World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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Prognostic Factors of Mortality in Patients Hospitalized for Severe COVID-19 Pneumonia

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World Journal of Advanced Research and Reviews, 2025, 28(02), 666-674

Publication history: Received on 23 September 2025; revised on 01 November 2025; accepted on 03 November 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.28.2.3541

Abstract

Objective: This study aims to identify and determine the association between prognostic factors and mortality in patients admitted to intensive care for severe COVID-19 pneumonia.

Method: This was an analytical case-control study conducted over a 6-month period (August 2020 to February 2021) in the COVID-19 intensive care unit of HMMV. The study included all patients with a positive COVID-19 PCR test who were admitted to intensive care for a severe form of the disease.

Results: During the study period, 300 patients were admitted to the intensive care unit. The average age of the patients was 67 ± 11 years, and 217 were men (72.3%), with a male-to-female ratio (M/F) of 2.61. The majority of patients had medical comorbidities, dominated mainly by diabetes (35.7%). ORc (95% CI) for age was 1.23 (1.09-1.40), for sex 1.051 (0.77-1.42), for diabetes 1.91 (1.33-2.72), for hypertension (HTA) 1.27 (0.92-1.76), for obesity 1.45 (1.02-2.06), for cardiovascular diseases 1.040 (0.98-2.32), for asthma 1.21 (0.39-3.70), for COPD 0.88 (0.35-2.16), for CKD 1.64 (0.56-4.78), for neoplastic pathologies 1.21 (0.39-3.70), and for hypothyroidism 1.23 (0.44-3.46). With logistic regression analysis, the ORa for age was 2.73 (1.47-5.086) and for diabetes was 2.55 (1.34-4.85).

Conclusion: In this study identifying prognostic factors for mortality, it appears that age and diabetes are the epidemiological factors associated with mortality in patients with severe COVID-19 pneumopathy.

Keywords: COVID19; Mortality; Prognostic; Pneumonia; Disease

1. Introduction

COVID-19 is a disease caused by an infection with the novel coronavirus (2019-nCoV), which is responsible for "Severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) [1]. Clinically, it is characterized by significant individual variability, ranging from an asymptomatic form to a severe form requiring admission to intensive care. Since the virus's appearance in China in December 2019, 5 million people have officially died, with a mortality rate of approximately 2.02% [2]. At the national level, data published by the Ministry of Health during this period showed that over a 5-week span, there were more than 25,537 new cases, averaging over 800 cases per day [3].

To mitigate a potential overload of the healthcare system, it is essential to identify objective clinical and paraclinical elements related to the disease's prognosis [4]. The ability to predict the severity of the disease and/or its negative progression could help identify patients at risk of complications, thereby optimizing resource management and critical care capacity. This approach also helps identify modifiable and non-modifiable factors involved in each patient's

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prognosis. Several studies have been conducted to find prognostic factors for mortality, which can be epidemiological, clinical, biological, and radiological [5,6].

The objective of our work was to investigate the association between epidemiological prognostic factors (sex, age, obesity, diabetes, hypertension, cardiac pathologies, asthma, COPD, neoplastic pathologies, chronic renal failure, and hypothyroidism) and mortality in patients who were hospitalized for severe COVID-19 pneumonia at the HMMV Intensive Care Unit between August 2020 and February 2021.

2. Materials and Methods

2.1. Study Type, Location, and Period

This was a case-control study conducted in the HMMV COVID-19 intensive care unit over a 6-month period, from August 2020 to February 2021.

2.2. Study Sample

The study included patients hospitalized in the intensive care unit for COVID-19 pneumonia, confirmed by a positive COVID-19 polymerase chain reaction (PCR) test. Patients met the intensive care admission criteria set by the SFAR (French Society of Anesthesia and Intensive Care) during this period:

- Polypnea > 22 breaths/min
- Pulse oximetry (SpO2) < 90% in ambient air
- Systolic blood pressure < 90 mmHg
- Altered consciousness, confusion, somnolence
- Sudden deterioration of general condition in elderly subjects

2.3. Data Collection

A medical form was created to collect data from the medical records of patients, which were written by the on-call physician in the COVID-19 intensive care unit at the time of their admission. The form included the following elements: age, sex, BMI, diabetes, hypertension (HBP), cardiac pathologies, asthma, COPD, CKD, hypothyroidism, and outcome (survival or death).

2.4. Variable Definitions

- **Outcome variable:** The primary outcome was mortality.
- **Exposure factors:**
- **Age:** (two groups: > 59 years and < 59 years)
- **Sex:** (male or female)
- **Obesity:** Any patient with a BMI > 30 was considered obese. (BMI > 30)
- **Diabetes:** (history of diabetes or fasting blood glucose > 1.26 measured twice)
- **Hypertension (HTA):** (history of HTA or BP > 140/90 measured twice after a 15-minute rest interval)
- **Cardiac pathologies:** (all subjects followed for ischemic, arrhythmogenic heart disease, or heart failure)
- **Asthma:** History of asthma.
- **COPD:** Cough + expectoration 3 months/year for two successive years.
- **Chronic Kidney Disease (CKD):** History of CKD (GFR < 60 mL/min/1.73 m^2 for more than 3 months).
- **Neoplastic pathology:** (history of neoplastic pathologies).
- **Hypothyroidism:** (history of hypothyroidism).

2.5. Data Analysis

Statistical analysis was performed using IBM SPSS statistical software (version 10). Continuous variables were expressed as mean +/- standard deviation and compared using the Student's t-test, while categorical variables were expressed as percentages and compared using the Chi-square test or Fisher's exact test. Bivariate and multiple logistic regression models were used to generate unadjusted odds ratios (ORc) and adjusted odds ratios (ORa) with 95% confidence intervals (CI) for significance testing. Variables that achieved a p-value < 0.05 in bivariate analysis were entered into the multiple logistic regression models.

2.6. Ethical and Regulatory Aspects

The work was approved by the ethics committee of the Biomedical Research Faculty of Medicine and Pharmacy in Rabat.

3. Results

During the study period, we collected 300 cases. The average age was 67 ± 11 years, with the most represented age group being those over 59 years old. Of the patients, 217 were male (72.3%), resulting in a male-to-female ratio (M/F) of 2.61.

The majority of patients (63.5%) had a medical history, with the most prevalent comorbidity being diabetes (35.7%) (Table I).

Table I Distribution of comorbidities in patients

		N	Pourcentage marginal
Sexe	F	82	27.3%
	M	218	72.7%
Age	<59	57	19.0%
	>59	243	81.0%
Obésité	Non	211	70.3%
	Oui	89	29.7%
Diabète	Non	193	64.3%
	Oui	107	35.7%
Hypothyroïdie	Oui	11	3.7%
	Non	289	96.3%
IRC	Oui	10	3.3%
	Non	290	96.7%
Pathologie néoplasique	Oui	13	4.3%
	Non	287	95.7%
Asthme	Oui	14	4.7%
	Non	286	95.3%
BPCO	Oui	21	7.0%
	Non	279	93.0%
Pathologie cardiaque	Oui	60	20.0%
	Non	240	80.0%
HTA	Non	205	68.3%
	Oui	95	31.7%
Décès	Oui	180	60.0%
	Non	120	40.0%

Bivariate and multiple logistic regression models were used to generate unadjusted odds ratios (ORc) and adjusted odds ratios (ORa) with 95% confidence intervals (CI) for significance testing. Variables that achieved a **p-value** of less than 0.05 in bivariate analysis were entered into the multiple logistic regression models (Tables II and III).

Table 2 Characteristics of hospitalized patients with severe COVID-19 by mortality status

Variable	Total N (%)	Death N (%)	Survival N (%)	p-value
Age				
<59	57 (19%)	22(38.6%)	35(61.4%)	<0.001
>59	243(81.3%)	158(65%)	85(35%)	
Sexe				
Feminine	82(27.3%)	48(58.6%)	34(41.5%)	0.75
masculine	218(72.7%)	132(60.6%)	86(39.4%)	
Diabate				
Oui	193(64.3%)	100(51.8%)	93(48.2%)	<0.001
Non	107(35.7%)	80(74.8%)	27(25.2%)	
HTA				
Oui	205(68.3%)	117(57.1%)	88(42.8%)	0.128
Non	95(31.7%)	63(66.3%)	32(33.7%)	
Obesity				
Oui	211(70.3%)	118(55.9%)	93(44.1%)	0.027
Non	89(29.7%)	62(69.7%)	27(30.3%)	
Path cardiaques				
Oui	240(80%)	137(57.1%)	103(42.9%)	0.039
Non	60(20%)	43(71.7%)	17(28.3%)	
Asthme				
Oui	14 (4.7%)	9(64.3%)	5(35.7%)	0.7
Non	286(95.3%)	171(59.8%)	115(40.2%)	
BPCO				
Oui	21(7%)	12(57.1%)	9(42.9)	0.78
Non	279	168(60.2%)	111(39.1)	
Hypothyroidie				
Oui	11(3.7%)	5(45.5%)	6(54.5%)	0.31
Non	289	175(60.6%)	114(39.4%)	
Path neoplasique				
Oui	13(4.3%)	6(46.2%)	7(53.8)	0.29
Non	287	174(60.6%)	113(39.4%)	
IRC				
Oui	10(3.3%)	6(60%)	4(40%)	1.00
Non	290	174(60%)	116(40%)	

Table III Multivariate logistic regression analysis for the risk of death in severe COVID-19 patients

Variable	Total N (%)	Death N (%)	Survival N (%)	ORc (CI95%)	ORa (CI 95%)
Age					
<59	57 (19%)	22(38.6%)	35(61.4%)	1.23(1.09-1.40)	2.73(1.47-5.086)*
>59	243(81.3%)	158(65%)	85(35%)		
Sexe					
Feminin	82(27.3%)	48(58.6%)	34(41.5%)	1.051(0.77-1.42)	
masculin	218(72.7%)	132(60.6%)	86(39.4%)		
Diabete					
Oui	193(64.3%)	100(51.8%)	93(48.2%)	1.91(1.33-2.72)	2.55(1.34-4.85)*
Non	107(35.7%)	80(74.8%)	27(25.2%)		
HTA					
Oui	205(68.3%)	117(57.1%)	88(42.8%)	1.27(0.92-1.76)	
Non	95(31.7%)	63(66.3%)	32(33.7%)		
Obesité					
Oui	211(70.3%)	118(55.9%)	93(44.1%)	1.45 (1.02-2.06)	1.18(0.57-2.48)
Non	89(29.7%)	62(69.7%)	27(30.3%)		
Pathologies cardiaques					
Oui	240(80%)	137(57.1%)	103(42.9%)	1.040 (0.98-2.32)	1.06(0.48-2.25)
Non	60(20%)	43(71.7%)	17(28.3%)		
Asthme					
Oui	14 (4.7%)	9(64.3%)	5(35.7%)	1,21(0.39-3.70)	
Non	286(95.3%)	171(59.8%)	115(40.2%)		
BPCO					
Oui	21(7%)	12(57.1%)	9(42.9)	0,88(0.35-2.16)	
Non	279	168(60.2%)	111(39.1)		
Hypothyroidie					
Oui	11(3.7%)	5(45.5%)	6(54.5%)	1,23(0.44-3.46)	
Non	289	175(60.6%)	114(39.4%)		
Pathologie neoplasique					
Oui	13(4.3%)	6(46.2%)	7(53.8)	1,21(0.39-3.70)	
Non	287	174(60.6%)	113(39.4%)		
IRC					
Oui	10(3.3%)	6(60%)	4(40%)	1,64(0.56-4.78)	
Non	290	174(60%)	116(40%)		

4. Discussion

4.1. Age

The average age was 67 ± 11 years, with the most represented age group being those >59 years old. The crude odds ratio (ORc) was 1.23 (1.09-1.40), and the adjusted odds ratio (ORa) was 2.73 (1.47-5.086).

A meta-analysis of 611,583 subjects with COVID-19 revealed that patients over 60 had a higher risk of mortality [9]. This aligns with our study, where subjects >59 were 2.73 times more likely to die from COVID-19 pneumonia than others.

Advanced age has been identified as a major independent predictor of mortality in SARS and MERS, two other viruses from the coronavirus family. Earlier studies on macaques inoculated with SARS-CoV showed that older macaques had stronger innate host responses to viral infection than younger adults, with increased expression of genes associated with inflammation while type I beta interferon expression was reduced. Cellular function and excessive production of Th2-type cytokines could therefore lead to a deficit in viral replication control and more prolonged pro-inflammatory responses, potentially resulting in a poor prognosis [11].

4.2. Sex

Our study included 217 male patients (72.3%), with a male-to-female ratio (M/F) of 2.61. The ORc was 1.051 (0.77-1.42), with a non-significant p-value.

A Chinese study on a cohort of 1,663 hospitalized COVID-19 patients found that male sex was a risk factor for mortality [14].

A large study published on February 9, 2021, conducted by ANSM, the Health Insurance, and Epi-Phare, involved a little over 87,800 people hospitalized for COVID-19, of whom 15,660 died in the hospital. This study found a significant difference between the sexes, with men being 1.4 times more likely to be hospitalized and 2.1 times more likely to die [15]. In our study, the OR was 1.051 (0.77-1.42) (95% CI), which means there was no association between sex and mortality. This suggests that while men were more likely to be hospitalized in intensive care for severe forms, the risk of death by sex in our context was practically the same, which is in disagreement with other studies.

In our context, this male predominance could be explained by differences in social and cultural activities between the sexes. Men are generally the financial providers for families, which pushes them to go to work. Being more mobile and typically in contact with a larger number of people than women, they are exposed to a higher risk of contamination than women, who are more often confined to the role of homemaker and are therefore more sedentary. Furthermore, according to the literature, the lower hospitalization rate of women in intensive care could be explained by their lower susceptibility to viral infections [16].

4.3. Comorbidity

The patient's medical history and comorbidities play a major prognostic role in the risk of developing a severe form or dying from a SARS-CoV-2 infection.

Our bivariate analysis demonstrated that diabetes (ORc 1.91 (1.33-2.72)), obesity (ORc 1.45 (1.02-2.06)), and cardiac pathologies (ORc 1.040 (0.98-2.32)) were significantly associated with mortality.

A study on data from 44,672 patients reported by the Chinese Center for Disease Control found that COVID-19-related mortality was significantly affected by patient comorbidities. Diabetes was the main predictor of mortality [17,18].

A meta-analysis concerning 4,659 COVID-19 patients reported that those with hypertension (OR= 2.5; 95% CI: 2.1-3.1), coronary artery disease (OR= 3.8; 95% CI: 2.1-6.9), and diabetes (OR= 2.0; 95% CI: 1.7-2.3) had a significantly higher risk of death [12].

A Chinese study on a cohort of 1,663 hospitalized COVID-19 patients showed that the risk factor for mortality was diabetes (OR= 2.34; 95% CI: 1.45-3.76) [13].

After integrating all variables that were significant in the bivariate analysis into logistic regression models, we concluded that advanced age and diabetes were independent factors for mortality in severely ill COVID-19 patients.

Table 4 shows a comparison between our study and the data from a meta-analysis

Table 4 Comparison between our study and a meta-analysis

Meta-analyse			**Notre etudes**	
	Nombre des patients (etudes)	**Odds ratio (95%CI)**	**Nombre des patients (etudes)**	**Odds ratio (95%CI)**
Age	11962 (19)	1.80 (1.54–2.10)	300 (1)	2.73(1.47-5.086) *
Sexe	31948 (58)	1.72 (1.5–1.98)	300 (1)	1.051(0.77-1.42)
Diabète	30303 (52)	1.84 (1.61–2.1)	300 (1)	2.55(1.34-4.85) *
HTA	31341 (52)	2.02 (1.71–2.38)	300 (1)	1.27(0.92-1.76)
Obésité BMI > 25–30	9127 (3)	1.41 (1.15–1.74)	300 (1)	1.18(0.57-2.48)
Pathologie cardiaque	37156 (51)	2.12 (1.77–2.56)	300 (1)	1.06(0.48-2.25)

Based on the study's findings, a new policy was implemented after the study period: any patient over 59 years old and/or with diabetes who tested PCR positive was systematically admitted to the intensive care unit, regardless of their initial clinical state. This approach allowed for earlier treatment and improved patient management, while also optimizing critical care resource and capacity management.

4.4. Limitations and Biases

Our study, however, has some limitations and biases. First, it was a retrospective study with data collection that led to the exclusion of some patients due to a lack of properly usable data.

While our data collection and recruitment method are easily reproducible, ensuring good internal validity, the demographic specificities of Morocco may limit the study's external validity.

At the time of this study, a vaccination campaign was underway and new SARS-CoV-2 variants were emerging. It would be valuable to repeat this study by taking into account the vaccination and serological status of hospitalized patients.

5. Conclusion

In this analysis of prognostic factors for mortality, advanced age and diabetes were found to be the epidemiological factors most associated with mortality in patients with COVID-19 pneumonia.

These findings raise crucial questions for the future of pandemic management. The significant correlation between age and diabetes and fatal outcomes for COVID-19 highlights the need for targeted public health strategies. How can health systems better adapt to protect vulnerable populations and patients with comorbidities? What early screening and treatment protocols are necessary for these high-risk groups? Furthermore, as new infectious diseases and variants continue to emerge, research must focus on understanding the underlying mechanisms that make certain populations more susceptible to infection. A better understanding of the impact of comorbidities and aging on the immune response could not only improve pandemic care but also inform new therapies for infectious diseases in general.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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