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Review

# EPIDEMIOLOGIC ASPECTS IN PREVENTION OF THE NEW CORONAVIRUS INFECTION (COVID-19) (LITERATURE REVIEW)

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*At the end of 2019 the mankind had to face a new coronavirus infection with higher virulence which resulted in its rapid spread all over the world and in an ultimate pandemic. Initially a new virus which causes COVID-19 was called 2019-nCoV but it soon acquired its well-known name, SARS-CoV-2. We can positively state that this new coronavirus infection will remain in the history of world public healthcare as a disease that caused a collapse in rendering medical aid. Undoubtedly, this new coronavirus infection has changed customary lifestyle of the overall world population.*

*This review can be considered problematic in its essence and focuses on examining contemporary trends in the official epidemiologic situation in the world regarding the new coronavirus infection (SARS-CoV-2). Having analyzed several foreign and domestic documents, the authors revealed a necessity to enhance levels and quality of COVID-19 epidemiologic diagnostics. There is a suggestion being considered at the moment on including additional clinical and diagnostic activities aimed at preventing further spread of the new coronavirus infection. We should note that data on COVID-19-related mortality and morbidity are renewed every day and every hour. Given that, it seems rather difficult to keep in line with the latest trends in COVID-19 prevention and epidemiologic diagnostics. However, the authors made an attempt to possibly collect all the latest data on epidemiological peculiarities related to the clinical course of the new coronavirus infection. The authors have a hope that this review will be useful for epidemiologists when they detect new cases of the disease as well as for lecturers at medical higher educational establishments when they train students and resident physicians.*

***Key words**: new coronavirus infection, SARS-CoV-2, COVID-19, basic reproductive number, pandemic, severe acute respiratory syndrome – SARS, children, pregnant women, fecal-oral transmission, prevention.*

Multiple research papers have been written with their focus on communicable diseases since the history of mankind has seen a great number of pandemics. Primarily, we should mention plague, variola, cholera, and Spanish influenza; these infections caused the longest pandemics that occurred repeatedly and claimed huge numbers of people's lives. At the beginning of the 20th century the Spanish influenza pandemic of 1918 caused as many as 20 million deaths [1, 2]. Given the peculiar features of that period, it is no wonder that the pandemic predominantly spread through trade and communication routes as well as due to military operations (the First World War, 1914–1918). Access to medical aid was limited and sanitary conditions were rather poor thus making for occurrence of factors facilitating the transmission of the disease [3].

A lot of contemporary authors mention in the research works that the mankind has to face a new viral pandemic, the coronavirus



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infection [1, 3–10]. S. Weston with colleagues (2020) emphasize that till the very end of 2019 there were only six coronaviruses which could cause a human disease. Four of them (hCoV-229E, hCoV-HKU1, hCoV-NL63 and hCoV-OC43) can only produce a mild cold and don't cause any special concern of world public healthcare. However, the remaining two viruses caused more severe diseases with typically high case fatality rate. Thus, in 2002 a coronavirus was discovered that caused severe acute respiratory syndrome (SARS-CoV) [11]. From 2002 to 2004 SARS−CoV coronavirus from the Betacorona virus genus (bats are its natural reservoir) caused an epidemic for the first time. The disease was called atypical pneumonia and caused 774 death cases in 37 countries all over the world [11, 12]. Since 2003 there have been no new registered cases of atypical pneumonia caused by SARS−CoV [11]. The second epidemic caused by another coronavirus occurred in 2012 on Arabian Peninsula and was called Middle East respiratory syndrome (MERS-CoV) [11, 12]. SARS-CoV and MERS-CoV outbreaks started with a patient who suffered from pneumonia and both outbreaks resulted from zoonosis [11, 13]. A search for MERS-CoV reservoir was first concentrated on bats since they were considered by many authors [13, 14] to be a natural reservoir for a great variety of coronaviruses, including those similar to SARS-CoV и MERS-CoV. However, serologic tests and enzyme-linked immunoassays (hereinafter ELISA) performed on Arabian camels in Saudi Arabia, Qatar, and the Canary Islands established that MERS-CoV was widely spread in those animals [14–16].

At the end of 2019 the mankind had to face a new coronavirus infection with greater virulence that made for its rapid spreads all over the world and resulted in a pandemic. Initially the new virus was called 2019-nCoV but now its official name is SARS-CoV-2 and it causes the disease called COVID-19. Undoubtedly, this new coronavirus infection has become a significant milestone in the history of the 21st century as it has changed the customary lifestyle of the whole mankind.

This new coronavirus SARS-CoV-2 is a single-stranded RNA-virus that belongs to Coronaviridae family, Beta-CoVB line. The virus is assigned into the pathogenicity group II, similar to some other viruses from this family (SARS-CoV, MERS-CoV). Coronaviruses are the most striking example of a virus that was twice able to overcome the interspecies barrier between wild animals and humans during SARS and MERS outbreaks. SARS-CoV-2 is suspected to possibly overcome this barrier for the third time [17]. SARS-CoV-2 coronavirus is probably a recombinant virus between the bat coronavirus (RaTG13-2013, identity is 96 %) and another coronavirus of unknown origin. The genetic sequence of SARS-CoV-2 is similar to that of SARS-CoV at least by 79 % [17, 18]. To scientists' opinion, it is vital to examine an intermediate host since it. According to provides a better insight into how SARS-CoV-2 became a human virus and how to develop prevention activities in future. It is much safer to create new vaccines for animal hosts thus preventing any infection from spread among people [19].

Sanche S. with colleagues (2020), having generalized their experience in examining the coronavirus infection, noted that at the end of 2019 the municipal public healthcare committee in Wuhan (China) reported 41 cases of "pneumonia with unknown etiology" to the World Health Organization. On January 08, 2020 an infectious agent was successfully identified and shortly after it was established that the virus could be transmitted between people. By January 21, 2020 multiple COVID-19 cases had been registered in most provinces in China. By March 16, 2020 there were more than 170,000 confirmed cases of the disease and more than 6500 deaths all over the world. An outbreak of "pneumonia with unknown etiology" turned into the COVID-19 pandemic in such a short time as 3 months [20].

COVID-19 spread rapidly due to people travelling all over the world (both within a country and between different countries) and the pandemic scales were reached during 2–3 months. Therefore, by November 03, 2020 COVID-19 was detected in more than 210 countries (includ-

ing autonomous areas). The disease was registered on all continents, Antarctica excluded, a number of infected people amounted to 47,327,323; deaths, 1,211,882; 33,942,600 people fully recovered [21].

*The basic reproduction number* ($R_0$) is a dimensionless parameter that is used in epidemiology to characterize how contagious a disease is. It is usually determined as a number of people who will be infected by a typical patient who is surrounded by completely non-immunized population and there are no specific epidemiologic measures aimed at preventing this disease from spreading (quarantine, for example) [22]. To estimate COVID-19 spread, a lot of authors apply the basic reproduction number $R_0$. When $R_0 > 1$, a number of infected people is likely to grow, and if $R_0 < 1$, the transmission is likely to stop [23].

Sanche S. with colleagues [20] point out that the initial values of the basic reproductive number varied from 2.2 to 2.7 at early stages in the COVID-19 outbreak. However, their further studies involved mathematical modeling based on 140 confirmed COVID-19 cases; the authors established that the infection spread was very rapid as $R_0$ amounted to 5.7 (95 % CI 3.8–8.9) (July 2020). Thus, the basic reproduction number $R_0$ depends on the exponential growth of an outbreak as well as on latent (a period from contagion to becoming contagious) and infectious periods. The authors concluded that the longer the latent and infectious periods were the higher was $R_0$ [20]. Ge H. and others gave other data and stated that $R_0$ varied from 1.4 to 6.49 [24]. We should note that the basic reproduction number might be different in different countries and depend on an applied mathematical model [23] or prevention activities, such as social distancing and facial mask wearing.

Akin L. with colleagues [1] performed a comparative examination of basic reproduction numbers determined for several pandemics including Spanish influenza (1918–1919), 1.7–2.8; Asian influenza (1957–1958), 1.8; Hong Cong influenza (1968–1969), 1.06–2.06; swine influenza (2009), 1.4–1.6; COVID-19 (2019), 5.7.

Therefore, values of the basic reproductive numbers described by several authors [1, 20, 23–25] can possibly indicate that SARS-CoV-2 is highly contagious. The assumption is further confirmed by studies based on analyzing genome parts in the virus; it is assumed that SARS-CoV-2 has much greater affinity with the human receptor ACE2 which is necessary to penetrate a cell than the SARS virus detected in 2003. Thus, high contagiousness of SARS-CoV-2 is provided with a solid molecular basis.

There are some very interesting works on COVID-19 incubation period [26, 27]. Lauer S.A. with colleagues (2020) examined an incubation period in 99 disease cases. The authors took a period of time from the first contact with an infected person and up to the first signs of fever. It was done to exclude a systematic mistake in examining incubation periods caused by calculating them from a moment when cough or sore throat were detected and we should remember that these symptoms can be caused by other, more widely spread microorganisms. The research results showed that average incubation period up to the moment when the fever set in amounted to 5.7 days (CI, from 4.9 to 6.8 days). 2.5 % people had the first fever attack during 2.6 days (CI, from 2.1 to 3.7 days) and 97.5 % during 12.5 days (CI, from 8.2 to 17.7 days) [28]. Ge H. and others reported the longest incubation period that amounted to 24 days [24].

There is an opinion that animals can be a possible source of SARS-CoV-2 [17]. Nevertheless, a man is the primary infection source (the disease is anthroponotic) just as in case of SARS CoV and MERS CoV. The virus is transmitted by droplets of moisture (during talking, coughing, or sneezing), by close contacts, or the transmission can be fecal-oral [24, 29]. Nucleic acids of SARS-CoV-2 are detected in liquid from the bronchial tree, phlegm, nose and throat swabs, feces, blood, and urine at different stages in the clinical course of the disease. Aerosols exhaled from the airways by an infected person can persist in the air and infect people who don't keep a proper social distance in a closed space [30, 31]. SARS CoV-2

virus is detected in the air during three hours in experimental models. However, Cheng V.C.C. with colleagues failed to detect SARS CoV-2 in 8 samples taken at a 10-m distance from the chin of a patient, both wearing a face mask and without it [30]. Similar results were produced by other experts who examined air samples taken at a 5-m distance from patients: no virus detected [29].

Fecal-oral transmission is another topical issue with respect to COVID-19 which hasn't been given an exact answer so far. Diarrhea was among clinical symptoms in a lot of patients with COVID-19 [29, 31]. The virus can probably be transmitted in a direct contact with an infected person as well as with contaminated surfaces or household appliances [32]. SARS CoV-2 has been established to remain viable for 72 hours on plastic and stainless steel; copper, more than 4 hours; and carton boxes, up to 24 hours. However, experts do not have an unambiguous answer to the question whether the virus is able to preserve its virulence when it persists on various surfaces. Another possible transmission route can be associated with the virus penetrating the oral cavity, nose, and eyes form dirty hands [31]. The assumption has been confirmed by Bulut C. with colleagues who detected viable viruses in samples of feces taken from patients with diarrhea [29, 31]. The most indicative data are provided by Dhama K. and others (2020): anal swabs give positive results as opposed to oral cavity swabs at later stages in the infection. This can be used as an additional diagnostic criterion when a patient with COVID-19 is ready to be released from hospital given negative swabs taken from the oral cavity or nasopharynx: there can still be a risk of fecal-oral transmission. The same data were obtained when experts analyzed feces of children infected with SARS-CoV-2 and with mild clinical course of the disease. An oral cavity swab was negative as opposed to anal swab that was SARS-CoV-2-positive during ten days [33]. Medical workers should adhere to strict safety precautions when working with feces samples taken from patients with suspected COVID-19 or already infected ones.

Occurrence of SARS-CoV-2 virus in feces can result in the fecal-oral transmission of the infection. Probably, if we want to prevent SARS-CoV-2 spread, we should believe healthy people to be those who not only have negative oral cavity swabs but also anal ones [33].

Therefore, SARS CoV-2 occurrence in feces can be either due to lesions of the gastrointestinal tract or phlegm digestion and this gives further causes to pay great attention to personal hygiene.

Waste waters are becoming another important aspect in studies focusing on COVID-19 since they can become a factor making for the transmission of the disease. Given that SARS-CoV-2 virus occurs in phlegm, blood, urine, and feces, we can assume that it can also occur in sewerage and waste waters. This requires further investigation due to the fecal-oral transmission being quite possible. Therefore, it seems reasonable to revise the existing procedures and stages in treatment of waste and sewage waters and to implement effective disinfection techniques that can also eliminate SARS-CoV-2 [33].

Previous epidemics of many viral infections could result in pregnancy pathologies, a virus being transmitted from a mother to a fetus, a perinatal infection and even death. Schwartz D.A. (2020) conducted a study where he indicated that COVID-19 didn't cause any pathology in 38 pregnant women. It should also be noted that there have been no confirmed cases when SARS-CoV-2 was transmitted from a mother to a fetus [34–36].

Cheng V.C.C. et al. [30] examined 9 women with diagnosed COVID-19 during the third trimester. The study showed that clinical signs were similar to those detected in women who weren't pregnant: 7 women had fever; 5, lymphopeny; 4, cough; 3, myalgia; 2, sore throat and overall sickness. All the examined women had pneumonia but none of the needed AV; moreover, the outcomes were quite positive in all the examined cases. They all gave birth by cesarean section. Absence of intrauterine or trans-placental transmission was also confirmed by the newborns' Apgar scores: 8–9 after 1 minute and 9–10 after 10 minutes [35].

People with inapparent infection are still its sources and are epidemiologically dangerous for their susceptible counterparts. There have also been some reports on atypical clinical signs of COVID-19 with fatigability being its only symptom. Such respiratory symptoms as fever, cough, and phlegm can be completely absent [33]. Therefore, early diagnostics and detection of patients with inapparent infection can considerably reduce the transmission of the infection to other, more susceptible people. Nevertheless, we should note that experts are still unable to provide exact data on the matter and there is no unified and correct opinion on factors and conditions of SARS CoV-2 transmission.

According to Rasmussen S.A. and others, an average age of hospitalized patients amounted to 49–56 years and 32–51 % of them had another disease [37]. Bulut C. with colleagues [29] concentrated on age-related peculiarities of hospitalized patients in different countries and detected authentically significant differences. Thus, in China 87 % patients were aged 30–39 years; in Italy, 35.8 % and 36 % were aged 50–59 and 70–79 years respectively. However, people aged 20–29 years accounted for more than 70 % of hospitalized patients in Germany [29].

Hospitalized patients tended to have such clinical signs as fever (83–100 %), cough (59–82 %), myalgia (11–35 %), headache (7–8 %), and diarrhea (2–10 %). However, 100 % patients had certain lesions in their lungs detected by chest x-ray examination (ground-glass opacity). Meanwhile, children rarely had COVID-19 and most of them had the disease in its very mild form [37].

Besides age- and sex-related factors, it was also established that middle-age and elderly patients with primary chronic diseases, especially hypertension and diabetes mellitus, were more susceptible to respiratory failure and, consequently, their prognosis could probably be rather unfavorable [33].

According to data provided by the WHO, the overall mortality rate amounted to 6.3 as of April 13, 2020. But there were differences in mortality detected between different countries. This rate tends to be higher in countries with older population. Thus, in Italy average age of people who died from COVID-19 amounted to 78 years and the mortality rate was 12.73 %; France, 15.23 %; Spain, 10.22 %; China, 4.01 %; Germany, 2.28 %; the Russian Federation, 0.81 % [29]. According to data provided by Bulut C. and others, a concomitant disease can increase mortality: cardiovascular diseases, by 10.5 %; diabetes mellitus, by 7.3 %; chronic respiratory diseases, by 6.3 %; hypertension, by 6.0 %; and cancer, by 5.6 % [29].

Experts also note that mortality among men (2.8 %) is higher than among women (1.7 %). ACE2 is known to be located on the X-chromosome which can possibly have some alleles that provide its carrier with resistance to COVID-19 and this fact can explain lower mortality levels among women. Sex hormones might be another reason as it is assumed by Tay M.Z. with colleagues. Estrogen and testosterone have different immune-regulatory functions that can possibly influence both immune protection and severity of COVID-19 [36].

COVID-19 pandemic created a tremendous burden on public healthcare all over the world. A drastic growth in a number of new cases has already exceeded any quantities of available medical consumables thus limiting a capability to provide patients with intensive care and making it available for only a small part of critical ones. This could also make for growing mortality rates during the COVID-19 outbreak [33].

Therefore, it is truly vital to implement effective anti-epidemic, preventive, and sanitary-hygienic activities in order to prevent further spread of the disease and its transmission from person to person.

An epidemic process of any infection, this new coronavirus one among them, includes the epidemiologic triad described by Gromashevskiy: an infectious agent, a transmission mechanism, and a susceptible organism. However, at present we can influence only the first two sections in the epidemic process until a safe and, more importantly, effective vaccine against this new coronavirus infection is created.

Some countries implement various activities aimed at preventing COVID-19 transmis-

sion and spread, some effective, others not [38–40]. Thus, in China many cities were closed and social contacts were seriously limited at early stages in the epidemic. The government made a decision to follow two basic principles, "four early" and "four centralizations" [41]. "Four early" principle included early detection and early isolation of people infected with SARS-CoV-2, early communication and early treatment. All these activities facilitated early diagnostics and treatment and, consequently, prevented further SARS-CoV-2 spread and reduced contagion levels. Contact people were thoroughly traced in order to detect and isolate a source of the infection at an early stage. Any mass events were postponed, schools and industrial enterprises were closed [42, 43].

"Four centralizations" principle meant that patients with the severe clinical course of the disease were placed in the best hospitals with the most effective therapeutic capabilities (centralization of patients). Centralization of doctors, resources, and treatment provided an opportunity to render high quality medical aid to seriously ill patients in accordance with the principle "one person – one strategy". We should note than more than 37,000 thousand medical workers from other provinces of China took an active part in treating patients with SARS-CoV-2 in Wuhan, Hubei province. This fact reflects noble qualities and high professionalism of medical personnel (centralization of doctors). All these aforementioned measures effectively reduced COVID-19 mortality [41].

In the United States, immigration was suspended and certain limitations were imposed on return of American citizens who could create a risk of the new coronavirus infection spread and transmission in the country. However, as it was noted by Patel A. and others, there was practically no quarantine and cities were not closed [44].

The British government adopted another strategy to fight against COVID-19. It was quite distinctive and was aimed at reaching "collective immunity" to SARS-CoV-2 virus. Thus, at least 40 million British citizens "were allowed" to get infected and the government hopes it would be enough to create durable national immunity. However, Yu J. with colleagues (2020) believe this strategy to be "absurd" since vaccination is the only way to create collective immunity whereas the governmental policy in Great Britain sacrifices a lot of people and this is considered to be inhuman in any civilized society. Besides, viruses can mutate and there is no evidence that a recovered person has some sort of durable immunity. Therefore, this strategy to fight the infection hardly seems reasonable [45].

At present most European and American countries haven't still adopted the effective Chinese strategy "to collect as many together as possible" but allow patients with mild clinical course of the disease to isolate themselves at home thus increasing risks of transmission and further spread of the virus.

Isolation and creation of vaccines and antiviral medications are top priorities. In case there is no safe and effective vaccine or a specific drug treatment, the only solution is to prevent the virus transmission, to provide people and medical personnel with basic information and to implement relevant prevention and control activities. Safety precautions can help people to prevent risks of contagion; for example, people should often wash their hands with soap or any alcohol-based disinfectant, cover their mouth with the elbow or a Kleenex when sneezing or coughing, avoid close contacts with people who have apparent symptoms, and apply for a medical aid instantly in case there is fever, cough, or labored breathing [38].

Creating a proper microclimate seems another possibly effective way to prevent SARS-CoV-2 from spreading. In particular, proper temperature and relative humidity can exert significant influence on frequency of COVID-19 cases and SARS-CoV-2 transmission [40].

According to data provided by Harmooshi N.N. (2020), SARS-CoV-2 is not a thermophilic virus; therefore, it becomes inactive just as air temperature drops [40]. However, other experts believe that SARS-CoV-2 disappears at 30 °C, and this is a mistake since the virus can become less viable under this temperature

but this doesn't mean it is eliminated completely [46]. Results produced in some latest research give grounds for an assumption that SARS-CoV-2 virus can survive on a surface during 4–28 days, but if air temperature drops below 30–40 °C, then its life span will decrease. In addition to temperature, coronaviruses are also sensitive to humidity; consequently, it is probable that SARS-CoV-2 virus can live longer under relative humidity being 50 %, than under that equal to 30 % [40].

Therefore, the most effective way to make SARS-CoV-2 virus less active is to use disinfectants which contain 60–70 % of ethanol or 70 % of isopropanol. Also, household detergents or soap can be used for disinfection. If your hands are relatively clean, you can use only a disinfectant, but in case they are dirty, you have to wash them with soap during at least 20 seconds [47].

Greater public awareness should be created by using posters with precise "DO" and "DO NOT DO" lists illustrating symptoms, ways of transmission and prophylaxis activities with a focus on personal hygiene aimed at preventing COVID-19 spread. Any campaigns on organizing physical and social distancing aimed at reducing physical contacts between people should be promoted. Fitbit devices and other applications on smartphones can be used for monitoring over symptoms during such outbreaks [48, 49]. Smartphones and Internet-services can also be used for spreading relevant information on how to prevent the infection from spreading.

Certain issues regarding SARS-CoV-2 still remain without an answer including factors that facilitated the virus overcoming the interspecies barrier and ultimate conclusion on its origin; differences in critical points of mutation in transmission and pathogenesis of the virus; the reason why it occurred; why some infected people die and others only have inapparent infection; repeated cases of the disease among recovered people.

However, one thing is known for sure: we can overcome SARS-CoV-2 virus only by joint efforts made by the whole world society and using lessons that we learned thanks to MERS and SARS outbreaks. Each day brings some new knowledge about the COVID-19 pandemic. It hasn't finished yet, and we should understand that unless we change our attitudes towards SARS-CoV-2 virus and become more demanding to ourselves, the virus will change our everyday life completely what it has been doing rather successfully all this time.

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