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A clinical profile and factors associated with severity of the disease among Polish patients hospitalized due to COVID-19 — an observational study

Abstract

Introduction: The coronavirus disease 2019 (COVID-19) is one of the greatest clinical challenges of the last decades. Clinical factors associated with severity of the disease remain unclear. The aim of the study was to characterize Polish patients hospitalized due to COVID-19 and to evaluate potential prognostic factors of severe course of the disease.

Material and methods: An observational study was conducted from March to July 2020 in the Pulmonology and Allergology Department of the University Hospital in Kraków, Poland. Consecutive patients with confirmed SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) infection were enrolled, and data about past medical history, signs and symptoms, laboratory results, imaging studies results, in-hospital management and outcomes was prospectively gathered.

Results: The study sample comprised 100 patients at the mean age of 59.2 (SD 16.1) years among whom 63 (63.0%) were male. Among them 10 (10.0%) died, 47 (47%) presented respiratory failure, 15 (15.0%) were transferred to the intensive care unit, 17 (17.0%) developed acute kidney injury, 7 (7.0%) had sepsis and 10 (10.0%) were diagnosed with pulmonary embolism. Multivariable analysis revealed age (OR 1.1; 95% CI 1.01–1.15), body mass index (BMI; OR 1.24; 95% CI 1.01–1.53), modified early warning score (MEWS; OR 3.95; 95% CI 1.48–12), the highest d-dimer value (OR 1.73; 95% CI 1.03–2.9) and lactate dehydrogenase (LDH; OR 1.16; 95% CI 1.03–1.3) to be associated with severe course of COVID-19.

Conclusion: This observational study showed that almost half of hospitalized patients with COVID-19 developed respiratory failure in the course of the disease. Increasing age, BMI, MEWS, d-dimer value and LDH concentration were associated with the severity of COVID-19.

Key words: clinical characteristics, coronavirus disease 2019, respiratory failure, risk factors, SARS-CoV-2

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Introduction

Clinical presentation of COVID-19 is highly variable and involves multiple organs, however, the respiratory system seems to be predominantly affected. There are several reports describing an increased incidence of injuries to the heart, kidneys, muscles, gastrointestinal tract and the

nervous system among COVID-19 patients [1–3]. Another significant factor influencing outcomes of persons infected with SARS-CoV-2 is an increased incidence of thromboembolic complications which is secondary to severe disturbances in coagulation and fibrinolysis as well as endothelial damage, sometimes referred to as COVID-19-associated coagulopathy [4, 5]. It is estimated that

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SARS-CoV-2 infection remains mildly symptomatic in about 80% of patients. However, approximately 15% of cases are severe, warranting hospitalization and the remaining 5% of patients are critically ill and require management in the intensive care unit (ICU) [6]. At the time of the study, only systemic glucocorticoids were recognized to reduce mortality in several randomized controlled trials [7].

The objective of this study was to characterize the first COVID-19 patients treated in the Pulmonology and Allergology Department of the University Hospital in Kraków, Poland in terms of patients' clinical, laboratory, diagnostic outcomes and factors associated with the severity of the disease.

Material and methods

Study design

This is an observational study conducted from March to July 2020 in the Pulmonology and Allergology Department, University Hospital in Kraków, Poland. The study was approved by the Ethics Committee of Jagiellonian University Medical College, Kraków, Poland (KBET 1072.6120.145.2020), and written informed consent was obtained from all participants.

Study sample and data collection

We enrolled all consecutive patients with SARS-CoV-2 infection confirmed using reverse transcription polymerase chain reaction, admitted to the Pulmonology and Allergology Department. We collected basic demographic (age, sex) and detailed clinical information about the patients (symptoms, comorbidities, medications, smoking status) based on the interviews and comprehensive analysis of medical records. In each patient, modified early warning score (MEWS) was calculated on admission. We recorded laboratory results on the day of admission, on the 2nd to 4th day of hospitalization and the 6th to 8th day of hospitalization as well as results of imaging studies (chest X-ray and computed tomography of the chest).

Outcomes

The patients were observed during the entire hospitalization in the University Hospital for the occurrence of the following outcomes: death, myocardial injury, myocardial infarction (both defined according to the Fourth Universal Definition of Myocardial Infarction [8]), stroke (defined as a new focal neurological deficit with

signs and symptoms lasting more than 24 hours), acute kidney injury (AKI, diagnosed according to the Kidney Disease Improving Global Outcomes definition) [9], sepsis, septic shock (both defined according to the 2016 Surviving Sepsis Campaign International Guidelines for Management of Sepsis and Septic Shock) [10], pulmonary embolism (diagnosed with computed tomography pulmonary angiogram) as well as transfer to the ICU and a need for mechanical ventilation.

Statistical analysis

Categorical variables were presented as numbers (percentages), whereas continuous variables were reported as medians (interquartile range) or means (standard deviation) depending on variable distribution. Associations of quantitative data were analyzed with Student t test and with the nonparametric Mann–Whitney U test. To assess the association between selected factors and a severe course of the disease (defined as necessity to administer oxygen therapy), a multivariable logistic regression model was created. The variables for the model (age, sex, the highest d-dimer value during hospitalization, MEWS on admission, baseline LDH concentration) were selected based on the available evidence. The model was validated using the Hosmer-Lemeshow test. This was a complete-case analysis. After application of Bonferroni correction due to multiple testing, a p-value < 0.00062 was considered statistically significant. Statistical analysis was performed with STATISTICA software (Statsoft, Tulsa, USA).

Results

Baseline characteristics

The study group consisted of 100 patients with the mean age of 59.2 (SD 16.1) years among whom 63 (63.0%) were male. The most common comorbidities were hypertension (49.0%), obesity (31.0%) and dyslipidemia (19.0%). Twenty-seven patients (27.0%) had history of smoking. The most commonly used medications were β -blockers (35.0%), diuretics (24.0%), ACE inhibitors and statins (both 19.0%). Detailed demographic and clinical characteristics are presented in Table 1.

Signs and symptoms

The most common symptoms described by the patients on admission were fever (73.0%), cough (67.0%) and dyspnea (44.0%). Additionally, diarrhea and dysgeusia or dysosmia were reported by 29 (29.0%) and 15 (15.0%) patients, respectively. The median time from the onset of symptoms

Table 1. Baseline characteristics

Characteristic	Total (n = 100)
Demographic	
Age [years], mean (SD)	59.2 (16.1)
Sex, male	63 (63.0%)
Smoking	27 (27.0%)
Symptoms	
Time from first symptoms to positive swab [days]	5.0 (1.0–7.0)
Time from first symptoms to admission [days]	7.0 (3.0–9.0)
Fever prior to admission	73 (73.0%)
Sore throat	16 (16.0%)
Dyspnea	44 (44.0%)
Pleuritic chest pain	13 (13.0%)
Ischemic chest pain	0 (0.0%)
Hemoptysis	1 (1.0%)
Cough	67 (67.0%)
Myalgia	27 (27.0%)
Syncope	2 (2.0%)
Diarrhea	29 (29.0%)
Dysgeusia or dysosmia	15 (15.0%)
Measurements & vital signs on admission	
Resting baseline SpO ₂ on admission [%]	95.0 (93.0–96.0)
BMI [kg/m ²]	27.7 (25.2–30.8)
Systolic blood pressure on admission [mm Hg]	130.0 (123.5–145.5)
Diastolic blood pressure on admission [mm Hg]	82.5 (77.0–90.0)
Heart rate on admission [beats/minute]	86.5 (77.0–95.5)
Respiratory rate on admission [breaths/minute]	16.0 (14.0–20.0)
Fever on admission	3 (3.0%)
MEWS on admission	1.0 (0.0–2.0)
Comorbidities	
Hypertension	49 (49.0%)
Atrial fibrillation	9 (9.0%)
Chronic heart failure	11 (11.0%)
Coronary artery disease	15 (15.0%)
History of myocardial infarction	9 (9.0%)
History of stroke	3 (3.0%)
Peripheral artery disease	3 (3.0%)
Dyslipidemia	19 (19.0%)
Hyperthyroidism	0 (0.0%)
Hypothyroidism	9 (9.0%)
Diabetes mellitus	16 (16.0%)
Obesity	31 (31.0%)
Chronic kidney disease	6 (6.0%)
Asthma	10 (10.0%)
COPD	7 (7.0%)

Table 1. cont. Baseline characteristics

Active neoplastic disease	6 (6.0%)
History of DVT/PE	7 (7.0%)
Medications	
Acetylsalicylic acid	14 (14.0%)
Oral anticoagulants	3 (3.0%)
Direct oral anticoagulants	4 (4.0%)
β-blockers	35 (35.0%)
ACE-I	19 (19.0%)
ARB	16 (16.0%)
Calcium channel blockers	15 (15.0%)
Statins	19 (19.0%)
Diuretics	24 (24.0%)
Insulin	5 (5.0%)

Data is presented as n [%] for categorical variables and median (interquartile range) unless otherwise specified. ACE-I — angiotensin converting enzyme inhibitors; ARB — angiotensin receptor blockers; BMI — body mass index; COPD — chronic obstructive pulmonary disease; DVT/PE — deep vein thrombosis/pulmonary embolism; MEWS — modified early warning score; SD — standard deviation

to admission to the hospital was 7.0 (IQR 3.0–9.0) days. Hypotension (defined as systolic blood pressure < 90 mm Hg), tachycardia (defined as heart rate > 100/min) and tachypnea (defined as respiratory rate > 20 breaths/min) were observed on admission in 0 (0.0%), 11 (11.0%) and 23 (23.0%) patients, respectively. The median MEWS on admission was 1.0 (IQR 0.0–2.0) point.

Laboratory results

Complete blood count most often revealed lymphopenia (35/100, 35.0%), while thrombocytopenia was present in 17 patients (17.0%). Coagulation tests commonly showed an increased concentration of fibrinogen (50/59, 84.7%), d-dimer (53/84, 63.1%) and prolonged APTT (16/89, 18.3%). Renal function, reflected by estimated glomerular filtration rate (eGFR), was normal in the majority of patients (82/100, 82.0%). Serum concentrations of liver enzymes were commonly elevated, i.e. alanine aminotransferase (ALT; 45/100, 45.0%), aspartate aminotransferase (AST; 48/91, 52.7%) and gamma-glutamyl transpeptidase (GGTP; 53/74, 71.6%). The majority of patients had elevated level of lactate dehydrogenase (LDH; 78/96, 81.3%). Among markers of inflammation we observed elevation of C-reactive protein (CRP), procalcitonin (PCT) and interleukin 6 (IL-6) in 79/100 (79.0%), 29/96 (30.2%) and 39/71 (54.9%) patients, respectively. Medians with IQR as well as proportions of patients with abnormalities in laboratory results are summarized in Table 2.

Imaging studies

Chest X-ray was performed in 99 patients (99.0%). There were no discernible pathological findings in 22 cases (22.0%). Interstitial infiltrates and consolidations were described in 22 (22.0%) and 19 patients (19.0%), respectively. The coexistence of interstitial infiltrates and consolidations was reported in 35 patients (35.0%). One subject had extensive neoplastic changes, which made chest X-ray analysis impossible.

Computed tomography was performed in 45 patients (45.0%) — computed tomography pulmonary angiogram in 43 cases and high-resolution computed tomography in 2 cases. Among patients with available CT results, ground-glass opacities were described in 38 cases (84.4%), consolidations were found in 29 patients (64.4%), and pleural fluid was detected in 11 individuals (24.4%).

Management

Low-molecular-weight heparin (LMWH) was administered in 90 patients (90.0%) with the maximal administered dose being prophylactic in 39 patients (39.0%), intermediate in 28 subjects (28.0%) and therapeutic in 23 patients (23.0%). The majority of patients (69/100, 69.0%) received antibiotics while chloroquine and ritonavir/lopinavir were administered in 36 (36.0%) and 2 (2.0%) individuals, respectively. Oxygen therapy was used in 47 patients (47.0%) during hospitalization, with the median maximal FiO₂ accounting for 50.0% (IQR 28.0–90.0).

Table 2. Baseline laboratory tests results

Parameter	Value; median (IQR)	Patients with abnormal values; n(%)
White blood count [$\times 10^3/\text{mm}^3$]	5.95 (4.56–7.59)	Leukopenia: 19/100 (19.0%) Leukocytosis: 11/100 (11.0%)
Neutrophils, count [$\times 10^3/\text{mm}^3$]	3.96 (2.69–5.69)	Neutropenia: 4/100 (4.0%)
Lymphocytes, count [$\times 10^3/\text{mm}^3$]	1.12 (0.88–1.50)	Lymphopenia: 35/100 (35.0%)
Hemoglobin [g/dl]	13.8 (12.7–14.8)	Anaemia: 18/100 (18.0%)
Platelets [$\times 10^3/\text{mm}^3$]	197.5 (159.5–257.0)	Thrombocytopenia: 17/100 (17.0%)
D-dimer on admission [mg/L]	0.84 (0.47–1.42)	Elevation: 53/84 (63.1%)
Highest d-dimer [mg/L]	1.20 (0.74–2.44)	Elevation: 67/81 (82.7%)
Fibrinogen [g/L]	4.7 (3.7–5.9)	Elevation: 50/59 (84.7%)
APTT [s]	31.9 (28.7–35.1)	Prolongation: 16/89 (18.3%)
INR	0.95 (0.90–1.02)	Elevation: 4/98 (4.1%)
eGFR [mL/min/1.73 m ²]	87.0 (66.9–104.7)	Decreased: 18/100 (18.0%)
Urea [mmol/L]	5.3 (3.8–6.9)	Elevation: 17/99 (17.2%)
Glucose [mmol/L]	5.7 (5.2–7.0)	Elevation: 48/93 (51.8%)
ALT [U/L]	31.5 (20.5–61.0)	Elevation: 45/100 (45.0%)
AST [U/L]	37.0 (27.0–56.0)	Elevation: 48/91 (52.7%)
Bilirubin [$\mu\text{mol/L}$]	7.3 (5.7–9.0)	Elevation: 0/85 (0.0%)
GGTP [U/L]	49.0 (26.0–107.0)	Elevation: 53/74 (71.6%)
Myoglobin [$\mu\text{g/L}$]	72.2 (42.9–118.2)	Elevation: 21/70 (30.0%)
Creatine kinase [U/L]	114.0 (64.0–189.0)	Elevation: 22/90 (24.4%)
Ferritin [$\mu\text{g/L}$]	400.0 (223.0–949.0)	Elevation: 35/71 (49.3%)
Lactate dehydrogenase [U/L]	270.0 (224.5–361.0)	Elevation: 78/96 (81.3%)
NT-proBNP [pg/mL]	186.0 (69.0–1061.0)	Elevation: 38/71 (53.5%)
Troponin I [ng/L]	5.3 (2.5–14.4)	Elevation: 7/80 (8.8%)
C-reactive protein [mg/L]	37.0 (9.8–91.0)	Elevation: 79/100 (79.0%)
Procalcitonin [ng/mL]	0.04 (0.02–0.11)	Elevation: 29/96 (30.2%)
Interleukin-6 [pg/mL]	19.1 (1.5–52.6)	Elevation: 39/71 (54.9%)

ALT — alanine transferase; APTT — activated partial thromboplastin time; AST — aspartate aminotransferase; eGFR — estimated glomerular filtration rate; GGTP — gamma-glutamyl transpeptidase; INR — international normalized ratio; NT-proBNP — N-terminal pro brain natriuretic peptide

Outcomes

Among 100 enrolled patients, 10 (10.0%) died, 47 (47.0%) developed respiratory failure, 15 (15.0%) were transferred to the ICU, 17 (17.0%) presented AKI, 7 (7.0%) had sepsis, and 10 (10.0%) were diagnosed with pulmonary embolism. The median time of hospitalization was 19.5 days (IQR 14.0–31.5) while median time of ICU stay accounted for 12.0 (IQR 6.0–19.0) days. The majority of patients (52/100, 52.0%) were discharged with positive result of nasal swab for SARS-CoV-2 and were isolated at home. The median time to viral clearance among 81 subjects with available negative result was 31.0 (IQR 20.0–37.0) days. Details concerning management and outcomes are summarized in Table 3.

Factors associated with severity of the disease — the univariable analysis

Patients with severe COVID-19 had a higher MEWS on admission and more often presented with dyspnea. Moreover, in terms of laboratory results, COVID-19 patients requiring oxygen therapy were characterized by a higher white blood cell and neutrophil count, lower lymphocyte count, higher d-dimer levels as well as higher concentrations of inflammatory markers, liver damage enzymes, LDH, myoglobin, NT-proBNP and troponin. Treatment differences between these groups included more frequent administration of antibiotics and chloroquine. Detailed information about between-group differences are summarized in Table 4. A complete comparison

Table 3. Treatment and outcomes

Treatment	Number of patients; n [%]
Treatment	
Prophylactic LMWH	39 (39.0%)
Intermediate dose LMWH	28 (28.0%)
Therapeutic dose LMWH	23 (23.0%)
Direct oral anticoagulants	11 (11.0%)
Antibiotics	69 (69.0%)
Chloroquine	36 (36.0%)
Ritonavir/lopinavir	2 (2.0%)
Oxygen therapy on admission	33 (33.0%)
FiO ₂ on admission	36.0 (28.0–40.0)
Oxygen therapy anytime during hospitalization	47 (47.0%)
Highest FiO ₂ during hospitalisation	5.0 (28.0–90.0%)
Outcomes	
Mortality	10 (10.0%)
Mechanical ventilation	8 (8.0%)
Transfer to the ICU	15 (15.0%)
Pulmonary embolism	10 (10.0%)
Myocardial injury	7 (7.0%)
Myocardial infarction	1 (1.0%)
Stroke	0 (0.0%)
Acute kidney injury	17 (17.0%)
Sepsis	7 (7.0%)
Septic shock	6 (6.0%)
Length of hospitalisation [days]	19.5 (14.0–31.5)
Length of ICU stay [days]	12.0 (6.0–19.0)
Positive swab at discharge	52 (52.0%)
Time to negative swab [days] (n = 81)	31.0 (20.0–37.0)

ICU — intensive care unit; LMWH — low molecular weight heparin

of demographic, clinical, laboratory data can be found in Supplementary Tables 1–3.

Factors associated with severity of the disease — the multivariable analysis

Multivariable analysis revealed that severe course of COVID-19 is associated with increased age (OR 1.10; 95% CI 1.01–1.15), BMI (OR 1.24; 95% CI 1.01–1.53), MEWS on admission (OR 3.95; 95% CI 1.48–12.0), the highest d-dimer value during hospitalization (OR 1.73; 95% CI 1.03–2.90) and baseline LDH concentration (OR 1.16; 95% CI 1.03–1.30). The validation of the model was performed using the Hosmer and Lemeshow

goodness of fit test ($X^2 = 18.12$, $p = 0.02$). Logistic regression results are summarized in Figure 1 and Supplementary Table 4.

Discussion

To our knowledge, this is one of the first manuscripts describing a prospective cohort of Polish COVID-19 patients, and we believe that it may be useful for local clinicians involved in the care of patients with SARS-CoV-2.

The presented study cohort consisted predominantly of males and the mean age amounted to 59.2 years, which confirms the results of several previous studies reporting higher representation of males in hospitalized patients [1, 2, 11, 12]. Elderly persons with COVID-19 are characterized by a high case fatality ratio and symptomatic infection rate [13, 14]. In a Chinese modeling study, the rate of hospitalization due to COVID-19 increased with age, ranging from 1% for patients aged 20 to 29 years, through 8% for those aged 50 to 59 years, up to 18% for individuals older than 80 years [15]. Underlying medical comorbidities are considered important risk factors for severe COVID-19 course and mortality. The most common comorbidities in the presented cohort were hypertension (49%), obesity (31%) and dyslipidemia (19%), which is comparable to several large studies from the United States and China. Upon initial presentation, COVID-19 symptoms are typically consistent with pneumonia [3, 16–18]. The majority of patients in this case series were hospitalized due to a cluster of flu-like symptoms, i.e. fever (73.0%), cough (67.0%) and dyspnea (44.0%). Additionally, we observed a significant representation of gastrointestinal symptoms as well as other typical COVID-19 symptoms, i.e. loss of smell or taste, which was present in 15% of cases. In a report published by the Centers for Disease Control and Prevention, the described symptoms of COVID-19 included: cough (50%), fever > 38°C (43%), myalgia (36%), headache (34%), dyspnea (29%), sore throat (20%), diarrhea (19%), nausea/vomiting (12%), loss of smell or taste, abdominal pain, and rhinorrhea in fewer than 10 percent each [19].

A number of observational studies involving COVID-19 patients revealed a unique pattern of laboratory changes, encompassing hemostatic derangements and pronounced hyperinflammatory state. First, there are numerous reports about significant coagulation abnormalities, including increased concentrations of fibrinogen and d-dimer as well as relatively common prolongation

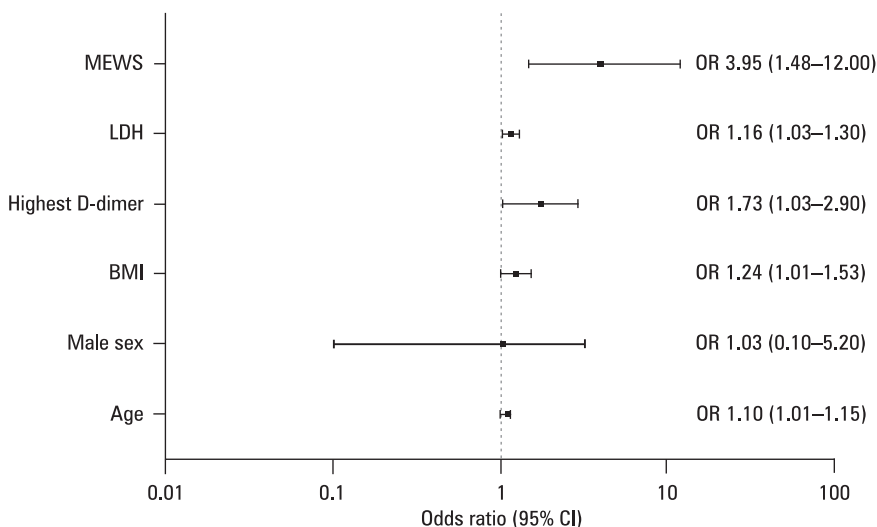


Figure 1. Summary of multivariable regression results. Dots and whiskers represent odds ratios with 95% confidence intervals. BMI — body mass index; LDH — lactate dehydrogenase; MEWS — modified early warning score; OR — odds ratio

of coagulation times. Coagulation tests in the presented cohort showed an increased concentration of fibrinogen and d-dimer in the majority of patients and prolonged APTT in nearly 20% of cases. Another frequently described laboratory anomaly is thrombocytopenia, which was present in 17% of the study group and in 5.0 to 41.7% of patients in the previous reports. According to the studies, utilizing global coagulation tests (rotational thromboelastometry, thrombography) COVID-19-associated coagulopathy represents severe hypercoagulability, which most probably is consistent neither with disseminated intravascular coagulation nor consumptive coagulopathy. Importantly, both abnormalities in coagulation tests and thrombocytopenia seem to be associated with disease severity and mortality [20]. Second, the majority of patients in the current study had laboratory findings suggestive of an exuberant inflammatory response reflected by markedly elevated concentrations of CRP, PCT, ferritin and IL-6. These observations are in line with some previous reports suggesting significant role of hyperinflammatory state with cytokine release syndrome in the pathogenesis of COVID-19 and its association with critical and fatal illness [1, 21]. Finally, recent data suggests that liver injury is quite common among patients with COVID-19 [22]. This was also observed in the current study cohort – serum concentrations of liver enzymes (ALT, AST, GGTP) and cellular damage markers (LDH) were frequently elevated. Importantly, according to the recent meta-analysis, liver injury seems to be more prevalent in severe cases of COVID-19 [23].

Radiological findings may vary depending on disease stage, patients age, immunity status and comorbidities [24]. Normal chest radiographs or CT are found in only 18% of patients with mild disease and this proportion drops to 3% in severely ill patients. Typical CT findings in COVID-19 include bilateral, multilobar ground glass opacities with a peripheral or posterior distribution, mainly in the lower lobes, while consolidation at the initial imaging are less common (more frequent in elderly people). Moreover, pleural effusion is an uncommon but a possible finding, sometimes accompanying the disease progression [25]. In the presented study, chest radiographs were performed in nearly all patients upon admission to the hospital and similarly to data presented above, were normal in 23.9% of cases, while the remaining patients presented interstitial infiltrates, consolidations or both. Important strength of this study is high availability of CT scans which were performed in almost half of the studied patients and most commonly showed ground glass opacities followed by consolidations and presence of fluid in the pleural space.

The frequency of reported complications in COVID-19 is strongly dependent on the studied population and disease severity. The most commonly observed organ involvement in patients with severe COVID-19 is lung injury manifested by acute respiratory failure. In this study, almost half of the studied cohort developed respiratory insufficiency, and 15% of patients were transferred to the ICU due to severe respiratory failure among whom more than a half required endotra-

Table 4. Comparison of selected variables between patients with severe and non-severe COVID-19

Characteristic	Severe cases (n = 47)	Non-severe cases (n = 53)	P-value
Demographic			
Age [years], mean (SD)	62.3 (15.9)	56.5 (15.8)	0.07
Sex, male	30 (63.8%)	33 (62.3%)	0.87
Symptoms			
Dyspnea	32 (68.1%)	12 (22.6%)	< 0.0001
Measurements and vital signs on admission			
BMI [kg/m ²]	28.4 (26.1–32.1)	26.8 (24.9–28.6)	0.009
Heart rate on admission	90.0 (80.0–100.0)	82.0 (71.0–91.0)	0.007
Respiratory rate on admission	20.0 (17.0–22.0)	15.0 (14.0–16.0)	< 0.0001
MEWS on admission	2.0 (1.0–2.0)	0.0 (0.0–1.0)	< 0.0001
Comorbidities			
Hypertension	29 (61.7%)	20 (38.5%)	0.02
Chronic heart failure	10 (21.3%)	1 (1.9%)	0.003
Laboratory results			
White blood count [$\times 10^3/\text{mm}^3$]	6.86 (5.70–9.83)	5.20 (3.87–6.58)	< 0.0001
Neutrophils, count [$\times 10^3/\text{uL}$]	5.34 (3.92–8.15)	3.02 (2.03–4.01)	< 0.0001
Lymphocytes, count [$\times 10^3/\text{uL}$]	1.00 (0.64–1.20)	1.38 (1.09–1.65)	< 0.0001
D-dimer on admission [mg/L]	1.10 (0.74–2.08)	0.54 (0.35–1.07)	< 0.0001
Highest d-dimer [mg/L]	2.20 (0.96–5.15)	0.91 (0.55–1.43)	< 0.0001
APTT [s]	33.9 (30.2–38.2)	30.8 (27.8–33.1)	0.02
AST [U/L]	46.0 (35.0–68.0)	31 (24.0–41.5)	0.0003
GGTP [U/L]	72.5 (31.0–174.0)	40.0 (23.0–59.0)	0.003
Myoglobin [$\mu\text{g/L}$]	115.5 (66.4–175.5)	57.9 (38.6–77.9)	< 0.0001
Ferritin [$\mu\text{g/L}$]	681.0 (379.0–1280.0)	308.0 (145.0–529.0)	0.0004
Lactate dehydrogenase [U/L]	354.0 (284.0–456.0)	232.0 (201.0–275.0)	< 0.0001
NT-proBNP [pg/mL]	482.5 (134.0–2084.0)	93.0 (35.0–321.0)	< 0.0001
Troponin I [ng/L]	12.7 (4.3–29.4)	3.7 (2.5–7.8)	0.0002
C-reactive protein [mg/L]	85.5 (34.5–170.0)	12.1 (2.3–48.2)	< 0.0001
Procalcitonin [ng/mL]	0.10 (0.04–0.20)	0.02 (0.02–0.04)	< 0.0001
Interleukin-6 [pg/mL]	29.3 (19.1–78.0)	1.5 (1.5–21.2)	< 0.0001
Treatment			
Antibiotics	45 (95.7%)	24 (45.3%)	< 0.0001
Chloroquine	25 (53.2%)	11 (20.8%)	< 0.0001
Outcomes			
Pulmonary embolism	8 (17.0%)	2 (3.8%)	0.04
Acute kidney injury	13 (27.7%)	4 (7.6%)	0.014
Positive swab at discharge	19 (42.2%)	33 (62.3%)	0.047

Data is presented as n [%] for categorical variables and median (interquartile range) unless otherwise specified. ALT — alanine transferase; AST — aspartate aminotransferase; BMI — body mass index; GGTP — gamma-glutamyl transpeptidase; MEWS — Modified Early Warning Score; NT-proBNP — N-terminal pro brain natriuretic peptide; SD — standard deviation. The $p < 0.00062$ is considered significant

cheal intubation and mechanical ventilation. In the previous studies from the USA, 12–24% of hospitalized patients required mechanical ventilation [3, 17]. In a nationwide cross-sectional study performed in China including approximately 44,500 cases, one in twenty patients was categorized as critically ill (i.e. with respiratory failure, shock, or multiorgan dysfunction) [6]. Importantly, thromboembolic complications are markers of severe COVID-19 and are associated with multiorgan failure and increased mortality [26]. The evidence to date supports the concept that the thrombotic manifestations of severe COVID-19 are due to the ability of SARS-CoV-2 to invade endothelial cells via ACE-2 (angiotensin-converting enzyme 2). Ten percent of patients in our cohort were diagnosed with pulmonary embolism despite the fact that LMWH was administered in 90% of the analyzed cases. Depending on the population and type of study (retrospective vs prospective with active screening for venous thromboembolism), the incidence of thromboembolic complications ranges from 3.9% to 79.4% in the ICU patients and from 1.3 to 14.7% among non-critically ill patients [27]. Kidney involvement in COVID-19 is frequent, with clinical presentation ranging from mild proteinuria to AKI necessitating renal replacement therapy [28]. In our study, a baseline renal function was normal in the majority of patients (82%). In the course of the hospitalization, 7% of our patients have developed AKI, which corroborates the results of the recently published meta-analysis estimating the incidence of AKI among hospitalized patients at the level of 8.9% [29]. It is important to note that a substantial proportion of AKI could have been missed due to limited sensitivity of serum creatinine. The role of secondary infections in COVID-19 may be overestimated, although data is limited [30, 31]. In a review, the rate of bacterial or fungal coinfections was only 8%, whereas in our study, 7% of hospitalized patients developed sepsis or septic shock [30].

Finding an effective treatment for COVID-19 was a long and tortuous road filled with many hopes and even more disappointments. The recruitment to our study was initiated at the beginning of pandemic in Poland, therefore, many patients received medications which are currently known to be ineffective. Chloroquine was administered to 36% of our patients while the combined protease inhibitor ritonavir/lopinavir was used extremely rarely (2% of cases). Unfortunately, the gradually emerging data from controlled trials revealed that these drugs do not improve outcomes in this

population [32, 33]. The available evidence shows a benefit associated with the administration of systemic glucocorticoids among patients requiring oxygen therapy. The use of remdesivir is currently suggested in patients with severe COVID-19 who are not critically ill. Despite initial positive signals from observational studies, the use of convalescent plasma proved to be ineffective. Routine use of IL-6 pathway inhibitors (tocilizumab, sarilumab) is not recommended, although these drugs given in the intensive care settings may benefit a selected group of critically ill patients [34].

The mortality rate in our cohort was 10% compared to estimated mortality rate of 2.8% among the entire population of Polish COVID-19 patients [35]. The estimated mortality rate among hospitalized patients accounts for 18.9% and varies greatly depending on a study, ranging from 0.7 to 61.5% [36]. Such variability in the death rate is probably secondary to inter-country differences in population characteristics, health-care-related factors as well as strategy concerning hospital admissions or outpatient treatment of COVID-19 patients.

Almost half the patients in this study were classified as severe cases based on the development of respiratory failure. Univariable analysis comparing severe and non-severe cases showed that patients with severe COVID-19 more commonly presented with dyspnea and increased baseline respiratory rate as well as higher MEWS on admission, thus suggesting a potential clinical utility of the latter as a risk stratification tool in this population [37]. Analysis of laboratory results revealed that severely ill patients had indicators of coagulopathy, hyperinflammatory state, liver damage and increased cardiac biomarkers [1, 16, 38].

Finding risk factors of severe COVID-19 is particularly relevant for clinician involved in management of COVID-19 patients. There are several papers reporting factors potentially associated with mortality of severe course of the disease, however, none of them is based on a Polish cohort [17, 39]. In a study of 5,279 people with COVID-19 in New York City by Petrilli *et al.* [17], among hospitalized patients, factors associated with critical illness were: age, heart failure, BMI (greater than 40) and male sex, with diabetes being also significant. On the other hand, in a large Chinese study, a multivariable logistic regression model showed 10 potential predictors of critical illness. These variables included chest X-ray abnormalities, age, hemoptysis, dyspnea, unconsciousness, the number of comorbidities, cancer

history, neutrophil-to-lymphocyte ratio, as well as concentrations of LDH and direct bilirubin [39]. A multivariable analysis in our study revealed rather similar results and suggested the increasing age, BMI, MEWS on admission, the highest d-dimer level during hospitalization and LDH concentration as factors potentially related to a severe course of COVID-19. Unfortunately, a relatively small study sample reduces the statistical power of this analysis while single-center character of this study may limit its generalizability.

There is very limited data concerning the clinical characteristics and outcomes of Polish patients hospitalized due to COVID-19. In a retrospective study by Nowak *et al.* [40], the authors reported similar distribution of signs and symptoms as well as comorbidities in their sample. Interestingly, the mortality in our cohort was more than two times lower despite a similar proportion of critically ill patients requiring a transfer to the ICU. This may be partially due to differences in treatment, i.e. our cohort was characterized by more common administration of currently recommended LMWH as well as less frequent use of chloroquine and ritonavir/lopinavir, both of which proved to be ineffective in the treatment of COVID-19. An univariable analysis performed in the aforementioned study suggested age, shortness of breath, cardiovascular disease, malignancy and bilateral patchy shadowing in chest X-ray as potential predictors of mortality in this population, which partially corroborates our results. It is however important to note that data presented in our study was gathered in a prospective manner, and therefore, offers more valuable insight into the clinical profile of Polish patients hospitalized due to COVID-19.

This study has several limitations. First, due to the limited study sample and a relatively low incidence of several outcomes of interest, such as mortality, AKI and pulmonary embolism, we were unable to perform multivariable analysis to assess risk factors for these events. Second, this study was performed in a single ward specialized in treating patients with respiratory failure, therefore, the presented cohort may consist of patients with more severe form of COVID-19 compared to other wards, thus limiting the generalizability of the results. Third, the incidence of several outcomes might be underestimated due to lack of routine screening, i.e. lack of active troponin level monitoring for myocardial injury or lack of routine deep vein ultrasound and CT pulmonary angiogram for venous thromboembolism. Finally, we believe that this cohort of first one hundred

patients with COVID-19 treated in our center comprises a relatively large proportion of mild cases compared to later stages of the pandemic.

Conclusion

In this observational study describing the clinical profile of 100 hospitalized patients with COVID-19, nearly half of the analyzed cases developed respiratory failure and approximately 10% died in the course of the disease. The multivariable analysis revealed increasing age, BMI, MEWS on admission as well as higher d-dimer and LDH concentration as factors associated with severe course of COVID-19.

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Conflict of interest

None declared.

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