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ANALYSIS OF THE IMPLEMENTATION OF CLINICAL MANIFESTATIONS OF COVID-19 IN CONTACT PERSONS

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Abstract

Introduction. The emergence of a new coronavirus infection (COVID-19) caused by the SARS-CoV-2 virus, which first appeared in December 2019, has led to a rapid spread and a global pandemic with 103 million cases reported worldwide. The clinical picture of COVID-19 develops within 14 days after infection, on average, 97,5% of people experience symptoms within 11.5 days. COVID-19 can progress from asymptomatic infection to extremely severe, critical (acute respiratory failure (ARF), acute respiratory distress syndrome (ARDS), shock, multiple organ failure syndrome (MOFS)).

Purpose of the study. To investigate the age characteristics, comorbidities and timing of the main clinical symptoms of COVID-19 in contact patients.

Methods. A retrospective study was carried out, including the collection of clinical data from electronic medical records of patients with COVID-19 who were hospitalized from March 13 to June 5, 2020, taken from the Integrated Medical Information System (CMIS) from all regions of Kazakhstan. The data obtained were processed by descriptive statistics methods.

Results. We analyzed 5326 electronic medical records of patients with COVID-19, of which 94,4% (n = 5011) patients at the time of laboratory confirmation (PCR +) had clinical manifestations of COVID-19 of varying severity, and the remaining 315 were hospitalized as contact persons with positive PCR SARS-CoV-2, in the process of further monitoring it was found that 5,6% of patients realized clinical manifestations of COVID-19 of varying severity during the period of inpatient treatment.

Conclusions. Early detection and monitoring of contact persons with COVID-19 allows the identification of patients from the "risk group" and timely treatment, which helps to reduce the risk of complications. Patients with a mild and asymptomatic course pose a high risk in the continuation of the pandemic and are the cause of a severe epidemiological situation. The results obtained show the importance of early detection, isolation and monitoring of persons in contact with COVID-19. This study with reliable and timely information obtained contributes to timely preventive, therapeutic and diagnostic measures, which contributes to a significant reduction in deaths among people of the "risk group".

Key words: coronavirus infection, COVID-19, clinical manifestations, asymptomatic course.

Резюме

АНАЛИЗ РЕАЛИЗАЦИИ КЛИНИЧЕСКИХ ПРОЯВЛЕНИЙ COVID-19 У КОНТАКТНЫХ ЛИЦ

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Резюме

Введение. Появление новой коронавирусной инфекции (COVID-19), вызванной вирусом SARS-CoV-2, впервые появившейся в декабре 2019 г., привело к быстрому распространению и глобальной пандемии с 103 млн. случаев, которые регистрировались во всех странах мира. Клиническая картина COVID - 19 развивается в течение 14 дней после заражения, в среднем у 97,5% людей симптомы реализуются в течение 11,5 дней. COVID-19 может протекать от бессимптомной инфекции до крайне тяжелой, критической (острая дыхательная недостаточность (ОДН), острый респираторный дистресс синдром (ОРДС), шок, синдром полиорганной недостаточности (СПОН)).

Цель исследования. Исследовать возрастную характеристику, сопутствующую патологию и сроки реализации основных клинических симптомов COVID-19, у контактных пациентов.

Методы. Проведено ретроспективное исследование, включающее сбор клинических данных с электронных историй болезней пациентов с COVID-19, находившихся на стационарном лечении с 13 марта по 5 июня 2020 г., взятых из Комплексной медицинской информационной системы (КМИС) со всех регионов Казахстана. Полученные данные обработаны методами описательной статистики.

Результаты. Нами проанализированы 5326 электронных историй болезней пациентов с COVID-19, из них 94.4% (n=5011) пациентов на момент лабораторного подтверждения (ПЦР+) имели клиническую манифестацию COVID-19 различной степени выраженности, а остальные 315 были госпитализированы, как контактные лица с положительным ПЦР SARS-CoV-2, в процессе дальнейшего мониторинга было установлено, что 5,6 % пациентов реализовали клинические проявления COVID-19 различной степени тяжести в период стационарного лечения.

Выводы. Раннее выявление и мониторинг контактных лиц с COVID-19 позволяют выявить пациентов из «группы риска» и провести своевременное лечение, что способствует снижению риска осложнений. Пациенты с легким и бессимптомным течением представляют высокий риск в продолжении пандемии и являются причиной тяжелой эпидемиологической ситуации. Полученные результаты показывают значимость раннего выявления, изоляции и мониторинга лиц, контактных COVID-19. Данное исследование с достоверной и своевременно полученной информацией способствует своевременным профилактическим и лечебно-диагностическим мероприятиям, что способствует существенному снижению летальных исходов среди лиц «группы риска».

Ключевые слова: коронавирусная инфекция, COVID-19, клинические проявления, асимптомное течение.

Түйіндеме

БАЙЛАНЫСТА БОЛҒАН АДАМДАРДА COVID-19 КЛИНИКАЛЫҚ КӨРІНІСТЕРІНІҢ ІСКЕ АСЫРЫЛУЫН ТАЛДАУ

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Кіріспе. Алғаш рет 2019 жылдың желтоқсанында пайда болған SARS-CoV-2 вирусынан туындаған жаңа коронавирустық инфекцияның (COVID-19) пайда болуы әлемнің барлық елдерінде тіркелген 103 миллион жағдаймен тез таралуына және жаһандық пандемияға әкелді. Covid - 19 клиникалық көрінісі инфекциядан кейін 14 күн ішінде дамиды, адамдардың орташа 97,5% - ында 11,5 күн ішінде белгілер байқалады. COVID-19 асимптоматикалық инфекциядан өте ауыр, критикалық (жедел тыныс жетіспеушілігі, жедел респираторлық стресс синдромы, шок, көп ағзалы жетіспеушілік синдромы) болуы мүмкін.

Зерттеу мақсаты. Байланыста болған пациенттерде жас ерекшелігін, қатар жүретін патологияны және COVID-19 негізгі клиникалық симптомдарының іске асырылу мерзімін зерттеу.

Әдістері. Қазақстанның барлық өңірлерінен кешенді медициналық ақпараттық жүйеден (КМАЖ) алынған 2020 жылғы 13 наурыз бен 5 маусым аралығында стационарлық емделуде болған COVID-19 бар пациенттердің электрондық ауру тарихының клиникалық деректерін жинауды қамтитын ретроспективті зерттеу жүргізілді. Алынған мәліметтер сипаттамалық статистика әдістерімен өңделеді.

Нәтижелері. Біз covid-19 бар пациенттердің 5326 электрондық ауру тарихын талдадық, олардың 94.4% (n=5011) зертханалық растау кезінде (ПТР+) пациенттердің әртурлі дәрежедегі COVID-19 клиникалық манифестациясы болды, ал қалған 315-і SARS-CoV-2 оң ПТР-мен байланыста болған адамдар ретінде ауруханаға жатқызылды, одан әрі мониторинг процесінде пациенттердің 5,6 % стационарлық емдеу кезеңінде әртүрлі ауырлықтағы COVID-19 клиникалық көріністерін жүзеге асырғаны анықталды.

Тұжырымдар. COVID-19-бен байланыста болған адамдарды ерте анықтау және бақылау "қауіп тобындағы" пациенттерді анықтауға және уақтылы емделуге мүмкіндік береді, бұл асқыну қаупін азайтуға көмектеседі. Жеңіл және асимптоматикалық курспен ауыратын науқастар пандемияның жалғасуында жоғары қауіп тудырады және ауыр эпидемиологиялық жағдайдың себебі болып табылады. Алынған нәтижелер COVID-19 байланысатын адамдарды ерте анықтау, оқшаулау және бақылаудың маңыздылығын көрсетеді. Дұрыс және уақтылы алынған ақпараты бар осы зерттеу уақтылы алдын алу және емдеу-диагностикалық іс-шараларға ықпал етеді, бұл "тәуекел тобындағы" адамдар арасындағы өлім-жітімді едәуір төмендетуге ықпал етеді.

Түйінді сөздер: коронавирустық инфекция, COVID-19, клиникалық көріністер, асимптоматикалық күрс.

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Introduction

The emergence of a new coronavirus infection (COVID-19) caused by the SARS-CoV-2 virus, which first appeared in December 2019, (Wuhan, China) led to a rapid spread and a global pandemic with 103 million cases reported in all countries of the world [8].

According to official statistics to date, in the United States of America (USA), the incidence rate has reached 26 million people, of which the mortality rate is 2,1%. [27]. Italy has 2.54 million registered cases, with a death rate of 3.8%. Data for the Russian Federation (RF) show 3.79 million people, with a death rate of 2.2%. In the Republic of Kazakhstan (RK), the first cases of COVID-19 (SARS-CoV- 2) were registered on March 13, 2020 and today, according to statistics, the number of cases has increased to 235.000. of which approximately 1,5-2% are children, the mortality rate was 1.5% of the total number of cases. This infection, taking into account its molecular and biological features, and the variability of the clinical course, is associated with a high risk of developing critical conditions, complications, and high mortality [5].

The disease patterns of COVID - 19 develops within 14 days after infection, on average, 97.5% of people have symptoms of infection within 11,5 days [8,5,15]. The symptoms of COVID - 19 vary from an asymptomatic infection to an extremely severe, critical one (AHRF, ARDS,

shock, MODS) [5,10,15]. Common symptoms of the disease may include: fever, cough, fatigue, shortness of breath, sore throat, headache, and conjunctivitis [5,15]. Therefore, it is difficult to distinguish COVID-19 from other respiratory diseases [16,22,31].

The defeat of the gastrointestinal tract, accompanied by diarrhea, nausea and vomiting, is noted in a smaller number of cases. It should be noted that in 80-90% of cases, there is a mild or asymptomatic course of infection, which in about 10% of patients at various times from the moment of infection is realized in a severe course with shortness of breath, hypoxemia and extensive (> 50%) radiological damage to the lung parenchyma. Critical condition with respiratory failure, pneumonia, shock, develops in about 5% of cases, accompanied by a fatal outcome, which almost always occurs as a result of the progression of acute respiratory distress syndrome and multiple organ failure [10,23,26].

Among hospitalized patients, about 10-20% enter the intensive care unit (ICU), 3-10% need intubation, and 2-5% die [30]. There is evidence that the mortality rate from COVID-19 is about 3% [9], which is therefore lower than from SARS-CoV (10%) and MERS-CoV (35%). However, given the relatively recent and rapid spread of COVID-19, it may be too early to determine the actual death rate from this disease. Current data show that the main risk factors for an adverse outcome include age, coronary heart disease, hypertension, diabetes mellitus, and chronic lung disease [13].

Patients with prolonged, delayed onset of the disease pose a high risk of continuing the pandemic and are the cause of a severe epidemiological situation in all countries.

Research Objective: to investigate the age characteristics, concomitant pathology, and timing of the main clinical symptoms of COVID-19 in contact patients.

Research materials

Study design: a retrospective, one-step study. Patient information (clinical data) is extracted from the database of

the integrated medical information system (IMIS) from all regions of Kazakhstan, formed on the basis of electronic medical records (5326) of patients with COVID-19 who were on inpatient treatment from March 13 to June 5, 2020.

Inclusion criteria: positive PCR analysis for the presence of SARS-CoV-2 nucleic acid, no clinical symptoms at the time of examination.

Indicators of descriptive statistics are calculated using the MS Excel analysis package.

Results

We analyzed 5326 electronic medical records of patients with COVID-19, of which 94,4% (n=5011) of patients at the time of laboratory confirmation had a clinical manifestation of COVID-19 of varying severity, the remaining 315 were hospitalized as contact persons with positive PCR SARS-CoV-2, in the course of further monitoring, it was found that 5.6 % of patients realized clinical manifestations of COVID-19 of varying severity during inpatient treatment.

An important task of epidemiological surveillance of infectious diseases for all countries is to identify the population groups that are most actively involved in the epidemic process. Our analysis of the age structure presented in Figure 1 showed that the highest percentage of morbidity was observed among the age group of 20-29 years and amounted to 26,7% of cases (n=84). Significant differences in the proportion of disease in age groups: 30-39 (17,1%), 40-49 years (19,4%), 50-59 years (17,1%) were observed, the same percentage of registered patients aged 10-19 years and 60-69 years was observed in 5,4% respectively, 3,2 % of cases (n=10) COVID-19 was observed in patients older than 80 years, not significantly different from age group of children aged 1-9 years (2,9%) and the minimum number of occurrence of the disease was observed in children under one year and 1.6% (n=5) and among those aged 70-79 years was 1,3% (n=4). Figure 1.

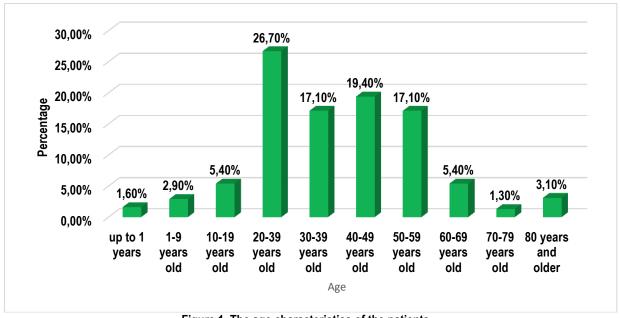


Figure 1. The age characteristics of the patients.

Our data coincide with the results of a study by Russian scientists, where the average age of COVID-19 patients was (46.41 \pm 20.58) (from March to July 2020). Patients with COVID-19 were characterized by a predominance of mainly middle-aged and elderly people. Most often, COVID-19 was registered in the age groups "40-59 years" and "19-39 years" – 35,7 % (35,5–35,9 %) and 30,8 % (30,6–31.0%), respectively [1]. Figure 2.

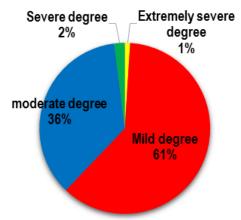


Figure 2. Severity of COVID-19 in patients

Of the 315 patients, clinical manifestations of varying severity were observed in 95,6% (n=301) of the patients. Accordingly, the remaining 14 patients did not realize any clinical manifestations and were attributed to asymptomatic viral transmission (4,4%). According to the clinical protocol for the diagnosis and treatment of COVID-19, a complex laboratory and instrumental examination was conducted,

based on the data of which the severity of the patients was determined (Figure 2). It is revealed that at 61,1% were prevalent lung disease (n=184), moderate degree was observed in 35,9% of patients (n=108), severe degree was noted in 2% of cases (n=6), noteworthy that in 1% of cases (n=3) patients required ICU due to the extremely severe course of the disease, given that all of them belong to the age group of 60 years and older and had a history of comorbidities in diabetes, obesity and hypertension.

Time of symptoms onset (day).

Table 1.

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Nº	Symptoms	Number of	Number of
	onset (day)	cases (abs.)	cases (%)
1	1-3	220	73
2	4-7	54	17,9
3	8-14	22	7,4
4	15-23	5	1,7
	Total:	301	100%

As shown in Table 1, the implementation of clinical manifestations in pre-symptomatic patients at the time of hospitalization in most cases, 73 % (n=220), occurred in the first three days of hospitalization, during the first week (from 4-7 days of hospitalization), the manifestations of the disease were noted in 17,9% of cases (n=54), in 7.4% of patients, symptoms appeared in the period from 8 to 14 days of hospital stay, the later onset of symptoms characteristic of COVID-19, the onset of which was registered between 15-23 days in 1,7% of patients (n=5). Figure 3.

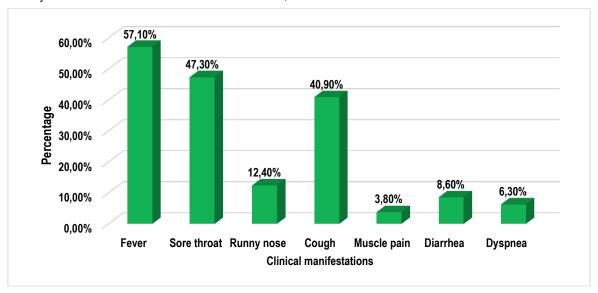


Figure 3. Clinical implications in patients with COVID-19.

According to the clinical protocol "Coronavirus infection-COVID-19", the characteristic clinical manifestations for this disease are: upper respiratory tract lesions (rhinitis, pharyngitis), lower respiratory tract lesions (COVID-associated pneumonia), extrapulmonary COVID-associated lesions (gastroenteritis, nephritis, myocarditis, olfactory nerve neuritis, meningitis, encephalitis, polyneuropathies, etc.). Among the analyzed patients, as shown in Figure 3,

the following clinical symptoms were registered with the highest frequency: more than half of the patients 57,1% had an increase in body temperature (n=171), sore throat and cough were observed in every second patient, and amounted to 47,3% and 40,9%, respectively, in significantly less frequent cases – runny nose (12,4%), diarrhea (8,6%), difficulty breathing (6,3%) and muscle pain - in 3,8% of patients. Figure 4

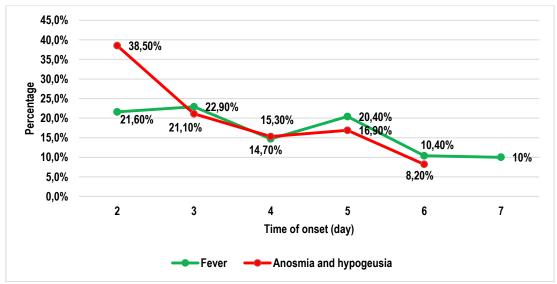


Figure 4. Time of onset (day) of fever, olfactory dysfunction and dysgeusia.

The time of onset of the reaction temperature from "presymptomatic" at the time of hospitalization of patients ranged from 2 to 7 days, while of the 171 patients, who had a fever the highest rates of implementation of this symptom of 22,9% (n=39) were observed on the 3rd day of hospitalization, in 21,6% (n=37) notes her onset on 2 day hospital stay, at least, the onset of temperature on day 4, which was 14,7% (n=25), with subsequent growth on day 5 – 20,4% (n=35), there was also a more delayed onset of this sign in the clinic, so on the 6th and 7th day of hospitalization, there was a relatively uniform initial registration of elevated temperature, which was 10.4% (n=18) and 10% (n=17), respectively.

Olfactory dysfunction (OD) - hyposmia and anosmia-is an important symptom of COVID-19 and is increasingly being used as a public health tool to identify COVID-19 patients, in particular asymptomatic carriers, who may unknowingly be the main drivers of the spread of the disease [3]. According to the results of our studies, all patients have a combination and simultaneous onset of OD

and dysgeusia. The highest of these symptoms is noted during the 2nd day of hospitalization, which is 38,5% (n=66) of the total number of patients celebrating the clinical symptom (n=134), some 21,1% (n=36), the changes observed on the 3rd day of hospitalization, 15.3 (n=26) and 16,9% (n=19) changes in the perception of taste and smell appear on 4 and 5 days hospital stay, respectively, OD and dysgeusia 8,2% was observed in patients after a week (6-day) after identifying a positive PCR for SARS-CoV-2.

Given the significant detection rate of OD and dysgeusia, this indicator may increase the sensitivity of COVID-19 screening strategies, in particular, to identify patients at the earliest stages of the disease. Despite the fact that the pathogenetic mechanism of olfactory dysfunction and its clinical characteristics in patients with COVID-19 remain unclear. Multiple cross-sectional studies conducted in the world have shown that the frequency of blood pressure in patients with COVID-19 ranges from 33,9 to 68% with a predominance of women [28]. Figure 5

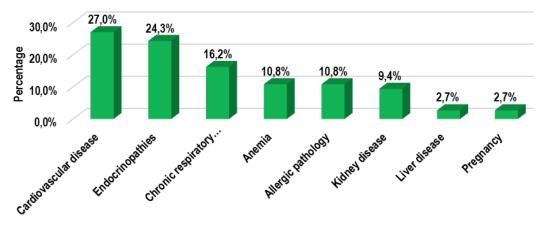


Figure 5. Background pathology in patients with COVID-19.

Of the 315 contact persons with a positive PCR result for SARS-CoV-2 at the time of hospitalization, 74 were found to have comorbidities. In the structure, diseases of the cardiovascular system prevailed, and amounted to 27%, chronic respiratory diseases were observed in 16,2% of patients, endocrinopathy occupied 24,3%, of which the

share of diabetes mellitus accounted for 8,1%, obesity was three times less (2,7%), with the same frequency: anemia and a burdened allergic background of 10,8%, respectively, concomitant pathology from the kidneys was observed in 9.4% of patients, liver diseases accounted for 2,7%. It should be noted that in 2,7% of cases, COVID-19 occurred

during pregnancy and the identified clinical manifestations in some cases occur in combination with each other.

Discussion of the results

Pandemic COVID-19 has caused a huge crash in the world, while molecular biological characteristics and variability of the clinical course, high risk of development of critical conditions, complications and significant mortality level [5].

Contact persons with positive PCR for SARS-CoV-2, and patients with an asymptomatic course of the disease pose a high risk of continuing the pandemic and are the cause of a severe epidemiological situation in all countries. The above data show the importance of proper management of patients with an asymptomatic course of COVID-19. Up-to-date, reliable, and timely data can help decision-makers better understand the situation and implement the necessary measures.

The asymptomatic course of COVID-19 is currently receiving a lot of attention, but its frequency remains unclear. A study conducted by American scientists showed that 55 asymptomatic carriers with confirmed SARS-CoV-2 infection at subsequent admission eventually had different symptoms and mainly a mild course of the disease, asymptomatic infection was noted mainly in young patients aged 18 to 29 years [25]. Another study involving 634 patients infected with COVID-19 on a cruise ship in Japan found that 17.9% of those examined were asymptomatic [20].

The analysis of the age structure in our study showed that the highest percentage (26,7%) of morbidity was observed among the age group of 20-29 years, and relatively the same level was observed in the age categories: 30-39 years (17,1%), 40-49 years (19,4%), 50-59 years (17,1%).

In our opinion, the obtained age ratio of COVID-19 cases is associated with the predominance of people of the most working age (20-59 years), and not with the features of SARS-CoV-2, which coincides with the data of Russian scientists [2].

The high rate of human-to-human transmission of SARS-CoV-2 [17] is partly due to the pronounced transmission during the pre-symptomatic course of the disease [11], when infection reaches a peak.

According to British scientists Eggo et. Al., in May 2020, only 20% of children under the age of 18 show symptoms of the disease. According to the results of a meta-analysis conducted by researchers from India co-authored by Meena., 91% (87-95%) of children had a history of contact with a SARS-CoV-2 infected patient. The results of seventeen studies showed that in 23% (17-30%) of cases, patients were asymptomatic. Twenty-three studies (n-1330) reported data on specific symptoms, where fever was the most common clinical sign and was observed in almost half of the patients, 45% of the patients had a cough, and only 11% had rapid breathing, and 4-9% had gastrointestinal manifestations. Most of these patients had mild to moderate disease severity (96%), with a very small proportion of patients having severe manifestations (3%), such as hypoxia, dyspnea, and cyanosis. Only 1% of all clinically confirmed cases were severe (acute respiratory distress syndrome, respiratory failure, shock, encephalopathy, myocardial injury or heart failure, acute kidney injury, etc.).

In the analyzed patients, mild (61,1%) and moderate (35,9%) course of the disease prevailed in terms of severity, but it should be noted that the severe degree occurred in 2% of cases (n=6), while 1% of patients (n=3) needed ICU due to the extremely severe course of the disease, given that this category of patients belong to persons 60 years and older and has a history of concomitant diseases in the form of diabetes, obesity and hypertension.

In a retrospective study by Klopfenstein et. al., 54 (47%) of 114 confirmed COVID-19 patients had anosmia [14]. The study also showed that anosmia in patients usually developed 4.4 days after the onset of SARS-CoV-2 infection with a duration of 8.96 days, while olfactory function in 98% of patients was restored within 28 days [14.19].

In our study, there is an earlier occurrence of OD with the highest rate of these symptoms on day 2 of hospitalization (38,5%), while all patients have a combination and simultaneous onset of OD and dysgeusia.

Data from a multicenter study conducted in patients with laboratory-confirmed COVID-19 infection, who were recruited from 12 European hospitals, showed that a total of 417 patients with mild to moderate COVID-19 were registered. Runny nose and nasal congestion were the most common catarrhal manifestations associated with the disease. While 85.6% and 88.0% of patients reported olfactory and taste dysfunction, respectively. There was a significant association between both disorders (p <0.001). OD appeared earlier than other symptoms in 11,8% of cases [12].

The vast majority of cases of SARS-CoV-2 infection are associated with contact-household transmission of the virus in the families of infected people with asymptomatic forms of COVID-19 [4,6,7,18,21].

According to the clinical Protocol of the Republic of Kazakhstan examination of the contact includes only the definition of PCR for COVID-19, while computer tomography (CT) of the lungs is not provided in the absence of implementation of clinical manifestations, but in individuals with no clinical manifestations, even in case of a positive PCR test may be significant changes in the lung on CT.

According to the author Nicole Varble et al., the importance of the significance of the asymptomatic population of people with a positive SARS-CoV-2 test was revealed, taking into account their study using early chest CT, which can clarify the dynamics of transmission. A better understanding of chest CT in an asymptomatic population with COVID-19 may provide information for predictive modeling or elucidate the potential role of CT as an epidemiological tool to contain or mitigate outbreaks. In their study, chest CT scans were analyzed in initially asymptomatic patients with a positive polymerase chain reaction to SARS-CoV-2. CT results were correlated with clinical and laboratory features and subsequent symptoms to characterize the nature of SARS-CoV-2 virus infection in the outbreak [24].

The importance of screening contact persons remains relevant, and according to Chinese scientists Xingfei Pan et al., in order to prevent and control COVID-19, it is necessary to examine and observe infected SARS-CoV-2 as early as possible, despite the absence of symptoms [29].

Given the ongoing COVID-19 pandemic, it is necessary to conduct similar studies, with an in-depth study of contact persons and patients with an asymptomatic course.

Conclusions

The analysis of the age structure showed that among the studied patients who were admitted without symptoms, as a rule, people of the most working age predominate. The highest percentage (26,7%) of morbidity was observed among the age group of 20-29 years, and relatively the same level was observed in the age categories: 30-39 years (17,1%), 40-49 years (19,4%), 50-59 years (17,1%).

When assessing the severity, it was revealed that 5.6 % of those initially admitted as contacts with positive PCR for SARS-CoV-2 subsequently implemented a clinic during their hospital stay with mild, moderate and severe severity, while 1% of patients (n=3) needed ICU due to the extremely severe course of the disease.

The study of the relationship of the severity and structure of chronic diseases, showed that the severity of the disease increases with increasing age and presence of comorbidities, among which are prevalent cardiovascular disease (27%), and endocrinopathies (24,3%).

Contact persons with positive PCR for SARS-CoV-2, and patients with an asymptomatic course of the disease pose a high risk of continuing the pandemic and are the cause of a severe epidemiological situation in all countries.

Early detection and monitoring of contacts with COVID-19 allows you to identify patients from the "risk group" and conduct timely treatment, which helps to avoid complications. Patients with a mild course and asymptomatic patients pose a high risk in the continuation of the pandemic and are the cause of a severe epidemiological situation. The results show the importance of early detection, isolation, and monitoring of COVID-19 contacts. This study, with reliable and timely information obtained, contributes to timely preventive and therapeutic and diagnostic measures, which would significantly affect the reduction of deaths among persons of the "risk group".

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Mynzhanova A. - the collection of data, writing of the draft articles, management of resources study.

Baesheva D.A. - scientific guidance, concept and conceptualization of research.

Omarova A.K., Khamitova M.O., Dauylbaeva A.U. - data set. Turdalina B.R., Seidullaeva A.J., Altynbekova A.V., Zhuzzhasarova A.A. - scientific management and scientific support article, revision of the draft articles, formal analysis.

Kirpicheva U.A. - statistical processing of the material.

Kushugulova A.R., Kozhakhmetov S.S.-critical analysis, scientific support of the article, revision of the article.

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