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## **RESEARCH ARTICLE**

# Clinical and epidemiological characteristics of 320 deceased patients with COVID-19 in an Italian Province: A retrospective observational study

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## Abstract

Studies have described clinical features of patients with coronavirus disease (COVID-19). However, limited data concerning the clinical characteristics of the Italian deaths are available. We aim to describe the clinical and epidemiological characteristics of 320 deceased from the Italian experience. We retrospectively collected all consecutive nonsurvivor patients with laboratory-confirmed COVID-19 infection admitted to the Emergency Rooms (ERs) Piacenza Hospital Network during the first month of COVID-19 pandemic in Italy. Clinical history, comorbidities, laboratory findings and treatment were recorded for each patient. A total of 1050 patients with confirmed COVID-19 pneumonia were admitted to the ERs between 24 February and 22 March 2020. Three hundred and twenty (30.5%) patients died with a median age of 78.0 years, 205 (64%) non-survivors were above 65 years old, 230 (71.9%) were male. Non-survivor patients showed frequently several coexisting medical conditions, with hypertension being the most common comorbidity (235 patients, 73.4%). The in-hospital mortality did not change during the progression of the pandemic. In this retrospective Italian study, most of COVID-19 deceased patients were elderly male aged over than 65 years. Hypertension was the most common coexisting disease. In-hospital mortality was high and showed no variation during the first month of the COVID-19 italian epidemic.

### KEYWORDS

COVID-19, deceased, hypertension, SARS-CoV-2

## 1 | INTRODUCTION

Coronavirus disease (COVID-19) is an acute respiratory syndrome caused by a new betacoronavirus (severe acute respiratory syndrome-related coronavirus 2 [SARS-CoV-2]), which erupted in China, in Hubei province, in December 2019.<sup>1</sup> It rapidly spreads worldwide and was declared a pandemic by the World Health Organization (WHO).<sup>2</sup> Given the high contagiousness and mortality of the infection most of the Countries have adopted stringent contagion restriction measures. Italy was the first European country to

detect the disease recording an exponential growth of the contagion. The high number of patients requiring hospitalization and intensive care unit (ICU), mainly located in the Northern regions, have put the healthcare system to the test.

COVID-19 is characterized by a spectrum of clinical manifestations ranging from mild or totally asymptomatic forms to severe pneumonia, acute respiratory distress syndrome, multi organ failure, and death.<sup>3</sup>

Older males (age  $\geq$ 65 years) with pre-existing comorbidities (cerebrovascular and cardiovascular disease) appeared to have a

higher risk of death.<sup>4</sup> Further risk factors for mortality were higher sequential organ failure assessment (SOFA) score, elevated D-dimer, CD3 + CD8 + T cells  $\leq$ 75 cell/µL, and cardiac troponin I  $\geq$ 0.05 ng/mL<sup>4.5</sup> As of 20 April 2020, a total of 178 972 confirmed cases and 23.660 deaths have been reported in Italy, indicating a 13% of mortality rate; on the contrary worldwide and Chinese mortality were significantly lower compared with Italy (6.8% and 4.3%, respectively).<sup>6.7</sup> Demand for ICU beds differed widely between countries, varying from 5% to 32%. Health system in the Northern Italy has been overwhelmed by the high number of infected patients with ICU needs.<sup>8,9</sup> The purpose of the study is to assess the epidemiological and clinical characteristics of COVID-19 deceased patients over a one-month period at the beginning of the infection in Italy.

## 2 | MATERIALS AND METHODS

All consecutive patients with laboratory-confirmed COVID-19 infection admitted to the Emergency Rooms (ERs) Piacenza Hospital Network, including three Hospitals in Piacenza Province, Italy (Guglielmo da Saliceto Piacenza Hospital, Castel San Giovanni Hospital and Fiorenzuola d'Arda Hospital) between 24 February and 22 March 2020. Patients were diagnosed with COVID-19 infection following WHO's guidance.<sup>10</sup> Positive laboratory test for SARS-Cov-2 infection was defined as a result of real-time reverse transcriptasepolymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swabs.<sup>10</sup> The exam was implemented in a local laboratory with the adjunct of RT-PCR assays. Clinical, laboratory, treatment findings and date of death were retrospectively collected for each patient through the electronic folder available at our institutes and the data were saved on an electronic worksheet. The end of the follow-up was set on the 20th April 2020.

We have further subdivided the deceases according to the date of admission to the hospitals into four groups (admission in week 1: from 24 February to 1 March; week 2: from 2 to 8 March; week 3: from 9 to 15 March; week 4: from 16 to 22 March) to assess possible differences in the clinical and treatment characteristics of the deceased during the course of the epidemic. Clinical investigations were conducted according to the principles of the Declaration of Helsinki. The study was approved by the Institutional Ethical Board of the "Emilia Nord Area" (Approval number: 2020/0029787); written informed consent was waived by the Ethics Commission due to the emergency of the infectious disease.

## 2.1 | Data collection

A total of 33 variables have been evaluated for each patient. Data on vital signs at presentation and laboratory findings were collected from the first readings taken in the ER. The recorded data included the following: age, sex, medical comorbidities, complete blood count, blood gas analysis at admission, renal and liver function, creatine kinase (CK), lactate dehydrogenase (LDH), and C-reactive protein

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(CRP). Data on ICU admission and respiratory support (mechanical ventilation with orotracheal intubation [OTI], noninvasive mechanical ventilation [NIV]) was recorded for each patient until the end of the follow-up. Confusion, uremia, respiratory (CURB-65) rate  $\geq$ 30 per minute, low blood pressure, age  $\geq$ 65 years),<sup>11</sup> Quick SOFA (qSOFA)<sup>12</sup> were calculated according to the original studies for each patient. The classification of severity of COVID-19 was defined according to the WHO-China Joint Mission report for COVID-19.<sup>13</sup>

## 2.2 | Statistical analysis

Continuous variables are expressed as mean ± standard; the independent samples *t* test or the Mann-Whitney *U* test was used to compare normally and non-normally distributed continuous variables, respectively. Categorical variables are summarized as frequency and percentage, compared using Pearson's  $\chi^2$  exact test. The statistical significance level was set at 0.05 (two-tailed). All analyses were conducted with SPSS version 25.0 statistical software (SPSS IBM).

## 3 | RESULTS

## 3.1 | General clinical characteristics

One thousand and fifty patients with confirmed COVID-19 pneumonia were admitted to the ERs of Piacenza Hospital network. The study population included 320 non-survivor patients with COVID-19; 230 (71.9%) were male and the median age was 78.0 years, ranging from 40 to 98 years. Thirty-two (10%) patients were younger than 65 years old, while 205 (64%) patients were above 65 years old. The median duration of the hospitalization before death was 7.6 days, (interquartile range [IQR]: 5.0-11.5); the median duration from the first symptoms to the hospital admission was 6.0 (IQR: 5.0-11.0). Forty-four (13.8%) patients died at the admission into the ERs due to the critical conditions.

## 3.2 | Comorbidities and clinical presentation

Non-survivor patients showed frequently several coexisting medical conditions; with hypertension being the most common comorbidity (235 patients, 73.4%), followed by dyslipidemia (91, 28.4%), diabetes (72, 22.5%), chronic obstructive pulmonary disease (56, 17.5%), atrial fibrillation (50, 15.6%), heart diseases (39, 12.2%), kidney diseases (31, 9.7%), malignant tumors (9, 2.8%), and stroke (12, 3.7%). Ninety-six patients showed at least three or more comorbidities, whereas only 58 patients (18.1%) did not present underlying diseases (Table 1). At onset of illness, fever and dyspnea were the most common symptoms reported, followed by cough, diarrhea, fatigue, and headache. Vital signs and laboratory findings recorded on day of hospital admission are reported in Table 2. In most patient vital signs at presentation revealed a critical condition: partial pressure of

**TABLE 1** Demography and clinical presentation in 320 decedents

 with COVID-19

Total emergency room access (n)	1050		
Hospitalization rate (n, %)	773 (73.6)		
In-hospital death (n, %)	320 (30.5)		
Death at emergency room admission (n, %)	44 (13.8)		
Hospitalization length (d, min-max)	7.6 (0-41)		
Age			
Mean (min-max)	78.0 (40-98.5)		
Sugroup (n, %), y/old			
<65	32 (10.0)		
65-75	83 (25.9)		
>75	205 (64.0)		
Male sex (n, %)	230 (71.9)		
Comorbidities (n, %)			
Hypertension	235 (73.4)		
Cardiopathy	39 (12.2)		
Atrial fibrillation	50 (15.6)		
Dyslipidemia	91 (28.4)		
Diabetes	72 (22.5)		
COPD	56 (17.5)		
СКD	31 (9.7)		
Stroke	12 (3.7)		
Malignancy	9 (2.8)		
Patients without comorbidities (n, %)	58 (18.1)		
Patients with 1 comorbidity (n, %)	84 (26.2)		
Patients with 2 or more comorbidities (n, %)	178 (55.6)		

Abbreviations: CKD, chronic kidney desease; COPD, chronic obstructive pulmonary disease; COVID, coronavirus disease.

oxygen in arterial blood/fraction of inspired oxygen (PAO<sub>2</sub>/FIO<sub>2</sub>) inferior to 300 was found in 277 (86.6%) patients. Patients showed increased levels of high sensitivity CRP, LDH, and CK muscle-brain isoform. Lymphocytopenia occurred in 237 (73.6%) patients. Kidney injury were not frequently found as expressed by normal elevated plasma urea and serum creatinine values. No liver injury was detected, with normal aspartate aminotransferase and alanine aminotransferase.

## 3.3 | Age-related analysis

To explore age-related differences a subgroup analysis was performed, stratifying by age as  $\leq 65$  year-old, between 65 and 75 yearold or  $\geq 75$  year-old. Vital signs and laboratory findings were not different between the age-groups (Table 3): in particular PAO<sub>2</sub>/FIO<sub>2</sub>, PaO<sub>2</sub>, systolic blood pressure, heart and respiratory rate were comparable, revealing similar cardiovascular, and respiratory settings. Compared with younger patients, older patients had a higher proportion of comorbidities: only 31.2% patients in the <65 years group showed two or more comorbidities, on the contrary patients

#### TABLE 2 Patients clinical characteristics at ER admission

Symptoms at onset of illnes (n, %) Fever Cough Dyspnea Diarrhea Others symptoms	274 (85.6) 104 (32.5) 234 (73.1) 14 (4.4) 14 (4.4)
Vital signs at admission Temperature (°C), (n, %) <37 37-38 >38 SBP, mm Hg SBP < 90 (n, %), mm Hg RR (breath per minute) RR > 22 breath/minute HR (beat per minute) HR > 100 bpm (n, %) pO <sub>2</sub> , mm Hg pCO <sub>2</sub> , mm Hg PAO <sub>2</sub> /FiO <sub>2</sub> PAO <sub>2</sub> /FiO <sub>2</sub> < 300 (n, %)	$37.4 \pm 2.3$ 83 (25.9) 84 (26.2) 153 (47.8) $127.4 \pm 22.3$ 16 (5.0) $24.5 \pm 6.9$ 199 (62.2) $92.8 \pm 17.0$ 67 (20.9) $63.6 \pm 27.6$ $36.0 \pm 12.7$ $193.9 \pm 90.3$ 277 (86.6)
Blood samples Serum creatinine, mg/dL BUN, mg/dL LDH, U/L C-reactive protein, mg/dL Bilirubin, mg/dL CK, U/L Hemoglobin, g/dL White blood cell count (103/L) Lynfocites (%) Platelets (103/L)	$1.6 \pm 1.2$ $35.1 \pm 22.9$ $513.2 \pm 273.2$ $14.6 \pm 13.2$ $0.8 \pm 0.6$ $577.6 \pm 184.2$ $13.4 \pm 3.0$ $8.3 \pm 4.1$ $12.1 \pm 9.1$ $205.2 \pm 90.9$
CURB-65 (n, %) 0-1 2 >3	63 (19.7) 191 (59.7) 66 (20.6)
COVID classification (n, %) Moderate Severe Critic	7 (2.2) 248 (77.5) 65 (20.3)

Abbreviations: BUN, blood urea nitrogen; CK, creatine kinase; COVID, coronavirus disease; ER, emergency room; HR, heart rate; LDH, lactate dehydrogenase;  $PaO_2/FiO_2$ , partial pressure of oxygen in arterial blood/ fraction of inspired oxygen;  $pO_2$ , partial pressure of oxygen;  $pCO_2$ , partial pressure of oxygen;  $pCO_2$ , partial pressure of oxygen;  $pCO_2$ , partial pressure of carbon dioxide; RR, respiratory rate; SBP, systolic blood pressure.

with multiple comorbidities were 60.2% and 57.6% in group 65 to 75 years and >75 years, respectively (P = .01). Hypertension was the most common comorbidity in the three groups, nevertheless it was less frequent in the younger group compared with the older groups (50% vs 72.3% vs 72.7%, respectively; P = .004). Distribution of comorbidities according to age groups are displaced in Figure 1.

**TABLE 3** Age-related comorbidities andvital signs at ER admission

	Age < 65 (n = 32)	Age 65- 75 (n = 83)	Age > 75 (n = 205)	P value
Male (n, %)	28 (87.5)	65 (78.3)	137 (66.8)	.01
Comorbidities				
	1( (50.0)	(0 (70 0)	1 40 (70 7)	004
Hypertension	16 (50.0)	60 (72.3)	149 (72.7)	.004 .002
Cardiopathy Atrial fibrillation	1 (3.1) 2 (6.2)	4 (4.8) 12 (14.4)	34 (16.6) 36 (17.6)	.002
				.10
Dyslipidemia Diabetes	4 (12.5)	32 (38.5)	55 (26.8)	.11
COPD	5 (15.6)	26 (31.3)	41 (20.0)	.07
СКД	1 (3.1) 3 (9.4)	20 (24.1) 3 (3.6)	35 (17.1) 25 (12.2)	.02
Stroke	3 (9.4) 0			.08
	-	1 (0.1)	11 (5.3)	.12
Malignancy	1 (3.1)	1 (0.1)	7 (3.4)	.58
Patients with two or more comorbidities (n, %)	10 (31.2)	50 (60.2)	118 (57.6)	.01
Vital signs at admission				
SBP, mm Hg	128.5 ± 19.0	127.1 ± 20.8	127.4 ± 23.4	.788
RR (breath per minute)	25.3 ± 7.9	24.5 ± 5.2	24.4 ± 7.4	.523
pO <sub>2</sub> , mm Hg	61.8 ± 21.4	56.7 ± 20.4	66.8 ± 30.7	.483
PAO <sub>2</sub> /FiO <sub>2</sub>	181.4 ± 97.3	194.8 ± 93.6	195.5 ± 88.1	.408
OTI (n, %)	12 (37.5)	19 (22.9)	5 (2.4)	<.001
NIV (n, %)	6 (18.7)	43 (51.8)	44 (21.5)	<.001
OTI time (da ER a iot)	6.1 ± 6.9	6.3 ± 7.9	2.6 ± 3.0	.302
NIV time	1.8 ± 1.9	2.7 ± 3.5	2.8 ± 2.9	.433
OTI duration	6.5 ± 7.5	8.3 ± 14.0	$13.8 \pm 10.0$	.116
NIV duration	6.8 ± 6.5	5.8 ± 5.9	3.6 ± 3.1	.046

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Abbreviations: CKD, chronic kidney desease; COPD, chronic obstructive pulmonary disease; ER, emergency room; OTI, orotracheal intubation; NIV, noninvasive mechanical ventilation; pO<sub>2</sub>, partial pressure of oxygen; PaO<sub>2</sub>/FiO<sub>2</sub>, partial pressure of oxygen in arterial blood/fraction of inspired oxygen; RR, respiratory rate; SBP, systolic blood pressure.



## **COMORBIDITIES IN AGE GROUPS**

**FIGURE 1** Distribution of comorbidities according to age groups

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#### TABLE 4 Clinical characteristics of patients during the first 4 wk of COVID-19

	•	•				
	ALL (n = 320)	Wk 1 (n = 33)	Wk 2 (n = 101)	Wk 3 (n = 134)	Wk 4 (n = 52)	P value
Total ER access (n)	1050	123	306	404	217	
In-hospital death (n, %)	320 (30.5)	33 (26.8)	101 (33.0)	134 (33.1)	52 (23.9)	.15
Age, y	78.0 ± 10.0	75.6 ± 8.2	79.4 ± 10.4	77.7 ± 10.4	77.4 ± 9.1	.23
Male (n, %)	230 (71.9)	24 (19.5)	67 (21.9)	98 (24.2)	41 (18.9)	.40
Comorbidities (n, %)						
Hypertension Cardiopathy Atrial fibrillation Dyslipidemia Diabetes	235 (73.4) 39 (12.2) 50 (15.6) 91 (28.4) 72 (22.5)	27 (81.8) 4 (12.1) 7 (21.2) 13 (39.4) 7 (21.2)	78 (77.2) 15 (14.9) 19 (18.8) 30 (29.7) 22 (21.8)	88 (65.7) 12 (9.0) 18 (13.4) 31 (23.1) 28 (20.9)	42 (80.8) 8 (15.4) 6 (11.5) 17 (32.7) 15 (28.8)	.06 .47 .44 .23 .69
COPD CKD	56 (17.5) 31 (9.7)	7 (21.2) 5 (15.2)	20 (19.8) 16 (15.8)	15 (11.2) 8 (6.0)	14 (26.9) 2 (3.8)	.06 .02
CURB-65 (n, %) 0-1 2 >3	63 (19.7) 191 (59.7) 66 (20.6)	6 (18.2) 24 (72.7) 3 (9.1)	18 (17.8) 64 (63.4) 19 (18.8)	24 (17.9) 80 (59.7) 30 (22.4)	15 (28.8) 23 (44.2) 14 (26.9)	.15
COVID classification (n, %) Moderate Severe Critic	7 (2.2) 248 (77.5) 65 (20.3)	3 (9.1) 19 (57.6) 11 (33.3)	1 (1.0) 77 (76.2) 23 (22.8)	1 (0.7) 112 (83.6) 21 (15.7)	2 (3.8) 40 (76.9) 10 (19.2)	.01
Treatment (n, %) OTI NIV OTI time (da ER a OTI) NIV time OTI duration NIV duration	36 (11.2) 93 (29.0) 5.7 ± 7.0 2.7 ± 3.1 8.4 ± 11.6 4.8 ± 4.9	8 (24.2) 12 (36.4) 1.2 ± 1.5 5.6 ± 6.0 9.2 ± 7.9 6.0 ± 6.3	15 (14.9) 27 (26.7) 6.9 ± 9.5 2.6 ± 2.2 9.2 ± 16.1 4,6 ± 4.6	10 (7.5) 37 (27.6) 7.2 ± 5.1 2.1 ± 2.4 6.3 ± 7.4 4,8 ± 4.2	3 (5.8) 17 (32.7) 6.7 ± 3.8 2.2 ± 1.7 9.6 ± 8.3 4,5 ± 5.7	.01 .66 .25 .005 .93 .85

Abbreviations: CKD, chronic kidney disease; COPD, chronic obstruction pulmonary disease; COVID, coronavirus disease; ER, emergency room; NIV, noninvasive ventilation; OTI, orotracheal intubation.

## 3.4 | Course of the pandemic

During the observation period local health and government officials in Emilia-Romagna responded to the outbreak by creating a network of ICUs; moreover, the availability of ICU beds provided for COVID-19 in Piacenza hospitals were progressively increased from 25 to 45 beds. Comparison of demographic and clinical characteristics of patients who were admitted to ICU during the first 4 weeks of COVID-19 revealed comparable severity of the disease (Table 4).

A CURB-65 greater than 2 (81.8% in week 1, 82.2% in week 2, 82.1% in week 3, 71.1% in week 4) and a COVID classification at least severe or critic (90.9% in week 1, 99% in week 2, 99.3% in week 3, 96.1% in week 4) have been found in the majority of the deceased patients at admission during each of the 4 weeks.

During the first month of COVID-19 epidemic in Piacenza the inhospital mortality rate was 30.5%. In weeks 2 and 3 the number of patients hospitalized for COVID-19 overwhelmed the ICUs resources. Despite the high rate of hospitalization and the low availability of ICU beds, patients admitted during weeks 2 and 3 showed an in-hospital mortality similar to the in-hospital mortality in weeks 1 and 4 (29.2% in week 1, 34.6% in week 2, 34.7% in week 3, 25.3% in week 4; P = .15). A total of 36 (11.2%) patients required invasive mechanical ventilation with a mean intubation time of  $8.4 \pm 11.6$  days. Ninety-three (29.0%) patients were treated with noninvasive ventilation and died in  $4.8 \pm 4.9$  days.

## 4 | DISCUSSION

In the current study, we presented the characteristics of a large cohort of consecutive deceased patients with COVID-19, referred to the ERs of the Piacenza Hospital network in Italy. The clinical characteristics of these patients indicated that the age, male sex, and underlying diseases were the most important risk factors for death. Moreover, in-hospital mortality was very high but has not changed during the epidemic.

In our population median age of deceased patients was 78.0 years. Two previous studies Chinese study reported an average age in non-survivors respectively of 65.8 and 70.7 year-old.<sup>14,15</sup> Our data are in line with the literature reaffirming that advanced age is one of the strongest predictors of death in patients with SARS-CoV-2.<sup>16</sup>

Most patients were men (230, 71.9%) confirming the greater prevalence of COVID-19 in males.<sup>7,17,18</sup> However, gender differences seems to become less important as prognostic factor for death in advancing age; the percentage of male was significantly higher in non-survivor younger patients than in the older ones. Our data are in line with the literature that confirms the increased susceptibility of older males to SARS-CoV-2 infection.<sup>19</sup> These data are corroborated in previous studies on SARS-COV and Middle East respiratory syndrome coronavirus (MERS-COV), but the reasons of the greater prevalence in males are not yet fully explained.<sup>20,21</sup>

Among the study population non-survivor patients frequently showed several comorbidities: half of the patients presented two or more associated disease, whereas only 58 patients (18.1%) had no comorbidities. Previous studies reported similar findings showing higher prevalence of coexisting chronic illness in non-survivor compared with survivor.<sup>16,19,22</sup> In particular Li et al<sup>23</sup> have identified hypertension has one of the strongest predictors of death or severe COVID-19. In our case series, hypertension (73.4%) was the most common comorbidity followed by dyslipidemia (28.4%) and diabetes (22.5%). The reason for this higher prevalence in severe COVID-19 may be found in the role of ACE2: it is a protein homolog of ACE, widely distributed in the heart, kidneys and lungs, and it acts as a negative regulator of the renine-angiotensine system. SARS-CoV-2 uses ACE2 receptor to enter in human alveolar epithelial cells. The altered expression of ACE2 should increase patient susceptibility to viral host cell entry and may partially explain the high prevalence of hypertension in deceased patients.<sup>23,24</sup>

Fever was to be the most common symptom at the hospital admission followed by dyspnea (73.1%). In a recent study dyspnea has been found as an independent risk factor for developing death in patients with SARS-CoV-2 pneumonia, being present at the hospital admission in the 74% of fatal cases.<sup>16</sup> Dyspnea is likely the consequence of increased hypoxemia linked to an advanced stage of Covid-19 lung disease.

We observed that the majority of the deceased have severe or critical clinical conditions at admission and a high CURB-65. CURB-65 is one of the most well-validated risk prediction models of community acquired pneumonia, with an in-hospital mortality that range from 3% to 57% in patient with a score of 2 points or more.<sup>25</sup> Previous studies have proposed qSOFA as scoring system for mortality prediction at admission for patients with SAR-CoV-2.<sup>5,7</sup>

Our data are in line with those of Zhou et al<sup>5</sup> who identified a significant higher proportion of qSOFA > 1, CURB-65 > 2 and severe and critical Covid-19 cases in non-survival compared with survivor.

We have further noticed that young non-survivors had a significant higher probability to receive mechanical ventilation compared with the older ones. Nevertheless, older patients received more frequently a respiratory support with NIV, particularly in the group of age between 65 and 75 years. Probably this was the result of a choice of allocation of limited resources made by physician based on the increased probability of survival of the youngest patients. MEDICAL VIROLOGY - WILEY

The rate of intra-hospital mortality observed during the first month of the epidemic was very high (30.5%) and diverges from the results reported in the previous studies. In a meta-analysis of nine Covid-19 studies concerning the Chinese population the average rate of in-hospital death is 5%, ranging from 4.3% to 14.6%.<sup>26</sup> A recent study of a cohort of 109 decedents reported an in-hospital mortality respectively of 16.5%, 9.6% and 9% in three different hospitals in the province of Wuhan.<sup>15</sup> Several reasons may explain the high number of deaths. First, Italian general population tends to be elderly with high median age and life expectancy compared with other countries, such as China.<sup>27</sup> Second, despite ICU resources were tripled, the very high number of ER admissions in a short period of time in a small province has led to a rapid depletion of hospital resources. Third, the ICU length period needed for each patients did not allow for rapid replacement. Grasselli et al<sup>28</sup> reported a median ICU length period of 9 days. In our report OTI median duration was 8.5 days (IQR: 6.0-13.5) and median ICU stay was 11.5 days (IQR: 7.0-17.0). Fourth, the proximity to the site proximity to the site of the italian outbreak had led to the widespread growth of the virus in the provincial territory before the beginning of the restriction measures.

In the course of the 4 weeks the in-hospital mortality rate remained unchanged. We observed a progressive decline in OTI rate in non-survivor patients after the second week, with an increase and earlier use of NIV and high flow-oxygen. This reflects well how the ventilation mode of the most severe patients had changed during the outbreak according to the available resources.

To date our study is the largest collection of non-survivor Covid-19 from western population yet described. Nevertheless, it has some limitations. First, we do not provide information of survivor patients, this does not allow a comparison and a better analysis of the results obtained. Second, despite the high number of patients, these refer to the population of a single Italian province and one of the most affected by the pandemic. Third, due to the retrospective nature of the study no definitive conclusions can be drawn. Therefore, additional studies are necessary to confirm our results.

## 5 | CONCLUSION

Most of Covid-19 deceased patient were elderly male aged over than 65 years with more than one chronic comorbidities. Hypertension was the most common coexisting disease. Patients frequently showed severe and critical clinical conditions at admission in the ER, resulting in a high in-hospital mortality. Despite the high rate of hospitalization during weeks 2 and 3 of the epidemic in-hospital mortality did not change.

#### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

#### AUTHOR CONTRIBUTION

AB and LR designed the work, co-wrote the paper and performed statistical analysis. AM and GQV supervised the study and approved

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the final version of the manuscript. AZ, CS, GC, AND SG were involved in data collection and analysis of the results.

## ETHICS STATEMENT

The study was approved by the Institutional Ethical Board of the "Emilia Nord Area" (Approval number 2020/0029787); written informed consent was waived by the Ethics Commission due to the emergency of the infectious disease.

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