Особенности клинического течения новой коронавирусной инфекции у студентов, находившихся под наблюдением в обсерваторе, в первую и вторую волну подъема заболеваемости

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Введение. Внезапное появление в мире новой коронавирусной инфекции (COVID-19) поставило перед наукой сложные задачи по определению основных клинических проявлений данного заболевания, а также по утверждению стандартов диагностики, лечения и профилактики. Продолжаются исследования по изучению симптомов легкого течения COVID-19. Данные, полученные в таких исследованиях, особенно актуальны для врачей первичного звена здравоохранения.

Цель исследования — оценить особенности клинического течения COVID-19 среди студентов СЗГМУ им. И.И. Мечникова, помещенных в обсерватор, в период первой и второй волны подъема заболеваемости.

Материалы и методы. Исследование проведено на базе обсерватора СЗГМУ им. И.И. Мечникова в два этапа: в период с 21.04.2020 по 31.08.2020 (первая волна) и с 16.09.2020 по 31.12.2020 (вторая волна). У всех участников исследования были зафиксированы демографические, эпидемиологические и клинико-анамнестические данные.

Результаты. В исследовании участвовали 309 человек: 39,8 % мужчин ($n = 123$) и 58,9 % женщин ($n = 182$). Средний возраст респондентов составил 21,5 ± 2,6 года. Количество участников в первую и вторую волну — 113 и 196 человек соответственно. Во вторую волну средний возраст больных COVID-19 был на 1,5 года меньше, чем в первую, и составил 21,2 ± 2,5 года ($p < 0,001$). У студентов, находившихся под наблюдением, во вторую волну повышения заболеваемости COVID-19 по сравнению с первой отмечено достоверное повышение частоты следующих симптомов: сухого кашля, потери обоняния, головной боли, общей слабости, повышения температуры тела до 38,0 °C, заложенности носа ($p < 0,05$). Частота встречаемости таких симптомов, как заложенность в грудной клетке, боли в пояснице и повышение температуры тела свыше 38,0 °C, достоверно уменьшилась ($p < 0,05$). Достоверно снизилась частота развития вирусной пневмонии у пациентов, наблюдавшихся в период второй волны, по сравнению с данными, полученными при наблюдении в период первой волны ($p < 0,001$).

Ключевые слова: новая коронавирусная инфекция; COVID-19; студенты; обсерватор; клиническое течение; симптомы; первая и вторая волна повышения заболеваемости.

Features of the clinical course of a new coronavirus infection in students who were observed in the observator in the first and second wave of morbidity increasing

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INTRODUCTION: The sudden appearance of a new coronavirus infection in the world has posed difficult challenges for science to determine the main clinical manifestations of this disease, as well as to approve standards for diagnosis, treatment and prevention. Research of the symptoms of mild COVID-19 is continuing. The data obtained in such studies are particularly relevant for primary care physicians.

THE AIM: To evaluate the features of the clinical course of COVID-19 among students of the North-Western State Medical University named after I.I. Mechnikov, placed in the observatory, during the first and second waves of rising morbidity.

MATERIALS AND METHODS: The study was conducted on the basis of the observatory of the NWSMU named after I.I. Mechnikov in two stages: in the period from 21.04.2020 to 31.08.2020 (the first wave) and from 16.09.2020 to 31.12.2020 (the second wave). Demographic, epidemiological, and clinical-anamnestic data were recorded in all participants of the study.

RESULTS: The study involved 309 people: 39.8% men ($n = 123$) and 58.9% women ($n = 182$). The average age of the respondents was 21.5 ± 2.6 years. The number of participants in the first and second waves was 113 and 196 people, respectively. The average age of participants with COVID-19 in the first wave was 1.5 years less and was 21.2 ± 2.5 years ($p < 0.001$). There was a significant increase in the frequency of the following symptoms: dry cough, loss of smell, headache, general weakness, increased body temperature to 38.0 °C, nasal congestion ($p < 0.05$) in students who were monitored in the second wave of increased incidence of COVID-19 compared to the first. The frequency of symptoms such as chest congestion, lower back pain, and fever above 38.0 °C significantly decreased ($p < 0.05$). There was a significant decrease in the incidence of viral pneumonia in patients who were observed during the second wave, compared with the data obtained during the first wave ($p < 0.001$).

Keywords: new coronavirus infection; COVID-19; students; observator; clinical course; symptoms; first and second waves of increased morbidity.

INTRODUCTION

In 2019, an outbreak of a new, previously unknown infection, subsequently named coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO), occurred in the People's Republic of China. In the first 4 months since the first report of COVID-19, more than 1 million people have been infected with more than 55,000 cases of lethal outcome [1]. The sudden emergence of a new coronavirus infection in the world has posed challenging tasks for science to determine the main clinical manifestations of this disease and to approve standard diagnostics, treatment, and prevention. In the process of accumulating information about the course of COVID-19, it was revealed that its severity is influenced by age, gender, and concomitant diseases [2–4]. Acute respiratory infection symptoms, such as fever, cough, shortness of breath, fatigue, and chest congestion, are considered characteristic signs of COVID-19 [5, 6]. However, the clinical manifestations of COVID-19 can vary significantly [5]. Based on the data obtained by Chinese specialists, the disease is mild in 80% of cases [7]. In this regard, the research continues to analyze the symptoms of mild COVID-19 [8]. It is of interest to evaluate the aspects of the clinical course of the new coronavirus infection during the first and second waves of incidence. The literature presents only a few cases focused on such analysis, and most studies concern only hospitalized patients [9]. There are almost no studies focused on the aspects of the mild clinical course of the new coronavirus infection, despite their relevance, especially for primary care physicians who monitor and treat this patient group in outpatient settings.

The study aimed to assess the aspects of the clinical course of COVID-19 among students of the North-Western State Medical University named after I.I. Mechnikov who stayed in an observation facility during the first and second waves of incidence.

Research objectives. This study has the following objectives:
1. Study the aspects of the clinical course of COVID-19 among students accommodated in the observation facility of the North-Western State Medical University named after I.I. Mechnikov from September 16 to December 31, 2020.
2. Conduct a comparative analysis of the course of the disease and symptoms of COVID-19 among students of the North-Western State Medical University named after I.I. Mechnikov who were monitored in the observation facility during the first (April 21 to August 31, 2020) and second waves (September 16 to December 31, 2020) of increase in incidence rates.

MATERIALS AND METHODS

The study was conducted in the observation facility of the North-Western State Medical University named after I.I. Mechnikov. The study protocol was approved by the local ethics committee of the North-Western State Medical University named after I.I. Mechnikov. The aspects of the organization of the observation facility work were published earlier [10]. Epidemiological and clinical anamnestic indices, namely, gender, age, close contact history with COVID-19 patients, complaints, physical data, and laboratory and instrumental research method data, were recorded in all patients transferred to the observation facility from April 21 to August 31, 2020 (first wave) and from September 16 to December 31, 2020 (second wave). Swab samples from the oropharynx/nasopharynx were collected for SARS-CoV-2 from all students transferred to the observation facility. Other examinations (laboratory and instrumental methods) were performed if indicated.

The principle of stratification into groups of patients staying in the observation facility at different periods of monitoring was described earlier [8]. Group 1 included patients without complaints or clinical upper respiratory tract infection (URTI) manifestations in the presence of negative results of oropharynx/nasopharynx swab tests for SARS-CoV-2 and had contact with a patient with coronavirus infection at the place of residence or in a medical organization. Group 2 included patients with any clinical URTI manifestations (except pneumonia) in the presence of negative results of oropharynx/nasopharynx swab tests for SARS-CoV-2. Group 3 included patients with positive results of oropharynx/nasopharynx swab tests for SARS-CoV-2 regardless of the presence or absence of any clinical URTI manifestations or with signs of viral pneumonia confirmed by objective research methods regardless of the results of oropharynx/nasopharynx swab tests for SARS-CoV-2 [8]. According to the WHO recommendations, due to the lack of proven efficacy, the antiviral drugs were not prescribed to the study participants [11]. COVID-19 patients were given vitamin D at a dose of 4000 IU once a day according to a protocol based on the experience of American doctors [12] and vitamin C at a dose of 500 mg twice a day. For prophylactic purposes, contact persons and URTI patients received vitamin D at a dose of 2000 IU and vitamin C at a dose of 500 mg twice a day.

RESULTS AND DISCUSSION

Of the 309 patients included in the study, 39.8% were men (*n* = 123) and 58.9% women (*n* = 182). The average age of the respondents was 21.5 ± 2.6 years. Table 1 presents the gender and age characteristics of the participants depending on the study period.

Table 1. Gender and age characteristics of the study participants

Таблица 1. Половозрастные характеристики участников исследования

Parameter	First wave (*n* = 113)	Second wave (*n* = 196)	*p*	Total sample (*n* = 309)
Average age, years ± SD	22.4 ± 2.5	21.0 ± 2.6	<0.001*	21.5 ± 2.6
Gender, men, *n* (%)	51 (45.1)	72 (36.7)	0.183**	123 (39.8)

Note. SD, standard deviation. * *t*-test for independent samples. ** Pearson χ^2 test.

Table 2. Distribution of participants into groups in the first and second waves

Таблица 2. Распределение участников на группы в первую и вторую волну

Group, *n* (%)	First wave (*n* = 113)	Second wave (*n* = 196)	*p*	Total sample (*n* = 309)
1	49 (43.4)	69 (35.2)	0.191*	118 (38.2)
2	20 (17.7)	43 (21.9)	0.461*	63 (20.4)
3	44 (38.9)	84 (42.9)	0.570*	128 (41.4)

Note. * Pearson χ^2 test.

Table 1 demonstrates that statistically significant age differences were revealed between the participants in the first and second waves (*p* < 0.001).

Among study participants (*n* = 309), the proportions of patients were 38.2% (*n* = 118) in group 1 (students who were in contact with a laboratory-confirmed COVID-19 patient and did not fall ill), 20.4% (*n* = 63) in group 2 (students with laboratory-unconfirmed COVID-19 and clinical URTI signs), and 41.4% (*n* = 128) in group 3 (patients with laboratory-confirmed COVID-19 or viral pneumonia). Table 2 shows the results of the analysis of incidence in the groups in the first and second waves.

Table 2 demonstrates that there were no statistically significant differences in the distribution of participants in groups in the first wave.

The average age of group 3 participants (patients with COVID-19 or viral pneumonia) was 22.7 ± 2.6 and 21.2 ± 2.5 years in the first and second waves, respectively. These indicators had statistically significant differences (*p* < 0.001). Spanish authors also noted an

Table 3. Frequency of occurrence of symptoms in patients with COVID-19 in the first and second waves

Таблица 3. Частота встречаемости симптомов среди больных COVID-19 в первую и вторую волну

Symptom, *n* (%)	First wave (*n* = 113)	Second wave (*n* = 196)	*p*	Total sample (*n* = 309)
Presence of at least one symptom of URTI	19 (43.2)	72 (85.7)	<0.001*	91 (71.1)
Dry cough	9 (20.5)	43 (51.2)	<0.001*	52 (40.6)
Productive cough	1 (2.3)	2 (2.4)	0.739*	3 (2.3)
Chest congestion	6 (13.6)	4 (4.8)	<0.05*	10 (7.8)
Ageusia	8 (18.2)	19 (22.6)	0.442*	27 (21.1)
Anosmia	11 (25.0)	38 (45.2)	<0.001*	49 (38.3)
Muscle pain	3 (6.8)	6 (7.1)	0.895*	9 (7.0)
Low back pain	2 (4.5)	0 (0)	<0.05*	38 (29.7)
Headache	7 (15.9)	31 (36.9)	<0.001*	38 (29.7)
Sore throat	4 (9.1)	10 (11.9)	0.568*	14 (10.9)
Diarrhea	0 (0)	0 (0)	–	0 (0)
Asthenia	11 (25.0)	55 (65.5)	<0.001*	66 (51.6)
Fever of 38.0°C and above	3 (6.8)	0 (0)	<0.001*	3 (2.3)
Fever below 38.0°C	11 (25.0)	37 (44.0)	<0.05*	48 (37.5)
Nasal congestion	7 (15.9)	27 (32.1)	<0.05*	34 (26.6)
Rhinorrhea	1 (2.3)	0 (0)	0.137*	1 (0.8)

Note. * Pearson χ^2 test. URTI, upper respiratory tract infection.

increase incidence of younger age patients with COVID-19 who underwent inpatient treatment during the second wave [9].

The gender composition of patients during the first and second waves did not differ significantly.

During the study, we assessed the prevalence of symptoms among participants in group 3 in the first and second waves (Table 3).

A significant increase in the incidence of dry cough, anosmia, headache, general asthenia, fever up to 38.0°C, and nasal congestion ($p < 0.05$) was noted in the second follow-up period than the first. The incidence of symptoms such as chest congestion, back pain, and fever above 38.0°C decreased significantly ($p < 0.05$). In addition, a gender- and age-adjusted multivariate analysis revealed that symptoms such as rhinorrhea, nasal congestion, and ageusia were not significant factors associated with the development of anosmia in participants with COVID-19. The data obtained are consistent with the results of other international studies, which also indicate the development of anosmia in COVID-19 patients. The pathogenesis of anosmia is currently unclear; various hypotheses have been proposed, and therefore, additional studies are required [13–15].

It should be noted that despite a significant increase in the prevalence of dry cough in group 3 participants in the second wave than the first wave, the incidence of productive cough did not significantly change. As a result of the analysis of the prevalence of dry and productive cough in group 3 participants, statistically significant differences were found in the first and second waves, and dry cough was registered significantly more often than productive cough ($p < 0.001$).

During the study, a significant decrease in the incidence of pneumonia from 11.5% to 0% was noted in group 3 participants during the second wave ($p < 0.001$). The multivariate analysis adjusted for gender and age revealed that the heaviness/compressing chest pain in the study participants was statistically significantly associated with pneumonia (diagnosed using objective research methods) and increased the probability of its presence by 17.8 times (95% confidence 1.5–298.3; $p < 0.05$).

CONCLUSIONS

1. Statistically significant differences in the age of COVID-19 patients during the first and second waves were revealed. Thus, the average age of COVID-19 patients in the second wave was 21.2 ± 2.5 years ($p < 0.001$), which is 1.5 years less than in the first wave.
2. The incidence of clinical symptoms of COVID-19 during the second wave has changed significantly than the first wave. Dry cough, anosmia, headache, general asthenia, fever up to 38.0°C, and nasal congestion ($p < 0.05$) were registered significantly more often. Meanwhile, the incidence of chest congestion, lower back pain, and fever above 38.0°C decreased significantly ($p < 0.05$).
3. A significant decrease was noted in the incidence of viral pneumonia in patients during the second wave than in the first wave ($p < 0.001$).

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