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EPIDEMIOLOGY OF THE INITIAL PERIOD OF NOVEL CORONAVIRUS (COVID-19) PANDEMIC IN THE REPUBLIC OF MOLDOVA

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Keywords: *COVID-19, infection, Republic of Moldova, prevention, epidemiological study.*

Introduction. *In the Republic of Moldova, the first case of COVID-19 was confirmed on March 7, followed by a significantly increasing incidence across the country. It is important to describe the clinical and epidemiological aspects that were adjusted to the national context in order to develop and implement optimal public health care measures.*

Material and methods*. A cross-sectional descriptive study was conducted from March 7 to April 6, 2020, using the surveillance system data of the Republic of Moldova on COVID-19 case incidence. All cases of COVID-19 were confirmed by Real-Time PCR.*

Results. *During the reference period, 965 cases of COVID-19 were registered, whereas the urban incidence rate was 1.4 times higher than the rural one. The mean age of infected population was 45.2 years, whereas the most affected age group was 50-59 years, found in 232 cases. Healthcare workers made up 26.6±1.4% out of 965 diseased patients. They included nurses – 34.2±3.0%, auxiliary medical staff – 29.6±2.8%, doctors – 27.2±2.8%, first-aid assistants – 7.4±1.6%, pharmacists – 1.2±0.7%, paramedics – 0.4±0.4%. The health status of people diagnosed with COVID-19 was severe in 8.0±0.9% of cases; moderate severity – in 34.7±1.5% and satisfactorily severe – in 57.3±1.6% of cases.*

Conclusions. *The identified clinical and epidemiological aspects allowed readjusting the public health policies in order to prevent the spread of COVID-19 infection among the elderly and medical workers.*

Cuvinte cheie: *COVID-19, infecție, Republica Moldova, prevenire, studiu epidemiologic.*

EPIDEMIOLOGIA INFECȚIEI CU NOUL TIP DE CORONAVIRUS (COVID-19) ÎN PERIOADA INIȚIALĂ A PANDEMIEI ÎN REPUBLICA MOLDOVA

Introducere. *Primul caz de infectare cu noul tip de coronavirus COVID-19 în Republica Moldova a fost confirmat la data de 7 martie 2020, ulterior a fost înregistrată o creștere semnificativă a îmbolnăvirilor. Aspectele clinico-epidemiologice ajustate contextului național sunt necesare a fi descrise pentru elaborarea și implementarea acțiunilor optime de sănătate publică.*

Material și metode. *Am realizat un studiu descriptiv transversal în perioada 7.03.2020 – 6.04.2020, folosind datele din sistemul de supraveghere a Republicii Moldova cu privire la cazurile de infecție COVID-19, care au fost confirmate prin tehnici de biologie moleculară (Real-Time PCR).*

Rezultate. *În perioada de referință au fost înregistrate 965 cazuri de COVID-19, mediul urban fiind afectat de 1,4 ori mai mult decât cel rural. Vârsta medie a celor infectați a fost de 45,2 ani, iar cel mai afectat grup de vârstă a fost cel de 50-59 ani – 232 cazuri. Dintre cele 965 persoane infectate, lucrătorii medicali reprezintă 26,6±1,4%: asistenți medicali – 34,2±3,0%; personal medical auxiliar – 29,6±2,8%; medici – 27,2±2,8%; felceri – 7,4±1,6%; farmaciști – 1,2±0,7%; paramedici – 0,4±0,4%. Starea de sănătate a persoanelor diagnosticate cu COVID-19 a fost gravă în 8,0±0,9%, de gravitate medie în 34,7±1,5% și satisfăcătoare în 57,3±1,6%.*

Concluzii. *Aspectele clinico-epidemiologice identificate permit reajustarea politicelor de sănătate publică referitor la prevenirea răspândirii infecției COVID-19 printre persoanele în vârstă și lucrătorii medicali.*

INTRODUCTION

Coronavirus belongs to a large family of viruses that can cause various symptoms such as pneumonia, fever, shortness of breath and lung infection (1). These viruses are common in animals around the world but are known to affect humans in some cases. Although coronaviruses are a large family of viruses, it is considered that only six (229E, NL63, OC43, HKU1, MERS-CoV, and SARS-CoV) could infect humans. Thus, 2019-CoV became the seventh (2, 3).

The World Health Organization (WHO) used the term new coronavirus 2019 to refer to a coronavirus that affected the lower respiratory tract of patients with pneumonia in Wuhan, China, on December 29, 2019 (4, 5, 6). The WHO has announced that the official name of the new type of coronavirus in 2019 is COVID-19 – coronavirus disease (6).

And the current reference name for the virus is Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). This is a single-stranded RNA coronavirus with positive polarity. The virus underwent a genomic sequence, following the nucleic acid testing on specimens from a patient with pneumonia during the 2019-2020 Wuhan coronavirus epidemic. Wuhan beta-coronavirus sequences have similarities to the beta-coronaviruses identified in bats. However, the virus is genetically distinct from other coronaviruses, such as SARS-CoV and MERS-CoV (7).

At the end of December 2019, a group of patients was hospitalized with an initial diagnosis of pneumonia with an unknown etiology. These patients have been epidemiologically related to a seafood and wet animals wholesale market in Wuhan, Hubei Province, China (8). Early reports predicted the emergence of a potential Coronavirus outbreak, by estimating the reproduction number of the novel Coronavirus (COVID-19, named by the WHO on 11 February 2020) as being significantly higher than 1 (intervals from 2.24 to 3.58) (9).

By April 6, 2020, more than 134,901 people were infected worldwide, by affecting almost every country across the globe. Moreover, at the beinning of April, the mortality rate was calculated in the following countries like Germany, this index being of 1.2%, compared to Italy – 11.9%, Spain – 8.6%, the Netherlands – 8%, the United Kingdom – 7.1% and France – 9.0% (10, 11). However, the overall mortality rate accounted for 2.2-3.4% (12).

Globally, about 3.4% of reported COVID-19 cases have died. By comparison, seasonal flu generally kills much less than 1% of those infected (13, 14). Virus susceptibility appears to be associated with age, gender and other health conditions (15). COVID-19 has now been declared by the WHO as public health emergency of international concern (16).

Due to the rapid spread of the new coronavirus and its effects on human health, the scientific community responded quickly to the new virus and many early research studies have already been published on this epidemic (9-14). This article is aimed to provide information and evidence on the evolution of the COVID-19 epidemic in the Republic of Moldova at its initial stage. This article can provide meaningful information for future research on this topic and justify the governmental decision-making on management strategies regarding this public health emergency at both community and national level. The combination of epidemiological data can provide an early understanding of the pandemic situation, thus promoting a balanced and well-targeted action from public health perspective.

MATERIAL AND METHODS

The present cross-sectional descriptive study was conducted from March 7 – April 6, 2020. The national surveillance system data of the Republic of Moldova have been reported cases based on standard case definition, namely, COVID-19 suspected, possible or confirmed cases during the initial stage of the epidemic. All cases of COVID-19 were confirmed via molecular biology (Real-Time PCR) techniques. The confirmed case definition was used according to the national legislation in force, namely "A person with laboratory confirmation of COVID-19 infection, regardless of clinical signs and symptoms." The statistical data have been processed via MicrosoftExcel and EpiInfo 7.2.

RESULTS

The first suspected COVID-19 case in the Republic of Moldova was reported on March 7, fol lowed by laboratory confirmation on 08 March in a person who entered the country. In the following

week, there was a steady increasing daily tendency, with unique cases being registered. A constant increase in the number of cases were reported over the next 2 weeks, viz. tens of newly-infected people per day, so that over the last week there was a sudden increase in the number of cases, being estimated to around 100 cases per day. On April 6.965 cases were registered, whereas 101 cases had been reported a day before (fig. 1).

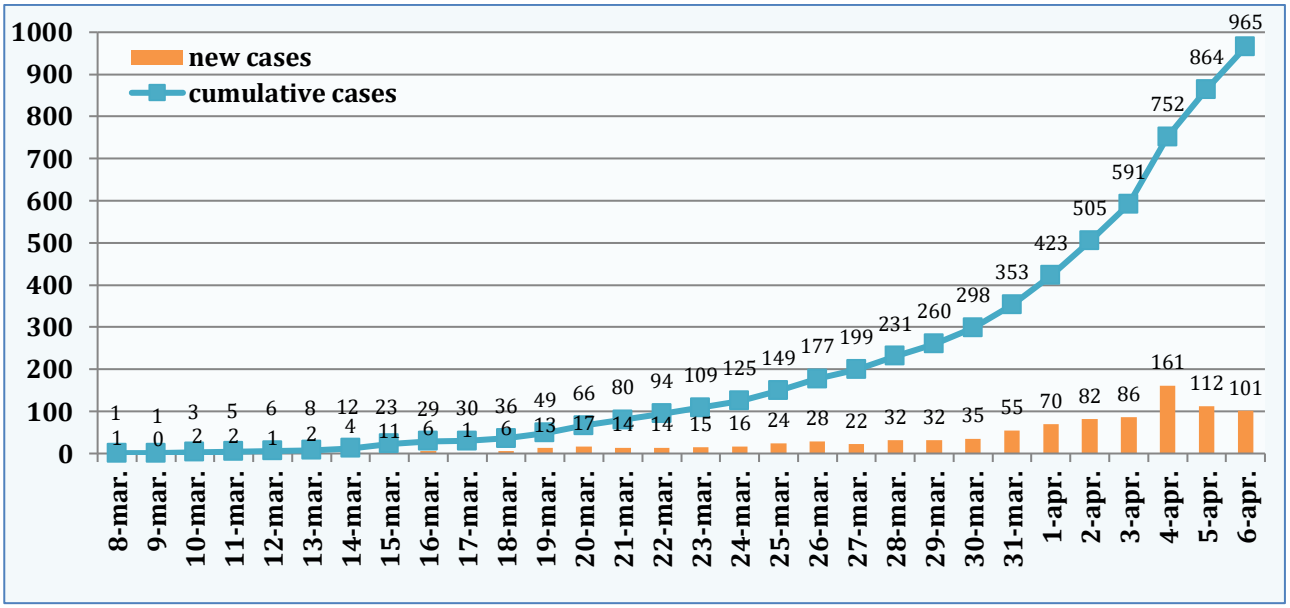

Figure 1. Number of new and cumulative cases of COVID-19 reported in the Republic of Moldova during the reference period (abs.).

However, along with the increasing number COVID-19 cases, various laboratory diagnostic activities were conducted in this regard (fig. 2).

The present data confirms that according to the case definition for COVID-19 infection, a signifycant number of people underwent testing. The number of investigations was continuously increasing until April 4, 2020, when it was at highest, when 681 investigated samples were performed. Afterwards on April 5 and 6, the number of tests decreased, more likely because these were the weekend days. It should be mentioned that an overall number of 4,598 tests have been performed so far, within the Virology laboratory of NAPH.

The geographical distribution of COVID-19 cases was also assessed, in order to identify the virus spreading intensity. Therefore, on April 6, 2020, almost all the administrative territories of the country were affected, except for Soldanesti and Rezina districts.

The highest levels of COVID-19 incidence were recorded in the following regions: Ștefan Vodă – 213.27‰ (148 cases), Soroca – 125.73‰ (125 cases), and Glodeni – 61.34‰ (36 cases). A high incidence rate was found in Chisinau – 37.94‰ (316 cases). As regarding the geographical distribution, the most affected were the Southern areas – 41.64‰ (219 cases), followed by the Northern areas – 37.94‰ (222 cases), and the Central areas – 14.51‰ (152 cases). The incidence rate in the administrative territories with special status, namely, ATU Gagauzia was 1.24‰ (2 cases), and Transnistria – 11.53‰ (54 cases) (tab. 1).
Therefore, the major outbreaks registered at this stage of the epidemic, also called as community transmission, occurred mainly in Chisinau, and Soroca and Stefan-Voda districts. The massive spread of disease was reported in Glodeni district.

During the initial period of the epidemic, the total number of people infected with the novel coronavirus accounted for 385 patients from rural areas and 539 patients from urban areas. Therefore, the incidence rate made up 41.7±1.6% cases – rural areas and 58.3±1.6% – urban areas, respectively. This phenomenon is probably due to the massive internal and exter

nal migration of people from urban areas, as well as due to a higher contact level among people in places with high population density and urban activities associated with people behavior and mass-gathering (fig. 3).

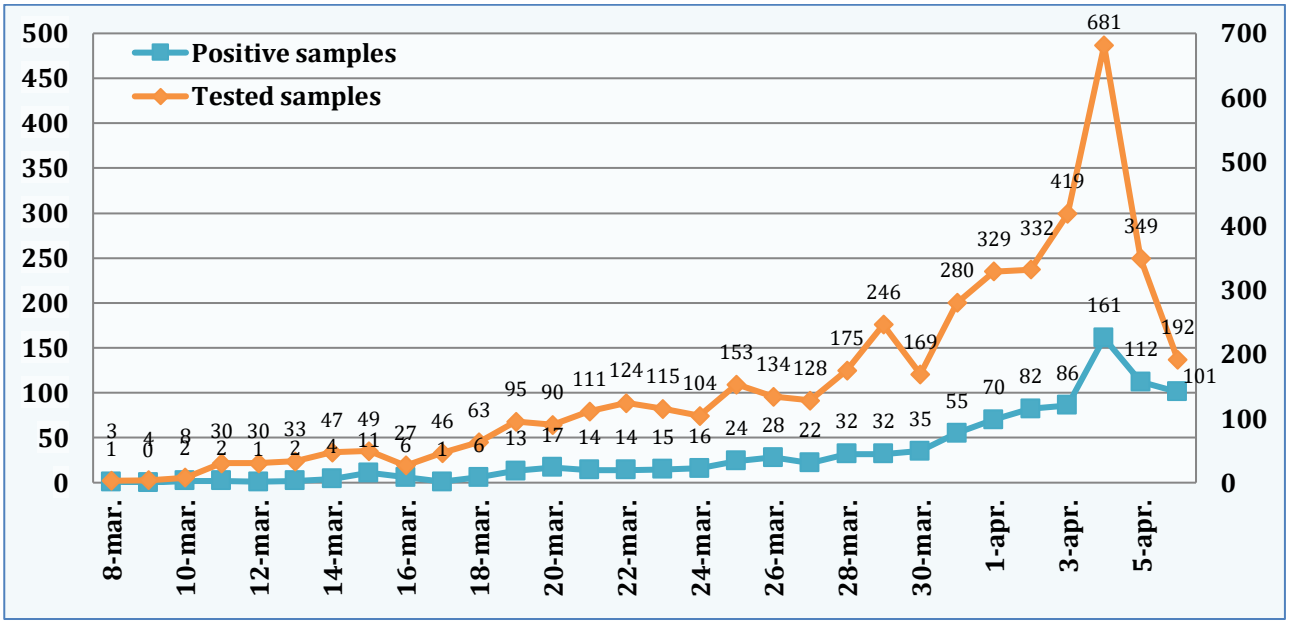

Figure. 2. Number of persons tested and found positive to COVID-19 in the Republic of Moldova, during the reference period (abs.).

Table 1. Geographical distribution of COVID-19 cases in the early stages of the epidemic in the Republic of Moldova (abs. and ‰).

Administrative territory	Number of population	Number of cases	Incidence
Chisinau	**832,865**	**316**	**37.94**
Northern areas	**974,558**	**222**	**22.78**
Balti	151,791	10	6.59
Briceni	71,447	4	5.60
Donduseni	41,719	1	2.40
Drochia	85,558	2	2.34
Edinet	79,160	5	6.32
Falesti	90,275	20	22.15
Floresti	85,643	2	2.34
Glodeni	58,691	36	61.34
Ocnita	52,948	1	1.89
Riscani	66,498	5	7.52
Singerei	91,412	11	12.03
Soroca	99,416	125	125.73
Central areas	**1,047,681**	**152**	**14.51**
Anenii Noi	82,998	12	14.46
Calarasi	76,551	4	5.23
Criuleni	73,371	6	8.18
Dubasari	34,969	1	2.86
Hincesti	118,619	32	26.98
Ialoveni	101,797	36	35.36
Nisporeni	64,797	10	15.43
Orhei	124,007	30	24.19
Rezina	49,891	0	0.00
Straseni	92,052	5	5.43

Soldanesti	40,942	0	0.00
Telenesti	70,982	10	14.09
Ungheni	116,705	6	5.14
Southern areas	**525,928**	**219**	**41.64**
Basarabeasca	27,997	1	3.57
Cahul	124,091	32	25.79
Cantemir	61,317	8	13.05
Causeni	89,356	13	14.55
Cimislia	58,604	3	5.12
Leova	51,990	2	3.85
Stefan-Voda	69,394	148	213.27
Taraclia	43,179	12	27.79
ATU Gagauzia	**161,676**	**2**	**1.24**
Transnistria	**468,414**	**54**	**11.53**
Total cases in cities	**984,656**	**326**	**33.11**
Total cases in districts	**2,558,052**	**585**	**22.87**
Total cases per Republic	**3,542,708**	**965**	**27.24**

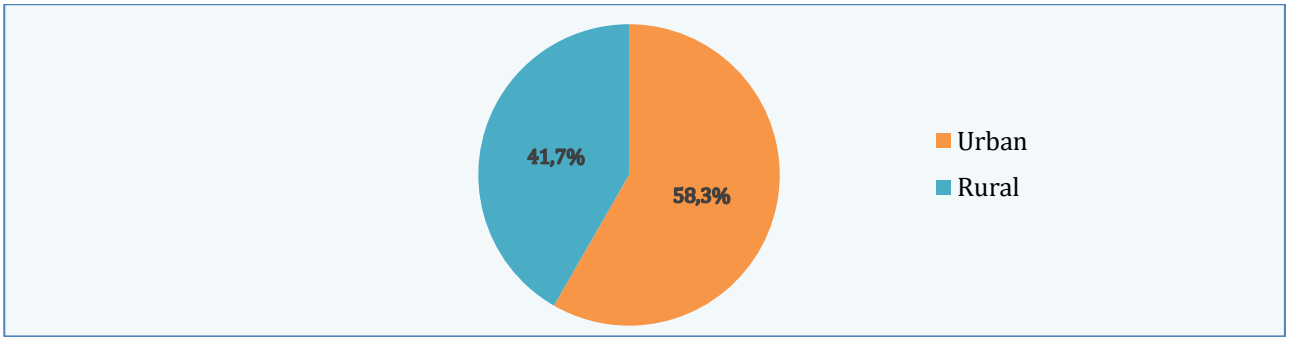

Figure 3. Distribution of COVID-19 cases depending on the living areas of the infected persons during the reference period in the Republic of Moldova (in %).

The average age of those infected was 45.2 years; the mean age for COVID-19 infected people from urban areas was 44.6 years, while those from rural areas – 46.1 years. The mean age of COVID-19 infected men was 42.9 (386 people) and infected women – 46.7 years (575 people).

According to gender distribution, 244 infected women and 141 infected men were from rural areas, which made up 63.4±2.5% vs. 36.6±2.5%, respectively. 316 COVID-19 infected women and 223 men were from urban areas, accounting for 58.6±2.1% vs. 41.4±2.1%, respectively. Thus, these data confirmed that gender distribution depending on the living environment presents a statistically significant difference ($p \leq 0.05$) (fig. 4).

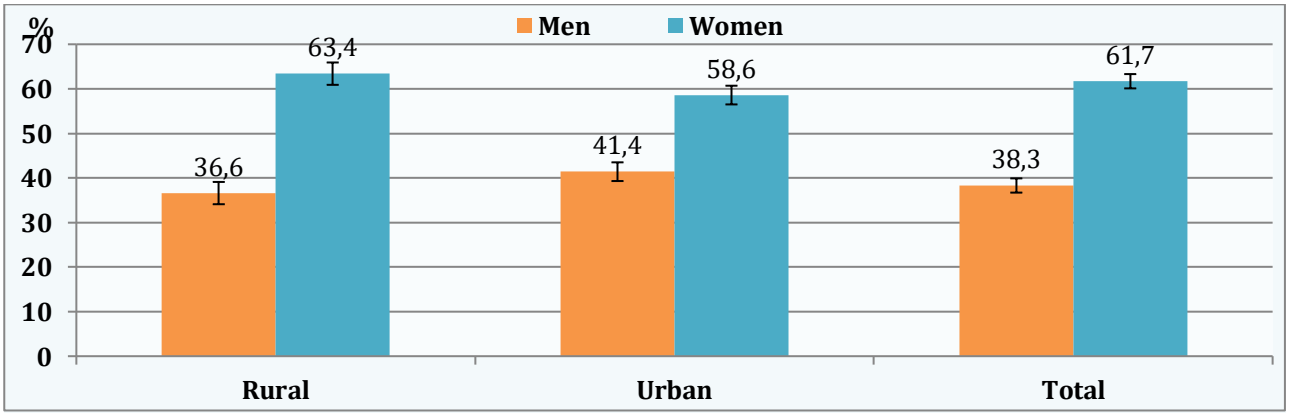

Figure 4. Gender distribution of infected persons depending on their living areas in the initial pandemic stages in the Republic of Moldova (in %).

Out the total number of women, 11 women were found pregnant, which made up 1.9% of pregnancy cases. Furthermore, 2 people pregnant were reported as being in the first trimester (25%), 5 pregnant women were in the second trimester of pregnancy (62.5%), and only one woman was in the third trimester of gestation (12.5%).

The study of age-related COVID-19 distribution showed that the most affected were people aged 50-59 years, which included 232 cases, followed by people aged between 40-49 years found in 170 COVID-19 cases. People aged 30-39 years were ranked third among total number, found in 152 confirmed cases, followed by a small difference in-group of people aged 60-69 years, accounting for 147 of infected cases. The least number of infected cases were reported in children (0-9 years) with a total of 37 cases and in those older than 80 years, where only 6 cases were recorded (fig. 5).

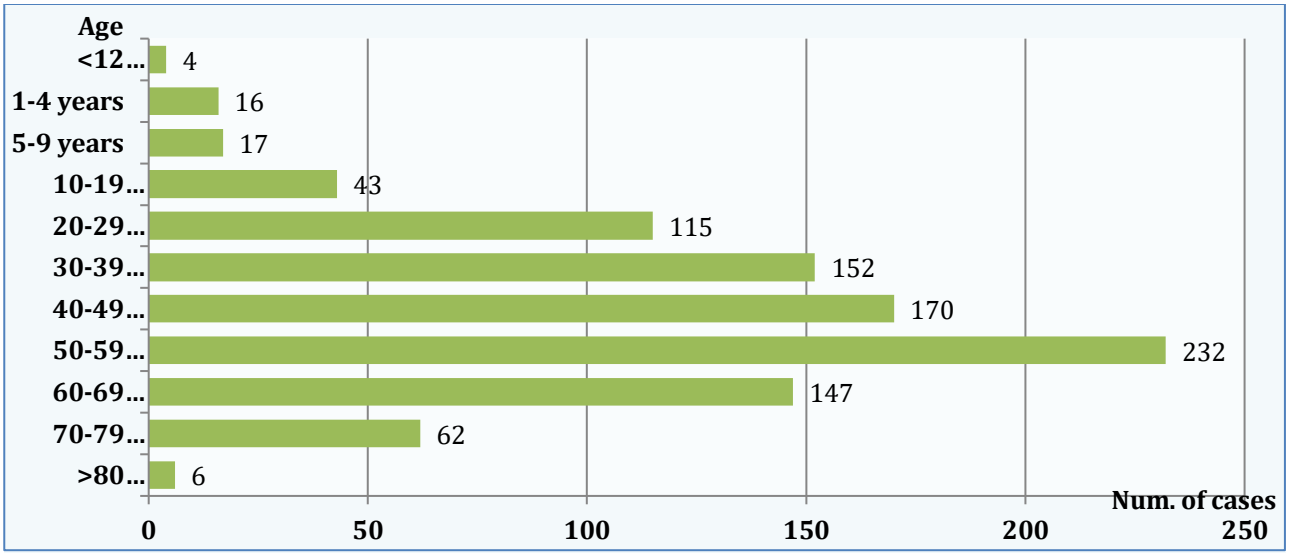

Figure 5. Age distribution of COVID-19 cases recorded during the reference period in the Republic of Moldova (abs.).

Another important epidemiological aspect included within the study refers to people traveling abroad in the last 14 days before the onset of disease. Therefore, the distribution of people who traveled abroad within 14 days before the onset of the disease was 20.2±1.6% (129 cases); those who did not travel abroad 79.8±1.6% (510 cases); those who traveled or admitted to have been in contact with a confirmed case of COVID-19 abroad – 22.7±4.0% (25 cases); 43.7±4.7% (48 cases) could not confirm or deny being in contact with infected people; 33.6±4.5% (37 cases) stated that they were not in contact with a confirmed case of COVID-19 abroad (fig. 6).

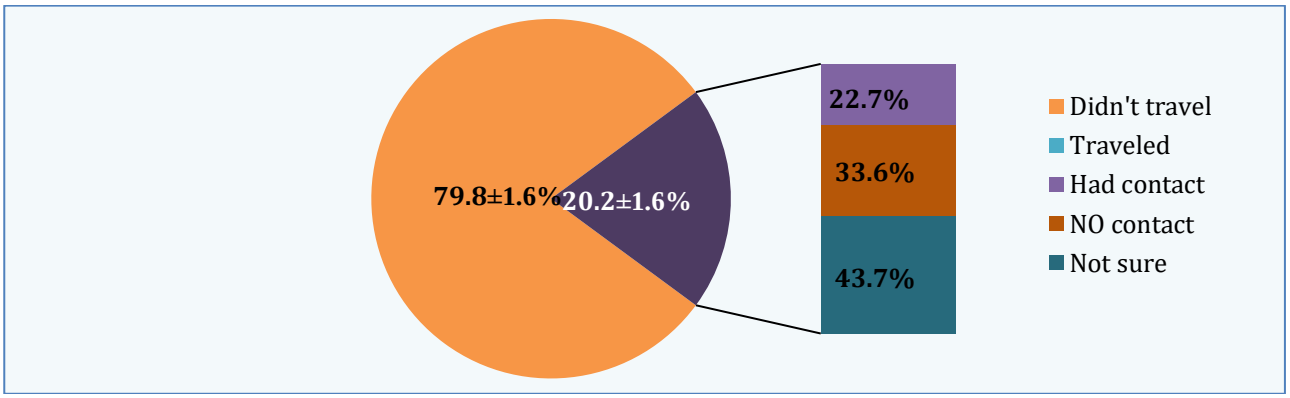

Figure 6. Distribution of people traveling abroad and being in contact with confirmed COVID-19 cases (in %).

Of those who traveled abroad during the last 14 days, most people were found to return from the UK (33 people), followed by those who returned from Italy (21 cases), and from Ukraine (14 cases), which are the most visited countries by Moldovans for business or travelling purposes. Other countries included France – 13 cases, Russia – 10, Romania 7, Dubai – 4, Czech Republic and Germany – per 2 cases each, Austria, Belarus, Bulgaria, Switzerland, Turkey – 1 case per each country. 18 epidemiological investigations did not reveal data upon the country visited by those who claimed to have traveled abroad.

All people diagnosed with COVID-19 and who had not traveled abroad during the last 14 days (being considered as local transmission of infection) were asked about their contacts with already confirmed COVID-19 cases. Therefore, based on epidemiological surveys, it was found that 430 people were in contact with a confirmed case (54.3±2.0%), 164 people stated that they were not in contact with COVID-19 positive people (20.7±1.5%) and 198 people did not know for sure (25.0±1.5%). Epidemiological data did not reveal any relevant information in 173 people (fig. 7).

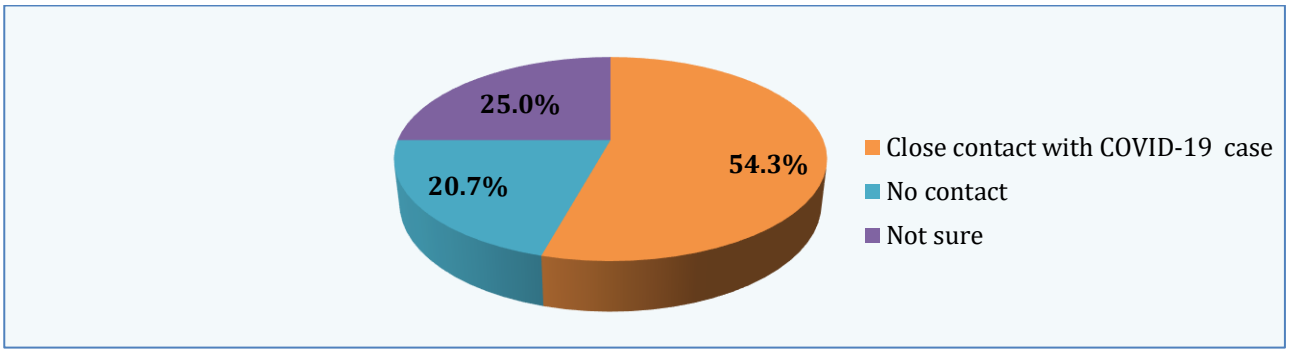

Figure 7. Distribution of cases that were in/no contact with people diagnosed with COVID-19 (in%).

The Republic of Moldova, as well as other countries registered a number of SARS-CoV-2 – infected health care workers. The HCWs were a subject of specific testing strategy, therefore some selection bias could influence the figures regarding the HCWs infection prevalence. The HCWs as general population have been tested in case of COVID-19 suspecting, when they were exposed to the risk in the health care facilities also when they were identified as being in contact with a confirmed case. The local initial epidemic stage revealed that out of the total of 965 infected people, 257 were healthcare workers, which made up 26.6±1.4% of cases. Out of these cases, 88 (34.2±3.0%) were nurses, 76 (9.6± 2.8%) – auxiliary medical staff, 70 (27.2±2.8%) – doctors, 19 (7.4±1.6%) – first-aid men, 3 (1.2± 0.7%) – pharmacists and a paramedic (0.4± 0.4%)(fig. 8).

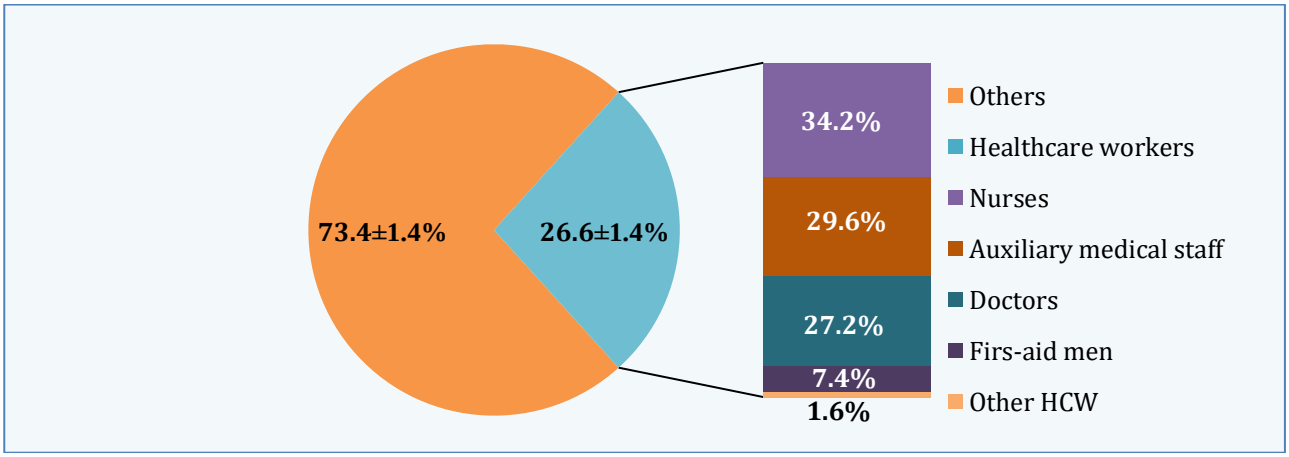

Figure 8. Distribution of infected healthcare workers out of the total number of cases and distribution depending on their professional category (in%).

Most cases of infections among healthcare workers were registered in Soroca – 86, Stefan Voda – 46, Glodeni – 15, Republican Clinical Hospital (Chisinau) – 14, Emergency Hospital Chisinau – 13, Clinical Psychiatric Hospital – 8, Orhei District Hospital – 7, National Center for Pre-Hospital Emergency Medical Assistance – 6. Of those 37 (14.4±2.2%) healthcare workers had contracted the infection within medical institutions, whereas the remaining 220 (85.6±2.2%) cases could not determine the path of transmission (fig. 9).

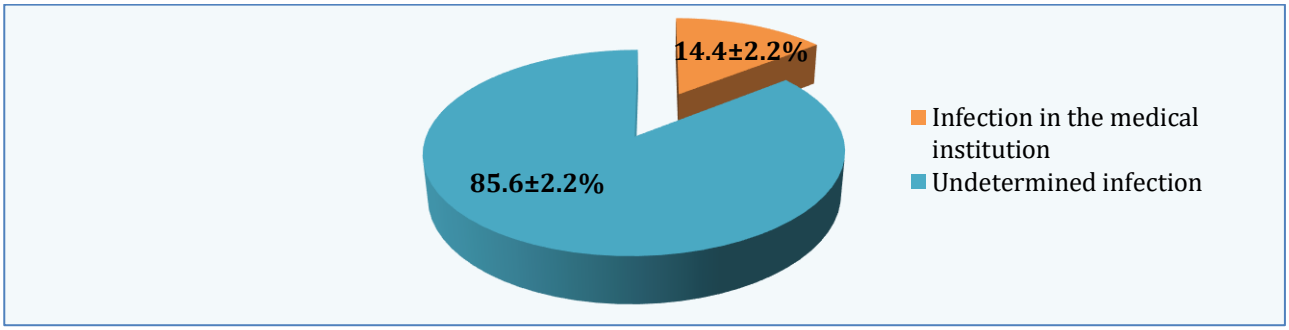

Figure 9. Distribution of COVID-19 cases within medical institutions during the reference period (in %).

Clinical manifestation of the diseases and health status of people diagnosed with COVID-19 have been assessed. Thus, it was established that on April 6, 2020 there were 77 (8.0±0.9%) people hospitalized with severe disease, 335 (34.7±1.5%) people had a medium severe disease, and 553 (57.3±1.6%) cases showed mild symptoms (fig. 10).

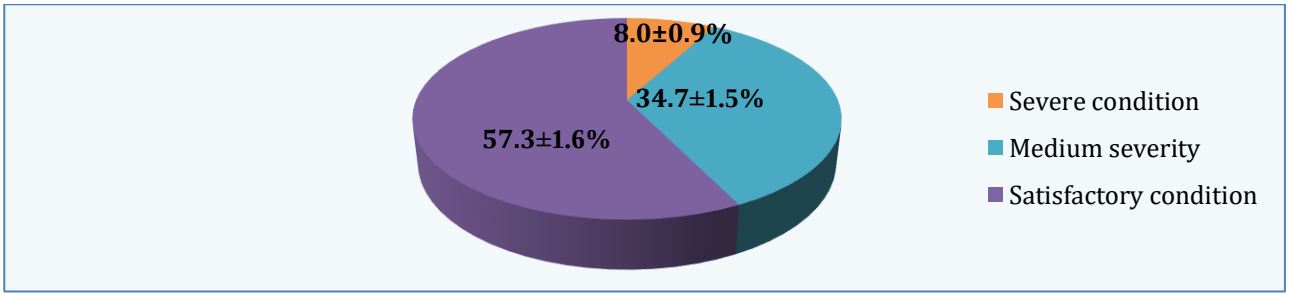

Figure 10. Distribution of patient health status with COVID-19 in the initial epidemic period in the Republic of Moldova (in %).

To date, the total number of people treated for COVID-19 is 40 (65.6±6.1%) and 21 (34.4±6.1%) people died. 904 (93.7±0.8%) cases are active and 6.3±0.8% are closed cases (deceased, discharged) (fig. 11).

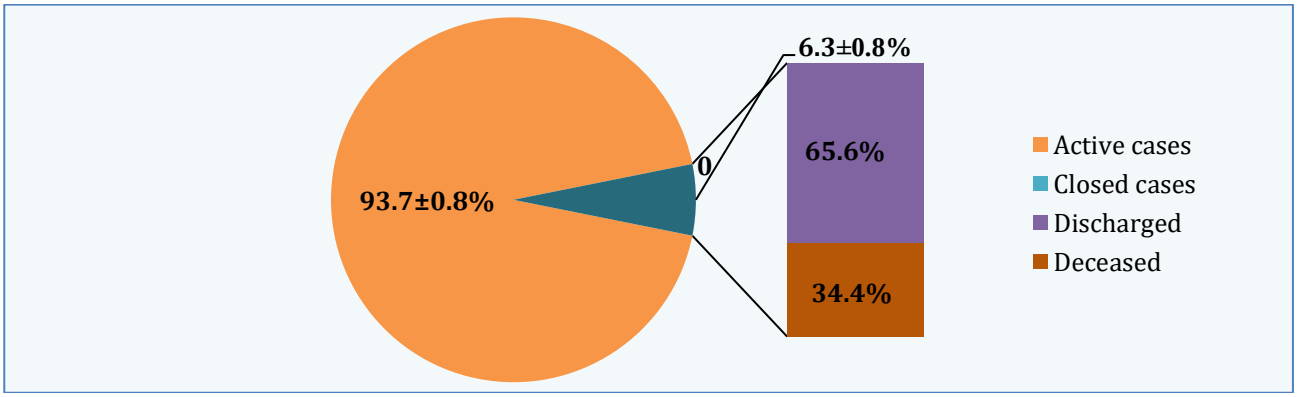

Figure 11. Distribution of closed cases and their classification in the initial COVID-19 epidemic period in the Republic of Moldova (in %).

DISCUSSIONS

The epidemiological situation in the Republic of Moldova has evolved following WHO well-known scenarios: ”zero”, imported cases, clusters and community transmission. The first COVID-19 case, which was confirmed on 8 March 2020, did not surprisingly occur. Furthermore, the infection transmitted among people through close contact, including family members. Clusters and later community transmission were registered.

The present study findings are similar to other studies that found a higher percentage of infected people in urban living environment. Thus, Fan J. et al. (17) found that in China's Gansu Province, the share of urban COVID-19 infected people was 58.3%. The same findings were reported by another study conducted in China in Tianjin Province by Cao C et al. (18) that determined COVID-19 infection in 52.4% of cases from urban areas and in suburban, whereas 47.6% cases were from rural areas. These findings as well as those of the present study can be explained by the fact that SARS-CoV-2 is more easily spread in urban areas due to higher population density, closer contact between subjects and less social distancing compared to rural living environment.

Regarding the age of patients with COVID-19 in the initial period, studies in outbreaks in China found that in Gansu Province, the patients identified in the early period were younger than those identified in the late period, but in general 54 of patients were younger (mean age 38 years) than patients identified in the early stage of the outbreak in Wuhan (mean age 59 years) (4). In this context, the mean age of 45.2 years was recorded in the early period of the COVID-19 epidemic in the Republic of Moldova, which tends to resemble the indices recorded in other (secondary) outbreaks, other than the initial one in the Chinese city of Wuhan. By assumption, COVID-19 have been registered among middle age group, because cases at the beginning of pandemic have been mainly imported, and represent middle-age people who are working abroad with following transmission of the virus among their family members, In the study of Fan J. (17) the distribution of the disease by sex did not differ significantly between the early and late periods, but number of female patients slightly predominated. In contrast, Chen and colleagues reported more men than female patients in the Wuhan outbreak (19). Cao C. and co-workers also reported higher prevalence of infection in men in their Tianjin study, accounting for 51.64% and women in 48.06% (18). In the context of these confusing data, it is still premature to interpret the obtained study data where the COVID-19 incidence in women is obviously higher than in men.

As regarding the most affected age group, almost all the studies showed that middle-aged people were the most affected, especially those aged 40-49 years, followed by people aged 50-59 (17, 18, 19). It could be assumed that this is associated with people migration particularly in Italy and Great Britain, middle-aged females being the most affected ones. The study conducted during the reference period revealed a tendency of increasing COVID-19-associated morbidity in people aged 50-59 years. However, further additional information is required to trace out final conclusions.

As regarding the population travelling, different studies divide information into the early epidemic stages of travelling to China and the later stages of the COVID-19 pandemic. Studies have drawn particular attention to the citizens who returned from the so-called "red zones" or countries with a large number of confirmed COVID-19 cases. Thus, according to Hien Lau et al. (20), 51.89% of those interviewed traveled to China in the initial stage and 28.26% travelled to other countries in the second stage. These data correspond to our study findings, where 20.2% of people reported travelling abroad in the last 14 days. The significant difference between the number of people who traveled to China in the initial pandemic stage and those who traveled to other countries during the second stage can be explained by an increase in number of cases of local (community) SARS-CoV-2 transmission.

An important feature of COVID-19 pandemic is the infection spread among healthcare workers, particularly of first-line medical assistance. A series of studies have been referred to this phenomenon, showing different incidence among infected healthcare workers. Thus, in the USA, the state of Ohio reported at least 16% of cases involving healthcare workers, while in Minnesota, this index was 28% (21) In the province of Brescia, the central outbreak in Italy, 10-15% of doctors and nurses were infected during the initial period of the pandemic (22). Subsequently, it appears that the share of infected health-

care workers in Italy has increased to 20% (23). Spain reported the latest figures for infected healthcare workers on March 30. At that time, around 12 thousand of healthcare workers were estimated to be infected, out of over 85 thousand cases, i.e. the incidence rate being of 14% (24).

In Romania, the last official and valid report was made on April 3. By that time, 474 doctors and other medical staff were infected in the neighboring country, out of a total 3,183 cases, the incidence rate being of 14.8%. It should be noted that 318 cases were reported within a hospital in Suceava. On March 30, the incidence rate was 14.5% (25). Compared to these data, our study revealed that the percentage of COVID-19 – confirmed cases among healthcare workers accounted for 26.6±1.4%.

Therefore, there is a great difference in the incidence of infected healthcare workers across the countries worldwide due to economic and socio-cultural differences, access to protective equipment, medical staff training and compliance to preventive and control measures etc.

As regarding the clinical aspects of COVID-19 infection worldwide, particularly of patient's condition, 4% of cases were reported as severe, followed by milder or moderate severity level (26). If compared to this index from the Republic of Moldova, our study revealed 8% of patients with severe clinical evolution; therefore, all suspected cases were admitted to the hospital. However, due to the differences among counties regarding hospitals admission criteria as well as assigning of the severity of cases it is difficult to affirm that there were any specific issues regarding the higher diseases' severity. Another indicator evaluated at this stage was the share of closed cases. The global indicator is 32.03% compared to 6.3% of closed cases from the Republic of Moldova. This gap is probably due to the late onset of the pandemic in the Republic of Moldova, considering that the recovery period of patients with COVID-19 lasts up to a month, however, it might vary, depending on the clinical form and manifestations. There are also great concerns regarding the high rate of lethal cases among patients in the Republic of Moldova – 34.4% compared to 21.0% worldwide, thus implicitly displaying a lower rate of discharged patients from Moldova – 65.6% compared by 79.0% globally (26).

CONCLUSIONS

1. The first month of COVID-19 epidemic exhibited a dynamic evolution, showing an increasing tendency to affect all the administrative territories of the Republic of Moldova.
2. The most COVID-19 affected age groups in the Republic of Moldova correspond to those from the other countries worldwide, thus, the prevailing female infected cases made up 63.4±2.5%, then people living in urban areas – 58.3±1.6%, the mean age of people was 45.2 years, with a tendency to increase among people aged up to 70 years.
3. The high rate of infected health care workers accounted for 26.6±1.4%, which was relatively higher, compared to other states, where this indicator was as following: Spain – 14.0%, Romania – 14.8%, Italy 20.0%.
4. The incidence of severe clinical forms, which required assisted ventilation, was higher in the Republic of Moldova compared to this index worldwide, thus being of 8% compared to 4% in other countries. Additional clinical resource management and practices are needed.

CONFLICT OF INTEREST

The authors do not declare any conflict of interest.

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