

## Impact of Covid 19 Among Hemodialysis Patients

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### ABSTRACT

**Background:** Global health and life are at risk from COVID-19, particularly for individuals who have several illnesses, such as renal disease. Hemodialysis (HD) patients make up a sizable subset of kidney failure patients with a variety of etiologies, most of which are thought to involve immune system impairment.

**Objective:** To describe the clinical characteristics, laboratory finding, short term outcomes and to estimate the mortality rate of COVID 19 infection in chronic HD patients in Assiut Governorate.

**Patients and Methods:** A retrospective study was conducted on 400 patients in upper Egypt (Assiut Governorate) with end stage renal disease on regular HD was carried out at Quarantine Department of Assiut Feverish Hospital, two hundred of them were infected with COVID-19 diagnosed by polymerase chain reaction (PCR). **Results:** Regarding the two hundred isolated HD patients infected with COVID-19, the mean age was (61.04 ± 14.57 years) older than those without COVID-19 (49.54 ± 11.78), gender distributed was (48% males and 52.6% females) with an incidence rate of occurrence about 15.4% of total HD patient in Assiut governorate. The total mortality rate was 31% higher in males than female. About 41.8% males died while the survivals were 58.2% of total males had COVID 19 infection, while 17.8% of females died with a total survival 82.2% of females had infected with COVID 19. The most frequent symptoms were gastritis (0.000), fever (0.001) and cough (0.009) respectively. While the most significant laboratory findings were elevated s. creatinine, high WBC counts, high absolute neutrophilic counts, and low platelet counts with  $p < 0.001$ .

**Conclusion:** At the area of COVID-19 infection, the incidence of COVID-19 infection was relatively low among HD patients in Assiut Governorate, with good prognosis among infected patients by COVID 19. The predictor factors for mortality were elderly, male gender, presence of cardiac diseases, elevated serum creatinine, elevated serum potassium, bilateral GGO in CT scan chest and hypoxemia with need for CAPAP or intensive care admission.

**Keywords:** HD, COVID-19, Chronic Kidney Failure.

### INTRODUCTION

The pandemic of COVID 19 had been a life threatening to the whole world. Patients who had heart illness, chronic liver disease, CKD, or other risk factors were put at risk<sup>(1)</sup>. Fever, cough, and dyspnea were the most symptoms of COVID -19 infection<sup>(2)</sup>.

HD patients were immune compromised and they had altered immune response to various infections including virus infection<sup>(3)</sup>. The most common cause of immune system dysregulation in HD patients may be elevated levels of circulating dialysis membrane-associated inflammatory marker along with uremic toxins<sup>(4)</sup>. A number of innate and adaptive immune response abnormalities are linked to the aforementioned alterations. HD patients' peripheral blood has higher levels of inflammatory cytokines<sup>(5)</sup>.

This study aimed to describe the clinical characteristics, laboratory finding, short term outcomes and to estimate the mortality rate of COVID 19 infection in chronic HD patients in Assiut Governorate.

### PATIENTS AND METHODS

In this retrospective study, two hundreds Egyptian patients' lives at Assiut Governorate with end stage kidney disease (ESKD) on regular HD with a confirmed diagnosis of COVID 19 was enrolled in this study. Those patients' data were collected from Quarantine Department, Assiut Feverish Hospital in a period from January 2021 to April 2022.

Assiut Quarantine Fever Hospital is a large hospital for isolation of cases infected with COVID-19 and it is considered the only hospital for isolation and

treatment of ESKD on HD patients infected with COVID-19 in Assiut Governorate. In addition, at the same period, Assiut population were around 4447417 population, while the total number of patients with ESKD on regular HD were 1299 patients.

**Patients were divided into two groups: Group (1):** included 200 HD patients with COVID-19 infection compared to **Group (2):** included 200 HD patients not infected with COVID-19.

Patients with ESKD on regular dialysis proved as having COVID 19 infection confirmed by real time polymerase chain reaction [RT-PCR] test. Patients who were <18 years old, patients with chronic lung disease, patients with major comorbidities or concomitant malignancies, patients under treatment of chemotherapy, pregnant and lactating females and non-compliant patients were excluded.

**All patients were subjected** to the following: Complete history taking and full clinical examination include assessment of general condition, vital signs. Abdominal, chest and heart examination were assessed with focus on manifestations of CKD.

**Laboratory investigations included;** CBC by Erma Automated Blood Count Machine (Tokyo, Japan), Latex agglutination slide test was performed for qualitative and semi quantitative determination of CRP in non-diluted serum, D-dimer level, Serum ferritin by using (TOSOH AIA-360 Automated Immunoassay Analyzer, Japan). AST, ALT by using a photometric unit of the auto-analyzer the Cobas 6000 analyzer

(c501 module) and nasopharyngeal and oropharyngeal swabs were collected for COVID-19 (PCR) test by using Rotor Gene real-time PCR with fluorescence system (QIAGEN, GmbH, Germany) before or soon after admission to the assigned hospitals.

**Imaging study included;** X-ray chest and HRCT chest. Patients with COVID-19 were classified as mild, moderate, severe and critical.

**Ethical approval:** Because the study was non-interventional and intended as an anonymous retrospective analysis, no subjects were solicited for informed permission. The study was carried out in compliance with the Helsinki Declaration and was authorised by the University of Al-Azhar Assiut Branch's Ethics Committee (protocol code 41-20; 04/05/2020).

**Statistical analysis:** Using the SPSS V. 18.0 for Windows®, the collected data were coded, processed,

and analysed. Relative percentages and frequencies were used to report the qualitative data. The difference between two or more sets of qualitative variables was computed using the Chi square test ( $\chi^2$ ). The mean±SD, of the quantitative values were displayed. Two independent groups of normally distributed variables (parametric data) were compared using the t-test for independent samples. A significant P value of 0.05 was determined.

**RESULTS**

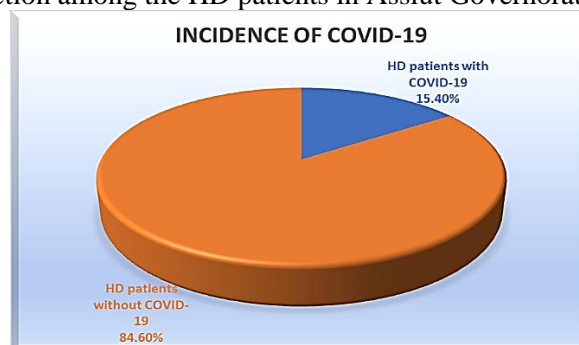
Four hundred HD patients were enrolled in this study, two hundred patients of them were infected with COVID-19. They were significantly older than those without COVID-19, had shorter dialysis duration, and had higher incidence of DM than the non-infected group (Table 1). White blood cells value was high in 25% (100 patients), the mean white blood cells value was  $8.857 \times 10^9/L$  (median:  $7.70 \times 10^9/L$ ) (Table 1).

**Table (1):** The demographic data and characteristics of the studied HD patients (infected with COVID group and non-infected group) (N=400).

Characteristics			Hemodialysis with COVID-19 (N=200)		Hemodialysis without COVID-19 (N=200)		P-value
		Total	Number	%	Number	%	
Gender	Male	225	108	48%	117	52%	0.364
	Female	175	92	52.6%	83	47.4%	
Hypertension	Present	305	114	37.4%	191	62.6%	<0.001*
	Absent	95	86	90.5%	9	9.5%	
Diabetes mellitus	Present	103	84	81.6%	19	18.4%	<0.001*
	Absent	297	116	39.1%	181	60.9%	
Ischemic Heart Disease	Present	31	18	58.1%	13	41.9%	0.350
	Absent	369	182	49.3%	187	50.7%	
			<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>	
Age/year			61.04	14.57	49.54	11.78	<0.001*
Duration of dialysis/year			2.10	0.49	2.94	0.71	0.000*
Blood urea (mg/dl)			142.58	34.42	149.97	37.17	0.209
Serum creatinine (mg/dl)			5.86	1.43	9.21	2.21	<0.001*
WBC ( $\times 10^9/L$ )			10.08	2.43	7.63	1.84	<0.001*
Absolute lymphocytic count ( $\times 10^9/L$ )			1.55	0.36	1.60	0.38	0.612
Absolute neutrophils count ( $\times 10^9/L$ )			7.86	1.82	6.02	1.41	<0.001*
Hemoglobin (g/dl)			10.54	2.38	9.92	1.99	0.005*
Platelets ( $\times 10^9/L$ )			215.43	52.31	247.93	60.38	<0.001*
Serum ferritin (mcg/L)			1018.84	251.83	913.31	226.82	0.366
Sodium (mEq/L)			140.08	11.93	136.04	5.28	<0.001*
Potassium (mEq/L)			4.271	1.01	5.01	0.81	<0.001*

\*: Significant

The incidence of COVID-19 infection among the HD patients in Assiut Governorate were 15.40% (Figure 1).



**Figure (1):** Incidence of COVID-19 among the HD patients in Assiut Governorate

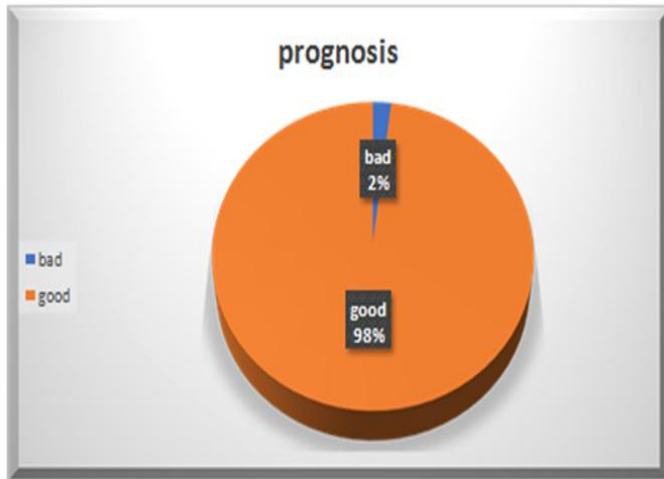
HD male patients with COVID-19 who died were significantly more than the female patients. The survivors were significantly younger than the non-survivors. Among HD patients with COVID-19, 31.6% of hypertensive patients died, 31% of diabetic patients died (**Table 2**). 36.4% of patients with dry cough and 26.9% of patients with productive cough died. Also, 47.7% of patients with chest pain, 53.8% of those with gastritis, and 33.3% of those with diarrhea died. Significantly more patients with bilateral ground glass opacity died compared to those with unilateral ground glass opacity (**Table 2**).

**Table (2):** Demographic features, clinical characteristics, and laboratory findings of the HD patients with COVID-19 stratified by mortality in the follow-up.

Demographic features		Total	Survivors (N=138)		Non-survivors (N=62)		P value
			Number	%	Number	%	
Gender	Male	110	64	58.2%	46	41.8%	<0.001*
	Female	90	74	82.2%	16	17.8%	
Cardiac Disease	Present	18	8	44.4%	10	55.6%	<b>0.018</b>
	Absent	182	130	71.4%	52	28.6%	
Gastritis	Present	52	24	46.2%	28	53.8%	<0.001*
	Absent	148	114	77%	34	23%	
Fever	Present	148	112	75.7%	36	24.3%	<0.001*
	Absent	52	26	50%	26	50%	
Cough	Dry	132	84	63.6%	48	36.4%	<b>0.009</b>
	Productive	52	38	73.1%	14	26.9%	
	no cough	16	16	100%	0	0%	
Chest pain	Present	38	20	52.6%	18	47.4%	<b>0.015</b>
	Absent	162	118	72.8%	44	27.2%	
Dyspnea	Present	188	126	67%	62	33%	<b>0.017</b>
	Absent	12	12	100%	0	0%	
Rhinitis	Present	2	0	0%	2	100%	<b>0.034</b>
	Absent	198	138	69.7%	60	30.3%	
CT scan Finding	Unilateral GGO	42	34	81%	8	19%	<b>0.019</b>
	Bilateral GGO	138	86	62.3%	52	37.7%	
	Bilateral Consolidation	2	2	100%	0	0%	
	Normal CT	18	16	88.9%	2	11.1%	
Need for oxygen Supply	Yes	156	94	60.3%	62	39.7%	<0.001*
	No	44	44	100%	0	0%	
Need for CPAP	Yes	36	16	44.4%	20	55.6%	<0.001*
	No	164	122	74.4%	42	25.6%	
Need for invasive mechanical ventilation	Yes	4	0	0%	4	100%	<b>0.003</b>
	No	196	138	70.4%	58	29.6%	
Need for intensive care in follow -up	Yes	78	42	53.8%	36	46.2%	<0.001*
	No	122	96	78.7%	26	21.3%	
Treatment regimens	Iverzine	96 (48%)	54	39.1%	42	67.7%	<b>0.613</b>
	Dexamethasone	82 (41%)	48	34.8%	34	54.8%	
	Remdesivir	42 (21%)	42	100%	0	0%	
	Solumedrol	14 (7%)	10	7.2%	4	6.5%	
	Aluvia	32 (16%)	24	17.4%	8	12.9%	
			Survivors (N=138)		Non-survivors (N=62)		P-value
			Mean	SD	Mean	SD	
Age/year			59.57	14.00	64.65	15.192	<b>0.022</b>
Blood urea (mg/dl)			130.09	30.51	170.39	40.94	<0.001*
Serum creatinine (mg/dl)			5.20	1.23	7.33	1.72	<0.001*
Sodium (mEq/L)			141.62	13.26	136.94	7.20	<b>0.001</b>
Potassium (mEq/L)			4.07	0.91	4.71	1.11	<b>0.000*</b>
Serum ferritin (mcg/L)			789.58	196.42	851.61	211.31	<b>0.4</b>
CRP (mg/dL)			67.72	15.51	73.94	17.43	<b>0.167</b>
AST			49.12	11.43	53.58	11.51	<b>0.532</b>
ALT			53.03	12.48	49.65	12.21	<b>0.638</b>
Hemoglobin (g/dl)			10.67	2.56	10.252	1.88	<b>0.193</b>
Platelets (*10 <sup>9</sup> /L)			212.32	51.76	222.33	54.34	<b>0.493</b>
Total WBC count(*10 <sup>9</sup> /L)			9.92	2.41	10.435	2.42	0.543
Absolute neutrophils count (*10 <sup>9</sup> /L)			7.71	1.88	7.80	1.92	0.903
Absolute lymphocytic count (*10 <sup>9</sup> /L)			1.57	0.38	1.65	0.38	0.727

\*: Significant

The prognosis was good in 98% of patients infected with COVID (Figure 2).



**Figure (2):** Percentage frequencies of studied HD patients according to prognosis

The most contributing factors for mortality were elevated serum creatinine  $\geq 7$  mg/dl, elevated serum potassium  $> 5$  meq/L, presence of gastritis, elevated blood urea  $> 150$  mg/dl, need for intensive care, and male gender, then need for CPAP therapy, and old age  $\geq 65$  years and the least contributing factors were association of cardiac disorders, and presence of bilateral ground glass opacity in CT (**Table 3**).

**Table (3):** Multivariable logistic regression analysis for factors affecting mortality among hemodialysis patients with COVID-19

Variable	Odds Ratio	95% CI		P value
		Lower	Upper	
Elevated serum creatinine $\geq 7$ mg/dl	2.643	1.840	3.798	<b>0.000</b>
Elevated serum potassium $> 5$ meq/L	3.339	1.715	6.499	<b>0.000</b>
Elevated blood urea $> 150$ mg/dl	1.922	1.404	2.631	<b>0.000</b>
Need for intensive care	1.908	1.373	2.652	<b>0.000</b>
Male gender	1.600	1.269	2.017	<b>0.000</b>
Need for CPAP therapy	2.782	1.550	4.995	<b>0.001</b>
Old age $\geq 65$ years	1.514	1.103	2.077	<b>0.014</b>
Cardiac disorders	2.782	1.154	6.708	<b>0.023</b>
Bilateral GGO	1.209	1.041	1.405	<b>0.028</b>

\*: Significant

## DISCUSSION

Hemodialysis (HD) patients are suffering from threatened forms of infection, which is associated with high mortality rate. In era of COVID-19 pandemic, the elderly patients and patients with multiple risk factors as DM, hypertension and cardiovascular disease have the severest form of infection, also HD patients more often are elderly and have comorbidities<sup>(4)</sup>.

In the current study we found that there were 15.4% of HD patients in Assiut Governorate had COVID-19. We found that HD patients with older age had higher rate of infection with COVID-19 more than others, but the sex of the patient had no significance. On concordance with the present study **Hsu et al.**<sup>(6)</sup> found the same result. Also, in agreement with the current study **Bao et al.**<sup>(7)</sup>, enrolled 46 HD patients with COVID-19 and 56 without COVID-19 with incidence of 45% which was much higher than our results. They concluded that there was no significant difference in sex between the groups under examination, but their findings contradicted our findings in that they discovered no significant difference in age. Their limited sample size may be the reason for this discrepancy of their study.

Regarding chronic diseases, moreover, our findings demonstrated that the HD patients with DM, hypertension, and shorter duration of dialysis had high incidence of COVID-19. Also, **Hsu et al.**<sup>(6)</sup> reported the same result regarding diabetes mellitus and hypertension. In contrast to our results **Bao et al.**<sup>(7)</sup> and **Zou et al.**<sup>(8)</sup> revealed that there was no significant difference between the studied HD groups with and without COVID-19 as regard all comorbidities and duration of HD. The disagreement might be attributed to their study's tiny sample size.

Regarding the relationship between COVID-19 and laboratory findings of the studied HD patients, we found a significant association between the incidence of COVID-19 and serum creatinine, WBC, absolute neutrophils count, hemoglobin, platelets, sodium and potassium. However, there was no significant difference as regard blood urea, absolute lymphocytic count and serum ferritin. According to **Zou et al.**<sup>(8)</sup>, who endorsed the current investigation, there were notable differences in creatinine and potassium levels between HD patients who had COVID-19 and those who did not. **Bao et al.**<sup>(7)</sup> found, in contrast to our findings, that WBC was not substantially greater in COVID-19 patients compared to HD patients without COVID-19.

Regarding outcome of the studied HD patients with COVID-19 it was found that (69%) were discharged with cure, (31%) died due to the development of acute respiratory distress syndrome and shock. Also, we found that the male gender and old age were significant predictors of mortality. While, **Hsu et al.**<sup>(6)</sup> reported that the mortality rate was 24.9%, in multivariable logistic regression analysis they found that older age but not gender was significant predictor of mortality in HD patients with COVID-19. The disagreement regarding gender may be due to the difference in the severity of the studied patients. As well, **Tang et al.**<sup>(9)</sup> revealed that older age was significant predictor of mortality in HD patients with COVID-19 in multivariable logistic regression analysis. (18%) died during hospitalization.

Among the comorbidities in HD patients, we

found that cardiac disorders were significant predictors of mortality. Our findings were corroborated by **Hsu et al.**<sup>(6)</sup> and **Turgutalp et al.**<sup>(10)</sup>, that the cardiac disorders is a good predictors of mortality .

Regarding clinical characteristics of the HD patients with COVID-19, we found that the non-survivors have significantly higher prevalence of dyspnea, fever, dry cough, chest pain, gastritis, and rhinitis. However, there was no significant association between death and diarrhea, sore throat, and lower limb edema. We also found that gastritis was a significant predictor of mortality.

Our results were supported by **Turgutalp et al.**<sup>(10)</sup> who reported that, most of non- survival HD patients with COVID-19 had symptoms like fatigue, dry cough, anorexia, dyspnea, myalgia, and diarrhea. Our results were further supported by **Hakami et al.**<sup>(11)</sup> who reported that the most frequently reported clinical symptoms in the hospitalized COVID-19 deceased patients with ESKD were fever, shortness and cough.

Regarding, laboratory findings of the HD patients with COVID-19, it was found that there was significant difference between survivors and non survivors as regard blood urea, serum creatinine, sodium and potassium. However, there was no significant association between mortality and WBC, absolute lymphocytic count, lymphocyte percentage, absolute neutrophils count, hemoglobin, platelets, serum ferritin, CRP, ALT and AST. We also found that elevated serum creatinine  $\geq 7$  mg/dl, elevated serum potassium  $> 5$  meq/L, and elevated blood urea  $> 150$  mg/dl were significant predictors of mortality. Also, **Hakami et al.**<sup>(11)</sup> revealed that blood urea was significantly associated with mortality. In contrast to our findings, **Turgutalp et al.**<sup>(10)</sup> who revealed that, ferritin, lymphocyte count, platelet count, CRP, and anemia were significantly related with mortality.

Regarding interventions needed for the HD patients with COVID-19, it was found that hypoxia, needs for CPAP and ICU were identified as significant predictors of mortality. In agreement with the current study **Hakami et al.**<sup>(11)</sup> and **Turgutalp et al.**<sup>(10)</sup> found that the need for ventilation and ICU admission conferred a significant risk for in-hospital mortality.

Among the predictors of mortality, we found that the presence of bilateral GGO was identified as significant predictor of mortality. In agreement with the current study **Bacharaki et al.**<sup>(12)</sup> revealed that the worse CT findings on admission were significantly associated with mortality. Also, in harmony with the current study **Zou et al.**<sup>(8)</sup> and **Turgutalp et al.**<sup>(10)</sup> revealed that, the presence ground glass opacities on chest CT was significantly associated with mortality of HD patients with COVID-19.

## CONCLUSION

COVID-19 pandemic had a significant morbidity and mortality among general population

worldwide in Assiut Governorate. COVID-19 infection among HD patients had been of low incidence and good prognosis compared with general populations. Elderly patients, males, cardiac disorders and clinical presentation with gastritis had linked to the rate of mortality. Elevated serum creatinine, urea, hyperkalemia, hypoxemia, bilateral GGO, need for intensive care and CPAP therapy were significantly associated with COVID-19 related mortality.

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