What Changed Between the Peak and the Plateau Periods of the First COVID-19 Pandemic Wave? A Multicentric Portuguese Cohort Study in Intensive Care.

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Research

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Abstract

Background

The COVID-19 pandemic represented a challenge for intensive care units (ICU) with overwhelming demand, heterogenous outcomes and clinical practices. To improve care a profound knowledge on severe COVID-19 patients during different time points is crucial. This data is still scarce. We aimed to analyze and compare COVID-19 patient demographics, clinical management, and outcomes between two periods from the first pandemic wave.

Methods

We performed a multicentric ambispective cohort study including severe COVID-19 patients between March and August 2020 from 16 Portuguese ICUs. A peak and a plateau period were defined, corresponding to weeks 10-16 and 17-34 of the first pandemic wave. All patients had SARS-CoV-2 pneumonia diagnosis and complete hospital follow-up.

Results

We included 541 adult patients with a median age of 65 [57-74] years and mostly male (71.2%). Severe acute respiratory distress syndrome developed in 63.9% of cases. Overall, 28-day mortality rate was 23.7% with age and SAPSII (both $p < 0.001$) as independent risk factors.

Between peak and plateau periods there were no significant differences in age (65 vs. 66, $p = 0.6$), SAPS II (40 vs. 39, $p = 0.8$), PaO₂/FiO₂ ratio (139 vs. 136, $p = 0.6$), and antibiotic therapy (57.2% vs. 63.8%, $p = 0.2$) at admission, nor in 28-day mortality (24.4% vs. 22.8%, $p = 0.7$). Adjuvant therapy with corticosteroids had no impact on 28-day mortality (26.9% vs. 22.5% without, $p = 0.4$). The peak period included 53.8% of patients and they had less comorbidities (no comorbidities 29% vs. 36%, $p = 0.01$), presented at admission a higher use of vasopressors (81% vs. 63%, $p < 0.001$), invasive mechanical ventilation (58 vs 49%, $p < 0.001$), prone positioning (60% vs 48%, $p = 0.009$), and hydroxychloroquine (80.2% vs. 13.4%; $p < 0.001$) and lopinavir/ritonavir (60.4% vs. 13.4%; $p < 0.001$) prescription, as compared with the plateau period. In the plateau period, there was a greater use of high flow nasal canula (5% vs 16%, $p < 0.001$) on admission, remdesivir (0.5% vs. 19.9%; $p < 0.001$) and corticosteroid (39% vs. 61%, $p < 0.001$) therapy, and a shorter ICU length-of-stay for survivors (12 days vs. 7, $p < 0.001$).

Conclusion

There were significant changes in patient comorbidities, therapies and ICU length-of-stay between peak and plateau periods of the first COVID-19 wave with similar 28-day mortality.

Introduction

The surge of the COVID-19 pandemic represented a tremendous challenge for healthcare systems worldwide due to overwhelming hospital admissions, particularly in intensive care units (ICU).

Six months after the COVID-19 pandemic declaration on the 11th March 2020, over 28 million cases of SARS-CoV-2 infection and 917,000 deaths had been reported.¹ Furthermore, it has been estimated that approximately 26% of hospitalized COVID-19 patients require ICU admission.² Worldwide reports of critical patient's mortality rates are very heterogenous, ranging between 26% and 97%.²⁻¹⁰

In Portugal during the first six months of the SARS-CoV-2 pandemic, between March and August, the total number of confirmed infections in the country reached 58,012 with an overall mortality rate of 3.1%. In the first wave, the peak of confirmed community infections took place on the 26th of March 2020 linked with increased healthcare system stress, risk of ICU bed shortage consequence of our low number of ICU beds (6.4/100000 habitants)¹¹ and the notion that a higher community infection rate could be associated with worse clinical outcomes in the hospital setting.¹¹⁻¹⁴

Early COVID-19 clinical practice and guidelines suffered changes as data emerged during the initial phases of the pandemic.¹⁵⁻²³ Nonetheless, epidemiologic data comparing distinct temporal periods of the first pandemic wave is scarce.³⁻¹⁰ Clinical data on severely ill COVID-19 patients in the ICU is crucial for improved care, in-hospital patient flow and healthcare system's organization.

This study aimed to analyze and compare COVID-19 patient's characteristics, clinical management and outcomes between the peak and plateau periods of the first pandemic wave in Portugal.

Methods

Study design and settings

We performed a multicentric ambispective observational cohort study open to all ICUs between the 1st of March and the 31st of August, 2020, in Portugal. The study was endorsed by the Portuguese National Society of Critical Care.²⁴ The ISARIC (International Severe Acute Respiratory and emerging Infections Consortium) was a key partner and source of the standardized clinical data collection tool used by each participating center before final database merger for this study.²⁵

Patients

Patients with a primary diagnosis of SARS-CoV-2 PCR confirmed pneumonia admitted in intensive care units between 01st of March and 31st of August 2020 were eligible for this study. Patients were consecutively included and followed-up until hospital discharge.

All patients without complete hospital stay by the end of the study period and SARS-CoV-2 infected patients admitted to the ICU for other reasons were excluded from the analysis.

Variables

Study variables were collected from the clinical records and included demographic, clinical data, comorbidities, signs and symptoms, laboratory results, infectious complications, therapeutics, LOS and mortality. These variables were collected at hospital admission, ICU admission and hospital discharge. Missing, illogical and outlier values were reported to local investigators for correction and the final database resulted from the combination of the datasets from each center collected independently.

For the analysis, the first wave of the SARS-CoV-2 pandemic was divided into an initial “peak” period, considering a cut-off of more than 20 new patients admissions per week, and a later “plateau” period, corresponding to weeks 10–16 and 17–34 of the year 2020.¹²

Statistical analysis

Categorical variables were described in count and percentage. Dichotomic variables were compared using chi-square test or Fisher’s exact test as appropriate.

Continuous variables were described in mean and standard deviation (SD) or median and interquartile range [IQR] as appropriate and comparison was made using t-test or ANOVA for parametric variables, and Mann-Whitney test was used for non-parametric variables. Logistic regression was used for multivariate analysis. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corporate software.

Ethics

This study was approved by the National Ethics Committee for Clinical Research (2020_EO_02) and the Ethics Committees of each center. The informed consent was waived given the observational character of this study and the exceptional context of the COVID-19 pandemic. This study complied with the ethical principles of the Declaration of Helsinki. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement guidelines for reporting observational studies were used for this manuscript.

Results

Participating centers and patients

Sixteen centers (Supplementary table 1) participated with 569 adult critical COVID-19 patients for the study. Twenty-eight patients (4.9%), from the plateau period, were excluded due to continued hospitalization at the time of database closure. The main analysis included 541 adult patients. Pediatric and neonatal ICUs from four centers provided clinical data for seven children that were separately described (Supplementary table 2).

Epidemiology

Adult patients in this study were mostly male (71.2%) with a median age of 65 [57–74] years and arterial hypertension (47.1%) was the most frequent comorbidity. Age group and associated comorbidities and ICU mortality rates are illustrated in Fig. 1. Approximately one third (32.7%) of patients had no comorbidities and these were younger than the others (63 [54–68] years vs. 67 [59–76], $p < 0.001$). Patient demographic characteristics and comorbidities are detailed in Table 1 and hospital presenting symptoms are presented in Supplementary table 3.

Table 1
COVID-19 patient's characteristics and respiratory support at ICU admission.

N = 541	n	%
Age (years, median [IQR])	65	[57–74]
Male gender	385	(71.2)
Comorbidities		
Hypertension	255	(47.1)
Obesity	150	(27.7)
Diabetes mellitus	131	(24.2)
Cardiovascular disease	81	(15.0)
Pulmonary disease ^a	65	(12.0)
Renal disease	55	(10.2)
Neurologic disease ^b	26	(4.8)
Neoplasm	26	(4.8)
Liver disease	22	(4.7)
Asthma	15	(2.8)
Hematologic disease	15	(2.8)
Dementia	8	(1.5)
HIV/AIDS	7	(1.3)
No comorbidities	177	(32.7)
Single comorbidity	91	(16.8)
Two or more comorbidities	273	(50.5)
SAPS II score	40	[30–52]
SOFA score (median [IQR]) (n = 117)	6	[3–9]
Cardiovascular	3	[0–4]
Respiratory	3	[2–3]
Renal	0	[0–1]
Hematologic	0	[0–0]
Neurologic	0	[0–0]
Hepatic	0	[0–0]
PaO2 / FiO2 (median [IQR])	138	[101–203]
Invasive mechanical ventilation	292	(62.9)
High flow nasal cannula	55	(11.9)
Non-invasive ventilation	34	(7.3)
ECMO	6	(1.3)
Hospital to ICU admission (median [IQR], days)	1	[0–3]
Onset of symptoms to hospital (median [IQR], days)	6	[3–9]
^a non-asthma pulmonary disease. ^b non-dementia neurologic disease. Abbreviations: COVID-19 - Coronavirus disease 2019, ICU - Intensive Care Unit, IQR - interquartile range, HIV - human immunodeficiency virus; AIDS - acquired immunodeficiency syndrome, SAPS - Simplified Acute Physiology Score, SOFA - sequential organ failure assessment, PaO2 - partial pressure of oxygen, fraction of inspired oxygen, ECMO - extra-corporeal membrane oxygenation.		

Clinical severity, management and mortality

At ICU admission Simplified Acute Physiology Score (SAPS) II (n = 527) presented a median value of 40 [30–52], and admission Sequential Organ Failure Assessment (SOFA) score (n = 117) was 6 points [3–9], mostly represented by respiratory (3 [2–3]) and cardiovascular (3 [0–4]) dysfunction or failure. The types of respiratory support provided during ICU admission day are detailed in Table 1.

Throughout the ICU stay nearly two thirds (63.9%) of the patients were reported to have severe acute respiratory distress syndrome (ARDS) criteria. Therapies in the ICU and outcomes are shown in Table 2. Antibiotic therapy was initiated 24 hours before or after ICU admission in 60.1% (n = 187) of patients and azithromycin was the most frequently used antibiotic (65.8%), particularly in combination with another class of antibiotic (91.1%).

Table 2
COVID-19 ARDS severity, therapies during the ICU stay and clinical outcomes.

(N = 541)	n	%
ARDS (n = 335)		
Mild	13	(3.9)
Moderate	107	(31.9)
Severe	214	(63.9)
Invasive mechanical ventilation (n = 520)	399	(76.7)
Non-invasive mechanical ventilation (n = 411)	112	(27.3)
ECMO (n = 414)	24	(5.8)
Prone positioning (n = 408)	221	(54.2)
Renal replacement therapy (n = 474)	91	(19.2)
Vasopressors (n = 409)	296	(72.4)
Corticosteroids (n = 403)	216	(53.6)
Lopinavir/ritonavir (n = 403)	144	(35.7)
Hydroxychloroquine (n = 403)	197	(48.9)
Remdesivir (n = 403)	38	(9.4)
Antibiotics ^a (n = 311)	187	(60.1)
Antifungals (n = 400)	39	(9.8)
Tracheostomy (n = 414)	42	(10.1)
ICU LOS (days, median [IQR])	11	[6–20]
Hospital LOS (days, median [IQR])	23	[14–38]
Mortality rate at 28 days	128	(23.7)
Mortality rate in the ICU	129	(23.8)
Mortality rate in the hospital	151	(27.9)
^a Antibiotic therapy initiated within ± 24 hours of ICU admission.		
Abbreviations: COVID-19 - Coronavirus disease 2019, ARDS - acute respiratory distress syndrome, ICU - Intensive Care Unit, ECMO - extra-corporeal membrane oxygenation, IQR - interquartile range, LOS - length-of-stay.		

Overall, 28-day mortality rate was 23.7%, in-ICU was 23.8% and in-hospital was 27.9% (Table 2). Patients receiving IMV (76.7%) during their ICU stay presented a 28-day mortality rate comparable to those receiving any other type of non-invasive oxygen support (respectively, 25.3% versus 17.4%, $p = 0.09$). Age groups, comorbidities and associated ICU mortality rates are depicted in Fig. 1. The number of comorbidities was not associated with increased mortality in univariate analysis ($p = 0.3$). Both age ($p < 0.001$) and SAPS II ($p < 0.001$) were independent risk factors for increased 28-day mortality in the ICU.

In our cohort, adjuvant therapy with corticosteroids was not associated with any impact on 28-day mortality in comparison with those without (26.9% vs. 22.5%, $p = 0.4$, respectively).

Peak and plateau phase of the first COVID-19 pandemic wave

The temporal distribution of ICU admissions, age and mortality rate between the peak and plateau periods are depicted in Fig. 2. The peak period occurred between weeks 10–16, with an abrupt increase of the number of ICU admissions to a maximum of 92 during week 13, followed by a plateau period between weeks 17–34. In fact, approximately half of the patients (53.8%) included in this study were admitted in the ICU during the peak period.

COVID-19 patient characteristics between peak and plateau of the first SARS-CoV-2 wave were analyzed as shown in Table 3. The number of days since the onset of symptoms until hospital admission was higher during the peak than in the plateau period (7 [4–9] vs. 5 [3–8], $p = 0.002$) and no differences were found regarding the time between hospital to ICU admission ($p = 0.6$), age ($p = 0.1$) or severity of illness, as assessed by SAPS II score ($p = 0.8$) between periods.

Table 3

Comparison of COVID-19 patient baseline characteristics on ICU admission day between peak and plateau periods of the first pandemic wave.

Clinical characteristics (N = 541) (n, %)	Peak (n = 291)		Plateau (week 17–34) (n = 250)		p-value
Age (years, median [IQR])	65	[58–71]	66	[57–76]	0.1
Male gender	206	70.8	179	71.6	0.9
Hypertension	126	43.3	129	51.6	0.1
Obesity	78	26.8	72	28.8	0.6
Diabetes mellitus	56	19.2	75	30.0	0.01
Cardiovascular disease	37	12.7	44	17.6	0.1
Pulmonary disease ^a	27	9.3	38	15.2	0.05
Renal disease	25	8.6	30	12.0	0.2
Neurologic disease ^b	12	4.1	14	5.6	0.4
Neoplasm	13	4.5	13	5.2	0.7
Liver disease	12	4.1	10	4.0	
Asthma	10	3.4	5	2.0	0.4
Hematologic disease	6	2.1	9	3.6	0.3
Dementia	1	0.3	7	2.8	0.03
HIV/AIDS	3	1.0	4	1.6	0.7
No comorbidities (n = 177)	105	36.1	72	28.8	0.04
Single comorbidity (n = 91)	53	18.2	38	15.2	0.2
Multiple comorbidity (n = 273)	133	45.7	140	56.0	0.01
SAPS II (median [IQR]) (n = 527)	40	[31–52]	39	[30–51]	0.8
PaO ₂ / FiO ₂ (median [IQR])	139	[100–211]	136	[101–195]	0.6
Invasive mechanical ventilation (n = 464)	169	58.1	123	49.2	< 0.001
Non-invasive ventilation	14	4.8	20	8.0	0.2
High flow nasal cannula	14	4.8	41	16.4	< 0.001
SOFA score (median [IQR]) (n = 117)					
Overall	7	[4–11]	5	[3–7]	< 0.001
Cardiovascular	3	[0–4]	1	[0–3]	< 0.001
Respiratory	3	[2–3]	3	[3–4]	0.2
Antibiotics (n = 311) ^c	99	57.2	88	63.8	0.2
Corticosteroids (n = 403)	85	39.4	131	60.6	< 0.001
Antifungal	17	7.8	22	12	0.1
Vasopressor	175	80.6	121	63	< 0.001
Prone positioning	130	59.9	91	47.6	0.009
Renal replacement therapy	47	20	44	18.4	0.4
Extra-corporeal membrane oxygenation	11	5.1	13	6.6	0.3
ICU length-of-stay (days, median) (n = 412) ^d	12	[5–22]	7	[4–14]	< 0.001

Peak period of the first COVID-19 pandemic wave is set between weeks 10–16, and post-peak period between week 17–34 of 2020.

^a Non-asthma pulmonary disease. ^b Non-dementia neurologic disease. ^c Antibiotic therapy initiated within $\pm$ 24 hours of ICU admission. ^d Including only patients who survived to ICU discharge (n = 412). ^e Including only patients who survived to hospital discharge (n = 390), from ICU admission date to hospital discharge.Abbreviations: COVID-19 - Coronavirus disease 2019, ICU - Intensive Care Unit, IQR - interquartile range, HIV - human immunodeficiency virus, AIDS - acquired immunodeficiency syndrome, SAPS - Simplified Acute Physiology Score, PaO₂ - partial pressure of oxygen, fraction of inspired oxygen, SOFA - sequential organ failure assessment.

Clinical characteristics (N = 541) (n, %)	Peak (n = 291)		Plateau (week 17–34) (n = 250)		p-value
Hospital length-of-stay (n = 390) ^e	24	[15–42]	21	[12–33]	0.001
Mortality rate at 28 days	71	24.4	57	22.8	0.7
Mortality rate in the ICU	76	26.1	53	21.2	0.2
Mortality rate in the Hospital	86	29.6	65	26.0	0.4
Peak period of the first COVID-19 pandemic wave is set between weeks 10–16, and post-peak period between week 17–34 of 2020.					
^a Non-asthma pulmonary disease. ^b Non-dementia neurologic disease. ^c Antibiotic therapy initiated within $\pm$ 24 hours of ICU admission. ^d Including only patients who survived to ICU discharge (n = 412). ^e Including only patients who survived to hospital discharge (n = 390), from ICU admission date to hospital discharge.					
Abbreviations: COVID-19 - Coronavirus disease 2019, ICU - Intensive Care Unit, IQR - interquartile range, HIV - human immunodeficiency virus, AIDS - acquired immunodeficiency syndrome, SAPS - Simplified Acute Physiology Score, PaO ₂ - partial pressure of oxygen, fraction of inspired oxygen, SOFA - sequential organ failure assessment.					

During the peak period patients displayed significantly more vasopressor use (81% vs. 63%, $p < 0.001$), higher frequency of IMV (58 vs 49%, $p < 0.001$) and prone positioning (60% vs 48%, $p = 0.009$) and presented less comorbidities (no comorbidities 36.1% vs 28.8%, $p = 0.04$, and multiple comorbidities 45.7% vs. 56.0%, $p = 0.01$). Conversely, in the plateau period there was an increase of high flow nasal cannula (HFNC) use (5% vs 16%, $p < 0.001$) at ICU admission, although there were no significant differences in PaO₂/FiO₂ ratio (139 vs 136, $p = 0.6$) between periods.

Significant therapeutic differences between the peak and plateau periods were observed with a reduction in hydroxychloroquine (80.2% vs. 13.4%; $p < 0.001$) and lopinavir/ritonavir (60.4% vs. 13.4%; $p < 0.001$) and an increase in remdesivir (0.5% vs. 19.9%; $p < 0.001$) and corticosteroid therapy (39% vs. 61%, $p < 0.001$). There was no significant difference in the proportion of overall antibiotic therapy initiated during the period of 24 hours before and after ICU admission (respectively, 57.2% vs. 63.8%, $p = 0.2$), including azithromycin (75.8% vs. 63.6%, $p = 0.08$), that could also be prescribed as COVID-19 adjunctive therapy, between peak and plateau periods.

Finally, there was a significant decrease in median ICU LOS (12 days vs 7, $p < 0.001$) and hospital LOS among survivors (24 days vs. 21, $p = 0.001$), and no significant difference in 28-day mortality (24.4% vs. 22.8%, $p = 0.7$) between peak and plateau periods. (Table 3)

Discussion

In this study we showed that patients admitted to the ICU during the peak and plateau period of the first COVID-19 pandemic wave in Portugal were different, while presenting similar age, severity of illness and 28-day mortality rates. In the peak period there were less comorbidities and a higher use of IMV, prone positioning, vasopressors, and hydroxychloroquine, lopinavir/ritonavir administration. The plateau period was characterized by higher rates of use of HFNC for respiratory support, increasing prescription of remdesivir and corticosteroid therapy and was associated with a shorter hospital and ICU LOS.

Although the majority of hospitalized patients and overall SARS-CoV-2 confirmed infections in Portugal were female gender (respectively, 59% and 55%), in this cohort of critically ill COVID-19 patients there was a preponderance of men, leading us to consider that male gender was more severely affected by COVID-19 than female.^{4,26–29} This observation is in line with other studies reporting male gender prevalence up to 60–80% in this setting.^{26–32} Gender specific immune responses could provide a possible explanation for these findings.³³

A high proportion of patients in our study presented comorbidities. The main comorbidity was hypertension, in nearly half of the study population, followed by obesity and diabetes, each present in approximately a quarter of the population. In contrast with other reports, the number of comorbidities was not associated with 28-day mortality.^{4,28,32,34–37} Importantly, almost one third of patients of these critically ill COVID-19 patients had no known comorbidities. These patients without known risk factors should be further studied to understand the role of genetic factors and particular immune phenotypes, helping to uncover severe SARS-CoV-2 disease pathophysiology.^{38,39}

There was a higher frequency of IMV at ICU admission during the peak period, although clinical severity (SAPS II and PaO₂/FiO₂ ratio) at ICU admission was similar between both periods. These differences could result from the delay between the onset of symptoms till the first hospital encounter in the emergency department leading to the need of urgent decision to “intubate and ventilate” in the peak period by impending severe respiratory failure due to COVID-19. Furthermore, initial COVID-19 recommendations considered that HFNC and non-invasive ventilation could be detrimental for the hypoxemic patient and increased viral shedding with potential higher risk for healthcare professionals, leading to patient’s intubation and ventilation in the emergency departments and wards for a safer ICU transfer.¹⁶ As safety data emerged, these recommendations were updated to include NIV and HFNC in the clinical management of hypoxemic patients and postponed the “intubate and ventilate” decision in the later plateau period of the pandemic.

Major differences regarding off-label compassionate use COVID-19 therapies were observed between periods including three repurposed drugs (hydroxychloroquine, lopinavir/ritonavir and remdesivir) and corticosteroids, in parallel with new data.⁴⁰ The use of hydroxychloroquine and lopinavir/ritonavir in the treatment of COVID-19 was initially suggested by their in vitro inhibition of coronavirus SARS infection.^{41–44} These drugs did not show any clinical benefit in randomized clinical trials (RCTs) and raised concerns for adverse reactions, such as cardiotoxicity, with prolongation of the corrected QT interval, particularly, in case of hydroxychloroquine co-administered with azithromycin, and gastrointestinal disorders.^{19,45–47} Remdesivir inhibited SARS-CoV-2 replication in human epithelial cells and double-blind placebo controlled RCTs reported a reduction in time to clinical improvement in COVID-19 hospitalized

patients as well as a significant reduction in 28-day mortality in patients requiring oxygen support.^{21,48-51} However, the larger SOLIDARITY open label RCT did not show any clinical benefit for hydroxychloroquine, lopinavir/ritonavir or remdesivir either in ventilated and non-ventilated patients.⁵⁶ Currently, these COVID-19 compassionate use therapies are not formally recommended in the treatment of critically ill patients.^{20,52}

Antibiotic therapy was consistently prescribed throughout our study. This reflected concerns of bacterial co-infection, however, its incidence in ICU COVID-19 patients has been reported to be low (8.1–14%).⁵³⁻⁵⁵ Additionally, the use of azithromycin in COVID-19, due to immunomodulatory properties, has shown no clinical benefit in several RCTs.⁵⁵⁻⁵⁹ Therefore, the routine use of antibiotics in COVID-19 patients is not supported by evidence.⁶⁰

Based on the results from the open label Recovery RCT, corticosteroid administration increased significantly during the plateau phase but we did not find any survival benefit in patients so treated. The results of the RECOVERY trial became available during our study period and showed a significant reduction in 28-day mortality in hospitalized patients who were receiving either IMV or oxygen alone and were treated with dexamethasone, but with a marked increase in mortality in those not requiring oxygen.¹⁷ These findings were later corroborated by the CoDEX trial with an improvement in the number of ventilator-free days over 28 days in moderate or severe ARDS patients.⁶¹ Both these studies were open-label RCT with high mortality rates well above of those of our cohort. The RECOVERY trial presented relatively high 28-day mortality rates among patients receiving IMV with 29.3% in the dexamethasone group and 41.4% in the usual care group). Similarly, the CoDEX trial, presented a very high 28-day mortality rates in mechanically ventilated patients with 56.3% in the dexamethasone group and 61.5% in the standard care group. In our study a large proportion of COVID-19 patients were treated with corticosteroids without improved survival rates. The benefit of corticosteroid therapy in COVID-19 may be equivocal in specific clinical settings, including older age.⁶²

The heterogeneity of results and outcomes during the early stages of the pandemic raise questions regarding the assessment of severity of illness, hospital settings and patient flow, as well as the characteristics of usual/standard care groups. Care must be taken when interpreting and comparing our results with the literature.

Finally, dynamic changes in the community, national policies, healthcare systems and clinical management could help to understand the differences in patient characteristics and outcomes observed between the peak and plateau periods of the first wave of the COVID-19. In Portugal, COVID-19 patient ICU admissions peak took place between the 10th and 16th weeks of 2020, while the state of National Emergency was declared between weeks 12–14 (March 19th and April 02th) due to the high community infection rate, effectively preventing a shortage of hospital beds and healthcare professionals.⁶³ The nationwide number of SARS-CoV-2 confirmed infections and ICU admissions both presented their maximum during week 13, implying that the national lockdown effectively contained the spread of the disease, reduced the number of severe COVID-19 patients and the demand on the healthcare system.^{64,65} Our study in a population of critically ill patients admitted in intensive care, appears to strengthen reports that COVID-19 hospitalized patient outcomes are associated with the community case rate, with worsening outcomes when the prevalence of COVID-19 was higher in the community.¹³

Strengths of this study include the first Portuguese description of a multicentric cohort of critically ill COVID-19 patients and the dynamic analysis between the peak and the plateau periods of the first pandemic wave. Limitations of this study include the inability to include all the Portuguese Intensive Care Medicine centers, retrospective data in some centers, and missing data regarding bed occupancy, therapies, rates of ventilator-associated pneumonia, bloodstream infections and other complications. Additionally, the proportion of patients that were excluded due continued hospitalization at the time of database closure, although small, may have precluded differences in outcomes.

Conclusion

During the first COVID-19 wave, patient characteristics, clinical management and outcomes in Intensive Care changed between peak and plateau periods. During the peak period, there was a higher rate of IMV, prone positioning, vasopressors, hydroxychloroquine and lopinavir/ritonavir. Patients in the plateau period were more comorbid, received greater respiratory support with HFNC, remdesivir and corticosteroid therapy and had a shorter ICU LOS. The mortality rate was similar in both periods. This study adds to the understanding of COVID-19 pandemic dynamics, contributes to healthcare policies, patient care and establishes a work frame for future research.

Declarations

Ethical approval and consent to participate

Institutional Ethics Committees from all the collaborating centers authorized this study and waived the need for patient informed consent.

Consent for publication

All the authors agree and consent with the publication of this manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available, upon reasonable request, from the corresponding author with the permission of the *Sociedade Portuguesa de Cuidados Intensivos*.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

RP and SMF were the national coordinators of the study, enrolled the participating centers, analyzed data and wrote the manuscript, JG and JJM analyzed the data and reviewed the manuscript. All authors collected data and approved the final manuscript.

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Figures

Age group, comorbidities and mortality rates in critically ill COVID-19 patients

Figure 1

Age group distribution, comorbidities and associated ICU mortality rates in critically ill COVID-19 patients.

Figure 2

Temporal distribution of ICU admissions between peak and plateau periods with associated median age and mortality rate.

Supplementary Files

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