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Pulmonary Medicine

HAEMODIALYSIS: A KING OR A CLOWN FOR COVID POSITIVE PATIENTS WITH PRE-EXISTING PULMONARY DISEASES!

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ABSTRACT **Background:** COVID-19 infection in patients with pre-existing respiratory diseases, manifesting as ARDS, while simultaneously affecting multiple organs severely worsened the outcome, raising the need to explore various treatment modalities. **Objective:** To study the impact of haemodialysis on outcomes of COVID-19 patients with pre-existing pulmonary diseases. Methods: Data of patients with known pulmonary comorbities admitted to COVID wards, undergoing haemodialysis for AKI at tertiary care centre, was collected from July 2020 to January 2022. The demographics, baseline parameters and outcomes were recorded. **Results:** Total 61 patients were included in this retrospective observational study. The percentage of different pre-existing pulmonary pathologies (COPD, Asthma, ILD, and Pulmonary Tuberculosis) were equally distributed among survivors(n=47) and non-survivors(n=14). The non-survivors were older(p=0.003), and had a higher percentage of males (p=0.02), higher percentage of smokers (p=0.02) and alcohol consumers(p=0.011), a lower mean systolic blood pressure, higher pulse rate, higher respiratory rate and lower SpO2. The non-survivors had a lower mean hemoglobin, platelet count, and a higher mean TLC, NLR, and D-dimer levels. On admission, the non-survivors had a higher mean blood urea level and serum creatinine level (p<0.001). The number of hemodialysis done was significantly higher(p=0.041) in the survivors as compared to non-survivors. **Conclusion:** Our study strongly suggests that haemodialysis can be used as a life saving treatment modality for AKI in COVID positive patients with pre-existing pulmonary disease. Also protocols need to be redefined for early initiation and increased frequency of haemodialysis in patients with acute on chronic multisystem insult.

KEYWORDS : Haemodialysis, COVID, pulmonary disease.

Introduction

Breath and by virtue of it lung health is fundamental to life. Respiratory diseases are the most common cause for patients to visit doctors in India[1]. Adding fuel to this proverbial ever simmering fire, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) attacked ACE-2 (angiotensin converting enzyme 2) in lung alveolar cells, heart, kidney, and GIT leading to ARDS, shock, acute renal injury, cardiac injury etc[2]. With an ever-increasing variety of mutant strains, COVID is still a major challenge that necessitates prompt planning of a multidisciplinary management strategy and early detection of multi-organ involvement. Acute kidney injury (AKI), which also raises the risk of death, is the most frequent extrapulmonary symptom of COVID-19. The kidney is susceptible to SARS-CoV-2 because ACE-2 receptors are highly expressed there. The RAAS (renin-angiotensin-aldosterone system) dysregulation, cytokine-induced hyper-inflammatory state, microvascular injury, and COVID-19-associated prothrombotic state are only a few of the components that are known to contribute to the pathophysiology of COVID-19-associated kidney injury.

Owing maximum mortality to lung and renal injury, we need to explore haemodialysis as a treatment modality to extinguish this multisystem blaze.

Our study exclusively takes into account the patients with already compromised respiratory system super-infected with COVID making them most vulnerable of all critical care patients and studies the role of haemodialysis as a holistic treatment modality to reduce the renal burden and systemic inflammatory response.

Subject and method

Institutional ethics committee–human research approved the study. Study procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

This retrospective observational study included patients admitted in COVID isolation wards, who have pre-existing pulmonary disease undergoing haemodialysis for AKI at tertiary care centre from July 2020 to January 2022. Their history of various pre-existing pulmonary disease (asthma, chronic obstructive pulmonary disease, interstitial lung disease, pulmonary tuberculosis), presenting complaints, baseline biochemical parameters (complete blood count, serum urea, serum creatinine, D-dimer, serum potassium, serum sodium) were taken before haemodialysis. Patients with chronic kidney disease on maintenance haemodialysis were excluded. All the patients were tested COVID positive by RT-PCR. Haemodialysis were performed using polysulfone membrane in these patients for any of the emergency indications of acute kidney injury (refractory acidosis, refractory hyperkalaemia, anuria, uraemia, refractory fluid overload). The patients were grouped on the basis of their outcomes into survivors and non-survivors, and then their biochemical parameters were compared between them.

Statistical Analysis

The presentation of the categorical variables was done in the form of number and percentage (%). The quantitative data were presented as the mean±SD. The statistical analysis was done using Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

Results

Total 61 patients (survivors= 47 and non-survivors=14) were included in this study. As shown in Table 1, the non-survivors were older with mean age 60.34 years with higher percentage of males(n=12,85.71%) as compared to survivors with mean age of 45.38 years and males (n=24,51.06%). The percentage of smokers and alcohol consumers in non-survivors was 57.14% and 50% respectively. There was no statistically significant discrepancy in BMI between survivors and non-survivors.

Table 1: Comparison of baseline characteristics between COVID survivors and non-survivors

		Survivors (n=47)	Non-survivors (n=14)	P-value
Demographics				
	Age (years)	45.28±15.21	60.34±15.06	0.003
	Males	24 (51.06%)	12 (85.71%)	0.020
	BMI (kg/m2)	22.38±3.88	23.12±4.70	0.596
	Smokers	12 (25.53%)	8 (57.14%)	0.02
	Alcohol	8 (17.02%)	7 (50%)	0.011
Vitals				
	Systolic BP (mm Hg)	132.44±17.30	115.85±11.24	0.021

	Diastolic BP (mm Hg)	79.21±5.25	71.29±2.78	0.083
	Pulse rate (bpm)	102.14±19.40	112.81±14.44	<0.001
	Respiratory rate (cpm)	25.43±5.23	31.57±5.24	<0.001
	SpO2 (%)	89.71±4.65	81.49±6.18	<0.001
Etiological diagnosis				
	COPD	23 (48.94%)	8 (57.14%)	0.872
	Asthma	11 (23.40%)	3 (21.43%)	0.712
	ILD	9 (19.15%)	2 (14.29%)	0.838
	PTB	4 (8.51%)	1 (7.14%)	0.321

A lower mean systolic blood pressure 115.85 mm Hg, higher pulse rate 112.81 bpm, higher respiratory rate 31.57 cpm and lower SpO2 81.49% was seen in non-survivors groups with significant p value. Diastolic blood pressure did not differ significantly between both the groups.

The different pre-existing pulmonary pathologies were equally distributed among both the groups.Chronic Obstructive Pulmonary Disease [COPD] 8(57.14%) vs 23(48.94%) , Asthma 3(21.43%) vs 11(23.40%), Interstitial Lung Disease (ILD) 2(14.29%) vs 9(19.15%), and Pulmonary Tuberculosis [PTB] 1(7.14%) vs 4(8.51%) among non-survivors and survivors group respectively.

A significant difference was seen between the groups on comparison of haematological parameters as shown in Table 2 and Figure 1. The non-survivors had a lower mean hemoglobin level 9.92 gm/dl , a higher mean TLC 23.53 (x 103/uL), a higher NLR 14.38±5.69, a lower platelet count 1.36±0.57 (lac/mm3), and a higher D-dimer level 6.69±2.86 (mg/l).

Table 2: Comparison of haematological parameters between COVID survivors and non-survivors

	Survivors	Non-survivors	P-value
Hemoglobin (g/dl)	12.35±2.47	9.92±2.51	0.004
TLC (x 103/uL)	14.23±4.32	23.53±8.08	<0.001
NLR	8.78±3.78	14.38±5.69	<0.001
Platelet count (lac/mm3)	1.87±0.29	1.36±0.57	<0.001
D-dimer (mg/l)	2.36±1.53	6.69±2.86	<0.001

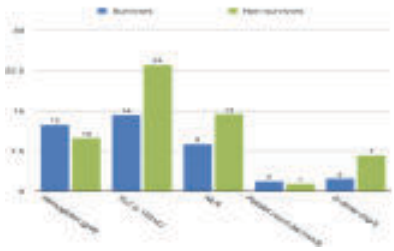

Figure 1: Comparison of haematological parameters between COVID survivors and non-survivors

Table 3 and Figure 2 shows the comparison between the baseline kidney function test of survivors and non-survivors. On admission, the non-survivors had a higher mean blood urea level 218.99±73.27 vs 147.40±35.74 mg/dl and a higher mean serum creatinine level 9.21 vs 6.76 mg/dl as compared to survivors group. On the contrary, there was no significant difference in the mean sodium and potassium level between survivors and non-survivors.

A noteworthy result here was that the number of hemodialysis done was significantly higher in the survivors 2.50±1.29 as compared to non-survivors 1.68±0.96.

Table 3: Comparison of baseline kidney function tests between COVID survivors and non-survivors

	Survivors	Non-survivors	P-value
Blood Urea (mg/dl)	147.40±35.74	218.99±73.27	<0.001
Serum Creatinine (mg/dl)	6.76±1.32	9.21±3.77	<0.001
Na+ (mEq/l)	140.15±7.60	142.23±9.37	0.403
K+ (mEq/l)	4.71±1.06	4.90±0.84	0.527
No. of HD done	2.50±1.29	1.68 ± 0.96	0.041

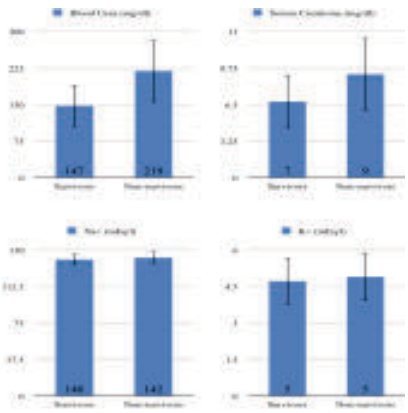

Figure 2: Comparison of baseline kidney function tests between COVID survivors and non-survivors

Discussion

2019 left us with a Pandora's box in the form of COVID, sparing next to nobody, some more vulnerable to it's clutches than the others. Our study is exceptional in terms of using haemodialysis as an intervention, in an unventured territory, for benefitting the most vulnerable of all COVID patients, those with already compromised respiratory system and renal involvement.

In this study, we find that our demographic data are close to the existing literature we have on COVID. Higher mean age (p=0.003) was seen in the non-survivors group which is similar in a meta-analysis by Biswas et al including 20 studies and a total of 64,476 patients, has shown a relative risk of mortality of 15.44 with age >=50 years[3].

The difference in sex distribution between survivors and non-survivors stood in consistence with our existing knowledge of COVID. For instance, a large multi-center retrospective cohort study involving 4300 females and 3808 males with COVID-19 infections compared the two sexes for their outcomes. Multivariate model correcting for age and comorbidities was applied and showed a significant association between mortality and male sex (OR 1.96, p=0.001)4. Since our patients also had renal involvement, comparison with existing literature on mortality of dialysis patients is necessary. Females had a better survival rate than males in a Korean study involving 4994 patients with a female-to-male mortality of 0.775 though this study included patients on maintenance haemodialysis and ours did not. In our patients, the difference in sex distribution between survivors (males-51.06%) and non-survivors (males-85.71%) but statistically significant (p=0.020)

The higher number of smokers (p=0.02) and alcohol consumers (p=0.011) among non-survivors is intuitive. Although smoking has been definitively linked to COVID mortality, same cannot be said about alcohol consumption. Dai et al6 have shown higher mortality in COVID with cigarette smoking but not so with alcohol consumption in 1547 patients from 4 hospitals of Wuhan. But if we look at another study from Bengaluru by Marimuthu et al7 both smoking and alcohol consumption were associated with higher mortality in COVID patients. Differences in patient population in both countries could be one of the reasons for the same.

Similarly, the almost equal percentage distribution of various etiologies of pulmonary involvement is important to interpret the data because the inherent differences in the mortality of the various causes could have been eliminated.

The significantly (p<0.001) higher mean pulse rate, respiratory rate and a lower SpO2 and a systolic BP (p=0.021) in the non-survivors is in consistency with data on COVID patients. Patients with a lower blood pressure and a higher pulse rate are more likely to suffer from worse outcomes. The higher respiratory rate and a lower O2 saturation adding

to the mortality can be explained by the fact that both COVID and pulmonary diseases can lead to it.

Haematological parameters are also consistent with our knowledge. A study from Saudi Arabia with clinical data of 6026 COVID patients showed that lower hemoglobin, higher D-dimer, TLC, and percentage of neutrophils were associated with mortality8 Similar results were shown in another study by Chapanduka et al9 though the platelet count was similar among survivors and non-survivors, in contrast to our data. Multiple factors could be at play here, for eg, more patients with MODS, co-existing causes of fever like malaria, dengue, etc. could have led to a lower platelet count in the non-survivors.

Since the patients were being dialyzed, a look at their kidney function at tests becomes mandatory. Non-survivors had a significantly higher ($p<0.001$) mean blood urea and serum creatinine than the non-survivors. This is true for patients with renal involvement, in general.
The poor outcome amongst non-survivors may point towards the lack of adequate sessions of haemodialysis owing to multiple factors could such as, severity at presentation, shorter hospital stay, threshold for deciding initiation of haemodialysis, logistical factors etc. But the truth remains undenied that Survivors underwent significantly greater number ($p=0.041$) of haemodialysis sessions as compared to non-survivors.

Conclusion

The substantial impact of COVID-19 on multiple organ systems leading to a baffling rate of mortality, calls upon an endeavour to seek and explore all life saving therapeutic measures in our arsenal.

What is important, is to acknowledge that the findings here apply to COVID positive patients with pre-existing pulmonary diseases and new onset renal involvement. Hence these patients represent the strata with poorest possible outcomes and most in need of critical care. Despite the grave prognosis haemodialysis proved to be a KING in reducing mortality significantly in upto three-fourth of patients included in our study. That being said, a higher number of haemodialysis received in the survivors group should be interpreted as a call for us to reconsider our decision making process regarding initiation and frequency of haemodialysis. To conclude, in patients with COVID dialysis may have remarkable effect on alleviation of the cytokine storm and consequent mortality, in addition to its effect on renal system.

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