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ORIGINAL ARTICLE

Infection

Current status of COVID-19 among hemodialysis patients in the East Azerbaijan Province of Iran

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Abstract

Introduction: Management of vulnerable patients during the COVID-19 pandemic requires careful precautions. Hemodialysis patients constitute a large group of at-risk patients that not only suffer from a compromised immune system but also are at a higher risk due to frequent admission to healthcare units. Therefore, a better understanding on the pathogenesis and possible risk factors of COVID-19 in hemodialysis patients is of high importance.

Methods: A total of 670 maintained hemodialysis patients from all dialysis units of the East Azerbaijan Province of Iran, including 44 COVID-19 patients were included in the present study. Possible associations between the backgrounds of patients and the incidence of COVID-19 were assessed. Also, hemodialysis patients with COVID-19 were compared to 211 nonhemodialysis COVID-19 patients.

Findings: Chronic glomerulonephritis patients and those with blood group A demonstrated a higher incidence of COVID-19. On the other hand, patients with blood group AB^+ and those with hypertension etiology of kidney failure demonstrated a lower incidence of COVID-19. Hemodialysis patients with COVID-19 had higher counts of polymorphonuclears (PMNs) in their peripheral blood compared to other COVID-19 patients.

Discussion: A better comprehension on the risk factors associated with COVID-19 in hemodialysis patients can improve our understanding on the pathogenesis of COVID-19 in different situations and help the enhancement of current therapeutics for COVID-19 in hemodialysis patients.

Keywords: COVID-19, hemodialysis, risk-factor, chronic glomerulonephritis, PMNs

INTRODUCTION

COVID-19 is a serious pandemic health problem endangering the lives of millions of people all around the globe. This pandemic condition is accompanied by social, economic, and emotional burdens moreover to life-threatening health problems. It has been shown that the life-threatening compilations of COVID-19 such as acute respiratory distress syndrome (ARDS) are more prevalent among elderly people and those suffering from at least one chronic disease.[1,2] As a result, the

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mortality rate of at-risk groups is relatively higher than the rest of the community.[3–5] Hence, chronic disease sufferers and vulnerable groups require special consideration in the case of COVID-19. Hemodialysis patients constitute a large group of kidney failure patients with heterogeneous etiologies that are generally considered to have a compromised immune system.[6] These patients exhibit altered inflammatory responses and disturbed antiviral immune functions.[7,8] Sustained uremia, uremic toxins, and dialysis membrane-associated inflammation are the common causes of immune system dysregulation in these patients.[6,9] The mentioned changes are associated with a series of malfunctions in innate and adaptive immune responses. Hemodialysis patients contain more inflammatory cytokines in their peripheral blood, accompanied by a higher expression and activity of Toll-like receptors (TLRs) on their monocytes and granulocytes.[10,11] The elevated levels of anaphylatoxins and inflammatory cytokines cause higher homing of inflammatory cells in tissues eventuating in tissue inflammation and malfunction.[12,13] The barrier properties of epithelial tissues also undergo a serious weakness in hemodialysis patients.[14] The dysregulated immune responses however might act as a double-edged sword upon encounter with COVID-19. So that, a limited inflammatory capacity might decrease the likelihood of the progression of COVID-19 to its severe inflammatory stages. Regarding the different kidney failure causes and various etiologies among the hemodialysis patients, the fate of COVID-19 in various patients could be different. Some hemodialysis patients such as lupus nephropathy cases receive immunosuppressive regimens.[15] Thus, the susceptibility of these patients to COVID-19 could be different than the others.[16] Therefore, uncovering the situation of COVID-19 in hemodialysis patients requires a precise analysis of the possible risk factors in patients with distinct etiologies.

To make a better understanding on the pathogenesis of COVID-19 in hemodialysis patients and to assess the possible risk factors associated with its incidence and mortality, the present cross-sectional study was carried out on a total of 670 hemodialysis patients of East Azerbaijan province in the northwest of Iran. The associations between the patient-related variables and the disease incidence were examined. Also, the disease course in hemodialysis patients with COVID-19 was compared to that of other COVID-19 sufferers.

MATERIALS AND METHODS

Patients selection

This study was conducted under ethical approval from the local ethics committee (registration code: IR.TBZMED.REC.1398.1311) and in accordance with the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects. Written informed consent was obtained from the all studied patients except the expired patients and those admitted to the intensive care unit. The patients were selected from all hemodialysis centers of the East Azerbaijan Province of Iran. The verified COVID-19 patients were selected from the University Hospital of Tabriz University of Medical Sciences. The histories of patients were recorded from the hospitalization documents and periodic laboratory tests of hemodialysis patients. Information such as age, sex, history of dialysis, cause of kidney failure, HBs antibody titer, blood group, and history of influenza vaccination were recorded.

Statistics

The normality of the obtained quantitative data was analyzed by the Kolmogorov–Smirnov test. Regarding that none of the data sets passed the normality test, the data were analyzed by the Mann–Whitney test to compare the two study groups. The nonparametric results are represented as median ± range. The qualitative data were analyzed by Fisher's exact test. All statistical analyses were carried out by GraphPad Prism software (version 6) and P values below 0.05 were considered statistically significant.

RESULTS

Association of patient history to the incidence of COVID-19

Among the 670 hemodialysis patients, 44 patients were polymerase chain reaction confirmed for COVID-19. Fourteen patients died of COVID-19 among the 44 infected patients (Table 1). Hemodialysis patients with and without COVID-19 exhibited no difference regarding the age, sex, and history of dialysis. Hemodialysis patients with the kidney failure etiology of hypertension exhibited a lower incidence of COVID-19 (48.8% vs. 29.5%; P = 0.018). Hereditary kidney failure causes such as autosomal dominant polycystic kidney disease and Alport syndrome demonstrated a trend for higher

Table 1 Demographic information of the hemodialysis patients and hemodialysis patients with COVID-19

	Hemodialysis patients n = 626	Hemodialysis with COVID-19 n = 44	P value
Age (y) (median ± range)	61.50 (19–88)	63.50 (22–83)	0.277
Sex			0.391
Male	401	31	
Female	225	13	
Dialysis history (mo) (median ± range)	23.50 (2–200)	23.50 (3–180)	0.564
Cause of kidney failure			
HTN	306 (48.8%)	13 (29.5%)	0.018
DM	248 (39.6%)	19 (43.1%)	0.636
Hereditary	20 (3.1%)	4 (9.0%)	0.065
Cancer	7 (1.1%)	1 (2.2%)	0.421
Post kidney	20 (3.1%)	2 (4.5%)	0.649
CGN	14 (2.2%)	4 (9.0%)	0.025
Other	11 (1.7%)	1 (2.2%)	0.560
Blood group			
• A	204 (32.5%)	21 (47.7%)	0.047
+	196 (31.3%)	20 (45.4%)	0.065
−	8 (1.2%)	1 (2.2%)	0.459
• B	149 (23.8%)	11 (25.0%)	0.855
+	137 (21.8%)	11 (25.0%)	0.578
−	12 (1.9%)	0 (0.0%)	1.000
• AB	52 (8.3%)	0 (0.0%)	0.040
+	52 (8.3%)	0 (0.0%)	0.040
−	0 (0.0%)	0 (0.0%)	1.000
• O	221 (35.3%)	12 (27.2%)	0.327
+	210 (33.5%)	11 (25.0%)	0.319
−	11 (1.7%)	1 (2.2%)	0.560
Influenza vaccine received	78 (12.4%)	1 (2.2%)	0.049
HBs antibody (IU/L) (median ± range)	68.50 (0–1100)	77.50 (0–1000)	0.323

CGN = chronic glomerulonephritis; DM = diabetes mellitus; HTN = hypertension.

Table 2 Demographic characteristics of survivor and nonsurvivor hemodialysis patients with COVID-19

	Nonsurvivor n = 14	Survivor n = 30	P value
Age (y) (median ± range)	67.5 (31–81)	65.5 (22–82)	0.884
Sex			0.498
Male	11	20	
Female	3	10	
Dialysis duration (m) (median ± range)	21.5 (3–180)	23.5 (7–110)	0.542

COVID-19 morbidity (3.1% vs. 9.0%; P = 0.065). Chronic glomerulonephritis (CGNs) patients showed a significantly higher incidence rate of COVID-19 (2.2% vs. 9.0%; P = 0.025). Hemodialysis patients with blood group A exhibited higher COVID-19 morbidity (32.5% vs. 47.7%; P = 0.047) that the majority of them were A^+ (31.3% vs. 45.4%; P = 0.065). On the other hand, patients with blood group AB^+ exhibited a significantly lower incidence of COVID-19 (8.3% vs. 0.0%; P = 0.040). Also, the patients with an influenza vaccination history exhibited a relatively lower incidence of COVID-19 (12.4% vs. 2.2%; P = 0.049).

Association of patient history with the mortality of COVID-19

There were no significant associations between age, sex, and dialysis age and the mortality of COVID-19 among the hemodialysis patients (Table 2).

Table 3 Comparison of COVID-19 patients with COVID-19 hemodialysis patients

	Hemodialysis with COVID-19 n = 44	COVID-19 n = 211	P value
Age (y) (median ± range)	63.50 (22.00–83.00)	62.00 (16.00–93.00)	0.647
Sex			0.389
Male	31	131	
Female	13	80	
WBCs (count/μL) (median ± range)	9800.5 (1100–21000)	5900 (520–23700)	0.012
PMNs (count/μL) (median ± range)	6885.5 (600–18690)	4480 (421.7–18618)	0.012
Lymphocyte (count/μL) (median ± range)	1065.5 (149–3772)	954 (56–8580)	0.504
CRP			0.541
Positive	42	193	
Negative	2	18	
Mortality rate (%)	31.81	22.74	0.245

CRP = c-reactive protein; PMNs = polymorphonuclears; WBCs = white blood cells.

Comparison between the hemodialysis patients with COVID-19 and other COVID-19 patients

To compare the disease course of COVID-19 in hemodialysis patients with that in other COVID-19 patients, we incorporated 211 COVID-19 patients into this study (Table 3). Hemodialysis patients with COVID-19 demonstrated higher absolute counts of white blood cells (WBCs; P = 0.012) and polymorphonuclears (PMNs; P = 0.012). Other parameters such as age, sex, lymphocyte count, and CRP positive cases did not differ significantly between the two studied groups. While the mortality rate of COVID-19 among hemodialysis patients was higher than that of nonhemodialysis COVID-19 patients, the observed difference was not statistically significant (P = 0.245).

DISCUSSION

Regarding the distinct causes of kidney failure in hemodialysis patients, the present study aimed at investigating the possible associations of various variables to the incidence and mortality of COVID-19. We observed significant associations between the incidence of COVID-19 and the etiology of kidney failure as well as the blood groups and influenza vaccination. In comparison with the ordinary COVID-19 patients, hemodialysis patients with COVID-19 exhibited higher levels of WBCs and PMNs in their blood.

Hemodialysis patients are among the at-risk groups for getting involved with COVID-19 and therefore, careful precautions are required for proper management of their condition.[17] While case reports are describing milder progress of COVID-19 in hemodialysis patients,[18–20] it has been shown that the mortality rate of COVID-19 is higher in hemodialysis patients compared to other COVID-19 sufferers.[21] Although the mortality rate of COVID-19 in hemodialysis patients was higher than the rest of COVID-19 patients of this study, the observed difference was not statistically significant. The obtained mortality rate of COVID-19 hemodialysis patients was comparable to the mortality rate obtained by Goicoechea et al.[21] for the COVID-19 in hemodialysis cases in Spain.

On the other hand, patients with specific kidney failure etiologies are under simultaneous therapies for their chief problem. For instance, CGN cases such as systemic lupus erymanthos (SLE) patients receive immunosuppressants for their main therapy. These cases might be more prone to opportunistic infections. In the current study, the CGN group of hemodialysis patients consisted mostly up of the SLE patients and exhibited a higher incidence of COVID-19 compared to the other etiologies. Li et al.[22] demonstrated that obstructive nephropathy patients exhibit a higher incidence of COVID-19 while they reported lupus nephropathy to not be associated with COVID-19. On the other hand, hypertension-associated kidney failure cases showed a lower incidence of COVID-19 in the present survey. A similar study by Li et al.[22] in China reported no association of hypertension to the morbidity of COVID-19. While another study carried out in China reports diabetes mellitus as an important risk factor for the incidence of COVID-19 in hemodialysis patients,[23] we did not observe an association between diabetes mellitus and COVID-19. Interestingly, the blood group and the history of influenza vaccination were associated with the morbidity of COVID-19. However, possible mechanisms underlying these observations are needed to be clarified. The COVID-19 mortality was not associated with age, sex, and the history of hemodialysis.

Neutrophils have been reported to contribute to the pathogenesis of COVID-19 through neutrophil extracellular traps (NETs) that help the alveolar thrombosis and facilitate the establishment of ARDS.[24–26] The count of neutrophils in peripheral blood is also positively correlated to the severity of the disease.[27] The neutrophil to lymphocyte ratio has also been introduced as an independent risk factor for the mortality of COVID-19.[28] While the hemodialysis patients usually have lower PMNs in their circulation compared to healthy individuals,[29,30] we demonstrated that hemodialysis patients with COVID-19 contain higher counts of PMNs that might reflect a more severe disease course. Our outcomes on the increased counts of PMNs are in accordance with a previous report examining the COVID-19 in hemodialysis patients in Wuhan, China.[22] The lymphocyte count of hemodialysis patients with COVID-19 did not exhibit significant difference with other COVID-19 patients and both were low in counts. Other studies have also reported a decreased count of lymphocytes in hemodialysis patients suffering from COVID-19. So that, the lower count of lymphocytes was associated with COVID-19-related mortality.[21,23,31] Therefore, COVID-19-associated risk factors are required to be more clarified for hemodialysis patients.

This study was a cross-sectional survey that examined the patients until July 1, 2020. While the incorporation of a large group of patients is an advantage for the present study, it was impossible to collect more information from the patients due to the multicentral nature of the study and the absence of specialized research staff in the all participated therapeutic centers in the COVID-19 crisis. Incorporation of the imaging results and examining the fate of COVID-19 in each etiology of kidney failure could better clarify the risk factors of COVID-19 in this group of at-risk patients.

CONCLUSION

Undoubtedly, at-risk groups require careful consideration during the pandemic COVID-19. Recognition of risk factors and specific disease course of COVID-19 in hemodialysis patients might improve our understanding of the pathogenesis of COVID-19 in hemodialysis patients and help the better management of the disease in this at-risk population.

DATA AVAILABILITY STATEMENT

The data responsible for the results of this study are available from the corresponding authors upon request.

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