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Original article

Clinical characteristics, management and in-hospital mortality of patients with coronavirus disease 2019 in Genoa, Italy

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Article info

Article history:
Received 29 April 2020
Received in revised form 14 July 2020
Accepted 16 July 2020
Available online 15 August 2020

Editor: M. Paul

Keywords:
Acute respiratory distress syndrome
Coronavirus disease 2019
Interleukin-6
Mortality
Severe acute respiratory syndrome coronavirus 2

Abstract

Objectives: To describe clinical characteristics, management and outcome of individuals with coronavirus disease 2019 (COVID-19); and to evaluate risk factors for all-cause in-hospital mortality.

Methods: This retrospective study from a University tertiary care hospital in northern Italy, included hospitalized adult patients with a diagnosis of COVID-19 between 25 February 2020 and 25 March 2020. Results: Overall, 317 individuals were enrolled. Their median age was 71 years and 67.2% were male (213/317). The most common underlying diseases were hypertension (149/317; 47.0%), cardiovascular disease (63/317; 19.9%) and diabetes (49/317; 15.5%). Common symptoms at the time of COVID-19 diagnosis included fever (285/317; 89.9%), shortness of breath (167/317; 52.7%) and dry cough (156/317; 49.2%). An 'atypical' presentation including at least one among mental confusion, diarrhoea or nausea and vomiting was observed in 53/317 patients (16.7%). Hypokalaemia occurred in 25.8% (78/302) and 18.5% (56/303) had acute kidney injury. During hospitalization, 111/317 patients (35.0%) received non-invasive respiratory support, 65/317 (20.5%) were admitted to the intensive care unit (ICU) and 60/317 (18.5%) required invasive mechanical ventilation. All-cause in-hospital mortality, assessed in 275 patients, was 43.6% (120/275). On multivariable analysis, age (per-year increase OR 1.07; 95% CI 1.04 to 1.10; p < 0.001), cardiovascular disease (OR 2.58; 95% CI 1.07 to 6.25; p = 0.03), and C-reactive protein levels (per-point increase OR 1.009; 95% CI 1.004 to 1.014; p = 0.001) were independent risk factors for all-cause in-hospital mortality.

Conclusions: COVID-19 mainly affected elderly patients with predisposing conditions and caused severe illness, frequently requiring non-invasive respiratory support or ICU admission. Despite supportive care,
Introduction

As the incidence of coronavirus disease 2019 (COVID-19) has increased [1,2], so has the clinical understanding of the disease. However, data on clinical presentation, complications, management and outcome are mainly obtained from relatively small case series [1,3-9], mainly collected from China [1,3-5,8,10-17] or including selected groups of critically ill patients [6,7,18-20]. Consequently, they do not necessarily represent the current situation in European hospitals.

The main objective of this study was to describe clinical characteristics, management and outcome of individuals with COVID-19 who were admitted to our hospital in Genoa, northern Italy. We also sought to investigate risk factors associated with all-cause in-hospital mortality.

Materials and methods

With the first reported COVID-19 case in Genoa occurring on 25 February 2020, we created a collaborative study group (GECOVID-19) with the aim of improving the care of COVID-19 patients and conducting research at our hospital. This group prospectively recorded all consecutive patients with COVID-19 admitted to our hospital and collected data according to a pre-established clinical form.

Study design

For the purpose of this study, we established a retrospective cohort including all adults hospitalized with COVID-19 during the period from 25 February to 25 March 2020. The present report was designed after data collection, but the analysis was planned before starting the data analysis.

Setting

This study was conducted in a 1200-bed university-affiliated hospital (San Martino Policlinico Hospital) in Genoa, northern Italy, attending a population of approximately 400 000. During the study period, individuals with COVID-19 were admitted to the hospital if they presented PaO₂ < 60 mmHg at rest in ambient air or if the exacerbation of their underlying diseases or severe symptoms were considered unmanageable at home.

Data collection and definitions

Detailed information regarding data collection and definitions used in this study are reported in the Supplementary material (Appendix S1). Briefly, the following data were collected from the patients’ medical records at the time of COVID-19 diagnosis (i.e. at the time of the first clinical sample recorded as positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA and before any antiviral or antibiotic treatment): demographics, underlying diseases, and clinical, laboratory and radiological findings. Data on treatments, COVID-19-related complications and outcome were also collected during the course of the disease.

A confirmed case of COVID-19 was defined by a positive result of an RT-PCR assay of a respiratory sample. Cardiovascular disease was defined as a history of coronary artery disease, congestive heart failure, or severe valvular heart disease with or without valve replacement. Non-invasive respiratory support techniques included high-flow nasal cannula, continuous positive airway pressure and non-invasive positive-pressure ventilation.

Data regarding the number of patients who had died, had been discharged and were still hospitalized were recorded as of 19 April 2020. The primary outcome measure was all-cause in-hospital mortality.

Microbiology

Respiratory samples were tested for SARS-CoV-2 using RT-PCR targeted at open reading frame 1ab and nucleocapsid protein genes. A cycle threshold (Ct) value < 37 defined a positive test whereas a Ct value ≥ 40 defined a negative result. Possible coinfection with respiratory viruses was ruled out by means of multiplex RT-PCR on the same respiratory sample (Allplex TM Respiratory Panel Assay, Seoul, South Korea). Bacterial and/or fungal cultures were collected according to physicians’ judgement, and microorganisms were identified with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and were tested for antimicrobial susceptibility with a Vitek 2 automated system (bioMérieux, Marcy l’Étoile, France).

Statistical analysis

No statistical sample size calculation was performed. Data were retrieved from an online database for anonymous and automatic data collection [21]. Quantitative variables were expressed as median and interquartile range (IQR), and qualitative variables as number and

![Fig. 1. Number of admissions to hospital according to age group.](image-url)
percentage. Qualitative variables were compared using the \( \chi^2 \) and Fisher’s exact tests, as appropriate. Quantitative variables were compared by Wilcoxon rank sum test. Missing data for each variable were excluded from the denominator. Univariable analysis was used to identify potential predictors of all-cause in-hospital mortality. Potential significant baseline predictors (i.e., variables collected at the time of the first clinical sample positive for SARS-CoV-2 RNA) on univariable comparisons (\( p < 0.10 \)) were considered for the multivariable regression model. A stepwise backward selection approach was used to select the predictors to include in the final multivariable model. For easier graphical interpretation, age was grouped as follows: 31–40 years, 41–50 years, 51–60 years, 61–70 years, 71–80 years and >80 years. The analyses were performed using SPSS Statistics version 21.0 (IBM Corp., Armonk, NY, USA).

**Ethical consideration**

The study protocol was approved by the Ethics Committee of Liguria Region (N.CER Liguria 114/2020-ID10420) and the need for written informed consent was waived because of the retrospective nature of the study.

**Results**

Overall, 317 COVID-19 patients were included in the study. The number of hospital admissions varied substantially according to the age group, with the highest number observed among patients aged >60 years (Fig. 1).

The median age was 71 years (IQR 60–82 years) and 213/317 (67.2%) were male. Overall, 65.3% (110/317) of patients had at least one underlying disease (Table 1). Hypertension was the most frequent underlying disease (149/317; 47.0%), followed by cardiovascular disease (63/317; 19.9%), diabetes mellitus (49/317; 15.5%) and neurological disease (28/317; 8.8%).

The median duration of symptoms before diagnosis was 5 days (IQR 2–8 days). At the time of COVID-19 diagnosis, the most common symptoms included fever (285/317; 89.9%), shortness of breath (167/317; 52.7%) and dry cough (156/317; 49.2%). Overall, 16.7% of the patients (53/317) presented with atypical clinical manifestations consisting of mental confusion, diarrhoea and nausea or vomiting in 9.1% (29/317), 5.7% (18/317) and 5.7% (18/317) respectively.

**Table 1**

Clinical characteristics of the 317 hospitalized patients at the time of COVID-19 diagnosis

| Characteristics | Patients (n = 317) |
|-----------------|-------------------|
| Age, years      | 71 (60–82)        |
| Sex, male       | 213 (67.2)        |
| Underlying disease |                |
| Hypertension    | 149 (47.0)        |
| Cardiovascular disease | 63 (19.9) |
| Diabetes mellitus | 49 (15.5)       |
| Neurological disease | 28 (8.8)     |
| Chronic kidney disease | 22 (6.9)     |
| Chronic obstructive lung disease | 18 (5.7) |
| Solid cancer    | 12 (3.8)          |
| Haematological malignancy | 11 (3.5) |
| Number of underlying diseases |        |
| 0               | 110 (34.7)        |
| 1               | 95 (30.0)         |
| 2               | 62 (19.6)         |
| ≥3              | 50 (15.8)         |
| Charlson co-morbidity index   | 4 (1.3)        |
| Time from illness onset to hospital admission, days | 5 (2–8) |
| Signs and symptoms |                |
| Fever (Temperature >37.3 °C) | 285 (89.9) |
| Shortness of breath         | 167 (52.7) |
| Dry cough                  | 156 (49.2)       |
| Arteria                  | 57 (18.0)         |
| Mental confusion           | 29 (9.1)          |
| Diarrhoea                  | 18 (5.7)          |
| Myalgia                   | 18 (5.7)          |
| Headache                  | 14 (4.4)          |
| Nausea and vomiting        | 14 (4.4)          |
| Sputum                     | 9 (2.8)           |
| Physical examination       |                  |
| Tachypnoea                 | 140 (44.2)        |
| Tachycardia                | 89 (28.1)         |
| Hypotension                | 3 (0.9)           |
| Laboratory findings        |                  |
| Lymphopenia                | 192/281 (68.3)    |
| Thrombocytopenia           | 114/272 (41.9)    |
| ALT >40 U/L               | 105/303 (34.7)    |
| AST >40 U/L               | 102/300 (32.8)    |
| Hypokalaemia               | 78/302 (25.8)     |
| Leukopenia                 | 53/303 (17.4)     |
| Inflammatory markers       |                  |
| C-reactive protein, mg/L (n = 301) | 79.3 (33.7-132.5) |
| D-dimer, μg/mL (n = 278)   | 1050 (630.7-1563.7) |
| Interleukin-6, ng/mL (n = 252) | 46.7 (20.0-97.9) |
| Hypoxaemic respiratory failure | 199/310 (64.2) |
| Acute kidney injury        | 56/303 (18.5)     |
| Radiological findings      |                  |
| Pulmonary consolidation    |                  |
| Bilateral                  | 200/294 (68.0)    |
| Monolateral                | 76/200 (38.0)     |
| Interstitial pattern       | 124/294 (42.2)    |
| Absence of lesions         | 35/294 (11.9)     |
| Pleural effusion           | 11/294 (3.7)      |

**Table 2**

Treatments and outcomes of hospitalized patients with COVID-19

| Characteristics | Patients (n = 317) |
|-----------------|-------------------|
| Anti-infectious drugs |                  |
| Hydroxychloroquine | 225 (71.0) |
| Darunavir/ritonavir | 155 (48.9) |
| Oseltamivir       | 32 (10.1)         |
| Lopinavir-ritonavir | 4 (1.3)       |
| Remdesivir        | 2 (0.6)           |
| Anti-inflammatory drugs |            |
| Corticosteroids | 122 (38.5) |
| Tocilizumab | 61 (19.2) |
| Antibiotics       |                  |
| Fifth-generation cephalosporin | 123 (38.8) |
| Third-generation cephalosporin | 46 (14.5) |
| Macrolides        | 26 (8.2)          |
| β-lactams/β-lactamase inhibitor | 24 (7.6) |
| Fluoroquinolones  | 9 (2.8)           |
| Others            | 7 (2.2)           |
| Complications during the hospitalization |  |
| ARDS development | 116 (36.6) |
| Non-invasive respiratory support | 111 (35.0) |
| ICU admission     | 65 (20.5)         |
| Invasive mechanical ventilation | 60 (18.9) |
| Septic shock      | 15 (4.7)          |
| CRRT              | 9 (2.9)           |
| ICU length of stay, days (n = 46) | 12.0 (6.5-21.5) |
| Hospital length of stay, days (n = 275) | 12.0 (5.0-19.0) |
| All-cause in hospital mortality | 120/275 (43.6) |

**Abbreviations:** ARDS, acute respiratory distress syndrome; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

**Abbreviations:** ARDS, acute respiratory distress syndrome; CRRT, continuous renal replacement therapy; ICU intensive care unit.

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and 4.4% (14/317), respectively (3 out of 317 patients (0.9%) presented with only atypical manifestations at the time of COVID-19 diagnosis).

Lymphopenia was the most common haematological abnormality (198/281; 68.3%) followed by thrombocytopenia (114/272; 41.9%) and elevated serum transaminase levels. Hypokalaemia was also a common finding, observed in 25.8% of the patients (78/302) at the time of diagnosis, as was acute kidney injury (AKI) (56/303; 18.5%).

Of the 294/317 (92.7%) chest radiographs that were performed, 259/294 (88.1%) revealed abnormal results. The most common pattern was pulmonary consolidations in 200/294 (68.0%) patients.

### Table 3

| Characteristics | In-hospital survivors (n = 155) | In-hospital non-survivors (n = 120) | p |
|-----------------|-------------------------------|---------------------------------|---|
| Age, years      | 65 (52–76)                    | 81 (72–87)                     | <0.001 |
| Sex, male       | 98 (63.2)                     | 85 (70.8)                      | 0.20   |
| Underlying disease |                               |                                |       |
| Hypertension    | 57 (36.8)                     | 75 (62.5)                      | <0.001 |
| Diabetes mellitus | 16 (10.3)                    | 26 (21.7)                      | 0.01   |
| Cardiovascular disease | 16 (10.3)               | 39 (32.5)                      | <0.001 |
| Chronic kidney disease | 5 (3.2)                   | 14 (11.7)                      | 0.01   |
| Neurological disease | 6 (3.6)                    | 20 (16.7)                      | <0.001 |
| Chronic obstructive lung disease | 4 (2.6)               | 11 (9.2)                       | 0.03   |
| Solid cancer    | 3 (1.9)                       | 7 (5.8)                        | 0.11   |
| Haematological malignancy | 3 (1.9)                  | 6 (5.0)                        | 0.19   |
| Number of underlying diseases |                           |                                |       |
| 0               | 80 (51.6)                     | 18 (15.0)                      | <0.001 |
| 1               | 44 (28.4)                     | 34 (28.3)                      | 1.00   |
| 2               | 20 (12.9)                     | 31 (25.8)                      | 0.08   |
| ≥3              | 11 (7.1)                      | 37 (30.8)                      | <0.001 |
| Charlson co-morbidity index | 2.0 (1.0–4.0)             | 5.0 (4.0–6.0)                  | <0.001 |
| Time from illness onset to diagnosis, days | 6.0 (3.0–8.0)             | 3.0 (2.0–7.0)                  | 0.001  |
| Signs and symptoms |                               |                                |       |
| Fever (<37.3°C) | 146 (94.2)                    | 104 (86.7)                     | 0.04   |
| Dry cough       | 86 (55.5)                     | 50 (41.7)                      | 0.03   |
| Shortness of breath | 67 (43.2)                  | 79 (65.8)                      | <0.001 |
| Asthenia        | 34 (21.9)                     | 16 (13.3)                      | 0.08   |
| Myalgia         | 15 (9.7)                      | 3 (2.5)                        | 0.03   |
| Headache        | 12 (7.7)                      | 2 (1.7)                        | 0.03   |
| Diarrhoea       | 8 (5.2)                       | 6 (5.0)                        | 1.00   |
| Nausea and vomiting | 8 (5.2)                   | 3 (2.5)                        | 0.36   |
| Sputum          | 7 (4.5)                       | 1 (0.8)                        | 0.14   |
| Mental confusion | 3 (1.9)                      | 22 (18.3)                      | <0.001 |
| Physical examination |                             |                                |       |
| Tachypnoea      | 55 (32.9)                     | 71 (59.2)                      | 0.01   |
| Tachycardia     | 36 (23.2)                     | 37 (30.8)                      | 0.14   |
| Hypotension     | 1 (0.6)                       | 2 (1.7)                        | 0.59   |
| Laboratory findings |                               |                                |       |
| Lymphopenia     | 84/137 (61.3)                 | 81/104 (77.9)                  | 0.008  |
| Hypoaemic respiratory failure | 72/152 (47.4)            | 104/116 (89.7)                 | <0.001 |
| ALT >40 U/L     | 49/145 (33.8)                 | 38/114 (33.3)                  | 1.00   |
| AST >40 U/L     | 45/131 (34.4)                 | 54/103 (52.4)                  | 0.01   |
| Leukopenia      | 38/145 (26.2)                 | 25/116 (21.6)                  | 0.47   |
| Hypokalaemia    | 33/146 (22.6)                 | 56/116 (48.3)                  | <0.001 |
| Thrombocytopenia | 23/146 (15.8)                | 19/116 (16.4)                  | 1.00   |
| Inflammatory markers |                               |                                |       |
| C-reactive protein, mg/L (n = 260) | 57.2 (20.0–111.5) | 109.0 (73.1–169.0)             | 0.001  |
| D-dimer, μg/L (n = 237) | 867.0 (480.6–1330.5)         | 1317.0 (935.9–2284.0)          | 0.22   |
| Interleukin-6, ng/L (n = 216) | 27.4 (15.0–54.3)         | 740.0 (43.8–142.0)             | 0.02   |
| Acute kidney injury | 12/146 (8.2)                | 38/116 (32.8)                  | 0.001  |
| Treatments      |                               |                                |       |
| Hydroxychloroquine | 109 (70.3)                | 78 (65.0)                      | 0.36   |
| Antibiotics     | 86 (55.5)                     | 81 (67.5)                      | 0.05   |
| Darunavir/ritonavir | 80 (51.6)                  | 52 (43.3)                      | 0.18   |
| Corticosteroids | 54 (34.8)                     | 40 (33.3)                      | 0.90   |
| Tocilizumab     | 33 (21.3)                     | 17 (14.2)                      | 0.16   |
| Oselatinavir    | 20 (12.9)                     | 9 (7.5)                        | 0.17   |

**Abbreviations: ARDS, acute respiratory distress syndrome; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRRT, continuous renal replacement therapy; ICU, intensive care unit.**

* Continuous values are shown as median (interquartile range); all other values are n (%).
of which 124/200 (62.0%) were bilateral. One hundred and twenty-four patients out of 294 had an interstitial pattern (42.2%).

As for treatment, most patients received hydroxychloroquine (225/317; 71.0%) and a combination treatment with darunavir/ritonavir (195/317; 48.9%) or oseltamivir (32/317; 10.1%). One-hundred and twenty-two individuals out of 317 (38.5%) were treated with tocilizumab (Table 2). Two-hundred and three patients out of 317 (64.0%) were treated with intravenous antimicrobials, most commonly a fifth-generation cephalosporin or a third-generation cephalosporin with either a macrolide or a fluoroquinolone.

The majority of patients received oxygen therapy and 111 out of 317 (35.0%) required non-invasive respiratory support. Among them, 47.8% (53/111) subsequently required invasive mechanical ventilation (Table 2).

Overall, 20.5% (65/317) of patients needed intensive care and 18.8% (60/317) underwent invasive mechanical ventilation for a median of 9 days (IQR 4.5–16.5 days). None received extracorporeal membrane oxygenation. During hospitalization, 9/317 (2.8%) patients developed AKI requiring continuous renal replacement therapy.

On 19 April 2020, a total of 275 (86.7%) patients were no longer hospitalized: 120/275 (43.6%) had died in the hospital and 155/275 (43.6%) were treated with methylprednisolone and 61/317 (19.2%) received ritonavir (155/317; 48.9%) or oseltamivir (32/317; 10.1%). One hundred and twenty-two individuals out of 317 (38.5%) were treated with methylprednisolone and 61/317 (19.2%) received tocilizumab (Table 2). Two-hundred and three patients out of 317 (64.0%) were treated with intravenous antimicrobials, most commonly a fifth-generation cephalosporin or a third-generation cephalosporin with either a macrolide or a fluoroquinolone.

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On 19 April 2020, a total of 275 (86.7%) patients were no longer hospitalized: 120/275 (43.6%) had died in the hospital and 155/275 (43.6%) were discharged alive. Comparison between survivors and non-survivors is shown in Table 3. On multivariable analysis, only age (per-year increase odds ratio OR 1.07; 95% CI 1.04–1.10; p < 0.001), cardiovascular disease (OR 2.58; 95% CI 1.07–6.25; p 0.03), and C-reactive protein (CRP) levels (per-point increase OR 1.009; 95% CI 1.004–1.014; p 0.001) retained an independent association with all-cause in-hospital mortality (Table 4). An additional multivariate model excluding CRP and IL-6 (i.e. those variables with the highest number of missing values) suggested that AKI at the time of COVID-19 diagnosis was a possible additional, independent predictor of increased in-hospital mortality (OR 3.31; 95% CI 1.53–7.16; p 0.002; complete model results are available in the Supplementary material, Table S1). Survival curves according to age groups for the entire study population and for those patients with no underlying disease are shown in Fig. 2 and see Supplementary material, Fig. S1, respectively.

**Discussion**

The findings of the present cohort study conducted in a teaching hospital in northern Italy can be summarized as follows: (a) COVID-19 is mainly a disease of the elderly, with multiple underlying conditions and frequent atypical presentations; (b) overall in-hospital mortality is particularly high (120/275; 43.6%) and complications are common; and (c) age, cardiovascular disease and increased CRP were associated with all-cause in-hospital mortality in our study.

In our series, we observed an uneven age distribution among hospitalized COVID-19 patients, with more than 50% being aged ≥70 years. This percentage is significantly higher than that observed in China 1,3,4,8,10–17. Indeed, the pooled mean age of patients hospitalized with COVID-19 in 14 previous Chinese studies that included unselected patients was only 50 years 1,3,4,8,10–17. Reasons for the predominance of old patients in our report are not clear, although they may be attributable to the ageing Italian population 22, or the fact that, compared with young patients, older ones have an increasing risk of chronic co-morbidities that predispose them to more severe form of COVID-19 4,6.

The clinical manifestations most commonly observed in our study included fever, shortness of breath and dry cough. Fever and shortness of breath were also common findings in case series of COVID-19 patients from China and the USA 1,3,4,8,10–17,24, and these findings have been considered as prognostic indicators for adult respiratory distress syndrome and higher mortality 18. Surprisingly, our data show that 16.7% of patients (53/317) with COVID-19 had ‘atypical’ clinical manifestations such as mental confusion, diarrhoea or nausea and vomiting. Although these atypical manifestations could potentially lead to a delay in diagnosis 25 with possible uncontrolled transmission of the infection, it should be addressed that in our cohort there were only 3/317 patients (0.9%) who presented with only atypical manifestations. Accordingly, even in our outbreak setting, the level of COVID-19 suspicion should be low in the absence of fever, cough or shortness of breath.

With regards to laboratory findings, we observed a high proportion of patients with AKI at the time of COVID-19 diagnosis. This finding was only occasionally reported in previous series 6,12; we believe that the likely contributing factors include dehydration due to diarrhoea and poor oral feeding and side effects of symptomatic drugs (i.e. non-steroidal anti-inflammatory drugs). Whether coronaviruses have a pathogenic effect on kidneys warrants further investigation 26. Contrary to what was expected, the rate of hypokalaemia in our population was also high, reaching 25.8% (78/302). This is consistent with that previously reported for the SARS-CoV outbreak in 2003 in Singapore 27. Although the mechanism of hypokalaemia is still unknown, a role of diarrhoea or vomiting might be postulated. Of note, hypokalaemia could predispose patients to develop cardiac arrhythmias, which previous authors observed in about 7%–16% of individuals with COVID-19 5,24.

In our cohort, the number of antibiotics prescribed to COVID-19 patients was particularly high, suggesting substantial inappropriate prescription of antibiotics. This finding might reflect the lack of scientific evidence on how to properly manage patients with COVID-19 in the early stages of the pandemic. Moreover, the high number of patients presenting with radiological images suggestive for pulmonary consolidation (200/294; 68.0%), could have increased the suspicion of bacterial co-infection. However, in our study, which was based on routine clinical practice, we were not able to document any bacterial co-infection. On the basis of these results, we think improving the differential diagnosis between SARS-CoV-2 and bacterial respiratory pathogens should become a critical research priority, to reduce, in line with antimicrobial stewardship principles, the rates of unnecessary antibiotic prescriptions in individuals with COVID-19.

With the exception of remdesivir 28, no other specific antiviral therapy has been found to provide benefit for COVID-19 to date, and
treatment mainly consists of supportive care [5,19,29,30]. In the present study, 71.0% (225/317) and 48.9% (155/317) of the patients received hydroxychloroquine and darunavir/ritonavir, respectively. Although no effective outcomes were observed for hydroxychloroquine [31] and protease inhibitors [32] in two recent studies, future randomized studies should be performed to clarify the impact of antiviral drugs on the natural history of the disease.

Despite aggressive supportive treatment of respiratory and renal complications, we observed a striking all-cause in-hospital mortality of 43.6% (120/275), which is greater than previously reported rates from Chinese and US patients [1,3,4,8,10-17,23,24]. Our main hypothesis was that the high mortality associated with COVID-19 probably reflects the old age of our patients and the severity of underlying diseases. However, increased CRP levels were also associated with death. High levels of CRP have also been associated with the severity of the disease [18], possibly suggesting the involvement of cytokine storm in the clinical outcome of the patients [18,33,34]. The implication of the host immune response in COVID-19 suggests a potential role of anti-inflammatory drugs as adjunctive therapy. However, the role of corticosteroids or tocilizumab—a recombinant humanized monoclonal antibody inhibiting membrane-bound and soluble interleukin-6 receptors [35]—remains controversial [29], even if case reports [36,37] and case series [38] have reported benefits. Although we cannot advocate the universal use of corticosteroids and tocilizumab in individuals with COVID-19, follow-up studies evaluating the role of anti-inflammatory drugs are warranted [30]. Finally, the independent association we found between AKI and increased mortality in the additional multivariable model may reflect the unfavourable prognostic effect of organ dysfunction and/or severe disease presentation.

Our study has several limitations. First, it is a retrospective analysis and we did not examine all aspects of care that potentially could influence the outcome. For example, data are lacking about some important clinical characteristics that have been found associated with COVID-19 severity, such as weight, body mass index and smoking status. Second, this study was performed at a single institution of northern Italy and the results may not be representative of other Italian or European centres. Third, some data were missing for certain patients included in this study. Therefore, studies with the inclusion of more patients would be needed to increase the statistical power and lend support to inflammatory markers (e.g. CRP, interleukin-6) as risk of in-hospital death. Finally, among our study population, 42/317 were still hospitalized at the time of writing this report. Therefore, all-cause in-hospital mortality could be underestimated.

In conclusion, in our cohort, COVID-19 mainly affected elderly individuals with predisposing conditions and caused severe illness that frequently required non-invasive respiratory support or admission to intensive care. Despite supportive care, COVID-19 remains associated with a substantial risk of all-cause in-hospital mortality.

Transparency declaration

M. Bassetti serves on scientific advisory boards for Angelini, AstraZeneca, Bayer, Cubist, Pfizer, Menarini, MSD, Nabriva, Paratek, Roche, Shionogi, Tetraphase, The Medicine Company and Astellas Pharma Inc. and has received funding for travel or speaker honoraria from Algorithm, Angelini, Astellas Pharma Inc., AstraZeneca, Cubist, Pfizer, MSD, Gilead Sciences, Menarini, Novartis, Ranbaxy, and Teva; D.R. Giacobbe reports honoraria from Stepstone Pharma.
Authors' contributions

Conceptualization was by A. Vena, D.R. Giacobbe, A.Di Biagio, M. Mikulska, L. Taramasso, A. De Maria, L. Ball, I. Brunetti, M. Loconte, N. A. Patroniti, C. Robba, E. Delfino, C. Dentone and L. Magnasco; methodology was by A. Vena, D.R. Giacobbe, M. Bavastro, M. Cerchiaro, P. Pelosi and M. Bassetti; the software programming was by M. Giacomini and S. Mora. A. Di Biagio, M. Mikulska, L. Taramasso, A. De Maria, L. Ball, I. Brunetti, M. Loconte, N. A. Patroniti, C. Robba, E. Delfino, C. Dentone, L. Magnasco, P. Pelosi, M. Bassetti, L. Nicolini, F. Toscanini, E. Barisione, F. Baldi, E. Balletto, M. Berruti, F. Briano, C. Sepulcri, S. Dettori, L. Labate, M. Mirabella, F. Portunato, R. Pincino, C. Russo and S. Tutino were responsible for validation and the investigation and data curation was by A. Vena, D.R. Giacobbe, P. Pelosi, M. Bassetti A., Di Biagio, M. Mikulska, L. Taramasso, A. De Maria, L. Ball, I. Brunetti, M. Loconte, N. A. Patroniti, C. Robba, E. Delfino, C. Dentone and L. Magnasco. A. Di Biagio, M. Mikulska, L. Taramasso, A. De Maria, L. Ball, I. Brunetti, M. Loconte, N. A. Patroniti, C. Robba, E. Delfino, C. Dentone, L. Magnasco, P. Pelosi and M. Bassetti supervised the study.

Acknowledgements

The authors thank Alessio Signori for statistical analysis.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2020.07.049.

Appendix. GECOVID-19 Study group

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