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Clinical and Laboratory Features of Hemodialysis Patients Suspected to Have COVID 19 Shifted to Isolation Hospitals: Retrospective Study

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Abstract

Background: The coronavirus disease (COVID-19) pandemic has greatly affected the dialysis community. The uremia caused by chronic kidney failure causes inflammation and immune suppression at the molecular level. 3 Immunosuppression, which occurs in chronic kidney failure, can change the immune response to viral diseases. Dialysis patients appear to be at increased risk for viral transmission with relatively high mortality rates ranging from 11% to 30%.

Aim of Study: To evaluate the importance of clinical and laboratory features for early detection and better management of Covid 19 patients under regular hemodialysis.

Patients and Methods: We included a total of 120 hemodialysis patients who were allocated into two groups; Group 1 included 75 patients who did not develop covid infection, while Group 2 included the remaining 45 patients who developed that serious infection. All patients were subjected to complete history taking, physical examination, radiological chest assessment (via X-ray and CT chest), as well as laboratory investigations (including CBC, d dimer, ferritin, and CRP).

Results: There was an increased hemodialysis frequency in group 1 compared to group 2.96% of patients in group 1 had dialysis three time per week compared to 80% in Group 2. The used access did not show a significant difference between the two groups, as AVF was used in 92% and 93.3% of patients in the same groups respectively, while the remaining cases used a permanent catheter. NLR showed a significant rise in the group 2 (5.9 vs. 1.9 in group 1). CRP had median values of 3 and 98gm/dl in groups 1 and 2 respectively, with a significant increase in association with covid infection. Serum d-dimer had median values of 220 and 900 in groups 1 and 2 respectively, with a significant rise in patients with covid infection. Serum ferritin had median values of 137 and 480 in the groups 1 and 2 respectively, with a significant rise in association with covid infection.

Conclusion: Covid infection is associated with a marked changes in the clinical and laboratory parameters in haemodialysis patients. It is associated with a marked deterioration of vital signs, decreased CBC parameters, and increased inflammatory markers.

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Key Words: *COVID-19 – Clinical and laboratory features – Hemodialysis patients.*

Introduction

COVID-19 is a serious pandemic disease discovered for the first time on December 2019. With high rate of human-to-human transmission **[1].**

Although much effort was done to control the disease the quantities of affirmed and suspected cases keep on rising. Doctors, medical caretakers, and emergency vehicle laborers are particularly susceptible to contamination than other groups. Of the affirmed cases around the world, 6%, or 90,000, were medical services workers **[2].**

Coronavirus (CoV) is among the main pathogenic organisms that affect there spiratory system in humans. An ongoing outbreak of pneumonia associated with a novel coronavirus, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was firstly reported in Wuhan, Hubei province, China in December 2019 **[3].**

Although lung involvement is the most common and most serious disease manifestation, it has been increasingly demonstrated that extra-pulmonary manifestations are quite common **[4].** In patients with Corona virus disease 2019 (COVID-19), the most common clinical symptoms arefever and cough, shortness of breath, and other breathing difficulties in addition to other nonspecific symptoms, including headache, dyspnea, fatigue, and musclepain **[5].** Moreover, some patients also report digestive symptom such as diarrhea and vomiting **[6].**

The kidney can be affected in several ways, and acute kidney injury (AKI) is relatively common aswell as hematuria and proteinuria. From the USA and the UK, AKI was found in 20-46% of patients

admitted to intensive care unit (ICU) and considerable sector of them needed kidney replacement therapy (KRT). AKI in Covid 19 patients dramatically increases the risk of mortality **[7]**.

Early reports from Italy pointed to that kidney replacement therapy (KRT) patients being at high risk of infection and mortality **[8]**. HD patients older than 70 years were at higher risk of dying from symptomatic COVID-19, whereas those younger than 70 years seemed to have a milder disease in most cases **[9]**.

The aim of the present study was to evaluate the importance of clinical and laboratory features for early detection and better management of Covid 19 patients under regular hemodialysis.

Patients and Methods

This was a retrospective study, we included a total of 120 hemodialysis patients who were allocated into two groups; Group 1 included 75 patients who did not develop covid infection, while Group 2 included the remaining 45 patients who developed that serious infection. Conducted at Nephrology Department, Police Hospitals, Cairo, Egypt.

The study included the data of the patients on regular haemodialysis who were admitted to the previous department during the period between December 2019 and August 2021.

Inclusion criteria:

HD patients age ≥18 years, and patients on HD for more than 6 months.

Exclusion criteria:

Patient's age <18, patients with malignant disease, and uncooperative patients.

Ethical consideration:

The study gained approval from the local scientific and ethical committee of Al-Azhar University. Patient confidentiality was preserved, and the collected data were used only for scientific purposes. An informed consent was obtained from all participants after explaining the benefits and drawbacks of each intervention.

Patients evaluation:

I- *History taking:*

- Personal history including patient name, age, gender, occupation, residence, and special habits.
- Current complaint including cough, vomiting, diarrhoea, fatigues, dyspnoea, anorexia, anosmia, headache or other symptoms.
- Analysis of each complaint regarding onset, course, duration, what increased, what decreased, and associations.
- Primary renal disease: e.g. primary glomerulonephritis, diabetes, hypertension, lupus nephritis, and others.
- Haemodialysis history including the duration of haemodialysis, dry weight, frequency of haemodialysis per week, and the type of vascular access (AV fistula, central venous catheter, or others).
- Current systemic comorbidities with its duration and commenced medications.

II- *Clinical examination:*

- General examination included patient look, body built, body mass index (BMI), and assessment of vital signs (heart rate, temperature, respiratory rate, and temperature).
- Measurement of oxygen saturation via pulse oximetry.
- Local chest examination including inspection, palpation, percussion, and auscultation.

III- *Laboratory investigations:*

About 10 cm of venous blood were obtained from a superficial forearm vein in all participants for assessment of the following parameters:

- Complete blood count (CBC) with its components including haemoglobin, platelets, and white blood cells with its differentials (neutrophils and lymphocytes).
- Neutrophil to lymphocyte ratio (NLR) was calculated by dividing the number of neutrophils by number of lymphocytes **[10]**.
- C-reactive protein was determined using immunoturbidimetric Protiline CRP assay kits (bioMerieux, Lyon, France) according to the manufacturer's instructions.
- D-dimer was determined via immune-turbidometric assay using STA®-Liatest D-Di ® kits (Cat. No. 00515) on STA®-analyzers (DiagnosticaStago S.A.S, 3 allee Theresa, 92600 Asnieressur Seine, France).
- Serum ferritin was measured by Chemiluminescence immunoassay (CLIA) on the Siemens Advia Centaur immunoassay analyzer using the manufacturer's recommendations.

IV- *Radiological investigations:* Chest X-ray, and chest computed tomography (CT).

Outcomes: Identification of clinical and laboratory parameters to detect covid infection in patients on haemodialysis.

Data collection:

1- Demographic data: Age, and gender.

2- Comorbidities: Smoking, hypertension, diabetes mellitus, and glomerulonephritis.

3- Haemodialysis related data: Frequency, dry weight, and angioaccess.

4- Covid related symptoms: Cough, vomiting, diarrhoea, fatigue, dyspnea, anorexia, and anosmia.

5- Clinical assessment: Temperature, respiratory rate, blood pressure, and oxygen saturation.

6- Laboratory parameters: Complete blood count, neutrophil lymphocyte ratio, CRP, D-dimer, and ferritin.

Statistical analysis:

The collected data were coded, processed and analysed using the SPSS (Statistical Package for Social Sciences) version 26 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples *t*-test was used to compare between two independent groups of normally distributed variables (parametric data) while Mann Whitney U test was used for non-normally distributed Data (non-parametric data). In all applied tests, the *p*-values associated with test statistics indicated the significance level at which the null-hypothesis (the hypothesis of no difference) was rejected and it was set at 0.05 so that a *p*-values ≥0.05 are statistically non-significant, *p*-values <0.05 are significant, and *p*-values <0.01 are highly significant.

Results

The mean age of the included cases was 60.63 and 59.6 years in groups 1 and 2 respectively. Men represented 76% and 73.3% of patients in the same two groups respectively, whereas the remaining cases were females. Both age and gender were statistically comparable between the two study groups (p=0.668 and 0.744 respectively) (Table 1).

The prevalence of smoking and other systemic comorbidities was significantly increased in Group 2 (p<0.05). Smokers represented 32% and 60% of the patients in Groups 1 and 2 respectively. In addition, hypertension was present in 60% and 80%, whereas diabetes was present in 64% and 93.3% of patients in the same two groups respectively. However, the prevalence of glomerulonephritis was statistically comparable between the two groups (p=0.06), as it was present in 4% and 13.3% of patients in the same previous groups respectively (Table 2).

The frequency of haemodialysis was significantly increased in Group 1, as 96% of its patients had dialysis three time per week compared to 80% in Group 2 (p=0.005). Dry weight had mean values of 84.44 and 82.87kg in Groups 1 and 2 respectively, which was comparable between the two groups. Likewise, the used access did not show a significant difference between the two groups, as AVF was used in 92% and 93.3% of patients in the same groups respectively, while the remaining cases used a permanent catheter (Table 3).

Regarding the manifestations of covid reported by patients in group 2, cough was reported by all patients (100%), while fatigue, dyspnea, and anorexia were present in the majority of patients (93.3%). Additionally, diarrhea was reported by 73.3% of patients, while anosmia and vomiting were detected in 53.3% (Table 4).

Regarding vital signs, temperature was significantly elevated in group 2 (38.8 vs. 36.82° in group 1 - p<0.001). Pulse was significantly increased in Group 2 (82.93 vs. 71.52 bpm in Group 1 - p<0.001). In addition, respiratory rate had mean values of 17.28 and 21.07 cycles/min in groups 1 and 2 respectively, with a significant increase in the latter (p<0.001). Although DBP was statistically comparable between the study groups (p=0.37), SBP showed a significant rise in Group 2 (p= 0.032). Oxygen saturation was significantly reduced in group 2 (86.67 vs. 97.24 in group 1 - p=0.37) (Table 5).

Haemoglobin level showed a significant decline in association with Covid infection (9.73 vs. 10.3gm/dl in group 1 - p=0.004). Total leucocytic count also showed a significant decline in group 2 (4.5 vs. 6.9 in group 1 - p<0.001). Lymphocytic count also showed the same changes (p<0.001). However, neutrophil count was statistically comparable between the two groups (p=0.435). Platelet count showed a significant decline in the covid infected group (189.4 vs. 226.68 in Group 1 -

p<0.001). Nonetheless, NLR showed a significant rise in the same group (5.9 vs. 1.9 in group 1 - p<0.001). CRP had median values of 3 and 98gm/dl, whereas serum d-dimer had median values of 220 and 900 in groups 1 and 2 respectively. Additionally, serum ferritin had median values of 137 and 480 in the same two groups respectively. All of the three parameters were significantly elevated in association with covid infection (Table 6).

Table (1): Analysis of demographic data in the two study groups.

	Group 1 [Haemodialysis without Covid-19] (N=75)	Group 2 [Haemodialysis with Covid-19] (N=45)	Test of significance	*p*-value
Age (Years)	60.36±9.67	59.60±8.86	*t*=0.430	0.668
Sex:				
Male	57 (76%)	33 (73.3%)	χ^2=0.107	0.744
Female	18 (24%)	12 (26.7%)		

χ^2: Chi-square test. *t*: Independent samples *t*-test.

Table (2): Analysis of risk factors and comorbidities in the two study groups.

	Group 1 [Haemodialysis without Covid-19] (N=75)	Group 2 [Haemodialysis with Covid-19] (N=45)	Test of significance	*p*-value
Smoking	24 (32%)	27 (60%)	χ^2=9.023	0.003*
HTN	45 (60%)	36 (80%)	χ^2=5.128	0.024*
DM	48 (64%)	42 (93.3%)	χ^2=12.907	<0.001*
Glomerul-onephritis	3 (4%)	6 (13.3%)	FET=3.532	0.060

χ^2 : Chi-square test.
FET : Fischer's exact test.
* : Statistically significant (p<0.05).

Table (3): Haemodialysis related data in the two study groups.

	Group 1 [Haemodialysis without Covid-19] (N=75)	Group 2 [Haemodialysis with Covid-19] (N=45)	Test of significance	*p*-value
Frequency of dialysis / Week:				
- Two times/ Week	3 (4%)	9 (20%)	FET=8	0.005*
- Three times/ Week	72 (96%)	36 (80%)		
- Dry Weight	84.44±12.11	82.87±13.19	*t*=0.666	0.507
Access:				
- AVF	69 (92%)	42 (93.3%)	FET=0.072	0.788
- Permeant catheter	6 (8%)	3 (6.7%)		

χ^2 : Chi-square test.
FET : Fischer's exact test.
* : Statistically significant (p<0.05).

Table (4): Analysis of the COVID-19 criteria in the two study groups.

	Group 1 [Haemodialysis without Covid-19] (N=75)	Group 2 [Haemodialysis with Covid-19] (N=45)	Test of significance	*p*-value
Cough	0 (0%)	44 (100%)	χ^2=120	0.564
Vomiting	0 (0%)	24 (53.3%)	χ^2=50	0.855
Diarrhea	0 (0%)	33 (73.3%)	χ^2=75.862	0.160
Fatigue	0 (0%)	42 (93.3%)	χ^2=107.692	0.547
Dyspnea	0 (0%)	42 (93.3%)	χ^2=107.692	0.547
Anorexia	0 (0%)	42 (93.3%)	χ^2=107.692	0.547
Anosmia	0 (0%)	24 (53.3%)	χ^2=50	0.855

χ^2 : Chi-square test.
t : Independent samples *t*-test.
* : Statistically significant (p<0.05).

Table (5): Analysis of vital signs in the two study groups.

	Group 1 [Haemo-dialysis without Covid-19] (N=75)	Group 2 [Haemo-dialysis with Covid-19] (N=45)	Test of signif-icance	*p*-value
Temperature (° C)	36.82±0.20	38.80±0.96	*t*=–17.381	<0.001*
Pulse (B/min)	71.52±3.75	82.93±6.51	*t*=–12.206	<0.001*
Respiratory rate (Cycle/min)	17.28±1.05	21.07±2.35	*t*=–12.121	<0.001*
SBP (mmHg)	143.60±17.76	150±11.08	*t*=–2.175	0.032*
DBP (mmHg)	85.60±11.42	87.33±7.80	*t*=–0.899	0.370
Oxygen saturation (%)	97.24±1	86.67±4.74	*t*=18.684	<0.001*

χ^2 : Chi-square test.
z : Mann-Whitney U-test.
* : Statistically significant (p<0.05).

Table (6): Analysis of laboratory findings in the two study groups.

	Group 1 [Haemo-dialysis without Covid-19] (N=75)	Group 2 [Haemo-dialysis with Covid-19] (N=45)	Test of signif-icance	*p*-value
HGB (gm/dl)	10.30±1.12	9.73±0.84	*t*=2.973	0.004*
WBCs (10^3/cmm)	6.9 (4.54-9.91)	4.5 (3-10.2)	z=–5.686	<0.001*
Lymphocytes (10^3/cmm)	2.15 (1.24-3.24)	0.66 (0.3-1)	z=–9.157	<0.001*
Neutrophils (10^3/cmm)	4.3 (2.43-6.66)	4.12 (2.65-11.1)	z=–0.781	0.435
PLTs (10^3/cmm)	226.68±46.55	189.40±61.08	*t*=3.770	<0.001*
NLR	1.9 (1.35-4.8)	5.9 (4.3-23.15)	z=–9.031	<0.001*
CRP	3 (0-8)	98 (40-145)	z=–9.205	<0.001*
D-dimer	220 (125-450)	900 (680-1100)	z=–9.156	<0.001*
Ferritin	137 (75-350)	480 (400-500)	z=–9.142	<0.001*

t: Independent samples *t*-test.
z: Mann-Whitney U-test.
*: Statistically significant (p<0.05).

Discussion

The current study was conducted at Police Hospitals aiming to evaluate the importance of clinical and laboratory features for early detection and better management of Covid 19 patients under regular hemodialysis. We included a total of 120 hemodialysis patients who were allocated into two groups; Group 1 included 75 patients who did not develop covid infection, while Group 2 included the remaining 45 patients who developed that serious infection. Based on group allocation, the incidence of covid infection in our hemodialysis setting was 37.5%.

Other authors reported a lower incidence of covid infection in hemodialysis patients, as this infection was diagnosed in 66 out of the included 602 patients (incidence rate = 11%) **[11]**. Another French study reported an incidence rate of 19% (38 out of 200 hemodialysis patients) **[12]**.

Difference between studies could be due to different preventive strategies against covid infection, patient criteria, methods of diagnosis, as well as the burden of pandemic in the tested region.

In the current study, the mean age of the included patients was 60.36±9.67 and 59.6±8.86 years in groups 1 and 2 respectively, with no significant difference between the two groups (p=0.668).

Likewise, Zou et al. **[11]** also noted no significant difference regarding age between the infected and non-infected hemodialysis patients (p=0.085). It had median values of 61 and 64.5 years in the non-infected and infected groups respectively. This is in line with our findings.

Our findings showed no significant difference between covid infected and non-infected groups regarding gender distribution (p=0.744). Men represented 76% and 73.3% of patients in groups 1 and 2 respectively, while the remaining patients were women.

Similar to the previous findings, Hsu and his colleagues **[13]** reported that male patients represented 60% and 57% of patients in the covid infected and non-infected groups respectively with no significant difference between the two groups (p=0.2).

Ghonimi et al. **[14]**, on the other hand, reported that male dialysis patients had double the incidence of covid 19 than females (9% versus 4.5% respectively; p<0.01), indicating that male gender is a significant risk factor for infection in this specific population.

In our study, smokers represented 32% and 60% of patients in groups 1 and 2 respectively, with a significant rise in association with covid infection (p=0.003).

There are currently no peer-reviewed studies that have evaluated the risk of SARS-CoV-2 infection among smokers. However, smoking is already known to be a risk-factor for many other respiratory infections, including colds, influenza, pneumonia and tuberculosis **[15]**. The effects of smoking on the respiratory system makes it more likely that smokers contract these diseases, which could be more severe **[16]**. Smoking is also associated with increased development of acute respiratory distress syndrome, a key complication for severe cases of COVID-19 **[17]**, among people with severe respiratory infections **[18]**.

Conversely, another study reported comparable smoking prevalence between covid infected and non-infected groups (p=0.799), which was 51.5% and 53.2% in the same groups respectively **[11]**. Tang et al. **[19]** also confirmed the previous findings.

In the current study, the prevalence of hypertension was 60% and 80% in groups 1 and 2 respectively, with a significant increase in the covid-infected group (p=0.024).

Likewise, Tang et al. **[19]** reported that hypertension was present in 24% and 10% of patients in the covid and non-covid hemodialysis patients, with a significant difference between the two groups (p<0.001).

In our study, diabetes mellitus was present in 64% and 93.3% of patients in groups 1 and 2 respectively, with a significant increase in group 2 (p<0.001).

In the same context, a previous similar study reported the increased prevalence of diabetes in covid-infected hemodialysis patients (69.9% vs. 58.2% in the non-infected group - p<0.001) **[13]**. Tang et al. **[19]** also noted the same findings.

In the current study, glomerulonephritis was present in 4% and 13.3% of patients in groups 1 and 2 with no significant difference between the two groups (p=0.06). Glomerulonephritis was present in non-covid patients as they were also patients with CKD.

In contrast to the previous findings, Zou et al. **[11]** reported that the incidence of glomerulonephritis was 36.4% and 40.1% in covid infected and non-infected groups, which was comparable on the statistical analysis (p>0.05). The previous

authors did not mention the criteria for glomerulonephritis diagnosis. In our opinion, the main cause of this differences is related to criteria used in diagnosis of glomerulonephritis.

Hours of hemodialysis per week found to be an important risk factor for acquiring Covid 19 infection in the current study. In the present study 96% of patients ingroup one regularly received the prescribed hours of hemodialysis versus 80% ingroup two with significant difference (p=0.005).

Conversely, other authors did not report a significant difference between covid infected and non-infected groups regarding hemodialysis frequency (p=0.4), as 59% and 55.4% of patients had dialysis three time per week in the previous two groups respectively. The remaining patients had dialysis < three times per week **[19]**.

In our study, the used access did not show a significant difference between the two groups, as AVF was used in 92% and 93.3% of patients in the same groups respectively, while the remaining cases used a permanent catheter.

In the same context, Zou and his colleagues **[11]** also reported no significant difference between the covid infected and non-infected patients regarding the angioaccess (p=0.388). Another study confirmed the previous findings **[14]**.

In the current study, fever predominate in Covid 19 patients the mean temperature among them was 38.8 centigrade versus 36.82 in non-infected group (p<0.001).

Fever is a complex cytokine-mediated physiological response that stimulates both the innate and adaptive arms of immunity involving adrenergic stimulation pathways **[20]**. Guan et al. **[21]** reported that history of fever was positive in 42.8% while 88.7% of the COVID-19 patients had fever at the time of hospitalization.

According to a recent systematic review, fever prevalence in adult COVID-19 patients ranged between 68.26% [95% CI: 60.46-76.07, I^2 = 51%] and 98.63% [95% CI: 95.96-100.00] **[22],** making it an important sign of this contagious infection.

In our study, cough was present in 100% of our Covid patients. Zou et al. **[11]** reported that cough was detected in 69.7% of covid patients, while Xiong et al., reported that only 37.4% of their patients with covid reported cough **[23]**.

In the current study, dyspnea was detected in 93.3% of the included covid cases. Huang et al. **[6]** found a prevalence of breathlessness as high as 92% amongst patients infected with covid. Others reported lower incidence, as in a systematic review and meta-analysis, Rodriguez-Morales et al. **[24]** found an overall dyspnoea prevalence of 45.6% (95% CI: 10.9-80.4%). In addition, Li et al., conducted a systematic review that included the data of 1,994 patients. The overall percentage of patients experiencing dyspnoea was 21.9% **[25]**. Some of the variation in dyspnoea prevalence within and between studies can be explained by differences in how it was investigated and documented.

In our study, anorexia was reported by 93.3% of covid patients. Other studies reported variable incidence ranging between 23.2% and 40% **[26, 27,28]**. The preexisting chronic kidney disease could explain our increased incidence, as diminished appetite is reported in as many as 40%-50% of dialysis patients **[29]**.

Our findings showed that fatigue was reported by 93.3% of patients infected with covid. Zou et al. **[11]** reported that the same manifestation was present in 34.8% of patients. Xiong et al. **[23]** reported an incidence of 45%.

Our findings showed that anosmia was present in 53.3% of patients with Covid infection. In agreement with our findings, in a retrospective study by Klopfenstein et al. **[30]**, 54 (47%) out of 114 confirmed COVID-19 patients presented with anosmia. An additional report stated that the incidence range of anosmia from 9.2% to 82% and an average anosmia incidence rate of 30.19% **[31]**.

In the current study, vomiting was present in 53.3% of patients infected with covid. In one study' s Nobel et al., noted that the presence of vomiting in as high as 22.7% patients **[32]**. Cholankeril et al. **[26]** and Hajifathalian et al. **[33]** reported the prevalence of symptoms of nausea and vomiting as 10.3 and 15.9%, respectively.

In our study, diarrhea was present in 73.3% of patients infected with covid. A previous report stated that the incidence of diarrhea with covid infection varied widely, ranging from 2% to 49.5% **[34]**.

In our study, respiratory rate showed a significant increase in group 2 (21.07 vs. 17.28 in group 1 - p<0.001). Hypoxemia-driven tachypnoea could explain the previous finding **[35]**.

In the current study, although DBP was statistically comparable between the study groups (p=0.37), SBP showed a significant rise in Group

2 (p=0.032). This could be due to the increased prevalence of hypertension in the covid infected group.

Another study noted no significant difference between the infected and non-infected groups regarding their measured systolic and diastolic blood pressures (p=0.514 and 0.672 respectively). The former had mean values of 138 and 144mmHg, while the latter had mean values of 87 and 85mmHg in the previous two groups respectively **[11]**. One should mention that the prevalence of hypertension was comparable between the two groups and that could explain the previous findings.

In the current study, the mean oxygen saturation on admission was significantly reduced in group 2 (86.67 vs. 97.24 in group 1 - p=0.37).

Desaturation in patients with covid infection could be explained by different mechanisms including; intrapulmonary shunting, perfusion diffusion mismatch, intravascular microthrombi, in addition to impaired diffusion capacity **[36]**.

In the current study, haemoglobin level showed a significant decline in association with covid infection (9.73 vs. 10.3gm/dl in group 1 - p=0.004).

Anemia was not a common laboratory finding of patients with SARS-CoV-2 infection, but the hemoglobin showed a descending tendency in fact. The first COVID-19 case in the USA showed a slight decrease in hemoglobin in illness day 6 and then recovered as the condition improved **[37]**. Hemoglobin was below the normal range in 51% of 99 patients with SARS-CoV-2 infection reported by Jin Yin-tan Hospital **[6]**. Indiscriminate use of anticoagulant before laboratory results may be a suggestive cause.

Inflammatory changes caused by SARS-CoV-2 infection could interfere with erythropoiesis, resulting in a decrease in hemoglobin **[38]**.

In contrast to the previous findings, another study reported that hemoglobin levels were comparable between infected and non-infected hemodialysis patients (p=0.98), and it had mean values of 10.36 and 10.37gm/dl in the two groups respectively **[11]**.

In the current study, the mean of total leucocytic count also showed a significant decline in group 2 (4.5 vs. 6.9 in group 1 - p<0.001).

Likewise, Tang et al. **[19]** reported a significant decline in mean total leucocytic count in association with covid infection in hemodialysis patients, which had a median value of 4.9 versus 5.57 in patients without covid infection (p=0.002). Another study also confirmed the previous findings **[39]**.

Our findings showed that the mean of lymphocytic count was significantly decreased in group 2 (0.66 vs. 2.15 in group 1 - p<0.001).

Lymphopenia is found to be a characteristic of COVID-19 and was found to be useful in differentiating between COVID-19 pneumonia and non-COVID-19 pneumonia. Researchers show that the decrease in lymphocyte is mainly caused by depletion of T-lymphocyte subsets, mainly T-helper and T-suppressor cells, and the presence of lymphopenia in COVID-19 patients suggests significant inflammation and tissue damage **[40]**.

Similarly, another study reported that lymphocytic count had median values of 0.86 and 0.97 in the covid infected and non-infected groups, with a significant decline with covid infection (p=0.01) **[19]**.

In the current study, platelet count showed a significant decline in the covid infected group (189.4 vs. 226.68 in Group 1 - p<0.001).

There are very few reports of the mechanisms of thrombocytopenia in patients with COVID-19, but thrombocytopenia is very common. Three mechanisms have been reported; direct infection of bone marrow cells by the virus and inhibition of platelet synthesis, platelet destruction by the immune system, and platelet aggregation in the lungs, resulting in microthrombi and platelet consumption **[41]**.

In the same context, Ma and his associated noted that platelet count had median values of 154 (range, 140-200) in hemodialysis patients with covid, compared to a median of 171 (range, 36-486) in patients without covid, with an increase in the latter **[42]**.

Our findings showed that neutrophil to lymphocyte ratio (NLR showed a significant rise in the group 2 (5.9 vs. 1.9 in group 1 - p<0.001).

The NLR parameter has been widely used to assess systemic inflammation in a variety of diseases. NLR has been studied and proved to be useful in differentiating between patients hospitalized with fever due to infection and those with fever due to non-infectious causes **[43,44]**.

Moreover, in both acute and chronic illness, NLR could predict disease severity regardless of

the aetiology, such as infection, autoimmune or malignancy **[45,46]**.

The NLR of the COVID-19 patients in a previous study was significantly higher in severe patients (median value 7.06; IQR 6.41) **[46]**.

In our study, C-reactive protein (CRP) had median values of 3 and 98 gm/dl in groups 1 and 2 respectively, with a significant increase in association with covid infection. CRP production is induced by inflammatory cytokines and by tissue destruction in patients with COVID-19 **[47]**.

Ma et al. **[42]** also noted a significant increase in CRP in hemodialysis patients infected with covid compared to controls. Patients with raised CRP constituted 47% of the covid infected patients compared to only 3% in patients without infection.

Contrarily, other authors did not notice a significant difference between the covid infected and non-infected individuals (p=0.3), as it had median values of 2 and 1.4mg/l in the same two groups respectively **[19]**.

In the current study, serum d-dimer had median values of 220 and 900 in groups 1 and 2 respectively, with a significant rise in patients with covid infection (p<0.001). Elevated D-Dimer is most likely due to the acute lung injury itself or due to the increased rate of thromboembolic complications observed in patients with covid infection **[17]**.

Tang and his coworkers **[19]** reported that the same marker had median values of 5.6 and 2.1 mg/l in the covid infected and non-infected groups respectively, with a significant difference on statistical analysis (p<0.001). Yau et al. **[48]** reported that serum d dimer ranged between 0.746 and 3.895ng/ml, and all patients had d dimer level >0.5ng/ml.

Our findings showed that serum ferritin had median values of 137 and 480 in the groups 1 and 2 respectively, with a significant rise in association with covid infection.

Active ferritin production during the course of inflammatory diseases can occur. Macrophages, which produce cytokines and account for the majority of the immune cells in the lung parenchyma, might be responsible of the secretion of serum ferritin **[49]**. Moreover, ferritin synthesis can be induced by several inflammatory stimuli including cytokines, such as IL-6, which is increased during the course of covid infection **[38]**.

In a previous study, serum ferritin in hemodialysis patients infected with covid had a median value of 1461.5ng/ml (range, 604-1500), and 75% of these cases had ferritin >900ng/ml **[48]**.

Our study has some limitations. First of all, it is a single center study that included a relatively small sample size. Also, it lacks the effect of covid infection on patient outcomes, especially mortality. These previous drawbacks should be well discussed in the upcoming studies.

Conclusion:

Based on the results of our study, it could be included that:

Covid infection is associated with a marked changes in the clinical and laboratory parameters in haemodialysis patients. It is associated with a marked deterioration of vital signs, decreased CBC parameters, and increased inflammatory markers.

Recommendations:

More studies including more cases from different nephrological centers should be conducted in the future.

Hemodialysis patients should be evaluated with laboratory parameters for early detection of covid infection.

References

1- SCHWARTZ I.B., KAUFMAN J., HU K. and BIANCO S.: Predicting the impact of asymptomatic transmission, non-pharmaceutical intervention and testing on the spread of COVID19. Med. Rxiv, 68 (5): 926-929, 2020.

2- LABRAGUE L.J. and DE LOS SANTOS J.A.A.: COVID-19 anxiety among front-line nurses: Predictive role of organisational support, personal resilience and social support. Journal of Nursing Management, 28 (7): 1653-1661, 2020.

3- WANG W., XU Y., GAO R., LU R., HAN K., WU G., et al.: Detection of SARS-CoV-2 in different types of clinical specimens. Jama, 323 (18): 1843-1844, 2020.

4- GUPTA S., RAGHUWANSHI G.S. and CHANDA A.: Effect of weather on COVID-19 spread in the US: A prediction model for India in 2020. Science of the Total Environment, 728: 138860, 2020.

5- MO P., XING Y., XIAO Y., DENG L., ZHAO Q., WANG H., et al.: Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. Clinical Infectious Diseases, 72 (10): 916-920, 2020.

6- HUANG C., WANG Y., LI X., REN L., ZHAO J., HU Y., et al.: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet, 395 (10223): 497-506, 2020.

7- HIRSCH J.S., NG J.H., ROSS D.W., SHARMA P., SHAH H.H., BARNETT R.L., et al.: Acute kidney injury in

patients hospitalized with COVID-19. Kidney international, 98 (1): 209-218, 2020.

8- ALBERICI F., DELBARBA E., MANENTI C., ECONIMO L., VALERIO F., POLA A., et al.: Management of patients on dialysis and with kidney transplantation during the SARS-CoV-2 (COVID-19) pandemic in Brescia, Italy. Kidney international reports, 5 (5): 580-585, 2020.

9- SMOLANDER J. and BRUCHFELD A.: The COVID-19 epidemic: Management and outcomes of hemodialysis and peritoneal dialysis patients in Stockholm, Sweden. Kidney and Blood Pressure Research, 46 (2): 250-256, 2021.

10- YODYING H., MATSUDA A., MIYASHITA M., MATSUMOTO S., SAKURAZAWA N., YAMADA M., et al.: Prognostic significance of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in oncologic outcomes of esophageal cancer: A systematic review and meta-analysis. Annals of surgical oncology, 23 (2): 646-654, 2016.

11- ZOU R., CHEN F., CHEN D., XU C.-L. and XIONG F. (2020). Clinical characteristics and outcome of hemodialysis patients with COVID-19: A large cohort study in a single Chinese center. Renal failure, 42(1), 950-957.

12- CREPUT C., FUMERON C., TOLEDANO D., DIACONITA M. and IZZEDINE H.: COVID-19 in patients undergoing hemodialysis: Prevalence and asymptomatic screening during a period of high community prevalence in a large Paris center. Kidney Medicine, 2 (6): 716-723. e711, 2020.

13- HSU C.M., WEINER D.E., AWEH G., MISKULIN D.C., MANLEY H.J., STEWART C., et al.: COVID-19 among US dialysis patients: Risk factors and outcomes from a national dialysis provider. American journal of kidney diseases, 77 (5): 748-756. e741, 2021.

14- GHONIMI T.A.L., ALKAD M.M., ABUHELAIQA E.A., OTHMAN M.M., ELGAALI, M.A., IBRAHIM, R.A.M., et al.: Mortality and associated risk factors of COVID-19 infection in dialysis patients in Qatar: A nationwide cohort study. PloS One, 16 (7): e0254246, 2021).

15- HEALTH, U.D.O. and SERVICES, H.: The health consequences of smoking-50 years of progress: a report of the Surgeon General. In: Atlanta, GA: US Department of Health and Human Services, Centers for Disease. Pp. 1-36, 2014.

16- MURIN S. and BILELLO K.S.: Respiratory tract infections: Another reason not to smoke. Cleveland Clinic Journal of Medicine, 72 (10): 916-920, 2005.

17- LEHMANN A., PROSCH H., ZEHETMAYER S., GYSAN M.R., BERNITZKY D., VONBANK K., et al.: Impact of persistent D-dimer elevation following recovery from COVID-19. PloS One, 16 (10): e0258351, 2021.

18- HSIEH S.J., ZHUO H., BENOWITZ N.L., THOMPSON B.T., LIU K.D., MATTHAY M.A., et al.: Prevalence and impact of active and passive cigarette smoking in acute respiratory distress syndrome. Critical Care Medicine, 42 (9): 2058, 2014.

19- TANG H., TIAN J.-B., DONG J.-W., TANG X.-T., YAN Z.-Y., ZHAO Y.-Y., et al.: Serologic detection of SARS-CoV-2 infections in hemodialysis centers: A multicenter retrospective study in Wuhan, China. American journal of kidney diseases, 76 (4): 490-499. e491, 2020.

20- EVANS S.S., REPASKY E.A. and FISHER D.T.: Fever and the thermal regulation of immunity: The immune system feels the heat. Nature Reviews Immunology, 15 (6): 335-349, 2015.

21- GUAN W.-J., NI Z.-Y., HU Y., LIANG W.-H., OU C.-Q., HE J.-X., et al.: Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine, 382 (18): 1708-1720, 2020.

22- ISLAM M.A., KUNDU S., ALAM S.S., HOSSAN T., KAMAL M.A. and HASSAN R.: Prevalence and characteristics of fever in adult and paediatric patients with coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis of 17515 patients. PloS One, 16(4): e0249788, 2021.

23- XIONG F., TANG H., LIU L., TU C., TIAN J.-B., LEI C.-T., et al.: Clinical characteristics of and medical interventions for COVID-19 in hemodialysis patients in Wuhan, China. Journal of the American Society of Nephrology, 31 (7): 1387-1397, 2020.

24- RODRIGUEZ-MORALES A.J., CARDONA-OSPINA J.A., GUTIÉRREZ-OCAMPO E., VILLAMIZAR-PEÑA R., HOLGUIN-RIVERA Y., ESCALERA-ANTEZANA J.P., et al.: Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel medicine and infectious disease, 34: 101623, 2020.

25- LI B., YANG, J., ZHAO, F., ZHI, L., WANG, X., LIU, L., et al.: Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clinical research in cardiology, 109 (5): 531-538, 2020.

26- CHOLANKERIL G., PODBOY A., AIVALIOTIS V.I., TARLOW B., PHAM E.A., SPENCER S.P., et al.: High prevalence of concurrent gastrointestinal manifestations in patients with severe acute respiratory syndrome coronavirus 2: Early experience from California. Gastroenterology, 159 (2): 775-777, 2020.

27- HAN C., DUAN C., ZHANG S., SPIEGEL B., SHI H., WANG W., et al.: Digestive symptoms in COVID-19 patients with mild disease severity: Clinical presentation, stool viral RNA testing, and outcomes. The American Journal of Gastroenterology, 27 (3): 341-351, 2020.

28- PAN L., MU M.I., YANG P., SUN Y., WANG R., YAN J., et al.: Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. The American Journal of Gastroenterology, 27 (9): 2349, 2020.

29- CARRERO J.J. and GONZÁLEZ-ORTIZ A.: Anorexia and appetite stimulants in chronic kidney disease. In Nutritional Management of Renal Disease (pp. 893-906): Elsevier, 2022.

30- KLOPFENSTEIN T., KADIANE-OUSSOU N.J., TOKO L., ROYER P.Y., LEPILLER Q., GENDRIN V., et al.: Features of anosmia in COVID-19. Médecine et Maladies Infectieuses, 50 (5): 436-439, 2020.

31- AANAND P., ANGRAL S., VARSHNEY S. and RAJ R.: Incidence of Anosmia among Covid 19 patients in India. Indian Journal of Otolaryngology and Head & Neck Surgery, 21: 1-10, 2021.

32- NOBEL Y.R., PHIPPS M. and ZUCKER J.: Gastrointestinal symptoms and COVID-19: Case-control study from the United States. Gastroenterology, 20: 5085-88, 2020.

33- HAJIFATHALIAN, K., KRISKO, T., MEHTA, A., KUMAR, S., SCHWARTZ, R., FORTUNE B., et al.: Gastrointestinal and hepatic manifestations of 2019 novel coronavirus disease in a large cohort of infected patients from New York: Clinical implications. Gastroenterology, 159 (3): 1137-1140, 2020.

34- WANG C., KANG K., GAO Y., YE M., LAN X., LI X., et al.: Cytokine levels in the body fluids of a patient with COVID-19 and acute respiratory distress syndrome: A case report. Annals of Internal Medicine, 173 (6): 499-501, 2020.

35- MARINI J.J. and GATTINONI L.: Management of COVID-19 respiratory distress. JAMA, 323 (22): 2329-2330, 2020.

36- DHONT S., DEROM E., VAN BRAECKEL E., DEPUYDT P. and LAMBRECHT B.N.: The pathophysiology of 'happy'hypoxemia in COVID-19. Respiratory Research, 21 (1): 1-9, 2020.

37- HOLSHUE M.L., DEBOLT C., LINDQUIST S., LOFY K.H., WIESMAN J., BRUCE H., et al.: First case of 2019 novel coronavirus in the United States. New England Journal of Medicine, 27 (1): 1-7, 2020.

38- LIU T., ZHANG J., YANG Y., MA H., LI Z., ZHANG J., et al.: The role of interleukin-6 in monitoring severe case of coronavirus disease 2019. EMBO Molecular Medicine, 12 (7): e12421, 2020.

39- QU R., LING Y., ZHANG Y.H.Z., WEI L.Y., CHEN X., LI X.M., et al.: Platelet to lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. Journal of Medical Virology, 92 (9): 1533-1541, 2020.

40- YANG A.-P., LIU J.-P., TAO W.-Q. and LI H.-M.: The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. International Immunopharmacology, 84, 106504, 2020.

41- XU D., ZHOU F., SUN W., CHEN L., LAN L., LI H., et al.: Relationship between serum SARS-CoV-2 nucleic acid (RNAemia) and organ damage in COVID-19 patients: A cohort study. Clinical Infectious Diseases, 2020.

42- MA Y., DIAO B., LV X., ZHU J., CHEN C., LIU L., et al.: Epidemiological, clinical, and immunological features of a cluster of COVID-19-contracted hemodialysis patients. Kidney International Reports, 5 (8): 1333-1341, 2020.

43- NAESS A., NILSSEN S.S., MO R., EIDE G.E. and SJURSEN H.: Role of neutrophil to lymphocyte and monocyte to lymphocyte ratios in the diagnosis of bacterial infection in patients with fever. Infection, 45 (3): 299-307, 2017.

44- NAESS A., MO R., NILSSEN S., EIDE G. and SJURSEN H.: Infections in patients hospitalized for fever as related to duration and other predictors at admittance. Infection, 42 (3): 485-492, 2014.

45- ISAAC V., WU C.-Y., HUANG C.-T., BAUNE B.T., TSENG C.-L. and MCLACHLAN C.S.: Elevated neutrophil to lymphocyte ratio predicts mortality in medical inpatients with multiple chronic conditions. Medicine, 95 (23), 2016.

46- SUKRISMAN L., SINTO R. and PRIANTONO D.: Hematologic Profiles and Correlation Between Absolute Lymphocyte Count and Neutrophil/Lymphocyte Ratio with Markers of Inflammation of COVID-19 in an Indonesian National Referral Hospital. International Journal of General Medicine, 14: 6919, 2021.

47- ALI N.: Elevated level of C-reactive protein may be an early marker to predict risk for severity of COVID-19. Journal of Medical Virology, 92 (11): 2409-2411, 2020.

48- YAU K., MULLER M.P., LIN M., SIDDIQUI N., NESKOVIC S., SHOKAR G., et al.: COVID-19 outbreak in an urban hemodialysis unit. American Journal of Kidney Diseases, 76 (5): 690-695. e691, 2020.

49- ROSÁRIO C., ZANDMAN-GODDARD G., MEYRON-HOLTZ E.G., D'CRUZ D.P. and SHOENFELD Y.: The hyperferritinemic syndrome: Macrophage activation syndrome, Still's disease, septic shock and catastrophic antiphospholipid syndrome. BMC Medicine, 11 (1): 1-11, 2013.

العلامات السريرية لمرضى الاستصفاء الكلوى المزمن المرجحة للاصابة بمرض كوفيد-١٩ والمحفزة للنقل لمستشفيات العزل دراسة مرجعية

خلفية الدراسة : لقد أثر جائحة فيروس كورونا (كوفيد-١٩) بشكل كبير على مجتمع غسيل الكلى. يتسبب التبول فى الدم الناجم عن الفشل الكلوى المزمن فى حدوث التهاب وتثبيط للمناعة على المستوى الجزيئى. ٣ يمكن أن يغير كبت المناعة، الذى يحدث فى الفشل الكلوى المزمن، الاستجابة المناعية للأمراض الفيروسية. يبدو أن مرضى غسيل الكلى معرضون لخطر متزايد لانتقال الفيروس مع معدلات وفيات عالية نسبياً تتراوح من ١١٪ إلى ٣٠٪.

الهدف من الدراسة : تقييم أهمية الميزات السريرية والمخبرية للكشف المبكر وإدارة أفضل لمرضى كوفيد-١٩ تحت غسيل الكلى المنتظم.

المرضى وطرق الدراسة : شملت هذه الدراسة على ١٢٠ من مرضى غسيل الكلى الذين تم تقسيمهم إلى مجموعتين، تضمنت المجموعة الأولى ٧٥ مريضاً لم يصابوا بعدوى كوفيد، بينما تضمنت المجموعة الثانية ٤٥ مريضاً متبقين أصيبوا بهذه العدوى الخطيرة. خضع جميع المرضى لأخذ التاريخ الكامل، والفحص البدنى، والتقييم الإشعاعى للصدر (عن طريق الأشعة السينية والصدر المقطعى المحوسب)، وكذلك الفحوصات المخبرية.

نتائج الدراسة : كان هناك زيادة فى تكرار غسيل الكلى فى المجموعة ١ مقارنة بالمجموعة ٢. ٩٦٪ من المرضى فى المجموعة ١ خضعوا للغسيل الكلوى ثلاث مرات فى الأسبوع مقارنة بـ ٨٠٪ فى المجموعة ٢. لم يظهر وسيلة الغسيل المستخدم فرقاً معنوياً بين المجموعتين، حيث تم استخدام الوصلة الشريانية الوريدية فى ٩٢٪ و ٩٣.٣٪ من المرضى فى نفس المجموعات على التوالى، بينما استخدمت الحالات المتبقية قسطرة دائمة. أظهر تعداد الكريات البيض الكلى أيضاً انخفاضاً ملحوظاً فى المجموعة ٢ (٤.٥ مقابل ٦.٩ فى المجموعة ١). تحليل دى دايمر كانت قيمته المتوسطة ٢٢٠ و ٩٠٠ فى المجموعتين ١ و ٢ على التوالى، مع ارتفاع معنوى فى المرضى المصابين بعدوى كوفيد. كانت قيم مصل الفيريتين ١٣٧ و ٤٨٠ فى المجموعتين ١ و ٢ على التوالى، مع ارتفاع معنوى مصاحب لعدوى كوفيد. كانت قيم بروتين سى التفاعلى وسيطة تبلغ ٣ و ٩٨جم / ديسيلتر فى المجموعتين ١ و ٢ على التوالى، مع زيادة معنوية مرتبطة بعدوى كوفيد.

الاستنتاج : ترتبط عدوى كوفيد بتغيرات ملحوظة فى المعايير السريرية والمخبرية فى مرضى غسيل الكلى. يرتبط بتدهور ملحوظ فى العلامات الحيوية، وانخفاض فى جميع معايير صورة الدم، وزيادة علامات التهابات المصل.