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Original Article

Internal Medicine Section

Outcome of COVID-19 in Patients Requiring Haemodialysis- A Retrospective Observational Study

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ABSTRACT

Introduction: Acute Kidney Injury (AKI) and Chronic Kidney Disease (CKD) are risk factors for COVID-19 infection. Patients with kidney disease also have other co-morbidities like hypertension, diabetes mellitus, cardiovascular disease that are risk factors for poor outcome in COVID-19 infections. Severe COVID-19 has multiorgan involvement including AKI. Compared to normal population, renal failure patients with COVID-19 have extensive lung involvement, need more ventilator support, and have higher mortality.

Aim: To assess outcome (mortality, recovery) and association between factors (age, gender, co-morbidities), biochemical parameters with mortality in COVID-19 patients requiring haemodialysis.

Materials and Methods: It was a retrospective observational study wherein, data was collected, entered and analysed with Statistical Package for the Social Sciences (SPSS) version 19.0 using medical records of all COVID-19 patients who had renal failure (AKI or CKD) requiring haemodialysis. The study period was from June-September 2020 at Vydehi Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India.

Results: Out of total 68 COVID-19 positive patients, mean age of presentation was 55.08 years and with 75% of the study population were males. Most patients presented with severe COVID-19 illness with tachypnoea and hypoxia. The AKI occurrence and mortality was noted in 44.1% and 47%, respectively. It was noted that medication usage was higher for corticosteroids, oseltamivir, vitamin C, zinc therapy.

Conclusion: In the present single centre study involving COVID-19 patients requiring haemodialysis, it was noticed that severe COVID-19 illness, presence of AKI, chronic respiratory illness and high inflammatory markers were associated with higher mortality.

Keywords: Acute kidney injury, Cardiovascular disease, Chronic kidney disease, Coronavirus disease-2019, Diabetes mellitus

INTRODUCTION

The COVID-19 presents with varied symptoms including being asymptomatic to having fever, cough, breathlessness and fatigue. Both AKI and CKD are risk factors for COVID-19 infection. The COVID-19 itself can cause AKI with incidence of 3-9% and presence of AKI, CKD, hypertension, diabetes mellitus, cardiovascular disease are risk factors for poor outcome in COVID-19 infections [1,2]. Compared to normal population, renal failure patients with COVID-19 have extensive lung involvement, need more ventilator support, and have higher mortality [2]. They have mortality between 3-6% reaching almost 30% in different geographical areas [1-4].

Literature search showed that there was lack of large scale data on mortality and lack of clinical management strategies in treatment of these vulnerable patients. So, this study was expected to provide information regarding the outcome (mortality, recovery) and association between factors (age, gender, co-morbidities), biochemical parameters with mortality in COVID-19 patients who had renal failure (AKI or CKD) requiring haemodialysis.

MATERIALS AND METHODS

This retrospective observational study was conducted using medical records of COVID-19 patients requiring haemodialysis during period June-September 2020 at Vydehi Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India, after obtaining Institutional Ethical Committee (IEC) approval (ECR/747/Inst/KA/2015/RR-18).

Inclusion criteria: All patients diagnosed as COVID-19 with positive pharyngeal swab Reverse Transcriptase-Polymerase Chain Reaction Test (RT-PCR) who had renal failure (AKI or CKD) requiring haemodialysis.

Exclusion criteria: The COVID-19 patients who had milder renal dysfunction not requiring dialysis.

The COVID-19 infection was classified as mild (clinical symptoms with pneumonia), moderate (fever with pneumonia), severe (with tachypnoea with respiratory rate greater rate 30 breaths per minute, hypoxia with saturation less than 93% at rest, arterial PO_2/oxygen concentration less than 300 mmHg) [5].

Outcomes/Endpoints observed were mortality and recovery. Recovery was defined as absence of fever with normal body temperature for more than three days, significant improvement in respiratory symptoms, improved chest imaging indicating reduced inflammation and a negative RT-PCR test.

Using medical records like patient's file, laboratory test reports from medical record section in the hospital, data was collected regarding patient's demography (age, gender), co-morbidities (hypertension, diabetes mellitus, pre-existent renal disease, cardiovascular disease, chronic respiratory illness), biochemical parameters like complete blood cell count, Liver function test, D-Dimer, Lactate Dehydrogenase (LDH), ferritin, C-Reactive Protein (CRP), radiological tests like chest radiograph.

STATISTICAL ANALYSIS

The data was collected, entered and analysed with SPSS version 19.0. Continuous variables was presented as mean±Standard Deviation (SD) or median with Interquartile Ranges (IQR). Categorical vaiables was presented as frequency and percentage (%). Chi-square test or Fischer's-Exact test was performed to see the association between any two categorical variables. The p-value <0.05 was considered statistically significant. Differences in quantitative parameters in two groups were assessed by t-test.

RESULTS

There were total 68 COVID-19 positive patients requiring haemodialysis. Male population was 51 (75%) with male:female ratio of 3:1 [Table/Fig-1]. Chronic respiratory illness was noted in

40 (58.8%). Thirty (44.1%) of COVID-19 patients had AKI. Severe COVID-19 illness was noted in 27 (37.9%).

Characteristics	Survivors	Non survivors	p-value (t-test)
Number (%)	36 (53)	32 (47)	-
Mean age (years) (M±SD)	54.47±13.34	61.56±13.64	1
Gender			
Male (%)	27 (75)	24 (75)	1
Female (%)	9 (25)	8 (25)	1
Co-morbidities (%)			
Hypertension	28 (78)	25 (78)	0.97
Diabetes mellitus	20 (56)	24 (75)	0.09
Chronic respiratory illness	12 (33)	28 (87)	0.001
Cancer	1 (3)	0	0.342
Smoking	17 (47)	20 (62)	0.2
Ishaemic heart disease	8 (22)	6 (19)	0.39
Old cerebrovascular accident	3 (8)	7 (22)	0.116
Presenting symptoms (%)			
Asymptomatic	2 (6)	0	0.176
Mild	17 (47)	2 (6)	0.001
Moderate	14 (39)	6 (19)	0.069
Severe	3 (8)	24 (75)	<0.001
AKI (%)	8 (22)	22 (69)	<0.001
Existent CKD (%)	22 (61)	14 (43)	0.152
Patients who skipped/ missed dialysis (%)	15 (41)	8 (25)	0.147

[Table/Fig-1]: Comparison of clinical parameters among COVID-19 survivors and non survivors (N=68).

In this study, occurrence of anaemia, high D-dimer, high LDH, hypoalbuminaemia, high serum ferritin and high CRP were noted in over more than half of the population, more frequently in mortality group [Table/Fig-2]. Further, it was noted that medication usage was higher for corticosteroids, oseltamivir, vitamin C, zinc therapy in mortality group [Table/Fig-2].

(a) Laboratory findings with normal cut-off values in units	Mean value among COVID-19 survivors (values in units)	Mean value among COVID-19 non survivors (values in units)	Number of patients with abnormal values among survivors n (%)	Number of patients with abnormal value among non survivors n (%)	Total number of patients with abnormal value among both groups n (%)
Anaemia (normal Hb 14-16 g/dL)	13	9.8	24 (67)	32 (100)	56 (82.4)
High D-dimer (normal 220-740 ng/mL)	367	1023	24 (67)	32 (100)	56 (82.4)
High LDH (normal <250 U/L)	261	578	24 (67)	32 (100)	56 (82.4)
High CRP (normal <10 mg/L)	9	45	25 (69)	32 (100)	57 (83.8)
Hypoalbuminaemia (normal 3.5-5 g/dL)	3.3	1.9	28 (78)	32 (100)	60 (88.2)
High S. Ferritin (normal 29-250 µg/L)	302	878	28 (78)	32 (100)	60 (88.2)

(b) Medications	Frequency among COVID-19 survivors (n,%)	Frequency among COVID-19 non survivors (n,%)	Total Percentage among both groups (n,%)
Corticosteroids	25 (69)	32 (100)	57 (83.8)
Oseltamivir	23 (64)	32 (100)	55 (80.9)
Vitamin C	33 (92)	32 (100)	65 (95.6)
Zinc	35 (97)	32 (100)	67 (98.5)

[Table/Fig-2]: Comparison of laboratory parameters (a) and medications usage (b) among survivors (n=36) and non survivors (n=32).

When outcome was analysed, mortality and recovery were noted in 32 (47%) and 36 (53%) patients, respectively. In the mortality group [Table/Fig-1], it was noted that chronic respiratory illness, AKI, severe COVID-19 illness were seen in 28 (87%), 22 (69%), 24 (75%) patients respectively. In the survivor group [Table/Fig-1], it was noted that chronic respiratory illness, AKI, severe illness were seen in 12 (33%), 8 (22%), 3 (8%) patients, respectively. Need of Intensive Care Unit (ICU) support, and stay in hospital more than 10 days were noted in 42 (61.8%) and 29 (42.6%), respectively.

DISCUSSION

The clinical course of COVID-19 infection varies from asymptomatic to mild respiratory illness to severe disease needing ICU care, mechanical ventilation support and sometimes haemodialysis [6-10].

Co-morbidities/Risk factors: Similar to other studies, it was noted that, higher occurrence of co-morbidities like diabetes mellitus [11,12], hypertension [11,12], chronic respiratory illness [13,14] and risk factor like smoking [15] were observed in mortality group in this study.

Clinical features: In the present study, higher occurrence of fatigue, fever, cough, breathlessness, both lung involvement, pneumonia was noted in mortality group like in other studies [15-18].

Complications: In the present study, occurrence of AKI (44.1%) was high compared to other studies (4.5-23%) [19]. In this study, higher need of oxygen support, ICU support were noted in mortality group as such patients are prone for sepsis, shock, cerebrovascular disease, venous thromboembolism [20], multiorgan involvement including respiratory events like dysponea, hypoxia, renal failure, altered mental status, liver dysfunction, coagulopathy, thrombocytopenia [1,20].

Treatment: In the present study, it was noted that medication usage was higher for corticosteroids, oseltamivir, vitamin C, zinc therapy similar to that quoted in other studies using various medications like corticosteroids [3,19,20], vitamin C [20], oseltamivir [11,21], zinc therapy [20] [Table/Fig-3] [11,15,20,21]. Mechanism of action of these drugs quoted are direct antiviral and immunomodulatory properties [9].

Other studies	Corticosteroids	Vitamin C	Oseltamivir	Zinc therapy
Present study	57 (83.8%)	65 (95.6%)	55 (80.9%)	67 (98.5%)
Flythe JE et al., [11]	52 (36%)	10 (7%)	-	-
Rosenthal N et al., [20]	19.8%	13.6%	-	9.6%
Stefan G et al., [15]	9 (24%)	-	-	-
Ozturk S et al., [21]	12 (3.8%)	-	228 (63.7%)	-

[Table/Fig-3]: Comparison of frequency of medications used for COVID-19 among different studies [11,15,20,21].

Though several drugs, medications were under investigations during the study period, there was no effective medications nor vaccine available for COVID-19. Hence, treatment was tailored according to patient co-morbidities and clinical condition, like in other studies [15]. This shows marked heterogeneity in therapeutic approach across globe [14].

Mode of dialysis: In the present study, all patients underwent single use dialyser treatment. All patients underwent regular dialysis or Sustained Low Efficiency Dialysis (SLED) according to their haemodynamic status. Continuous Renal Replacement Therapy (CRRT) was not offered due to non affordability by patients.

Investigations: Consistent with other studies, it was noted that occurrence of anaemia, high D-dimer, high LDH, hypoalbuminaemia, high serum ferritin and high CRP were higher in mortality group [Table/Fig-4] [3,11,14,19,22]. This indicates significant role of inflammation in mortality in COVID-19.

Other studies	D-dimer	Serum albumin	Serum ferritin	CRP	LDH
Present study	1023 ng/mL	1.9 g/dL	878 µg/L	45 mg/L	578 U/L
Kooman JP and van der Sande FM [19]*	-	-	-	CRP>175 mg/dL	-
Flythe JE et al., [11]*	1347 ng/mL	-	3406 ng/mL	170 mg/L	-
Tortonese S et al., [14]*	715 IU/L	3.2 g/dL	-	65 mg/L	313 U/L
Bellan M et al., [22]*	1356 µg/mL	-	-	7.1 mg/dL	706 IU/L

[Table/Fig-4]: Laboratory findings influencing mortality in various studies [11,14,19,22]. *In all these studies, laboratory parameters were abnormal.

Outcome (Recovery and Mortality): On analysis of mortality rate, it was noted that mortality and recovery were seen in 32 (47%) and 36 (53%) patients, respectively. Interestingly it was noted that COVID-19 patients with renal failure on haemodialysis had higher mortality compared to those without [9,10,23,24]. This shows that mortality in COVID-19 was higher in presence of renal failure (AKI, CKD) [3-5,21].

In this study, mortality was related to presence of chronic respiratory illness, AKI and severe COVID-19 illness with possible underlying malnutrition and less efficient immunity in this group like in other studies [22,23,25,26].

In this study, mortality rate was 47%, higher than compared to other studies like 27.7% [23], 13.3% [10], 12% [5]. Reasons could be different baseline characters, difference in co-morbidities, study included AKI in significant numbers unlike in other studies which included predominantly CKD patients, genetic factors, variation in local testing facilities and difference in referring local health care centres.

Limitation(s)

Retrospective study, sample size was small, single centre study, follow-up time was short, and the study lacked a comparable group (COVID-19 patients without renal failure).

CONCLUSION(S)

In the present single centre study, involving COVID-19 patients with renal failure requiring haemodialysis, it was noticed that mortality was associated with presence of severe COVID-19 illness, chronic respiratory illness, AKI and inflammatory biochemical markers. Further it was noticed that during this period, there was no definitive treatment for COVID-19 infection leading to random use of multiple, different medications as target therapy. In this current scenario, use of biochemical parameters, relating co-morbidities to determine COVID-19 prognosis needs further validation and also effective antiviral therapy, vaccines are needed to control this COVID-19 pandemic.

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