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SARI Surveillance System in Senegal: Factors Associated with Death among Hospitalized SARI Patients

Amadou Moustapha NDOYE

amadoumoustapha.ndoye@pasteur.sn

Institut Pasteur de Dakar

Viviane Marie-Pierre Ciss DIALLO

De Fann University Hospital Center (CNHU FANN)

Billo TALL

Institut Pasteur de Dakar

Aboubacry GAYE

Université du Sine Saloum El-Hâdj Ibrahima NIASS

Cheikh TALLA

Institut Pasteur de Dakar

Antoine SYLVA

Centre Hospitalier Universitaire Idrissa Pouye Grand Yoff,

Ndongo DIA

Institut Pasteur de Dakar

Adji Astou Mbow

Institut Pasteur de Dakar

Louise FORTES

Centre Hospitalier National Dalal Jamm

Samba Niang Sagne

Institut Pasteur de Dakar

Mamadou Seck

De Fann University Hospital Center (CNHU FANN)

Fatimata Wone

Centre Hospitalier National Dalal Jamm

Margarite Diatta

Institut Pasteur de Dakar

Coura SECK

Centre Hospitalier Universitaire Idrissa Pouye Grand Yoff,

Joseph FAYE

Institut Pasteur de Dakar

Mamadou Cissé
Institut Pasteur de Dakar

Mamadou Aliou Barry
Institut Pasteur de Dakar

Boly Diop
Ministère de la Santé et de l'Hygiène Publique

Inès Vigan-Womas
Institut Pasteur de Dakar

Cheikh LOUCOUBAR
Institut Pasteur de Dakar

Moussa SEYDI
De Fann University Hospital Center (CNHU FANN)

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Abstract

The Severe Acute Respiratory Infection (SARI) surveillance system plays a crucial role in monitoring respiratory diseases, including COVID-19, in Senegal. SARI remains a significant public health concern, particularly in the context of the COVID-19 pandemic. To track the spread and severity of respiratory infections, Senegal has implemented a robust surveillance system. Vaccination is a key strategy to reduce severe cases and mortality, yet multiple factors influence its effectiveness.

Objectives: This study describes the SARI surveillance system, identifies the types of COVID-19 vaccines administered, and analyzes the factors associated with mortality among SARI patients.

Methods: A multicenter prospective cohort study including inpatients with laboratory-confirmed testing was conducted at three SARI surveillance hospitals in Senegal. Demographic, clinical, and immunological data were extracted from the medical records of patients who had been discharged or had died. We described the clinical characteristics of patients at admission and during hospitalization. We analyzed clinical status (discharged or died) after admission among adult patients (≥ 18 years) who were eligible for COVID-19 vaccination in Senegal.

Results: A total of 224 patients were included in the final analysis. The median age was 47 years and 45.1% of patients were female. The majority of patients (67.9%) reported at least one pre-existing condition. Vaccination was significantly associated with a lower risk of mortality (OR = 0.43; 95% CI: 0.19–0.94, p = 0.037). Heart disease was an independent risk factor (OR = 3.14; 95% CI: 1.15–8.48, p = 0.023). Dyspnea was strongly associated with mortality, although the association did not reach conventional statistical significance (OR = 2.70; 95% CI: 1.04–7.96, p = 0.052). ICU admission was the strongest predictor of mortality, with an OR of 3.70 (95% CI: 1.70–8.19, p = 0.001).

Conclusions: This study investigated factors associated with mortality in patients presenting with severe acute respiratory infections, including COVID-19. The findings highlight several demographic, clinical, and vaccination-related variables that are significantly associated with an increased or decreased risk of death.

1 Introduction

Sentinel influenza surveillance systems have been developed in recent years and are sometimes used as platforms to estimate influenza vaccine effectiveness against influenza-associated SARI hospitalizations.

The World Health Organization (WHO) has advised countries with hospital-based sentinel influenza surveillance to adapt their systems to include surveillance of severe SARS-CoV-2 infection and, where possible, to collect data to measure the effectiveness of COVID-19 vaccines [1–3].

For several years, the Institut Pasteur International Network, in support of the Ministries of Health of the countries concerned, has participated in sentinel surveillance networks set up for influenza and later

extended to respiratory infections (ASIDE program). In 2012, Senegal established a fever surveillance network, the Senegal Sentinel Syndromic Surveillance Network (4S Network). The 4S Network, based on syndromic surveillance of fevers at community sites (health posts) and in health centers, enables rapid identification of unusual health events in different epidemiological contexts, thus contributing to a faster health response. Its current aim is to detect, in addition to influenza-like syndromes, other febrile syndromes with a major public health impact in Senegal, such as COVID-19, malaria, arboviral diseases, and bloody diarrhea [4].

Thanks to its experience in SARI surveillance, the Institut Pasteur de Dakar is heavily involved, on behalf of the health authorities, in the diagnosis of COVID-19. Through the 4S Sentinel Network, it intends to conduct studies to assess, following Emergency Use Authorization, the effectiveness of COVID-19 vaccines in preventing severe forms of the disease, particularly SARI associated with laboratory-confirmed SARS-CoV-2 infection.

Many questions remain about the effectiveness of vaccines against COVID-19 in real-world settings. Only post-introduction studies of vaccine effectiveness can provide answers. This study describes the SARI surveillance system, identifies the types of COVID-19 vaccines administered in Senegal, and analyzes the factors associated with mortality among SARI patients.

2 Materials and Methods

2.1 Study design

A multicenter prospective cohort study including inpatients with laboratory-confirmed testing was conducted at three SARI surveillance hospitals in Senegal. The cohort protocol was adapted from the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC)/WHO Clinical Characterization Protocol (CCP).

2.2 Setting

The study was conducted in hospitals belonging to the Sentinel Fever Syndromic Surveillance Network. The study sites were three hospitals in Dakar: Hôpital Fann (Infectious Diseases Department), HOGIP (Hôpital Général Idrissa Pouye de Grand Yoff), and the Dalal Jamm Guediawaye Hospital.

Data were collected from patients hospitalized between November 2022 and July 2024, in line with the national strategy set out by the Senegalese Ministry of Health. Swab specimens and blood samples were transported the same day to the Institut Pasteur de Dakar for virological and immunological analyses.

2.3 Participants

The surveillance population consisted of people of all ages hospitalized with SARI symptoms in a hospital of the SARI surveillance network.

Inclusion criteria

- Meets the SARI case definition:

History of fever or measured fever ≥ 38°C, and cough, with symptom onset within the last 10 days. A minimum hospital stay of 24 hours is required for a person to be considered hospitalized.

- - Belongs to a target group for COVID-19 vaccination on the date of hospital admission.
- - Written informed consent.

Non-inclusion criteria

Is ineligible for swabbing due to severe septal deviation, nasal obstruction, or any other condition contraindicating swabbing;

Has a history of hospitalization in the 14 days before this hospital admission (including transfer from another hospital)

2.4 Data sources

Clinical data were collected from patients' medical records. Collected data included sociodemographic characteristics, medical history (comorbidities), and symptoms at admission, as well as daily vital signs, oxygen saturation, clinical symptoms, and medication administration until discharge. Intensive care unit (ICU) admission and ventilator use were also recorded. Routine laboratory test results were also collected when available.

A dedicated paper Case Report Form (CRF) was completed at each site by the research team using data from medical records and laboratory results.

2.5 Laboratory data

For all SARI patients, a nasopharyngeal sample was collected, placed in 2 mL of Universal Transport Medium, and sent daily to the National Influenza Center (NIC) of Senegal at the Institut Pasteur de Dakar (IPD). For respiratory pathogens, a two-step real-time reverse transcription–polymerase chain reaction (RT-PCR) was performed using the CFX96 785BR3027 system and the Seegene Allplex respiratory pathogen panel assay.

2.6 Variables Assessed

End Point

Clinical status at discharge: alive versus dead.

Candidate risk factors for SARI mortality were grouped as follows:

Demographic factors: Advanced age, male sex.

Clinical factors: Presence of comorbidities (hypertension, diabetes, cardiovascular diseases, renal failure).

Immunological factors: Vaccination status, time between vaccination and infection.

Healthcare access: Delayed hospitalization, limited access to oxygen therapy and intensive care.

2.7 Statistical Analysis

Continuous and categorical variables were presented as median (IQR) and as frequencies and percentages, respectively. We compared categorical variables using Fisher's exact test and continuous variables using ANOVA. To explore the risk factors associated with clinical status, unadjusted and covariate-adjusted multivariate logistic models were fitted. All covariates included in the multivariate models were chosen for their clinical relevance. Collinearity was assessed. Missing data affected several variables to varying degrees. Missing values were not imputed, and multivariable models were fitted using complete cases for the included covariates. We conducted all analyses using R software, version 4.0.1 [33].

2.8 Ethical considerations:

The study was conducted in accordance with the Declaration of Helsinki and approved by the Senegalese National Ethics Committee (CNERS) (protocol code SEN22/19; date of approval: 08 April 2022).The Senegalese National Ethics Committee approved this study (reference number N°00000083 MSAS/CNERS/SP).

3 Results

3.1 3.1. Characteristics of Patients

The median age (IQR) was 47 years (35–63), and 101 patients (45.1%) were female. Regarding comorbidities, 67.9% of participants had at least one condition. The main coexisting conditions were hypertension (25%), obesity (17%), immunosuppression (14.7%), heart disease (10.3%), and diabetes (8.5%). Regarding symptoms, the most frequent were fever (86.6%), asthenia (78.1%), cough and dyspnea (both approximately 65.6%), headache (62.5%), and myalgia (48.2%). The median duration of symptoms was 5 days (IQR: 3–9), and the median SpO2 was 95% (IQR: 89–98). In terms of COVID-19 vaccination, 51.8% were unvaccinated, and among those vaccinated, 51.4% had received two doses. The most common first-dose vaccines were Janssen (37.4%), AstraZeneca (22.2%), and Sinopharm (22.2%). The most common second-dose vaccines were AstraZeneca (36.1%) and Sinopharm (32.8%), while third doses were rare, the most common being Janssen (50.0%). Influenza vaccination coverage was low, with only 2.7% of patients having received the vaccine that year. Pneumococcal vaccination coverage was also minimal, with 1.8% having received PPSV23 and 0.9% PCV13. Among SARI cases, the most frequently detected pathogen was rhinovirus (5.8%), while no pathogen was identified in 82.1%. In-hospital mortality was 19.6%, and 80.4% of patients survived (Table 1).

Table 1

summarizes the baseline demographic, clinical, immunological, and vaccination-related characteristics of the study population, stratified by vital status at discharge.

Age	**Alive (N = 180)**	**Death (N = 44)**	**Total (N = 224)**	**p value**
				0.2071
Median	47.000	53.500	47.000	
Q1, Q3	32.000, 63.000	39.750, 65.250	35.000, 63.250	
Age categories				0.1232
]0, 30]	39 (90.7%)	4 (9.3%)	43 (100.0%)	
]30, 60]	90 (79.6%)	23 (20.4%)	113 (100.0%)	
> 60	51 (75.0%)	17 (25.0%)	68 (100.0%)	
Sex				0.1022
Female	86 (85.1%)	15 (14.9%)	101 (100.0%)	
Male	94 (76.4%)	29 (23.6%)	123 (100.0%)	
Virological COVID-19 results at admission				0.1542
Negative	172 (79.6%)	44 (20.4%)	216 (100.0%)	
Positive	8 (100.0%)	0 (0.0%)	8 (100.0%)	
COVID-19 vaccination				0.0062
No	85 (73.3%)	31 (26.7%)	116 (100.0%)	
Yes	95 (88.0%)	13 (12.0%)	108 (100.0%)	
Flu vaccination				0.8522
No	175 (80.3%)	43 (19.7%)	218 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value	
				0.2071	
Yes	5 (83.3%)	1 (16.7%)	6 (100.0%)		
Previous flu vaccination				0.3892	
No	177 (80.1%)	44 (19.9%)	221 (100.0%)		
Yes	3 (100.0%)	0 (0.0%)	3 (100.0%)		
Pneumococcal Polysaccharide Vaccine, 23-valent (PPSV23)				0.3182	
No	176 (80.0%)	44 (20.0%)	220 (100.0%)		
Yes	4 (100.0%)	0 (0.0%)	4 (100.0%)		
Pneumococcal Conjugate Vaccine (PCV)				0.4822	
No	178 (80.2%)	44 (19.8%)	222 (100.0%)		
Yes	2 (100.0%)	0 (0.0%)	2 (100.0%)		
Number of preexisting disorders					0.0602
0		64 (88.9%)	8 (11.1%)	72 (100.0%)	
1		44 (80.0%)	11 (20.0%)	55 (100.0%)	
≥2		72 (74.2%)	25 (25.8%)	97 (100.0%)	
Cancer				0.1842	
No	173 (79.7%)	44 (20.3%)	217 (100.0%)		
Yes	7 (100.0%)	0 (0.0%)	7 (100.0%)		
Heart disease				< 0.0012	
No	168 (83.6%)	33 (16.4%)	201 (100.0%)		
1. * Linear Model ANOVA					
2. Pearson’s Chi-squared test					

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
Yes	12 (52.2%)	11 (47.8%)	23 (100.0%)	
Hypertension				0.0072
No	142 (84.5%)	26 (15.5%)	168 (100.0%)	
Yes	38 (67.9%)	18 (32.1%)	56 (100.0%)	
Kidney disease				0.2982
No	171 (81.0%)	40 (19.0%)	211 (100.0%)	
Yes	9 (69.2%)	4 (30.8%)	13 (100.0%)	
Liver disease				0.3892
No	177 (80.1%)	44 (19.9%)	221 (100.0%)	
Yes	3 (100.0%)	0 (0.0%)	3 (100.0%)	
Lung disease				0.5112
No	172 (80.0%)	43 (20.0%)	215 (100.0%)	
Yes	8 (88.9%)	1 (11.1%)	9 (100.0%)	
Asthma				0.5242
No	167 (79.9%)	42 (20.1%)	209 (100.0%)	
Yes	13 (86.7%)	2 (13.3%)	15 (100.0%)	
Diabetes				0.1712
No	167 (81.5%)	38 (18.5%)	205 (100.0%)	
Yes	13 (68.4%)	6 (31.6%)	19 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
Immunosuppression				0.2322
No	156 (81.7%)	35 (18.3%)	191 (100.0%)	
Yes	24 (72.7%)	9 (27.3%)	33 (100.0%)	
Neurologic disorder				0.2472
No	177 (80.8%)	42 (19.2%)	219 (100.0%)	
Yes	3 (60.0%)	2 (40.0%)	5 (100.0%)	
Rheumatoid pathology				0.8422
No	173 (80.5%)	42 (19.5%)	215 (100.0%)	
Yes	7 (77.8%)	2 (22.2%)	9 (100.0%)	
Anemia				0.0912
No	169 (81.6%)	38 (18.4%)	207 (100.0%)	
Yes	11 (64.7%)	6 (35.3%)	17 (100.0%)	
Tuberculosis				0.5142
No	172 (80.8%)	41 (19.2%)	213 (100.0%)	
Yes	8 (72.7%)	3 (27.3%)	11 (100.0%)	
Obesity				0.5122
No	148 (79.6%)	38 (20.4%)	186 (100.0%)	
Yes	32 (84.2%)	6 (15.8%)	38 (100.0%)	
Weight				0.6761
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
N-Miss	24	2	26	
Median	68.000	64.000	66.000	
Q1, Q3	56.000, 78.000	55.250, 72.000	56.000, 76.875	
Height				0.7021
N-Miss	45	14	59	
Median	1.700	1.700	1.700	
Q1, Q3	1.650, 1.750	1.623, 1.750	1.650, 1.750	
BMI				0.9361
N-Miss	46	14	60	
Median	23.262	22.704	23.148	
Q1, Q3	20.164, 27.155	18.964, 25.615	20.129, 27.029	
Other chronic condition				0.6592
No	155 (79.9%)	39 (20.1%)	194 (100.0%)	
Yes	25 (83.3%)	5 (16.7%)	30 (100.0%)	
Days since symptom onset, median (IQR)				0.7021
Median	6.000	5.000	5.000	
Q1, Q3	3.000, 9.000	3.000, 10.000	3.000, 9.000	
Fever				0.1252
No	21 (70.0%)	9 (30.0%)	30 (100.0%)	
Yes	159 (82.0%)	35 (18.0%)	194 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	**Alive (N = 180)**	**Death (N = 44)**	**Total (N = 224)**	**p value**
				0.2071
Axillary temperature on admission				0.2591
N-Miss	16	4	20	
Median	38.500	38.000	38.400	
Q1, Q3	38.000, 38.900	37.800, 38.500	37.900, 38.800	
SpO2				< 0.0011
N-Miss	25	5	30	
Median	96.000	89.000	95.000	
Q1, Q3	90.000, 98.000	86.000, 96.000	89.000, 98.000	
Desaturation				< 0.0012
No	107 (88.4%)	14 (11.6%)	121 (100.0%)	
Yes	48 (65.8%)	25 (34.2%)	73 (100.0%)	
Headache				0.8622
No	68 (81.0%)	16 (19.0%)	84 (100.0%)	
Yes	112 (80.0%)	28 (20.0%)	140 (100.0%)	
Ageusia				0.0602
No	98 (85.2%)	17 (14.8%)	115 (100.0%)	
Yes	82 (75.2%)	27 (24.8%)	109 (100.0%)	
Coryza				0.3642
No	146 (81.6%)	33 (18.4%)	179 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
Yes	34 (75.6%)	11 (24.4%)	45 (100.0%)	
Sore throat				0.0462
No	144 (83.2%)	29 (16.8%)	173 (100.0%)	
Yes	36 (70.6%)	15 (29.4%)	51 (100.0%)	
Dyspnea				0.0012
No	71 (92.2%)	6 (7.8%)	77 (100.0%)	
Yes	109 (74.1%)	38 (25.9%)	147 (100.0%)	
Shortness of breath				0.9952
No	94 (80.3%)	23 (19.7%)	117 (100.0%)	
Yes	86 (80.4%)	21 (19.6%)	107 (100.0%)	
Tachypnea				0.0602
No	68 (87.2%)	10 (12.8%)	78 (100.0%)	
Yes	112 (76.7%)	34 (23.3%)	146 (100.0%)	
Apnea				0.5462
No	175 (80.6%)	42 (19.4%)	217 (100.0%)	
Yes	5 (71.4%)	2 (28.6%)	7 (100.0%)	
Anosmia				0.0042
No	131 (85.6%)	22 (14.4%)	153 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
Yes	49 (69.0%)	22 (31.0%)	71 (100.0%)	
Anorexia				0.1962
No	59 (85.5%)	10 (14.5%)	69 (100.0%)	
Yes	121 (78.1%)	34 (21.9%)	155 (100.0%)	
Dysgueusia				0.4662
No	105 (82.0%)	23 (18.0%)	128 (100.0%)	
Yes	75 (78.1%)	21 (21.9%)	96 (100.0%)	
Vomiting				0.6342
No	141 (81.0%)	33 (19.0%)	174 (100.0%)	
Yes	39 (78.0%)	11 (22.0%)	50 (100.0%)	
Nausea				0.3652
No	167 (81.1%)	39 (18.9%)	206 (100.0%)	
Yes	13 (72.2%)	5 (27.8%)	18 (100.0%)	
Asthenia				0.5762
No	38 (77.6%)	11 (22.4%)	49 (100.0%)	
Yes	142 (81.1%)	33 (18.9%)	175 (100.0%)	
Myalgia				0.2032
No	97 (83.6%)	19 (16.4%)	116 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
Yes	83 (76.9%)	25 (23.1%)	108 (100.0%)	
Abdominal pain				0.3182
No	147 (81.7%)	33 (18.3%)	180 (100.0%)	
Yes	33 (75.0%)	11 (25.0%)	44 (100.0%)	
Diarrhea				0.6022
No	153 (81.0%)	36 (19.0%)	189 (100.0%)	
Yes	27 (77.1%)	8 (22.9%)	35 (100.0%)	
Palpitations				0.0022
No	137 (85.6%)	23 (14.4%)	160 (100.0%)	
Yes	43 (67.2%)	21 (32.8%)	64 (100.0%)	
Chest pain				0.0062
No	95 (88.0%)	13 (12.0%)	108 (100.0%)	
Yes	85 (73.3%)	31 (26.7%)	116 (100.0%)	
Dizziness				0.1482
No	155 (82.0%)	34 (18.0%)	189 (100.0%)	
Yes	25 (71.4%)	10 (28.6%)	35 (100.0%)	
Chills				0.1232
No	141 (78.3%)	39 (21.7%)	180 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
Yes	39 (88.6%)	5 (11.4%)	44 (100.0%)	
Dermatosis				0.4782
No	169 (80.9%)	40 (19.1%)	209 (100.0%)	
Yes	11 (73.3%)	4 (26.7%)	15 (100.0%)	
Confusion				0.2222
No	166 (81.4%)	38 (18.6%)	204 (100.0%)	
Yes	14 (70.0%)	6 (30.0%)	20 (100.0%)	
Positivity				0.2512
No	11 (68.8%)	5 (31.2%)	16 (100.0%)	
Yes	151 (80.7%)	36 (19.3%)	187 (100.0%)	
Positivity (Wantai total Ig, S/RBD protein)				0.6142
No	1 (100.0%)	0 (0.0%)	1 (100.0%)	
Yes	161 (79.7%)	41 (20.3%)	202 (100.0%)	
Positivity (ID.Vet IgG, N protein)				0.1152
No	36 (72.0%)	14 (28.0%)	50 (100.0%)	
Yes	130 (82.3%)	28 (17.7%)	158 (100.0%)	
SARI infection				0.0572
Adenovirus	1 (50.0%)	1 (50.0%)	2 (100.0%)	
Coronavirus NL63	1 (100.0%)	0 (0.0%)	1 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

Age	Alive (N = 180)	Death (N = 44)	Total (N = 224)	p value
				0.2071
Influenza	7 (100.0%)	0 (0.0%)	7 (100.0%)	
SARS-CoV-2	8 (100.0%)	0 (0.0%)	8 (100.0%)	
Haemophilus influenzae	1 (50.0%)	1 (50.0%)	2 (100.0%)	
Influenza A	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Klebsiella pneumoniae	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Metapneumovirus	2 (66.7%)	1 (33.3%)	3 (100.0%)	
Moraxella pneumoniae	0 (0.0%)	1 (100.0%)	1 (100.0%)	
Parainfluenza virus 4	1 (100.0%)	0 (0.0%)	1 (100.0%)	
Rhinovirus	10 (76.9%)	3 (23.1%)	13 (100.0%)	
Unknown	149 (81.0%)	35 (19.0%)	184 (100.0%)	
Intensive Care Unit				< 0.0012
No	149 (88.7%)	19 (11.3%)	168 (100.0%)	
Yes	31 (55.4%)	25 (44.6%)	56 (100.0%)	
1. * Linear Model ANOVA				
2. Pearson’s Chi-squared test				

The Kaplan–Meier curve describes a gradual decline in the proportion of patients remaining event-free over the observation period, with a steeper early decline followed by a flatter portion at longer follow-up times. For the time-to-event analysis, the date of hospital admission was used as the time origin (time zero). Follow-up time was calculated in days from hospital admission to either in-hospital death (event) or hospital discharge alive (censoring), whichever occurred first. Kaplan–Meier estimates were used to descriptively illustrate the probability of remaining free from in-hospital death over time. Because the analysis was descriptive and no between-group survival comparison was planned, neither a log-rank test nor a Cox proportional-hazards model was performed. This analysis is presented as a purely descriptive illustration of the timing of in-hospital death rather than as a formal comparative survival analysis (Fig. 2).

3.2 Bivariate analysis

The bivariate analysis showed that several factors were significantly associated with mortality. Advanced age (> 60 years) was a risk factor, with an OR of 3.25 (95% CI: 1.10-11.98, p = 0.048). Vaccination was significantly associated with a reduced risk of death (OR = 0.38; 95% CI: 0.18–0.75, p = 0.007). The presence of multiple comorbidities was also associated with an increased risk of death (OR = 2.78; 95% CI: 1.21–6.98, p = 0.021), particularly heart disease (OR = 4.67; 95% CI: 1.88–11.55, p = 0.001) and hypertension (OR = 2.59; 95% CI: 1.27–5.20, p = 0.008). Among symptoms, dyspnea (OR = 4.13; 95% CI: 1.77–11.31, p = 0.002), anosmia (OR = 2.67; 95% CI: 1.36–5.28, p = 0.004), palpitations (OR = 2.91; 95% CI: 1.46–5.78, p = 0.002), and chest pain (OR = 2.67; 95% CI: 1.34–5.59, p = 0.007) were strongly associated with an increased risk of death. Finally, ICU admission showed the strongest bivariate association with mortality, with an OR of 6.32 (95% CI: 3.13–13.05, p < 0.001); as noted in the Discussion, this likely reflects disease severity rather than an independent causal effect (Table 2).

Table 2
Factors Associated with In-Hospital Mortality: Univariable Analysis

Patient's Characteristics		**Alive**	**Death**	**OR (univariable)**
Age	Mean (SD)	48.5 (18.9)	52.5 (16.8)	1.01 (0.99–1.03, p = 0.207)
Age Categories (years)	]0, 30]	39 (90.7)	4 (9.3)	-
	]30, 60]	90 (79.6)	23 (20.4)	2.49 (0.89–8.92, p = 0.112)
	> 60	51 (75.0)	17 (25.0)	3.25 (1.10-11.98, p = 0.048)
Sex	Female	86 (85.1)	15 (14.9)	-
	Male	94 (76.4)	29 (23.6)	1.77 (0.90–3.60, p = 0.105)
COVID-19 vaccination	No	85 (73.3)	31 (26.7)	-
	Yes	95 (88.0)	13 (12.0)	0.38 (0.18–0.75, p = 0.007)
Number of preexisting disorders	0	64 (88.9)	8 (11.1)	-
	1	44 (80.0)	11 (20.0)	2.00 (0.75–5.55, p = 0.169)
	≥ 2	72 (74.2)	25 (25.8)	2.78 (1.21–6.98, p = 0.021)
Heart disease	No	168 (83.6)	33 (16.4)	-
	Yes	12 (52.2)	11 (47.8)	4.67 (1.88–11.55, p = 0.001)
Hypertension	No	142 (84.5)	26 (15.5)	-
	Yes	38 (67.9)	18 (32.1)	2.59 (1.27–5.20, p = 0.008)
Kidney disease	No	171 (81.0)	40 (19.0)	-
	Yes	9 (69.2)	4 (30.8)	1.90 (0.49–6.16, p = 0.305)
Lung disease	No	172 (80.0)	43 (20.0)	-
	Yes	8 (88.9)	1 (11.1)	0.50 (0.03–2.83, p = 0.519)

Patient's Characteristics		Alive	Death	OR (univariable)
Asthma	No	167 (79.9)	42 (20.1)	-
	Yes	13 (86.7)	2 (13.3)	0.61 (0.09–2.33, p = 0.528)
Diabetes	No	167 (81.5)	38 (18.5)	-
	Yes	13 (68.4)	6 (31.6)	2.03 (0.68–5.49, p = 0.178)
Immunosuppression	No	156 (81.7)	35 (18.3)	-
	Yes	24 (72.7)	9 (27.3)	1.67 (0.68–3.81, p = 0.236)
Neurologic disorder	No	177 (80.8)	42 (19.2)	-
	Yes	3 (60.0)	2 (40.0)	2.81 (0.36–17.47, p = 0.266)
Rheumatoid pathology	No	173 (80.5)	42 (19.5)	-
	Yes	7 (77.8)	2 (22.2)	1.18 (0.17–5.08, p = 0.843)
Anemia	No	169 (81.6)	38 (18.4)	-
	Yes	11 (64.7)	6 (35.3)	2.43 (0.79–6.80, p = 0.100)
Tuberculosis	No	172 (80.8)	41 (19.2)	-
	Yes	8 (72.7)	3 (27.3)	1.57 (0.33–5.71, p = 0.517)
Obesity	No	148 (79.6)	38 (20.4)	-
	Yes	32 (84.2)	6 (15.8)	0.73 (0.26–1.77, p = 0.513)
Other chronic condition	No	155 (79.9)	39 (20.1)	-
	Yes	25 (83.3)	5 (16.7)	0.79 (0.26–2.06, p = 0.660)
Fever	No	21 (70.0)	9 (30.0)	-

Patient's Characteristics		Alive	Death	OR (univariable)
	Yes	159 (82.0)	35 (18.0)	0.51 (0.22–1.27, p = 0.130)
Headache	No	68 (81.0)	16 (19.0)	-
	Yes	112 (80.0)	28 (20.0)	1.06 (0.54–2.14, p = 0.862)
Ageusia	No	98 (85.2)	17 (14.8)	-
	Yes	82 (75.2)	27 (24.8)	1.90 (0.98–3.78, p = 0.062)
Coryza	No	146 (81.6)	33 (18.4)	-
	Yes	34 (75.6)	11 (24.4)	1.43 (0.64–3.05, p = 0.366)
Sore throat	No	144 (83.2)	29 (16.8)	-
	Yes	36 (70.6)	15 (29.4)	2.07 (0.99–4.23, p = 0.049)
Dyspnea	No	71 (92.2)	6 (7.8)	-
	Yes	109 (74.1)	38 (25.9)	4.13 (1.77–11.31, p = 0.002)
Shortness of breath	No	94 (80.3)	23 (19.7)	-
	Yes	86 (80.4)	21 (19.6)	1.00 (0.51–1.93, p = 0.995)
Tachypnea	No	68 (87.2)	10 (12.8)	-
	Yes	112 (76.7)	34 (23.3)	2.06 (0.99–4.65, p = 0.064)
Apnea	No	175 (80.6)	42 (19.4)	-
	Yes	5 (71.4)	2 (28.6)	1.67 (0.23–8.03, p = 0.550)
Anosmia	No	131 (85.6)	22 (14.4)	-
	Yes	49 (69.0)	22 (31.0)	2.67 (1.36–5.28, p = 0.004)
Anorexia	No	59 (85.5)	10 (14.5)	-

Patient's Characteristics		Alive	Death	OR (univariable)
	Yes	121 (78.1)	34 (21.9)	1.66 (0.79–3.75, p = 0.199)
Dysgueusia	No	105 (82.0)	23 (18.0)	-
	Yes	75 (78.1)	21 (21.9)	1.28 (0.66–2.48, p = 0.467)
Vomiting	No	141 (81.0)	33 (19.0)	-
	Yes	39 (78.0)	11 (22.0)	1.21 (0.54–2.54, p = 0.634)
Nausea	No	167 (81.1)	39 (18.9)	-
	Yes	13 (72.2)	5 (27.8)	1.65 (0.50–4.66, p = 0.369)
Asthenia	No	38 (77.6)	11 (22.4)	-
	Yes	142 (81.1)	33 (18.9)	0.80 (0.38–1.80, p = 0.576)
Myalgia	No	97 (83.6)	19 (16.4)	-
	Yes	83 (76.9)	25 (23.1)	1.54 (0.79–3.02, p = 0.204)
Abdominal pain	No	147 (81.7)	33 (18.3)	-
	Yes	33 (75.0)	11 (25.0)	1.48 (0.66–3.17, p = 0.320)
Diarrhea	No	153 (81.0)	36 (19.0)	-
	Yes	27 (77.1)	8 (22.9)	1.26 (0.50–2.90, p = 0.603)
Palpitations	No	137 (85.6)	23 (14.4)	-
	Yes	43 (67.2)	21 (32.8)	2.91 (1.46–5.78, p = 0.002)
Chest pain	No	95 (88.0)	13 (12.0)	-
	Yes	85 (73.3)	31 (26.7)	2.67 (1.34–5.59, p = 0.007)

Patient's Characteristics		Alive	Death	OR (univariable)
Dizziness	No	155 (82.0)	34 (18.0)	-
	Yes	25 (71.4)	10 (28.6)	1.82 (0.77–4.06, p = 0.152)
Chills	No	141 (78.3)	39 (21.7)	-
	Yes	39 (88.6)	5 (11.4)	0.46 (0.15–1.16, p = 0.130)
Dermatosis	No	169 (80.9)	40 (19.1)	-
	Yes	11 (73.3)	4 (26.7)	1.54 (0.41–4.76, p = 0.481)
Confusion	No	166 (81.4)	38 (18.6)	-
	Yes	14 (70.0)	6 (30.0)	1.87 (0.63-5.00, p = 0.228)
Positivity	No	11 (68.8)	5 (31.2)	-
	Yes	151 (80.7)	36 (19.3)	0.52 (0.18–1.75, p = 0.258)
Positivity (ID.Vet IgG, N protein)	No	36 (72.0)	14 (28.0)	-
	Yes	130 (82.3)	28 (17.7)	0.55 (0.27–1.18, p = 0.118)
Intensive Care Unit	No	149 (88.7)	19 (11.3)	-
	Yes	31 (55.4)	25 (44.6)	6.32 (3.13–13.05, p < 0.001)

3.3 Multivariable analysis

In the multivariable analysis, heart disease (aOR = 3.14 [1.15–8.48]), dyspnea (aOR = 2.70 [1.04–7.96]), and ICU admission (aOR = 3.70 [1.70–8.19]) were associated with higher odds of death. In contrast, vaccination (aOR = 0.43 [0.19–0.94]) was associated with lower odds of death (Fig. 1).

4 Discussion

This study investigated factors associated with mortality in patients presenting with severe acute respiratory infections, including COVID-19. The findings highlight several demographic, clinical, and

vaccination-related variables that are significantly associated with an increased or decreased risk of death.

Older age, particularly above 60 years, was found to be a significant risk factor for mortality in the bivariate analysis (OR = 3.25; p = 0.048). Indeed, other studies have shown that advanced age is a major determinant of poor outcomes in respiratory infections, owing to immunosenescence and a higher burden of chronic disease among older people [5, 6].

Male sex showed a trend toward increased mortality (OR = 1.95; p = 0.088 in multivariable analysis), although this was not statistically significant. Previous studies have likewise reported higher mortality in men, potentially owing to behavioral and immunological differences [7].

COVID-19 vaccination was significantly associated with a lower risk of death in both univariable (OR = 0.38; p = 0.007) and multivariable analysis (OR = 0.43; p = 0.037). This finding is directionally consistent with real-world evidence of reduced hospitalization and mortality among vaccinated individuals [8]; however, this cohort was not restricted to laboratory-confirmed COVID-19: only 8 of 224 patients were SARS-CoV-2 PCR/antigen-positive at admission (none of whom died), and vaccination status was analyzed as a simple binary exposure without accounting for time since last dose, number of doses, vaccine product, or the variant period in which infection occurred. Given the observational design and these limitations, this association should be interpreted as hypothesis-generating rather than as firm evidence of a causal, vaccine-specific protective effect, and residual confounding by indication (e.g., healthier or more health-engaged patients being more likely to be vaccinated) cannot be excluded.

Having multiple comorbidities was associated with higher mortality (OR = 2.78; p = 0.021). In particular, heart disease emerged as an independent risk factor in multivariable analysis (OR = 3.14; p = 0.023). This is consistent with existing literature indicating that cardiovascular conditions exacerbate the severity of respiratory infections and increase the risk of complications [9].

Hypertension was also associated with increased risk in univariable analysis, although it was not included in the final multivariable model. These findings reinforce the need to closely monitor patients with underlying cardiovascular diseases during respiratory infection outbreaks. It should be noted that, with 44 deaths distributed across the covariates considered, the events-per-variable ratio for the multivariable model is limited, which constrains the number of covariates that can be reliably estimated and increases the risk of overfitting. The choice of covariates (sex, vaccination, heart disease, dyspnea, ICU admission) was based on clinical relevance rather than a pre-specified, formally documented selection strategy. Baseline severity indicators with strong bivariate associations (SpO2, desaturation) were not included in the final model. These modeling choices should be interpreted as exploratory, and a pre-specified admission-only model (excluding downstream variables such as ICU admission) would strengthen causal interpretation in future analyses.

Among clinical signs, dyspnea was associated with higher mortality (adjusted OR = 2.70; p = 0.052), although this did not reach conventional statistical significance; this likely reflects respiratory

compromise. Symptoms such as palpitations, chest pain, and anosmia were also associated with increased mortality in univariable analysis, suggesting that both respiratory and cardiovascular manifestations can indicate more severe disease progression [10].

Admission to the intensive care unit (ICU) showed the strongest statistical association with death, with odds ratios of 6.32 in the bivariate analysis and 3.70 in the multivariable analysis ($p = 0.001$). This association should, however, be interpreted as a marker of illness severity rather than as an independent causal risk factor: ICU admission occurs downstream of clinical deterioration and may also reflect triage decisions and bed availability, so its inclusion in a mortality-prediction model can introduce overadjustment or collider bias. Accordingly, this variable is presented separately from the admission-time predictors (age, comorbidities, dyspnea) and should not be interpreted as an actionable or modifiable risk factor; it nonetheless underscores the importance of early risk stratification at admission, before ICU-level deterioration occurs.

Limitations of the Study

Our study has several limitations. First, only patients who were hospitalized at the three sentinel sites were included, which excluded SARI cases managed on an outpatient basis; this may lead to an underestimation of overall SARI incidence and limits the representativeness of the findings for the full spectrum of disease severity. Second, the retrospective, hospital-based design does not allow us to confirm consecutive, unselected enrollment, and residual selection and information bias cannot be excluded; a participant flow diagram would strengthen transparency in a future version. Third, ICU admission was included in the multivariable model despite likely reflecting illness severity rather than an independent causal factor, so the corresponding association should not be interpreted causally (see Discussion above). Fourth, the multivariable model was based on a limited number of events (44 deaths) and a clinically rather than statistically pre-specified covariate set, without formally reported model diagnostics; these estimates should be considered exploratory pending external validation. Fifth, an etiological diagnosis could not be established for 82.1% of SARI cases, and only 8 patients had a laboratory-confirmed SARS-CoV-2 infection; this limits our ability to attribute the observed vaccination–mortality association specifically to protection against COVID-19. The study is more accurately viewed as an analysis of all-cause SARI mortality with COVID-19 vaccination as one covariate among several. Finally, missing data for several clinical variables (notably anthropometric measures and SpO2, see Methods) may have affected the precision of some estimates.

5 Conclusions

This study identifies advanced age, heart disease, and dyspnea as admission-time factors associated with mortality in patients with severe respiratory infections, while ICU admission was strongly associated with death but most likely reflects underlying illness severity rather than an independent causal factor. COVID-19 vaccination was associated with a lower risk of death in this cohort; however, given the observational design, the limited number of laboratory-confirmed SARS-CoV-2 cases, and the binary

definition of vaccination status used, this finding should be considered preliminary and hypothesis-generating rather than definitive evidence of vaccine effectiveness against SARI mortality. These findings nonetheless highlight the need for targeted monitoring and early risk stratification in high-risk groups, and support further prospective, etiology-stratified studies to clarify the specific contribution of COVID-19 vaccination.

Abbreviations

SARI
Severe Acute Respiratory Infection
NIC
National Influenza Center
SARS
Severe Acute Respiratory Syndrome
ICU
Intensive Care Unit
OR
Odds Ratio
CI
Confidence Interval
PPSV23
Pneumococcal Polysaccharide Vaccine 23-valent
PCV13
Pneumococcal Conjugate Vaccine 13
aOR
Adjusted Odds Ratio
WHO
World Health Organization
CRF
Case Report Form
BMI
Body Mass Index

Declarations

Author Contributions: Conceptualization, M.S., C.L., and A.M.N.; methodology, M.S., A.M.N., and B.T.; software, M.C.; validation, N.D., I.V.-W., and A.A.M.; formal analysis, A.G. and C.T.; investigation, A.M.N., B.T., A.S., L.F., M.S., F.W., and C.S.; writing—original draft preparation, A.M.N.; writing—review and editing, B.T., A.M.N., and M.S.; data management, J.F.; supervision, V.M.-P.C.D.; B.T., A.S., L.F., C.S., M.D., M.A.B., B.D., and A.S.; funding acquisition, M.S. and M.A.B. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author because of ethical restrictions.

Conflicts of Interest: The authors declare no conflicts of interest.

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Figures

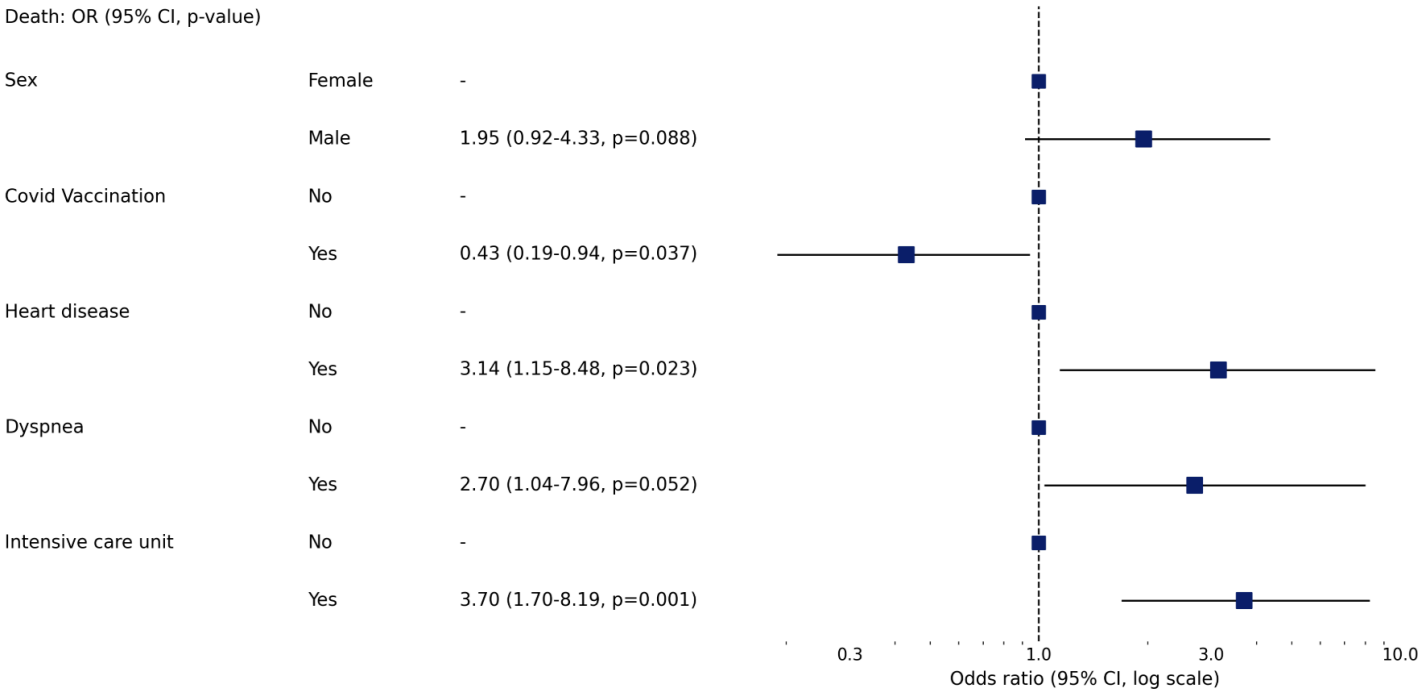


Figure 1

Multivariable analysis of clinical status at hospital discharge

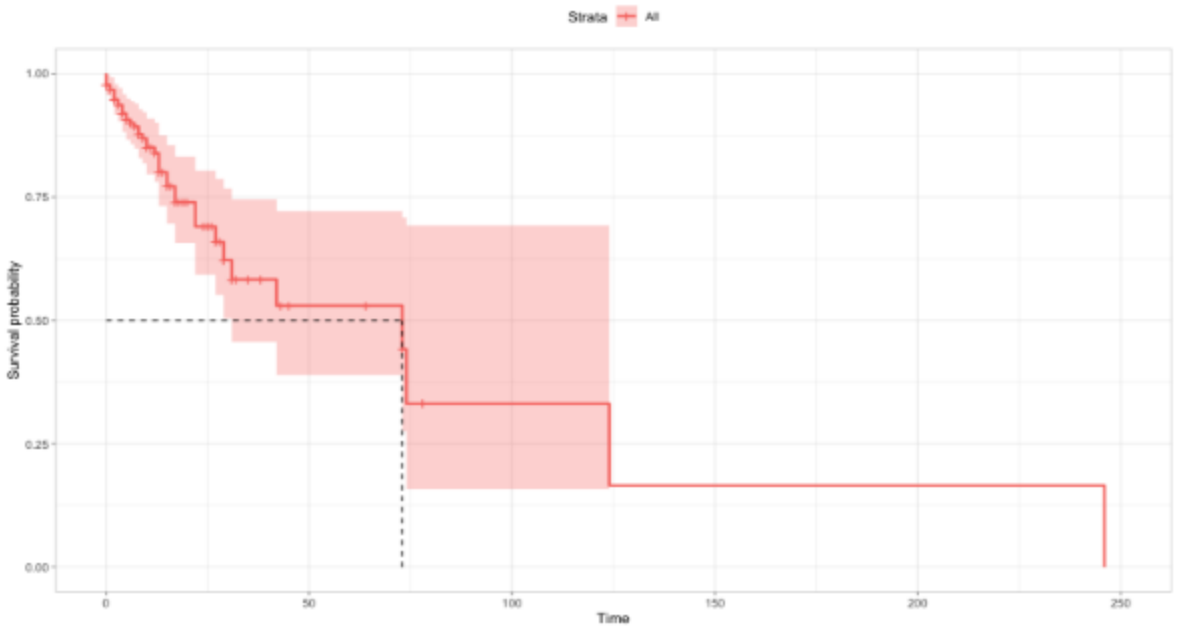


Figure 2

Overall Survival Curve Estimated by the Kaplan–Meier Method