Clinical and laboratory characteristics of the COVID-19 disease in adult patients

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ORIGINAL ARTICLE

Abstract

BACKGROUND: In December 2019, a new coronavirus, SARS-CoV-2, appeared in Wuhan, China. This virus is the cause of the COVID-19 disease. This infection later spread to the whole world. The goal of this article is to present the clinical and laboratory characteristics of patients with COVID-19 treated in the Faculty Hospital Pilsen.

METHODS: In this monocentric, retrospective study, clinical and biochemical data of 89 adult patients with COVID-19 was analyzed. These patients were in the care of the Faculty Hospital Pilsen between March 14 and April 7.

RESULTS: In this cohort, made up of 89 patients, 63 were treated as outpatients and 26 were hospitalized. 10 patients required intensive care. The most common symptoms among patients were cough and fever. Dyspnea was present in 29 patients. A CT scan showed bilateral pneumonia in 23 of the admitted patients. Fever and bilateral pneumonia were significantly more common in patients ≥ 60 years old ($p=0.047$, and $p=0.001$, respectively). Of lab results, the patients in intensive care had significantly higher values of C-reactive protein, procalcitonin, lactate dehydrogenase, interleukin 6, myoglobin and ferritin.

CONCLUSION: The most common symptoms of COVID-19 are fever and cough. These two symptoms are simultaneously present in more than half the cases. Approximately 1/10th of patients requires intensive care. Higher values of lactate dehydrogenase, myoglobin and ferritin on patient admission appear to be a strong predictive factor of the patient's status progressing into requiring ICU attention.

INTRODUCTION

Coronaviruses are enveloped, single-strand RNA viruses belonging into the *Coronaviridae* family (Weiss *et al.* 2011). Until the discovery of the new SARS-CoV-2 virus, 6 CoV strains were known to cause disease in humans. (Su *et al.* 2016).

The most common coronaviruses, 229E, OC43, NL 63 and HKU1, cause only minor diseases with symptoms of the common cold (Cui *et al.* 2019). Severe respiratory diseases are caused by two strains of zoonotic origin, known as SARS-CoV and MERS-CoV, in which fatal disease course is more frequently described. (Zhong *et al.* 2003). In the SARS disease, mortality is reported around 10%, in MERS it

is as high as 35% (Yin *et al.* 2018; Song *et al.* 2019). Since December 2019, a growing number of pneumonia cases caused by a new coronavirus was being observed in the Chinese city of Wuhan, in the Hubei province. (Zhu *et al.* 2020). The first patients to be admitted to the hospital were epidemiologically tied to the Chua-nan market directly in Wuhan (Bogoch *et al.* 2020; Lu *et al.* 2020). The source of the disease was identified as the new coronavirus SARS-CoV-2. The virus spread rapidly, and at the end of January, cases were being reported from other Chinese cities and from several countries around the world (Munster *et al.* 2020).

It was found that SARS-CoV-2 enters the human cell by binding to the peptidase ACE2 (Xu *et al.* 2020), which is the binding site of the glycopeptide S. This is the trimeric glycopeptide which forms the spikes of the viral envelope. (Yan *et al.* 2020). Interhuman transmission was observed shortly after the disease was reported (Carlos *et al.* 2020; Zhu *et al.* 2020). The average incubation period was observed to be 5.2 days, and based on its distribution timeline, the maximal incubation period was declared to be 14 days (Li *et al.* 2020). Therefore the quarantine, when eventually implemented, was set to last 14 days. Deaths are observed particularly among elderly – this is probably due to a weaker immune system and higher likelihood of a more severe disease manifestation (Li *et al.* 2020; Wang *et al.* 2020). Death is most commonly observed in the range of 6 to 41 days from symptom onset, the median being 14 days (Li *et al.* 2020).

METHODS

This monocentric, retrospective study analyzes 89 adult patients, who were diagnosed with COVID-19 in the Faculty Hospital Pilsen between March 14, 2020 and April 7, 2020. The Faculty Hospital Pilsen is the largest hospital in the Pilsen region, which has approximately 585 thousand inhabitants. All the patients we approached agreed to be included and to have their data be used. Patients in outpatient care were consulted by telephone, respecting their mandatory home isolation. The patients treated in the hospital were consulted directly in the specialized ward they were staying in. A record about the interview was always included in the patients' medical documentation.

The laboratory values (leucocytes, C-reactive protein, procalcitonin, lactate dehydrogenase, interleukin 6, myoglobin and ferritin) were obtained from the hospital information system Medicalc4 (Medicalc software s.r.o., Pilsen, Czech Republic), and subsequently the values for the group being treated in a regular ward (n=16) and the ICU (n=10) were compared. Furthermore, the incidence of the major symptoms of COVID-19 (cough, fever, dyspnea and bilateral pneumonia) was analyzed in the group of patients ≤ 59 years old and in the group of patients ≥ 60 years old.

The statistical calculations were performed in the program STASTISTICA (version 11, TIBCO Company). To statistically process the data, the Shapiro-Wilk test of normality was used, and the two-sample t test was used in variables fulfilling the condition of normality. In the variables not fulfilling the condition of normality, the non-parametric two-sample Mann-Whitney U test was used. Values of $p < 0.05$ were considered significant.

RESULTS

The sample is made up of 89 patients over the age of 18; 46 of them are men (51.7%) and 43 are women (48.3%). The age median was 53.0 years. 52 patients were in the group ≤ 59 years (n = 52; 58.4%) and 37 patients were in the group ≥ 60 (n = 37; 41.6%). Patient history showed 20 (22.5%) patients had arterial hypertension, 15 (16.9%) patients were obese with a BMI over 30, 12 (13.5%) patients had type 2 diabetes mellitus, and 7 (7.9%) patients had ischemic heart disease (Table 1).

63 (70.7%) patients were treated as outpatients in home isolation. 26 (29.3%) patients required hospital admission, of which 16 (18%) patients were admitted

Tab. 1. Demographic and health characteristics of COVID-19 patients

	Patients (n = 89)
Age	
Average (SD)	51.4 (18.5)
Range	20-87
≤ 39	30 (33.7%)
40-49	9 (10.1%)
50-59	13 (14.6%)
60-69	23 (25.9%)
≥ 70	14 (15.7%)
Sex	
Women	43 (48.3%)
Men	46 (51.7%)
Chronic diseases	
High blood pressure	20 (22.5%)
Chronic ischemic hearth disease	7 (7.9%)
Bronchial asthma	8 (9%)
Chronic obstructive pulmonary disease	2 (2.2%)
Chronic kidney disease	4 (4.5%)
Diabetes mellitus	12 (13.5%)
Hypothyroidism	4 (4.5%)
Oncology disease	3 (3.4%)
Obesity	
Yes	15 (16.9%)
No	74 (83.1%)

Tab. 2. Overview of clinical symptoms of COVID-19 patients

	Total (n=89)	Outpatient (n=63)	Hospitalized (n=26)
Fever	66 (74.2%)	41 (65.1%)	25 (96.2%)
Cough	67 (75.3%)	50 (79.4%)	17 (65.4%)
Dyspnea	29 (32.6%)	17 (22.2%)	12 (46.2%)
Nasal congestion	8 (9%)	8 (12.7%)	0 (0%)
Hemoptysis	3 (3.4%)	2 (3.2%)	1 (3.8%)
Sore throat	5 (5.6%)	4 (6.3%)	1 (3.8%)
Headache	22 (24.7%)	15 (23.8%)	7 (26.9%)
Chest pain	4 (4.5%)	1 (1.6%)	3 (11.5%)
Arthralgia	22 (24.7%)	17 (22.2%)	5 (19.2%)
Myalgia	22 (24.7%)	16 (25.4%)	6 (23.1%)
Fatigue	20 (22.5%)	13 (20.6%)	7 (26.9%)
Weakness	38 (42.7%)	20 (31.7%)	18 (69.2%)
Anorexia	10 (11.2%)	4 (6.3%)	6 (23.1%)
Vomiting	4 (4.5%)	0 (0%)	4 (15.4%)
Diarrhea	14 (15.7%)	8 (12.7%)	6 (23.1%)
Anosmia	17 (19.1%)	16 (25.4%)	1 (3.8%)
Ageusia	8 (9%)	7 (11.1%)	1 (3.8%)
Fever + cough	49 (55.1%)	33 (52.4%)	16 (61.5%)
Fever + cough + dyspnea	21 (23.6%)	10 (15.9%)	11 (42.3%)

to the regular ward and 10 (11%) patients were admitted to the ICU. 16 (18%) patients were treated by oxygen therapy, 8 (9%) patients were connected to mechanical ventilation. 3 (3.4%) patients died. A CT scan was performed in all 26 patients admitted to the hospital. Bilateral pneumonia was confirmed in 23 hospitalized patients. Unilateral pneumonia was present in 3 patients. In the overall cohort of patients with COVID-19, cough was present in 67 (75.3%) of all patients. There was no observed significant difference in the incidence of cough between the groups of patients $\leq$ 59 years and $\geq$ 60 years ($p = 0.169$). Fever was present in 66 (74.2%) of all patients and significantly more often present in the group $\geq$ 60 years ($p = 0.047$). Fever was present in 25 (96.2%) of hospitalized patients. The simultaneous presence of cough and fever was observed in 49 (55.1%) of all patients. Dyspnea was present in 29 (32.6%) patients. There was no observed significant difference in the incidence of dyspnea between the patient groups $\leq$ 59 years and $\geq$ 60 years ($p = 0.260$). Bilateral pneumonia was diagnosed in 23 (25.8%) patients and was more frequently present in patients $\geq$ 60 years ($p = 0.001$) (Table 2).

The values of select laboratory parameters were compared between patients treated in the regular ward (group 0; n = 16) and patients in the ICU (group 1; n = 10). The median leucocyte count in group 0 was 6.95 x 109; in group 1, it was 7.15 x 109. However, this difference was not significant ($p = 0.202$) (Figure 1).

The median value of C-reactive protein in group 0 was 54.5 mg/L, and it was 139.0 mg/L in group 1. Significantly higher C-reactive protein values were recorded in the ICU group ($p = 0.003$) (Figure 2). The median value of procalcitonin in group 0 was 0,13 µg/L and in group 1 it was 0.89 µg/L. Significantly higher values were observed in patients admitted to the ICU ($p = 0.006$) (Figure 3). The median value for lactate dehydrogenase in group 0 was 4.56 µkat/L and it was 7.33 µkat/L in group 1. Significantly higher values of lactate dehydrogenase were observed in patients in the ICU group ($p = 0.000$) (Figure 4). The median value of interleukin 6 in group 0 was 25,15 ng/L, in group 1 it was 86.10 ng/L. Significantly higher values were observed in patients in the ICU ($p = 0.014$) (Figure 5). The median value of myoglobin in group 0 was 45.45 µg/L and it was 96.75 µg/L in group 1. Significantly higher values were present in patients admitted to the ICU ($p = 0.043$) (Figure 6). The median value of ferritin in group 0 was 405 µg/L, and in group 1 it was 1219 µg/L. Significantly higher values were observed in patients from the ICU group ($p = 0.000$) (Figure 7).

DISCUSSION

COVID-19 is a completely new disease and there still doesn't exist enough valid data regarding its epidemiological, clinical, laboratory and, most importantly, therapeutic characteristics. Considering
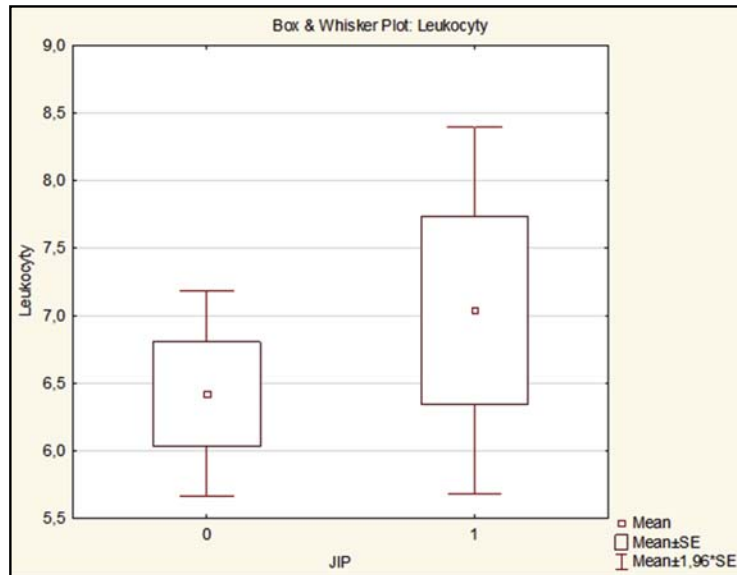
Fig. 1. The median leucocyte count in a regular hospital ward (group 0) was 6,95 x
109; in the ICU (group 1), it was 7,15 x109.

clinical symptoms, lots of shared characteristics with the previous SARS-CoV virus have been described (Huang *et al.* 2020). Some of the most common and important symptoms are fever, cough and fatigue (Carlos *et al.* 2020; Ren *et al.* 2020). In our sample, the most common symptom was cough, appearing in 75.3% of our patients. Some Chinese authors describe this symptom in 76–82% of all cases in the research they have published (Huang *et al.* 2020; Chen *et al.* 2020). The most common symptom in our study was not fever, contrary to our expectation – it was present in 74.2% patients. Most Chinese authors describe fever as the major symptom of the disease (Liu *et al.* 2020; Pan *et al.* 2020). One study done on 138 patients describes fever prevalence to be as high as 98.6% of all its cases (Wang *et al.* 2020).

A common symptom of ongoing pneumonia, regardless of cause, is dyspnea. In our sample, this symptom appeared in 32.6% of all patients. This observation is not in conflict with other authors, who usually note this symptom in approximately 31% of all cases (Chen *et al.* 2020; Wang *et al.* 2020). One study even found a prevalence as high as 55% (Huang *et al.* 2020). Fever, cough and dyspnea are also among the symptoms of other respiratory infectious diseases, often they are observed in the flu (Lam *et al.* 2016; Monto *et al.* 2000), and as such the differentiation between these two diseases, occurring during a flu epidemic and based solely on
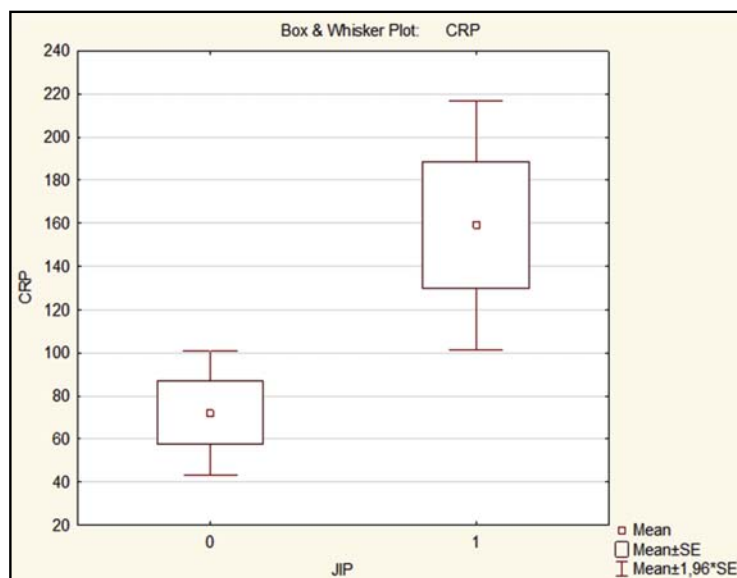

Fig. 2. The median value of C-reactive protein in a regular hospital ward (group 0) was
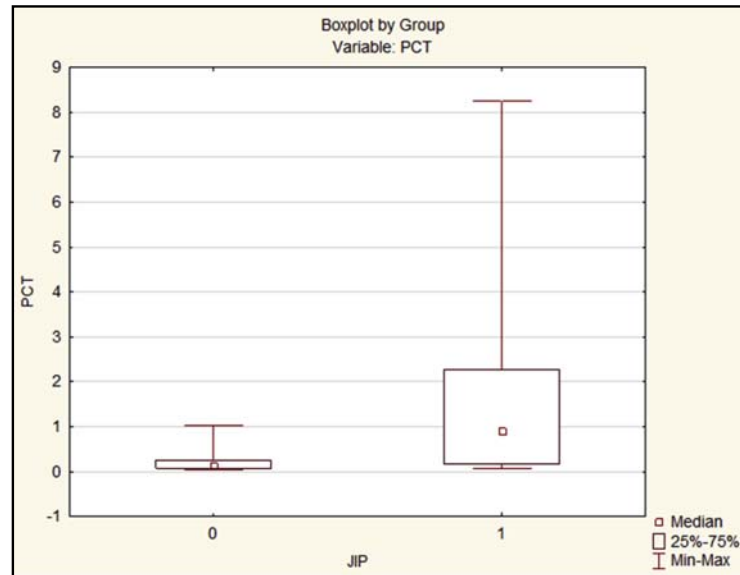54,5 mg/L; in the ICU (group 1), it was 139,0 mg/L.

Fig. 3. The median value of procalcitonin in a regular hospital ward (group 0) was 0,13 µg/L; in the ICU (group 1), it was 0,89 µg/L.

clinical presentation, can be a tough nut to crack. The presence of non-specific symptoms or a subclinical manifestation can significantly delay the diagnosis of the real disease (Song *et al.* 2020).

Headaches, muscle pain and arthralgia are all often present in respiratory infections including COVID-19. All 3 of these symptoms have been identified in 22% of our patients. Other studies present different findings. Headaches are often reported as being less common, between 6.5 and 8% (Huang *et al.* 2020; Wang *et al.* 2020). Muscle pain is described with a large variability of prevalence from 11% (Chen *et al.* 2020), to over 34.8% (Wang *et al.* 2020) up to 44% (Huang *et al.* 2020). The figure that we have arrived at falls within this broad range.

Regarding gastrointestinal symptoms, we observed diarrhea in 15.7% of our patients, and in 4.5% we also observed vomiting. The prevalence of diarrhea in our sample was larger than declared by studies of different authors, where we usually encounter this symptom in less than 10% of cases (Guan *et al.* 2020; Huang *et al.* 2020). Loss of appetite, and resulting decreased food intake, was experienced by 11.2% of our patients. In some patients, we observed also a decreased fluid intake and resulting dehydration.

Among newly observed neurological symptoms of the disease caused by SARS-CoV-2 were ageusia and anosmia (Russell *et al.* 2020). In a sample of 214 patients with a clinical manifestation of the disease, ageusia was
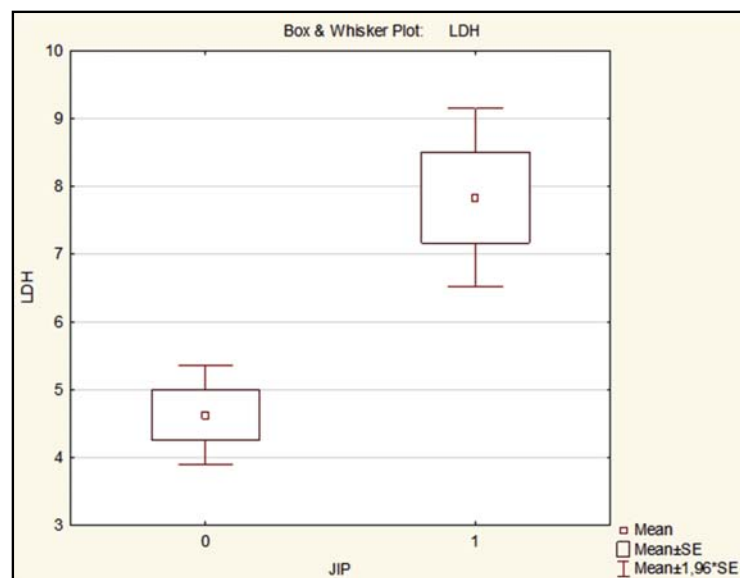

Fig. 4. The median value for lactate dehydrogenase in a regular hospital ward (group 0) was 4,56 µkat/L; in the ICU (group 1), it was 7,33 µkat/L.
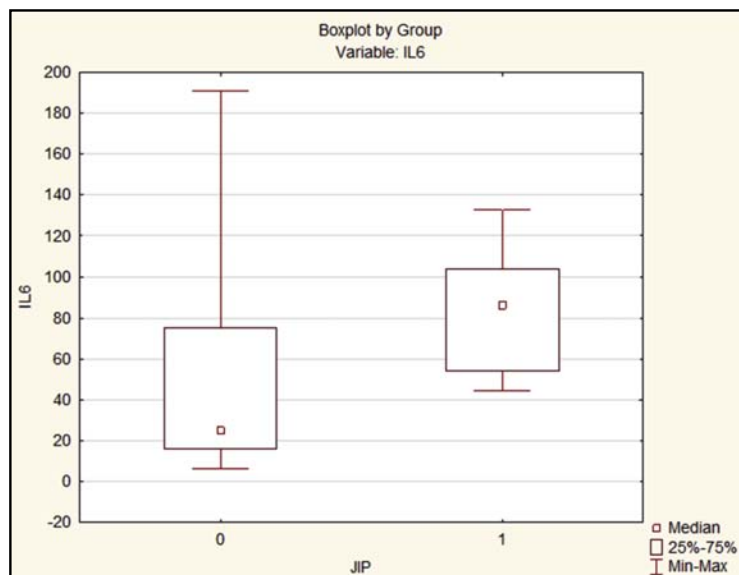
Fig. 5. The median value of interleukin 6 in a regular hospital ward (group 0) was 25,15 ng/L; in the ICU (group 1), it was 86,10 ng/L.

present in 5.6% of the cases and anosmia in 5.1% of the cases (Mao *et al.* 2020). In our cohort of patients, we recorded anosmia in 17% patients and ageusia in 9% of our patients. Usually, these symptoms were present in patients with a mild disease course, who were treated in home isolation.

Regarding laboratory findings, in the patients treated in a regular ward, the median value of C-reactive protein was 83.5 mg/L. In patients requiring intensive care, the median value of C-reactive protein was 139 mg/L. The increase of C-reactive protein values in patients requiring intensive care was caused by a more frequent presence of bacterial coinfection. In studies of other authors, lower average values of C-reactive protein

are reported (Chen *et al.* 2020; Guan *et al.* 2020). The median value of procalcitonin in patients treated in the regular ward was 0.17 µg/L and in patients requiring intensive care it was 0,89 µg/L. These values correspond with values reported by other authors (Chen *et al.* 2020; Huang *et al.* 2020). We also followed the median value of interleukin 6, a cytokine involved in the induction, growth and differentiation of the cells of the immune system (Qiu *et al.* 2013). Interleukin 6 plays a role in handling stress and depression (Kontoangelos *et al.* 2014), which could be significant in a disease as severe as COVID-19. In patients treated in the regular ward, we found the median value of interleukin 6 to be 58.7 µg/L, in the ICU patients it was 86.1 µg/L. The
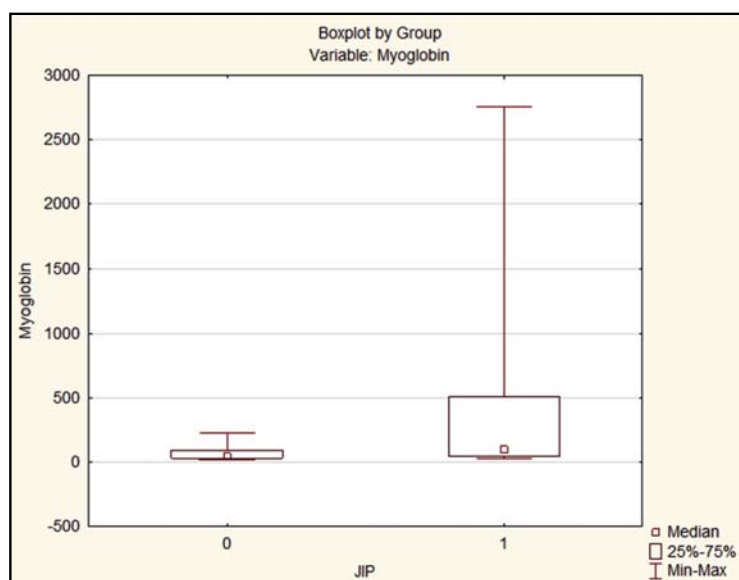

Fig. 6. The median value of myoglobin in a regular hospital ward (group 0) was 45,45 µg/L; in the ICU (group 1), it was 96,75 µg/L.
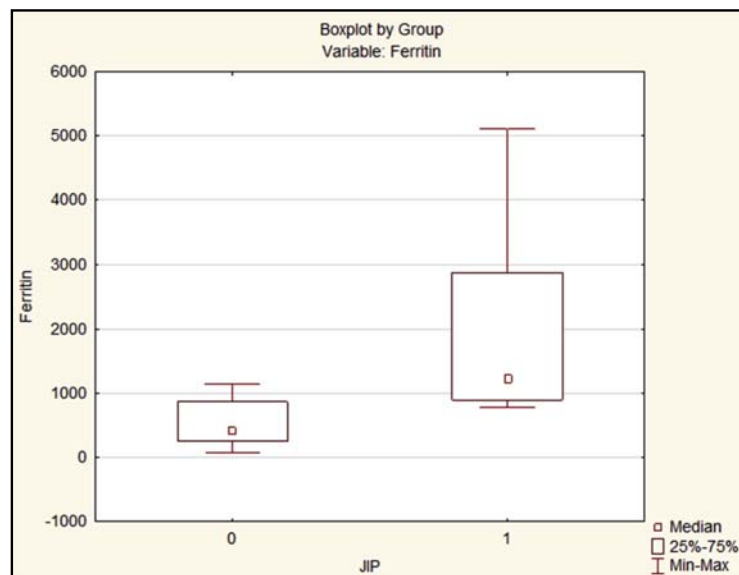
Fig. 7. The median value of ferritin in a regular hospital ward (group 0) was 405 µg/L; in the ICU (group 1), it was 1219 µg/L.

value of ferritin is a highly predictive factor of a more severe disease course requiring intensive care. In our cohort the median value of ferritin in patients treated in the regular ward was 858.5 µg/L and in the ICU group it was 1219 µg/L.

Our study is limited by a small sample of 89 COVID-19 adult patients. Data collection is ongoing in patients who are newly diagnosed and treated in our center. Regarding laboratory data, our goal is to find predictive parameters indicating that the patient will experience a severe course of the disease. We are currently also analyzing the values of vitamin D as a factor which positively affects the immune system (Grzechocinska *et al.* 2013). It is becoming more and more clear from various studies that the deficiency of this vitamin is connected to an increased risk and more severe course of respiratory infections in both children and adults (Gunville *et al.* 2013). In the COVID-19 patients admitted to our hospital, we have so far recorded vitamin D deficiency in most of the cases.

CONCLUSION

The new infectious disease COVID-19 is caused by the SARS-CoV-2 virus, which was first discovered in China at the end of 2019. The disease currently affects humans of all age categories all over the world. The most vulnerable group are people over 60. Among important risk factors are cardiovascular disease, diabetes and obesity. To combat the disease, it is essential to take preventative measures and to provide early treatment to the sick. Different countries of the world have taken very different approaches in implementing anti-epidemic measures. In most patients, the disease course is asymptomatic or with only mild symptoms. However,

approximately one tenth of patients require intensive care. Death is most often caused by acute respiratory distress syndrome and multiorgan failure.

ACKNOWLEDGMENTS

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