



# Journal of Umm Al-Qura University for Medical Sciences

Journal homepage: <https://uqu.edu.sa/en/mj>

## COVID-19 Vaccine and Its Impacts on Dental Practice in Saudi Arabia

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### ARTICLE INFO

#### Article History:

Submission date: 18/09/2021

Accepted date: 26/01/2022

#### Keywords:

COVID-19; Vaccine types; Dental Practice; Herd Immunity, Saudi Arabia.

### ABSTRACT

Despite of various COVID 19 mitigation measures done by health authorities and governments all over the world, severe acute respiratory syndrome coronavirus-2 (SARS CoV2) transmissibility is still high and threatens population. Immunization by safe, effective newly developed vaccines remains the best hope to end the COVID-19 pandemic. Saudi Arabia was one of the first countries in the world to begin vaccination program where dental practitioners were among health care providers who were prioritized to get the vaccine. The aim of this review is to discuss the developed anti-COVID 19 vaccines and to highlight the anticipated impacts of these vaccines on dental practice in Saudi Arabia. Different strategies for vaccine development were introduced either by conventional methods such as live attenuated virus, inactivated or killed virus, or by next-generation vaccines. So far, out of many clinical trials made for vaccines, few types were agreed for emergency use. The major vaccine types tested in these trials are viral vector-based vaccines, mRNA vaccines, attenuated vaccines, and protein-based vaccines. In Saudi Arabia, the national immunization technical advisory group has authorized Pfizer-BioNTech BNT162b2 and ChAdOx1 nCoV-19 Oxford-AstraZeneca vaccines and started mass campaigns to vaccinate its citizens and residents on track to reach herd immunity. Although wide-scale vaccination among dental practitioners is expected to have many positive impacts on dental practice and return the profession to pre COVID stage, the high transmission rate and emerging new variants of the virus strongly recommend adherence to guidelines for SARS- CoV- 2 infection prevention during dental practice.

### 1. Introduction

The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) had infected at least 224 511 226 globally, leading to 4 627 540 deaths and still counting despite of implementation of many precaution measures [1]. The key measures used to mitigate the virus transmission by most countries around the world include social distancing, enforcing masks policy, frequent hand hygiene, travel restrictions, partial or complete lockdowns, and schools' closures [2]. Since such preventive measures could not completely stop the spread of COVID-19 as well as none of the explored therapies can directly kill the virus, so, the vaccine is the most promising health intervention strategy to mitigate the spread of SARS-CoV-2 [3,4].

In Saudi Arabia, the total number of COVID-19- positive cases to date (14<sup>th</sup> September 2021), are 546,067 with 8,628 associated deaths [5]. Since reporting of the first case in the kingdom on March 2nd, 2020, the Saudi Ministry of Health implemented multiple strategies to decrease the number of cases and slow the spread of SARS-CoV-2 infection [6]. To accomplish that strategy, multiple protective measures were implemented on 9<sup>th</sup> March including travel restrictions, lockdown, and curfews (suspending Umrah and prayers at mosques; closing all shopping malls, schools and universities; suspending employee attendance at governmental and private workplaces (except for critical staff as health care workers, police and military soldiers,.....etc ) [7]. Saudi Arabia was at the forefront of countries in the world to begin vaccination programs. The first vaccine approved for use by the Saudi FDA and by the national immunization technical advisory group was in mid-December 2020. Later on, in February 2021, a second vaccine was authorized for use in the kingdom [8].

The dental practice carries a very high potential risk of transmitting COVID-19 infection as considered by the Occupational Safety and Health Administration (OSHA) [9]. The risk of COVID-19 infection is high in countries with higher community spread while this risk is reduced when community spread is low [10]. To the best of our knowledge, there are no published reviews elucidating COVID- 19 vaccine impacts on dental practice after the vaccination campaign started in Saudi Arabia. So, the aim of this review is to elucidate the various types of vaccines developed against SARS -CoV- 2 and discuss their impacts on dental practice in Saudi Arabia.

### 2. Viral vaccines

#### 2.1. Categories and principles of viral vaccines:

For the preparation of any viral vaccine, one of two main approaches is used: either conventional or next generation. Conventional approaches deliver either *live attenuated virus and inactivated or killed virus* while next-generation vaccine approaches protein subunit vaccines, virus- like particles or nucleic acid- based (DNA or mRNA) vaccines) [11].

##### 2.1.1. Conventional viral vaccines:

The conventional viral vaccines including *Live attenuated and inactivated/ killed virus vaccines* had successfully decreased the burden of a significant number of viral diseases, leading to the eradication of small pox and significant limitation of some diseases, such as polio. However, these vaccines may be not suitable in outbreaks, as live attenuated vaccines carry the risk of reversion, and chemicals used for inactivation or killing of inactivated/ killed virus vaccines can lead to undesired effects. Furthermore, during outbreaks, conventional vaccine development may be limited, as it requires cultivation and propagation of the pathogen [12].

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### 2.1.2. Next-generation viral vaccines:

**2.1.2.1 Viral vector-based vaccines** that based on the delivery of one or more antigens of a modified virus engineered to encode for those antigens, which are then introduced into the host cells by the vector. In vivo, the antigen is expressed, and the host can induce an immune response against the target virus [13].

**2.1.2.2. Viral protein subunit vaccines** contain protein of the target virus or portions of it and act by inducing the production of neutralizing antibodies. Proteins or peptides alone are poorly immunogenic and always require repeated administration with the use of an adjuvant [14].

**2.1.2.3. Virus-like particles** are particles composed of several structural viral proteins that are co-expressed and are non-infectious although it is structurally identical to the infectious virus but lacks the viral genome [15].

**2.1.2.4 Viral nucleic acid-based vaccines** use genetic material encoding the antigen (plasmid DNA or RNA, as messenger RNA or viral replicon) from a disease-causing virus to stimulate an immune response against it. Once inserted into host cells, protein-making machinery recognizes it as foreign, read and manufacture antigens, which then trigger humoral as well as cell-mediated immune responses [16].

### 3. Anti- COVID-19 vaccines:

Several COVID-19 vaccine types and candidates were immediately started by vaccine research and development (R&D) on 11 January 2020, ten days after the SARS-CoV-2 virus was isolated and the full genetic sequence of it was released and made available to scientists [17].

The vaccine-targeted antigens were selected after the description of structural proteins present in the infectious virion. Three of these proteins are inserted into a lipid envelope derived from the host cell membrane and include spike (S) protein, membrane (M) protein, and envelope (E) protein. The fourth protein named N protein coats the large RNA and is encased by the lipid envelop (Figure 1) [11]. It was found that the only antibodies that can neutralize the virus and prevent infection are those directed to (S) protein as it is responsible for host cell receptor binding and membrane fusion (Figure 2) [12,13].

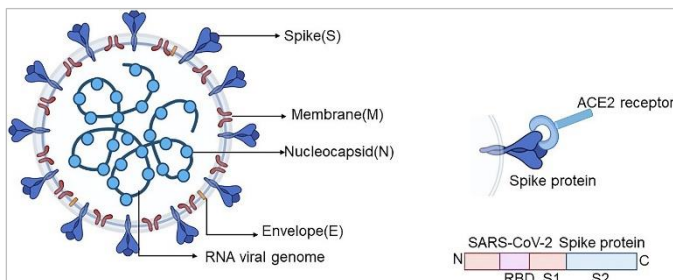


Figure 1: Schematic diagram of the SARS-CoV-2 coronavirus particle [11]

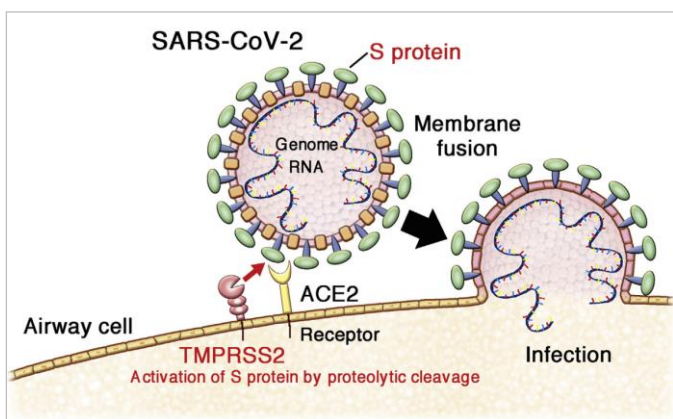


Figure 2: SARS-CoV-2 S protein receptor binding and membrane fusion [12]

In response to rapidly disseminated SARS-CoV-2 causing COVID-19, scientists and pharmaceutical companies have been in a race to produce vaccines. About 200 official vaccine projects were started by

December 2020 with approximately 80 of them have already reached human experimentation as confirmed to be active in vitro [19,20].

### 3.1. Conventional anti-COVID-19 vaccines:

Two *live attenuated SARS-CoV-2 vaccines*: projects of active preclinical development were commenced at Indian institutions, one in collaboration with a New York private biotech and the other in collaboration with an Australian university. A third project developed at a Turkish university was started but none of these three projects reached the stage of clinical trials. On the other hand, only *Inactivated or killed SARS-CoV-2 vaccines* already approved for limited use in the general population after passing phase III trials were available. These vaccines include Sinovac Biotech; Sinopharm, Wuhan; Inst Biol Products, China; and Bharat Biotech, India [20].

### 3.2. Next-generation anti- COVID-19 vaccines

**3.2.1 SARS-CoV-2 protein subunit vaccines**: projects based on SARS-CoV-2 proteins, their fragments, or their fragments combination. COVID-19 vaccines based on Spike protein, are the most immunogenic and activated by combination with new adjuvants either of bacterial or synthetic origin [22]. Some of these candidate vaccines are already in human trials and others are in Phase II trial [20].

**3.2.2 SARS-CoV-2 Virus-like particles (VLP) vaccines**: are plant-based vaccines, where genetic modification of tobacco plants was done by inserting the spike protein gene of the virus into a bacterium to infect it. Tobacco plant cells then act as spike protein producers where the protein aggregate as virus-like particles. Medicago; Canada and GlaxoSmithKline; Italy are two producers of VLP-based vaccine candidates for COVID-19 that are in the phase III trial [21].

**3.2.3. Recombinant SARS-CoV-2 viral-vectored vaccines**: among those vaccines which underwent the stages of preclinical studies, the adenovirus-based vectors were the most accepted ones approved to elicit a strong antibody response. *Sputnik V* vaccine, created in Russia, uses different adenoviruses for the first and second doses and was the first COVID-19 vaccine to be registered and authorized for use by the Russian Ministry of Health, in August 2020. However, to date, neither the European Medicines Agency (EMA) nor the World Health Organization (WHO) had approved the Russian Sputnik V vaccine for emergency use. The second adenovirus-based vector vaccine was *Oxford AstraZeneca ChAdOx1 nCoV-19*, utilizing adenovirus from chimpanzees, which was approved at the end of December 2020, in the United Kingdom and used for vaccination in many countries all over the world starting from January 2021. The third adenovirus-based vector vaccine is *Johnson & Johnson* developed by Janssen Pharmaceutica, a Belgium-based division in collaboration with Beth Israel Deaconess Medical Center, and has been authorized for emergency use by the European Union, the United States, and other countries by end of February 2021. The fourth adenovirus-based vector vaccine developed is *CanSino*, China's CanSino Biologics Inc, and China obtained a limited authorization for administration of Chinese health care workers and military soldiers [22,23].

### 3.2.4. SARS-CoV-2 Virus nucleic acid-based vaccines:

**3.2.4.1. DNA based vaccines**: use plasmid DNA that contains mammalian expression promoters and the gene that encodes the spike protein of SARS-CoV-2 virus, which is then expressed in the vaccinated individual on delivery and stimulates an immune response. However, vaccines using this approach are still in phase I/II clinical trials [24].

**3.2.4.2. SARS -CoV- 2 mRNA vaccines**: two mRNA vaccines were generated in less than one year after the virus genetic sequence was released. These two vaccines including mRNA-1273 (developed by Moderna) and BNT162b (developed by Pfizer and BioNTech Ltd.) represent only 11% of all the vaccines developed on various platforms. Both types of vaccines were approved for emergency use in many countries [3].

### 4. Impacts of SARS -CoV- 2 infection on dental practice:

During dental procedures, exposure to SARS-CoV-2 is highly anticipated to occur via generated droplets and aerosols either from confirmed, suspected, or asymptomatic patients. Another important risk factor that creates cross-infection in dental practice is the

prolonged close contact between patients and operators during different treatment procedures [9]. So, early after the emergence of the pandemic, on March 18<sup>th</sup>, the American Dental Association (ADA), and the U.S. Centers for Disease Control and Prevention (CDC) have urged all dentists to cancel or postpone all elective and non-urgent dental visits and accordingly routine dental practice has been suspended in several countries [25, 26]. Furthermore, the continued community spread of COVID-19 can lead to accidental aerosol exposure from infected patients in dental practices [27].

The high risk of COVID-19 infection transmission among dental healthcare practitioners has mandated the health authorities to develop new guidelines and recommendations [28]. In Saudi Arabia, the guidelines, and recommendations of both the World Health Organization (WHO) and the Centre for Disease Control (CDC) USA, have promptly been adopted and are available to all dental practitioners by the Ministry of Health (MOH) on the official website [29].

### 5. Impacts of COVID- 19 pandemic on dental education:

University dental clinics and dental hospitals may potentially create a reservoir for the spread of the SARS-CoV-2 virus as patients, students and teachers share the same spaces during clinical teaching sessions [9]. So, shortly after the emergence of the COVID-19 pandemic, higher education institutions all over the world prioritized the safety and wellbeing of their students and staff. They shift campus teaching and exams to online distance learning and assessment on various internet platforms. On the other hand, laboratory, preclinical, and clinical sessions, which are core components of the dental education program, were postponed [30]. This was also the case for Saudi dental students during the early wave of the pandemic, in the second semester of the academic year 2019-2020. Nevertheless, at the same time, some dental schools in Europe extend their program dates and reschedule examinations in order to not reduce their clinical graduation requirements [31]. In the United States, most dental schools suspended clinical activities allowing only management of dental emergencies where students were participating in teledentistry consultations to continue their learning. However, the remaining schools practiced social distancing in their preclinical simulation laboratory activities [32]. Yet, among the problems facing online education, a major factor was that although most students had experience in using technology with online educational platforms, many faculty members lacked that experience [33].

In order to help students to compensate for their lost educational time at the first pandemic wave, educational institutions followed CDC guidelines for re-opening institutions of higher education based on risk levels associated with an educational activity. In dental education, it was critical to provide safe and healthy clinic environments, where dental school activities cover all the risk levels from low risk in online classes to high risk in the clinics [33].

Accordingly, during the second wave, most of the dental schools across the globe switched from the usual way of teaching to a hybrid model with online learning for theoretical sessions and on-campus face-to-face clinical sessions. This policy was followed in the attempt to minimize the virus transmission and compensate for various unlearned practical and cognitive skills, that are necessary to the profession [34]. A number of policies, tools, and guidelines were recommended by CDC, ranging from patient triage, social distancing, and direct patient management using various precautions, such as air purifiers and, personal protective equipment (PPE) especially during aerosol-generating procedures [35].

Lately, after the development of an effective vaccine against SARS-CoV-2 virus, CDC guidelines for institutions of higher education (IHEs) stated that learning can be returned to full capacity at the universities without masking or physical distancing, provided that all faculty staff and students are fully vaccinated. But the recommendations also emphasize at the same time, the continued implementation of general protective measures like hand hygiene, cough etiquette, cleaning, and disinfection. Furthermore, the guidelines recommended the utilization of appropriate preventive strategies in the presence of not fully vaccinated individuals on the campus [35].

### 6. Impacts of COVID- 19 pandemic on the psychological health of dental practitioners:

Anxiety and fear of becoming infected with SARS-CoV-2 virus, during dental practice were investigated in a cross-sectional study in March 2020. A number of 669 dentists in 30 different countries were included and the conclusions reported that 87% of participants feared that they could become infected from either a patient or a co-worker [36]. On the other hand, 60% of dental students in a Saudi college were anxious and worried to be infected by SARS-CoV2 while treating their patients [37]. Moreover, a study of the impact of the COVID-19 pandemic on the financial health of dental students concluded that they were worried about their financial situation, expressing fear about meeting their financial responsibilities, and were also anxious about finding a job after graduation [33].

### 7. COVID- 19 vaccination in Saudi Arabia:

After launching the vaccination program, Saudi MOH planned a phased approach that initially targeted the healthcare workers (HCWs), high-risk populations with comorbid illnesses, and the elderly. A second and third phase followed targeting vaccination of at least 70% of the whole population in the kingdom [19]. This target was set to achieve the goal of WHO stated that all countries are of utmost need to develop herd immunity. To reach herd immunity, WHO stated that vaccination coverage for 60–70% of the population must be achieved either through vaccinations or exposure to the virus [8]. The very active strategy put by KSA to provide immunization to all citizens and residents on track to reach herd immunity. By September 13<sup>th</sup>, 2021, almost 39,822,645 doses of COVID-19 vaccine were given (to more than 50 % of the total population recently estimated of more than 35 million) [38-40]. Herd immunity is expected to be achieved soon in Saudi Arabia after the announcement of the Saudi Ministry of Human Resources and Social Development On 7 May 2021 that COVID vaccination will be mandatory for employees of all sectors to attend workplaces starting from 1 August 2021. The same announcement was also stated by the Ministry of Education for entry to educational and administrative facilities.

The two approved vaccines in Saudi Arabia; Pfizer–BioNTech and AstraZeneca–Oxford vaccines have reported efficacy relative risk reductions of 95% and 67% respectively [41]. Moreover, the approved efficiency of Pfizer BNT162b2 vaccine against a new SARS-CoV-2 variant, emerged in the United Kingdom in December 2020 and is estimated to be almost 50% more contagious, validates the kingdom choice of the vaccine [19].

### 8. Impacts of COVID-19 vaccine on dental practice in Saudi Arabia

In the first phase of the COVID-19 vaccination campaign, Saudi MOH had made the vaccine priorities to health care professionals at healthcare sectors including the MOH facilities, institutions, private hospitals and clinics as well as large public pharmacies [8]. General immunity achieved by anti-COVID vaccine among practice staff will offer a much safer environment for providing dental services, reassuring patients, and the dental team. Immunization not only protects dental health care workers but also protects their families, patients, and service users, from an occupationally acquired infection. Additionally, it protects vulnerable patients who may not respond well to their own immunization [42]. However, ADA recommended that even if the whole members of the dental team in any treatment center have been vaccinated, it is still vital to follow preventive strategy put pre-vaccination including frequent hand hygiene, wearing appropriate PPE, keeping adequate physical spaces even in absence of patients in the clinic. Their recommendation is based on the fact that none of the currently available vaccines is 100% effective [43]. Besides, the presence of more than 80 genotypes of COVID-19, risk of asymptomatic carriers, rapid neutralization of the antibodies within a short period after recovery from COVID, and the likelihood of recurrent infection. Thus, there are still some worries on whether vaccination alone will provide long-term immunity against COVID-19 and its variants. So, in spite of the development of effective vaccines, post-COVID -19 dental practice is expected to have permanent changes, with new perspectives. These changes rely on the core operating protocols, regional COVID-19 rates, and subsequent predicted risk of infection [44].

## 9. Conclusion:

Undoubtedly, the current COVID-19 vaccination program, for various cohorts in the kingdom, will have a positive impact on dental practice in the context of safe patient management, decreasing the cost of extra precautions taken during treatment and relieving the psychological burden on dental practitioners. In addition, it will help dental students regain their confidence and acquire manual skills during clinical training, which is the core element of the dental profession. However, even after vaccination of practitioners and patients, implementation of the adopted preventive strategies against COVID-19 is still highly recommended until the SARS-CoV-2 virus becomes less virulent, and its spread rate naturally diminishes.

**Financial support and sponsorship:** None.

**Conflict of interest:** The authors declare no conflict of interest, financial or otherwise.

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