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Morbidity and Mortality of Acute Renal Failure in COVID-19 Patients in Intensive Care According to Waves/Variant: Case of the Grand Hôpital de l'Est Francilien Site de Meaux

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Abstract

Introduction: The incidence of acute renal failure (ARF) varies between 20% and 40% of cases for COVID-19 patients admitted to the intensive care unit, with very high mortality, but heterogeneous according to the different epidemic waves, probably due to the genetic variant phenomenon of the virus. The aim of this study is to determine the morbidity and mortality of COVID-19 patients admitted with ARF to the intensive care unit of the Grand Hôpital Est Francilien (GHEF) according to the waves and variants. **Methods**: Cross-sectional observational study of COVID-19 patients with ARF admitted to the intensive care unit of the GHEF site in Meaux covering the period from March 1st 2020 to December, 31st 2021. Per-hospitalisation and outcome data were collected and analysed with SPSS version 25.0 software using the Chi-square or Fischer's exact test or Student's t-test and logistic regression for $p < 0.05$. **Results**: A total of 86 patients were included. The mean age was higher (70 ± 8.5) in patients in the fourth wave than in the other waves ($p = 0.015$), with male predominance in all waves without signif-

icant difference. Co-morbidities: hypertension, diabetes, heart disease, dyslipidaemia and arrhythmia complete with fibrillation were present in all waves. The majority of patients were classified as KDIGO 1 for the different waves (1st: 61.9%, 2nd: 86.5%, 3rd: 80%, and 4th: 75%), with the same trend according to variant (alpha: 80%, beta: 75%, delta: 81.3%, omicron: 75%). Mortality by the wave was: 1st: 28.5%, 2nd: 37.5%, 3rd: 23% and 4th: 11%) and by variant: alpha: 24.2%, beta: 44.8%, delta: 20.7%, omicron: 10.3%). Overall mortality was 33.7%. Case fatality was higher in the fourth wave. Hypertension, shock, failure to recover renal function, acute lung oedema, ventilator-associated lung disease and hyperkalaemia were factors associated with mortality ($p < 0.001$). **Conclusion**: Acute renal failure is common in COVID-19 patients admitted to the intensive care unit, and mortality is not negligible. The beta variants and the second wave presented more cases of renal impairment, although the mechanism is still unknown. Further studies are needed to understand this mechanism and perhaps to be able to identify the cause.

Keywords

Mortality, COVID-19 Morbidity, Renal Failure, Intensive Care Unit

1. Introduction

Acute renal failure (ARF) is a complication frequently encountered during SARS-COV-2 pneumonia, with an incidence of 20% to 40% in COVID-19 patients admitted to the intensive care unit (ICU) [1], and different histological phenotypes ranging from acute tubular necrosis to glomerular damage, in particular the collapsing form, have been found [2] [3] [4] [5].

Studies have shown that the mortality rate of COVID-19 patients developing renal failure is high, ranging from 8% to 23% [1]. One study found that 6.7% of patients with COVID-19 developed renal failure, and mortality in this sub-population was estimated at 91.7% [1]. Hirsch JS et al in the USA in 2020 found that out of 1395 COVID-19 patients admitted to intensive care, 76% developed ARF, with a mortality rate of 23.5% [6]. A multicentre study carried out in 4 intensive care centres in Paris found that out of 379 COVID-19 patients admitted to intensive care, half had developed ARF, including 15% stage 1, 12% stage 2 and 25% KDIGO stage 3, with a mortality rate on day 28 of 25.4% [7]. In China, Cao in 2020 reported an incidence of acute kidney injury (AKI) of 44.4% and a mortality rate of 32.3% [8]. In Africa, in Burkina-Faso: Delma, working on the prevalence and factors associated with acute renal failure during COVID-19 in patients admitted to the intensive care unit, found a prevalence of 16.07% and a mortality rate of 1.8% [9]. In Tunisia, in 2020, out of 28 patients admitted to intensive care, Karray found an incidence of 25% for AKI with a mortality rate of 26.3% [10]. The management of this ARF, in particular extrarenal purification, which concerns 17% to 21% of patients [11] [12], is not unusual [5].

These variations in mortality could be partly explained by genetic factors, in particular mutation, the different variants of the SARS-COV-2 virus and their waves of contamination. There are no published studies that have investigated the morbidity and mortality of COVID-19 patients developing ARF according to waves and variants. This study was conducted at the Grand Hôpital Est Francilien with this objective in mind.

2. Methods

2.1. Type and Population of the Study

This is a cross-sectional observational study conducted in the intensive care unit of the Grand Hôpital Est Francilien (GHEF) site in Meaux from March, 1st 2020 to December, 31st 2021. The population consisted of all COVID-19 patients who had developed acute renal failure during hospitalisation in the intensive care unit.

2.2. Patients Selection

Patients at least 18 years of age, with a positive COVID-19 PCR test and variant typing, who developed acute renal failure during hospitalisation in intensive care were included. The following were excluded: patients transferred to another intensive care unit for any reason, patients with renal failure prior to admission to the intensive care unit, and patients whose records were missing variables of interest. Patients were recruited consecutively according to order arrival. We selected patients over four covid waves, the first wave from March 2020 to August 2020, the second wave from September 2020 to February 2021, the third wave from March 2021 to June 2021 and the fourth wave from August 2021 to December 2021. Period of appearance of the different variants were: alpha in May 2020, beta in January 2021, delta in May 2021 and omicron in November 2021.

2.3. Data Collection

Data were collected by the principal investigator from the patients' computerised records from admission to the ICU up to day 28. The variables of interest were:

- Socio-demographic: age, sex, race, wave of the epidemic. We have selected 4 waves: first, second, third and fourth.

- Clinical: weight, height, co-morbidities, systolic and mean arterial pressure, peripheral oxygen saturation (SpO_2), episodes of hyper- or hypotension, diuresis.

- Paraclinical: creatinemia (day 1 to day 10 and day 28), urea, natremia, kalemia, blood gas, COVID-19 PCR, variant, bacteriology, chest CT scan. Four variants have been selected: alpha, beta, delta and omicron.

- Therapeutics: ventilatory parameters: tidal volume (Vt), positive end-expiratory pressure (PEEP), FiO_2, fraction of inspired oxygen (FiO_2), respiratory rate (RR) and plateau pressure; use of catecholamines; vascular filling (quantity and quality); other nephrotoxic treatments, recourse to extra-renal purification

(ERP).

- Evolutionary: complications, length of stay in intensive care, mortality at Day 10 and Day 28 and causes of death.

In this work the definition of acute renal failure is that of KDIGO 2012 (see Table 1) which is based on:

1) Increase in creatinemia between 2 samples taken within 48 hours.

2) An increase of more than 50% in creatinine levels within a known or presumed interval of 7 days.

3) Diuresis between 6 and 12 hours.

Table 1. KDIGO classification of renal failure.

Severity stage	Serum creatinine	Urine output
1	- rise ≥ 0.3 mg/dl (26.5 µmol/l) over 48 hours - increase of 1.5 to 1.9 times the baseline value over 7 days	- oliguria < 0.5 ml/kg/h for 6 to 12 hours
2	- 2 to 2.9 fold increase on baseline	- oliguria < 0.5 ml/kg/h for more than 12 hours
3	- elevation ≥ 3 times the basal value - elevation ≥ 4.0 mg/dl (≥353.6 µmol/l) or initiation of extrarenal purification	- oliguria < 0.3 ml/kg/h for more than 24 hours - anuria for 12 hours.

2.4. Statistical Analysis

The data were entered using Microsoft Excel version 2013, double-checked, encoded and transferred to SPSS version 25.0 for analysis. The Chi-square or Fischer's exact test was used to compare proportions, and the Student's t-test was used to compare means. The search for associated factors was carried out using logistic regression with calculation of the Odd ratios and their 95% confidence intervals. For all tests, the p-value was set at ≤0.05.

2.5. Ethical and Regulatory Aspects

The protocol was approved by the local ethics committee and authorised by the head of department. The principles of the Helsinki Convention, in particular confidentiality and anonymity, were respected throughout the data collection and analysis process. Informed consent was impossible because we worked on the files. We have no conflict of interest in this study.

3. Results

3.1. Patient Flow Diagram

During this period, 216 patients were admitted to the intensive care unit, 130 had an ARF and 44 were excluded, transferred to other health structures for extracorporeal membrane oxygenation (ECMO), 24 patients or the presence of an ARF before admission (24) on and therefore excluded. Finally, we analysed the records of 86 patients, *i.e.* 39.8%.

3.2. General Characteristics of Patients by Wave

Table 2 shows the general characteristics of patients by wave.

The mean age (year) was higher (70 ± 8.5) for patients in the fourth wave and lower (59 ± 11.3) for those in the first wave; it was (67 ± 11.9) in the second wave and (65.1 ± 11.8) in the third wave, and the difference was significant ($p = 0.015$). Male gender predominated in all waves with no significant difference ($p = 0.833$). Comorbidities (arterial hypertension, diabetes, heart disease, dyslipidaemia, complete arrhythmia due to atrial fibrillation) were present in patients in all waves with no significant difference ($p > 0.05$). Kalaemia was often below 6mmol/l in many patients in all waves and above 6 mmol/l in few patients with no significant difference ($p = 0.244$). Mean creatinemia was higher in patients in the third wave on day 5 (155 ± 105.8), ten (425.3 ± 172.9) and twenty-eight (439.6 ± 76, 4) compared with those in the other waves (109.2 ± 39 to 134.8 ± 56.6 on day 5, 266.2 ± 132.5 to 367.5 ± 61.5 on day 10 and 168.7 ± 120.1 to 355.5 ± 194.4 on day 28) with a significant difference ($p < 0.001$).

3.3. Distribution of Patients by Wave and Variant

Table 3 shows the distribution of patients by wave and variant.

The first wave had 21 patients (24.4%), of whom 10 (47.6%) had variant alpha, 11 (52.4%) had variant beta and none had variants delta or omicron. The second wave had 37 patients (37%), 16 (43.2%) with variant alpha, 21 (56.8%) with variant beta and none with variant delta or omicron. The third had 20 patients (23.3%), none with the alpha variant, 4 (20%) with the beta variant and 16 (80%) with the delta variant and none with the omicron variant. The fourth had 8 patients (9.3%), all with the omicron variant (100%). The variants were: alpha, 26 patients or 30.2%, beta, 36 patients or 41.86%, delta, 16 patients or 18.6% and omicron 8 or 9.3% with a significant difference.

3.4. Therapeutic Characteristics

Table 4 shows the therapeutic characteristics

The mean inspired oxygen fraction (FiO_2) was 91.22%, positive end-expiratory pressure (PEEP) was 12.65 cmH_2O, plateau pressure was 28.32 cmH_2O, oxygen saturation was 81.88%, respiratory rate was 27.73, tidal volume was 469.80 ml, P/F ratio was 80.97 mmHg. ARDS was moderate in 29 patients (33.7%) and severe in 57 (66.3%). The mean number of days in prone position was 1.86. Intubation was required in 65 patients (75.6%) and the mean duration of intubation was 21.15 days. All patients had received claforan and rovamycin, 83 patients (96.5%) had received radiological contrast media, 60 patients (69.8%) had received corticosteroids, 34 patients (39.5%) had received aminoglycosides, 59 patients (68.6%) had been curarised, 26 patients (30.2%) had received tazocillin and 25 patients (29.1%) had received extrarenal renal replacement therapy (ERT). The average duration of ERT was 17.2 days and the average ERT time was 8.4 days.

Table 2. General characteristics of patients by wave.

Variables	Waves				p
	1st	2nd	3rd	4th	
	n = 21	n = 37	n = 20	n = 8	
Age, year					
Mean ± SD	59 ± 11.3	67 ± 11.9	65.1 ± 11.8	70 ± 8.5	**0.015**
Sex					0.833
Male	12 (57.1)	24 (64.9)	13 (65)	6 (75)	
Female	9 (42.9)	13 (41.9)	7 (35)	2 (25)	
Comorbidities					
HTA					
No	10 (47.6)	19 (51.4)	8 (40)	5 (62.5)	0.722
Yes	11 (52.4)	18 (48.6)	12 (60)	3 (37.5)	
Diabetes					
No	12 (57.1)	25 (67.6)	11 (55)	4 (50)	0.684
Yes	9 (42.9)	12 (32.4)	9 (45)	4 (50)	
Heart disease					
No	16 (76.2)	23 (62.2)	10 (50)	5 (62.5)	0.388
Yes	5 (23.8)	14 (37.8)	10 (50)	3 (37.5)	
Dyslipidemia					
No	19 (90.5)	29 (78.4)	14 (70)	6 (75)	0.434
Yes	2 (9.5)	8 (21.6)	6 (30)	2 (25)	
AFA					
No	20 (95.2)	29 (78.4)	16 (80)	4 (50)	0.053
Yes	1 (4.8)	8 (21.6)	4 (20)	4 (50)	
Biology					
Kalaemia (mmol/l)					
>6	8 (38.1)	6 (16.2)	5 (25)	1 (12.5)	0.244
<6	13 (61.9)	31 (83.8)	15 (75)	7 (87.5)	
Creat (µmol/l) D5					
Mean ± SD	109.2 ± 39	134.8 ± 56.6	155 ± 105.8	114 ± 4.2	**<0.001**
Creat (µmol/l) D10					
Mean ± SD	357.7 ± 197.6	266.2 ± 132.5	425.3 ± 172.9	367.5 ± 61.5	**<0.001**
Creat (µmol/l) J28					
Mean ± SD	355.5 ± 194.4	168.7 ± 120.1	439.6 ± 76.4	260 ± 70.7	**<0.001**

Legend: HTA = arterial hypertension, AFA = atrial fibrillation arrhythmia, Creat = creatinemia, SD = standard deviation, D = day.

Table 3. Distribution of variants according to the different waves and variants.

Variant	Waves					p
	Total	1st	2nd	3rd	4th	
	n = 86 (%)	n = 21 (%)	n = 37 (%)	n = 20 (%)	n = 8 (%)	
Alpha	26 (30.2)	10 (47.6)	16 (43.2)	0	0	**<0.001**
Beta	36 (41.86)	11 (52.4)	21 (56.8)	4 (20)	0	
Delta	16 (18.6)	0	0	16 (80)	0	
Omicron	8 (9.3)	0	0	0	8 (100)	

Table 4. Therapeutic characteristics.

Variable	n = 86	%
FiO_2, *%,* mean ± ET	**91.22** (89.46 - 93.07) ± 9.11	
$PaCO_2$, *mm Hg,* mean ± SD	**38.12** (35.69 - 40.51) ± 11.28	
PaO_2, *mm Hg, mean* ± SD	**59.43** (57.58 - 61.49) ± 8.69	
PEEP, *cm H_2O, mean* ± SD	**12.65** (12.31 - 13.06) ± 1.76	
Plateau pressure, *cm H_2O* mean ± SD	**28.32** (27.63 - 28.91) ± 2.48	
Saturation, %, mean ± SD	**81.88** (80.61 - 82.84) ± 4.38	
PAM, mm Hg, mean ± SD	**57.33** (56.27 - 58.60) ± 4.90	
RR, mean ± SD	**27.73** (26.85 - 28.34) ± 3.75	
VTE, mean ± SD	**469.80** (448.80 - 488.74) ± 82.05	
P/F mm Hg, mean ± SD	**80.97** (76.01 - 86.03) ± 26.58	
ARDS (P/F)		
Moderate	**29**	**33.7**
Severe	**57**	**66.3**
Variable	**n = 86**	**%**
Number PP: mean ± SD	1.86 (1.29 - 2.45) ± 2.32	
Duration OTI	21.15 (18.48 - 24.91) ± 13.95	
Curare	59	68.6
Intubation	65	75.6
Contrast agent	83	96.5
Corticosteroids	60	69.8
Aminoglycoside	34	39.5
Tazocillin	26	30.2
Claforan	86	100.0
Rovamycin	86	100.0
EEP	25	29.1
Duration EEP, day, mean ± SD	17.20 (11.36 - 23.03) ± 16.48	
Admission time-EEP, day, mean ± SD	8.40 (6.05 - 11.55) ± 6.65	

Legend: FiO_2 = fraction inspired in oxygen, SD = standard deviation, PEEP = positive end-expiratory pressure, PP = prone position, VTE = tidal volume, P/F = partial pressure of oxygen in arterial blood on fraction inspired in oxygen, RR = respiratory rate, ARDS = acute respiratory distress syndrome, prone position, OTI = orotracheal intubation, EEP = extra-renal purification.

3.5. Characteristics of Patients with Acute Renal Failure According to KDIGO, by Wave and Variant

Table 5 shows the characteristics of patients with acute renal failure according to KDIGO, by wave and variant.

Table 5. Characteristics of patients with acute renal failure according to KDIGO as a function of waves and variant.

Variables		KDIGO 1st stage	KDIGO 2nd stage	KDIGO 3rd stage
Variant	**Total**			
Alpha	26 (100%)	21 (80.8%)	3 (11.5%)	2 (7.7%)
Beta	36 (100%)	27 (75%)	8 (22.2%)	1 (2.8%)
Delta	16 (100%)	13 (81.3%)	2 (12.5%)	1 (6.3%)
Omicron	8 (100%)	6 (75%)	2 (25%)	0 (0%)
Waves				
1st	21 (100%)	13 (61.9%)	6 (28.6%)	2 (9.5%)
2nd	37 (100%)	32 (86.5%)	4 (10.8%)	1 (2.7%)
3rd	20 (100%)	16 (80%)	3 (15%)	1 (5%)
4th	8 (100%)	6 (75%)	2 (25%)	0 (0%)

There were 26 patients with variant alpha, 21 (80.8%) of whom were at KDIGO stage 1, 3 (11.5%) at KDIGO stage 2 and 2 (7.7%) at KDIGO stage 3. There were 36 patients with the beta variant, of whom 27 (75%) were KDIGO stage 1, 8 (22.2%) were KDIGO stage 2 and 1 (2.8%) was KDIGO stage 3. There were 16 patients with the delta variant, 13 (81.3%) of whom were at stage 1 of KDIGO, 2 (12.5%) at stage 2 and 2 (7.7%) at stage 3 of KDIGO. There were 8 patients with the omicron variant, of whom 6 (75%) were KDIGO stage 1, 2(25%) were KDIGO stage 2 and none were KDIGO stage 3. During the first wave with 21 patients: 13 (61%) were at stage 1 of KDIGO, 6 (28.6%) at stage 2 and 2 (9.5%) at stage 3 of KDIGO. During the second wave with 37 patients: 32 (86.5%) were at stage 1 of KDIGO, 1 (10.8%) at stage 2 and 1 (2.7%) at stage 3 of KDIGO. In the third wave of 20 patients: 16 (80%) were at KDIGO stage 1, 3 (15%) at KDIGO stage 2 and 1 (2%) at KDIGO stage 3.

3.6. Changes in Creatinemia, Diuresis and Mortality by Wave and Variant

Figure 1 shows changes in creatinemia, diuresis and mortality by wave and variant.

The first wave had 28.5% deaths, the 2nd wave 37.5%, the 3rd wave 23% and the 4th wave 11%. Mortality by variant was: Alpha 24.2%, Beta 44.8%, Delta 20.7%, Omicron 10.3%. Diuresis decreased from day 5 to day 28 for all variants except for the alpha variant whose diuresis increased from day 10 to day 28. Creatinine increased from day 5 to day 28 for all variants and for all waves except for waves 3 and 4, where it remained constant from day 10 to day 28. Diuresis decreased from day 5 to day 28 for all variants and waves except for variant alpha where it increased from day 10 to day 28 and for waves 2 and 4 where it increased from day 5 to day 28.

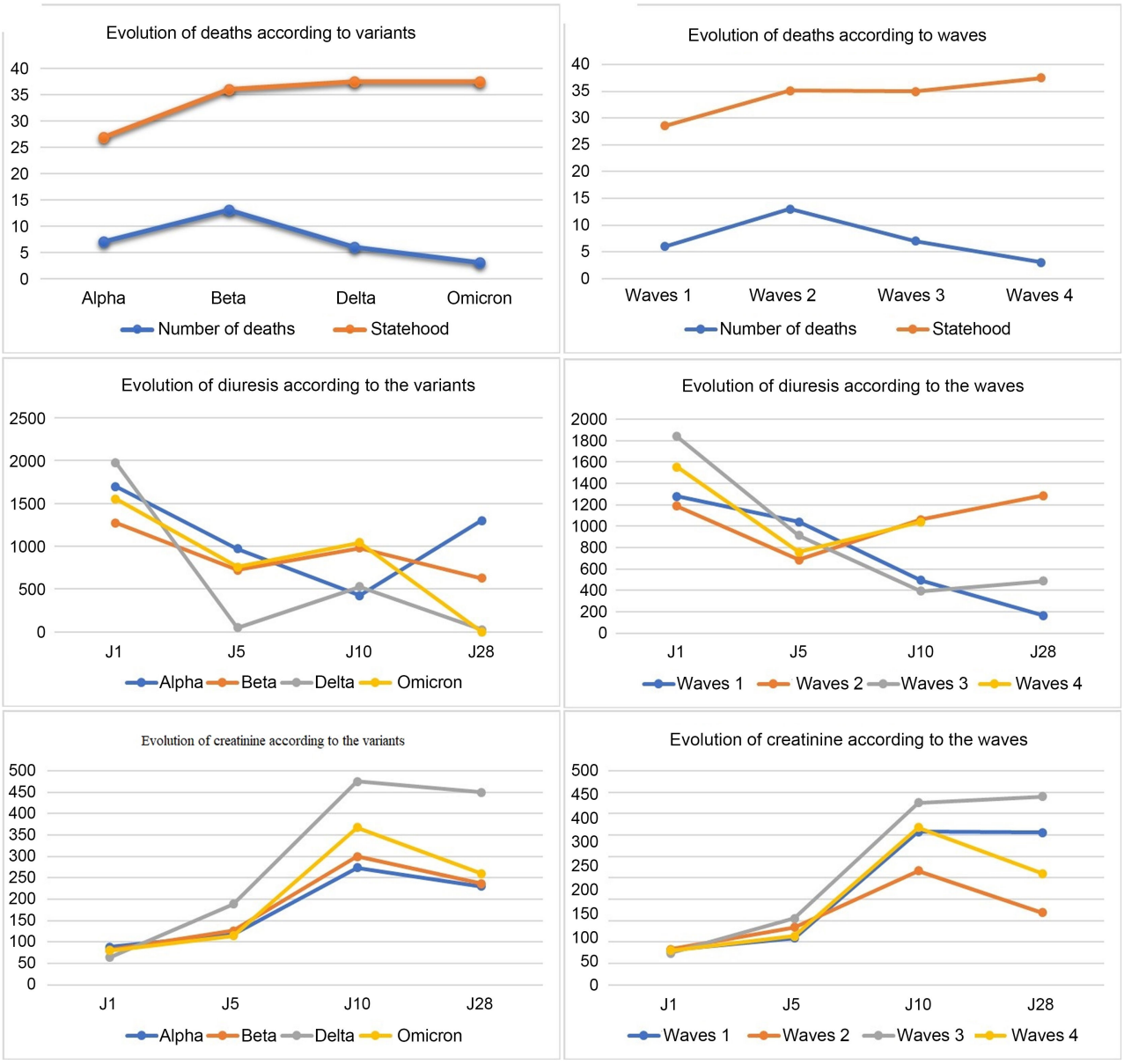

Figure 1. Trends in creatinemia, diuresis and mortality according to wave and variant.

3.7. Overall Mortality

Figure 2 presents the overall mortality

Overall mortality was 29 of the 86 patients with renal impairment 33.7% *i.e.*

3.8. Factors Associated with Mortality for All Patients

Table 6 presents the factors associated with mortality.

In multivariate analysis, hypertension (ORa: 8.8 (2.9 - 26.8)), the presence of heart disease (ORa: 2.5 (1 - 6.3)), hyperkalaemia (ORa: 3.5 (2.1 - 6)), acute lung oedema (ORa: 6.9 (1.9 - 24.8), failure to recover normal renal function (ORa2.5 (1 - 4.5), mechanically ventilated lung disease (ORA:6.5 (2.6 - 11.3) and shock ORa:8 (2.4 - 25.9) were associated with mortality ($p < 0.05$). The presence of

pressure sores (eschar), which was associated with mortality in the univariate analysis (p = 0.013), did not persist in the multivariate analysis (p = 0.064).

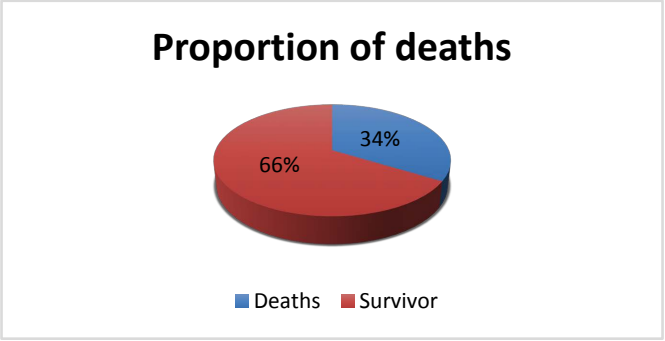

Figure 2. Overall mortality.

Table 6. Factors associated with mortality.

Variables	Univariate analysis		Multivariate analysis	
	P	OR (CI 95%)	p	ORa (CI 95%)
Comorbidities				
HTA				
No		1		1
Yes	<0.001	1.9 (1.3 - 2.7)	**0.001**	8.8 (2.9 - 26.8)
Heart disease				
No		1		1
Yes	0.047	1.3 (1 - 2)	**0.041**	2.5 (1 – 6.3)
Clinic/biology				
Hyperkalaemia				
No		1		1
Yes	<0.001	1.2 (1 - 3.2)	**<0.001**	3.5 (2.1 - 6)
APO				
No		1		1
Yes	0.001	2.5 (1.1 - 5.9)	**0.002**	6.9 (1.9 - 24.8)
Complications				
Recover of normal renal fonction				
Yes		1		1
No	<0.001	1 (0.8 - 1.5)	**0.001**	2.5 (1.1 - 4.5)
VAP				
No		1		1
Yes	0.040	2.9 (1.2 - 4.6)	**0.021**	6.5 (2.6 - 11.3)
Shock				
No		1		1
Yes	<0.001	1.8 (1.3 - 2.4)	**<0.001**	8 (2.4 - 25.9)
Eschar				
No		1		1
Yes	0.013	0.3 (0.2 - 0.4)	0.064	0.1 (0.01 - 0.3)

Legend: HTA = high blood pressure, APO = acute pulmonary oedema, VAP = ventilator-associated pneumonia.

4. Discussion

This study found that 86 patients (39.8%) presented with kidney damage during hospitalisation. Mortality was higher in the second wave and with the omicron variant. Renal damage was more frequent with the beta variant in 36 out of 86 patients (41.2%) and the alpha variant in 26 out of 86 patients (30.2%). Recovery of diuresis was more rapid with variant alpha and waves 2 and 4, although renal damage was more numerous in the second wave. Only 4 patients were at KDIGO stage 3. Overall mortality was 33.7%, associated with factors described in the literature (hypertension, diabetes, heart disease, etc.).

The mean age of our patients was 64.89 ± 11.82 years, with the majority (58.1%) aged ≥ 65 years. These results corroborate the data in the literature [9] [13] [14]. However, Nlandu [15] in the Democratic Republic of Congo, a country with a short life expectancy, reported a younger average age of 55.6 ± 13.2 [13]. Similarly, males predominated in our study, as other authors have noted [13] [15] [16]. It is probable that the reduction in expression of the angiotensin 2 receptor (ACE2), the SARS-Cov2 receptor, by oestrogens explains this difference, testosterone increasing the expression of this receptor [17]. The beta variant predominated in the first and second waves, the delta in the third and the omicron in the fourth, probably because of the adaptation of the immune system to control the virus and the change in the virus genes to escape the immune system, without excluding the potential role of vaccination. Many of the patients had comorbidities, particularly cardiovascular, as reported in the literature [13] [14] [15].

The use of invasive ventilation was 75.6%, the mean inspired oxygen fraction was 91% ± 22%, and positive expiratory pressure was high in both young and old patients, with a mean of 12.65% ± 1.76%. Geehan Suleyman found that 90% of patients requiring invasive ventilation had a FiO_2 greater than 50% [15]. However, Nlandu et al in a context of limited resources reported 26.4% recourse to artificial ventilation without determining the ventilatory parameters of these patients [13]. Giacomo Grasselli *et al.*: the use of invasive ventilation was 99%, the pep level was very high in both young and adult patients, with an average of 14 cmH_2O, inspiration oxygen fraction was over 50% in young patients and over 70% in adult patients [13]. It should be noted that the need for ventilation, as well as the level of pep and FiO_2, depends on the severity of the patient.

In our series, the majority of patients were KDIGO 1 (77.90%), followed by KDIGO 2 (17.40%) and KDIGO 3 (4.70%). Xia reported more than 40% of patients classified as KDIGO stage 3. However, Rubin found: stage I (35%), stage II (35%) and stage III (30%). Chan L found: stage I 39%, stage II 19% and stage III 42% [18] [19] [20]. The timing of the assessment of the KDIGO stage may explain the differences between the results of the different authors. Wave 2 and variant beta seem to be accompanied by the most renal damage, without any clear explanation.

We recorded a death rate of 37.5% in wave 2, 28.5% in wave 1, 23% in wave 3

and 11% in wave 4. The beta variant was associated with a higher death rate than the other variants (Beta 44.8%, Alpha 24.2%, Delta 20.7%, Omicron 10.3%). The beta variant appeared to be associated with severe disease. Mutation of the omicron variant reduced virulence and lethality. Overall mortality in our series was 33.3%, higher than Grasseli (26%) [13], Khalil [16]: 11.2% with a larger sample size. In DR Congo, Nlandu [15] and Makulo [21] reported rates of 6 and 20.3% respectively in intensive care patients, who were therefore less serious. The factors associated with mortality, in particular comorbidities, are those cited in the literature [11] [14].

5. Limitations

The study being monocentric, the results cannot be generalised without risk of error. In addition, a comparative study on the mortality of COVID-19 patients with renal insufficiency and those without would have provide more insights. Some statistical tests were not carried out because of the small sample size (for example, to compare the frequency of ARF and mortality by wave and variant.

The strength of this study is that it confirms that renal failure is frequent in COVID-19 patients, with a significant mortality rate.

6. Conclusion

Acute renal failure is common in COVID-19 patients admitted to intensive care, with a significant mortality rate. The beta variants and the second wave presented more cases of renal impairment, although we do not know the mechanism. Further studies are needed to understand this mechanism and perhaps be able to implement preventive measures.

Authors' Contributions

Khazy Anga: conception of the study and drafting of the manuscript.
Wilfrid Mbombo: conception of the study and drafting of the manuscript.
Vivien Hong Tuan HA: conception of the study.
Éric Amisi: conception of the study and reading of the manuscript.
All other authors: reading and correction of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Martinez-Rojas, M.A., Vega-Vega, O. and Bobadilla, N.A. (2020) Le rein est-il une

cible du SRAS-CoV-2? *American Journal of Physiology-Renal Physiology*, **318**, F1454-F1462. https://doi.org/10.1152/ajprenal.00160.2020

[2] Wang, D., Hu, B., Hu, C., Zhu, F., Liu, X. and Zhang, J. (2020) Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*, **323**, 1061-1069. https://doi.org/10.1001/jama.2020.1585

[3] Gupta, S., Coca, S.G. and Chan, L. (2020) AKI Treated with Renal Replacement Therapy in Critically Ill Patients Covid-19. *Journal of the American Society of Nephrology*, **32**, 161-176. https://doi.org/10.1681/ASN.2020060897

[4] Hoffman, M., Kleine-Weber, H. and Schroeder, S. (2020) ARS-Cov-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*, **181**, 271-280. https://doi.org/10.1016/j.cell.2020.02.052

[5] Mizuiri, S. and Ohashi, Y. (2015) ACE and ACE2 in Kidney Disease. *World Journal of Nephrology*, **4**, 74-82. https://doi.org/10.5527/wjn.v4.i1.74

[6] Hirsch, J.S., Ng, J.H., Ross, D.W., Sharma, P., Shah, H.H., Barnett, R.L., *et al.* (2020) Acute Kidney Injury in Patients Hospitalized with Covid-19. *Kidney International*, **98**, 209-218. https://doi.org/10.1016/j.kint.2020.05.006

[7] Gabarre, P., Dumas, G. and Zafrani, L. (2021) Insuffisance rénale aiguë chez les patients COVID-19 en soins intensifs. *Médecine Intensive Réanimation*, **30**, 43–52. https://doi.org/10.37051/mir-00069

[8] Cao, M., Zhang, D., Wang, Y., *et al.* (2020) Clinical Features of Patients Infected with the 2019 Novel Coronavirus (Covid-19) in Shanghai, China. https://doi.org/10.1101/2020.03.04.20030395

[9] Delma, S., Akodmo, S.I., Bonzi, Y.J., Zochinga, P., Traore, S.H., Sanogo, S.E., *et al.* (2021) L'insuffisance rénale aigue au cours de la Covid-19 au Burkina Faso: Prévalence et facteurs associés. *Néphrologie & Thérapeutique*, **17**, 383. https://doi.org/10.1016/j.nephro.2021.07.084

[10] Karray, R., Jamoussi, A., Ayed, S., Lakhdhar, D., Rachdi, E., Ben Khelil, J., *et al.* (2020) Surmortalité de l'insuffisance rénale aiguë oligoanurique au cours de la COVID-19: Étude prospective tunisienne. *Néphrologie & Thérapeutique*, **16**, 312. https://doi.org/10.1016/j.nephro.2020.07.170

[11] Cheng, Y., Luo, R., Wang, K., Zhang, M., Wang, Z. and Dong, L. (2020) Kidney Disease Is Associated with in Hospital Death of Patients with COVID-19. *Kidney International*, **97**, 829-838. https://doi.org/10.1016/j.kint.2020.03.005

[12] Yang, X., Yu, Y., Xu, J., Shu, H., Xia, J. and Liu, H. (2020) Clinically Course and Outcomes of Critically Ill Patients with SARS-Cov-2 Pneumonia in Wuhan, China: A Single-Centered, Retrospective Observational Study. *The Lancet Respiratory Medicine*, **8**, 475-481. https://doi.org/10.1016/S2213-2600(20)30079-5

[13] Grasseli, G., Zangrillo, A., *et al.* (2021) Baseline Characteristics and Outcomes of 1591 Patients Infected with SARS-CoV2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA*, **323**, 1574-1581. https://doi.org/10.1001/jama.2020.5394

[14] Suleyman, G., Fadel, R.A., Malette, K.M., *et al.* (2020) Clinical Characteristics and Morbidity Associated with Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Network Open*, **3**, e2012270. https://doi.org/10.1001/jamanetworkopen.2020.12270

[15] Nlandu, Y., *et al.* (2021) Predictors of Mortality in Covid-19 Patients at Kinshasa Medical Center and a Survival Analysis: Retrospective Cohort Study. *BMC Infectious Diseases*, **21**, Article No. 1272. https://doi.org/10.1186/s12879-021-06984-x https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06984-x

[16] Khalil, M., Mehdi, R., *et al.* (2023) Analyse de survie de la durée du séjour des pa-

tients ateints de la Covid-19 dans la province d'Ilam, en Iran. *Journal of Clinical Medicine*, **12**, Article 6678. https://doi.org/10.3390/jcm12206678

[17] Murrel, D.F. and Murase, J.E. (2020) The Potential Protectrice Effect of Estrogen: A Plausible Theory for Why COVID-19 Mortality Is Lower in Females. *International Journal of Women's Dermatology*, **6**, 152-153. https://doi.org/10.1016/j.ijwd.2020.04.011

[18] Xia, P., Wen, Y., Duan, Y., *et al.* (2020) Clinicopathological Features and Outcomes of Acute Kidney Injury in Critically Ill COVID-19 with Prolonged Disease Course: A Retrospective Cohort. *Journal of the American Society of Nephrology*, **8**, 475-481. https://doi.org/10.1681/ASN.2020040426

[19] Rubin, S., Orieux, A., Prevel, R., *et al.* (2020) Characterization of Acute Kidney Injury in Critically Ill Patients with Severe Coronavirus Disease 2019. *Clinical Kidney Journal*, **13**, 354-361. https://doi.org/10.1093/ckj/sfaa099

[20] Chan, L., Chaudhary, K., Saha, A., *et al.* (2020) AKI in Hospitalized Patients with COVID-19. *Journal of the American Society of Nephrology*, **32**, 151-160. https://doi.org/10.1681/ASN.2020050615

[21] Makulo, J.R., Manzambi, B.M., Nlandu, Y.M., Mandina, M.N., Kutoloka, C.M., *et al.* (2020) Surveillance des décès aux Cliniques Universitaires de Kinshasa (RDC): La COVID-19 a-t-elle entraîné une surmortalité? *Annales Africaines de Médecine*, **14**, 3923-3929.