Original Research Article

Clinical profile and outcome of patients on Maintenance Hemodialysis hospitalized with Covid 19 infection – A retrospective study from a tertiary care centre of Eastern India

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Abstract

Background: Patients on maintenance hemodialysis (MHD) are more vulnerable to SARS-CoV-2infection because of uraemia related immune dysfunction leading to impaired immune defences and pro-inflammatory state, increased comorbidity burden, frequent hospital admissions and the risk of cross-contamination in the dialysis centres. Presence of comorbidities is associated with poor outcome.This study primarily designed to assess the clinical profile, treatment and outcome in MHD patients hospitalized with COVID-19 infection. **Methods:** This was a retrospective hospital record based study, including all the patients on MHD admitted with COVID-19 infection between1st may2020 to 1st March 2021. Categorical and Continuous variable were presented as proportions and mean ± SD.The statistical significance level was set at 0.05 (two-tailed). **Results:** 56 patients(Male 47 and Female 9) on MHD were admitted during the study period.We observed that half of the patients admitted survived and were discharged from the hospital and median hospital stay being 13.5 (6-17) days.The mean age of non survivors was significantly higher as compared to survivors. 56.9 years (14.9) vs 47.8 (16.8)years (P<0.05)No statistical significant difference was found in outcome based on gender or comorbidities. Significantly higher mortality was noted among patients on invasive ventilation (87.1%) Among lab variables Lymphopenia and hypoalbuminemia were significantly associated with poor outcome. **Conclusions:** We observed a high mortality rate among maintenance hemodialysis patients hospitalized for COVID-19.Lower serum albumin and lymphocyte count at admission were associated with poor prognosis.

Key words: Maintenance Hemodialysis, COVID 19, SARS CoV2 Infection

Key message: Patients on Maintenance hemodialysis are a high risk group and presence of lower albumin and lymphocyte count was associated with higher mortality in the group. Vaccination may be protective and we need further studies to assess their effectiveness in MHD patients.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS- CoV-2) infection which emerged in Wuhan, China in December 2019 was declared pandemic later[1].

In the general population, the 2019 coronavirus disease (COVID-19) has a mortality rate of around 6%[1], similar to SARS-CoV1(10%) but lower than MERS-CoV (around 40%)[2-4].

Co-morbidities like obesity, hypertension, diabetes mellitus, cardiovascular disease, advanced age, or superimposed acute kidney injury made patients with COVID-19 infection, susceptible to higher risk of intensive care admission or death[4-10].

Patients on maintenance hemodialysis were found to be particularly vulnerable to COVID-19 infection due to uraemiarelated immune system dysfunction leading to impaired immune defence and pro-inflammatory state, increased comorbidity burden, frequent hospital admissions and the risk of cross-contamination in the dialysis centres[10-12].Most studies that included dialysis patients focused on infection susceptibility and strategies to limit the disease spread[11,13]. As with increased vulnerability patients, clinical presentation and outcome could be different from the general population. Moreover, regional differences are also conceivable since the extend and severity of outbreaks varied among countries.

Therefore, in this observational retrospective cohort study we aimed to assess the clinical profile, treatment and outcome in MHD patients hospitalized with COVID-19 infection from a tertiary care centre in Eastern India.

Methodology

Approval of the Institutional Ethics Committee was obtained, and a retrospective study of hospital records spanning 13 months (1/05/2020- 01/03/2021) was conducted at All India Institute of Medical Sciences, Patna. Relevant clinical information was obtained and analysed to determine the profile and evaluate the outcome of patients on maintenance haemodialysis suffering from COVID 19 admitted at the institute during the relevant study year. Patient with

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nasal and pharyngeal specimen tested positive for COVID 19 through RTPCR/TrueNat/Rapid antigen test were considered confirmed case of COVID 19. Demographic information, details of comorbidities, relevant clinical features, laboratory parameters including the inflammatory markers were retrieved for each patient. Data regarding clinical features comprised of saturation at room air (SpO2) at admission , respiratory rate, severity of COVID 19 infection and requirement of ventilatory support both invasive and non-invasive during the course of treatment were also collected.The data collection was done by resident from medical records department (MRD).Two faculty independently reviewed the data and validated it.

Severity of COVID 19 infection was categorised as mild/moderate and severe according to "National Clinical Management Protocol COVID-19"

Statistical Analysis plan

Categorical variables in the study such as gender, comorbidities, severe COVID 19 infection, invasive ventilation and non-invasive ventilation were presented as proportions. Group comparison of these variables across the outcome of patients was done by applying chi square test. Continuous variable such as age, respiratory rate, SPO2, and different laboratory parameters, will be first checked for the normal distribution of data using the Q- Q plot. According to the distribution, they will be presented as mean (SD) or median (IQR). Group comparison for continuous variables across the outcome of the patients was done by applying independent sample t test or Mann Whitney U test. The statistical significance level was set at 0.05 (two-tailed).

Results

Over 56 COVID 19 patients who were on maintenance haemodialysis were identified from the records. Of those, half of the patients survived and were discharged from the hospital The median hospital stay being 13.5 (6-17) days. The mean age of admitted patients was 55.3 (±16.4) years which was significantly higher among those who died [56.9 (14.9)] years as compared with the survivors [47.8 (16.8)] years. Majority were male (83.9 %). Regarding comorbidities, majority patients were suffering from diabetes (78.5 %) and hypertension (80.3%) whereas only 32.1 % and 8.9% patients were suffering from coronary artery disease and COPD respectively. However, no statistically significant difference was found for the gender and comorbidity distribution across the survivors and non survivors.(Table 1) Initial clinical assessment of patients done at the time of admission revealed that approximately one third (39.7 %) patients had severe COVID 19 infections.

Table 1: General characteristics of patients according to outcome (N= 56)

Characteristics		Discharge (n-28)	Death (n-28)	p value (Test of significance)
Age (years) Mean (SD)		47.8 (16.8)	56.9 (14.9)	0.03*(Independent sample t -test)
Gender n (%)	Female	4 (44.4)	5 (55.6)	1.00 (Fisher exact test)
	Male	24 (51.1)	23 (48.9)	
Comorbidities n (%)	Diabetes mellitus	23 (52.3)	21 (47.7)	0.515 (Pearson chi square)
	Hypertension	24 (53.3)	21 (46.7)	0.503 (Fisher exact test)
	COPD	4 (80)	1 (20)	0.352 (Fisher exact test)
	Coronary artery disease	10 (55.6)	8 (44.4)	0.567(Pearson chi square)
Transplant n (%)		0(0)	1(100)	
Vascular access n (%)	AVF	23 (41)	19 (33.9)	0.19 (Pearson chi square)
	CVC	05 (8.9)	09 (16.0)	0.57 (Pearson chi square)

COPD-Chronic Obstructive Pulmonary Disease, AVF-Arteriovenous Fistula, CVC-Central venous catheters

Although, there was no statistically significant difference in mortality rate across the severity of COVID infections among the patients. Approximately, one fourth patients (26.8%) received non-invasive ventilation and more than half of the patients (55.4%) were placed on ventilator during the course of treatment at the hospital. Significantly higher mortality was noted among patients on invasive ventilation (87.1%)(Table 2).

Table 2: Clinical characteristics of patients at admission and after admission (N= 56)

Characteristics		Discharge (n-28)	Death (n- 28)	p value (Test of significance)
SpO2 (Oxygen Saturation) mean (± SD)		95.1 (2.9)	94 (3.9)	0.255(Independent sample t -test)
Severity of COVID 19 infection n (%)	Mild/Moderate	19 (55.9)	15 (44.1)	0.274 (Pearson chi square)
	Severe	9 (40.9)	13 (59.1)	
RR Mean (SD)		26.6 (4.2)	31.3 (5.7)	0.001(Independent sample t -test)
Invasive ventilation n (%)	No	24 (96)	1 (4)	<0.001 (Fisher exact test)
	Yes	4 (12.9)	27 (87.1)	
Non-Invasive ventilation n (%)	No	14 (34.2)	27 (65.9)	<0.001 (Fisher exact test)
	Yes	14 (93.3)	1 (6.7)	

RR- Respiratory Rate

Furthermore, on a positive note patients receiving non-invasive ventilation had significantly higher discharge rate (93.3%). As far as laboratory parameters are concerned, lymphocyte count and serum albumin were significantly decreased among those who died as compared with those who survived. Distribution of rest of the laboratory parameters was similar across the survivors and non survivors (Table 3).

Table 3: laboratory parameter of patients according to outcome (N= 132)

Characteristics [(mean (SD)/ median (IQR)]	Discharge	Death	p value (Test of significance)
TLC (count /µl)	10.2 (5.2)	15.5 (6.7)	0.255 (Independent sample t -test)
Lymphocyte (%)	10.7 (2.9- 11.5)	5.8 (2.5- 9.4)	0.017* (Mann-Whitney U test)
Platelet count (count /µl)	137 (106.5- 210)	134.5 (85- 227.5)	0.844 (Mann-Whitney U test)
Albumin (gm/dl)	3.1 (0.5)	2.8 (0.4)	0.013* (Independent sample t -test)
LDH (U./L)	828 (559.3- 1212.5)	960.7 (659.2- 1481.7)	0.272 (Mann-Whitney U test)

CRP (mg/dl)	66.2 (35.9- 137.5)	157.5 (46.5- 225.4)	0.093 (Mann-Whitney U test)
D- dimer (mcg /mL)	2.9 (1.9- 6)	2.5 (1.6- 3.8)	0.272 (Mann-Whitney U test)
Procalcitonin(ng/ml)	2.1 (0.8- 5)	2.1 (0.4- 8.8)	0.824 (Mann-Whitney U test)
Serum Ferritin(ng/ml)	729.9 (440.3- 1491.8)	647.3 (396.7- 1474.7)	0.481 (Mann-Whitney U test)
Interleukin 6	33.8 (8.8-84.7)	53.1 (13.3- 141.2)	0.244 (Independent sample t -test)

TLC= Total leucocyte count, LDH= Lactate dehydrogenase, CRP= C- reactive pro

42 patients had Arterio-Venous fistula (AVF) as their vascular access and 19 patients were dialysed through central venous catheters (CVC). Out of 42 of the patient with AVF 19 didn'tsurvive while amongst the rest 14 who had CVC there was 9 deaths. There was no statistically significant difference in mortality based on type of vascular access.

Amongst 13 patients during the second wave of the pandemic, 4 had received one dose of vaccine while 1 patient received 2 doses of vaccine. The patient who received two doses of vaccine was discharged after 10 days of hospital stay, in spite of being admitted with severe disease . Only one amongst those who received single dose of vaccine survived.

Discussion

The mortality rate in our cohort of maintenance hemodialysis patients was found to be higher when compared to previous studies. Mortality rate reported by Gabriel et al was around 19%, Yiqiong et al reported 16.2% (China), studies from Spain reported 30.5% and from Italy (25-41%)[14-18]. In a recently published study from Turkey by Turgutalp et al[19]. 16.3% mortality was reported, while in a study including a large cohort of patients from India by Prasad et al[20]. there was only 13.3% mortality. Higher mortality in our study may be attributed to the fact that our study included only admitted patients who had more rapid and severe course of illness.

More than half of patients on MHD were eventually put on ventilators while one fourth were on non-invasive ventilation and those who could not survive were of higher age.

There was no statistically significant difference in survivors when compared to non-survivors based on gender and presence of comorbidities.Most commonly observed co-morbidity was hypertension followed closely by diabetes. Only about one-third of the patient had coronary artery disease.

Regarding laboratory investigation only decreased serum albumin and low lymphocyte count were found to be associated with higher mortality. Even in general population afflicted with SARS-CoV2 virus, lower albumin and lymphocyte count has been suggested to predict mortality[21]. While in the study by Turgutalp et al[19]. thrombocytopenia and high Aspartate Transaminase (AST) level during hospitalization in COVID19 MHD patients were found as risk factors of mortality.

Inpatients on MHD low serum albumin may be associated with the malnutrition-inflammation complex syndrome, an important risk factor for cardiovascular mortality[22].

COVID 19 patients who died from Acute Respiratory Distress Syndrome(ARDS), on autopsy had severe endothelial injury[23]. Increased endothelial dysfunction renders an individual prone to severe form of COVID 19 infection. MHD patients owing to their uremic milieu have an abnormal immune response and enhanced endothelial dysfunction leading to an increased risk of mortality[24,25]. Recently published study showed presence of chronic kidney disease (CKD) in COVID-19 infection indecently increased the risk of mortality even after normalisation of age and other comorbidity like diabetes and hypertension[26].

There was no clotting of the dialysis circuit was in this study with routine anticoagulation with unfractionated heparin. Other studies reported a high incidence of clotting mainly during continuous renal replacement therapy CRRT[27]. The pathogenesis of high thrombosis in COVID-19 infection is incompletely understood but endothelial inflammation, hyper viscosity and pulmonary hypoxemia leading to vasoconstriction may contribute[28].

We in our study observed that outcome was poorer amongst older people and those with low serum albumin and lymphocyte count.

Limitation

Small number of patients and the study being a single centre are the major limitations of this study. The mortality of non-COVID patients on MHD during the same study period in the dialysis unit was not analysed. The effect of various treatment on this group of patients needs to be determined. Follow up of the discharged patient is also required.

Conclusion

We observed a high mortality rate among maintenance hemodialysis patients hospitalized for COVID-19. Lower serum albumin and lymphocyte count at admission were associated with poor prognosis .There was an increased risk of death in patients admitted with severe disease.

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