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Predictive Factors of Renal Failure in Covid 19 Patients at the Anti-Covid Center in Lome, Togo

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Abstract

Background: Angiotensin-converting enzyme 2 has been identified as the receptor that allows the entry of SarsCov2 into the human cell. Its expression in the kidney is 100 times higher than in the lung; thus, making the kidney an excellent target for SarsCov2 infection manifesting as renal failure (RF). The objective of this study was to determine the predictive factors of RF during covid-19 in the Togolese context.

Patients and Methods: This was a retrospective descriptive and analytical study conducted at the Lomé Anti-Covid Center including the records of patients hospitalized for covid 19, of age ≥ 18 years and having performed a creatinemia. RF was defined by a GFR < 60 ml/min/1.73 m2 calculated according to the MDRD formula. Patients were randomized into 2 groups according to GFR<60 or not. Statistical tests used were Pearson's Chi-2 test or Fisher's exact test for qualitative variables and Mann-Whitney test or Wilcoxon test for quantitative variables. The significance level was set at 0.05. Univariate and multivariate logistic regression was performed to search for associated factors.

Results: 482 patients were selected for this study with a mean age of 58.02 years. Sixty-five percent of the patients were men, i.e., a sex ratio of 1.88. Fifty-two patients had RF, i.e., a frequency of 10.8%. There were 65% men (315 cases), for a sex ratio (M/F) of 1.88. Risk factors for renal failure in covid-19 were age ≥ 65 years (ORa 2.42; CIa95% [1.17 - 4.95]; p=0.016), anemia (ORa 2.49; CIa95% [1.21 - 5.26]; p=0.015), moderate (ORa 13; CIa95% [2.30 - 2.44]; p=0.017), severe (ORa 26.2; CIa95% [4.85 - 4.93]; p= 0.002) and critical (ORa 108; CIa95% [16.5 - 21.76]; p<0.001) severity stages at admission.

Conclusion: Renal failure would therefore be related to the severity of covid 19 and is the most formidable factor, conditioning the course of the disease and the patient's vital prognosis.

Keywords: Covid-19, renal failure, risk factors, Togo

Introduction

Covid 19 is a global pandemic caused by SarsCov2 (Severe Acute Respiratory Syndrome Coronavirus 2) identified in China and is responsible for unexplained severe pneumonitis [1,2]. As of June 30, 2022, this infectious disease has affected more than 550 million people worldwide and killed nearly 6,500,000 people. This has earned it the status of a Public Health Emergency of International Concern (PHEIC) by the WHO because of its high capacity for spread [3]. Angiotensin-converting enzyme 2 (ACE2) has been identified as the receptor that allows the entry of SarsCov2 into the human cell. Its

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expression in the kidney is 100 times higher than in the lung; thus, making the kidney an excellent target for SarsCov2 infection manifesting as renal failure (RF) [4, 5]. RF is the impairment of the emunctory function of the kidney, preventing the internal balance of the organism, either by a decrease in renal blood flow, or by damage to the renal tissue with filtration disorders, or by abnormalities in the excretion of the urine formed [6]. The incidence of renal failure varies from 0.5 to more than 20% in patients undergoing conventional hospitalization and from 14-35% in intensive care [7]. However, in general, and particularly in Togo where there is no data concerning renal damage, the parameters that allow the prediction of renal evolution and prognosis when Covid-19 is discovered remain unknown, despite the high frequency of renal failure during this condition. Thus, it seemed necessary to us to conduct the present study whose objective is to determine the predictive factors of renal failure in Covid-19 patients at the Lomé Anti-Covid Center.

Patients And Method

This was a retrospective study with a descriptive and analytical aim covering the period from 21 March 2020 to 28 February 2021 (12 months) and focusing on the records of patients infected with SarsCov2 hospitalized at the Lomé Anti-Covid Center. Were included the records of patients of age ≥ 18 years, in whom the diagnosis of Covid-19 was made by PCR; having performed a minimum assessment made of creatinine. Not included in the study were the records of patients aged <18 years and those with renal failure before admission. Data were collected from the hospitalization register and individual patient records. The parameters studied were socio-demographic, clinical, paraclinical, therapeutic and evolutionary. Renal failure was defined as glomerular filtration rate (GFR) <60 ml/min/1.73m2 and was calculated using the simplified MDRD formula. Patients were randomized into 2 groups: 1 with GFR <60 ml/min/1.73m2 and the other with GFR ≥60 ml/min/1.73m2.

Data were entered into an electronic xlsform deployed through the Kobo Toolbox platform, which is a national platform set up to contain all data on Covid-19-positive patients. The resulting database was analyzed with R 4.0.4 software (R Core Team, Vienna) in the RStudio 1.4 environment. A comparative analysis was performed between the two groups. Statistical tests used were Pearson's Chi-2 test or Fisher's exact test for qualitative variables and Mann-Whitney test or Wilcoxon test for quantitative variables. The significance level was set at 0.05. Univariate and multivariate logistic regression was performed to search for associated factors. From an ethical point of view, we obtained the agreement of the bioethics committee and the written consent of all patients included in the study for the use of their biomedical data. Patients were informed about the nature and objectives of the study. The confidentiality of the biomedical data collected was ensured by the anonymity of the survey forms.

Results

During the study period, of the 801 inpatients in Covid 19, 503 had achieved creatinine levels. And of the 503 patients, we retained 482 and excluded 21 (18 for age <18 years and 3 for renal failure before Covid). 52 patients had renal failure, a frequency of 10.8% [CI95% 8.02-13.56%]. The mean age in the general population with creatinine was 45.72 ± 15.9 years (extremes 18-100 years). There were 65% men (315 cases), for a sex ratio (M/F) of 1.88.

Comparative analysis

In comparative analysis, in terms of sociodemographic and clinical parameters, there was a statistically significant difference between the proportion of renal failure patients and non-renal failure patients ($p<0.05$) according to age ($p<0.001$), educational level ($p=0.027$) hypertension ($p<0.001$), diabetes ($p=0.002$), dyspnea ($p<0.001$), abdominal pain ($p=0.031$), vomiting ($p=0.006$), asthenia ($p=0.003$), respiratory rate ($p<0.001$), oxygen saturation ($p<0.001$), and presence of signs of respiratory struggle ($p=0.005$). The existence of renal failure was proportional to the severity of clinical signs on admission ($p<0.001$) (Table I).

Predictive factors for renal failure in covid-19

In univariate analysis, the risk factors for developing renal failure on covid 19 were: Age greater than or equal to 65 years (OR=1.22; CI95% [1.13-1.32] $p<0.001$); history of hypertension (OR=1.17; CI95% [1.10-1.24] $p<0.001$) and diabetes (OR=1.12; CI95% [1.04-1.20] $p=0.002$); dyspnea (OR=1.21; CI95% [1.14-1.29]; $p<0.001$); vomiting (OR=1.29 ; CI95% [1.11-1.50]; $p<0.001$); respiratory rate >30 (OR=1.34; CI95% [1.26-1.44]; $p<0.001$); pulse room air saturation <92% (OR=1.21; CI95% [1.11-1.33] $p<0.001$); existence of signs of respiratory struggle (OR=1.25; CI95% [1.09-1.42]; $p=0.001$); gravity moderate at the entrance (OR=1.14; CI95% [1.05-1.23] $p=0.002$), severe (OR=1.34, CI95% [1.24-1.45] $p<0.001$), and critical (OR=1.73, CI95% [1.51-1.99] $p<0.001$) severity stages; anemia (OR=1.13; CI95% [1.07-1.20] $p<0.001$); hyperleukocytosis (OR=1.24 ; CI95% [1.16-1.34] $p<0.001$); elevated CRP (OR=1.19; CI95% [1.05-1.35] $p=0.006$); accelerated sedimentation rate (OR=1.14; CI95% [1.06-1.23] $p<0.001$) ; uremia >0.4g/l (OR=1.83; CI95% [1.73-1.93] $p<0.001$) and hyperkalemia (OR=1.42; CI95% [1.15-1.76] $p=0.001$). University education level (OR=0.85; CI95% [0.76-0.96] $p=0.007$), secondary education level (OR=0.83; CI95% [0.72-0.94] $p=0.005$), and primary education level (OR=0.81; CI95% [0.72-0.92] $p=0.002$) education levels were protective factors for renal failure. In multivariate analysis, after adjustment for other factors in the original model, age greater than or equal to 65 years, moderate to critical admission severity, and anemia were associated with renal failure (Table IV).

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Table I: Distribution by socio-demographic and clinical data

	GFR (ml/min/1.73m²)			p
	Total	≥ 60	< 60	
	n= 482	n= 430	n= 52	
Age				<0.001
< 65 years	406 (84%)	375 (87%)	31 (60%)	
≥ 65 years	76 (16%)	55 (13%)	21 (40%)	
Gender				0.12
Female	167 (35%)	144 (33%)	23 (44%)	
Male	315 (65%)	286 (67%)	29 (56%)	
Marital status				0.11
Married	263 (73%)	236 (73%)	27 (71%)	
Divorced	17 (4.7%)	13 (4%)	4 (11%)	
Widower	16 (4.4%)	13 (4%)	3 (7.9%)	
Single	65 (18%)	61 (19%)	4 (11%)	
Level of education				0.027
Not in school	27 (8.3%)	20 (6.8%)	7 (23%)	
Primary	76 (23.2%)	72 (24%)	4 (13%)	
Secondary	59 (18%)	55 (19%)	4 (13%)	
University	165 (50.5%)	149 (50%)	16 (52%)	
Comorbidities				
High blood pressure	132 (27%)	103 (24%)	29 (56%)	<0.001
Diabetes	90 (19%)	72 (17%)	18 (35%)	0.002
Asthma	13 (2.7%)	11 (2.6%)	2 (3.8%)	0.6
HIV infection	17 (3.5%)	15 (3.5%)	2 (3.8%)	0.7
Obesity	32 (6.6%)	26 (6%)	6 (12%)	0.14
Fever	140 (29%)	120 (28%)	20 (38%)	0.11
Rhinitis	31 (6.4%)	30 (7%)	1 (1.9%)	0.2
Pharyngitis	6 (1.2%)	6 (1.4%)	0 (0%)	>0.9
Dyspnea	133 (28%)	100 (23%)	33 (63%)	<0.001
Cough	164 (34%)	142 (33%)	22 (42%)	0.2
Arthralgia	22 (4.6%)	20 (4.7%)	2 (3.8%)	>0.9
Headaches	94 (20%)	88 (20%)	6 (12%)	0.12
Anosmia	25 (5.2%)	23 (5.3%)	2 (3.8%)	>0.9
Agueusia	21 (4.4%)	20 (4.7%)	1 (1.9%)	0.7
Abdominal pain	12 (2.5%)	8 (1.9%)	4 (7.7%)	0.031
Diarrhea	15 (3.1%)	12 (2.8%)	3 (5.8%)	0.2
Vomiting	17 (3.5%)	11 (2.6%)	6 (12%)	0.006
Asthenia	79 (16%)	63 (15%)	16 (31%)	0.003
Obesity	75 (31%)	65 (31%)	10 (33%)	0.8
Respiratory rate >30 cycle/min	89 (18%)	58 (13%)	31 (60%)	<0.001
Pulse room air saturation <92%	71 (22%)	50 (18%)	21 (44%)	<0.001
Signs of respiratory struggle	22 (4.6%)	15 (3.5%)	7 (13%)	0.005
Gravity at the entrance				<0.001
Asymptomatic	150 (31%)	149 (35%)	1 (1.9%)	
Mild	169 (35%)	159 (37%)	10 (19%)	
Moderate	75 (16%)	65 (15%)	10 (19%)	
Severe	70 (15%)	49 (11%)	21 (40%)	
Critical	18 (3.7%)	8 (1.9%)	19 (19%)	

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Table II: Distribution by biological data

	GFR (ml/min/1.73m²)			p
	Workforce	≥ 60	< 60	
	n/N	n= 430	n= 52	
Anemia				<0.001
Mild	87/461	76 (83.4%)	11 (12.6%)	
Moderate	59/461	51 (86.4%)	08 (13.6%)	
Severe	22/461	10 (45.5%)	12 (54.5%)	
Leukocytes				<0.001
Leukopenia	47/458	44 (93.6%)	03 (6.4%)	
Hyperleukocytosis	74/458	53 (71.6%)	21 (28.4%)	
Neutrophils				<0.001
Neutropenia	31/436	31 (100%)	0 (0%)	
Polynucleosis	69/436	47 (68.1%)	22 (31.9%)	
Lymphococytes				0.6
Lymphopenia	01/458	01 (100%)	0 (0%)	
Lymphocytosis	411/458	368 (89.5%)	43 (10.5%)	
Plates				0.006
Thrombopenia	75/452	60 (80%)	15 (20%)	
Thrombocytosis	31/452	26 (83.9%)	05 (16.1%)	
Accelerated sedimentation rate	159/258	135 (84.9%)	24 (15.1%)	<0.001
Elevated C-reactive protein	74/124	58 (78.4%)	16 (21.6%)	0.006
Hyponatremia	29/175	19 (65.5%)	10 (34.5%)	0.079
Kaliemia				0.009
Hypokaliémie	14/173	11 (78.6%)	03 (21.4%)	
Hyperkaliémie	15/173	7 (46.7%)	08 (53.3%)	
Chloremia				0.009
Hypochloremia	48/175	35 (72.9%)	13 (27.1%)	
Hyperchloremia	18/175	10 (55.6%)	08 (44.4%)	

Table III: Distribution by treatment received

		GFR (ml/min/1.73m²)		p
	Total	≥ 60	< 60	
	n= 482	n= 430	n= 52	
Admission to the intensive care unit	141 (30%)	105 (25%)	36 (73%)	<0.001
Oxygen therapy	99 (21%)	67 (16%)	32 (65%)	<0.001
Corticosteroids	34 (7.3%)	24 (5.8%)	10 (20%)	0.001
Anticoagulants	118 (25%)	90 (22%)	28 (57%)	<0.001
Chloroquine - azithromycin	338 (83%)	344 (82%)	44 (90%)	0.2
Aminopenicillins	65 (14%)	52 (12%)	13 (27%)	0.007
Cephalosporins	57 (12%)	45 (11%)	12 (24%)	0.006
Quinolones	33 (7.1%)	24 (5.8%)	09 (18%)	0.004
Imidazoles	17 (3.6%)	12 (2.9%)	05 (10%)	0.024
Aminosides	05 (0.9%)	04 (1%)	0 (0%)	>0.9
Macrolides	391 (84%)	347 (83%)	44 (90%)	0.2

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Table IV: Multivariate Analysis

	Initial model			Final model		
	OR	$IC_{95\%}$	p^1	ORa	$ICa_{95\%}$	p^2
Age ≥ 65 years	1.99	[0.89 – 4.42]	0.09	2.42	[1.17 – 4.95]	0.016
Gravity at the entrance						
Asymptomatic						
Mild	6.99	[1.22 – 1.33]	0.072	7.13	[1.31 – 1.33]	0.065
Moderate	11.3	[1.78 – 2.21]	0.03	13	[2.30 – 2.44]	0.017
Severe	18.8	[2.97 – 3.71]	0.009	26.2	[4.85 – 4.93]	0.002
Critical	78.9	[9.44 – 17.71]	<0.001	108	[16.5 – 21.76]	<0.001
Anemia						
No						
Yes	2.63	[1.20 – 5.88]	0.016	2.49	[1.21 – 5.26]	0.015

Discussion

This study, like most retrospective studies, was confronted with the lack of certain information in the patients' medical records. The lack of a computerized system for the management of patients' records was a difficulty in the search for records and in the traceability of patients. The absence of biological data such as 24-hour proteinuria, urine dipstick at a minimum, creatininemia and blood count in some patients, and cytology and pathological anatomy data useful for the diagnosis of certain kidney diseases was also a limitation. These difficulties could be a source of bias and thus limit these results, which could not then be generalized to the entire population of patients with Covid-19. However, our study is still of interest because, to our knowledge, it is the first study in Togo to provide data on the risk factors for the occurrence of RF in Covid-19. In the literature [7], the incidence of renal failure varies from 0.5 to over 20%. In our study, the incidence of RF during Covid-19 was 10.8%. See et al (Singapore) [8]; and Lin et al (China) [9] reported a prevalence of 8.1% and 10.6% respectively. This result is therefore consistent with the data in the literature. We had found in our series, as risk factors of renal disease during Covid-19: age ≥ 65 years with a risk of 2.42 times compared to those with age below 65 years; anemia with 2.49 times the risk of having renal failure associated with Covid-19; and finally, the moderate, severe, and critical stages of severity on admission with the risks of 13 times, 26.2 times,108 times respectively. Usually, patients with renal failure during Covid-19 have oligo-anuria, anemia, hematuria and moderate to critical stage severity [10 – 12]. Comorbidities such as advanced age, hypertension and diabetes are common in patients with impaired renal function [13]. Our results therefore confirm the data in the literature. Indeed, renal failure correlates with high expression of CEA2 in the renal parenchyma (thus favoring direct access of the virus), the severe form of Covid-19, high C reactive protein (CRP) levels and anemia [14]. The main factor incriminated in the occurrence of renal failure during SarsCov2 infection is the elevated expression of ACE2, the key receptor of this virus within the renal parenchyma [4, 5]. It may be promoted by other factors, such as hypovolemia (fever, diarrhea, diuretic), viral pneumonitis (hypoxemia, mechanical ventilation), viral heart disease (cardio-renal syndrome), nephrotoxic drugs (nonsteroidal anti-inflammatory drugs, iodinated contrast media, antibiotics, etc.) [15]. Cheng et al (China), using multivariate regression analysis, found that higher age, severe disease, and anemia were risk factors for renal failure [16]. Hirsch et al (in the USA) found a significant association of renal failure with advanced age, severe infection, cardiovascular disease, hypertension, diabetes mellitus, black race, need for ventilation and vasopressor drugs [17]. In the series of Henry et al (UK); age greater than or equal to 65 years, comorbidities, anemia, high neutrophil count and CRP value greater than 6mg/L were significantly associated with the occurrence of renal failure [18]. In the general population, it is known that RF is more associated with advanced age since once SarsCov2 infected elderly patients, morbidity and mortality rates increased, probably implying a weakening of the immune system of elderly patients and aging of tissues thus leading to greater susceptibility to viral replication [9]. Our results also showed that a severity of infection on admission ranging from moderate to critical to severe was a risk factor for renal failure during Covid-19. Indeed, one possible explanation is that Covid-19 can be complicated by acute respiratory distress syndrome and septic shock in severe cases, and the subsequent hypotension and vasoconstriction would contribute to the development of acute tubular necrosis, as evidenced by histological findings in renal tissues from patients with Covid-19 [16]. The relationship between anemia and renal failure during Covid-19 is not well elucidated. It is well known that renal failure may contribute to the development of anemia due to reduced erythropoietin production, increased risk of bleeding, and reduced red blood cell life span. Anemia has also been shown to be a risk factor for the development of renal failure in patients undergoing

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major surgery leading to increased mortality. However, it is not always clear whether the presence of anemia is simply a reflection of a comorbid disease that increases the risk of renal failure or a direct contributor to renal failure, e.g., due to anemia-induced hypoxia in the renal cortex. The kidney, particularly the proximal tubule, is known to be sensitive to ischemic damage. Using an animal model, Madu et al (Nigeria) [19] showed a sustained reduction in renal cortical and medullary oxygenation in rats that were subjected. It should also be noted that anemia is the prerogative of black subjects with respect to the African diet. This would then constitute a favorable terrain for the development of renal failure once associated with the severe form of the infection.

Conclusion

We conducted a retrospective descriptive and analytical study over a period of one year at the Lomé Anti-Covid Center in which we performed comparative analysis and univariate and multivariate logistic regression to investigate the predictive factors for the occurrence of renal failure during Covid-19. At the end of this study, the risk factors for renal failure during Covid-19 were age ≥ 65; anemia; and moderate, severe, and critical stages of severity on admission. RF is the most formidable factor, conditioning the course of the disease and the patient's vital prognosis. Therefore, it should be emphasized in the follow-up of patients with Covid-19. In addition, a study on the efficacy of therapies in Covid-19 patients with renal failure could allow a better management of these patients in our context.

List of Abbreviations

SarsCov2=Severe Acute Respiratory Syndrome Coronavirus 2.

PHEIC=Public Health Emergency of International Concern.

ACE2=Angiotensin-converting enzyme 2.

RF=Renal Failure.

GFR = Glomerular Filtration Rate

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Author's Contributions

Kossi Akomola SABI, Awéréou KOTOSSO, Yoan Makafui AMEKOUDI, Conceived and wrote the first draft of the manuscript

Laune Odilon BLATOME, Badomta DOLAAMA, Ayodélé Jonathan SABI, Oscar GNIRIMI GBAHBANG, Loutou Ahoub-Laye AFFO, have collected the data

Both authors read and approved the final manuscript

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Availability of Data and Materials

The datasets used and/or analysed during the current study available from the author [Kossi Akomola SABI, Nephrology and Hemodialysis department of CHU Sylvanus Olympio, Lomé (Togo); Mail: kossi.sabi@gmail.com] on reasonable request

Ethical approval and Consent to Participate

This study was approved by "Comité de Bioéthique pour la Recherche en Santé (CBRS)" (Bioethics Committee for Health Research) from the Togo Ministry of Health (CBRS N°004/2020/CBRS). Written informed consent was provided by all participant prior to participation. All methods were carried out with relevant guidelines of Helsinki.

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