Original Article

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Predictors of in-Hospital and 90-day Outcome of Hemodialysis Patients with COVID-19 Admitted to a Tertiary Hospital, Chattogram, Bangladesh

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Abstract

Background: Renal impairment is common in Coronavirus Disease-2019 (COVID-19) and the impact of renal impairment on patient outcomes may differ due to geographical area, differences in healthcare systems or hospital capacities. This study investigated the factors associated with in-hospital and 90 days outcomes in COVID-19 patients who needed hemodialysis for their renal impairment in a public tertiary hospital in Bangladesh.

Materials and methods: This prospective observational study was conducted in Chittagong Medical College Hospital (CMCH) Chattogram, Bangladesh. Consecutive COVID-19 patients (Both confirmed and suspected) with renal impairment and subjected to hemodialysis were included. The demographic characteristics, clinical course and laboratory parameters were recorded. Outcome measures were in-hospital and 90 days mortality.

Results: 315 patients were included in the study and 301 patients completed the 90 days follow up. The in-hospital mortality rate was 29.8% and 90 days mortality rate was 31.2%. Age was significantly higher in patients who died in hospital (47.5±14.3 vs 51.6±16.3 years, p=0.028) and died within 90 days (44.5±14.0 vs 50.9±3.2 years, p=0.002) of admission than who survived. Mortality in patients with End Stage Renal Disease (ESRD) on Maintenance Hemodialysis (MHD) were less than AKI and CKD patients (p=0.007) regarding in-hospital outcome. Total WBC count was also higher in expired patients both in-hospital (p=0.023) and 90 days (p=0.031) than survived patients. Median blood urea (188.0 vs 210.0 mg/dL) SGPT (31.0 vs 36.0 U/L) and D-dimer (2.6 vs 4.6 ug/mL) were significantly higher and Lymphocyte count was significantly lower in expired group than survived group regarding in-hospital mortality (p<0.05). There was no significant difference of serum creatinine, CRP, serum ferritin between expired and survived groups.

Conclusions: This study showed that patients with COVID-19 who required hemodialysis were higher mortality rate both in-hospital and 90 days follow up. Older age, leukocytosis, lymphopenia, uremia, increased SGPT and D-dimer were predictors of in-hospital mortality. ESRD on MHD had good outcome. Older age and leukocytosis were predictors of 90 days mortality.

Key words: AKI; CKD; COVID-19; Hemodialysis.

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Introduction

Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCoV-2) infection emerged in Wuhan, China in December 2019 and rapidly developed in a pandemic. On February 11, 2020, the world health organization officially named the disease caused by SARS-CoV-2 as Coronavirus Disease 2019 (COVID-19).[1]

COVID-19 is primarily manifested as an acute respiratory illness but it can affect multiple organs.[2] The kidneys are the second most frequently affected organ by SARS-CoV-2, after the lungs.[3] Preliminary data from Wuhan, China reported AKI was uncommon in COVID-19 and SARS-CoV-2 infection does not result in AKI or aggravate Chronic Kidney Disease (CKD) in the COVID-19 patients.[4] However, later on data from Europe and the United States (US) revealed an incidence of up to 34%.[5-8] The pathogenesis is multifactorial including possible viral invasion, hypovolemia, systemic inflammation, nephrotoxin exposure, endothelial dysfunction, coagulopathy and organ crosstalk.[9,10]

The incidence of AKI varies among geographical regions and clinical settings, ranging from 7 to 57% in hospitalized patients and 19–80% in patients in the intensive care unit (ICU).[11-18] Renal

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Replacement Therapy (RRT) is utilized in 20–60%.[12,18] Both AKI and RRT are associated with adverse hospital outcomes and increased mortality.[19]

Survivors of COVID-19 are shown to be at an increased risk of long-term adverse outcomes including, mortality, chronic kidney disease, end-stage renal disease and reduced quality of life. The impact of renal impairment with hemodialysis on patient outcomes may differ due to factors such as geographical area, differences of health-care systems or hospital capacities. There is no large-scale study which documents the outcomes of AKI in COVID-19 patients from Bangladesh. In addition, although the increased mortality risk in CKD patients with COVID 19 has been well demonstrated.[20,21]

Therefore, we planned to conduct this prospective observational study to evaluate the clinical profile of these patients and to determine the risk factors for adverse in-hospital and 90 days outcome in hospitalized patients with COVID-19 who received hemodialysis in CMCH.

Materias and methods

This prospective observational study was studied at CMCH, Bangladesh from January, 2021 to December, 2022. The ethical review committee of Chittagong Medical College approved this study. Patients were selected consecutely according to selection criteria. Inclusion criteria were patients with COVID-19 (Both confirmed or suspected cases), admitted in the COVID dedicated zone (Red or Yellow zone) of CMCH and needed to hemodialysis for renal insufficiency. Exclusion criteria were transferred to other hospitals during treatment and refused to participate. The full demographic and clinical history was obtained from the legal relatives of the patients. All investigations report including the renal function were measured and note. Treatment details and in-hospital outcome were noted. After discharge patients were advised to attend follow-up visit 90 days after to review their renal function status. Outcome variables were predictors of in-hospital and 90 days mortality.

Participants were categorized according to their outcome (Expired and survived groups). Categorical variables were summarized as frequencies and percentages. Normally distributed continuous data were expressed as mean ± Standard Deviation (SD) or median and interquartile range (25%-75%). Independent t and Mann–Whitney U tests were used to compare grouped continuous variable data where appropriate. Chi-square test was used to perform intergroup and categorical comparisons as appropriate. Variables that were found to be significant ($p<0.05$).

Results

315 patients were studied. Among them, follow up of 301 patients were completed after 90 days.

Table I Demographic, clinical and laboratory characteristics of the patients

Variables, units □	□	Frequency □	Percentage
Age, Years □	□	48.8±15.1	
Age, Years			
□	<40 □	83 □	26.3
□	40-60 □	180 □	57.1
□	>60 □	52 □	16.5
Gender			
□	Male □	221 □	70.2
□	Female □	94 □	29.8
Residence			
□	Urban □	93 □	29.5
□	Rural □	222 □	70.5
RT-PCR results			
□	Positive □	127 □	40.3
□	Negative □	188 □	59.7
Renal status			
□	AKI □	26 □	8.25
□	AKI on CKD □	196 □	62.22
□	ESRD on MHD □	93 □	29.52
Respiratory rate, breaths/min □			24.5±5.4
Pulse, beats/min □			95±14.7
Systolic Blood Pressure (SBP) mm of Hg □			138.8±29.7
Diastolic Blood Pressure (DBP) mm of Hg □			85±18
Total count of WBC, /mm^3 □			12800 (9500-16500)
Neutrophil, % □			80.7±9.5
Lymphocyte, % □			10(8-17)
Monocyte, % □			3(2-5)
CRP, mg/L □			63 (24-105)
Serum creatinine, mg/dL □			10.3 (8.3-12.9)
Blood urea, mg/dL □			196 (156-238)
Serum ferritin, ng/mL □			662 (410-1000)
SGPT, U/L □			32 (23-51)
D-dimer, µg/mL □			3.2 (1.5-5.3)

Data were expressed as frequency and percentage, mean±SD, median (25%-75%)

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The mean age was 48.8 (±15.1) years. The highest proportion of the patients were from the 40-60 years age group (57.1%). There was a male predominance with a male to female ratio of 2.4:1. About three quarter (70.5%) of the patients were from rural areas. Most of the patients (59.7%) were RT-PCR negative (COVID suspected) and RT-PCR positive (confirmed COVID) patients were 40.3%. Most of the patients were AKI on CKD (62.22%) followed by ESRD on MHD (29.52%). AKI was present in only 8.25%. This study showed mean respiratory rate, pulse, SBP and DBP were 24.5 breaths/min, 95 beats/min, 138.8 mm of Hg and 85 mm of Hg respectively. There was neutrophilic leukocytosis (median WBC- 12800/mm^3, mean Neutophil-80.7%, median lymphocyte-10% and median monocyte-3%). Median CRP, serum creatinine, blood urea, serum ferritin, SGPT and D-dimer were 63 mg/L, 10.3 mg/dL, 196 mg/dL, 662.2 ng/mL, 32 U/L and 3.2 ug/mL respectively (Table I).

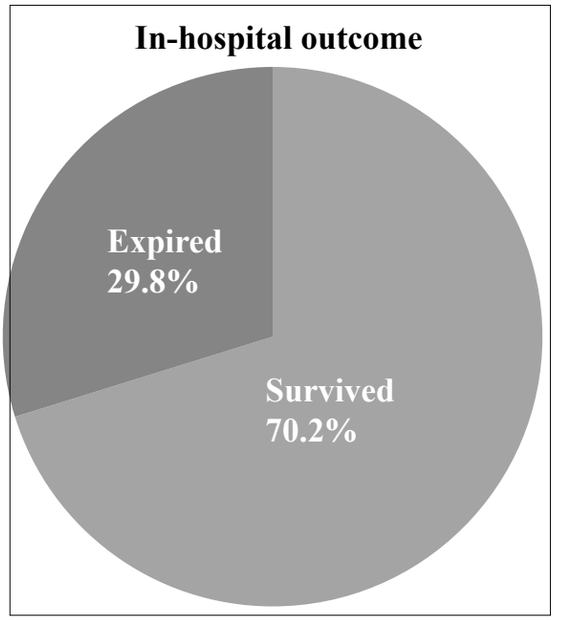

Figure 1 In-hospital outcome of the patients

Out of 315 patients, 221 (70.2%) improved and discharged from the hospital. Other 94 patients expired giving the mortality rate of 29.8% (Figure 1).

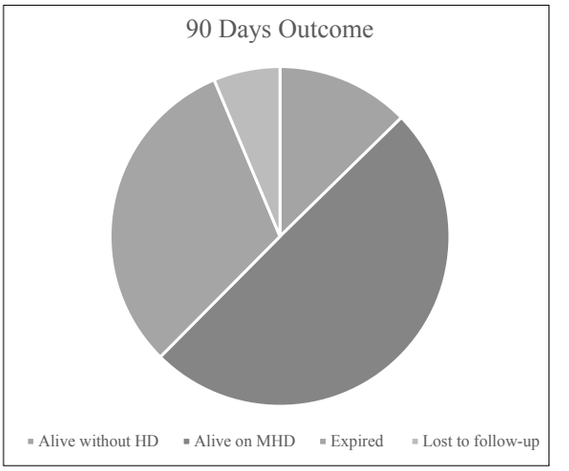

Figure 2 Outcome of the patients after 90 days follow up

Out of 221 discharged patients, 69 (31.2%) patients expired, 110 (49.8%) patients were taking MHD, only 28 (12.7%) patients didn't need any MHD and 14 (6.3%) patients were lost to follow-up (Figure 2).

Table II Association of different demographic, clinical and laboratory parameters with in-hospital mortality

Variables, unit	In-hospital outcome		p value
	Survived (n=221)	Expired (n=94)	
Age, Years	47.5±14.3	51.6±16.3	0.028*
Age, Years			
<40	61 (27.6)	22 (23.4)	
40-60	133 (60.2)	47 (50.0)	0.007†
>60	27 (12.2)	25 (26.6)	
Renal status			
AKI	16 (7.2)	10 (10.6)	0.336†
AKI on CKD	130 (58.8)	66 (70.2)	0.054†
ESRD on MHD	75 (33.9)	18 (19.1)	0.007†
Gender Male	154 (69.7)	67 (71.3)	0.777†
Female	67 (30.3)	27 (28.7)	
Residence Urban	65 (29.4)	28 (29.8)	0.947†
Rural	156 (70.6)	66 (70.2)	
Respiratory rate, breaths /min	24.3±5.5	25.2±5.3	0.187*
Pulse, beats/min	94.0±15.2	97.3±13.4	0.073*
SBP, mmHg	140.5±30.0	135.0±28.7	0.132*
DBP, mmHg	85.4±18.1	84.2±17.8	0.615*
Total WBC count, /mm^3	12200 (9250-16400)	14000 (10425-18600)	0.023‡
Neutrophil, %	80.3±8.6	82.1±11.2	0.133*
Lymphocyte, %	12.0 (8.0-18.0)	10.0 (7.0-15.0)	0.033‡
Monocyte, %	4.0 (2.0-5.0)	3.0 (2.0-5.0)	0.107‡
CRP, mg/L	61.0 (24.0-98.5)	65.5 (24.0-105.4)	0.767‡
Serum creatinine, mg/dL	10.2 (8.2-13.4)	10.0 (7.7-12.4)	0.533‡
Blood urea, mg/dL	188.0 (148.3-230.0)	210.0 (172.9-252.4)	0.009‡
Serum ferritin, ng/mL	647.4 (379.7-1032.0)	712.5 (490.0-998.5)	0.332‡
SGPT, U/L	31.0 (22.0-46.0)	36.0 (25.1-70.0)	0.018‡
D-dimer, µg/mL	2.6 (1.3-4.6)	4.6 (2.2-6.9)	0.001‡

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Table II shows that age (Both numerical and categorical) had statistical significant association in in-hospital mortality (p<0.05). That means, expired patients (51.6±16.3 years) of in-hospital follow up were in older age compared to survived patients (47.5±14.3 years). ESRD on MHD patients were more survived than AKI and AKI on CKD group which was statistically significant. Median WBC count was more in expired group than survived group (14000 vs 12000 /mm3, p=0.023). In other hand, median lymphocyte was more reduced in expired group than survived group (10 vs 12%, p=0.033). Moreover, median blood urea (210 vs 188 mg/dL), median SGPT (36 vs 31 U/L) amd median D-dimer (4.6 vs 2.6 µg/mL) were significantly more in expired group than survived group. None other parameters were significantly different in both groups.

Table III Association of different demographic, clinical and laboratory parameters with 90 day mortality (n=208)

Variables, unit	90-day mortality		p value
	Survived (n=141)	Expired (n=68)	
Age, Years	44.48±14.0	50.9±13.2	0.002†
	Age, Years		
<40	52 (36.9)	10 (14.7)	0.004*
40-60	75 (53.2)	50 (73.5)	
>60	14 (9.9)	8 (11.8)	
Renal status			
AKI	11 (8.0)	5 (7.2)	0.876*
AKI on CKD	80 (58.0)	37 (53.6)	0.494*
ESRD on MHD	47 (34.0)	27 (39.2)	0.427*
Gender Male	97 (68.8)	48 (70.6)	0.792*
Female	44 (31.2)	20 (29.4)	
Residence Urban	42 (29.8)	21 (30.9)	0.874*
Rural	99 (70.2)	47 (69.1)	
Respiratory rate, breaths/min	23.8±5.6	25.0±5.0	0.125†
Pulse, beats/min	93.9±14.5	92.9±16.3	0.670†
SBP, mmHg	141.7±32.7	141.0±23.7	0.882†
DBP, mmHg	85.5±18.9	86.1±17.2	0.938†
Total WBC count, /mm3	12200 (9200-16500)	14350 (9935-17100)	0.031*
Neutrophil, %	80.4±8.4	80.5±8.8	0.938†
Lymphocyte, %	11.0 (8.0-18.0)	13.0 (6.0-17.5)	0.620*
Monocyte, %	4.0 (2.0-5.0)	3.0 (2.0-4.6)	0.408*
CRP, mg/L	60.0 (24.0-98.0)	83.2 (32.3-160.0)	0.066*
Serum creatinine, mg/dL	10.5 (8.9-14.0)	8.4 (7.1-10.6)	0.620*
Blood urea, mg/dL	192.6 (155.0-233.0)	165.0 (134.6-233.5)	0.149*
Serum ferritin, ng/mL	709.9 (400.0-1050.0)	398.7 (259.3-569.0)	0.487*
SGPT, U/L	32.0 (23.0-46.0)	24.5 (20.0-61.0)	0.301*
D-dimer, µg/mL	2.6 (1.3-4.6)	2.6 (1.3-4.3)	0.669*

Data were presented as frequency (Percentage) mean±SD, median (25%-75%). †Independent t test, **Mann-Whitney U test, *Chi square test.

Table III shows that age (numerical and categorical) had statistical significant association in 90 days mortality (p<0.05). Expired patients (50.9±13.2 years) were older than survived patients (44.48±14.0 years). WBC count had significant association with 90 days mortality (Median count 14350 vs 12200 /mm^3, p=0.031). Other than these, none had significant association.

Table IV Multivariate logistic regression of independent predictors of 90 days mortality

Variables	B	OR	95% CI for OR		p value
			Lower	Upper	
Age (Numerical)	0.126	1.134	1.019	1.263	0.022
Age (Categorical)	-1.068	0.344	0.048	2.458	0.287
Total WBC count	0.000	1.000	1.000	1.000	0.022
Serum bi-carbonate	-0.245	0.782	0.653	0.937	0.008
Serum SGPT	-0.001	0.999	0.992	1.006	0.798
Constant	-1.299	0.273	-	-	0.508

Discussions

The present study showed out of 315 patients, 221 (70.2%) survived and discharged from the hospital. In-hospital mortality rate was 29.8%. Among in-hospital survived patients 69 patients were expired (31.2%). Mortality in Japanese hemodialysis people with COVID-19 were 30.8%.[22] Expired patients of both in-hospital and 90 days follow up were in older age which was statistically significant in comparison to survived group. There was similar findings in previous studies.[23,24-26] Most of the patients were male (70.2%) and lived in rural area (70.5%) in the country. These observations were not different in both survived and expired group regarding in-hospital and 90 days outcome (p>0.05). Among 315 patients, 127 patients (40.3%) were RT-PCR positive and rest were RT-PCR negative but had COVID symptoms. Percentage of mortalities were more observed in AKI group and less observed in ESRD on MHD group which were statistically significant (p=0.028) regarding in-hospital outcome. Both survived and expired groups of in-hospital and 90 days outcome had share similar findings related to respiratory rate, pulse rate, SBP and DBP. There was neutrophilic leukocytosis (median WBC- 12800/mm^3, Neutophil-82%, lymphocyte-10% and monocyte-3%). WBC count

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was significantly higher in expired group than survived group regarding in-hospitality and 90 days outcome. Differential count of lymphocyte was significantly lower in expired group than survived group regarding in-hospital outcome. There were studies that supported these hematological observations.[23,24,27,28]

Blood urea, D-dimer and SGPT were significantly higher in expired group than survived group regarding in hospital outcome. There was no difference in results of other parameters regarding in-hospital and 90 days outcome. Blood urea is more increased in expired group, might be due to presence of sepsis and dehydration. Analysis of serum creatinine and blood urea regarding outcome were similar to an Indian study by Sing et al.[27] Other study also supported these findings.[24,25,29-31]

COVID-19 disease is nightmare of 21st century. Patients with renal impairment (CKD and AKI) have been suffering for this outbreak. This study focuses on predictors of mortality both in hospital and 90 days after hospitalization to predict baseline characteristics of worse outcome of patients and thus can take necessary measures to overcome it.

Limitations

It was a single center study. No comparison was done between hemodialysis and non-hemodialysis COVID patients. Both Confirmed COVID patients (RT-PCR positive) and suspected COVID patients (RT-PCR negative) were studied together.

Conclusions

The present study suggests that older age and leucocytosis are predictors of both in-hospital and 90 days mortality. Lymphopenia, increased blood urea, SGPT and D-dimer are also a predictors of in-hospital mortality. ESRD on MHD patients have good outcome than CKD and AKI patients regarding in-hospital mortality.

Recommendations

This study recommends that COVID-19 patients who required hemodialysis have increased mortality rate both in-hospital and 90 days outcome. Some demographic (Age) clinical (Age, ESRD on MHD) and laboratory (Total count of WBC, differential count of lymphocyte, blood urea, SGPT and D-dimer) parameters may influence the outcome. Further, multicenter studies are needed to support these findings as predictors of mortality in Bangladeshi COVID-19 patients who required hemodialysis.

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Contribution of authors

MNH-Conception, design, interpretation of data, critical revision & final approval.

SMUI-Interpretation of data, drafting, critical revision & final approval.

MSHC-Data analysis, interpretation of data, critical revision & final approval.

MA-Acquisition of data, data analysis, drafting & final approval.

RBK-Acquisition of data, data analysis, drafting & final approval.

SH-Acquisition of data, data analysis, drafting & final approval.

Disclosure

All the authors declared no conflict of interest.

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