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Ethiological, Clinical and Epidemiological Overview of Covid-19 Pandemia

Semiha Yalçın*[1], Selva Zeren[2] , Abdullah Yüksel Barut[3], Sema Aydın[4]

1 Mugla Sitki Kocman University, Faculty of Milas Veterinary Medicine, Department of Preclinical Sciences, Department of Microbiology, Turkey. 2 Istanbul Gelisim University, Faculty of Health Science, Department of Audiology, Turkey. 3 Istanbul Gelisim University, Faculty of Health Science, Department of Nutrition and Dietetics, Turkey. 4 Istanbul Gelisim University, School of Applied Sciences Department of Gastronomy,Turkey.

Abstract

The cause of COVID-19 disease has been named as the SARS-CoV-2 virus, which is defined in the category of betaCOV viruses. The disease has been declared as a COVID-19 pandemic by the World Health Organization (WHO). Coronaviruses (CoV) are viruses, some of which are zoonotic, have a crown-like appearance under an electron microscope and contain a single stranded RNA genetic material. The SARS-CoV-2 virus that causes COVID-19 is transmitted through respiratory droplets and direct contact with people. Contagious from the presymptomatic period, COVID-19 can be presented with the symptoms of simple upper respiratory tract infection; it may as well cause severe disease characterized by severe respiratory failure. While the first step in radiological evaluation is x-ray, examination of the lungs with computed tomography has diagnostic value. Prevention is important because there is no medical treatment and immunization method specific to the disease. The most important factor in protection is to limit the exposure to the virus. Therefore, attention is constantly paid to the importance of personal protectors and hygiene.

Key words: *Covid-19, Pandemia, Coronaviruses*

***Corresponding Author:** Semiha Yalçın. Institution: Mugla Sitki Kocman University, Faculty of Veterinary Medicine, Department of Microbiology Becin Mah. Universite Cad. No:2 Milas/Mugla **E-mail:** semihayalcin82@gmail.com **Received:** Dec, 2020. **Accepted:** Feb, 2021.

Introduction

The cause of the pandemic which began during the last months of 2019 in Wuhan province of China, has been named as the SARS-CoV-2 virus, which is defined in the category of betaCOV viruses. The disease has been declared as a COVID-19 pandemic by the World Health Organization (WHO). The World is still struggling with the pandemic; it had deep impacts mainly on health and economic parameters and is still affecting them. The pandemic was handled with patience by health communities and professionals in our country and vast scientific data about the virus and the disease caused by it was collected in a short period of time. However, in our country, various measures are taken by the Ministry of Health regarding the coronavirus pandemic and the society continues to be informed in various ways. In this review article it is aimed to share information about the structure of Coronaviruses, it's contagiosity, pathogenesis of COVID-19 disease, clinical and radiological findings and protection methods according to current scientific data.

Ethiology

Coronaviruses (CoV) is a large family of viruses some of which have zoonotic character and may cause diseases like Middle East Respiratory Syndrome (MERS-CoV), Severe Acute Respiratory Syndrome (SARS-CoV). Coronaviruses (CoV) have envelopes and spiky glycoprotein structures on the envelope give them a crown-like appearance under the electron microscope. They contain a single stranded RNA genetic material (1, 2) Coronaviruses mainly cause respiratory and gastrointestinal system infections and has 4 genetic groups named Alphacoronavirus (alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus (deltaCoV) and Gammacoronavirus (gammaCoV) in the Orthocoronaviriade subfamily of Coronaviridae family. AlphaCoV and betaCov usually cause infection among mammals while others infect birds (3). Members of this big virus family may cause respiratory, enteric, hepatic and neurological diseases among different animal species like camels, cows, cats and bats. 6 different human CoV (HCoV) was defined which can infect humans. α-CoV HCoV-229E, HCoV-NL63, βCoVs HCoV-HKU1, HCoV-OC43 cause mild, low pathogenic, respiratory flu-like symptoms. β-CoV, SARS-CoV ve MERS-CoV on the hand cause serious and deadly respiratory infections (4). These viruses cause serious flu like symptoms and lower respiratory infections especially when immune system is compromised like in geriatric or diabetic patients; patients with AIDS or patients taking chemotherapy (1). They recently have caused epidemics with different clinical severities of respiratory and extra-respiratory symptoms (SARS CoV: 2002–2003, MERS CoV: 2012, SARS CoV-2: 2020) (5). SARS-CoV-2 virus causing COVID-19, has 30 kb length of RNA genetic material (5), round, eliptic or pleomorphic form and has a diameter of 60-140 nm (1). SARS CoV-2 (NC-045512.2) has a total of 11 gene regions; These are: ORF1ab, ORF2 (Spike protein), ORF3a, ORF4 (Envelope protein), ORF5 (Membrane protein), ORF6, ORF7a, ORF7b, ORF8, ORF9 (Nucleocapside protein) and ORF10 genes. ORF1ab gene expresses a poly protein. ORF1ab poly protein consists of 16 different nonstructural proteins (from NSP 1 to NSP16) (5). ORF2, Spike (S) protein, is a glycoprotein that assists binding of virus to host cell. The structure of S protein is defined; it detects Human-Angiotensin 2 (ACE2) protein on host cell (6, 7). A different division zone was detected on SARS CoV-2's S

protein, which is not present on S protein of SARS CoV's S protein; this is considered as one of the reasons of the difference of pathogenity of two viruses. ORF3a protein is an ion channel protein related to NLRP3 inflamasome activation. ORF4, Envelope (E) protein is an integral membrane protein which can oligomerise, form an ion channel and has a role in viral replication turnover, viral construction and pathogenesis. This protein interacts with nucleocapsid (N) protein and helps capsulation of the viral RNA genome. ORF6 has a role in viral pathogenesis. Type I transmembrane protein ORF7a and ORF7b protein which can be localized in Golgi area are accessory proteins. SARS CoV-2 has one ORF8 protein while SARS CoV has two ORF8 proteins named a and b. Nucleocapsid (N) protein of coronaviruses is a structural protein directly linked to viral RNA and provides stability (5). Genomic studies about the virus indicates SARS-CoV-2 is probably evolved from a strain existing among rats. Genomic sequence of SARS-CoV-2 has 96,2% similarity with CoV RaTG13 (GenBank: MN996532) coronavirus of rats; similarity of SARS-CoV with this strain is 79,5% (4, 5). No mammal host was detected to be the potential link between rats and humans. It is also possible that a mutation of the original strain has created a virus that can directly infect humans without an intermediate host. The lipid envelope covering the virus is sensitive to ultraviolet and heat like in other type of CoV's. These viruses can effectively be inactivated with lipid solvents like ether (75%), ethyl alcohol, chlorine based disinfectants, peroxyasetic acid and chloroform (1).

Transmission Iathways of the Infection

Respiratory infections are generally transmitted via invisible (<10nm) droplets which are physically emitted around through different size of airways. According to World Health Organization informations COVID-19 is transmitted among humans primarily through respiratory droplets and contact pathways. In the analysis of 75.465 COVID-19 cases in China no transmission through respiration was reported. Transmission through droplets occur in the presence of close contact of 1-1,5 meters with infected people. Virus loaded droplets ,sprayed via coughing, sneezing of infected people, reaching oral and nasal mucosa and conjunctiva of healthy individuals and inhalation of droplets is one of the main transmission pathways. Coughing and sneezing of infected person or hands infected by coughing and sneezing may contaminate objects (all surfaces around, contacted objects, personal belongings) with virus loaded droplets. So contact of these objects with healthy people and thus movement of virus towards contact with mouth, nose and eyes may also cause transmission. Not following hygiene rules, especially hand hygiene , plays an important role in transmission. Since particles smaller than 5 nm can hang in the air for longer durations, in virus dense environments like patients rooms, areas crowded with infected people; respiratory transmission may occur within distances longer than 1-1,5 meters. Some patients with COVID-19 infection developed intestinal infection so there is data about faecal viral presence. In some studies virus was detected in faecal specimens. But no cases with faecal-oral (faecal derived) transmission was reported so far. But the presence of faecal virus once again implies the importance of hygiene rules (8).

Potential Transmission of Covid-19 via Food

Covid-19 is a viral respiratory disease (9). There is no evidence for transmission of respiratory viruses via food or food packaging. It is known that Coronaviruses cannot duplicate in food and they need an animal or human as a host (10). But one can touch the contaminated surface or object and infect himself by touching his mouth, nose and/or eyes (11) Survival time of Covid-19 virus on different surfaces was reported in many studies in the literature. The virus was reported to last 72 hours on plastic and stainless steel, 24 hours on cardboard and 4 hours on copper (12). It must be considered that studies were held in laboratory conditions and controlled relative moist and temperature conditions may differ from actual life parameters. Prejudices towards unpackaged food has occurred after the pandemic. Doubts towards salad bars, open food shelves, unpackaged bakery products are noteworthy. But there is no scientific data about transmission through these products. Businesses should watch 'Hazard Analysis and Critical Control Point' (HACCP) rules to manage food safety risks and to avoid food contamination (13). Another point to be noted is the risk factors occurring during the transport of food. Staff responsible for food transport should be aware of the risk of Covid-19 transmission. Drivers have the potential to be infected by touching contaminated surfaces or by handshaking infected people (11). An infected driver may pass the virus on during the delivery of the food (9). Besides steering wheels, doorknobs, mobile devices etc. are among surfaces potentially contaminated with virus. Thus; In order to avoid cross contamination with food and devices used for food production and delivery, social distancing, hand and surface hygiene rules must be strictly followed. Drivers must follow social distance rules when loading food and when delivering it to the customers and must be aware of the need for providing top level personal hygiene and wearing clean personal protectors.

Pathogenesis

Angiotensin converting enzyme II (ACE2) is a carboxypeptidase forming Ang 1-7 and Ang 1-9 from Angiotensin (Ang) II. ACE2 was defined on renal vessel endothelium; on heart, hypothalamus and testical tissue. ACE2 expression was reported to increase in myocardial infarcts and cardiac failure and noted to have a regulatory effect on heart function. Animal models has shown respiratory SARS-CoV infection may cause ACE2 related SARS-CoV infection in the heart and may decrease myocardial ACE2 mRNA expression (14). ACE2 has an important role on regulation of vascular response to Ang II. ACE2; since it regulates the balance of Ang 1-7 , plays a critical role on the effects of these substances on kidneys and thus protecting the kidneys (15). The interesting point is the definition of ACE2 as the receptor of coronaviruses which are the cause of severe acute respiratory syndrome (SARS) . SARS-CoV-2 attaches the membrane by ACE2 via the receptor region of the S protein (16). ACE; adds to pulmonary tissue damage and edema by producing Ang II. ACE2 may avoid these effects but bonding of SARS virus to ACE2 and its replication decreases the expression of ACE2. Applying recombinant ACE2 to rats is shown to have protective effects from sepsis caused acute pulmonary damage (15).

ACE2 is present in gastrointestinal system, glial cells and neurons besides Type II alveolar pneumocytes. Neurological problems in COVID-19 patients range from common neurological symptoms like headache and dizziness to loss of taste and sense of smell, loss of consciousness, acute cerebral disease, ataxia, neuralgia and epilepsy. The mechanisms which can lead to neurological symptoms and complications may be related to the existence of ACE2 receptors in the glial cells and neurons of the central nervous system (17). Higher IL-6, IL-2, IL-7, IL-10, INFɣ induced protein (IP10), monocyte chemoattractant protein (MCP1), macrophage inflamattory (MIP1A) and TNF-α plasma levels were detected in COVID-19 patients followed in the ICU. This can be seen in severe viral infections like COVID-19 due to excess release of cytokines in the circulation and it is named 'cytokine storm'. IL-6 plays the most important role on the cytokine storm because of the effect on B cell proliferation, anticore release and stimulation of diffuse intravascular coagulation. Excess cytokine release is thought to have a relation with the severity of the disease and the mortality (18) Fever, cachexia, vasodilatation and laboratory findings like anemia, increase in ferritin, hypertrigliserydemia, hypofibrinogenemia, hypoalbuminemia and increase in liver enzymes are also the results of excess cytokine release.

Clinical Findings

Mean incubation period of COVID-19 after exposure to virus (infection) is 5-6 days but incubation period can be up to 14 days. This period is named 'presymptomatic' period and some infected people can be contagious in this period. Contamination can occur before the onset of the symptoms (19). In the COVID-19 guideline of Public Health Office of Turkish Ministry of Health, patients with no respiratory distress (Number of respirations 93% in room air) but with symptoms like fever, muscle/joint pain, cough and sore throat; patients with no co-morbid diseases (Cardiovascular diseases, DM, HT, cancer, chronic lung disease and other immunsupressive diseases) and patients younger than 50, patients with no negative prognostic factors in the initial blood test (blood lymphocytes >10x normal , ferritin >500 ng/ml or D-Dimer>1000 ng/ml etc.), patients with normal lung x-ray and/or CT are categorized as 'non-complicated cases'. Patients presenting with pneumonia are divided into 2 subgroups like mild and sever pneumonia. Mild pneumonia is defined as; patients with fever, muscle/joint pain, cough and sore throat and with number of respirations less than 30 per minute, SpO2 higher than 90% in room air and mild findings of pneumonia in the chest x-ray or CT scan. When the case proceeds to tachypnea (>30 per minute), SpO2 level lower than 90% in room air and bilateral diffuse pneumonia image on chest X-ray or CT scan, patient is categorized as 'severe pneumonia. Dyspnea or respiratory distress, respiration count >30 per minute, PaO2/FiO2100/min), acute renal failure, abnormalities in acute liver function tests, confusion, acute organ disorders like acute bleeding disorder, presence of immunsupression, high troponin values, arrhythmia, lactate levels higher than 2 mmol, capillary turnover failure and skin lesions like cutis marmaratus are the criteria to consider intensive care unit transfer of the patient (20). Mean recovery time of the disease is 2 weeks; healing time for severe or critical cases is 3 to 6 weeks. Death time for the patients that are lost range from 2 weeks to 8 weeks (21). Patients recovered from the disease have immune response but it is unknown yet for how long the patients recovered

from COVID-19, having anticors are protected and if they are immune from a second infection or not (22).

Radiological Findings

PA (Postero anterior) lung X-ray is in the first line in choice for radiological imaging for COVID-19 cases. This is a cheap and easy radiological inspection method and it is important because of its availability. Distinctive diagnosis of the lesions in the X-ray is made with computerized tomography (CT). CT scans became more available in the applied process of health revolution in our country thus made an impact on early diagnosis. Dose of radiation absorbed differ between PA lung X-rays and CT scans but with the help of current technology low dose CT devices lowered this risk. Diagnostic chance of PA lung X-rays is between 30-60% so in cases with normal X-rays if clinical symptoms (fever, cough, dyspnea etc.) support the diagnosis of Coronavirus 2019 (COVID-19), a CT scan must be performed (23). If the lung X-ray reflect low-density lesions with irregular borders in the mid and lower lung zones, if deletion of blood vessel clarity of the lower lung zones is bilateral a viral pneumonia must be considered. If a CT scan is planned it is better to scan lung zones with thinner sections before applying the intravenous contrast material. Lower dose or high definition CT can be performed depending on the clinical findings. The distinctive image of the case is lesions with different sizes, containing air bronchograms, with irregular borders and with an iced glass appearance in both lung zones but mainly in mid and lower zones (24). Iced glass images due to edema and hyaline layer formation in the lungs cause neighboring septae to thicken. In advanced stages of the disease fybromixoid fluid collection in the lung alveolus may occur. This coexistence in the lesions cause a pavement like image. Enlargement of the vessels on the borders of this image can be observed (25). In cases , usually bilateral lesions close to the pleural face towards the parenchyma, in the back area are observed (26). Literature about Coronavirus 2019 (COVID-19) state that CT scans are diagnostic for the cases (27).

Methods of Protection, Dysinfection and Control

In healthcare centers surfaces, furniture, fixed objects (tables, chairs, walls, computers) and medical equipment must frequently be cleaned with detergents and be disinfected. Disinfectans that were shown effective against SARS-CoV-2 like 70-90% ethanol, chlorine based products (hypochlorite), 0,1% hydrogen peroxide for general enviromental disinfection, 0,5% hydrogen peroxide for blood can be used as disinfectants. In crowded places out of health centers surfaces, furniture and fixed objects like counters, stair railings, bases and walls and all surfaces that can be contaminated by people must be disinfected. Routine application of disinfectants on surfaces in crowded places with increased contamination risks (gyms, offices, restaurants, hotels) is a method that will lower

the risk of SARS-CoV-2 transmission. But organic materials must be removed from the surfaces beforehand in order to effectively disinfect the area with methods like spraying disinfectants. Disinfection must be performed after the surface is cleaned by hand (brushing, rubbing). Performing these methods on people and spraying chemicals like chlorine is dangerous; it may cause toxication, irritate areas like eyes and skin and may cause respiratory distress by bronchospasm. Especially in areas where regular cleaning and disinfection cannot be done; frequent hand washing, and avoiding contact with the face must be considered as the primary protection method. It is important to follow personal protective precautions in order to stop the transmission. Social isolation must be achieved to avoid contact with infected people and contaminated surfaces. Methods like avoiding presence in crowds, wearing surgical masks, not touching the mask, using the mask with coverage over the nose and mouth, not wearing used masks, washing the hands frequently, using non-irritant antiseptics (antiseptics containing minimum 70-90% alcohol) if water can't be found, avoiding face, eye contact with hands, following disinfection rules at home must be followed personally (28). Today many countries aim to decrease disease transmission by promoting strict application of social distancing rules. Many businesses were closed because of that and people started working from home. But this is not applicable for food businesses. So it is important to keep all workers in the food production and supply chain safe from Covid-19 in terms of not creating a more negative situation in the current pandemic.

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