



EFFECT OF HEMODIALYSIS ON OUTCOME OF COVID 19 PATIENTS WITH RENAL FAILURE

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ABSTRACT

Background & Objectives: COVID19 has the capacity to injure organs such as the heart, nervous system, or the kidney besides causing interstitial and alveolar pneumonia^{1,2}. Acute Kidney Injury (AKI) is an independent risk factor for mortality in Covid 19 and is the most frequent extra-pulmonary organ dysfunction associated with ARDS. CKD patients have worsened Covid 19 outcomes due to increased risk of infection-related mortality as a consequence of impaired immunity. However, data comparing AKI and CKD patients on Maintenance Haemodialysis (MHD) in Covid-19 are sparse. So we undertook this study. The purpose of this present work was to evaluate the Effect of Haemodialysis on Outcome of Covid 19 Patients with Renal Failure in a tertiary care hospital in rural settings during the 1st and 2nd wave of Covid – 19 pandemic. **Methodology:** 342 eligible Covid 19 patients were selected from case files of patients admitted during first and second wave of Covid 19 at our institute from July 2020 to June 2021. These patients were divided into two groups viz. patients with renal failure (n=171) and without renal failure (n=171). Those with RF were further subdivided into CKD & AKI (n=49 & n=122 respectively). Outcomes were compared in both the groups and intragroup analysis was also done. **Results:** We found that, in patients with Renal Failure, CKD patients on Maintenance Hemodialysis fared better than AKI patients who did not require Dialysis (mortality - 24.5% vs 35.2% respectively). Also mortality was slightly lower in CKD patients on MHD i.e. 24.5% as compared to non-RF patients i.e. 25.1%. Similarly, mortality was higher among patients with AKI who did not need HD i.e. 35.2% when compared to non-RF patients 25.1%. **Conclusion:** Thus, Acute Kidney Injury (AKI) patients were at risk for more severe disease and worst outcomes, when compared to Chronic Kidney Disease (CKD) patients on MHD. Also CKD patients on Maintenance Hemodialysis (MHD) fared equally or better when compared to non-RF patients. Therefore Haemodialysis could have played a protective role and needs to be explored as a novel treatment modality for SAR-COV-2 infection.

KEYWORDS :

INTRODUCTION

The pandemic of Covid 19 has affected more than 685,441,381 people and is responsible for more than 6,841,333 deaths till now (Worldometer, 14 April, 2023). Mortality rates of Covid 19 are subject to wide variability, with reports of infection-associated death rates fluctuating between 11% and 45%³.

Acute Kidney Injury (AKI) is an independent risk factor for mortality in Covid 19 and is the most frequent extra-pulmonary organ dysfunction associated with ARDS.

Presence of Chronic kidney disease (CKD), as a comorbidity in a patient, when compared to the general population, in previous epidemics, such as influenza has been correlated with increased mortality.

All patients with chronic kidney disease (CKD) on Kidney Replacement Therapy, are immuno-suppressed making them more susceptible to infection. Infection is one of the leading causes of mortality in end-stage renal disease, with patients being older and suffering from additional diseases and decreased immunity^{4,5}. The influence of SARS-CoV-2 on patients undergoing Maintenance Hemodialysis (MHD) is unknown.

The purpose of this present work is to evaluate Effect of Haemodialysis on Outcome of Covid 19 Patients with Renal Failure during the 1st and 2nd wave of Covid – 19 pandemic.

MATERIAL & METHODS:

The present study was a hospital based Retrospective Case Control Study.

We included 342 patients, 18 years of age and above, of either sex, diagnosed as Covid-19 on RTPCR or HRCT with or without Renal Failure patients, admitted at Covid Hospital of Hind Institute of Medical Sciences, Safedabad, Barabanki, Uttar

Pradesh, during first & second wave of Covid 19 pandemic from July 2020 to June 2021.

We had 574 patients in Wave 1 of the pandemic in 2020 and 694 patients in 2021 during delta wave, thus a total of 1272 patient records/files were checked. It was found that out of these 49 patients had Chronic Kidney Disease and underwent Hemodialysis (HD) while 122 had Acute Kidney Injury (a total of 171) and were selected as the sample for Renal Failure Group and compared with sample of patients (n=171) who did not have Renal Injury based on baseline S. Creatinine levels, which served as control.

Hence 342 Covid 19 patients with or without Renal failure were divided into two groups as follows:

1. Covid 19 Patients with Renal Failure: n = 171 (122 AKI + 49 CKD)
2. Covid 19 Patients without Renal Failure : n = 171 (Control Group)

Outcomes were compared in both the groups and intra group analysis was also done. Ethical Clearance was taken from the Institutional Ethics Committee of our institute prior to commencement of the study.

Data Compilation and Statistical Analysis

Mean, median, S.D. and interquartile range(IQR) values were used to express Continuous variables and categorical variables were described as frequency rates and percentages in each category. To compare the continuous variables, the Mann-Whitney test (data were not normally distributed) and Independent group t tests (data were normally distributed) was used. Fisher Exact and Chi Squared test were used to compare Proportions for categorical variables. SPSS version 26.0 software (SPSS Inc.) and Advanced Excel were used to do the Statistical Analysis. The P value of 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS

In the present study, we analysed the records of 342 patients. It was a comparative analysis of two groups of 171. One with RF and the other without RF. The two groups of 171 patients each, were compared with regards to the various outcomes viz. Death, Discharge, Referral to L3 Centre and DOPR(Discharge on Patient Request), Intra group comparison was done of patients with Renal Failure(RF). They were divided as: those patients with CKD who were on Maintenance Hemodialysis(MHD) (n=49) and those who did not require Hemodialysis(HD) (n=122) but had altered renal physiology and raised baseline Serum Creatinine levels(AKI) on admission. This group of 49 patients on MHD was also compared with the group which had no Renal Failure (RF) (n=171) on presentation. Similarly the group of 122 AKI patients was also compared with group of non-RF patients.

Table no.1- Frequency Distribution according to gender, Age-group, Haemodialysis, HRCT Chest and Outcome (n=342)

		Count	(%)
Gender	Male	246	71.9
	Female	96	28.1
Age-group	18-40	89	26.0
	41-60	139	40.6
	61-80	110	32.2
	81 or Above	4	1.2
Haemodialysis	0 times	293	85.7
	1 times	21	6.1
	2 times	12	3.5
	>= 3 times	16	4.7
HRCT Chest	0-5/25	0	.0
	6-10/25	9	2.6
	11-15/25	17	5.0
	16-20/25	14	4.1
	21-25/25	15	4.4
	NA	287	83.9
Outcome	Death	98	28.7
	Discharge	143	41.8
	Refer to Level 3 Hospital	33	9.6
	DOPR/LAMA	68	19.9

A majority of patients were males (71.9%). More than one third of patients were between 41-60 years of age (40.6%). Hemodialysis was given to 14.3% patients while rest 85.7% did not need it. HRCT chest CT severity score was 11-15/25 in 5% patients. Overall Mortality was 28.7% in both the groups. And overall 41.8% patients were discharged.

Table No.2- Past medical history/Co-morbidities Frequencies (n=342)

		Responses	
		Count	(%)
Co-morbidities ^a	Obesity/Overweight	2	1.2%
	Hypertension	49	30.2%
	Diabetes	73	45.1%
	Hypothyroidism	4	2.5%
	HEART DISEASE/ IHD etc	9	5.6%
	CVA/CNS	5	3.1%
	CLD/ LIVER DISEASES	12	7.4%
	RESP. DISEASES	8	4.9%
Total		162	100.0%
α. Multiple response			

Diabetes was the most common co-morbidity (45.1%) and hypertension was the second most common co-morbidity (30.2%).

Table No. 3 - Association of Outcome & Presence or Absence of RF (n=342)

Outcome	With RF (n=171)		Without RF (n=171)		p-value ¹
	No.	%	No.	%	
Death	55	32.2	43	25.1	0.151
Discharged	58	33.9	85	49.7	0.003*
Referred to L3	19	11.1	14	8.2	0.359
DOPR	39	22.8	29	17.0	0.175

¹Chi-square test, *Significant

Mortality was higher among patients with RF (32.2%) than without RF (25.1%). And rate of Discharge to home care was higher in non RF (49.7%) as compared to those with RF (33.9%) and was significant, p-value – 0.003.

Table No.4 - Association between Outcome and RF patients (n=171) with HD(CKD) and without HD(AKI)

Outcome	RF Present (n=171)				p-value ¹
	RF with No HD(AKI) (n=122)		RF with HD (CKD) (n=49)		
	No.	%	No.	%	
Death	43	35.2	12	24.5	0.173
Discharge	32	26.2	26	53.1	0.0008
Refer to Level 3 Hospital	11	9.0	8	16.3	0.169
DOPR/LAMA	36	29.5	3	6.1	0.0009

Mortality was higher among patients of AKI with No HD (35.2%) than CKD patients on MHD (24.5%) with insignificant (p>0.05) association. However significantly more patients were discharged in CKD on MHD group (53.1%) when compared to AKI patients not requiring HD (26.2%) with a P-value – 0.0008.

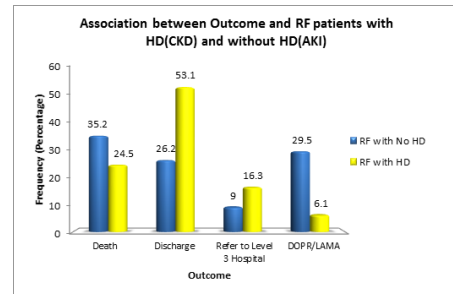


Fig. 1 - Association between Outcome and RF patients (n=171) with HD(CKD) and without HD(AKI)

Table No.5 - Association between Outcome of CKD patients on MHD and those without RF

Outcome	RF Present with HD(CKD) (n=49)		RF Absent (n=171)		p-value ¹
	No.	%	No.	%	
Death	12	24.5	43	25.1	0.925
Discharge	26	53.1	85	49.7	0.678
Refer to Level 3 Hospital	8	16.3	14	8.2	0.094
DOPR/LAMA	3	6.1	29	17.0	0.057

Mortality was lower among patients of CKD on MHD (24.5%) than those without RF (25.1%) with similar discharge rates amongst the 2 groups.

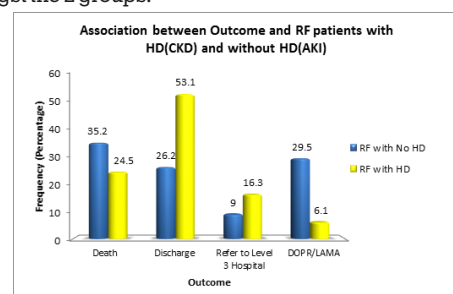
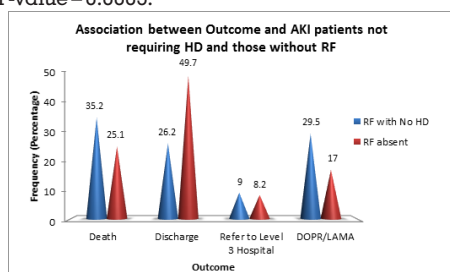


Fig. 2 - Association between Outcome and CKD patients on MHD and those without RF**Table No.6 – Association between Outcome and AKI patients not requiring HD and those without RF**

	RF(AKI) without HD (n=122)		RF Absent (n=171)		p-value ¹
	No.	%	No.	%	
Death	43	35.2	43	25.1	0.061
Discharge	32	26.2	85	49.7	0.0005
Refer to Level 3 Hospital	11	9.0	14	8.2	0.802
DOPR/LAMA	36	29.5	29	17.0	0.010

Mortality was higher among patients with AKI who did not need HD (35.2%) when compared to those without RF (25.1%) but with insignificant ($p > 0.05$) association however significantly more patients were discharged in non-RF group (49.7%) when compared to AKI group not needing HD (26.2%) with a P-value – 0.0005.

**Fig. 3 - Association between Outcome and AKI patients not requiring HD and those without RF**

Major findings of this study can be summed up as below:

1. In our study we found that significantly more patients were discharged in CKD group on Maintenance Hemodialysis (MHD) (53.1%) when compared to AKI group not requiring Hemodialysis (HD) (26.2%) with a significant P-value – 0.0008 (Ref. – Table 4, Fig. 1).
2. Similarly significantly more patients were discharged in non-RF group (49.7%) when compared to AKI group not requiring Hemodialysis(HD) (26.2%) with a significant P-value – 0.0005 (Ref. – Table 6, Fig. 3).
3. Also mortality was higher among patients of AKI who did not require Hemodialysis(HD) (35.2%) when compared to CKD patients who underwent Hemodialysis(HD) (24.5%), though it was not found to be statistically significant p value - 0.173 (Ref. – Table 4, Fig. 1) but was contrary to previous assumptions.
4. On comparing CKD patients on Maintenance Hemodialysis(MHD) with those without RF, it was found that, mortality was slightly lower among patients of CKD on Maintenance Hemodialysis(MHD) (24.5%) than non RF patients (25.1%).(Ref. – Table 5, Fig. 2) Therefore outcomes in CKD patients on MHD and non-RF group were similar which again was contrary to previous assumptions.
5. In analysis of AKI patients not requiring HD, with those without Renal Failure (RF), it was found that, Mortality was higher among patients with AKI who did not need HD (35.2%) when compared to those without RF (25.1%) (Ref. – Table 6, Fig. 3)

DISCUSSION

Acute Kidney Injury (AKI) in COVID-19 has been reported to be an independent predictor for poor prognosis of patients⁶.

Viral particles were detected in both renal glomerular and tubular cells by transmission electron microscopy and light microscopy on histopathological analysis.. Besides, researchers⁷ analysed kidney samples of 26 deceased COVID-19 patients and have provided direct evidence of renal viral invasion in those samples.

Investigators⁸ showed that, renal dysfunction was present in high percentage of COVID-19 patients at the time of hospitalization, and the most important of these symptoms were increased creatinine, haematuria and proteinuria. Based on these results, it can be said that AKI likely occurs early in the disease and in parallel with lung damage.

The present retrospective case control study was conducted with the objective to Study the Effect of Haemodialysis on Outcome of Covid 19 Patients with Renal Failure as compared to those without Renal Failure. A total of 342 patients were included in the study.

We found that, mortality was higher among patients with RF (32.2%) than without RF (25.1%). Rate of Discharge to home care was higher in non-RF (49.7%) as compared to those with RF (33.9%) and was significant, p-value – 0.003. In an analysis by a group⁹, the pooled estimates from primary studies for mortality in patients with CKD and COVID-19 showed a Relative risk of 1.6 (95% CI 0.88–2.92) (Low certainty), Hazard Ratio of 1.48 (95% CI 1.33–1.65) (Moderate certainty), and an Odds ratio of 1.77 (95% CI 1.54–2.02) (Moderate certainty). These results point to the impact of CKD on the poor outcomes of COVID-19, emphasizing the importance of strategies to prevent COVID-19 infection in CKD patients.

Workers in India¹⁰ showed, 83.1% had associated hypertension, 75 (35.2%) diabetes mellitus, 7% coronary artery disease, and 5.2% hypothyroidism. 165 (77.5%) were on Maintenance Hemodialysis (MHD), and 72.8% had arteriovenous fistula as vascular access. They found that the overall mortality was 24.4%, with similar mortality rates in both groups ($P = 0.709$) and 20.7% needed ICU transfer.

In our study, Increased Serum creatinine and urea was found among patients with RF with S. Creatinine of 4.21 with SD of 4.33 and average S. Urea 120.85 with SD of 88.94 both of which were significantly higher than non-RF group.

In this study, the 2 most prevalent comorbidities in both the groups were Hypertension(30.2%) and Diabetes(45.1%) & there was no significant ($p > 0.05$) association of Co-morbidities with outcome (death) according to presence and absence of RF.

Also there was no significant ($p > 0.05$) association of HRCT chest with outcome (Death) according to presence and absence of RF though number of patients who underwent HRCT was small. In another study Researchers¹¹ showed that among COVID-19 patients with and without CKD, no differences were found regarding ICU admission, chest computed tomography findings and death.

We found that, mortality was higher among patients of AKI not requiring HD (35.2%) when compared to CKD patients on MHD (24.5%) which was contrary to previous assumptions. Significantly more patients with CKD requiring MHD (53.1%) were discharged when compared to AKI patients not requiring HD (26.2%) with a significant P-value – 0.0008.

On comparing CKD patients on MHD with those without RF, it was found that, Mortality was slightly lower among patients of CKD on MHD (24.5%) than non-RF patients (25.1%) with similar discharge rates. Therefore, outcomes in CKD patients on MHD and patients without RF were similar which again was contrary to previous assumptions.

Lastly analysis of AKI patients not requiring HD, with those without RF, it was found that, Mortality was higher among patients with AKI who did not need HD (35.2%) when compared to those without RF (25.1%) but with insignificant ($p > 0.05$) association.

Similar findings were noted by Researchers in US¹² in their analysis of 3905 patients admitted to 3 hospitals in New York area. They concluded that patients with ESKD appear to had better outcomes than those with nondialysis CKD.

Researchers in US¹² examined presentations and outcomes among patients admitted to three hospitals in the New York retrospectively using electronic health records. Classification of patients was done as those with ESKD, those without CKD, and those with nondialysis CKD, with outcomes including ICU admission, hospital mortality and mortality rates. A total of 3905 patients were studied, of which 128 (3%) had ESKD and 588 (15%) had nondialysis CKD. There was a greater prevalence of comorbidities and higher admission D-dimer levels in ESKD and nondialysis CKD groups, whereas patients with ESKD had lower C-reactive protein levels at admission. The overall, unadjusted hospital mortality was 25%, and the mortality was 24% for those without CKD, 27% for those with ESKD, and 34% for those with nondialysis CKD.

Although patients with nondialysis CKD had higher odds of overall mortality versus those without CKD in univariate analysis (OR, 1.58; 95% CI, 1.31 to 1.91), this was no longer significant in fully adjusted models (OR, 1.11; 95% CI, 0.88 to 1.40). Also, ESKD status did not associate with a higher risk of mortality compared with non-CKD in adjusted analyses, but did have reduced mortality when compared with nondialysis CKD (OR, 0.57; 95% CI, 0.33 to 0.95). The study concluded that there was higher crude mortality rates for patients with nondialysis CKD and, to a lesser extent, ESKD, which were not significant after risk adjustment. Moreover, patients with ESKD appear to had better outcomes than those with nondialysis CKD.

Similarly, investigators¹³ reported higher probability for mortality in AKI patients when compared to those without AKI (OR, 14.208; 95% CI, 6.434–31.375; P = 0.003).

The possible mechanisms as to why CKD patients fared better could be because of the fact that:

a. CKD Patients on HD are immunocompromised and are unable to mount a proper immune response to the invading pathogen, and cytokine storm being the major cause of death during this pandemic was not seen in such immunocompromised patients with chronic debilitating illness like CKD.

b. It could also be possible that Haemodialysis(HD) helped to play a protective role, as during HD, there is a re-setting of bodies physiological parameters towards the normal, in that, fluids and electrolytes are corrected, Acid-Base balance is normalized, there is overall harmonizing effect on physiological internal milieu which might favor the CKD patient on MHD and is missing in patient with AKI or deranged physiology in terms of dehydration, electrolyte disturbances and Acid-base dis-balance.

c. Also during dialysis the blood and thus the Virus comes in contact with dialysate, other fluids, electrical charges and is outside the body for an extended period of some hours and this may adversely affect the pathogen(virus) in that it may decrease the virulence of the pathogen or decrease the viral load consequently helping the patient to fight the illness.

d. Therefore there is plenty of scope for the researchers to look into this in the future and to understand and pin point the actual mechanisms at play that protect the CKD patient on HD from the lethality of this abomination SARS-COV-2. It may add another useful weapon in our armamentarium in the quest to win over this pandemic and those that may land upon us in the future.

CONCLUSIONS:

We draw 3 important conclusions:

1. Our study shows that CKD patients on Maintenance Hemodialysis (MHD) fared equally or better when compared to non-RF patients, which was contrary to previous assumptions.
2. Acute Kidney Injury (AKI) patients with mild to moderately deranged physiology not requiring dialysis were expected to have better outcomes, however we observed that their outcomes were worse than that of CKD patients on MHD which was contrary to previous understanding.
3. Haemodialysis could have played a protective role in Covid patients with renal failure and can be used as a novel treatment modality in such patients. This needs to be explored in further studies.

Limitatons Of The Study:

1. This being a Retrospective observational study, no actual contact could be made with the patients and they could not be followed and thus it is not possible to know about the morbidity and mortality over an extended period of time.
2. Since the data is compiled from records of patients admitted during the two waves of Covid Pandemic, but these two groups/waves of Pandemic were very different as Virus had mutated and was no longer behaving the way it previously did as seen by higher mortality during the 2nd/Delta wave of the pandemic and thus comparing patients from two different waves together does not constitute a homogenous group, as they are inherently very heterogenous.

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