Overview of COVID-19 patients treated in University Hospital Split, Croatia - specifics related to patients age

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Abstract

Different aspects of the coronavirus disease 2019 (COVID-19) infection have been widely investigated since the onset of a pandemic in December 2019. Several studies investigated differences in disease development and presentation compared to patient characteristics. In this paper we present an overview of the first COVID-19 pandemic wave in Dalmatia, Croatia with specifics related to patients' age.

Demographic, clinical and radiological data from hospitalized COVID-19 positive patients in the Clinical Hospital Split over a three-month period were collected and analyzed. Subgrouping and additional analysis were performed: *Octogenarians vs Non-octogenarians*, and senior residence *vs* non-senior residence.

160 COVID-19 positive patients were enrolled. Of those, 61% were females. Median age was 78. More than a half of all patients were senior residents. No differences in final outcome were observed comparing specific medicament treatment. Among Octogenarians group, there were more asymptomatic cases, and higher mortality rate. Some differences in radiological presentation were also observed.

Senior COVID-19 positive patients are more often asymptomatic but with higher mortality rates. More attention should be paid to early detection on COVID-19 infection in the senior population.

Introduction

Since December 2019, when the dramatic public health threat novel coronavirus disease 2019 (COVID-19) started to spread worldwide,[1] many scientific papers covering different aspects of the disease were published. Currently, more than 66 million cases were confirmed, and more than 1.5 million people have died.[2]

According to the available data, Croatia is one country that had an appropriate response to the pandemic, with only 2269 confirmed cases and 107 deaths in *a first pandemic wave*. The Split-Dalmatia county was most heavily impacted, with 558 incidents and 33 deaths. The most dangerous *COVID-19 infiltration* occurred in three nursing homes, with a high incidence among tenants and mortality. However, the Croatian health care system was not congested with severe forms of disease in the first pandemic wave. Given so, both symptomatic and asymptomatic COVID-19 patients with some other chronic disease could be admitted to hospital for detailed monitoring and the most adequate health care.

In this paper, we present an overview of COVID-19 clinical presentation in patients treated at University Hospital Split with some findings which sheds new light in COVID-19 infection in elderly.

Materials and Methods

Study design

This is a retrospective observational (non-interventional) study approved by the Institutional Review board of the University Hospital Split. Given the retrospective nature of study, the need for written informed consent was waived.

According to World Health Organization (WHO) interim guidance, all hospitalized patients with COVID-19 were enrolled. The diagnosis was based on clinical symptoms, epidemiologic anamnesis and positive reverse-transcription polymerase chain reaction assay (RT-PCR).[3]

Data were retrieved from their hospital electronic records. Observed period was from March 23rd to May 20th which corresponds to *first epidemic wave* in Split's hospital. We collected the demographic data (age, sex, senior resident); presence of comorbidity, drug use, signs and symptoms at admission (fever, caught, dyspnea, *other* consisting of all other reported symptoms - diarrhea, nausea, loss of smell and taste, fatigue, sore throat, headache, nasal congestion, shivering, myalgic syndrome); body temperature (axillary measured), radiologic findings [chest X-ray and multi-slice computed tomography (MSCT)]; drug treatment and clinical outcome.

A sub analysis was performed to find differences related to the age of the patients. Two age groups were formed: *Octogenarians* (years 80+) and *Non-octogenarians*.

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Imaging diagnostic workup

A chest X-ray was performed on all patients admitted to the hospital. Data extracted included lung parenchymal consolidation, interstitial thickening, pleural effusion, signs of peri bronchial infiltration and data negative for pneumonia. Since chest radiography has been reported to have relatively low specificity,[4] chest X-ray was not repeated on a daily basis to all patients. Only patients with described changes on first chest X-ray exam, and those with clinical deterioration during hospital stay had repeated chest X-ray.

For several patients during their hospital stay chest MSCT scanning was performed to rule out clinically suspected intrathoracic complications such as pulmonary embolism, superimposed bacterial pneumonia, lung abscess or empyema.[3]

Statistical analysis

Pearson's χ^2 test was used for categorical parameters and Student's unpaired or paired *t*-tests were conducted to compare between-group and intra-group differences in the results.

To evaluate impact of different medicament treatments on final outcome (deceased *vs* recovered) frequency tables and χ^2 test were conducted. It was followed by Z test if positive correlation was observed.

Statistical analysis was performed using Statistica 8.0 software (StatSoft Inc., Tulsa, OK, USA), and a two-sided P value <0.05 was considered significant.

Data are presented as means ± standard deviation or number (percentage). Where appropriate, data were presented as median (25^{th}-75^{th} quartile range).

Results

The study enrolled a total number of 160 COVID-19 positive patients. Of those, 98 (60.87%) were females.

The median age of enrolled patients was 78 (Q1-Q3 64-85) while mean age ± standard deviation was 7218. The 82 (51.25%) patients were senior residents.

Regarding symptoms, 116 patients (72.5%) were symptomatic. The clinical presentations of the COVID-19 positive patients are listed in Table 1.

Average body temperature at admission was found to be 38.10.7 degrees of Celsius.

At admission, routine blood laboratory testing was performed to all patients. As expected for viral infection, average C-reactive protein value was elevated 7180.73, and leukocyte count was in reference interval 7.74.08. (Values are presented as mean ± standard deviation).

A total of 249 chest X-rays were performed, averaging 1.59 per patient. All patients had at least one chest X-ray examination. Of that, 66 patients (41.25%) had no radiologic evidence of pneumonia, while the rest of 94 patients (58.75%) had some abnormalities: lung parenchyma consolidation in 68 subjects (71.58%), pleural effusion in 20 subjects (21.05%), peri bronchial infiltration in 10 subjects (10.53%) and interstitial thickening in 27 subjects (28.42%) (Figure 1).

From total number of hospitalized patients, 129 (80.1%) were discharged and showed less frequent parenchymal consolidation, pleural effusion and interstitial thickening (P value: 0.01, <0.001, 0.005; χ^2 test) in comparison to those deceased in hospital 32 (19.9%). Regarding age, subgroup analysis was performed and results are presented in Table 2.

Patients classified as *Octogenarians* had statistically higher average body temperatures at reception in comparison with those classified as *Non-octogenarians*: 38.30.6 *vs* 37.80.64 (P value 0.002, Student's *t*-test).

18 MSCT examinations were performed: 11 chest, 4 abdominal and 3 brain MSCT scanning. Each chest MSCT had some abnormalities described: peripheral bilateral area of ground glass opacification in 6 patients, 9 patients had bilateral parenchymal consolidation, dominant in lower lobes, 4 patients had pleural effusion, for 1 patient crazy paving was described and 1 patient had spontaneous pneumothorax. Representative MSCT findings are presented in Figure 2.

Table 3 presents selected data of specific medicament COVID-19 treatment. Patients were treated in line with best available evidence.[5] No differences in final outcome were found when comparing different medicament treatments (Frequency tables and χ^2 test were done. P value is 0.474, DF 4. χ^2 test for trend - significance level P 0.252, DF 1).

Results of additional sub analysis comparing differences between patients who were senior residence and others are presented in Table 4.

Table 1. Clinical presentations of the COVID-19 positive patients.

Symptom	Number of symptomatic patients, N (%)
Fever	88 (75.86%)
Cough	63 (54.31%)
Shortness of breath	32 (27.59%)
Diarrhea and nausea	17 (14.66%)
Myalgia	15 (12.93%)
Chills	11 (9.48%)
Anosmia	7 (6.03%)
Headache	6 (5.17%)
Symptoms of urinary infection	6 (5.17%)
Sore throats and nasal congestion	5 (4.31%)
Vertigo	1 (0.86%)
Macular rash	1 (0.86%)

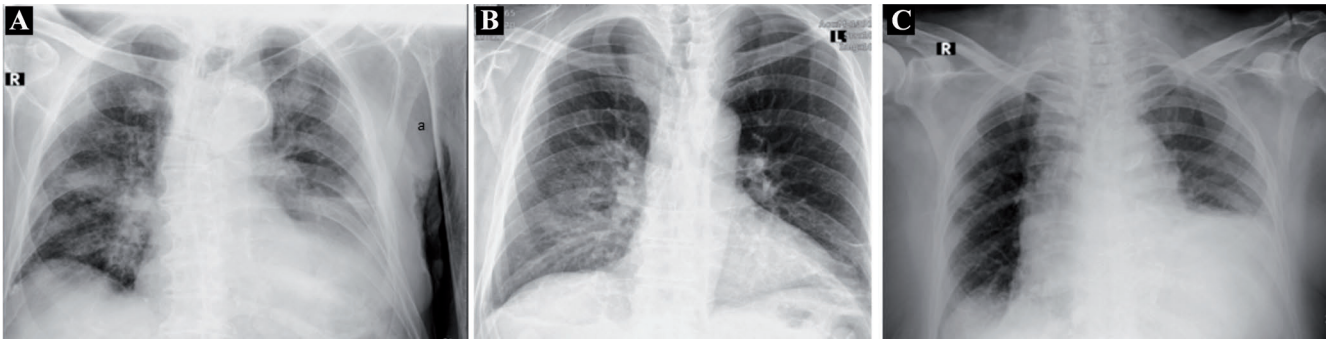

Figure 1. Representative chest X-rays. A) Peripheral parenchymal consolidation in right medial pulmonal field; B) right peri bronchial infiltration and interstitial thickening; C) pleural effusion left.

Discussion

Due to a well-controlled epidemiological situation in Split, Croatia during the first epidemic wave, detailed monitoring of all detected COVID-19 positives was conducted.

Following the initial occurrence of the virus in senior homes, spreading was comparatively low. All contacts of patients who tested positive for COVID-19 underwent further testing. Additionally, those who tested positive were admitted to hospital for adequate care, thus providing better insight of disease development within the population.

Of the total number of patients, more females were affected than males. Half of all patients were older than 79 years. However, demographically more females fall within this age group in Croatia.[6] Given so, this result was expected.

Almost three quarters of detected patients presented some symptoms. Previous reports suggested that the percentage of asymptomatic patients could be up to 45%.[7] However, we only tested those patients that were suspected COVID-19 cases due to clinical status; their contacts were tested at the end of a 14-day quarantine, unless symptoms were developed earlier. We did not test asymptomatic patients at the end of quarantine.

From our sample, 75% of patients had a

Figure 2. Representative chest multi-slice computed tomographic images. A) Ground glass opacifications (GGO), crazy paving, bilateral pleural effusion; B) GGO, parenchymal consolidation; C) right spontaneous pneumothorax and pneumomediastinum.

Table 2. Patient characteristics and clinical outcomes by subgroup analysis (<80 *vs* >80).

	<80	>80	P value*
Number of patients	83 (51.87)	77 (48.12)	-
Age (mean ± standard deviation)	60±11	87±5	-
Females	37 (44.58)	61 (79.22)	<0.001
Senior residence	18 (21.69)	64 (83.12)	<0.001
Symptoms at admission	71 (85.54)	44 (57.14)	<0.001
Fever	58 (69.88)	29 (37.66)	<0.001
Cough	41 (49.40)	21 (27.27)	0.004
Dyspnea	21 (25.3)	11 (14.29)	0.081
Radiologic abnormalities	45 (54.22)	50 (64.93)	0.168
Parenchymal consolidation	36 (43.37)	32 (42.56)	0.816
Pleural effusion	7 (8.43)	13 (16.88)	0.106
Peri bronchial infiltrate	6 (7.23)	4 (5.19)	0.595
Interstitial thickening	9 (10.84)	18 (23.38)	0.034
Deceased in hospital	10 (12.05)	22 (28.57)	0.009

*χ^2 test, values are presented as N (%).

Table 3. Clinical outcomes by treatment groups.

Therapy	Deceased	Recovered
Azithromycin, chronic and supportive therapy	6	12
Chloroquine, chronic and supportive therapy	5	26
Azithromycin and chloroquine, chronic and supportive therapy	7	19
Chronic and supportive therapy	15	71
Antiviral, chronic and supportive therapy	1	6
Total	33	127

Final data of conducted statistical analysis are reported in text.

Table 4. Patient characteristics and clinical outcomes by subgroup analysis (senior *vs* non-senior residence).

	Senior residence	Non-senior residence	P value*
Number of patients	82 (51.25)	78 (48.75)	-
Females	68 (82.93)	30 (38.46)	<0.001
Symptoms	42 (51.22)	73 (93.59)	<0.001
Fever	26 (31.71)	61 (78.21)	<0.001
Cough	18 (21.95)	44 (56.41)	<0.001
Dyspnea	12 (14.63)	20 (25.64)	0.082
Radiologic abnormalities	44 (53.66)	46 (58.97)	0.498
Parenchymal consolidation	27 (32.93)	41 (52.56)	0.012
Pleural effusion	13 (15.85)	7 (8.97)	0.188
Peri bronchial infiltrate	3 (3.66)	7 (8.97)	0.165
Interstitial thickening	14 (17.07)	13 (16.67)	0.945
Total number of deceased	20 (24.39)	12 (15.38)	0.155
Azithromycin in therapy	15 (18.29)	26 (33.33)	0.029
Chloroquine in therapy	22 (26.83)	33 (42.31)	0.039
Antiviral drugs in therapy	1 (1.22)	6 (7.69)	0.045

*χ^2 test, values are presented as N (%).

mild fever, a little above half were coughing, and less than a third felt dyspneic. This is in accordance with previous reports on the main COVID-19 symptoms.[8] Untypical presentation with gastrointestinal symptoms in almost 15% of patients was observed. Several studies already showed that nausea and diarrhea could be one of the symptoms during COVID-19 infection.[9-12] Other rare symptoms including vertigo,[13] and macular rash,[14] were also observed.

Following available radiologic guidelines, each patient's chest X-ray was done at the time of hospital admission.[15] 41% of patients displayed no evidence of pneumonia after analyzing radiograms. The remaining presented typical COVID-19 results including bilateral peripheral multifocal opacities or consolidation, lower lung zone predominant.[3]

During the hospital stay, several patients required MSCT scanning. Most scans were thoracic, which showed typical COVID-19 presentation with signs of ground glass opacifications, parenchymal consolidations, interstitial thickening and pleural effusion.[3] In 6 patients, signs of pulmonary embolism were found. All described goes in line with previously reported publications.[16,17] Cases of spontaneous pneumothorax were rarely described.[18-20]

Since there were not clear guidelines on medication therapy for treating COVID-19 patients, some differences in treatment were observed. All patients received chronic supportive therapy, as well as symptomatic therapy. Some patients were additionally treated with azithromycin, chloroquine or their combination and some received antiviral therapy (ritonavir). However, no differences in the outcome were found. This is also consistent with recent publications questioning successfulness of listed therapies which were previously described as potentially effectual.[21,22]

Given that half of patients were in their 80's and 90's, an additional analysis was performed to see possible specifics within this age group. As previously stated, most patients categorized as *Octogenarians* were females and lived in senior care facilities. Less than half experiences symptoms in comparison to those categorized as *Non-octogenarians*. Those with symptoms primarily experienced fever, with lower values compared to *Non-octogenarians*. This could be explained with *anergic* older organism and immune system which develop less tempestuous responses to infection.

All symptomatic patients from the *Octogenarians* group had abnormalities on chest radiograms. In comparison to the *Non-octogenarians* group, interstitial thickening was reported slightly less often. Isolated interstitial thickening is characteristic for mild viral pneumonia[23] and was more often presented in *Non-octogenarians*. *Octogenarians* with changes on radiograms had more often several associated radiographic lung changes such as consolidation and pleural effusion.

Finally, an additional analysis was performed to see differences within patients who were senior residents and the rest of the hospitalized COVID-19 positive patients (Table 4). Recommendation and instruction of the Croatian Institute of public Health was to hospitalize all positive patients who were senior residence (total of 82 subjects). Since all COVID-19 positive patients from senior facilities were hospitalized, it is expected that significant lower was the number of symptomatic cases. Patients who were not senior residence had more often fever and cough. Regarding to chest X-ray analysis, non-senior residence had more often signs of parenchymal consolidation, in line with more symptomatic cases. Comparing medicament treatment, senior residence received less often antiviral drugs, probably more often contraindicated. At the end, despite higher number of asymptomatic patients in senior residence group, mortality rate in this population was significant above the non-senior residence patients.

Conclusions

Our data support the general observation that COVID-19 infection is more fatal in senior patients with multiple comorbidities. As we shown here, in comparison with *Non-octogenarians, Octogenarians* were more often asymptomatic, with lower incidence of fever and caught, but with higher mortality rate. In a future, more attention should be pay to early detection of COVID-19 infection in senior population, including senior residence.

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