*RESEARCH ARTICLE*

## EPIDEMIOLOGY OF COVID -19 HEMODIALYSIS PATIENTS AT THE MILITARY HOSPITAL OF RABAT

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*Manuscript Info*

*Abstract*

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**Introduction:**Sars Cov2 infection is a risk factor for mortality in chronic hemodialysis (HD) patients and those with chronic kidney disease. In addition, it can be responsible for acute kidney injury (AKI) with a poor prognosis in patients requiring renal replacement therapy.The objective of our study is to determine the epidemiological and evolutionary profile of Covid 19 patients undergoing hemodialysis sessions.

**Method:**This is a monocentric retrospective study including patients with the severe form of Covid-19 referred to the Mohammed V military instruction hospital and undergoing one or more dialysis sessions between March 2020 and April 2021.

**Results:**Of 30 dialysis patients, 63.3% (n=19) were on chronic hemodialysis, 20% (n=6) presented an acutization of their chronic renal failure, and 16.7% (n=5) developed acute kidney injury. The average age was 64.4 years with a male predominance (70%).

Type 2 diabetes was the most common comorbidity (50%), followed by hypertension (33.3%) and cardiovascular disease (13.3%). About two-thirds of the patients presented with severe lesions on the chest CT classified as Co-RADS 5.

The overall mortality rate was 51.7%. This rate was 100% (n=5) in the AKI group, 66% (n=4) in the case of pre-existing renal failure and 33% (n=7) in the group of chronic hemodialysis patients.

There is a statistically significant difference in mortality between the group of hemodialysis patients and that of patients with AKI (p=0.034). The hospitalization departmentalso seems to be statistically associated with patient mortality (p=0.014). Among the comorbidities, only diabetes was statistically associated with patient mortality (p=0.05).

In our study, the levels of C reactive protein (CRP), ferritin, Lactate Dehydrogenase (LDH), white blood cells were lower in the chronic hemodialysis group compared to the other groups.

**Conclusion:**Our results underline the vulnerability of chronic hemodialysis patients to Covid 19 infection. They also confirm the poor prognosis of patients who develop AKI requiring hemodialysis, as well as those with diabetes.

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## Introduction:-
Morocco, like other countries, suffered the effects of the Covid 19 pandemic due to SARS Cov 2 with more than 8,000 deaths and 490,000 cases of infection(1), and a mortality rate of 1.8%.

While covid 19 infection generally results in mild to moderate symptoms, it can lead to severe respiratory complications requiring hospitalization in intensive care units, particularly in presence of significant comorbidities.

The impact of covid19 infection on the nephrological level is twofold: it constitutes a risk factor for mortality in patients undergoing hemodialysis and those with chronic kidney disease, in addition acute kidney injury is a common complication of severe cases and is associated with high mortality(2).

The prevalence of chronic kidney disease in Morocco is1.6 %( 3). Therefore, the prevention of Covid19 infection is important, particularly in this population.

## Method:-
### Study design:
This is a single-center retrospective study including patients with Covid 19 undergoing one or more hemodialysis sessions between March 2020 and April 2021.

### Study setting and population:
The inclusion criteria were the positivity of the SARS COV2 polymerase chain reaction (PCR) on a nasal swab, the presence of severe to moderate symptoms requiring treatment in a hospital setting.

The exclusion criteria are asymptomatic patients, or patients with minor forms, as well as suspected cases according to the recommendations of the Ministry of Health.

### Variables:
Patient-leveldata included demographics and comorbidities; values, physiologic parameters, and organ support (including RRT) for the first 14 days following admission; and clinical outcomes, includingacute organ injury and death. Baseline serum creatinine (SCr) is defined as the lowest value 365–7 day's prior tohospitalization. If a prehospital baseline SCr was not available, we used the SCr value on hospital admission as the baseline

All patients underwent a chest scan with evaluation of parenchymal lesions according to the CO-RADS classification, as well as a biological assessment on admission

### Data resource and measurement:
We collected the epidemiological data, the clinical-biological, radiological data relating to the patients thanks to the Dx care system, and we specified the outcomes of the patients. Data were analyzed on an SPSS version 20 file.

### Data analysis:
The association between qualitative variables was assessed with the chi-square test. Quantitative variables were analyzed using Student's t test. A p-value of less than 0.05 was considered significant.

## Results:-
30 patients were included in the study. Only 6% (n=2) of the patients came from our hemodialysis center.

The average age of our population was 64.4 years (standard deviation 11.2), of which 70% were male.

About half of the patients (46.7%) were admitted to an isolation unit; 38.7% (n=12) in the intensive care unit while 16.1% (n=5) stayed in an intensive care unit. The mean length of hospitalization was 10.77 days (standard deviation 3.72).

Type 2 diabetes was the most common comorbidity (50%), followed by hypertension (33.3%) and cardiovascular disease (13.3%). The other comorbidities are represented by smoking (6.7%) and the presence of neoplasia (3.3%).

Concerning the nephrological status, 60% (n=18) were on chronic hemodialysis, 23.3% (n=7) presented an acutisation of their chronic kidney disease, and 16.7% (n=5) developed an acute kidney injury.

On admission, approximately two-thirds of the patients presented with severe lesions on the chest CT scan classified as Co-RADS 5; 16.7% (n=5) had Co-RADS 4 lesions.

Pulsed oxygen saturation in free air was 83.27% on average (standard deviation: 9.37).

The results of the biological assessments are represented in Tables 1-3.

Regarding the dialytic data, the average number of sessions performed was 3.73 sessions (standard deviation 2.51), the blood pressure during was between 90 and 140 mmhg in 73.3% of cases. Hemodialysis was performed through an arteriovenous fistula (60%), followed by simple catheters (40%).

We noted noted3 cases (10%) of coagulation of the hemodialysis circuit.

The overall mortality rate was 51.7%. This rate was 100% (n=5) in the AKI group, 66% (n=4) in the case of pre-existing CKD and 33% (n=7 ) in the group of chronic hemodialysis patients.

There is a statistically significant difference in mortality between the hemodialysis group and the AKI group (p=0.034).

There is no difference in terms of mortality between the group of chronic hemodialysis patients and CKD patients .

Admission to intensive care unit also seems to be statistically associated with mortality (p=0.014).

Among the comorbidities, only diabetes was statistically associated with mortality (p=0.05).

In our study, the factors influencing mortality in the group of chronic hemodialysis patients were the long duration of hospitalization (9.92 days vs 12.17 days p=0.046), low oxygen saturation on admission (84.83% vs 84.67% p=0.05) and biologically serum potassium (4.79 mmol/l vs 4.88 mmol/lp=0.038) and the number of white blood cells (6416/mm3 vs 5966/mm3 p =0.031).

Among the risk factors established in the general population such as age, diabetes, hypertension, cardiovascular diseases, only diabetes was statistically associated with the mortality of chronic hemodialysis patients.

The levels of C-reactive protein, ferritin, LDH, white blood cells were lower in the HDC group compared to the other groups.

Comparing the evolution of patients with prior CKD, deceased patients were older (74 years vs 72.6 years, p=0.023) with lower serum sodium levels (139mmol/l vs 134 mmol/l, p=0.003) .

## Discussion:-

The mean age of chronic hemodialysis patients in our study was 61.94 years (standard deviation 10.35). In a meta-analysis including 396,062 chronic hemodialysis patients(4), the average age was 64.9 years indicating that HD patients infected with COVID-19 are in general older than other patients(5,6).

The mortality rate in the chronic hemodialysis group was 33%. Valeri et al. reported a mortality rate of 31% among 59 dialysis patients (7), another study of 36 hemodialysis patients showed that the mortality rate was 30.5%(8). This rate was 22.4% in the meta-analysis by Chen et al. (4).

The prognosis of patients with ARI was unfavorable with a mortality rate of 100%. This rate was 79.3% in a study of 638 patients presenting with AKI requiring dialysis (9). Hirsch et al.(10) evaluated 5449 hospitalized patients and showed that 37% of patients developed AKI. They also revealed that the mortality rate for AKI patients requiring hemodialysis was 55.1%.

Indeed Moledina et al demonstrated that COVID-19 is associated with an increased risk of AKI (11), which may be due either to a direct cytopathic effect on renal cells or indirectly through cytokine-induced damage ( 10.12–14).

The increase in the mortality rate in our series compared to the other studies is explained by the small size of our sample and the fact that the patients requiring dialysis are those who present the most serious complications with a significant inflammatory reaction, a unstable hemodynamic state, severe ARDS with multi-visceral failure. In addition, the worsening of renal function most often occurred in the hours or days following intubation, emphasizing the role of the alteration in the hemodynamic state as a mechanism for the occurrence of AKI.

The most common comorbidities in our series were diabetes and hypertension, which represent the leading cause of CKD.

In our study, the factors influencing mortality in the group of chronic hemodialysis patients were the long duration of hospitalization, low oxygen saturation on admission, diabetes and biologically the potassium level and the number of white blood cells.

In a study reporting data from 37 chronic hemodialysis patients(15), the risk factors for mortality were low oxygen saturation on admission, anemia and hypoalbuminemia.

Hyperleukocytosis has been described as associated with a poor prognosis in chronic hemodialysis patients in a Chinese study of 66 patients (16) .

Biochemical parameters associated with poor prognosis in the general population (D-dimer, C-reactive protein, pro-calcitonin, or albumin levels) were not associated with excess mortality in our study.

The indications for initiating hemodialysis in AKI patient with covid19 do not differ from the standard indications(17).

However, certain logistical constraints must be taken into account, such as the isolation of the patient, the protective measures for the nursing staff and the disinfection of the equipment.

Covid 19 infection is associated with a high risk of thrombosis(18).In our study, we noted 3 cases (10%) of circtuit clotting .Helms et al. reported 28 cases of circuit clotting in 29 patients(19). Al-Sarmkari et al reported repeated circuit coagulation in 8 of 12 patients even though these patients were initially on preventive anticoagulation(20).

In our study, the hemodialysis sessions were carried out either in intensive care or in a room dedicated to covid patients for stable patients, respecting protective measures.

In patients who did not have a vascular access, recourse to a temporary vascular access was necessary.

Intermittent methods were used in our department, however continuous methods are preferable in patients with covid19 in case of hemodynamic instability. All chronic hemodialysis patients received 3 sessions of 4 hours, using a membrane adapted to their body surface with Low-molecular-weight heparin-based anticoagulation.

**Limitations :**
Our study has several limitations. First, the reduced number of our sample, which makes it difficult to assess mortality risk factors in a relevant way in the absence of a control group. Secondly, due to the retrospective nature of our study, certain biological data (D-dimers, IL-6, procalcitonin) as well as the clinical characteristics (use of invasive ventilation, treatments received) of the patients were not evaluated. Finally, the fact that our hospital only receives patients with severe covid 19 forms explains the significant mortality found in our study.

## Conclusion:-
Our results highlight the vulnerability of chronic hemodialysis patients to Covid 19 infection. Low oxygen saturation, hyperleukocytosis and diabetes were associated with a poor prognosis. They also confirm the high mortality rate of patients who develop AKI with use of hemodialysis.

**What is known about this topic :**
1. Patients on maintenance hemodialysis appear particularly vulnerable to SARS-CoV-2 infection
2. Acute kidney injury (AKI) ascribed to COVID- 19 is a frequent complication of severe cases and moreover is associated with high mortality .

**What this study adds :**
1. the bad prognosis of AKI related to covid 19 infection
2. the outcome and risk factors of death in patients who were on maintenance hemodialysistherapy

**Competing interests :**
The authors declare no competing interests

**Authors' contributions**
Conception and study design :DrD.Montasser, DrM.Hallak ,Data analysis andinterpretation : D.Montasser, DrM.Hallak , DrD.Elkabbaj ,Manuscript revision: D.Montasser, DrM.Hallak , DrD.Elkabbaj .All authors read andapproved the final version of the manuscript.

**Table 1:-** Clinical and biological characteristics of hemodialysis patients with COVID-19.

| Chronic hemodialysis | | | | |
| --- | --- | --- | --- | --- |
| | Survival (n=12) | Death (n=6) | Overall (n=18) | P value |
| Age | 62,17 | 61,50 | 61,94 | 0,057 |
| Length of hospitalization (days) | 9,92 | 12,17 | 10,67 | **0,046** |
| Admission saturation (%) | 84,83 | 84,67 | 84,78 | **0,050** |
| Natremia (mmol/l) | 135,42 | 134,50 | 135,11 | 0,300 |
| Serum potassium (mmol/l) | 4,7917 | 4,8667 | 4,8167 | **0,038** |
| alkaline reserve (mmol/l) | 22,75 | 20,17 | 21,89 | 0,231 |
| C-reactive protein (mg/l) | 179,75 | 153,00 | 170,83 | 0,259 |
| Ast (IU/l) | 54,92 | 26,67 | 45,50 | 0,213 |
| Alt (IU/l) | 27,33 | 10,00 | 21,56 | 0,073 |
| Ferritinemia (ng/ml) | 1122,00 | 1489,50 | 1269,00 | 0,470 |
| LDH (IU/l) | 357,00 | 458,50 | 390,83 | 0,737 |
| Hemoglobin (g/dl) | 9,98 | 11,42 | 10,46 | 0,116 |
| White blood cells (/mm3) | 6416,6667 | 5966,6667 | 6266,6667 | **0,031** |
| platelet count (/mm3) | 221500,00 | 204500,00 | 215833,33 | 0,437 |
| neutrophils (/mm3) | 5218,00 | 4785,67 | 5073,89 | 0,064 |
| Lymphocytes (/mm3) | 634,67 | 581,83 | 617,06 | 0 ,376 |
| Prothrombin (%) | 86,92 | 91,33 | 88,39 | 0,052 |

**Table 2:-** Clinical and biological characteristics of patients with With Preexisting Kidney Disease.

| Outcomes | | | | |
| --- | --- | --- | --- | --- |
| Survival Preexisting Kidney Disease(n=2) | | Death (n=5) | Overall (n=7) | P value |
| Age (years) | 72,00 | 74,60 | 73,86 | **0,023** |
| length of hospitalization (days) | 12,00 | 9,00 | 9,86 | 0,411 |
| Admission saturation (%) | 91,00 | 81,20 | 84,00 | 0,990 |
| Natremia (mmol/l) | 139,00 | 134,60 | 135,86 | **0,003** |
| Serum potassium (mmol/l) | 4,9500 | 4,5600 | 4,6714 | 0,197 |
| alkaline reserve (mmol/l) | 18,50 | 21,20 | 20,43 | 0,723 |
| C-reactive protein (mg/l) | 305,50 | 212,68 | 239,20 | 0,540 |
| Ast (IU/l) | 24,50 | 92,60 | 73,14 | 0,244 |
| Alt (IU/l) | 10,50 | 40,80 | 32,14 | 0,278 |
| Hemoglobin (g/dl) | 11,10 | 11,98 | 11,73 | 0,247 |
| White blood cells (/mm3) | 9600,0000 | 8320,0000 | 8685,7143 | 0,373 |

| | | | | |
|---|---|---|---|---|
| platelet count (/mm3) | 161500,00 | 200800,00 | 189571,43 | 0,052 |
| neutophils (/mm3) | 8346,00 | 7069,80 | 7434,43 | 0,330 |
| Lymphocytes (/mm3) | 546,00 | 684,60 | 645,00 | 0,677 |
| prothrombin (%) | 83,50 | 66,25 | 72,00 | 0,490 |

**Table 3I:-** Clinico-biological characteristics according to nephrological status.

| | nephrological status | | | | | |
|---|---|---|---|---|---|---|
| | AKI (n=5) | | Pre existing CKD (n=7) | | Chronic hemidalysis (n=18) | |
| | Mean | Standard Deviation | Mean | Standard Deviation | Mean | Standard Deviation |
| Age (years) | 60,20 | 8,758 | 73,86 | 10,730 | 61,94 | 10,350 |
| length of hospitalization (days) | 12,40 | 3,647 | 9,86 | 3,761 | 10,67 | 3,789 |
| Admission saturation (%) | 82,80 | 8,815 | 84,00 | 9,469 | 84,78 | 9,956 |
| Creatinine (mg/l) | 35,40 | 59,597 | 55,57 | 31,262 | 108,94 | 61,512 |
| Urea (g/l) | 1,2820 | 1,79994 | 1,6457 | ,68036 | 1,2133 | ,53685 |
| Natremia (mmol/l) | 137,20 | 3,899 | 135,86 | 6,094 | 135,11 | 2,423 |
| Serum potassium (mmol/l) | 4,3000 | 1,39821 | 4,6714 | 1,00617 | 4,8167 | ,90245 |
| alkaline reserve (mmol/l) | 20,40 | 6,504 | 20,43 | 2,507 | 21,89 | 4,213 |
| C-reactive protein (mg/l) | 200,60 | 125,271 | 239,20 | 137,771 | 170,83 | 88,314 |
| Ast (IU/l) | 57,20 | 41,385 | 73,14 | 85,743 | 45,50 | 70,397 |
| Alt (IU/l) | 30,80 | 14,738 | 32,14 | 39,738 | 21,56 | 22,479 |
| Ferritinemia (ng/ml) | 2344,00 | 1653,078 | 3565,25 | 5409,152 | 1269,00 | 650,555 |
| LDH (IU/l) | 887,50 | 543,369 | 809,00 | 445,530 | 390,83 | 184,012 |
| Hemoglobin (g/dl) | 12,46 | 3,361 | 11,73 | 3,208 | 10,46 | 1,781 |
| White blood cells (/mm3) | 11180,0000 | 5857,64458 | 8685,7143 | 5517,97927 | 6266,6667 | 2612,63896 |
| platelet count (/mm3) | 287800,00 | 136856,494 | 189571,43 | 101475,542 | 215833,33 | 101137,792 |
| Neutrophils (/mm3) | 9932,00 | 6868,314 | 7434,43 | 5416,597 | 5073,89 | 2431,626 |
| Lymphocytes (/mm3) | 455,25 | 251,287 | 645,00 | 182,044 | 617,06 | 272,514 |
| prothrombin (%) | 72,40 | 9,099 | 72,00 | 28,086 | 88,39 | 5,078 |

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