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Original Article

Clinical and epidemiological characterization of severely ill patients with community-acquired infections during COVID-19

Clinical epidemiological characterization of critical ill patients with community-acquired infections during COVID-19

Clinical-Epidemiological Characterization of Critical Patients with Community Infections During COVID-19

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SUMMARY

Introduction: Severely ill patients require admission to intensive care units due to community-acquired infections.

Aim: To characterize, from a clinical and epidemiological perspective, severely ill patients with community-acquired infections during COVID-19.

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Methods: observational, descriptive, case series study,The study was conducted from September 1, 2020, to January 31, 2022. A total of 277 patients were included. Epidemiological and clinical variables were obtained. Statistical analysis was based on descriptive and association summary measures.

Results: 52.7% of the patients were female.The mean age was 40.2 years (95% CI: 37.8–42.4).*Acute Physiology and Chronic Health Evaluation II***(**The mean APACHE II score was estimated at 11.8 (95% CI: 9.7–12.2). The mean Sequential Organ Failure Assessment (SOFA) score was 1.8 (95% CI: 1.4–2.2). 31.7% of patients were hypertensive and 19.4% diabetic. Intra-abdominal infection was the main site of infection (52.7%), followed by pneumonia (34.7%). 98.7% were receiving antimicrobials at admission and 26.3% were receiving mechanical ventilation.

ConclusionsPatients are predominantly female, in their forties, with physiological system disorders and organ dysfunction, high blood pressure, diabetes mellitus, intra-abdominal infection or pneumonia, and requiring treatment with antimicrobials, invasive mechanical ventilation, and vasoactive drugs.

Keywords: Community-acquired infections; Epidemiology; Critical patient; Intensive care unit; COVID-19.

ABSTRACT

Introduction: Critically ill patients require admission to intensive care units due to community-acquired infections.

Objective: to characterize, from a clinical and epidemiological point of view, critical ill patients with community-acquired infections during COVID-19.

Results: 52.7% of the patients were female. The mean age was 40.2 years (95% CI: 37.8-42.4). The mean Acute Physiology and Chronic Health Evaluation II (APACHE II) was estimated at 11.8 (95% CI: 9.7-12.2). The mean Sequential Organ Failure Assessment (SOFA) scale was 1.8 (95% CI: 1.4-2.2). 31.7% of the patients were hypertensive and 19.4% diabetic. Intra-abdominal infection was the main location (52.7%), followed by pneumonia (34.7%). 98.7% had antimicrobials on admission and 26.3% had artificial mechanical ventilation.

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Conclusions: the patients are mostly characterized by being female, being in the fourth decade of life, developing alterations in their physiological systems and organ dysfunction, and having high blood pressure and diabetes mellitus; intra-abdominal infection or pneumonia as well as requiring treatment with antimicrobials, invasive mechanical ventilation and vasoactive drugs.

Keywords: Community-acquired infections; Epidemiology; Critical patient; Intensive care unit; COVID-19.

SUMMARY

Introduction: Critical patients require hospitalization in intensive care units due to infections acquired in the community.

Aim: To characterize, from a clinical and epidemiological point of view, severe patients with community infections during COVID-19.

Methods: Observational, descriptive, case series study, period from September 1, 2020 to January 31, 2022. Foram included 277 patients. Foram obtained epidemiological and clinical variables. A statistical analysis is based on measures-summary of descriptive and association statistics.

Results:52.7% two patients were female. The average age was 40.2 years (95% CI: 37.8-42.4). The Acute Physiology and Chronic Health Evaluation II (APACHE II) mean was estimated at 11.8 (95% CI: 9.7-12.2). The average Sequential Organ Failure Assessment (SOFA) scale was 1.8 (95% CI: 1.4-2.2). 31.7% two patients were hypertensive and 19.4% diabetic. Intra-abdominal infection was the main location (52.7%), followed by pneumonia (34.7%). 98.7% contain antimicrobials in the intake and 26.3% contain artificial mechanical ventilation.

Conclusões: Most two female patients, in the fourth decade of life, develop alterations in their physiological systems and organic dysfunction, in addition to arterial hypertension and diabetes mellitus; Intra-abdominal infection or pneumonia, in addition to requiring treatment with antimicrobials, invasive mechanical ventilation and vasoactive drugs.

Keywords: Infections acquired in the community; Epidemiology; Critical patient; Intensive Care Unit; COVID-19.

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Introduction

Severely ill patients require admission to intensive care units (ICUs) for community-acquired infections (CAIs), primarily pneumonia, central nervous system (CNS) infections, and urinary tract infections. Approximately 20% to 40% of these patients receive intensive treatment due to the magnitude of the disease or because they require adequate monitoring. (1)

The number of patients in intensive care with severe community-associated pneumonia (CASP) is increasing globally, especially among the elderly, those with comorbidities, and those with immunocompromised conditions. Twenty-one percent require ICU admission, and 26% require mechanical ventilation (MV). Mortality rates range from 25% to 50% or higher. (2)

Likewise, 20% of patients with CNS infections present signs of neurological focus and 30% seizures, requiring neurointensive treatment. (3) Urinary tract (24.8%) and intra-abdominal (24.3%) infections are frequent sites of CAI in patients admitted to the ICU due to sepsis and septic shock. The sepsis stage may appear in 32.7% of patients with CAI and septic shock in 28.5%. (4)

Despite the significant contribution of CAIs to morbidity and mortality in the ICU, research on this topic is limited at the national and international levels, as it generally focuses on healthcare-associated infections (HAIs). However, CAIs have different clinical-epidemiological patterns, risk factors, and prognoses compared to HAIs. Meanwhile, COVID-19 has generated variations in the morbidity and mortality of infectious diseases in general and CAIs in particular. (5)

Given this problem, this study aims to characterize, from a clinical and epidemiological perspective, critically ill patients with community-acquired infections during COVID-19.

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Methods

An observational, descriptive, case series study was conducted in the ICU of the "Carlos Manuel de Céspedes" Provincial General Hospital in Bayamo, Granma province, Cuba, from September 1, 2020, to January 31, 2022. During this period, the service was also dedicated to the care of patients with COVID-19.

Inclusion criteria

All patients with IAC whose diagnosis was based on the Centers for Disease Control and Prevention (CDC) criteria for the disease and its locations were consecutively included during the study period. (6)

Operationalization of variables

To characterize seriously ill patients from a demographic point of view, the following variables were selected:

- Sex: Male and female were considered according to the reference biological sex.
- Age: taken in completed years.

The following were obtained as baseline clinical variables to characterize seriously ill patients:

- Severity: This was assessed using the Acute Physiology and Chronic Health Evaluation II (APACHE II) prognostic score. The study included the worst indicators present in each patient during the first 24 hours after admission to the ICU. (7)
- Organ dysfunction: This was defined using the Sequential Organ Failure Assessment (SOFA) scale. SOFA was assessed within the first 24 hours of the patient's admission. (8)
- Place of origin: This was determined according to the service from which the patients came upon admission to the ICU: from the operating room, the emergency department, the hospital ward, other ICUs (coronary intensive care, intermediate care, or stroke intensive care), and another hospital.
- Systemic inflammatory response syndrome (SIRS) and sepsis/septic shock: The Consensus Conference of Chest Physicians/Society of Critical Care Medicine criteria for SIRS and the Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) criteria for sepsis/septic shock were applied. (9,10)

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- Comorbidity: pathological states present in the patient upon admission were considered, according to the criteria established for its diagnosis, such as: arterial hypertension (AHT), diabetes mellitus (DM) type 1 and 2, ischemic heart disease, bronchial asthma, HIV, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD) and ischemic and hemorrhagic stroke. (24)

The location of IAC was defined according to the CDC diagnostic criteria. (1) These included mild and severe pneumonias caused by COVID-19, according to the criteria of the National Action Protocol for COVID-19, version 1.5. (11)

The treatments required during the stay in the ICU to be assessed were:

a) Invasive artificial mechanical ventilation: with endotracheal intubation.
b) Renal cleansing methods: conventional hemodialysis, hemodialysis with ultrafiltration or plasmapheresis.
c) Parenteral nutrition (TPN): complete or total (the regimen meets more than 90% of the patient's daily nutritional needs) or partial (incomplete) when the regimen meets less than 40% of the daily nutritional needs.
d) Antimicrobial on admission: Antimicrobial prescription upon admission to the ICU, in accordance with the department's antimicrobial policy and action protocols.
e) Vasoactive and inotropic drugs: when norepinephrine, epinephrine, dopamine or dobutamine were used at the established doses for a minimum period of 24 hours.

The association of all variables with outcome was estimated; outcomes were grouped into two categories: patient discharged alive or death from the ICU.

Sources and techniques for collecting information:

The data needed to form the study variables were obtained from the patient's medical records and entered into an electronic database using the Statistical Package for the Social Sciences version 21.0 (SPSS) for subsequent analysis.

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Statistical analysis

In the statistical analysis, absolute frequencies and percentages were estimated for qualitative variables. Quantitative variables were expressed as mean, 95% confidence intervals (95% CI), median, interquartile range (IQR) (25th–75th percentiles), and standard deviation (±SD) according to the data distribution. To estimate the associations of clinical and epidemiological characteristics with patient outcomes (alive or deceased), mean age, APACHE II, and SOFA scores were compared using the Student t test; medians were compared using the median test; and qualitative data were compared using the chi-square test. The hypothesis that the difference between alive and deceased was statistically significant was tested, with a p value of < 0.05. SPSS version 21.0 was used for data processing.

Ethical aspects

The study was conducted with data from clinical practice. Informed consent was obtained from the patient or their family (when the severity of the condition did not allow it) for the invasive therapeutic procedures indicated during the care process. No new therapeutic measures were tested during the study. Furthermore, data confidentiality was guaranteed, and the bioethical regulations of the Helsinki Code for biomedical studies were applied. The study was approved by the Research Ethics Committee.

Results

A total of 277 patients with CAI were identified during the study period, representing 10.6% of the total admissions; of these, 55 died (19.9%). In the case series, 146 patients (52.7%) were female and 131 were male (47.3%). Of the deceased, 69.1% were men; significant differences were observed between those who were alive and those who died according to sex (p=0.000). The mean age was 40.2 years (95% CI: 37.8–42.4); in the deceased, it was 53.3 years (95% CI: 49.5–57.1) compared with 42.2 years in the living (95% CI: 39.7–44.6) (p=0.000). The median (IQR) age was 38 years (28), but significantly higher in the deceased (52 years, IQR: 16, p=0.000). (Table 1)

Table 1. Demographic characteristics of critically ill patients with community-acquired infections.

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Variable	All patients n=277	Alive n=222	Deceased n=55	p*
Sex				0.000
Male (no, %)	131-47.3	93-41.9	38-69.1	
Female (no, %)	146-52.7	129-58,1	17-30.9	
Age				
Mean age (95% CI†)	40.2 (37.8-42.4)	42.2 (39.7-44.6)	53.3 (49.5-57.1)	0.000
Standard deviation of the mean	8.3	18.5	14.0	
Median age (IQR‡)	38.0 (28.0)	39.0 (29.0)	52.0 (16.0)	0.000

*p< 0.05. Comparisons were made between living and deceased patients † 95% confidence interval ‡ interquartile range.

Table 2 shows the baseline clinical characteristics of critically ill patients admitted with CAI. Regarding severity, the mean APACHE II score was estimated at 11.8 (95% CI: 9.7–12.2); 24.3 (95% CI: 21.3–27.2) in deceased patients, and 5.4 in those who were alive (95% CI: 4.7–6.0) (p=0.000). The median APACHE II score (IQR) was 10.8 (9.5) and showed significant differences between those who were alive and those who were deceased (4.0 vs. 22.0, p=0.000). The mean overall SOFA was 1.8 (95% CI: 1.4-2.2) from 9.4 (95% CI: 8.7-10.2) in non-survivors and 2.0 (95% CI:1.7-2.4)in survivors (p = 0.000). Significant differences were noted in the median SOFA scores between those alive and deceased (2.0 vs. 10, p = 0.000). 52.7% of patients came from the operating room, 20.6% from inpatient wards, and 12.3% from the Emergency Department as the most frequent places of origin. The differences between those alive and deceased were significant in terms of origin (p = 0.000). It is noteworthy that 45.5% of those deceased came from other ICUs. SIRS developed in 50.9% of patients; in 100% of those who progressed to death, and in 38.7% of those discharged alive from the intensive care unit (p = 0.000). Sepsis/septic shock developed in 23.5% of patients.

Table 2. Basic clinical characteristics of critically ill patients with community-acquired infections.

Variable	All patients n=277	Alive n=222	Deceased n=55	p*
Gravity				
APACHE II† average (95% CI)	11.8 (9.7-12.2)	5.4 (4.7-6.0)	24.3 (21.3-27.2)	0.000

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Standard deviation of the mean	7.6	4.8	10.8	
APACHE II median (RIC)	10.8 (9.5)	4.0 (8.0)	22 (10.0)	0.000
Organ dysfunction				
Mean SOFA (95% CI)	1.8 (1.4-2.2)	2.0 (1.7-2.4)	9.4 (8.7-10.2)	0.000
Standard deviation	2.1	2.5	2.6	
SOFA ‡ median (IQR)	1.9 (3.0)	2.0 (3.0)	10 (4)	
Place of origin				0.000
Operating room (no, %)	146-52.7	134-60.3	12-21.8	
Hospitalization rooms (no, %)	57-20.6	53-23.9	4-7,3	
Emergencies (no, %)	34-12,3	22-9.9	12-21.8	
Other ICU (no, %)	33-11.9	8-3.6	25-45.5	
Other hospital (no, %)	9-3,2	7-3.2	2-3.6	
*S*RIS				0.000
But, %)	141-50.9	86-38.7	55-100	
No no, %)	136-49,1	136-61.3	0-0.0	
Sepsis/Septic Shock				0.000
But, %)	65-23.5	12-5,4	53-96.4	
No no, %)	212-76.5	210-94.6	2-3.6	

p< 0.05. Comparisons between living and deceased † Prognostic index Acute Physiology and Chronic Health Evaluation II.

‡ Sequential Organ Failure Assessment Scale

In the study, 177 patients with CAI presented comorbidity. Table 3 highlights that 31.7% of them had a diagnosis of hypertension, 19.4% diabetes mellitus, 5.8% ischemic heart disease, and 3.9% bronchial asthma. 2.9% had a history of other diseases such as COPD, stroke, or HIV. Only arterial hypertension (p = 0.005) and diabetes mellitus (p = 0.001) were associated with death.

Table 3. Comorbidity of critically ill patients with community-acquired infections.

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Comorbidity	All patients n=277		Alive n=222		Deceased n=55		p*
	No	%	No	%	No	%	
High blood pressure							0.005
Yeah	88	31.7	62	27.9	26	47.2	
No	189	68.3	160	72.1	29	52.8	
Diabetes mellitus							0.001
Yeah	54	19.4	35	15.7	19	34.5	
No	223	80.6	187	84.3	36	65.5	
Ischemic heart disease							0.068
Yeah	16	5.8	10	4.5	6	10.9	
No	261	94.2	212	95.5	49	89.1	
Bronchial asthma							0.529
Yeah	11	3.9	8	3.6	3	5.5	
No	266	6.1	214	96.4	52	94.5	
Others							0.204
Yeah	8	2.9	5	23	3	5.4	
No	269	97.1	217	97.7	52	94.6	

* p< 0.05. Comparisons were made between living and deceased individuals.

Table 4 shows that intra-abdominal infection (146 patients, 52.7%), pneumonia (34.7%), and CNS infection were the most common sites of CAI, but only the first two had a statistically significant association with death (p=0.000, respectively). Skin and soft tissue infections were identified in only 1.1% of subjects. Of the total number of patients, 66 presented mild or severe COVID-19 pneumonia (23.8%), which also represented 68.7% within this site.

Table 4 Location of community-acquired infection.

Location of the infection	All patients n=277		Alive n=222		Deceased n=55		p*
	No	%	No	%	No	%	
Intra-abdominal infection							0.000
Yeah	146	52.7	134	60.4	122	1.8	
No	131	47.3	883	9.6	437	8.2	
Pneumonia							0.000
Yeah	96	34.7	552	4.8	417	4.5	
No	181	65.3	167	75.2	142	5.5	
Urinary infection							0.503
Yeah	9	3.2	8	3.6	1	1.8	
No	268	96.5	214	96.4	549	8.2	
Central Nervous System							0.415

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Infection							
Yeah	9	3.2	9	4.1	0	0.0	
No	268	96.5	213	95.9	54	100.0	
Skin and soft tissue infection							0.785
Yeah	3	1.1	3	1.4	0	0.0	
No	274	98.9	219	98.6	55	100.0	
Others							0.221
Yeah	14	5.1	13	5.9	1	1.8	
No	263	94.9	209	94.1	54	98.2	

*p< 0.05. Comparisons were made between living and deceased individuals.

Table 5 shows the treatments required by patients with CAI in the intensive care unit. Ninety-eight percent of patients were admitted to the ICU with antimicrobials, 26.3% required IV, 23.5% vasoactive drugs, and 8.3% renal depurative methods. Only 2.3% required PN. Antimicrobial treatment was not significantly associated with adverse outcomes, while the need for IV, vasoactive drugs, renal depurative methods, and PN were associated with death.

Table.5 Treatments required by seriously ill patients with community-acquired infections.

Variable	**All patients n=277**		**Alive n=222**		**Deceased n=55**		**p***
	No	**%**	**No**	**%**	**No**	**%**	
Antimicrobials upon admission							0.386
Yeah	274	98.9	219	98.6	55	100.0	
No	3	1.1	3	1.4	0	0.0	
Artificial mechanical ventilation							0.000
Yeah	74	26.7	20	9.0	54	98.2	
No	203	73.3	202	91.0	1	1.8	
Kidney cleansing methods							0.000
Yeah	23	8.3	5	23	18	32.7	
No	254	91.7	217	97.7	37	67.3	
Parenteral nutrition							0.015
Yeah	10	3.6	5	23	5	9.1	
No	267	96.4	217	97.7	50	90.9	
Vasoactive drugs							
Yeah	65	23.5	12	5.4	53	96.4	0.000
No	212	76.5	210	94.6	2	3.6	

*p< 0.05. Comparisons were made between living and deceased individuals.

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Discussion

Regarding the frequency of CAI, Westphal et al. (12) found 41.2% in hospitals in Brazil. A similar study conducted in Hungary by Szabo et al. (1) showed 34.0% of patients affected by CAI admitted to tertiary centers. An incidence of 17.3% was estimated in the Thai multicenter Ubon-sepsis study. (13) In the ICU of the hospital where this project was carried out, a previous report confirmed that 47% of patients were admitted for CAI. (14)

Most international studies have found a high incidence of IAC in men, which is contrary to the trend observed in this case series. In Cuba, according to statistical data from the national multicenter DINUCIs project, a higher proportion of women are admitted to the ICU, which could be influencing this result. (15)

The behavior of mortality in relation to sex is very similar to that of the Ubon-sepsis study, which confirmed a lower frequency of survivors in men compared to non-survivors (63.0% vs. 69.5%). (13) Analysis of prognostic factors in that same investigation confirmed that male sex was independently associated with death. It is now recognized that sex may contribute to the differential risk for the development of infection and sepsis. Genetic conditions that confer susceptibility include complement component deficiencies, agammaglobulinemia; defects in phagocytosis, myeloperoxidase deficiency, and leukocyte adhesion molecule deficiency. Many studies have focused on polymorphisms in genes encoding proteins involved in the pathogenesis of sepsis. (16)

There is general agreement with other case series regarding the average age and the differences between the living and deceased (13,16), but in those published by authors such as Lindström et al. (17) and Westphal GA et al. (12), it was slightly higher. With increasing age, the risk and severity of infection increases due to changes in immunity. Variables such as comorbidity, nutritional status, and the causes of CAI may also influence this behavior.

Patients with CAI who are admitted to the ICU are more severely ill, due to alterations in the main organ systems and the development of multiple organ dysfunction. Therefore, the APACHE II and SOFA scores in this study are not coincidental. The significant pathophysiological changes caused by infection and sepsis explain the decline of vital body systems. Organ dysfunction is identified in

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approximately 50% of severely ill patients with CAI, and up to 60% may develop respiratory and circulatory dysfunction; hence the SOFA score in this series. (18)

Comorbidity in patients with CAI has been analyzed less frequently in epidemiological studies conducted to date, and the preexisting pathological states evaluated in them are varied. The frequency of diabetics in the present case series is very similar to that observed by Thomas-Rüddel et al. (19) It is also similar to that of Vidal et al. (20) who confirmed that diabetes mellitus was present in 17.91% of patients with CAI.

There are differences in the frequency of IAC locations from one study to another; however, the results in the present series are similar to those reported in studies published in other countries. The presence of IAC, in particular, is due to the fact that the intensive care unit primarily caters to surgical patients, as the institution is equipped with other intermediate care units with a monovalent clinical profile and is equipped with the material and human resources to treat patients with other non-surgical infections. The need for peritoneal lavage, relaparotomy, nutritional support, and antimicrobial therapy requires a more intensive treatment regimen for surgical patients.

The high prescription of antimicrobials has been documented by all authors, since this therapy constitutes the first line of treatment in sepsis. In the multicenter study "AbSeS", all patients received treatment with carbapenems and fluoroquinolones. (21) Regarding the need for IMA, the study by Chen et al. (22) showed that 50% of patients required it, specifically in the stages of sepsis and septic shock. Arumairaj et al. identified the use of invasive IMA in 64% of patients. (23) Another study reports a 33% use of invasive IMA, a statistic closer to ours. (24) Regarding the need for vasoactive drugs, the study by Chen et al. (22) confirmed that 52% of patients required it, specifically in the stages of sepsis and septic shock.

Between 17% and 20% of patients treated in the ICU require renal replacement therapy. In different prediction models, the risk of acute kidney injury doubles and triples in patients with infection who progress to sepsis and septic shock. Due to the higher frequency of IAI, a proportion of patients require TPN. The trend observed in the series regarding this treatment is similar to that of previous studies in the unit and to international studies, which ranges between 10% and 20%. (25)

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The associations estimated in the present study denote the need to continue channeling other research that delves into the interaction of the treatments required in patients with IAC and their prognosis, using designs based on prospective observational and experimental studies.

Conclusions

Severely ill patients with community-acquired infections are predominantly female, in their forties, develop alterations in their physiological systems and organ dysfunction, and have comorbidities such as high blood pressure and diabetes mellitus; a diagnosis of intra-abdominal infection or pneumonia; and require treatment with antimicrobials, invasive mechanical ventilation, and vasoactive drugs. There is an association between some characteristics of severely ill patients with community-acquired infections and death, including male status; older age, severity of illness, comorbidities (high blood pressure and diabetes mellitus), and the need for life-sustaining treatment.

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Conflict of interest

The authors declare no conflicts of interest.

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