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Mini Review

COVID-19, An Eye Opening Pandemic - A Mini Review

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Abstract

Corona virus disease (Covid-19) is an infectious disease of newly discovered Corona virus variant towards the end of the year 2019. It quickly infected thousands and millions of people all over world, spreading widely like a wildfire. By the end of January 2020, World Health organization declared the outbreak as global health emergency and later in March 2020, they announced COVID-19 as a global Pandemic. The uniqueness of Covid -19 was how little was known about the disease. Hence, it was a battle for many researchers, scientists, doctors, dentists, governments and the masses to understand the ongoing Pandemic situation. Although predominantly COVID-19 affects lungs, it did have manifestations on other parts of the human body. Here in this mini literature review, we tried to shed some light on basic aspects of COVID-19 along with oral manifestations, pathophysiology from the dental aspect along with recent advances in Vaccine and the ongoing clinical trials. We encourage active participation of Dentists in promoting the awareness and preventing the spread of covid -19 by understanding and equipping themselves with recent updates on this very disease.

Keywords: Corona Virus Disease; Oral Manifestations of Corona Virus Disease; Vaccines for COVID-19; Clinical Trials on Corona Virus; Dental Aspects of COVID-19; Mini Review of COVID-19

Introduction

Corona Virus Disease 2019 (COVID-19) is the disease caused by a new corona virus called SARS-CoV-2 (Severe acute respiratory syndrome coronavirus) [1].

History of the disease

During the month of December 2019, a considerable number of patients developed pneumonia of unknown cause in the capital city Wuhan of Hubei, a province in China; with clinical presentations greatly resembling viral pneumonia but some rapidly progressed to severe illness and fatal outcome [1,2].

These cases had a history of exposure to Wuhan Seafood Wholesale Market where live animals were also on sale. The disease then rapidly spread from Wuhan to other areas. By the first week of January 2020, a novel coronavirus was identified by the Chinese Centre for disease control and prevention (CDC) from the throat swab sample of these patients, and the virus was named 2019 novel coronavirus (2019-nCoV). Due to rapid global spread the World Health Organization (WHO) on January 30,2020; declared the outbreak as a public health emergency of international concern [1,2].

On 11 February 2020, WHO announced that "COVID- 19" (meaning coronavirus disease-2019) will be the official name of the dis-

ease. WHO has been deeply concerned by the alarming levels of spread and therefore, on 11 March 2020 made the assessment that COVID-19 can be characterized as pandemic [1,2].

Structure of the virus

COVID-19 is an RNA virus, with a typical crown-like appearance under an electron microscope due to the presence of glycoprotein spikes on its envelope, which give them the appearance of a solar corona. Due to, genetic similarities between the new coronavirus and the coronavirus that caused the SARS outbreak in 2002-2003, recently the new virus has been renamed as SARS-CoV-2 [1,2].

Pathophysiology

The unusually high pathogenicity for 2019-nCoV has not been completely understood as yet. Respiratory droplet transmission is the main route and it can also be transmitted through person-to-person contacts by asymptomatic carriers. The virus might pass through the mucous membranes, especially nasal and larynx mucosa, then enters the lungs through the respiratory tract.

Then the virus would attack the targeting organs that express angiotensin converting enzyme 2 (ACE2), such as the lungs, heart, renal system, gastrointestinal tract, skeletal muscle, tongue and salivary glands. Virus particles spread through the respiratory mucosa and infect other cells, induce a cytokine storm in the body.

Generate a series of immune responses, and cause changes in peripheral white blood cells such as lymphocytes that have role in body immune response. It progresses rapidly with acute respiratory distress syndrome (ARDS) and septic shock, which was eventually followed by multiple organ failure [1-4].

General clinical features

Reported studies have described the illnesses that have ranged from mild to severe disease, including death. The WHO has reported an incubation period for COVID-19 between 2 and 10 days. However, some literature suggests that the incubation period can last longer than two weeks and it is possible that a very long incubation period could reflect double exposure. The severity of the clinical picture seems to be correlated with age (> 70 years), comorbidities such as: diabetes, chronic obstructive pulmonary disease (COPD), hypertension, obesity and male sex but currently no scientifically valid explanations have been developed. The most common symptoms of COVID-19 are Fever, dry cough, fatigue. Other symptoms that are less common and may affect some patients include: Loss of taste or smell, nasal congestion, conjunctivitis, sore throat, headache, muscle or joint pain, different types of skin rash, Nausea or vomiting, diarrhea, chills or dizziness [1-4].

Symptoms of severe COVID-19 disease include: Shortness of breath, loss of appetite, Confusion, Persistent pain or pressure in the chest, High temperature (above 38°C) [1-4].

Oral manifestations [4-9]

The most common sites of involvement in descending order were tongue > labial mucosa > palate > gingiva> buccal mucosa > oropharynx > and tonsil [4,5].

Most common oral manifestation seen are Dysgeusia/loss of taste [3], Xerostomia [6], Aphthous-like ulcerations [7,8], Recurrent oral herpes simplex virus (HSV-1) infection [7,8], Erythema multiforme like ulcerative and erosive lesions [8], Unspecific oral ulcerations/mucositis, Oral candidiasis, angular cheilitis, Petechiae, Hyperpigmentation, Gingivitis, Necrotizing periodontal disease, Cervical facial lymphadenopathy, Acute non suppurative parotitis, Kawasaki-like lesions, Drug eruption lesions, Angina bullosa-like, Atypical Sweet syndrome, Melkersson-Rosenthal syndrome [9].

Vaccine and drugs for Covid-19

Vaccine has been the long-known technology that has helped our human community surpass the pandemics and epidemics in the past [10]. The Covid-19 disease caused by the Sars-Cov2 virus was a colossal pandemic wave after the H1NI influenza in 2009 [11]. In the past year, since the start of the COVID-19 pandemic, a vast array of research teams arose across the world to the challenge posed by this pandemic and has successfully developed vaccines that protect from the SARS-CoV-2 virus that causes COVID-19 [10].

There are currently 8 vaccines that are EAU (Emergency Authorization use) approved, and there ongoing 67 projects in various clinical trials across the world working towards manufacturing the vaccine and making it available globally [10]. The ongoing clinical trials that would eventually lead to mass production of vaccines will be the key to making it available in all countries, not just the developed and rich countries [10]. The 8 are EAU (Emergency Au-

thorization use) approved, are categorized based on their type and mechanism of action (MOA) below [15].

mRNA vaccine type

MOA: The covid-19 virus has a surface protein called the SPIKE. The vaccine is made of mRNA, which has the code to synthesize the same protein as in covid-19. When vaccinated, the mRNA(code) instructs the cell to synthesize the protein (spike) and is expressed on its surface. After this is accomplished, the mRNA is destroyed. Our immune system recognizes the new protein as an antigen and develops antibodies against the same and hence immunizes one to symptomatic COVID-19 disease [12].

	Efficacy	Dosage	Dosage frequency	Administration
Pfizer-BioNTech-COVID-19 Vaccine.	95% [12]	0.3 ml [12]	21 days [12]	Intramuscular [12]
Moderna	94.1% [12]	0.5 ml [12]	28 days [12]	Intramuscular [12]

Table 1

Adenovirus vector-based vaccine

MOA- These vaccines are manufactured based on the adeno-virus-based vector technology. The adeno-vector (vehicle) is the adenovirus without the genetic material that causes the infection and replication. To this vector(vehicle), the genetic code required to synthesize the Spike protein present in Sars-Cov-2 is introduced. The injected genetic code is incapable of infecting the individual instead triggers the immune system to build immunity against the COVID-19 disease [13]. Types are:

- Covishield: This vaccine uses the adenovirus-vector that causes common cold in chimpanzees [13].
- Sputnik: This vaccine uses the adenovirus-vector that cause common cold in humans [14].

Inactivated vaccine type

MOA - The inactivated whole virion (virus cell) is used to vaccinate. As these vaccines are made of dead virus cell they are incapable of infecting the individual but in turn triggers the immune system to build immunity against the COVID 19 disease [17].

Vaccine name	Manufacturer	Dosage	Dosage frequency	Efficacy	Administration
COVISHIELD	Astrazenaka-UK	~5 x 1010 viral particles [13]	12 weeks [13]	70.1% [13]	Intramuscular [13]
SPUTNIK V	Gamaleya Research Institute-Russia	0.5 ml [14]	21 days [14]	91.6% [14]	Intramuscular [14]

Table 2

Vaccine name	Manufacturer	Dosage	Dosage frequency	Efficacy	Administration
Coronavac	Sinovac-China	3 µg [17]	14 days [17]	50.4% [17]	Intramuscular [17]
Covaxin	BharathBiotech-IN	6 µg [18]	28 days [18]	91.6% [18]	Intramuscular [18]
BBIBP-CorV	Sinopharm-China	No Data available	14/28 days [15]	No data available	Intramuscular [15]

Table 3

Peptide vaccine

MOA- Peptide vaccines are synthetic vaccine that are manufactured by mimicking the genetic code (peptide sequence) to trigger the immune response and provide immunity against the disease-causing agent. Because they would be synthetic, there would be no risk of mutation or reversion, little or no risk of contamination by

pathogenic or toxic substances, and chemical manipulation of the peptide structure could possibly increase stability and decrease unwanted side effects seen in the native sequence [20].

There are about 67 ongoing clinical trials of which close to 20 are reaching the final stage of the clinical trial and 89 ongoing pre-clinical trials. The few of promising vaccine candidates in development and are yet to be approved are categorized below on the basis of their clinical development [10].

Vaccine name	Manufacturer	Dosage	Dosage frequency	Efficacy	Administration
Epivac-corona	State Research Center of Virology and Biotechnology-Russia	No data available	21 - 28 days [21]	No Data available	Intramuscular [21]

Table 4

Briefly, clinical trial is an experimental study involving humans, that compares therapeutic benefit of a treatment and placebo [10].

It has 4 phases as follows: Phase 1: It is determined whether the treatment/ medicine is safe, while assessing the mechanism and toxicity [10]. Phase 2: It is determined whether the medication/ treatment actually works, asses the dose and adverse effects [20]. Phase 3: It is determined whether the treatment is better to others [10]. Phase 4: It is determined whether the treatment/medication can stay by assessing the long-term adverse effects [10].

Therapeutic management for covid-19 disease caused by Sars-Cov2 virus, there are thousands of ongoing research and clinical trials worldwide in the hope of finding the most potential treatment option to manage the disease therapeutically.

Vaccine candidate	Mechanism	Trial Phase	Developer
CORVax12	DNA vaccine (plasmid)	Phase 1	OncoSec; Providence Cancer Institute-Portland
SCB-2019	Protein subunit vaccine	Phase 1	Linear Clinical Research -Australia
pVAC	Multi-peptide vaccine candidate	Phase 1	University Hospital Tuebingen
AG0301-COVID19	DNA vaccine	Phase 1/2	AnGes, Inc.; Japan Agency for Medical Research and Development-Japan
Soberana 1 and 2	Monovalent/conjugate vaccine	Phase 1/2	Finlay Institute of Vaccines- Cuba
BNT162	mRNA-based vaccine	Phase1/2/3	Multiple study sites in -Europe, North America and China
CVnCoV	mRNA-based vaccine	Phase 2b/3	CureVac
Convidicea (Ad5-nCoV)	Recombinant vaccine (adenovirus type 5 vector)	Phase 3	Tongji Hospital; Wuhan, China
NVX-CoV2373	Nanoparticle vaccine	Phase 3	Novavax
JNJ-78436735 (formerly Ad26. COV2.S)	Non-replicating viral vector	Phase 3	Johnson and Johnson

Table 5

In the past year, advances are moving in this direction with a better understanding of the virus [22]. At present, the therapy for Covid-19 fall into three major categories, these approaches along with their mechanism of action (MOA), are mentioned below [22]:

1. Antiviral: MOA - Prevents replication of the virus. Remdesivir is the only FDA-approved drug, another antiviral drug

such as favipiravir is authorized in different countries [23]. There are a few others that are under clinical trial, such as ritonavir, umifenovir, lopinavir [23].

2. Anti-inflammatory: MOA - It helps prevent hyperactivity of the immune system that would lead to dangerous complication. Dexamethasone a corticosteroid, an anti-inflammatory drug, administered only to hospitalized patients in need of adjuvant oxygen supply, first known drug to increase the survival rate, other drugs like baricitinib plus remdesivir (Baricitinib is used for treating rheumatoid arthritis and has anti-inflammatory properties, it is used along with remdesivir when corticosteroid cannot be used) [23]. Another anti-inflammatory drug that has been approved in other countries is Itolizumab (a drug used for the treatment of psoriasis). Researchers are currently studying interferon therapy. It is known to modulate immune response for viral infections [24].
3. Immune therapy: MOA - Support the immune system to fight the virus. This approach is used on critically ill patients. Convalescent plasma is currently approved. It is antibody-rich plasma of someone who has recovered from Covid-19, thereby boosting the recipient's immunity to fight the disease. Other therapies such as monoclonal antibody that inhibits interleukin-6 that is important in the treatment of covid-19 are currently under clinical trial and are called tocilizumab [23].

Conclusion

This literature overview on this article is intended to collect all the published data on Covid-19 caused by the Sars-Cov2 virus to understand the structure, the pathophysiology and the oral manifestations of the virus. We briefly outline the different kinds of vaccines currently available along with the ongoing clinical trials and various treatment protocols, medications used currently. However, it should be taken into consideration that due to the high fluidity of the evolving nature of this pandemic and the unraveling natural history of the disease process, it is very crucial for the dental community always to keep informed about the new developments and protocols issued. It is always wiser to know the basic knowledge alongside recent advances in such given situations. Dentists' awareness and participation in prevention, education, vaccination plays a pivotal role in promoting dental public health during such eye-opening Pandemics.

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