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The impact of common chronic diseases on the severity of clinical symptoms of COVID-19

Wpływ powszechnych chorób przewlekłych na nasilenie objawów klinicznych COVID-19

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ABSTRACT

INTRODUCTION: Most available research on the etiopathogenesis of COVID-19 predominantly focuses on adult populations with chronic diseases in advanced stages – including severe respiratory and cardiovascular disorders, as well as oncological conditions – where correlations with the clinical course of the disease have been observed. The clinical course of COVID-19 is highly variable, ranging from asymptomatic or mild manifestations to severe respiratory and circulatory failure and death. The objective of the study was to assess whether common chronic diseases influence the severity of the clinical symptoms of COVID-19.

MATERIAL AND METHODS: A retrospective study was conducted on a group of 208 patients between October 2022 and February 2023. An author-designed questionnaire collected data on post-COVID-19 symptoms and their severity (mild, moderate, or severe), frequency, and links to comorbidities. Descriptive statistics were used, with significance set at $p < 0.05$. Comparisons of variables were made using the χ^2 test.

RESULTS: Among the patients, 50.48% had chronic diseases, of which 55% experienced mild symptoms of COVID-19 and 40% experienced moderate symptoms. In the group without chronic diseases (49.52%), mild symptoms were observed in 58% of patients and moderate symptoms in 36%. No significant correlation was found between chronic diseases and the severity of symptoms ($p = 0.809$).

CONCLUSIONS: No significant correlation was found between mild chronic diseases and the severity of COVID-19 symptoms. The type, severity, and duration of the conditions and the level of viremia influence the prognosis. Further studies are needed to consider additional factors, such as gender and age.

KEYWORDS

chronic comorbidities, COVID-19, clinical symptoms

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STRESZCZENIE

WSTĘP: Większość dostępnych raportów naukowych na temat etiopatogenezy COVID-19 koncentruje się głównie na populacjach dorosłych z zaawansowanymi stadiami chorób przewlekłych, w tym ciężkimi zaburzeniami układów oddechowego i sercowo-naczyniowego, a także schorzeniami onkologicznymi, w których zaobserwowano korelację z przebiegiem klinicznym choroby. Przebieg kliniczny COVID-19 jest bardzo zmienny, od bezobjawowych lub łagodnych objawów do ciężkiej niewydolności oddechowej i krążeniowej oraz zgonu. Celem badania była ocena, czy powszechne choroby przewlekłe wpływają na nasilenie objawów klinicznych COVID-19.

MATERIAŁ I METODY: Badanie retrospektywne prowadzono w grupie 208 pacjentów w okresie od października 2022 r. do lutego 2023 r. Autorski kwestionariusz zawierał dane dotyczące objawów po COVID-19 i ich nasilenia (łagodne, umiarkowane lub ciężkie), częstości występowania oraz związku z chorobami współistniejącymi. Zastosowano statystyki opisowe, przy istotności statystycznej $p < 0,05$. Porównania zmiennych dokonano za pomocą testu χ^2.

WYNIKI: Spośród pacjentów 50,48% cierpiało na choroby przewlekłe, z czego u 55% wystąpiły łagodne objawy COVID-19, a u 40% umiarkowane. W grupie bez chorób przewlekłych (49,52%) łagodne objawy zaobserwowano u 58%, a umiarkowane u 36%. Nie stwierdzono istotnej korelacji między chorobami przewlekłymi a nasileniem objawów ($p = 0,809$).

WNIOSKI: Nie stwierdzono istotnej korelacji między powszechnymi chorobami przewlekłymi a nasileniem objawów COVID-19. Rodzaj, nasilenie i czas trwania schorzeń, a także poziom wiremii wpływają na rokowanie. Konieczne są dalsze badania uwzgledniające dodatkowe czynniki, takie jak płeć i wiek.

SŁOWA KLUCZOWE

przewlekłe choroby współistniejące, COVID-19, objawy kliniczne

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has shown that the presence of lifestyle comorbidities – hypertension, diabetes, heart disease, and obesity – significantly increases the risk of severe COVID-19. Patients with these conditions are more likely to be hospitalized and to have post--COVID complications [1]. It has been shown that in most patients hospitalized due to COVID-19, the most common comorbidities were hypertension, diabetes, and obesity [2]. Meta-analyses show that chronic diseases, such as respiratory, cardiovascular, and metabolic diseases, significantly increase the risk of severe complications of COVID-19. In older people with comorbidities, the mortality rate was much higher: in the over-80 age group, the hospital mortality rate was 26.6% [2,3]. In the case of COVID-19, the most common comorbidities were cardiovascular diseases. Data on complications after COVID-19 emphasize the importance of early diagnosis and the monitoring of patients with chronic diseases to improve the prognosis in the case of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [4]. Due to the wide range of clinical courses of COVID-19, symptoms are categorized as mild, moderate, severe, or critical. The first of them most often occur after 11 days of SARS-CoV-2 infection, with the median being about 4–5 days [5]. Patients who showed symptoms mostly had a mild or moderate course of the disease (81%), while 14% had a severe course and around 6% had a critical course [6]. Importantly, differences in the intensity of symptoms were observed between infections with individual strains – in the case of the omicron variant, the course is asymptomatic or mild, requiring hospitalization less often than the previous variants [7]. The mild form causes flu-like symptoms and may be only the initial phase of an incipient disease associated with viral replication [2]. This form most often includes headache, nasal congestion, cough, fever, loss or reduction in sense of smell (anosmia and hyposmia, respectively), disturbance of the sense of taste (dysgeusia), and muscle pain [8]. As variants of the virus emerged, the incidence of myalgia increased with a decreased incidence of anosmia and dysgeusia [6,8]. Rapid clinical deterioration was observed in some patients, probably due to an exacerbated immune response [2], and there were cases in which mild symptoms persisted for 12 months after diagnosis [9]. Moderate clinical symptoms are differentiated from mild symptoms based on abnormalities in chest imaging studies – mainly pneumonia. Dyspnea and a fever of $\geq 39.0°C$ that is resistant to paracetamol also appear [10]. In the severe course, in addition to the combination of the above-mentioned symptoms, tachypnea (a respiratory rate of ≥ 30 breaths per minute), hypoxia with a saturation of $< 93\%$, and significant pulmonary infiltrates occur [6,11]. Typically, this type of clinical picture is a consequence of the inflammation caused by the SARS-CoV-2 virus damaging the epithelium of type II pneumocytes. The inflammation results from increased release of proinflammatory cytokines such as IL-1β, IL-6, TNF-α, and IFN-γ [2,9]. The critical form of the severe course is characterized by acute respiratory distress syndrome (ARDS) and, as a result, multi-organ failure. ARDS appears about

8–9 days after the first symptoms appear. It is estimated that multi-organ failure may develop in about 2% of patients [6,9].

MATERIAL AND METHODS

In the study group (N = 208), 105 of the women had previously been diagnosed with chronic diseases, while the remaining 103 women had no history of disease. The decision to study the female population was informed by the subjective considerations of the researchers. The objective for subsequent studies is to direct the focus onto the male population. Chronic comorbidities in the patients included cardiovascular diseases – hypertension (15.66%), type 2 diabetes (14.50%), thyroid disease (20.48%), rheumatoid arthritis (6.02%), and allergies (20.48%). Other chronic conditions were reported by 24 women – 22.86% of the study group (Figure 1). There were no significant statistical differences in the incidence of chronic diseases, including hypertension, rheumatoid arthritis, and thyroid diseases in the patients.

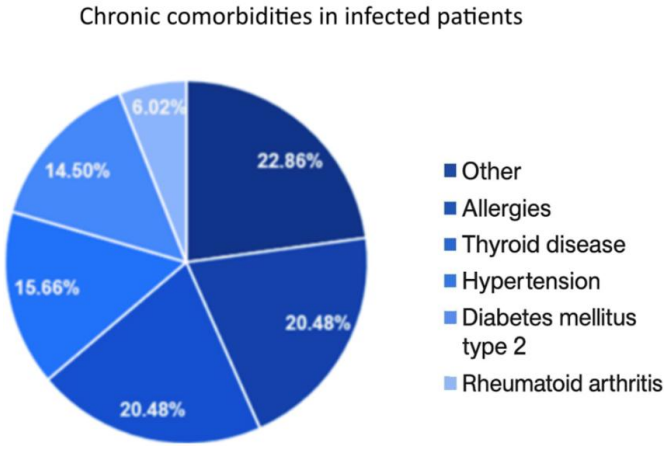

Fig. 1. Percentage of individual chronic diseases in the study group.

Study questionnaire

In the author's original questionnaire, respondents indicate clinical symptoms after SARS-CoV-2 infection. The demographic data (age, gender, education) were analyzed, as were comorbidities of various systems: the lungs and bronchi, e.g., bronchial asthma or chronic obstructive pulmonary disease; the genitourinary system, e.g., chronic cystitis; the heart and circulatory system, e.g., chronic heart failure, heart rhythm disorders, or coronary artery disease; the nervous system, e.g., neuralgia or concentration and memory disorders; the digestive system, e.g., stomach ulcers; the musculoskeletal system, e.g., degenerative diseases; diseases of the veins and peripheral arteries; hormonal disorders, e.g., hyperthyroidism or hypothyroidism; metabolic diseases, e.g., type 2 diabetes; autoimmune disorders, e.g., allergies and rheumatic diseases, e.g., rheumatoid arthritis. The place and time of infection with the SARS-CoV-2 virus were determined, the presence of the virus was confirmed by a diagnostic test (genetic, antigen, or antibody), and the clinical symptoms of COVID-19 were assessed, along with their severity (mild, moderate, or severe). The study group was divided into subgroups depending on the time of SARS-CoV-2 infection and the type and severity of clinical symptoms of COVID-19.

Statistical analysis

Statistical analysis was performed using the software program Statistica 12.0 (Krakow, Poland). Results were presented as means with standard deviation or percentages for nominal and ordinal scale data. Results with a p-value of less than 0.05 were considered statistically significant.

RESULTS

The majority of patients (56.73%) presented mild symptoms of COVID-19, regardless of the presence of chronic diseases (Table I). In the subgroup of patients with chronic diseases, 55.24% had mild symptoms, which was similar to those without chronic diseases (58.25%). Severe symptoms occurred in 5.29% of patients, with minimal differences between subgroups (chronic diseases – 4.76%, no chronic diseases – 5.83%).

Table I. Presence of chronic diseases and degree of symptoms after COVID-19

Degree of symptoms	Presence of chronic diseases*		Total (n, %)
	No (n, 95% CI)	Yes (n, 95% CI)	
Mild	60 (47.22–72.80)	58 (45.34–70.72)	**118 (56.73%)**
Moderate	37 (26.21–47.84)	42 (30.58–53.25)	**79 (38.36%)**
Severe	6 (1.25–10.82)	5 (0.62–9.36)	**11 (4.91%)**
Total (n, %)	**103 (49.52%)**	**105 (50.48%)**	**208 (100%)**

*p = 0.809, χ^2 test

Of the 105 women diagnosed with chronic disease, 55% had mild COVID-19 symptoms and 40% had moderate symptoms. In turn, among the women without chronic diseases (n = 103), mild symptoms dominated (58%), followed by moderate symptoms (36%). No statistical significance was observed (Figure 2).

Figure 3 presents the percentage distribution of participants with and without chronic comorbidities in the studied cohort. A total of 49.52% of individuals reported no chronic conditions, whereas 50.48% had at least one comorbidity.

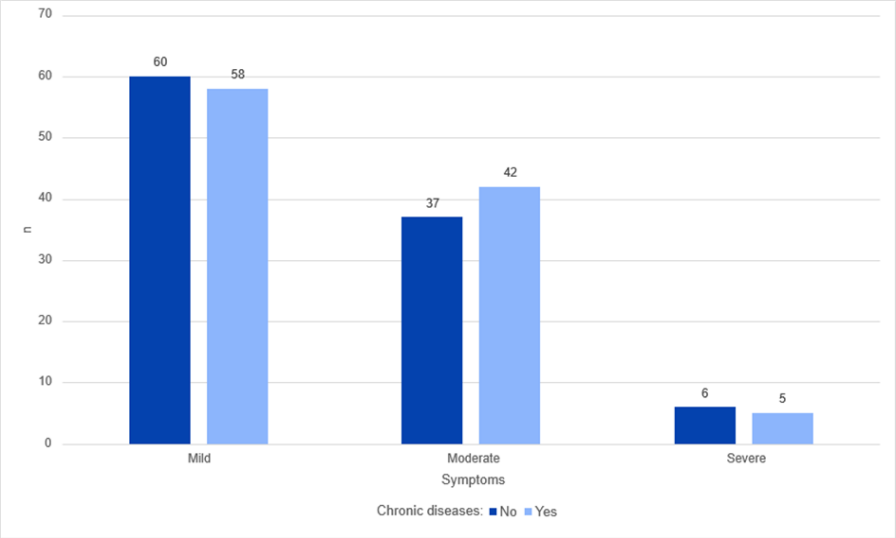

Fig. 2. Comparison of the occurrence of chronic diseases and the degree of symptoms after COVID-19 (*p = 0.809, χ^2 test).

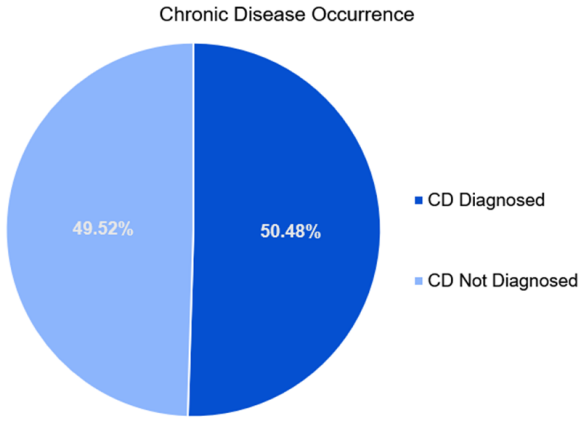

Fig. 3. Percentage of study group diagnosed with chronic diseases.

The diseases co-occurring with COVID-19 were ranked and assessed as percentages, as illustrated in Figure 1.

The chi-square test (χ^2) was used to compare the distribution of the degree of COVID-19 symptoms depending on the presence of chronic diseases. Since the calculated χ^2 value (0.809) was lower than the critical value (5.991), there was no basis to reject the null hypothesis. This means that no statistically significant relationship was found between the presence of chronic diseases and the severity of COVID-19 symptoms. This finding does not mean that such a relationship does not exist, but that sufficient evidence was not found to confirm the alternative hypothesis (which assumes the existence of a relationship).

DISCUSSION

Chronic diseases, according to the generally accepted definition, are characterized by a long-term course of a pathological condition with recurrent complaints after periods of improvement in the patient's health. They require continuous treatment and monitoring, often of the patient's vital signs and functional parameters by a specialist physician [12]. The COVID-19 pandemic, which directly contributed to the isolation of a group of patients with chronic diseases, had a negative impact on their general health – both somatic and mental. Fewer new cases of viral infection were detected, especially in this group of patients, which could be related to their isolation or asymptomatic course [13]. The most common chronic diseases that appeared in clinical statistics were diseases of civilization, e.g., diabetes, cardiovascular diseases, chronic lung diseases, and obesity. The analysis consisted of assessing the impact of their presence on the risk of severe COVID-19 [14]. One of the most common cardiovascular diseases in patients with COVID-19, during the pandemic and currently, is arterial hypertension [15]. Isolated hypertension is not an independent prognostic factor for the severity of the disease, but the co-occurrence of type 2 diabetes in patients significantly increased the risk of death in COVID-19 [16]. It has been suggested that hypertension may lead to a worsening of the course of SARS-CoV-2 infection, but this remains an open topic for further discussion and molecular mechanisms are still being sought to confirm these assumptions [17].

In our study, among the patients with hypertension, no direct correlation was found between the presence of this chronic disease and the severity of symptoms. A relationship with the co-occurrence of other risk factors, including age and other comorbidities, is suspected. Our study showed no statistical correlation between the occurrence of chronic diseases and the degree of clinical symptoms of COVID-19 ($p = 0.809$). Findings from other studies have suggested that less common chronic conditions may significantly worsen the clinical course of COVID-19. This impact largely depended on the characteristics of the study population as well as the severity and health consequences of the specific comorbid condition [18,19]. It has been indirectly shown that COVID-19 contributed to elevated blood pressure in patients who had not been ill before. However, the impact of the virus on the development of hypertension has not been confirmed [20], which was also documented in our work. However, some reports suggest that in patients with hypertension, COVID-19 is associated with a significant deterioration of their health [21]. This is most likely related to the occurrence of SARS-CoV-2--dependent chronic heart failure, which is significantly more severe in patients with high systolic blood pressure and less common in patients with high diastolic blood pressure. According to the latest reports, neglect of blood pressure treatment, especially in patients infected with SARS-CoV-2, often leads to the need for hospitalization in intensive care units, and in extreme cases there is a high risk of death [22]. Shalaeva et al. [23] suggest that despite the lack of a direct effect on the severity of symptoms, hypertension significantly prolongs their duration. Our work confirmed the lack of a direct effect of hypertension on the severity of symptoms associated with the course of the disease. However, it is noteworthy that Yoshihara [24] indicated no or a small causal relationship between hypertension and the exacerbation of clinical symptoms after SARS-CoV-2 infection. This suggests the need for further research to determine a specific relationship or lack thereof in a given clinical situation, the potential variability and individual dependence of which may additionally complicate the drawing of specific conclusions.

COVID-19 has also become a threat to patients with diabetes [25]. The immunological disorders that appear in the course of the disease itself – as well as the immune system response to SARS-CoV-2 infection – intensify inflammation, leading to glycemic disorders [26], which increases the probability of circulatory and respiratory failure in patients with a given clinical profile [27]. Patients with diabetes were at significantly higher risk of developing a more severe form of the disease. Symptoms of COVID-19 in this group may be less specific, which delays diagnosis and treatment. Maddaloni and Buzzetti [28] suggest developing separate risk scores for patients with diabetes to better assess their condition and to implement appropriate interventions that will be appropriately selected for a given patient, depending on their clinical condition. This is also because of the observed higher mortality rate (almost threefold) in coronavirus-infected patients with diabetes than in patients without diabetes [29]. Wu et al. [30] drew attention to the importance of chronic diseases in predisposing patients to a more severe course of the disease. Diabetes, circulatory and vascular diseases, and hypertension were the most common, and patients with these diseases were more susceptible to complications, including the development of acute respiratory distress syndrome. In turn, other studies have shown that in patients hospitalized due to COVID-19 infection, diabetes and heart disease had the strongest impact on the risk of death [31]. The presence of at least two chronic diseases predicted a worse course of COVID-19 and the patients had a higher risk of developing a severe course of the disease. The most common chronic diseases that worsened the course of infection were hypertension and diabetes, but this depended on the patient's age, the type, severity, and duration of chronic disease, and the

pharmacotherapy used [32,33]. Obese patients (body mass index (BMI) > 30) with comorbid cardiovascular disorders and diabetes showed higher mortality rates and a more severe course of COVID-19; a particularly high risk of complications was observed in people with cardiovascular diseases [34]. Szarpak et al. [35] drew attention to ischemic heart disease, in which a viral infection leads to the release of proinflammatory cytokines, which causes a disturbance in the homeostasis of the endothelium of blood vessels, especially cascades related to thrombocyte coagulation. The resulting clots are a direct cause of ischemic conditions due to embolic mechanisms, including ischemic disease, which is a direct threat to life.

Near the beginning of the COVID-19 pandemic, it was assumed that allergic diseases, including bronchial asthma, were one of the factors exacerbating the course of the disease and increasing susceptibility to infection. As the COVID-19 pandemic developed, it was noticed that the course of coronavirus was similar in patients with and without asthma. No difference in the frequency of hospitalization or mortality was observed between these groups [36], as in our study. Terry et al. [37] drew attention to the risk of infection, which was lower in people with asthma than in those without it, and one of the probable reasons was these patients' heightened awareness of the risk of infection and increased caution, where early isolation, social distancing, and personal hygiene played the main role. The opposite situation was observed in patients with chronic obstructive pulmonary disease (COPD), who have a high rate of hospitalization in intensive care units (ICUs). The essence of the problem is chronic inflammation causing impaired functionality of the respiratory epithelium. It induces a worse antiviral response, leading to reduced production of interferons, which makes patients more susceptible to infection. Increased expression of ACE2 in the epithelium facilitates the penetration of the SARS-CoV-2 virus into the lungs. Also, in COPD, hypoxia of the pulmonary vessels develops as a result of impaired lung ventilation, which is associated with increased prothrombotic potential. In SARS-CoV-2 infection, pulmonary clots form, which leads to hypoxia and ultimately to pulmonary embolism [38].

The criteria for the severity of clinical symptoms of COVID-19 in the questionnaires were the patients' subjective perceptions. Indirectly, the results indicated that the severity of COVID-19 symptoms may be influenced by various predisposing factors, such as age, genetics, lifestyle (i.e., diet and physical activity) and access to medical care – not only the co-occurrence of chronic diseases. However, it has been proven that coronavirus itself can also worsen the course of these diseases in patients who have already been diagnosed [39]. Our analysis did not confirm a statistically significant relationship between the presence of chronic diseases and the severity of COVID-19 symptoms in the women participating in this study. Of the 105 patients with chronic diseases, 55% had mild symptoms and 40% had moderate symptoms. In the subgroup without chronic diseases (n = 103), mild symptoms occurred in 58% and moderate ones in 36%. The lack of statistical significance suggests that the exclusive presence of chronic diseases did not directly affect the severity of the course of COVID-19.

While the results may prove useful in the assessment of health risks and the planning of therapeutic strategies, the factors contributing to a more severe course of the disease should be considered in the context of a wide spectrum of clinical parameters and not limited to only the presence of individual chronic diseases. Moreover, special attention should be given to the specific characteristics of the study population analyzed in the present research.

The survey was conducted exclusively among women who were relatively young and were not selected on the basis of any particular criteria. This may provide a rationale for the observed differences in comparison to other studies, where the participants were characterized by a much higher average age and fulfilled more specific criteria, such as BMI or the potential influence of other factors. Furthermore, the data encompassed subjective assessments by the researchers, which had the potential to restrict the analysis. In the future, it is recommended that further research be conducted to identify any additional factors that determine the course of the disease. This will allow for more precise adjustment of medical strategies to the specific needs of patients from different age groups.

CONCLUSIONS

1. No significant correlation with mild chronic diseases: In young women, no significant correlation was found between mild and moderate chronic diseases and the severity of clinical symptoms of COVID-19.
2. Impact of specific disease characteristics: The type, severity, and duration of chronic diseases play a key role in predicting the course of COVID-19, although the presence of such diseases alone does not necessarily determine the severity of infection.
3. The importance of viral load: In mild cases of COVID-19, the viral load is much lower than in patients with a severe disease course, indicating its key role in prognosis.
4. Study limitations and further research: The study was limited to individuals with chronic diseases who did not require hospitalization, which could have influenced the results. It is necessary to consider additional factors, such as gender and age, when planning medical strategies.

Authors' contribution

Study design – B. Pietrzyk, P. Dolibog, A. Joniec, T. Fajferek, J. Mikołajczyk
Data collection – T. Fajferek, B. Pietrzyk, A. Joniec, S. Kaczara, E. Kołodziej, J. Mikołajczyk, P. Dolibog
Data interpretation – B. Pietrzyk, A. Joniec, T. Fajferek, P. Dolibog
Statistical analysis – A. Joniec, T. Fajferek, S. Kaczara, E. Kołodziej, J. Mikołajczyk
Manuscript preparation – B. Pietrzyk, T. Fajferek, J. Mikołajczyk, P. Dolibog, A. Joniec, E. Kołodziej
Literature research – T. Fajferek, A. Joniec, J. Mikołajczyk, S. Kaczara, E. Kołodziej, P. Dolibog, B. Pietrzyk

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