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FEATURES OF THE CLINICAL COURSE OF A NEW CORONAVIRUS INFECTION IN STUDENTS WHO WERE UNDER OBSERVATION IN THE OBSERVATORY

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The emerging epidemic of a new coronavirus infection (COVID-19), received the status of an emergency of international importance and attracted the attention of not only health professionals, but also the population around the world. Although the risk of severe health consequences from COVID-19 for young people without

comorbidities is relatively low, an increase in the incidence of infection in this age group may lead to an increase in the proportion of people with severe disease, as well as the spread of infection among older age groups who are in close contact with them and are at high risk of mortality from COVID-19.

The aim of the study was to evaluate the clinical features of the new coronavirus infection among students of the North-Western State Medical University named after I.I. Mechnikov, placed in the observatory.

Materials and methods. The study was conducted on the basis of the observatory of the North-Western State Medical University named after I.I. Mechnikov. All persons transferred to the observatory in the period from 21.04.2020 to 31.08.2020, epidemiological and clinical-anamnestic data were recorded. In a prospective study, all participants were asked to complete a Health Questionnaire (EQ-5D) over the phone 3 months after their stay at the observatory.

Results. 113 people participated in the study: 45.1% of men (n = 51) and 54.9% of women (n = 62). The average age of the respondents was 22.4 ± 2.5 years. When conducting a multivariate analysis, it was found that gender, age, belonging to an ethno-linguistic group, and chronic diseases are not reliable factors associated with the development of COVID-19 participants. According to the results of a prospective study, a statistically significant difference between the responses of respondents who had and did not have COVID-19 was obtained with a positive answer to the question about the presence of pain and discomfort (p < 0.05).

Keywords: new coronavirus infection; COVID-19; students; clinical course.

ОСОБЕННОСТИ КЛИНИЧЕСКОГО ТЕЧЕНИЯ НОВОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИИ У СТУДЕНТОВ, НАХОДИВШИХСЯ ПОД НАБЛЮДЕНИЕМ В ОБСЕРВАТОРЕ

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Эпидемия новой коронавирусной инфекции (COVID-19) получила статус чрезвычайной ситуации международного значения и привлекла внимание не только специалистов здравоохранения, но и населения всего мира. Несмотря на то что риск тяжелых последствий для здоровья от COVID-19 у молодых людей без сопутствующих заболеваний относительно низок, распространение инфекции в данной возрастной группе может привести к увеличению заболеваемости среди людей более старших возрастных групп, находящихся с ними в тесном контакте и входящих в группу высокого риска смертности от COVID-19.

Цель исследования — оценить особенности клинического течения новой коронавирусной инфекции среди студентов СЗГМУ им. И.И. Мечникова, помещенных под наблюдение в обсерватор.

Материалы и методы. Исследование проведено на базе обсерватора СЗГМУ им. И.И. Мечникова, куда были помещены обучавшиеся, которые контактировали с заболевшими новой коронавирусной инфекцией, с легкими ее проявлениями, а также с клиническими проявлениями острого респираторного заболевания. У всех лиц, переведенных в обсерватор в период с 21.04.2020 по 31.08.2020, были зафиксированы эпидемиологические и клинико-анамнестические данные. В рамках проспективного

исследования спустя 3 мес. после пребывания в обсерваторе всем участникам по телефону было предложено заполнить «Опросник по здоровью» (EQ-5D).

Результаты. В исследовании приняли участие 113 человек: $45,1\,\%$ мужчин (n=51) и $54,9\,\%$ женщин (n=62). Средний возраст респондентов составил $22,4\pm2,5$ года. При проведении многофакторного анализа было установлено, что пол, возраст, принадлежность к этнолингвистической группе, хронические заболевания не являются достоверными факторами, ассоциированными с развитием COVID-19. Согласно результатам проспективного исследования статистически значимая разница между ответами респондентов, переболевших и не переболевших COVID-19, была получена при ответе на вопрос о сохранении ощущения дискомфорта или боли спустя 3 мес. от острого периода заболевания (p < 0,05).

Ключевые слова: новая коронавирусная инфекция; COVID-19; студенты; клиническое течение.

Introduction

In December 2019, the WHO China Country Office officially announced the new coronavirus infection (COVID-19) [1]. The first cases of SARS-CoV-2 infection in Russia were recorded in January 2020. The epidemic obtained the status of a global emergency and drew the attention of not only health professionals but also the world's population. Despite a significant scientific breakthrough in the study of the etiology, pathogenesis, and therapy of COVID-19 compared to the beginning of 2020, work is being carried out in all fields on the study of the characteristics of this disease course [2-4]. In response to the COVID-19 pandemic, the public healthcare service aims primarily to prevent or minimize the spread of SARS-CoV-2 to those most at risk of severe outcomes. Furthermore, elderly patients with concomitant chronic pathology, especially with cardiovascular diseases, are among the groups at high risk of mortality from COVID-19 [5].

The study of the characteristics of the infection course among the young population is no less urgent task, not only because of the high prevalence of the disease among all age groups. In early autumn, the opening of educational institutions poses new problems and increases the risk of transmission of infection among students. Although there is a relatively low risk of severe health effects from COVID-19 in young people without comorbidity, an increase in the incidence of infection in this age group can lead to an increase in the proportion of patients with severe disease, as well as to the spread of infection among older groups who are in close contact with young people and who are at high risk of death from COVID-19. The relevance of this problem has already been considered in foreign literature, which also reflects the results of an analysis of COVID-19 prevalence among students [6]. In addition, the analysis of the clinical course of the new coronavirus infection in young people is of interest, since at the time of data collection and analysis, the literature primarily described the symptoms registered in the severe course of infection. These include a decrease in sense of smell and taste (33.9-68%) [7], signs of conjunctivitis (31.6%) [8], as well as myalgia (11%), mental confusion (9%), headache (8 %), hemoptysis (5%), diarrhea (3%), nausea, vomiting, and palpitations. In the severe course of COVID-19, the severity of these symptoms can become specific. However, milder forms of the disease can be manifested with symptoms that are difficult to discern from other acute respiratory infections. This aspect of the course of the disease posed difficulties in differential diagnosis of COVID-19 and other upper respiratory tract infections (URTI) when deciding on the transfer of students from the dormitory building, where common areas were not individualized, to the observation facility to limit the spread of infection.

The goal of the study was to assess the aspects of the clinical course of a new coronavirus infection among students of the North-Western State Medical University named after I.I. Mechnikov staying in the observation facility.

Study objectives

- 1. To examine the effect of social and demographic characteristics on the incidence of COVID-19 among students of the North-Western State Medical University named after I.I. Mechnikov.
- 2. To identify the aspects of the clinical course of COVID-19 among students of the North-Western State Medical University named after I.I. Mechnikov.
- 3. To assess the impact of COVID-19 on the health status of students of the North-Western State Medical University named after I.I. Mechnikov in the post-viral period.

Materials and methods

The study was conducted in the observation facility of the North-Western State Medical University named after I.I. Mechnikov. Moreover, 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 regulated by the order of the rector

of the North-Western State Medical University named after I.I. Mechnikov (Order No. 663-0 of 04/21/2020 "On the organization of the observation facility in the dormitory building of the North-Western State Medical University named after I.I. Mechnikov, the Ministry of Health of Russia, at 45 Prosveshcheniya Ave., and the appointment of responsible persons to ensure its functioning") and published earlier [9]. Responsible persons, including residents of the Department of Family Medicine, who conducted daily monitoring of all students living in the dormitory, reported contacts with COVID-19 patients at their place of residence or place of work, as well as persons with URTI symptoms or positive results of oropharyngeal/nasopharynx swab tests for SARS-CoV-2 for isolation at the observation facility. Epidemiological and clinical-anamnestic data of all patients transferred to the observation facility during the period from 04/21/2020 to 08/31/2020 were recorded, namely, gender, age, place of residence, nationality, history of close contact with COVID-19 patients, complaints, physical data, chronic diseases, laboratory data. and instrumental studies. All students transferred to the observation facility were subjected to oropharyngeal/nasopharyngeal swab testing for SARS-CoV-2. Where specified, the rest of the examinations (laboratory and instrumental) were carried out.

When analyzing the data, all residents of the observation facility were distributed into three main groups. Group 1 included patients who had contact with a coronavirus-infected patient at the place of residence or in a medical organization or who had no complaints or clinical manifestations of URTI in the presence of negative results of swab testing from the oropharynx/ nasopharynx for SARS-CoV-2; Group 2 included patients with some clinical manifestations of URTI, excluding pneumonia, or with negative results of swab testing from the oropharynx/nasopharynx for SARS-CoV-2; Group 3 included patients with positive test results for SARS-CoV-2 oropharynx/nasopharynx swabs, irrespective of the presence or absence of any clinical manifestations of URTI, or with signs of viral pneumonia, verified by physical examination methods, regardless of the results of SARS-CoV-2 oropharynx/nasopharynx swabs. As recommended by the World Health Organization, all participants received a prophylactic dose of vitamin D (2000 IU) daily without antiviral therapy [10]. Moreover, COVID-19 respondents were given vitamin C at a dose of 500 mg twice daily and vitamin D at a dose of 4000 IU once daily, in accordance with a protocol based on the experience of American doctors [11]. If pneumonia was suspected, azithromycin at a dose of 500 mg once for 5 days was prescribed. As part of a prospective study, all participants were asked by telephone to complete a Health Questionnaire (EQ-5D) 3 months after staying at the observation facility [12].

Statistical data analysis was carried out using the SPSS 22.0 software (SPSS Inc., Chicago, Illinois, USA). Using a one-sample t-test, confidence intervals for quantitative variables were assessed. The confidence intervals of the shares were determined according to Clopper-Pearson. Further, the relationships of some variables with others, including quantitative, ordinal, and nominal ones in any combination, were assessed using multivariate analysis. To assess the significance of differences in categorical variables, the Pearson χ^2 test was used. With a distribution other than normal, independent samples were compared using the Mann-Whitney U test. The criterion for the statistical significance of the results was considered p < 0.05.

Results and discussion

In this study, 113 patients were enrolled, including 45.1% (n=51) of men and 54.9% (n=62) of women. The respondents had an average age of 22.4 ± 2.5 years. In addition, the majority (73.5%) were citizens of the Russian Federation; 26.5% were citizens of other states, namely, Moldova, Transnistria, Syria, Tajikistan, Turkmenistan, Uzbekistan, Brazil, Egypt, Jordan, Kazakhstan, Kenya, Kyrgyzstan, and Latvia. Moreover, the citizens of the Russian Federation were residents of 40 different regions of the country. In addition,



Results of stratification of the study participants depending on their belonging to the ethno-linguistic family, n=113

Результаты стратификации участников исследования в зависимости от принадлежности к этнолингвистической семье, n=113

all study participants (n = 113) were stratified into five main ethnolinguistic families depending on nationality (Figure).

Among all study participants (n=113), the proportion of individuals classified as group 1 (students who were in contact with a laboratory-confirmed COVID-19 patient and those without the disease), group 2 (students with laboratory-unconfirmed COVID-19 with clinical symptoms of URTI), and group 3 (laboratory-confirmed COVID-19 or viral pneumonia patients) was 46.9% (n=53), 17.7% (n=20), and 35.4% (n=40), respectively.

Table 1 presents the main characteristics of the study participants and reveals that a significant proportion of students in each of the groups had one or another chronic disease despite their young age, but no statistical differences were observed in the severity of concomitant diseases.

Table 2 presents the data on the prevalence of clinical symptoms characteristic of COVID-19. The study results showed that patients with clinical signs of URTI and laboratory-negative COVID-19 results (p < 0.05) complained of sore throat significantly more often (Table 2).

The multivariate analysis revealed that gender, age, and ethnolinguistic group affiliation are not significant factors associated with the development of COVID-19 (Table 3).

Table 1 / Таблица 1
Main characteristics of the study participants
Основные характеристики участников исследования

Parameter	Group 1 (n = 53)	Group 2 (n = 20)	Group 3 (n = 40)	p	Total sample (<i>n</i> = 113)
Average age, years ± SD	22.2 ± 2.4	22.5 ± 2.7	22.7 ± 2.6	0.340*	22.4 ± 2.5
Gender, men, n (%)	28 (52.8)	9 (45.0)	14 (35.0)	0.134**	51 (45.1)
Presence of at least one chronic disease, n (%)	19 (35.8)	8 (40.0)	12 (30.0)	0.628**	39 (34.5)

Note: Chronic diseases taken into account included bronchial asthma, chronic diseases of the ENT organs, chronic diseases of the gastrointestinal tract, anemia, diabetes mellitus, obesity, arterial hypertension, chronic kidney disease, allergic diseases in history. *T-test for independent samples; **Pearson χ^2 test. SD, standard deviation.

Table 2 / Таблица 2 The frequency of symptoms among affected individuals, depending on the results of oropharyngeal/nasopharyngeal smears for SARS-CoV-2

Частота встречаемости симптомов среди заболевших лиц в зависимости от результатов мазков из рото-/носоглотки на SARS-CoV-2

Symptom	Group 2 (n = 20)	Group 3 (n = 40)	р
Dry cough, n (%)	7 (35.0)	9 (22.0)	0.443*
Productive cough, n (%)	1 (5.0)	1 (2.5)	0.799*
Chest congestion, n (%)	1 (5.0)	6 (15.0)	0.477*
Ageusia, n (%)	5 (25.0)	8 (20.0)	0.912*
Anosmia, n (%)	7 (35.0)	11 (27.5)	0.765*
Muscle pain, n (%)	1 (5.0)	3 (7.5)	0.855*
Lumbar pain, n (%)	0	2 (5.0)	0.799*
Headache, n (%)	4 (20.0)	7 (17.5)	0.906*
Sore throat, n (%)	7 (35.0)	4 (10.0)	0.045*
Diarrhea, n (%)	1 (5.0)	0	0.721*
Asthenia, n (%)	7 (35.0)	11 (27.5)	0.765*
Body temperature 38.0 $^{\circ}\mathrm{C}$ and above, n (%)	2 (10.0)	3 (7.5)	0.869*
Body temperature below 38.0 °C, n (%)	10 (50.0)	11 (27.5)	0.151*
Nasal congestion, n (%)	3 (15.0)	7 (17.5)	0.903*
Rhinorrhea, n (%)	2 (10.0)	1 (2.5)	0.530*

Note: p value less than 0.05 (statistically significant result) is in bold. *Pearson χ^2 test.

Table 3 / Таблица 3 Dependence of the presence of COVID-19 on various factors, n=113 Зависимость наличия COVID-19 от различных факторов, n=113

Parameter	Response options	Presence of COVID-19, OR (95% CI)	p
Gender	Men	0.53 (0.21-1.32)	0.174
Age	under 25 years	1	_
	25 years and older	0.62 (0.16-2.40)	0.49
Ethnolinguistic family	Indo-European	1	_
	Afrasian	1.12 (0.13-8.22)	0.43
	Altai	1.66 (0.57-4.82)	0.35
	Korean	4.47 (0.28-71.65)	0.29
	North Caucasian	4.88 (0.30-80.92)	0.27
Presence of at least one chronic disease	Yes	0.52 (0.21-1.29)	0.16

Note: OR, odds ratio; CI, confidence interval.

Table 4 / Таблица 4 Results of the survey of the health status of respondents 3 months after discharge from the observation facility Результаты исследования состояния здоровья респондентов спустя 3 мес. после выписки из обсерватора

Sign	Group 1 (n = 43)	Group 2 (n = 17)	Group 3 (n = 36)	p
Difficulty in mobility, n (%)	1 (1.9)	1 (5.0)	5 (12.5)	0.155*
Difficulty in self-care, n (%)	0 (0)	0	0	_
Difficulty in daily activities, n (%)	1 (1.9)	0	2 (5.0)	0.892*
Pain or discomfort, n (%)	3 (5.7)	2 (10.0)	10 (25.0)	0.035*
Anxiety or depression, n (%)	3 (5.7)	2 (10.0)	2 (5.0)	0.927*
Health status, average score ± SD	92.3 ± 8.6	92.7 ± 10.9	92.0 ± 8.5	0.780*

Note: SD, standard deviation. p value less than 0.05 (statistically significant result) is in bold. *Pearson χ^2 test.

Among all study participants (n=113), patients who had viral pneumonia confirmed by computed tomography were in the observation facility. Some of them were transferred to the observation facility after staying in a hospital, whereas some were monitored and received therapy on an outpatient basis. The proportion of pneumonia of viral etiology among all COVID-19 cases was 20.0% (n=8). Among them, the incidence of pneumonia of I, II, and III degrees of severity was 62.5% (n=5), 25.0% (n=2), and 12.5% (n=1), respectively. Of the eight patients with pneumonia, 37.5% (n=3) were hospitalized.

It is noteworthy that among all cases of viral pneumonia confirmed by computed tomography, only 25.0% (n=2) of the study participants tested positive for SARS-CoV-2 with oropharyngeal/nasopharyngeal swabs.

More and more works are published in foreign literature based on a term such as "post-COVID syndrome" or "long COVID" [13]. This term refers to a multisystem disease that often occurs even after a relatively mild form of the disease. The most prominent nonspecific manifestations of this syndrome include fatigue and shortness of breath [13]. That is why the aims of the study included the analysis of the participants' condition during the convalescence period. In the prospective study, 85.0% (n=96) of all respondents (n=113) answered the phone call. All participants agreed to complete the questionnaire by telephone. Table 4 summarizes the results of the study of the health status of respondents 3 months after discharge from the observation facility.

Table 4 also shows that the findings demonstrated a statistically significant difference with a positive response to the question of the occurrence of pain or discomfort of a different nature (head, lumbar, thoracic, etc.) (p < 0.05).

In addition, for a detailed analysis of pain or discomfort in the post-viral period, all respondents with laboratory-confirmed COVID-19 or vi-

Table 5 / Таблица 5

The frequency of pain and discomfort in the post-viral period in individuals with various forms of COVID-19 Частота встречаемости болей и дискомфорта в поствирусном периоде у лиц с различными формами течения COVID-19

Sign	Group 1 (n = 21)	Group 2 (n = 11)	Group 3 (n = 8)	p
Pain or discomfort, n (%)	4 (19.0)	3 (27.3)	3 (37.5)	0.579*

^{*}Pearson χ² test.

ral pneumonia (n=36) were stratified into three groups. Group 1 included patients with a positive oropharyngeal/nasopharyngeal swab test for SARS-CoV-2 without signs of SARS or viral pneumonia; group 2 included patients with a positive oropharyngeal/nasopharyngeal swab test for SARS-CoV-2 with signs of URTI without viral pneumonia; and group 3 included patients with viral pneumonia.

Table 5 reveals that there was no statistically significant difference in the frequency of pain and discomfort in different groups during the clinical course of COVID-19.

Conclusions

- 1. There was no statistically significant association of COVID-19 with gender, ethnolinguistic group, and chronic diseases in the study participants.
- 2. There were no statistically significant differences in the clinical symptoms of COVID-19, with the exception of sore throat, which was more common in other acute respiratory infections.
- 3. In the post-viral period, respondents with a history of COVID-19 have a higher risk of pain or discomfort, which should be studied in detail in further research.

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