0.503**	**NS**
Cough	56	70.0%	36	43.4%	11.747	**0.001**	**HS**
Respiratory distress	53	66.3%	61	73.5%	1.017	**0.313**	**NS**
Diarrhea	11	13.8%	6	7.2%	1.854	**0.173**	**NS**
Malaise	18	22.5%	2	2.4%	15.274	**0.000**	**HS**
Sore throat	3	3.8%	2	2.4%	0.246	**0.620**	**NS**
Anosmia	0	0.0%	0	0.0%	NA	**NA**	**NA**
Ageusia	0	0.0%	0	0.0%	NA	**NA**	**NA**
DCL	7	8.8%	16	19.3%	3.725	**0.054**	**NS**
secondary infection	3	3.8%	5	6.0%	0.451	**0.502**	**NS**

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS), *:Chi-square test

Table 3 shows that there were non-statistical differences between patients with no AKI and patients with AKI regarding severity of disease in the form of Additional treatment (Actemra/ Remedisvir), Mechanical ventilation, and Cause of Death, while there were highly statistical differences between two groups regarding ICU admission which was higher among patients with AKI.

Table (3): Severity of diseases among studied patients

		Pts with no AKI		Pts with AKI		Test value*	P-value	Sig.
		No.=80	%	No.=83	%			
Additional treatment (Actemra/ Remedisvir)	Protocol	71	88.8%	77	92.8%	**3.189**	**0.363**	**NS**
	Actemra	6	7.5%	6	7.2%			
	Remedisvir	1	1.3%	0	0.0%			
	Actemra and Remedisvir	2	2.5%	0	0.0%			
ICU admission	No	36	45.0%	17	20.5%	**11.160**	**0.001**	**HS**
	Yes	44	55.0%	66	79.5%			
Mechanical ventilation	No	59	73.8%	56	67.5%	**0.773**	**0.379**	**NS**
	Yes	21	26.3%	27	32.5%			
Cause of Death	Not dead	61	76.3%	49	59.0%	**5.711**	**0.058**	**NS**
	Covid	14	17.5%	27	32.5%			
	Non-covid	5	6.3%	7	8.4%			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS), *:Chi-square test

Table 4 shows that there were non-statistical differences between patients with no AKI and patients with AKI regarding AST, Na, Ca, mg, CRP, D-dimer, ferritin, LDH, and TLC, while there were highly statistical differences between two groups regarding ALT, BUN, creatinine, K, PO4 which was higher among patients with AKI.

Table (4): Laboratory Data among studied cases

		Pts with no AKI	Pts with AKI	Test value	P-value	Sig.
		No. = 80	No. = 83			
ALT (SGPT) (U/L)	**Mean ± SD**	33.5 ± 5.12	38 ± 5.32	**-3.230ǂ**	**0.001**	**HS**
AST (SGOT) (U/L)	**Mean ± SD**	45 ± 10.12	42 ± 9.31	**-1.443ǂ**	**0.149**	**NS**
BUN (mg/dL)	**Mean ± SD**	24.50 ± 1.92	73.23 ± 8.55	**-14.125•**	**0.000**	**HS**
Creatinine (mg/dl)	**Mean ± SD**	0.95 ± 0.25	3.73 ± 0.38	**-10.395•**	**0.000**	**HS**
Normal **Abnormal**		79 (98.8%) 1 (1.3%)	6 (7.2%) 77 (92.8%)	**136.737***	**0.000**	**HS**
Na (mmol/l)	**Mean ± SD**	136.16 ± 5.86	135.01 ± 7.49	**1.090•**	**0.277**	**NS**
Normal **Abnormal**		47 (58.8%) 33 (41.3%)	34 (41.0%) 49 (59.0%)	**5.155***	**0.023**	**S**
K (mEq/L)	**Mean ± SD**	3.95 ± 0.53	4.34 ± 0.90	**-3.337•**	**0.001**	**HS**
Normal **Abnormal**		60 (75.0%) 20 (25.0%)	51 (61.4%) 32 (38.6%)	**3.445***	**0.063**	**NS**
Ca (mg/dL)	**Mean ± SD**	8.39 ± 0.65	8.56 ± 0.78	**-1.470•**	**0.144**	**NS**
PO4 (mmol/L)	**Mean ± SD**	2.82 ± 0.01	4.17 ± 1.18	**-6.175•**	**0.000**	**HS**
Mg (mg/dL)	**Mean ± SD**	2.05 ± 0.35	2.04 ± 0.30	**0.078•**	**0.938**	**NS**
CRP (mg/L)	**Mean ± SD**	49.5 ± 8.36	53 ± 11.84	**-1.963ǂ**	**0.050**	**NS**
Normal **Abnormal**		5 (6.3%) 75 (93.8%)	1 (1.2%) 82 (98.8%)	**2.925***	**0.087**	**NS**
D-dimer (mg/L)	**Mean ± SD**	1 ± 0.18	0.7 ± 0.12	**-1.749ǂ**	**0.080**	**NS**
Normal **Abnormal**		12 (15.8%) 64 (84.2%)	39 (47.0%) 44 (53.0%)	**17.724***	**0.000**	**HS**
Ferritin (ng/mL)	**Mean ± SD**	439 ± 98.91	208 ± 47.64	**-1.920ǂ**	**0.055**	**NS**
Normal **Abnormal**		30 (37.5%) 50 (62.5%)	44 (53.0%) 39 (47.0%)	**3.954***	**0.047**	**S**
LDH (IU/L)	**Mean ± SD**	420.65 ± 27.00	501.40 ± 84.31	**-1.761•**	**0.081**	**NS**
Normal **Abnormal**		9 (17.6%) 42 (82.4%)	7 (8.4%) 76 (91.6%)	**2.550***	**0.110**	**NS**
TLC (x10^3/ul)	**Mean ± SD**	8 ± 1.34	8 ± 1.12	**-0.862ǂ**	**0.389**	**NS**
Normal **Abnormal**		52 (65.8%) 27 (34.2%)	58 (69.9%) 25 (30.1%)	**0.306***	**0.580**	**NS**
Hb (g/dL)	**Mean ± SD**	11.99 ± 1.92	10.00 ± 2.17	**6.182•**	**0.000**	**HS**
PLT (x10^3/ul)	**Mean ± SD**	243.04 ± 9.80	203.55 ± 13.39	**2.500•**	**0.013**	**S**
INR	**Mean ± SD**	1.15 ± 0.22	1.22 ± 0.19	**-1.241•**	**0.217**	**NS**

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
*:Chi-square test; •: Independent t-test; ‡: Mann Whitney test

Table 5 shows that there was non-statistical significant correlation between creatinine levels and each of gender, condition on admission, CT findings, ICU admission, and death while there was highly significant difference regarding AKI resolution.

Table (5): Patients with AKI (correlation between creatinine level and clinical data of studied cases)

		Creatinine		Test value	P-value	Sig.
		Mean ± SD	Range			
Gender	Male	3.74 ± 2.67	1.5 – 12	0.041	0.967	NS
	Female	3.72 ± 2.02	1.3 – 8			
Condition on admission	Mild	3.13 ± 2.1	1.8 – 8.5	0.268	0.848	NS
	Moderate	3.83 ± 2.53	1.5 – 11			
	Severe	3.7 ± 2.42	1.3 – 12			
	Critical	4.01 ± 2.41	1.4 – 10			
CT-findings: CO-RADS	Low probability	1.6 ± 0	1.6 – 1.6	0.500	0.609	NS
	Intermediate probability	4.04 ± 2.89	1.5 – 11			
	High probability	3.71 ± 2.31	1.3 – 12			
ICU admission	No	3.45 ± 1.92	1.6 – 8.5	-0.547	0.586	NS
	Yes	3.8 ± 2.5	1.3 – 12			
Death	Alive	3.61 ± 2.3	1.3 – 11	-0.539	0.591	NS
	Died	3.9 ± 2.52	1.4 – 12			
AKI resolution	CR	3.17 ± 1.66	1.3 – 8	10.691	0.000	HS
	PR	7.21 ± 3.05	2.1 – 11			
	Died	3.7 ± 2.46	1.4 – 12			

Table 6 shows that in patients with AKI; the Mean ± SD of BUN was73.23 ± 28.55, Mean ± SD of creatinine was 3.73 ± 2.38, most cases were Stage II of AKI, 21 (25.3%) had proteinuria, 26 (31.3%) had hematuria, 60 (72.3%) were of normal platelets type, and only 11 (13.3%) had normal Schistocytes.

Table (6): Kidney function tests among patients with AKI

		Pts with AKI (no. = 83)
BUN (mg/dL)	Mean ± SD	73.23 ± 28.55
Creatinine (mg/dl)	Mean ± SD	3.73 ± 2.38
Stage of AKI	I	21 (25.3%)
	II	35 (42.2%)
	III	27 (32.5%)
Proteinuria	No	62 (74.7%)
	Yes	21 (25.3%)
Hematuria	No	57 (68.7%)
	Yes	26 (31.3%)
Type of platelets	Normal	60 (72.3%)
	Low	23 (27.7%)
Schistocytes	Negative	72 (86.7%)
	Positive	11 (13.3%)

Table 7 shows that there were non-statistical difference between ICU admission and each of LDH, CRP, and d-dimer, while there significant differences between ICU admission and BUN, creatinine, and serum ferritin.

Table (7): Relation between ICU admission and kidney function tests

		ICU admission		Test value	P-value	Sig.
		No	Yes			
Bun	Mean±SD	33.98 ± 26.43	56.70 ± 33.18	**-4.360•**	**0.000**	**HS**
Creatinine	Mean±SD	1.74 ± 1.60	2.67 ± 2.39	**-2.565•**	**0.011**	**S**
LDH	Mean±SD	457.86 ± 340.82	475.37 ± 224.82	-0.345•	0.731	NS
CRP	Mean±SD	60 ± 12.35	47 ± 4.51	-0.200‡	0.841	NS
D. dimer	Mean±SD	0.8 ± 0.12	1 ±0.4	-1.339‡	0.181	NS
Ferritin	Mean±SD	200 ± 42.36	463 ± 103.36	**-2.795‡**	**0.005**	**HS**

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)
•: Independent t-test; ‡: Mann Whitney test

Table 8 shows that majority of AKI patients did not need for HD, 59% had improved fate, while as regard AKI resolution; 50.6% showed complete resolution, 41.0% were died and 8.4% showed partial resolution.

Table (8): Distribution of patients with AKI regarding fate and outcomes

		Patients with AKI	
		No.	**%**
Need for HD	Yes	11	13.3%
	No	72	86.7%
Fate	Improved	49	59.0%
	Died	34	41.0%
AKI resolution	CR	42	50.6%
	PR	7	8.4%
	Died	34	41.0%

Table 9 shows that each of presence of chronic kidney disease, mechanical ventilation, CRP > 74, and TLC >13 had high predictive value for occurrence of AKI among hospitalized COVID 19 patients.

Table (9): Logistic regression analysis for predictors of AKI

	Uni-variety				Multi-variety			
	P-value	**Odds ratio (OR)**	**95% C.I. for OR**		**P-value**	**Odds ratio (OR)**	**95% C.I. for OR**	
			Lower	**Upper**			**Lower**	**Upper**
Chronic Kidney disease	0.000	0.138	0.048	0.395	0.005	0.179	0.054	0.591
MV	0.006	3.949	1.469	10.612	0.039	3.350	1.063	10.553
CRP > 74	0.011	3.494	1.326	9.209	0.409	1.624	0.514	5.137
TLC >13	0.016	3.828	1.290	11.358	0.357	1.849	0.499	6.844

DISCUSSION

The COVID-19 pandemic is a serious, multidimensional problem with tremendous detrimental consequences for healthcare, occupation, and economy. COVID-19 primarily manifests as an acute respiratory illness with interstitial or alveolar pneumonia, but can also affect multiple organs, such as the kidneys, heart, liver, blood, and nervous system [(7)].

There is a dearth of accurate consensus regarding the incidence, pathogenesis, diagnosis, management, and outcomes of AKI. The aim of the study was to study the incidence and prognosis of acute kidney injury among patients hospitalized with COVID-19.

In the present study, we found that there were non-statistically significant differences between patients with AKI and patients without AKI regarding age, sex, CT findings, and APACHE II while there were high significant differences between two groups regarding duration of admission and smoking. Furthermore, there were non-statistically significant differences between two groups regarding co morbidities as hypertension, diabetes, obesity, heart disease while there were highly significant differences regarding malaise, chronic kidney diseases and cough.

In agreement with our findings, the study of **El-Sayed *et al.*** [(8)] who aimed to assess the incidence rate of AKI in Egyptian COVID-19 patients, comparisons were carried out between home-isolated COVID-19 patients, hospitalized COVID-19 patients, and ICU COVID-19-patients with or without AKI, and reported that the median age was 56 years, with 57.9% of patients being male (377/651)**.** The characteristics of COVID-19 patients without AKI are presented with cough (91.4%), fever (54.3%), sore throat (62.3%), and dyspnea (64.1%), while the features of COVID-19 patients with AKI were presented with cough (72.5%), fever (85.7%), sore throat (18.7%), and dyspnea (84.6%). In this cohort study, there is no statistically significant difference regarding age between COVID-19 patients with or without AKI (mean, 57.5 years versus 55.0 years, respectively).

Furthermore, **Jewell *et al.*** [(9)] who aimed to investigate the epidemiology, risk factors and outcomes of AKI in patients with COVID-19 in a large UK tertiary center, and reported that mean age was 69 years (SD 17.1), 58.8% were male, 49.1% were of white and 27.4% of black ethnicity. A diagnosis of pre-existing CKD stages 3–5 (baseline eGFR< 60 ml/min/1.73m^2) was present in 16.6%; 14.0% had CKD stage 3, 2.1% CKD stage 4 and 0.5% CKD stage 5 (not on RRT). A total of 487 patients (39%) developed AKI and the proportion of these with pre-existing CKD was significantly higher at 26.7%, compared to those without AKI (10.1%, $p < 0.001$). Hypertension (54.6%) and diabetes (32.7%) were the most common comorbidities and were both significantly more frequent among patients with AKI (68.8 and 40.9%, respectively) than those without (45.5 and 27.4%, respectively, $p < 0.001$for both).

In the current study, we found that there were non-statistically significant differences between patients with no AKI and patients with AKI regarding

severity of disease in the form of Additional treatment (Actemra/ Remedisvir), Mechanical ventilation, and Cause of Death, while there were highly statistical differences between two groups regarding ICU admission which was higher among patients with AKI.

Ghosn *et al.* [10] reported in their study that fifty patients (45.4%) developed severe AKI (stage 2 or 3), and 60 (54.5%) had no AKI (46.4%) or AKI stage 1 (8.2%); the median time from ICU admission to AKI occurrence was 0 days (IQR: 0–7 days). Among patients who developed severe AKI (stages 2 or 3), 27 (54%) required renal replacement therapy. The median time from ICU admission to renal replacement therapy was 2 days (IQR: 0–9 days), Patients in the severe AKI group were older and had a higher rate of comorbidities, higher severity scores, and lower a mean arterial pressure on ICU admission than the other group. Regarding laboratory data on ICU admission, only leucocyte, D-dimer, and creatinine levels were significantly higher in the severe AKI group than in the other group.

In the present study, there were non-statistical differences between patients with no AKI and patients with AKI regarding AST, sodium, calcium, magnesium, CRP, D-dimer, ferritin, LDH, and TLC, while there were highly statistical differences between two groups regarding ALT, BUN, creatinine, K, PO4 which was higher among patients with AKI.

Furthermore, we found that there were highly statistically significant differences between two groups regarding arterial blood gases in form of Ph and HCO3, while there was a non-statistical difference between groups regarding O_2 saturation.

Similar to our results, **Wang *et al.* [11]** which reported that in comparison with patients without AKI, patients who developed AKI were older, tended to have chronic kidney disease, had higher Sepsis-Related Organ Failure Assessment score on day 1, and were more likely to receive invasive ventilation and develop acute organ dysfunction. Importantly, **Wang *et al.* [11]** reported also that increasing AKI severity was associated with increased in-hospital mortality when adjusted for other potential variables: odds ratio of stage 1 = 5.374 (95% CI: 2.147–13.452; $p < 0.001$), stage 2 = 6.216 (95% CI: 2.011–19.210; $p = 0.002$), and stage 3 = 34.033 (95% CI: 9.723–119.129; $p < 0.001$). Among laboratory parameters on day 1 after ICU admission, AKI patients had higher white cell count, neutrophil count, neutrophil-to-lymphocyte ratio (NLR), C-reactive protein level, and D-dimer. Moreover, patients with AKI had lower platelet count and albumin level and had more organ dysfunction indicated by different laboratory parameters than patients without AKI **[11].**

Acute kidney injury (AKI) is a major cause of morbidity and mortality in hospitalized patients, particularly in the critically ill. For patients admitted to the ICU, the incidence of AKI is reportedly as high as 25%, with a hospital mortality of 86% [12].

In the current study, we demonstrated that there was non-statistical significant correlation between creatinine levels and each of gender, condition on admission, CT findings, ICU admission, and death while there was highly significant difference regarding AKI resolution.

In comparison with our findings, **Samuels *et al.* [12]** demonstrated that the mean serum creatinine level on admission to the ICU was 0.9±0.6 mg/dl. The baseline creatinine was higher in patients who died (1.2±0.9 mg/dl) than in those who survived (0.9±0.5 mg/dl), as was peak creatinine during the first week following ICU admission (1.9±1.4 mg/dl for those who died vs 1.1±0.9 mg/dl for survivors). Patients whose creatinine did not rise more than 0.1 mg/dl after admission had a mean (SD) length of ICU stay of 5 days (8.6 days). Those with any increase in creatinine of 0.2 mg/dl or more during the first 3 days of ICU admission remained in the ICU for a significantly longer period.

On the other hand, we found that in patients with AKI; the Mean ± SD of BUN was73.23 ± 28.55, Mean ± SD of creatinine was 3.73 ± 2.38, most cases were Stage II of AKI, 21 (25.3%) had proteinuria, 26 (31.3%) had hematuria, 60 (72.3%) were of normal platelets type, and only 11 (13.3%) had normal Schistocytes. Moreover, we reported that there were non-statistical difference between ICU admission and each of LDH, CRP, and d-dimer, while there significant differences between ICU admission and BUN, creatinine, and serum ferritin.

Come in line with our findings, **El-Sayed *et al.* [8]** reported that in patients with AKI; the median of BUN was 135 (70–200), median of creatinine was 7.5 (1.3–13.7), this group of patients had also the highest levels of inflammatory markers and kidney function tests [D-dimer (1495.5 vs. 1445.7 mg/ml), C-reactive protein (1017 vs. 626.5 mg/dl), while **Jewell *et al.*[9]** reported that Of the 487 cases of AKI, 51% met KDIGO criteria for stage 1 (n = 248), 13% (n = 64) stage 2 and 36% (n = 175) stage 3. A total of 109 patients (8.7% of total, 22% of all AKI) required RRT and the relevant modalities included CVVHDF, HD, PD or any combination of those (different modalities for a single patient were used at different times and according to clinical indication and resource availability). None of the patients required RRT following discharge from the hospital. Of those discharged alive, AKI had resolved in 84.0% of all patients affected, and 69.7% of those with AKI3 prior to discharge**.**

Furthermore, **Sang *et al.* [13]** reported that patients with AKI had markedly higher levels of serum creatinine (median: 75.5 vs. 67.1 μmol/L, $P = 0.002$), interleukin-6 (median: 17.9 vs. 12.3 pg/ml, $P < 0.001$) and serum ferritin (median: 2001.0 vs. 985.4 ng/ml, $P < 0.001$). Hypoxemia and hypercapnia were also more frequently identified in patients with AKI (both $P < 0.001$).

In addition to above findings, we found that there were non-statistical significant correlation between

presence of hematuria and outcomes of studied cases in form of ICU admission, mechanical ventilation, death and fate of disease.

Furthermore, we found that there were non-statistical significant correlation between presence and severity of proteinuria and outcomes of studied cases in form of ICU admission, death and fate of disease except mechanical ventilation. Additionally, our study demonstrated that there were non-statistical significant correlation between presence of Schistocytes and outcomes of studied cases in form of ICU admission, mechanical ventilation, death and fate of disease.

In a harmony with our findings, **Han *et al.* [14]** reported that throughout the follow-up period, 1270 (67.4%) of all ICU patients died, and the mortality rate was 69.9 deaths per 100000 patient-days, the presence of proteinuria or hematuria worsened the mortality, irrespective of the effects of covariates. Although the AKI was further adjusted, the overall correlations between mortality and proteinuria or hematuria were significant. The trends in the correlations of mortality with proteinuria (Ptrend < 0.001) and hematuria (Ptrend = 0.010) were also significant after further adjustment of AKI. When patients with both proteinuria (trace or more) and hematuria (1+ or more) were compared with patients without both markers, the adjusted HR for mortality was 2.07 (1.545–2.772) (P < 0.001).

Several previous studies of **Paudel *et al.* [15] and Xu *et al.* [16]** had demonstrated that AKI, especially severe AKI was associated with poorer clinical outcomes. The AKI-EPI study of **Hoste *et al.* [17]** showed that patients with stage 1 AKI did not have a higher risk of mortality compared to patients without AKI. However, **Han *et al.* [14]** reported that only AKI KDIGO stage 3 was associated with ICU 28-day mortality, patients with KDIGO stage 1 and 2 AKI did not have a higher mortality compared to patients without AKI.

On the other hand, we found that majority of AKI patients did not need for HD, 59% had improved fate, while as regard AKI resolution; 50.6% were CR, 41.0% were died and 8.4% were PR.

In comparison with the study of **El-Sayed *et al.* [8]** who reported that he absolute number of patients needing hemodialysis was 34 (37%). This appeared in 5.2% of all patients and 37% of COVID-19 cases with AKI. COVID-19 AKI cases who needed hemodialysis had significant higher percentages with comorbid conditions including diabetes mellitus (73.5% vs. 14%), cardiac disease (23.5% vs. 5.2%), cancer (20.6% vs. 7%), and hypertension (79.4% vs. 28%). This group of patients had also the highest levels of inflammatory markers and kidney function tests [D-dimer (1495.5 vs. 1445.7 mg/ml), C-reactive protein (1017 vs. 626.5 mg/dl), serum creatinine (8.9 vs. 2.65 mg/dl), and blood urea (137.5 vs. 60 mg/dl)] in comparison to AKI patients who did not require hemodialysis.

Finally, we can report that each of presence of chronic kidney disease, mechanical ventilation, CRP > 74, and TLC >13 had high predictive value for occurrence of AKI among hospitalized COVID 19 patients.

Jewell *et al.* [9] reported that Multivariate logistic regression analysis revealed that pre-existing CKD (baseline eGFR< 60 ml/min/1.73m^2) was associated with a 3-fold risk of AKI (OR 3.05; 95%CI 2.24–4.18, p < 0.0001) adjusted for demographics and comorbidities. Other variables independently associated with increased AKI risk were male sex (OR 1.45; 95%CI 1.12–1.89, p = 0.005), black ethnicity (OR 1.76; 95%CI1.26–2.45, p < 0.005), hypertension (OR 1.66; 95%CI1.23–2.24, p < 0.005) and inpatient diuretic use (OR 1.79; 95%CI 1.27–2.53, p < 0.005).

It is possible that early on during the pandemic, there was concern that COVID-19 patients were at risk of capillary leak linked to the hyperinflammatory state and consequently clinicians were cautious about excess fluid replacement. As the pandemic unfolded, the clinical community became rapidly aware of the high rates of AKI and clinical picture of volume depletion that evolved during the course of the disease. In the absence of published data, our local practice changed as we developed more experience in managing these patients during the first wave, adopting a more liberal fluid management strategy and actively withholding diuretics upon admission.

CONCLUSION

It could be concluded that COVID-19 cases, particularly those in the ICU, should be closely monitored for the progression of AKI. Early detection of AKI and prompt meditation may improve COVID-19 patients' outcomes.

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