Review Article

Coronavirus disease 2019 (COVID-19): Insights into the recent trends and the role of the primary care in diabetic patients

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Abstract

Diseases with viral etiology continue to emerge in the last years and may represent serious problems that affect various aspects of life. Coronaviruses are a large family of RNA viruses that cause illness affecting the respiratory tract ranging from common cold to severe respiratory distress syndrome. In the last weeks of 2019, enormous cases of unexplained pneumonia were reported in China. Few days later, a novel type of coronavirus was identified as the causative agent of these cases and the disease was named as coronavirus disease 2019 (COVID-19) by the World Health Organization. The disease was rapidly spreading in China and all over the world and now it is considered as pandemic catastrophe. It can be transmitted from animals to human and from human to human. Diabetes mellitus may represent a potential risk factor for the development of COVID-19, possibly due to the relative state of immunosuppression frequently encountered in diabetic patients. This review sheds light on COVID-19 based on the currently available data with reference to the role of the primary care in diabetic patients.

Keywords: Coronavirus, COVID-19, diabetes mellitus, primary care, respiratory distress syndrome

Introduction

In the last decades, many diseases with viral etiology continue to emerge and represent serious problems that may affect various aspects of life and even hinder the development of various countries.[1] About 20 years ago, the severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic was identified and the Middle East respiratory syndrome coronavirus (MERS-CoV) was recorded in Saudi Arabia in 2012.[2] On the last days of December 2019, an epidemic of cases with unexplained low respiratory infections was reported in Wuhan, China. At first, the causative agent of these cases was not identified and they were identified as cases of "pneumonia of unknown etiology." Later on, the exact etiology of this illness was identified as a novel member of the coronavirus (CoV) family, and was referred to as "COVID-19."[3]

Epidemiologic studies found that COVID-19 virus is very contagious and has a rapid rate of spread. In January 30, 2020, the world health organization (WHO) considered the outbreak of COVID-19 as a Public Health Emergency of International Concern (PHEIC) because it extended to 18 countries with four countries reporting human-to-human transmission.[4] Because of its close similarity to the coronavirus that caused the SARS

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outbreak (SARS-CoVs), COVID-19 was termed later on as the SARS-CoV-2 virus.[5]

In the last decades, coronaviruses which are a large family of single-stranded RNA viruses that were isolated from different animal species were implicated in the emerging respiratory disease outbreaks.[6] Several studies reported that COVID-19 may probably originate from bats and then moving into other mammalian hosts such as camels before being transmitted to humans.[4]

On February 28, 2020, the WHO raised the threat concerning the COVID-19 epidemic to the "very high" level as the situation is quickly evolving. Various governments all over the world cooperate together to establish countermeasures to limit the deleterious effects of this disease.[7] On the same line, scientists all over the world try to rapidly develop new methods for rapid diagnosis and prevention and to establish effective strategies for management of this disease. The aim of this review was to shed light on COVID-19 regarding its etiology, pathogenesis, clinical features, methods of diagnosis, relation to diabetes mellitus, and possible lines of management based on the currently available data with reference to the role of the primary care.[8]

Etiology of COVID-19

Coronaviruses are RNA viruses which have spike glycoproteins on the envelope that give them the characteristic crown-like appearance under an electron microscope.[6] The subfamily Orthocoronavirinae of the Coronaviridae family has four genera namely Alphacoronavirus (alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus (deltaCoV), and Gammacoronavirus (gammaCoV). Genomic studies reported that rodents and bats may be the gene sources of alphaCoVs and betaCoVs while avian species may be the gene sources of deltaCoVs and gammaCoVs.[9] Each of these members may be the etiological factor for various respiratory, gastrointestinal, and neurological diseases in different animal species, including camels, rodents, and bats. Up till now, seven human CoVs capable of infecting humans were identified.[10]

Epidemiological studies found that about 2% of the general population may be silent carriers of CoVs and about 10% of acute respiratory infections are caused by CoVs.[11] Common human CoVs such as human CoV-HKU1 and human CoV-OC43 may cause common cold and self-limiting upper respiratory infections in immunocompetent patients and in the elderly, and lower respiratory tract infections in the immunocompromised patients and those with advanced age. Other human CoVs such as SARS-CoV-2 and MERS-CoV may be involved in acute respiratory distress syndrome epidemics with a mortality rate reaching up to 35% particularly in immunocompromised subjects.[12]

SARS-CoV-2 belongs to the betaCoVs subfamily. Its diameter ranges between 60 and 140 nm. It is sensitive to ultraviolet rays and heat and can be inactivated by lipid solvents such as ethanol, chlorine-containing disinfectants, and chloroform.[13] The single-stranded RNA genome isolated from a cluster-patient with atypical pneumonia in Wuhan was found to contain 29891 nucleotides, encoding for 9860 amino acids. Owing to the fact that this genomic structure is closely similar to that reported in a strain found in bats, bats were considered as the most probable sources for this virus. However, the potential intermediate mammalian host between bats and humans is not yet known.[14]

The animal-to-human transmission was initially incriminated as the main mechanism of transmission of the disease. Further studies reported that COVID-19 may be also transmitted from human-to-human, especially from the symptomatic persons.[15] Nevertheless, recent reports concluded that asymptomatic people also may also transmit COVID-19, which makes isolation is the best way to ameliorate this serious epidemic. The transmission frequently occurs through respiratory droplets from coughing or sneezing, particularly in closed places.[16] Data from Wuhan concluded that close contact between individuals is necessary for transmission, particularly in family members, physicians, nurses and other close contacts. Data from the cases in Wuhan reported that the incubation period of COVID-19 varies from 3 to 14 days.[17] However, further studies are urgently required to determine the exact mechanisms of transmission, the incubation period and the potential duration of infectivity of the patients.[16]

Diabetes mellitus, the primary care, and COVID-19

Recent reports from the infected areas with COVID-19 stated that the old people with disease states characterized by immunosuppression are at high risk for the development of severe respiratory distress syndrome and sepsis.[18] Chronic hyperglycemia in diabetic patients may have a negative impact on the immune system and increase the morbidity and mortality rates due to the increased liability to infections and related complications.[19] In 2003, the presence of diabetes mellitus was considered as an independent risk factor for complications and death during severe acute respiratory syndrome (SARS) outbreak.[20] Diabetes mellitus was reported to triple the risk of hospitalization during Influenza A (H1N1) pandemic in 2009 and quadrupled the risk of admission to the intensive care units upon hospitalization.[21] Seasonal influenza vaccine was proven to significantly reduce the secondary in diabetic patients.[22] Reports from Wuhan, China during the recent COVID-19 pandemic stated that among the fatality cases, major comorbid diseases were hypertension (53.8%), diabetes mellitus (42.3%), CHD (19.2%), and cerebral infarction (15.4%).[10]

Iwata-Yoshikawa *et al.*[23] studied the effect of diabetes in worsening severity of infection with Middle East respiratory syndrome Coronavirus in transgenic mice expressing dipeptidyl peptidase IV (DPP-IV) receptors on the pulmonary alveolar epithelium. They reported that as SARS-CoV binds to DPP-IV receptors in the alveoli, this aggravates pulmonary inflammation and infiltration with macrophages compared to control mice

not suffering from diabetes mellitus. From these results, it may be concluded that providing primary care measures to patients with diabetes mellitus may effectively reduce the morbidity and mortality rates from COVID-19.[18] These measures include maintaining strict glycemic control, more frequent monitoring of blood glucose levels, healthy nutrition, and adequate protein intake with correction of vitamins and minerals deficiencies and daily physical exercise to improve immunity.[19]

Pathogenesis of COVID-19

The viral characteristics and the genomic structure SARS-CoV-2 should be considered when investigating the pathogenesis of COVID-19. The pathophysiology and virulence mechanisms of SARS-CoV-2 are closely linked to the function of the structural and non-structural proteins produced by the virus.[24,25] These proteins were reported to block the host innate immunity and significantly ameliorate the host immune response to infection.[26] According to recent studies, mutations in the spike glycoproteins occurred in November 2019, which probably triggered the rapid transmission of COVID-19 in between humans. Studies on a large scale are required to determine the structural characteristics and mutations of SARS-COV-2 that might underlie the pathogenic mechanisms.[27,28]

Clinical characteristics of COVID-19

The clinical picture of COVID-19 is greatly variable from asymptomatic forms to severe cases characterized by respiratory failure that require mechanical ventilation.[28] More advanced cases may progress to severe septicemia with multi-organ failure. The clinical outcomes largely depend on the immune state of the individual and the severity of infection.[29] For the majority of the affected subjects, the clinical course of the disease seems to predict a favorable outcome. Patients with mild illness usually present with symptoms of an upper respiratory tract infection, including mild fever, dry cough, sore throat, nasal congestion, headache, malaise, or myalgia. Cases with moderate disease often present with respiratory symptoms such as cough, tachypnea, and shortness of breath without signs of severe pneumonia.[30]

Patients with severe disease usually present with signs of established pneumonia including high fever, severe dyspnea, tachypnea, respiratory distress, and hypoxia and may even progress to acute respiratory distress syndrome with subsequent respiratory failure.[31] Sepsis and septic shock with a life-threatening organ dysfunction may represent the end stage of a patient with severe COVID-19. Signs and symptoms include severe dyspnea and hypoxemia, altered consciousness, impairment of renal functions, severe hypotension, hyperbilirubinemia, lactic acidosis, thrombocytopenia, disseminated intravascular coagulation, and even signs of septic shock.[32]

Diagnosis of COVID-19

Most countries are utilizing some epidemiologic features that determine the persons who need to be tested for COVID-19. These features include any individual who has had close contact with a patient with laboratory-confirmed COVID-19 within 14 days of symptom onset or a history of traveling from areas known to be affected by COVID-19 within 14 days of the onset of symptoms.[7] It was recommended to collect specimens from both the upper and the lower respiratory tract of the suspected individuals.[5] The genetic material extracted from these specimens is amplified via a reverse polymerase chain reaction, which involves the synthesis of a double-stranded DNA from a single-stranded RNA mold. If the test is positive, it should be repeated for verification. In patients with confirmed diagnosis of COVID-19, the reverse polymerase chain reaction should be repeated to evaluate for complete clearance of the virus before being released from observation.[26]

Complete blood count may support the diagnosis and predict the prognosis of COVID-19 infection.[33] In the early stages of the disease, the total white blood cell count may be normal or mildly decreased with lymphopenia which may be considered as a negative prognostic indicator of COVID-19. Also, increased levels of C-reactive protein, liver enzymes, and lactate dehydrogenase may be reported.[16] In patients with sepsis, D-dimer value is usually increased. Blood lymphocytes show persistent decrease with laboratory results denoting multi-organ failure.[27]

In the early stages of the disease, differential diagnosis should take into consideration the possibility of other causes of infectious and non-infectious respiratory disorders including influenza and parainfluenza virus, respiratory syncytial virus, adenovirus, human metapneumovirus, and rhinoviruses. Rapid antigen detection tests and other investigations should be employed to exclude other respiratory pathogens and non-infectious causes.[34]

Prevention of COVID-19

Till now, the preventive measures are considered the main stay to limit the spread of COVID-19 in the community.[35] These measures include isolation of the confirmed patients and their close contacts and effective implication of the infection control strategies including appropriate precautions during specimen collection and avoidance of sputum induction.[36]

The most important strategy for prevention of COVID-19 is frequent hand washing, the use of portable hand sanitizer and avoiding contact with the face and mouth after interacting with a possibly contaminated environment. Healthcare workers caring for infected patients should utilize protective measures such as gowns, masks, eye glasses, and gloves to prevent transmission of the pathogen.[37] Individuals with symptoms of acute airway infection must keep their distance, cover coughs or sneezes with disposable tissues or masks and frequently wash their hands. People who are immunocompromised and the elderly persons should avoid public gatherings.[38]

Treatment of COVID-19

Up till now, no specific antiviral agent and no vaccine were recommended for COVID-19. The treatment is generally symptomatic, and oxygen therapy represents the treatment

strategy of choice for patients with severe infection.[39,40] Mechanical ventilation may be needed in severe cases with respiratory failure not responding to oxygen therapy. Measures of hemodynamic support with intravenous fluids, vasopressors, positive inotropics, and antibiotics may be essential for management of septic shock.[4]

On January, 2020, the WHO released a document summarizing guidelines for management of COVID-19 based on the acquired experiences from treatment of previous HCoVs epidemics.[7] These guidelines recommended protective mechanical ventilation and high-flow nasal oxygen or non-invasive ventilation for management of COVID-19 cases with respiratory failure.[16] Although no specific antiviral agents were yet approved for treatment of COVID-19, alpha-interferon aerosol inhalation, and lopinavir/ritonavir had been suggested.[9] Inhibitors of RNA polymerase such as remdesivir were suggested to be effective for both prophylaxis and therapy of HCoVs infections.[8] Recent studies reported that chloroquine and hydroxychloroquine might be available weapons to fight COVID-19, owing to their immunomodulatory effects. Hydroxychloroquine may be a promising agent for large-scale use due to its availability, the relatively low cost and the proven safety records.[41]

Prognosis of COVID-19

According to the data retrieved from the epidemiological studies, the estimated death rate of COVID-19 ranges from 1% to 2% depending on the study and the country.[37] The majority of deaths have occurred in patients over 50 years of age and those suffering from debilitating conditions that significantly affect the immune system such as rheumatoid diseases and diabetes mellitus. Infection tends to be generally mild in young children although they may represent a vector for further transmission of the disease.[4]

Conclusion

The outbreak of COVID-19 that originated in China had spread to more than one hundred countries outside China by 20 March 2020. Diabetes mellitus may represent an important risk factor for the morbidity and mortality of COVID-19. Scientists had achieved an interesting progress in the characterization of the novel coronavirus and are working hard to find therapeutic strategies and develop effective vaccines against this virus. However, further studies are urgently needed to explore the possible ways of transmission and the exact mechanisms by which the new corona viruses undergo entry and replication, which may represent the basis of future research on developing effective therapeutic agents and vaccines. Strict implication of the preventive measures with special care to the immunosupressed patients including diabetic individuals remains the worldwide corner stone for control of this epidemic.

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Conflicts of interest

There are no conflicts of interest.

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