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RESEARCH ARTICLE

Severe community-acquired pneumonia in Reunion Island: Epidemiological, clinical, and microbiological characteristics, 2016–2018

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Abstract

Purpose

No data are available on severe community-acquired pneumonia (CAP) in the French overseas department of Reunion Island. This is unfortunate as the microorganisms responsible for the disease are likely to differ from those in temperate regions due to a tropical climate and proximity to other islands of the Indian Ocean region. The aim of this study was to assess the epidemiological, clinical, prognosis, and microbiological characteristics of patients with severe CAP in Reunion Island.

Materials and methods

This retrospective study evaluated all patients with CAP aged >18 years and hospitalized in one of the two intensive care units of Reunion Island between 2016 and 2018. Microorganisms were identified by culture from blood and respiratory samples, multiplex polymerase chain reaction from respiratory samples, urinary antigen tests, and serology.

Results

Over the study period, 573 cases of severe CAP were recorded, with a mean incidence of 22 per 100,000 person-years. The most frequently isolated microorganism was influenza (21.9%) followed by *Streptococcus pneumoniae* (12%). The influenza virus was detected in affected patients all year round. Twenty-four patients with severe CAP came from another island of the Indian Ocean region (4.2%), mainly Madagascar (>50%). Two of these patients presented with melioidosis and 4 were infected with *Acinetobacter spp.*

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Abbreviations: CAP, Community-acquired pneumonia; ICU, Intensive care unit; PCR, Polymerase chain reaction.

Conclusions

Our findings have major implications for the management of severe CAP in tropical regions. The most frequently isolated microorganism in patients with severe CAP in Reunion Island is influenza followed by *S. pneumoniae*. Physicians should be aware that influenza is the main cause of severe CAP in patients living in or returning from Reunion Island, where this virus circulates all year round.

Introduction

Community-acquired pneumonia (CAP) is an acute infection of the lung parenchyma that is acquired outside hospital or health care facilities. It is the most common life-threatening infectious disease. National and international guidelines for the management of severe CAP [1, 2] are based on data collected in regions with a temperate climate, where *Streptococcus pneumoniae*, viruses, and *Legionella* are the main cause of the disease [3, 4]. Accordingly, they recommend to initiate antibiotic therapy effective against all strains of *S. pneumoniae* and *Legionella* (i.e., combination therapy with cephalosporin and a macrolide or monotherapy with respiratory fluoroquinolone) [5] and to consider the possibility of influenza infection during the winter season [6].

These guidelines are also applied in tropical regions, where the microorganisms responsible for the disease are likely to differ from those in temperate regions. This is the case in Reunion Island, a French overseas department with a population of 850,000 inhabitants located in the Indian Ocean region. This tropical island is characterized by two distinct seasons, the hot and humid southern summer from December to May and the milder and drier southern winter the rest of the year. Patients from the entire Indian Ocean region (Madagascar, Mauritius, and the Comoros Archipelago) are regularly evacuated to Reunion, both for reasons of proximity and because the medical infrastructure meets European standards (P3 microbiology laboratories, coronarography, all types of surgeries, circulatory assistance, etc.). This raises the possibility that microorganisms endemic to Madagascar and other neighboring islands, such as *Burkholderia pseudomallei* [7] and *Yersinia pestis* [8], are responsible for some of the cases of severe CAP observed on the island. In spite of this, no comprehensive study of the etiology of severe CAP in Reunion have been conducted to date. A better knowledge of the microbiological characteristics of severe CAP in the region could improve the management of residents or travelers from Reunion Island by helping physicians choose the best antimicrobial treatment according to the season.

The aim of this study was to assess the epidemiological, clinical, prognosis, and microbiological characteristics of patients with severe CAP hospitalized in intensive care unit (ICU) in Reunion Island.

Materials and methods

Selection of the study sample

We performed a retrospective chart review of all adult patients diagnosed with severe CAP and hospitalized in one of the two ICUs of Reunion Island (Félix Guyon University Hospital and Saint Pierre University Hospital) between January 2016 and December 2018.

Ethics

A written notice was provided to all participants or their legally authorized representative. Informed consent was not needed due to the retrospective and non-interventional nature of the study.

This observational study was approved by the French Ethics Committee of Infectious Disease and Tropical Medicine (CER-MIT) and declared to the French National Commission for Data Protection and Liberties (CNIL, #2206739). It complies with the Strengthening the Reporting of Observational studies in Epidemiology recommendations statement [9].

Definitions

Community-acquired pneumonia was defined as pneumonia acquired outside hospital and diagnosed within 48 hours of hospital admission. Diagnosis was established in the presence of a new lung infiltrate on chest x-ray or computed tomography scan together with one or more of the following symptoms and signs: fever $>38^{\circ}\text{C}$, cough, expectoration, chest pain, dyspnea, and signs of invasion of the alveolar space [10].

A severe case of CAP was defined as any patient hospitalized in ICU with 1 of the major criteria and/or 3 or more of the minor criteria established by the American Thoracic Society [1]. Major criteria were septic shock with need for vasopressors and respiratory failure requiring mechanical ventilation. Minor criteria were respiratory rate >30 breaths/min, PaO₂/FIO₂ ratio <250 , multilobar infiltrates, confusion or disorientation, blood urea nitrogen level >20 mg/dL, white blood cell count <4 G/L, platelet count <100 G/L, hypothermia $<36^{\circ}\text{C}$, and hypotension requiring aggressive fluid resuscitation.

Microbiological investigations

Blood and respiratory samples (sputum samples from non-intubated patients and tracheal or bronchoalveolar lavage from intubated patients) were collected from all patients. Microorganism identification was performed on both types of samples using Gram staining followed by culturing for definite identification. Alternatively, identification was performed using matrix-assisted laser desorption ionization time-of-flight mass spectrometry.

Respiratory samples were tested by multiplex polymerase chain reaction (PCR) (Seegene Allplex™ respiratory panel, Eurobio-ingen, Les Ulis, France) for the following microorganisms: influenza, respiratory syncytial virus, adenovirus, enterovirus, parainfluenza, human metapneumovirus, human bocavirus, rhinovirus, coronavirus (NL63, 229E, and OC43), *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella spp*, *Haemophilus influenzae*, *S. pneumoniae*, *Bordetella pertussis*, and *B. parapertussis*.

Pneumococcal and *Legionella* urinary antigen tests were routinely performed on admission to ICU.

Serology for atypical respiratory microorganisms was performed at the physician's discretion.

Data collection

Patient comorbidities were recorded at hospital admission.

Clinical and biological data were collected at the time of CAP diagnosis.

Average rainfall data for the 2016–2018 period were obtained from *Météo France*, Bureau of Meteorology, Saint-Denis, Reunion Island.

Study outcome

The primary outcome was to determine the ICU mortality and morbidity of patients with CAP.

The secondary outcome was to identify the microorganisms responsible for CAP in patients hospitalized in ICU.

Statistical analysis

Results were expressed as total number (percentage) for categorical variables and as median [25th-75th percentiles] for continuous variables. Continuous variables were compared using the Mann-Whitney test and categorical variables using the Chi-square test or Fisher's exact test, as appropriate. Survival functions in ICU at 30 days were estimated using the Kaplan-Meier method and compared using the log-rank test. A *P* value <0.05 was considered significant. Analyses were performed using the SAS statistical software (8.2, Cary, NC, USA).

Results

Incidence and isolated microorganisms

From January 2016 to December 2018, 1,283 patients were admitted to ICU for suspected or confirmed lower tract respiratory infection. Of these, 710 patients were excluded (12 were <18 years old, 698 had nosocomial pneumonia or non-infectious pneumonia). The remaining 572 patients formed the study cohort. The mean incidence of severe CAP was 22 per 100,000 person-years. The median age was 62 [52–73] years and the median simplified acute physiology score II on admission was 44 [31–57]. Patients presented with acute respiratory distress syndrome in 396 cases (69.2%) and with sepsis or septic shock in 347 cases (60.7%). Patient characteristics at ICU admission are shown in Tables 1 and 2.

The microorganism(s) responsible for severe CAP were identified in 67% of cases. The most frequently isolated microorganisms were influenza (21.9%), *S. pneumoniae* (12%), *Staphylococcus* spp (10.8%), *Enterobacteriaceae* (9.8%), and *H. influenzae* (7.5%). Pantone-Valentine leukocidin-positive *Staphylococcus aureus* accounted for 11.3% of all *Staphylococcus* spp strains. *Legionella pneumophila* and other intracellular bacteria were responsible for 3% of cases (Table 3). Other isolated viruses were rhinovirus in 10 cases (1.7%), human metapneumovirus in 9 cases (1.6%), coronavirus OC43 in 9 cases (1.6%), parainfluenza in 9 cases (1.6%), respiratory syncytial virus in 8 cases (1.4%), and adenovirus in 2 cases (0.3%). In the group of patients with influenza CAP, infection was polymicrobial in 52 cases (41.6%).

The incidence of influenza vs. *S. pneumoniae* according to rainfall is shown in Fig 1.

Twenty-four patients with severe CAP came from another island of the Indian Ocean region (4.2%), mainly Madagascar (>50%). Two of these patients presented with melioidosis (which is caused by *B. pseudomallei*) and 4 were infected with *Acinetobacter* spp (2 with *Acinetobacter baumannii* and 2 with *A. pittii*).

Prognosis

Over the study period, ICU mortality for the entire cohort was 20.8%. Survival rates according to microorganism are shown in Fig 2.

In univariate analysis, mortality was higher in patients with influenza CAP (24%) than in patients with non-influenza CAP (18.9%, *P* = 0.04).

The median duration of ICU stay was 7 [4–17] days in patients with influenza CAP vs. 6 [3–11] days in patients with non-influenza CAP (*P* = 0.018).

Table 1. Clinical characteristics at intensive care unit admission.

Clinical characteristics	Missing data	Total	Influenza CAP	Non-Influenza CAP	P-value
		(n = 572)	(n = 125)	(n = 447)	
Age (years)	0	62 [52–73]	61 [48.3–69]	63 [52.2–74]	0.099
Male	0	376 (65.7)	73 (58.4)	303 (67.8)	0.013
Body mass index (kg/m ²)	45	24.1 [21.4–29]	25.47 [22–29.9]	23.8 [21.1–28.63]	0.079
¹ Foreign residence	0	26 (4.5)	3 (2.4)	23 (5.1)	0.091
Duration of symptoms before ICU admission (days)	0	2 [1–5]	3 [2–6]	2 [1–5]	0.018
² CURB-65 score	8	3 [2–3]	3 [2–4]	3 [2–3]	0.122
SAPS II	12	53 [28–68]	55 [37–58.5]	48.5 [28.7–68.7]	0.795
Pulmonary abscess	0	38 (6.6)	7 (5.6)	31 (6.9)	0.147
Influenza-like illness	0	175 (30.6)	68 (54.4)	107 (23.9)	<0.001
Immunosuppression	0	47 (8.2)	9 (7.2)	38 (8.5)	0.136
Corticosteroids	0	53 (9.3)	7 (5.6)	46 (10.3)	0.04
³ Hazardous alcohol use	3	159 (27.8)	26 (20.8)	133 (29.8)	0.13
Chronic obstructive pulmonary disease	0	144 (25.2)	26 (20.8)	118 (26.4)	0.042
Asthma	0	33 (5.8)	13 (10.4)	20 (4.5)	0.009
Hypertension	0	248 (43.3)	56 (44.8)	192 (43)	0.076
Chronic renal failure with dialysis	0	28 (4.9)	5 (4)	23 (5.1)	0.171
Diabetes mellitus	0	197 (34.4)	48 (38.4)	149 (33.3)	0.048
Liver cirrhosis	0	22 (3.8)	4 (3.2)	18 (4.0)	0.2
Cancer < 4 months	0	51 (8.9)	6 (4.8)	45 (10.1)	0.026
History of congestive heart failure	0	114 (19.9)	18 (14.4)	96 (21.5)	0.022
Pregnancy	0	7 (1.2)	2 (1.6)	5 (1.1)	0.294

Results are expressed as n (%) or median [25th–75th percentiles], as appropriate.

CAP: Community-acquired pneumonia; ICU: Intensive care unit; SAPS 2: Simplified acute physiology score 2 [11].

¹Wounded and sick patients transported from foreign countries.

²CURB-65 (confusion: 1 point; blood urea nitrogen > 19 mg per dl: 1 point; respiratory rate > 30: 1 point; systolic blood pressure < 90 mmHg and/or diastolic blood pressure < 60 mmHg: 1 point; age > 65 years: 1 point) [12].

³Alcohol Use Disorders Identification Test Consumption \geq 4 for men or 3 for women [13].

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The median duration of mechanical ventilation was 4 [0–14] days in patients with influenza CAP vs. 2 [0–8] days in patients with non-influenza CAP ($P = 0.04$).

The need for extracorporeal membrane oxygenation was 8% in patients with influenza CAP vs. 2.5% in patients with non-influenza CAP ($P = 0.005$).

Discussion

This is the first epidemiological study to assess the clinical, microbiological, and prognostic characteristics of severe CAP in Reunion Island. It is also one of the rare studies on CAP in the Indian Ocean region [14, 15]. The incidence of severe CAP in our cohort was 22 per 100,000 person-years. The most frequently isolated microorganism was influenza (21.9%) followed by *S. pneumoniae* (12%). These epidemiological data can help to implement appropriate anti-infective treatment in residents or travelers from Reunion Island with severe CAP [16].

The rate of microbiological identification in our study was relatively high (68.3%) compared to other studies on the subject (around 50%) [3, 17–20]. This difference may be explained by our use of multiplex PCR, which allowed to detect both viral and bacterial agents of the disease. As in our study, recent studies using PCR for microbiological identification [20–22] found viruses (and especially influenza) to be the most common cause of severe CAP.

Table 2. Prognostic factors and laboratory findings at intensive care unit admission.

Variables	Missing	Total	Influenza CAP	Non-Influenza CAP	P-value
	data	(n = 572)	(n = 125)	(n = 447)	
Prognostic factors					
Temperature (°C)	23	38 [36.6–38.7]	38.3 [37.1–39]	37.7 [36.5–38.6]	0.017
Glasgow Coma Scale score	1	15 [3–15]	15 [3–15]	15 [3–15]	0.348
Extracorporeal membrane oxygenation	0	21 (3.7)	10 (8)	11 (2.5)	0.005
Mechanical ventilation	0	325 (56.8)	76 (60.8)	249 (55.7)	0.049
Non-invasive ventilation	0	122 (21.3)	31 (24.8)	91 (20.4)	0.054
High-flow oxygen therapy	0	72 (12.6)	17 (13.6)	55 (12.3)	0.11
Renal replacement therapy	0	74 (12.9)	19 (15.2)	55 (12.3)	0.08
Catecholamines	0	283 (49.5)	64 (51.2)	219 (49)	0.073
PaO ₂ /FiO ₂ ratio (mmHg)	6	166 [110.25–240]	152 [97.5–205.5]	179.5 [115–252.8]	0.003
Laboratory findings					
Creatinine level (μmol/L)	0	109 [70–178]	106 [70–148.25]	110 [71.25–187]	0.335
Total bilirubin level (μmol/L)	12	10 [6–16]	9 [6–15]	11 [6–16]	0.414
Prothrombin time (%)	8	70 [55–83]	72.5 [58.75–87]	67 [53–81]	0.029
Platelet count (G/L)	1	188 [129–271]	158 [119–218]	203.5 [136–285.5]	<0.001
Leucocyte count (G/L)	0	11.7 [7.5–16.3]	8.9 [5.5–14.5]	12.1 [8.15–16.65]	<0.001
Lactate level (mmol/L)	9	1.95 [1.3–3.4]	2 [1.3–3.2]	1.9 [1.3–3.5]	0.859
Creatine phosphokinase (mg/dL)	18	210 [87–604]	260 [122–947]	184 [83–513]	0.036
Hemoglobin level (g/dL)	0	12 [10.1–13.6]	12.75 [11.25–14]	11.76 [10–13.5]	0.001
Alanine aminotransferase level (UI/L)	11	28 [17–51.25]	32 [16–55]	26 [17–51]	0.271
Troponin level (ng/dL)	24	37 [16–104]	25 [11–82]	38 [18–116.25]	0.017
C-reactive protein level (mg/L)	54	170 [73.25–304.25]	148 [71.5–250.5]	177.5 [73.1–324]	0.558

Results are expressed as n (%) or median [25th-75th percentiles], as appropriate.

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Table 3. Isolated microorganisms.

Microorganisms	Total	Influenza CAP	Non-Influenza CAP
	(n = 572)	(n = 125)	(n = 447)
Viruses	168 (29.3)	125 (100)	43 (9.6)
Bacteria	283 (49.5)	50 (40)	233(52.1)
<i>Staphylococcus spp</i>	62 (10.8)	24 (19.2)	38 (8.5)
Panton-Valentine Leukocidin-positive	7 (1.2)	4 (3.2)	3 (0.7)
<i>Streptococcus pneumoniae</i>	69 (12)	16 (12.8)	53 (11.8)
<i>Haemophilus influenzae</i>	43 (7.5)	5 (4)	38 (8.5)
Enterobacteriaceae	56 (9.8)	3 (2.4)	53 (11.8)
Non-fermenting gram-negative bacilli	26 (4.5)	2 (1.6)	24 (5.4)
<i>Legionella</i>	9 (1.5)	0	9 (2)
Intracellular	9 (1.5)	0	9 (2)
Fungi	8 (1.4)	2 (1.6)	6 (1.3)

Results are expressed as n (%).

Polymicrobial infection was found in 52 cases of influenza CAP (41.6%).

Bacteremia was found in 97 cases of severe CAP (16.9%).

Bacteremia was found in 44 cases of influenza CAP (35.2%) and in 53 cases of non-influenza CAP (11.8%).

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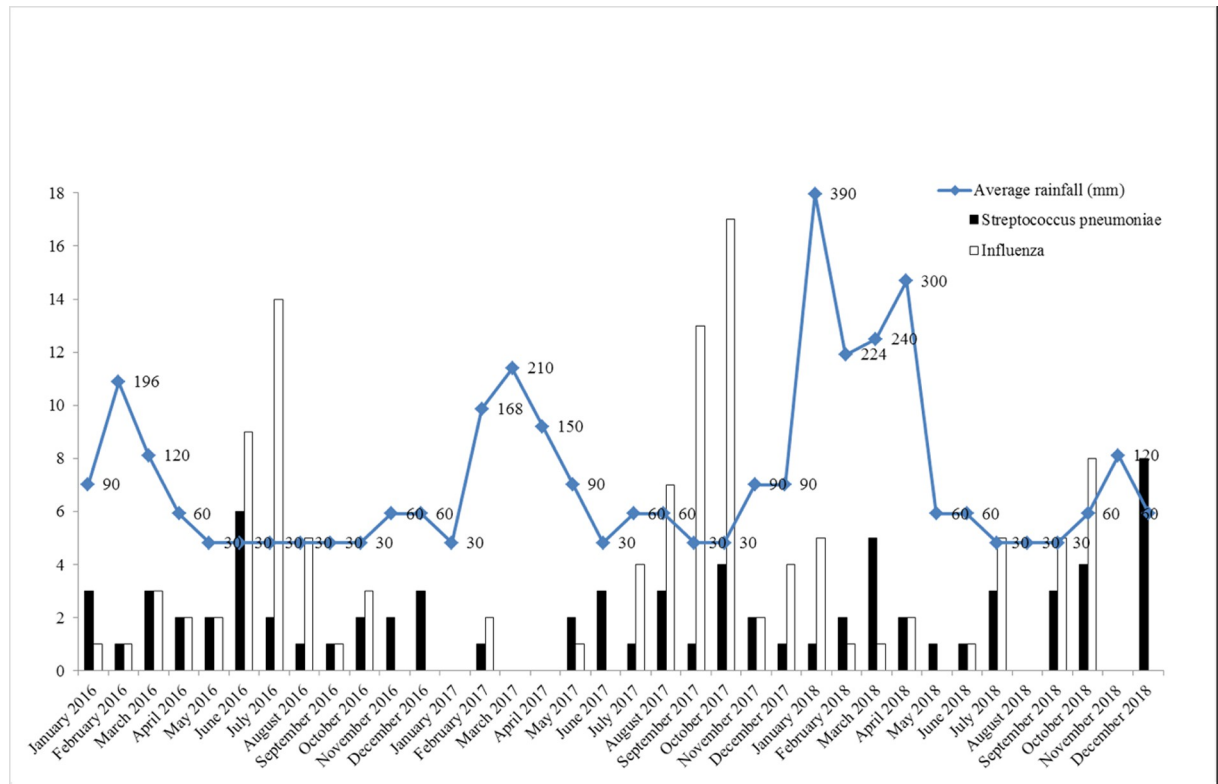


Fig 1. Incidence of influenza vs. *S. pneumoniae* according to rainfall, 2016 to 2018, Reunion Island.

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Thus, in the 2016 retrospective study conducted by Visseaux *et al.* in mainland France [21], 29.2% of 5,000 ICU patients with severe CAP had a viral infection. This finding is in line with our study, which detected viruses in 29.3% of patients with severe CAP. By contrast, the influenza virus accounted for 74.7% of all detected viruses in our study compared to 34.4% in the study by Visseaux *et al.* Siow *et al.* [23] have stressed the importance of using PCR for the detection of viruses causing severe CAP in tropical environments, where the incidence of viral infections is less dependent on the seasons than in temperate regions [24, 25]. In our study, this approach showed that influenza circulates all year round in Reunion Island. In spite of this, peaks of influenza incidence were observed during the southern winter and monthly incidence was found to be inversely proportional to temperature and rainfall. Several other studies conducted in tropical regions have found an association between seasons and the occurrence of influenza infections [25–29]. However, the physio-pathological explanation for this association remains to be established [24].

In our cohort, *S. pneumoniae* was the second (12%) most frequently isolated microorganism. This contrasts with most available studies, which identify *S. pneumoniae* as the main cause of severe CAP. However, many of these studies do not provide the incidence of viral infections [1, 2, 5, 18, 23] or underestimate it due to the non-systematic use of PCR for microorganism detection. In the last epidemiological study on severe CAP in Reunion Island, Paganin *et al.* [18] identified *S. pneumoniae* (42.9%) and *Klebsiella pneumoniae* (22.4%) as the main cause of the disease. Yet, this 2004 study did not establish the viral etiology of severe CAP because multiplex PCR was not systematically used in local ICUs at the time.

In our study, 2 patients returning from Madagascar presented with melioidosis. Given the recent emergence of *B. pseudomallei* in the Indian Ocean islands [7], clinicians and

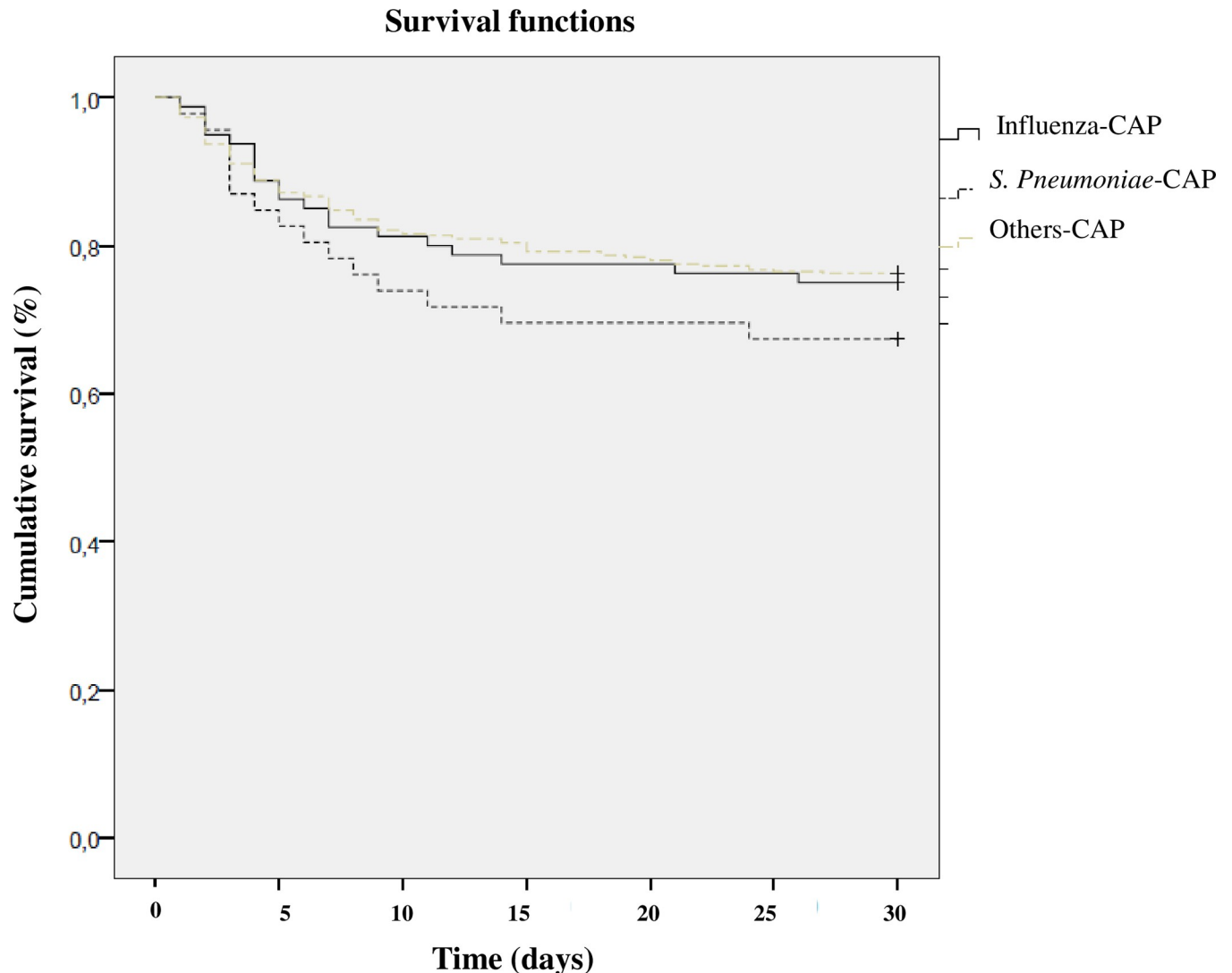


Fig 2. Survival rate according to microorganism using Kaplan–Meier analysis.

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microbiologists should consider melioidosis as a differential diagnosis in patients returning from the region, in particular from Madagascar. Other atypical microorganisms were detected, namely 2 strains of *A. baumannii* and 2 strains of *A. pittii*, with a mortality of 50%. While *Acinetobacter spp* strains are mainly known as nosocomial infectious agents, they have been shown to cause severe CAP in tropical areas. Thus, an observational study [30] conducted in Australia reported 41 cases of CAP caused by *Acinetobacter spp*, with *A. baumannii* accounting for 85% of strains. In that study, 88% of infectious episodes occurred during the rainy season, and 80% of patients required hospitalization in ICU.

The mortality rate for our entire cohort was 20.8%. This figure is consistent with those reported in the recent studies by Ferrer *et al.* (22%) [31] and Cavallazzi *et al.* (27%) [32]. By contrast, a UK study found mortality to reach 50% in patients with CAP hospitalized in ICU [33]. In the study conducted by Dupuis *et al.* in mainland France, hospital mortality was 22.8% in a cohort of 1,665 patients with severe pneumococcal CAP [34]. In our study, mortality and morbidity (including the need for extracorporeal membrane oxygenation and mechanical

ventilation) were higher in patients with influenza CAP than in those with non-influenza CAP. Likewise, in the Spanish study by Abelleira *et al.*, patients with CAP caused by influenza A H1N1 had a poorer prognosis than those with non-influenza CAP [35]. In a study conducted during the 2009 AH1N1 pandemic, Vandroux *et al.* [36] found mortality and the need for extracorporeal membrane oxygenation to be extremely high in Reunionese patients with AH1N1 influenza. Interestingly, Vandroux *et al.* reported numerous co-infections (31%), nearly half of which were caused by influenza and *S. aureus*. This is consistent with our results, since 41.6% of influenza infections were polymicrobial in our cohort, with half of them involving *S. aureus*. Other studies have found that mixed viral-bacterial infections are associated with an increased risk of mortality in patients with severe CAP [37, 38].

In line with the recommendations of the Infectious Diseases Society of America and the World Health Organization, the French Society of Infectious Disease and the French National Authority for Health recommend initiating curative treatment with oseltamivir in patients at risk of severe influenza [39]. Several recent studies confirm the potential benefit of early treatment with oseltamivir [40–43].

Our study has many limitations. First, the retrospective nature of the study could have introduced biases in our results. Second, only patients with severe CAP were included in the sample, which means that our results do not reflect the exact etiological agents of CAP in Reunion Island. Third, since our study covers the 2016–2018 period, it does not account for changes in the ecology of severe CAP that likely resulted from the COVID-19 pandemic and the implementation of social distancing measures [44–46]. Lastly, in the absence of multivariate analysis, we cannot discard the possibility that the difference in mortality rates observed between patients with influenza CAP vs. non-influenza CAP is due to the fact that the first group of patients had more comorbidities (age over 65 years, asthma, diabetes mellitus, etc.).

Conclusion

Our findings have major implications for the management of severe CAP in tropical regions. The most frequently isolated microorganism in patients with severe CAP in Reunion Island is influenza followed by *S. pneumoniae*. Physicians should be aware that influenza is the main cause of severe CAP in patients living in or returning from Reunion Island, where this virus circulates all year round.

Supporting information

S1 Dataset.

(XLS)

Author Contributions

Conceptualization: Axel de Mangou, Agathe Combe, Nathalie Coolen-Allou, Guillaume Miltgen, Nicolas Traversier, Olivier Belmonte, David Vandroux, Margot Caron, Charles Vidal, Jérôme Allyn, Nicolas Allou.

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Writing – original draft: Charles Vidal, Jérôme Allyn, Nicolas Allou.

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References

1. Metlay J.P, Waterer G.W, Long A.C, Anzueto A, Brozek J, Crothers K et al., « Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America », *Am. J. Respir. Crit. Care Med.*, vol. 200, n° 7, p. e45-e67, 01 2019, <https://doi.org/10.1164/rccm.201908-1581ST> PMID: 31573350
2. Agence Française de Sécurité Sanitaire des Produits de Santé—Société de Pathologie Infectieuse de langue Française-Société de Pneumologie de Langue Française: Antibiothérapie par voie générale dans les infections respiratoires basses de l'adulte: Pneumonie aiguë communautaire, Exacerbations de Bronchopneumopathie Chronique Obstructive—juillet 2010.
3. Lim TK, Siow WT. Pneumonia in the tropics. *Respirology* 2018; 23: 28–35. <https://doi.org/10.1111/resp.13137> PMID: 28763150
4. Cilloniz C, Martin-Loeches I, Garcia-Vidal C, San Jose A, Torres A. Microbial Etiology of Pneumonia: Epidemiology, Diagnosis and Resistance Patterns. *Int J Mol Sci* 2016 Dec 16; 17(12):2120. <https://doi.org/10.3390/ijms17122120> PMID: 27999274
5. Société de Pathologie Infectieuse de Langue Française. [15th consensus conference about management of lower respiratory tract infections in immunocompetent adult]. *Med Mal Infect.* mai 2006; 36:235–44. <https://doi.org/10.1016/j.medmal.2006.04.003> PMID: 16967525
6. Société de Pathologie Infectieuse de Langue Française. Procédure actualisée de prise en charge globale d'un patient suspect de grippe saisonnière. 2016. <https://www.coreb.infectiologie.com/UserFiles/File/medias/coreb/grippe/proced-grippe-saison-coreb-site-15fev16-1.pdf>.
7. Allou N, Martinet O, Allyn J, Bouchet B, Jaffar-Bandjee M-C, Galas T, et al. Emergence of melioidosis in the Indian Ocean region: Two new cases and a literature review. *PLoS Negl Trop Dis.* déc 2017; 11(12):e0006018. <https://doi.org/10.1371/journal.pntd.0006018> PMID: 29240770
8. Ratsitorahina M, Rabarijaona L, Chanteau S, Boisier P. Seroepidemiology of human plague in the Madagascar highlands. *Trop Med Int Health* 2000; 5:94–8. <https://doi.org/10.1046/j.1365-3156.2000.00521.x> PMID: 10747268
9. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Lancet* 2007 Oct 20; 370(9596):1453–7. [https://doi.org/10.1016/S0140-6736\(07\)61602-X](https://doi.org/10.1016/S0140-6736(07)61602-X) PMID: 18064739
10. Berdyev D, Scapin R, Labille C, Lambin C, Fartoukh M. Serious community infections—Acute bacterial community-acquired pneumonia in adults. *Réanimation* 2011; 20:S566–S575.
11. Le Gall JR, Lemeshow S, Saulnier F. A New Simplified Acute Physiology Score (SAPS II) Based on a European/North American Multicenter Study. *JAMA* 1993; 270: 2957–63. <https://doi.org/10.1001/jama.270.24.2957> PMID: 8254858
12. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003; 58:377–382. <https://doi.org/10.1136/thorax.58.5.377> PMID: 12728155

13. Bradley KA, DeBenedetti AF, Volk RJ, Williams EC, Frank D, Kivlahan DR. AUDIT-C as a brief screen for alcohol misuse in primary care. *Alcohol Clin Exp Res* 2007 Jul; 31(7):1208–17. <https://doi.org/10.1111/j.1530-0277.2007.00403.x> PMID: 17451397
14. Rakotoson JL, Rakotomizao JR, Andrianarisoa ACF. Acute community acquired pneumonia: 96 cases in Madagascar. *Med Trop* 2010; 70(1):62–4. PMID: 20337118
15. Razanajatovo NH, Guillebaud J, Harimanana A, Rajatonirina S, Ratsima EH, Andrianirina ZZ, et al. Epidemiology of severe acute respiratory infections from hospital-based surveillance in Madagascar, November 2010 to July 2013. *PLoS One*. 2018 Nov 21; 13(11):e0205124. <https://doi.org/10.1371/journal.pone.0205124> PMID: 30462659
16. Fally M, von Plessen C, Anhøj J, Benfield T, Tarp B, Clausen LN, et al. Improved treatment of community-acquired pneumonia through tailored interventions: Results from a controlled, multicentre quality improvement project. Gupta V, éditeur. *PLoS ONE*. 11 juin 2020; 15(6):e0234308. <https://doi.org/10.1371/journal.pone.0234308> PMID: 32525882
17. Ewig S, Ruiz M, Mensa J, Marcos MA, Martinez JA, Arancibia F, et al. Severe community-acquired pneumonia. Assessment of severity criteria. *Am J Respir Crit Care Med* 1998; 158:1102–8. <https://doi.org/10.1164/ajrccm.158.4.9803114> PMID: 9769267
18. Paganin F, Lillenthal F, Bourdin A, Lugagne N, Tixier F, Génin R, et al. Severe community-acquired pneumonia: assessment of microbial aetiology as mortality factor. *Eur Respir J* 2004; 24:779–85. <https://doi.org/10.1183/09031936.04.00119503> PMID: 15516672
19. De Pascale G, Bello G, Tumbarello M, Antonelli M. Severe pneumonia in intensive care: cause, diagnosis, treatment and management: a review of the literature. *Curr Opin Pulm Med* 2012; 18(3):213–21. <https://doi.org/10.1097/MCP.0b013e328351f9bd> PMID: 22388582
20. Olson G, Davis AM. Diagnosis and Treatment of Adults With Community-Acquired Pneumonia. *JAMA* 2020; 323:885–6. <https://doi.org/10.1001/jama.2019.21118> PMID: 32027358
21. Visseaux B, Burdet C, Voiriot G, Lescure F-X, Chougar T, Brugière O, et al. Prevalence of respiratory viruses among adults, by season, age, respiratory tract region and type of medical unit in Paris, France, from 2011 to 2016. *PLoS ONE*. 2017; 12(7):e0180888. <https://doi.org/10.1371/journal.pone.0180888> PMID: 28708843
22. Ruuskanen O, Lahti E, Jennings LC, Murdoch DR. Viral pneumonia. *Lancet* 2011; 377:1264–75. [https://doi.org/10.1016/S0140-6736\(10\)61459-6](https://doi.org/10.1016/S0140-6736(10)61459-6) PMID: 21435708
23. Siow WT, Koay ES-C, Lee CK, Lee HK, Ong V, Ngerng WJ, et al. The Use of Polymerase Chain Reaction Amplification for the Detection of Viruses and Bacteria in Severe Community-Acquired Pneumonia. *Respiration* 2016; 92:286–94. <https://doi.org/10.1159/000448555> PMID: 27649510
24. Zhang Y, Ye C, Yu J, Zhu W, Wang Y, Li Z, et al. The complex associations of climate variability with seasonal influenza A and B virus transmission in subtropical Shanghai, China. *Sci Total Environ* 2020; 701:134607. <https://doi.org/10.1016/j.scitotenv.2019.134607> PMID: 31710904
25. Monamele GC, Vernet M-A, Nsaibirni RFJ, Bigna JJR, Kenmoe S, Njankouo MR, et al. Associations between meteorological parameters and influenza activity in a subtropical country: Case of five sentinel sites in Yaoundé-Cameroon. Shaman J, éditeur. *PLoS ONE* 2017; 12(10):e0186914. <https://doi.org/10.1371/journal.pone.0186914> PMID: 29088290
26. Moya ML, Palekar R, Widdowson MA, Azziz-Baumgartner E, Kiang RK. Associations between seasonal influenza and meteorological parameters in Costa Rica, Honduras and Nicaragua *Geospat Health* 2015 4; 10(2):372. <https://doi.org/10.4081/gh.2015.372> PMID: 26618318
27. Adegboye OAA, McBryde ES, Eisen DP. Epidemiological analysis of association between lagged meteorological variables and pneumonia in wet-dry tropical North Australia, 2006–2016. *J Expo Sci Environ Epidemiol* 2020; 30(3):448–458. <https://doi.org/10.1038/s41370-019-0176-8> PMID: 31591495
28. Tang JW, Lai FYL, Nymadawa P, Deng YM, Ratnamohan M, Petric M, et al. Comparison of the incidence of influenza in relation to climate factors during 2000–2007 in five countries. *J Med Virol* 2010; 82(11):1958–65. <https://doi.org/10.1002/jmv.21892> PMID: 20872724
29. Kramer SC, Shaman J. Development and validation of influenza forecasting for 64 temperate and tropical countries. *PLoS Comput Biol* 2019 Feb 27; 15(2):e1006742. <https://doi.org/10.1371/journal.pcbi.1006742> PMID: 30811396
30. Davis JS, McMillan M, Swaminathan A, Kelly JA, Piera KE, Baird RW, et al. A 16-year prospective study of community-onset bacteremic *Acinetobacter* pneumonia: low mortality with appropriate initial empirical antibiotic protocols. *Chest* 2014; 146:1038–45. <https://doi.org/10.1378/chest.13-3065> PMID: 24901292
31. Ferrer M, Travieso C, Cilloniz C, Gabarrus A, Ranzani OT, Polverino E, et al. Severe community-acquired pneumonia: Characteristics and prognostic factors in ventilated and non-ventilated patients *PLoS One* 2018 Jan 25; 13(1):e0191721. <https://doi.org/10.1371/journal.pone.0191721> PMID: 29370285

32. Cavallazzi R, Furmanek S, Arnold FW, Beavin LA, Wunderink RG, Niederman MS, et al. The Burden of Community-Acquired Pneumonia Requiring Admission to ICU in the United States. *Chest* 2020; 158(3):1008–1016. <https://doi.org/10.1016/j.chest.2020.03.051> PMID: 32298730
33. Woodhead M, Welch CA, Harrison DA, Bellin G, Ayres JG. Community-acquired pneumonia on the intensive care unit: secondary analysis of 17,869 cases in the ICNARC Case Mix Programme Database. *Crit Care*. 2006; 10 Suppl 2:S1. <https://doi.org/10.1186/cc4927> PMID: 16934135
34. Dupuis C, Sabra A, Patrier J, Chaize G, Saighi A, Féger C, et al. Burden of pneumococcal pneumonia requiring ICU admission in France: 1-year prognosis, resources use, and costs. *Crit Care* 2021 Jan 10; 25(1):24. <https://doi.org/10.1186/s13054-020-03442-z> PMID: 33423691
35. Abelleira R, Ruano-Ravina A, Lama A, Barbeito G, Toubes ME, Domínguez-Antelo C, et al. « Influenza A H1N1 Community-Acquired Pneumonia: Characteristics and Risk Factors-A Case-Control Study. *Can Respir J* 2019 Mar 17; 2019:4301039. <https://doi.org/10.1155/2019/4301039> PMID: 31007805
36. Vandroux D, Allyn J, Ferdynus C, Gaüzere B-A, Kerambrun H, Galas T, et al. Mortality of critically ill patients with severe influenza starting four years after the 2009 pandemic. *Infectious Diseases* 2019; 51:831–7. <https://doi.org/10.1080/23744235.2019.1668957> PMID: 31538824
37. Gillet Y, Issartel B, Vanhems P, Fournet JC, Lina G, Bes M, et al. Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. *Lancet*. 2002 Mar 2; 359(9308):753–9. [https://doi.org/10.1016/S0140-6736\(02\)07877-7](https://doi.org/10.1016/S0140-6736(02)07877-7) PMID: 11888586
38. Voirit G, Visseaux B, Cohen J, Nguyen LBL, Neuville M, Morbieu C, et al. Viral-bacterial coinfection affects the presentation and alters the prognosis of severe community-acquired pneumonia. *Crit Care* 2016; 20(1):375. <https://doi.org/10.1186/s13054-016-1517-9> PMID: 27852281
39. Uyeki TM, Bernstein HH, Bradley JS, Englund JA, File TM, Fry AM, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clin Infect Dis* 2019; 68:e1–47.
40. Hsu J, Santesso N, Mustafa R, Brozek J, Chen YL, Hopkins JP, et al. Antivirals for Treatment of Influenza: A Systematic Review and Meta-analysis of Observational Studies. *Annals of Internal Medicine* 2012; 156:512–4. <https://doi.org/10.7326/0003-4819-156-7-201204030-00411> PMID: 22371849
41. Hernu R, Chroboczek T, Madelaine T, Casalegno J-S, Lina B, Cour M, et al. Early oseltamivir therapy improves the outcome in critically ill patients with influenza: a propensity analysis. *Intensive Care Med* 2018; 44:257–60. <https://doi.org/10.1007/s00134-017-4953-3> PMID: 29026934
42. Lytras T, Mouratidou E, Andreopoulou A, Bonovas S, Tsioufas S. Effect of Early Oseltamivir Treatment on Mortality in Critically Ill Patients With Different Types of Influenza: A Multiseason Cohort Study. *Clin Infect Dis* 2019; 69:1896–902. <https://doi.org/10.1093/cid/ciz101> PMID: 30753349
43. Chen L, Han X, Li Y, Zhang C, Xing X. Impact of early neuraminidase inhibitor treatment on clinical outcomes in patients with influenza B-related pneumonia: a multicenter cohort study. *Eur J Clin Microbiol Infect Dis* 2020; 39:1231–8. <https://doi.org/10.1007/s10096-020-03835-6> PMID: 32026193
44. Krol P, Coolen-Allou N, Teyssyre L, Traversier N, Beasley F, Nativel M, et al. Differential diagnoses of severe COVID-19 in tropical areas: the experience of Reunion Island. *Trop Med Int Health*. 2020 Dec 22. <https://doi.org/10.1111/tmi.13542>
45. Sullivan SG, Carlson S, Cheng AC, Bn Chilver M, Dwyer DE, Irwin M, et al. Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020. *Euro Surveill* 2020 Nov; 25(47):2001847.
46. Melidou A, Pereyaslov D, Hungnes O, Prosenc K, Alm E, Adlhoch C et al. Virological surveillance of influenza viruses in the WHO European Region in 2019/20 –impact of the COVID-19 pandemic. *Euro Surveill*. 2020 Nov 19; 25(46): 2001822. <https://doi.org/10.2807/1560-7917.ES.2020.25.46.2001822> PMID: 33213683