

Clinical characteristics, management and health-related quality of life in young adults with COVID-19

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Research Article

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Abstract

Background The outbreak of COVID-19 has rapidly spread to Italy, including Pesaro-Urbino province. Data on young adults with COVID-19 are lacking. We report the characteristics, management and health-related quality of life (HRQoL) in patients with COVID-19 aging ≤ 50 years.

Methods A retrospective analysis was performed in all patients ≤ 50 years with a confirmed diagnosis of COVID-19 admitted to Emergency department (ED) of San Salvatore Hospital in Pesaro from February 28th to April 8th, 2020. Data were collected from electronic medical records. HRQoL was investigated after one month from hospital discharge. Outcomes were evaluated between hospitalized and not hospitalized patients.

Results: Among 673 patients admitted to the ED and diagnosed with COVID-19, 104 (15%) were ≤ 50 years old: 74% were discharged at home within 48 h, 26% were hospitalized. Fever occurred in 90% of the cases followed by cough (56%) and dyspnoea (34%). Chest X-ray and/or CT scan revealed ground glass opacity, bilateral patch shadow or focal lesions in 27%, 37% and 10% of the patients, respectively. The most frequent coexisting conditions were hypertension (11%), thyroid dysfunction (8%) and neurological and/or mental disorders [NMDs] (6%). Mean BMI was 27. Hypokalaemia and NMDs were significantly more common in patients who underwent mechanical ventilation. Regardless of hospitalization, there was a significant impairment in both the physical and mental functioning.

Conclusions Overweight and hypertension are frequent conditions in young adults with COVID-19. Hypokalaemia and NMDs are commonly associated with progressive disease. There is a significant impact on HRQoL in the early stage of post-discharge.

Introduction

In early December 2019 41 cases of coronavirus disease 2019 (COVID-19) were described in Wuhan in Hubei Province (1). The outbreak of the new pandemic coronavirus pneumonia has rapidly spread all over the world including Europe and Italy with an increasing number of cases. People have been facing this new virus changing their habits and their behaviours with a huge impact on mental and physical health.

The first two cases in Italy were reported on the 23rd of January 2020 coming from Wuhan (2). Since then, severe acute respiratory syndrome coronavirus 2 (SARS Cov-2) has overwhelmed Italy with approximately 215.000 infected subjects. Among the most affected areas in Italy (Figure 1), Marche region counted almost 6.400 cases (3). The median age of the Italian patients was 62 years old; patients between 19-50 years old represented the 28% of the infected population, while patients older than 50 were the 70% (3).

Then, a remarkable interest of COVID-19 has been focused on older people (4) (5) (6). Conversely, only little clinical information on young people is available. Therefore, the aim of this study was to illustrate the epidemiological, demographic, clinical, laboratory, radiological characteristics and the clinical outcomes of laboratory-confirmed patients with COVID 19 ≤ 50 years old.

The study also aims to investigate the impact of the COVID-19 on patients' quality of life.

Materials And Methods

Patients

A retrospective analysis was performed on the confirmed cases of COVID-19, who were admitted to Emergency department (ED) of San Salvatore Hospital in Pesaro from February 28th to April 8th, 2020. All adults patients with age ranging from 18 to 50 years were considered in this study. A confirmed case of infection with SARS Cov2 was defined by RT-PCR assay on nasopharyngeal swab.

Data collection and definitions

Data were extracted from electronic medical records including patient demographic information, tobacco smoke addiction, underlying comorbidities, triage vital signs, referred symptoms on admission and the interval time lapse between illness onset and ED access. Fever was defined as axillary temperature of at least 37.5°C. Respiratory distress syndrome was defined as $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 300 according to the Berlin Definition (7). Laboratory tests and radiological data on admission were also collected.

Short form health survey (SF-36)

After one month from hospital discharge patients were interviewed and requested to answer to the short form health survey (SF-36). The SF-36 is an internationally instrument to measure Health-Related Quality of Life (HRQoL) that has been used in many different diseases to evaluate the quality of life for patients with other respiratory infections such as Middle East Respiratory Syndrome (MERS) (8) and SARS CoV-1 (9). The SF-36 includes 36 questions analysing eight health domains including physical functioning, role physical and bodily pain which evaluates physical sphere, mental health, role emotional, and social functioning items analysing mental component. Scores for each domain can range from 0 (worst) to 100 (best), higher scores indicate better HRQoL.

Statistical analysis

Continuous variables were expressed as median (IQR) and compared with the Mann-Whitney U test or independent group *t* tests, when data were normally distributed; categorical variables were expressed as number (%) and compared by χ^2 test or Fisher's exact test. Comparison analysis was carried out between hospitalized and not hospitalized patients (i.e.: discharged at home within 48 h upon ED arrival). A two-sided α of less than 0.05 was considered statistically significant. All the statistical analyses were supported by SPSS (Statistical Package for the Social Sciences) version 25.0 software (SPSS Inc).

Results

Among 673 patients admitted to the ED and diagnosed with COVID-19 from February 28th to April 8th, 2020, 104 (15%) were \leq 50 years old. Demographic, clinical, laboratory and radiological characteristics of the patients are shown in Table 1. Age ranged from 22 to 50 years with a mean of 41 years, the majority were men and the mean of BMI was 27. Hypertension was the most frequent coexisting condition being observed in 11% of the patients, followed by thyroid dysfunction (8%), and neurological and/or mental disorders (6%). Mean days from illness onset to first hospital access was 8.8. Common symptoms at the onset were fever (94%), cough (58%) and dyspnoea (34%), less common symptoms were fatigue (17%), anosmia (16%), diarrhoea (15%) and chest pain (14%). Respiratory distress was present in 13% of the patients. Laboratory findings showed that values of lactate dehydrogenase, CRP and D-dimer were in the upper limits while the remaining parameters were all within the normal ranges. Chest X-ray and/or CT scan revealed ground glass opacity, bilateral patch shadow or focal lesions in 27%, 37% and 10% of the patients, respectively. In 26% of the cases, chest X-ray was negative.

Seventy-one patients (74%) were managed in ED and discharged at home within 48h, 33 patients (26%) were hospitalized. Compared with patients who did not require hospitalization, in-patients were significantly older and were more likely to be overweight. Fever and dyspnoea were significantly more common in hospitalized patients. As expected, a significantly higher proportion of hospitalized patients had respiratory distress. Additionally, this group was more likely to have lymphocytopenia, hepatic dysfunction, higher inflammation biomarkers (i.e.: PCT, CRP and D-dimer [p ranging from <0.001 to 0.034]), and more extensive lung involvement ($p < 0.001$).

Six out of 33 hospitalized patients (18%) required mechanical ventilation (Table 2). Respiratory distress syndrome and hypokalaemia at the infection onset were significantly more common in patients requiring mechanical ventilation (p 0.001 and 0.028, respectively). No difference was noticed in other laboratory findings between patients who required and did not require ICU care. Among coexisting conditions, only neurological and/or mental disorders were significantly more common in patients requiring ICU care ($p=0.014$). Table 3 details clinical features of six patients who required ICU care. Except for patient n. 5, who did not suffer from any underlying disease, the remaining five patients died from one to 39 days upon the admission in ICU.

Among 104 patients, 85 were contacted one month from hospital discharge and requested to answer to SF-36. Sixty-four subjects (75%) answered the SF-36 questionnaire. The results of the survey are reported in Table 4. Early HRQoL revealed that physical functioning, general health and mental health reached the highest scores (74, 63, and 59, respectively) while physical role, vitality, social functioning and emotional role reached the lowest scores (30, 48, 45 and 46, respectively). Additionally, there were no significant differences between hospitalized and not hospitalized patients in physical component or mental component scores.

Discussion

Data on young adults with COVID-19 are lacking. Although one study from China reported a median age of 41 years, the overall population ranged from 41 to 65 years and it included even older patients (10).

Data from European countries describe patients who are generally older than those reported from Asiatic countries (11) (12) . Despite this, older age represents an independent risk factor for mortality in all reports. For this reason, this study focused on clinical characteristics, management and health related quality of life in young adults with COVID 19 admitted to the ED of Pesaro Hospital. During the epidemic, Marche, and particularly the Province of Pesaro-Urbino, was one of the most affected regions in Italy.

Overall, our data highlight distinctive features of COVID 19 in young patients.

First, as many as 26% of the patients was hospitalized upon arrival to the ED. This is a remarkable percentage considering the age. Even if there is a lack of data describing the management of patients after ED access, it is reasonable to think, looking at the regional prevalence of SARS CoV2, that many patients with mild symptoms were managed at home according to WHO indications (13). Second, in contrast to many reports in which SARS CoV2 seems to affect more males than females, our population included approximately an equal number of men and women. Conversely, we observed a slightly higher number of men (57%) requiring hospitalization after ED access. It has been demonstrated that for SARS-CoV2, as for other similar infections (i.e.: MERS and SARS-CoV1), the male gender is more affected than female thereby reflecting sex predisposition associated with genetic factors (14). Third, several coexisting conditions were quite frequent in this population. In concert with other studies focused on patients with COVID-19 without age selection, an increase of BMI even in young adults has been observed. As it has been already demonstrated in Influenza A virus (15), obesity may worsen the severity of respiratory diseases. One study showed that SARS-CoV2 patients having BMI ≥ 35 are at higher risk of mechanical ventilation, compared to those with BMI < 25 (16). This could be due to multiple factors. Accumulation of adipose tissue in the mediastinum and in the abdominal cavities seen in obese subjects determines lung mechanical dysfunction (17). Additionally, fat causes an abnormal cytokine production and an increasing inflammatory pathway activation thereby favouring the infection *per se* and worsening its clinical course. (18)

Hypertension is one of the most frequent underlying diseases in patients with COVID-19 (19). In our study, 11% of young patients suffered from this clinical condition. Although hypertension has been commonly described to increase the severity illness in patients with COVID 19 (20), it is still unclear whether hypertensive subjects are more likely to be infected by coronavirus. It is reasonable to think that angiotensin-converting enzyme 2 expression, frequently increased in these patients, and the activation of the renin-angiotensin system can be involved either in the entrance of the virus into the cell or in the inflammatory response (21). Further studies are warranted to elucidate this issue.

Thyroid dysfunction was seen in 8% of our patients. Little is known about the correlation between COVID-19 and thyroid dysfunction. Thyroid hormones play an important role in regulating the immune response and in modulating pulmonary system and alveolar ventilation. Hypothyroid patients can have a

decreased lung function (22) but there is no evidence that those who have a thyroid disorder, unless they are under immunosuppressive treatment, are at higher risk to be infected by coronavirus (23).

Fourth, we identified several features more frequently associated with young patients requiring ICU admission, namely the respiratory distress syndrome, the hypokalaemia and neurological diseases and mental disorders. While the more severe respiratory syndrome the greater risk of mechanical ventilation is easily explained, the relationship between the other two parameters and ICU admission is less clear.

Hypokalaemia has been already reported among patients with COVID-19 with progressive disease (24). It can occur first through virus action on angiotensin-converting enzyme 2 with an increased potassium excretion by the kidneys and secondly through loss, with vomiting or diarrhoea, in patients with gastrointestinal symptoms (25). Hypokalemia might worsen acute respiratory distress syndrome and acute cardiac injury, which are common complications in COVID-19 (24) (25) .

There are no data on underlying mental health disease and higher risk of developing SARS Cov-2 pneumonia. Similarly, no information on the effect of chronic benzodiazepines use in patients with COVID-19 infection is available. It is interesting to note how four out of six patients, who underwent mechanical ventilation, were taking benzodiazepines. The mechanism of action of these drugs is enhancing the effect of γ -amino-butyric acid type A ($GABA_A$) at the $GABA_A$ receptors. Chronic benzodiazepine exposure could be associated with an increased risk of developing pneumonia (26) as GABA can play an important role in regulating the secretion of a great number of cytokines (27) (28).

A severe respiratory infection generally affects HRQoL. This has been demonstrated in subjects recovering from MERS (8), SARS-CoV-1 (9) and H1N1 (29). Batawi et al. (8) demonstrated that subjects with MERS experiencing ICU admission scored low values for physical function, general health, vitality, emotional role and physical components. To our knowledge, there are still no studies considering the impact of COVID-19 on mental health and quality of life among these patients. Despite the young age population analysed in this study and the majority of patients who were discharged early after ED arrival, we observed lowest rating scores in items regarding physical role, vitality, social functioning and emotional role. It is interesting to note how the quality of life reported by hospitalized patients did not differ from non-hospitalized ones, as shown by similar physical and mental component summary scores (around 50 in both groups). This can be due by the fact that patients discharged early from ED experienced the lockdown period, so their psychological and physical spheres were possibly affected as the ones hospitalized.

The present study has some limitations. First, being a single-centre study, the number of patients considered is low. The suspected but undiagnosed cases were ruled out in the analyses. This feature has certainly weakened the statistical power of the study. Nevertheless, we considered all patients admitted to the ED of Pesaro Hospital in a very limited time which represented the period with highest COVID-19 incidence in our country. Second, this was a retrospective analysis. Although we tried to collect as many clinical data as possible, we may have still missed useful information for the management of these

patients. In particular, due to the massive burden of patients admitted at the ED, several laboratory parameters (i.e.: D-dimer, ferritin, IL-6 etc.) or second level radiological examinations (i.e.: CT scan) were not always performed, mainly at the beginning of the pandemic period. Third, we performed only one early SF-36 survey (within one month from hospital discharge), while late and repeated surveys (i.e.: three or six months thereafter) might be more useful either in differentiating HRQoL based on severity illness or showing a quality of life improvement.

Conclusions

These data showed that overweight and hypertension are frequent coexisting conditions in young adults with COVID-19. Respiratory distress and hypokalaemia at the infection onset such as neurological and/or mental disorders are commonly associated with progressive disease. Regardless of hospitalization, either physical or mental status are deeply affected in the early stage of post-discharge.

Declarations

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Authors' contributions Conceived and designed the experiments: FB, CT, SG, ZP, and BC. Analyzed the data: RM, UG, AP, and FB. Wrote the paper: FB, CT and AP. All authors drafted the article, revised it critically for important intellectual content, and approved the final article.

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Availability of data and materials

The data that support the findings of this study are available from Azienda Ospedaliera Ospedali Riuniti Marche Nord but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Institutional Review Board of Azienda Ospedaliera Ospedali Riuniti Marche Nord.

Ethics approval and consent to participate The present research has been performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. The Institutional Review Board of the Azienda Ospedaliera Ospedali Riuniti Marche Nord granted retrospective access to the data without need for individual informed consent.

Consent for publication Not applicable.

Competing interests The authors report no competing interests. FB is Associate Editor of BMC Infectious Diseases Journal. The authors alone are responsible for the content and the writing of the paper.

Bibliography

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China [published correction appears in *Lancet*. 2020 Jan 30;]. *Lancet*. 2020;395(10223):497-506
2. Giovanetti M, Benvenuto D, Angeletti S, Ciccozzi M. The first two cases of 2019-nCoV in Italy: Where they come from? *J Med Virol*. 2020; 92(5): 518–521.
3. Sorveglianza Integrata COVID-19 in Italia. Available at https://www.epicentro.iss.it/coronavirus/bollettino/Infografica_8maggio%20ITA.pdf. Accessed 8 May 2020.
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA*. 2020; 323(11): 1061–1069.
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020; 395(10223): 507-513.
6. Liu Y, Sun W, Li J, Chen L, Wang Y, Zhang L, et al. Clinical features and progression of acute respiratory distress syndrome in coronavirus disease 2019. medRxiv 2020.02.17.20024166; doi:<https://doi.org/10.1101/2020.02.17.20024166>
7. Ranieri V, Rubenfeld GD, Thompson B, Ferguson ND, et al. The ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012; 307(23): 2526- 2533.
8. Batawi S, Tarazan N, Al-Raddadi R, et al. Quality of life reported by survivors after hospitalization for Middle East respiratory syndrome (MERS). *Health Qual Life Outcomes*. 2019; 17(1): 101. Published 2019 Jun 11.
9. Ngai JC, Ko FW, Ng SS, To KW, Tong M, Hui DS. The long-term impact of severe acute respiratory syndrome on pulmonary function, exercise capacity and health status. *Respirology*. 2010; 15(3): 543-550.
10. Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. [published correction appears in *BMJ*. 2020 Feb 27; 368: m792]. *BMJ*. 2020; 368: m606. Published 2020 Feb 19.
11. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ*. 2020;369: m1985. Published 2020 May 22
12. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. [published online ahead of

- print, 2020 Apr 6]. *JAMA*. 2020; 323(16):1574-1581.
13. Home care for patients with COVID-19 presenting with mild symptoms and management of their contacts. Available at [https://www.who.int/publications/i/item/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications/i/item/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts). Accessed 30 May 2020.
 14. Sharma G, Volgman AS, Michos ED. Sex Differences in Mortality from COVID-19 Pandemic: Are Men Vulnerable and Women Protected? [published online ahead of print, 2020 May 4]. *JACC Case Rep*. 2020; 10.1016/j.jaccas.2020.04.027.
 15. Honce R, Schultz-Cherry S. Impact of Obesity on Influenza A Virus Pathogenesis, Immune Response, and Evolution. *Front Immunol*. 2019; 10: 1071. Published 2019 May 10
 16. Simonnet A, Chetboun M, Poissy J, et al. High Prevalence of Obesity in Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Requiring Invasive Mechanical Ventilation [published online ahead of print, 2020 Apr 9]. *Obesity (Silver Spring)*. 2020;10.1002/oby.22831.
 17. Dixon AE, Peters U. The effect of obesity on lung function. *Expert Rev Respir Med*. 2018; 12 (9): 755-767.
 18. Sattar N, McInnes IB, McMurray JJV. Obesity a Risk Factor for Severe COVID-19 Infection: Multiple Potential Mechanisms [published online ahead of print, 2020 Apr 22]. *Circulation*. 2020;10.1161/CIRCULATIONAHA.120.047659
 19. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *JAMA*. 2020; 323 (20): 2052–2059.
 20. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020; 395(10229): 1054-1062.
 21. Pranata R, Lim MA, Huang I, Raharjo SB, Lukito AA. Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: A systematic review, meta-analysis and meta-regression. *J Renin Angiotensin Aldosterone Syst*. 2020; 21(2): 1-11.
 22. Sadek SH, Khalifa WA, Azoz AM. Pulmonary consequences of hypothyroidism. *Ann Thorac Med*. 2017; 12(3): 204-208. .
 23. Boelaert K, Visser WE, Taylor PN, Moran C, Léger J, Persani L. ENDOCRINOLOGY IN THE TIME OF COVID-19: Management of hyperthyroidism and hypothyroidism. *Eur J Endocrinol*. 2020;183(1):G33-G39.
 24. Chen D, Li X, Song Q, et al. Assessment of Hypokalemia and Clinical Characteristics in Patients With Coronavirus Disease 2019 in Wenzhou, China. *JAMA Netw Open*. 2020;3(6): e2011122. Published 2020 Jun 1.
 25. Lippi G, South AM, Henry BM. Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). *Ann Clin Biochem*. 2020; 57(3): 262-265.
 26. Obiora E, Hubbard R, Sanders RD, Myles PR. . The impact of benzodiazepines on occurrence of pneumonia and mortality from pneumonia: a nested case-control and survival analysis in a

- population-based cohort. *Thorax*. 2013; 68(2): 63-170.
27. Bhandage AK, Jin Z, Korol SV, et al. GABA Regulates Release of Inflammatory Cytokines From Peripheral Blood Mononuclear Cells and CD4⁺T Cells and Is Immunosuppressive in Type 1 Diabetes. *EBioMedicine*. 2018;30: 283-294.
28. Sanders RD, Godlee A, Fujimori T, et al. Benzodiazepine augmented γ -amino-butyric acid signaling increases mortality from pneumonia in mice. *Crit Care Med*. 2013; 41(7): 1627-1636.
29. van Hoek AJ, Underwood A, Jit M, Miller E, Edmunds WJ. The impact of pandemic influenza H1N1 on health-related quality of life: a prospective population-based study. *PLoS One*; 6(3): e17030, 2011.

Tables

Table 1. Demographic, clinical, laboratory and radiological characteristics of 104 young adults with COVID-19 considered in this study

Characteristics	All patients (n=104)	Outpatients (n=71)	Inpatients (n=33)	p value
Mean age \pm SD - years	41.1 \pm 7.4	39.5 \pm 7.5	44.8 \pm 5.8	<0.001
Male gender - no. (%)	56 (53.8%)	37 (52.1%)	19 (57.6%)	0.757
Healthcare worker - no. (%)	13 (12.5%)	11 (15.5%)	2 (6.1%)	0.218
Mean BMI (Body mass index) \pm SD	27.1 \pm 5.01	26.37 \pm 5.12	28.6 \pm 4.46	0.029
Smoking habit - no. (%)	11 (10.6%)	9 (13.8%)	2 (7.1%)	0.495
Coexisting conditions				
Hypertension	11 (10.6%)	8 (11.3%)	3 (9.1%)	>0.999
Diabetes	4 (3.8%)	2 (2.8%)	2 (6.1%)	0.590
Chronic obstructive pulmonary disease	2 (1.9%)	2 (2.8%)	0	>0.999
Cerebrovascular disease	1 (1%)	1 (1.4%)	0	>0.999
Chronic liver disease	3 (2.9%)	2 (2.8%)	1 (3%)	>0.999
Neurological disease and mental disorder	6 (5.8%)	2 (2.8%)	4 (12.1%)	0.079
Malignancy	3 (2.9%)	3 (4.2%)	0	0.550
Thyroid diseases	8 (7.7%)	7 (9.9%)	1 (3%)	0.431
Days from illness onset to visit hospital	8.8 \pm 6.05	8.5 \pm 6.49	8.5 \pm 6.07	0.996
Signs and symptoms at the onset				
Fever	94 (90.4%)	61 (85.9%)	33 (100%)	0.028
Cough	58 (55.8%)	35 (49.3%)	23 (69.7%)	0.082
Dyspnoea	35 (33.7%)	18 (25.4%)	17 (51.5%)	0.016
Chest pain	15 (14.4%)	9 (12.7%)	6 (18.2%)	0.551
Fatigue	18 (17.3%)	13 (18.3%)	5 (15.2%)	0.906
Sore throat	9 (8.7%)	9 (12.7%)	0	0.054
Anosmia	17 (16.3%)	14 (19.7%)	3 (9.1%)	0.280
Diarrhoea	16 (15.4%)	9 (12.7%)	7 (21.2%)	0.406
Vomiting	5 (4.8%)	4 (5.6%)	1 (3%)	>0.999
Headache	8 (7.7%)	6 (8.5%)	2 (6.1%)	>0.999
Myalgia	11 (10.6%)	7 (9.9%)	4 (12.1%)	0.740
Syncope	6 (5.8%)	4 (5.6%)	2 (6.1%)	>0.999
Respiratory distress syndrome	14 (13.95%)	2 (2.8%)	12 (36.4%)	<0.001
Vital signs				
Systolic blood pressure. mm Hg	96 \pm 15.51 [89]	128 \pm 14 [59]	132 \pm 18.1 [30]	0.289
Heart rate	91.7 \pm 17.45 [71]	90.3 \pm 18.3 [47]	94.6 \pm 15.6 [24]	0.329
Respiratory rate	18 (17-24) [30]	17 (16-18) [19]	18 (17-24) [11]	0.171
Laboratory findings				
White blood cell count, \times 10 ⁹ /L (normal range 4-11)	5.820 \pm 2.489 [101]	5.614 \pm 2.259 [69]	6.264 \pm 2.913 [32]	0.224
Lymphocyte count, \times 10 ⁹ /L (normal range 1-4)	1.318 \pm 0.609 [101]	1.415 \pm 0.597 [69]	1.109 \pm 0.592 [32]	0.018
Platelet count, \times 10 ⁹ /L (normal range 150-400)	186 (152-248) [101]	183 (161-246) [69]	190.5 (142-250) [32]	0.693
Alanine aminotransferase, U/L (normal range 0-35)	28 (18-40) [99]	21 (15-33) [67]	36.2 (26.7-50) [32]	0.001
Aspartate aminotransferase, U/L (normal range 0-35)	24 (42-20.5) [95]	24 (19-30) [63]	42 (29.7-51) [32]	<0.001
Creatinine, mg/dl (normal range 0.67-1.17)	0.844 \pm 0.21 [101]	0.823 \pm 0.19 [69]	0.890 \pm 0.24 [32]	0.128
Potassium, mEq/L (normal range 3.5-5.1)	3.99 \pm 0.36 [99]	3.96 \pm 0.348 [68]	4.05 \pm 0.38 [31]	0.248
Lactate dehydrogenase, U/L (normal range 0-247)	250.5 (176.5-326.5) [67]	179 (150-221) [39]	317 (259-448) [28]	<0.001
Creatine kinase, U/L (normal range 0-195)	73 (49.25-124.5) [46]	67.5 (49-90.7) [28]	116 (59-270) [18]	0.034
Procalcitonin ng/mL (normal range 0.38)	0.03 (0.02-0.08) [49]	0.02 (0.02-0.04)	0.07 (0.02-0.132)	0.018

		[29]	[20]	
C-reactive protein mg/mL (normal range 0-0.49)	1.74 (0.49-5.72) [99]	0.89 (0.195-2.44) [67]	7.63 (2.66-11.72) [32]	<0.001
D-dimer, ng/L (normal range 0-500)	587 (298-920) [41]	406 (263-494) [21]	861 (591-1165) [20]	0.001
Involvement on chest radiographs				
No involvement	27 (26%)	26 (37.7%)	1 (3%)	
Ground-glass opacity	28 (26.9%)	23 (33.3%)	5 (15.2%)	
Bilateral lung patch shadow	37 (35.6%)	12 (17.4%)	25 (75.8%)	
Focal lesions	10 (9.6%)	8 (11.6%)	2 (6.1%)	<0.001

Data are expressed as mean±SD, median (IQR) or n (%).

p values indicate differences between out and in-patients. $P < .05$ was considered statistically significant.

In round brackets are expressed percentages and IQR, in brackets subjects analysed.

Table 2. Demographic, clinical, laboratory and radiological characteristics of 33 hospitalized young adults with COVID-19 considered in this study

Characteristics	Inpatients (n=33)	No ICU care (n=27)	ICU care (n=6)	p value
Mean age \pm SD - years	44.8 \pm 5.8	45.48 \pm 5.09	42.5 \pm 8.26	0.257
Male gender - no. (%)	19 (57.6%)	16 (59.3%)	3 (50%)	>0.999
Healthcare worker - no. (%)	2 (6.1%)	2 (7.4%)	0	>0.999
Mean BMI \pm SD	28.6 \pm 4.46	28.7 \pm 4.8	28.6 \pm 2.84	0.989
Smoking habit - no. (%)	2 (7.1%)	1 (4%)	1 (33.3%)	0.206
Coexisting conditions				
Hypertension	3 (9.1%)	3 (11%)	0	>0.999
Diabetes	2 (6.1%)	2 (7.4%)	0	>0.999
Chronic liver disease	1 (3%)	1 (3.7%)	0	>0.999
Neurological disease and mental disorder	4 (12.1%)	1 (3.7%)	3 (50%)	0.014
Thyroid diseases	1 (3%)	0	1 (16.7%)	0.182
Signs and symptoms at the onset				
Fever	33 (100%)	100%	100%	-
Cough	23 (69.7%)	21 (77.8%)	2 (33.3%)	0.053
Dyspnoea	17 (51.5%)	13 (48.1%)	4 (66.7%)	0.656
Chest pain	6 (18.2%)	6 (22.2%)	0	0.563
Fatigue	5 (15.2%)	5 (18.5%)	0	0.556
Anosmia	3 (9.1%)	3 (11.1%)	0	>0.999
Diarrhoea	7 (21.2%)	6 (22.2%)	1 (16.7%)	>0.999
Vomiting	1 (3%)	1 (3.7%)	0	>0.999
Headache	2 (6.1%)	1 (3.7%)	1 (16.7%)	0.335
Myalgia	4 (12.1%)	4 (14.8%)	0	>0.999
Syncope	2 (6.1%)	6 (22.2%)	1 (16.7%)	0.335
Respiratory distress syndrome	12 (36.4%)	6 (22.2%)	6 (100%)	0.001
Vital signs				
Systolic blood pressure. mm Hg	(30) 132 \pm 18.1	132 \pm 18.1 [25]	(5) 131 \pm 20	0.895
Heart rate	94.6 \pm 15.6 [24]	(21) 93.3 \pm 16.3	(3) 103 \pm 3.51	0.291
Laboratory findings				
White blood cell count, \times 10 ⁹ /L (normal range 4-11)	6.264 \pm 2.913 [32]	6.437 \pm 2.981 [26]	5.511 \pm 2.714	0.492
Lymphocyte count, \times 10 ⁹ /L (normal range 1-4)	1.109 \pm 0.592 [32]	1.091 \pm 0.460 [26]	1.183 \pm 1.051	0.739
Platelet count, \times 10 ⁹ /L (normal range 150-400)	190.5 (142-250) [32]	199(144.750-260.500) [26]	156.5 (138.750-181.750)	0.308
Alanine aminotransferase, U/L (normal range 0-35)	36.2 (26.7-50) [32]	39 (30.2-52) [26]	25 (17.5-28.7)	0.055
Aspartate aminotransferase, U/L (normal range 0-35)	42 (29.7-51) [32]	43 (28.5-49.7) [26]	35 (30.7-67)	0.906
Creatinine, mg/dl (normal range 0.67-1.17)	0.890 \pm 0.24 [32]	0.86 \pm 0.218 [26]	1 \pm 0.294	0.093
Potassium, mEq/L (normal range 3.5-5.1)	4.05 \pm 0.38 [31]	4.1 \pm 0.332 [26]	3.7 \pm 0.460	0.028
Lactate dehydrogenase, U/L (normal range 0-247)	317 (259-448) [28]	297 (255-365) [22]	483 (362-729)	0.141
C-reactive protein mg/mL (normal range 0-0.49)	7.63 (2.66-11.72) [32]	6.5 (2.55-11.25) [26]	11.7 (11.1-14.1)	0.097
Involvement on chest radiographs				
No involvement	1 (3%)	1 (3.7%)	0 (0%)	0.865
Ground-glass opacity	5 (15.2%)	4 (14.8%)	1 (16.7%)	
Bilateral lung patch shadow	25 (75.8%)	20 (74.1%)	5 (83.3%)	
Focal lesions	2 (6.1%)	2 (7.4%)	0 (0%)	

Data are expressed as mean \pm SD, median (IQR) or n (%).

p values indicate differences between out and in-patients. $P < .05$ was considered statistically significant.

Table 3. Demographic, underlying diseases and outcome of six patients admitted to Intensive Care Unit

Case no.	Gender	Age	Underlying disease	Home treatment	Days from hospital admission to ICU care	Length of stay in ICU (days)	Outcome
1	F	48	Friedreich's ataxia	No treatment	-	1	Death
2	M	37	Epilepsy, intellectual disability, obesity	clonazepam, carbamazepine, olanzapine	6	19	Death
3	M	47	Duodenal ulcer, obesity	Esomeprazole	2	10	Death
4	M	47	Depressive disorder, obesity	Alprazolam	0	39	Death
5	F	48	No disease	No treatment	1	27	Discharged
6	F	28	Blindness, epilepsy, hypothyroidism	sodium valproate, clobazam, topiramate, levothyroxine	0	9	Death

Table 4 Average score of SF36 components reported by 64 COVID-19 patients

	All patients (n=64)	Outpatients (n=49)	Inpatients (n=15)	p value
Physical functioning	74.3±25.48	76.22±25.34	68±25.76	0.277
Physical role	30.47±42.13	31.12±42.86	28.33±41.04	0.825
Bodily pain	54.34±30.39	51.88±28.50	62.40±35.80	0.244
General health	63.06±17.91	62.10±19.37	66.27±12.19	0.436
Vitality	48.44±23.20	47.65±21.22	51±29.47	0.629
Social functioning	45.12±29.52	43.62±27.85	50±35.04	0.468
Emotional role	46.87±45.50	45.57±45.99	51.11±45.19	0.684
Mental health	59.06±20.35	58.04±20.38	62.40±20.61	0.472
Physical component summary	49.87±24.25	55.32±23.48	56.25±23.15	0.894
Mental component summary	55.54±23.22	48.72±23.14	53.63±28.11	0.498

Figures

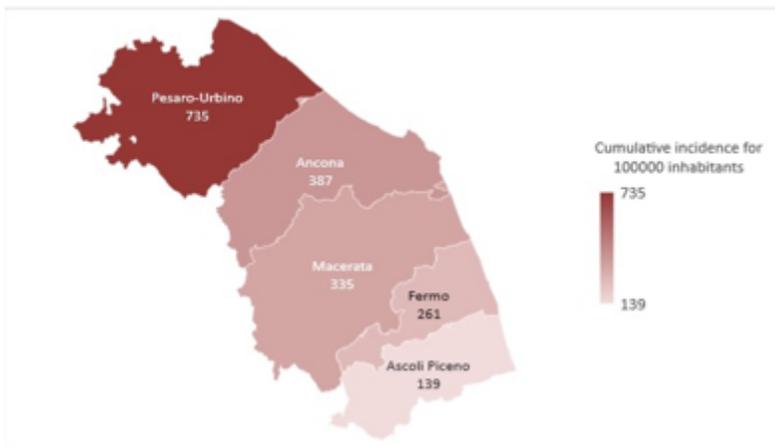
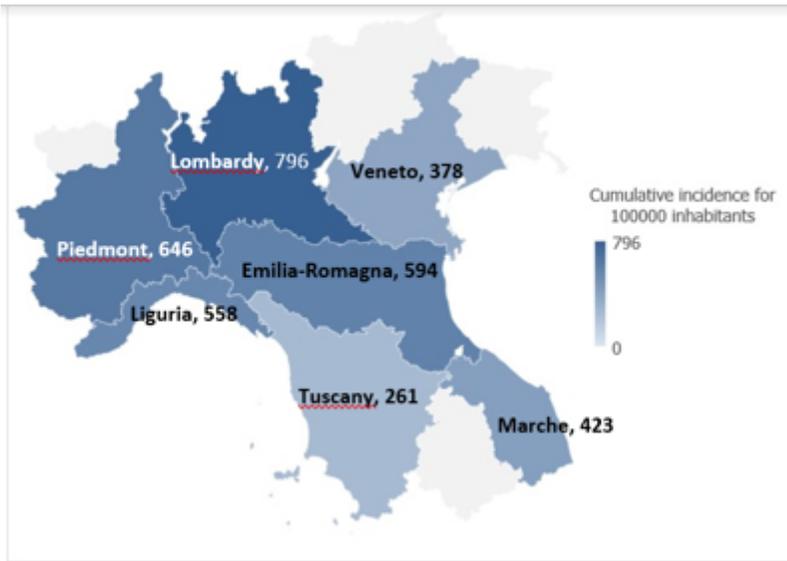


Figure 1

a. Distribution of Patients with Covid-19 from the seven Italian regions mainly involved in the pandemic. Shown are the official statistics of all documented, laboratory-confirmed cases of coronavirus disease 2019 (Covid-19) throughout Northern and Center Italy according to the Italian Civil Protection as of May 8, 2020. b. Distribution of Patients with Covid-19 across Marche region. Shown are the official statistics of all documented, laboratory-confirmed cases of coronavirus disease 2019 (Covid-19) throughout Marche according to the GORES (Operative Regional Group for Sanitary Emergencies) report as of May 8, 2020.