



Review Article

Global acceptance and hesitancy of COVID-19 vaccination: A narrative review

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Abstract

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a major global health threat to human civilization and has disrupted many aspects of the community around the globe. Vaccination is one of the prominent measures to control the COVID-19 pandemic. More than 120 vaccines have entered human clinical trials and at least 8 vaccines have been fully approved. However, the success of the COVID-19 vaccination programs depends on how the community accepts the vaccines. Despite COVID-19 vaccination having been initiated for a while now, more than 50% of the global population have not been vaccinated. In some low- and middle-income countries (LMICs), the vaccine coverage is less than 20%. Since the decision to accept the new vaccine is complex, understanding the factors underpinning vaccine acceptance is critical. This review aimed to summarize the COVID-19 vaccine acceptance rate around the globe as well as its associated determinants. Information from this study might be important to formulate effective strategies to increase the COVID-19 vaccine coverage, and to be able to achieve herd immunity.

Keywords: COVID-19, COVID-19 vaccine, vaccination, vaccine acceptance, vaccine hesitancy

Introduction

In December 2019, the coronavirus disease 2019 (COVID-19) outbreak started in Wuhan, China. The COVID-19 outbreak was declared as a pandemic by the World Health Organization (WHO) on March 11, 2020 and as of October 9, 2021, there have been more than 236.5 million confirmed cases and more than 4.8 million deaths worldwide [1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, is closely related to other newly emerging coronaviruses such as severe acute respiratory syndrome (SARS) coronavirus that emerged in 2002-2003, and the Middle East respiratory syndrome (MERS) coronavirus which emerged in 2012 [2]. The SARS-CoV-2 is a single-stranded, positive-sense RNA virus [3]. These viruses contain spike proteins (S-proteins) that bind with angiotensin-converting enzyme 2 (ACE2) receptors present on the surface of human lung epithelial cells [3]. ACE2 receptors are the same receptors utilized by the SARS-CoV [4]. After adhering to the cell



membrane, the virus hijacks the cell machinery, integrating its RNA into the cell's replication cycle, causing its further proliferation in the body and activating host immune responses [3].

The mortality rate of COVID-19 is lower than SARS and MERS and varies among countries. However, COVID-19 is significantly more contagious than SARS and MERS, hence the number of cases skyrocketed and outweighed both MERS and SARS [3]. SARS-CoV-2 is primarily transmitted through respiratory droplets (i.e., coughs, sneezes, and mucus that contain viral particles) [5]. On average, the droplets can travel not more than 2 meters and do not linger in the air [6, 7]. However, under experimental conditions, the SARS-CoV-2 remains viable in aerosols for 3 hours [7]. In addition, the viruses have also been shown to be transmitted through fomites (transmitted through contaminated surfaces) [7]. SARS-CoV-2 could contaminate different surfaces for several hours to up to 3 days depending on their material [7]. The median incubation period of COVID-19 is five days; however, it could be up to two weeks [3]. There is mounting evidence that COVID-19 can be transmitted while the person is asymptomatic, subsequently making it difficult to control and contain the spread [3].

The symptoms experienced by individuals infected by the SARS-CoV-2 include but are not limited to fever, cough, shortness of breath, and fatigue [8, 9]. Patients with severe COVID-19 suffer from acute respiratory distress syndrome (ARDS), multiple organ failure, and death [9]. In the absence of a definitive treatment, one of the best strategies is the vaccine [1] and high vaccination coverage is urgently required to achieve herd immunity against COVID-19. Vaccine development began as soon as the first genome sequence of SARS-CoV-2 was identified and published. Approximately 185 COVID-19 vaccines are in the preclinical stage and 102 have been entered clinical trials [10]. Currently, 31% of the COVID-19 vaccines in clinical development are protein subunits, succeeded by 16% of viral vector (non-replicating), 16% of mRNA and, 16% are made with the inactivated virus [10].

The COVID-19 vaccination programs are only successful when they are highly accepted by the community [11]. However, vaccine acceptance and demand are complicated; it is driven by various context-specific factors, including time, space, and most importantly, perceived behaviors of the community [12, 13]. This review sought to summarize the COVID-19 vaccine acceptance and hesitancy around the globe as well as its associated determinants. With this intent, effective strategies to increase the COVID-19 vaccine coverage and eliminate the current COVID-19 pandemic could be formulated.

COVID-19 vaccine: An update

Type of COVID-19 vaccines

Currently, several COVID-19 vaccines have been approved and multiple vaccine candidates are at the clinical stage of development. The vaccines and vaccine candidates were produced with different approaches. Some vaccine developing companies like Pfizer and Moderna employed synthetic mRNA by encoding the sequence of SARS-CoV-2 S-protein, which is then encapsulated within a lipid nanoparticle to preserve its integrity [14]. Oxford-AstraZeneca, Gamaleya (Sputnik V), Janssen, and CanSino developed the recombinant vaccines based on a DNA sequence encoding the S-protein inserted into the genome of a modified safe adenovirus [15]. The pathogen's genetic material is destroyed by heat, chemicals, or radiation so that they cannot replicate but their presence can still stimulate immunogenicity [15]. Sinopharm, Sinovac, and Bharat Biotech's vaccines were produced by inactivating the SARS-CoV-2 (grown in Vero cells) with β -propiolactone and absorbed onto aluminum hydroxide but keeping all the viral protein intact. Novovax, a recombinant protein subunit vaccine, was developed by using full-length S protein with a mutation at S1/S2 cleavage sites which safely generate an immune response against COVID-19 [16]. Without introducing viable pathogen particles, these subunit vaccines contain a fragment of the pathogen, either a protein (Pro-subunit), a polysaccharide, or a combination of both [17].

Efficacy of vaccines

There is a wide variation in the efficacy and safety of different vaccines. After completion of the phase 3 trial, Moderna showed a 93.2% efficacy in preventing COVID-19 and 98.2% in preventing severe COVID-19 cases in participants aging at least 18 years old, while the efficacy of Moderna on adolescents (12-17 years old) is ongoing phase 2/3 trial of and it was difficult to assess due to low incidence of COVID-19 cases in this population [18, 19]. Meanwhile, the first dose of Sputnik V showed 91.6% (16 of 14964 participants) efficacy, and only 0.3% (45/16427 participants) had serious adverse events [20]. Single-dose of Janssen Ad26.COVS.2 S also has a higher efficacy against severe-critical COVID-19 infection based on phase 3 clinical trial (Efficacy: 76.7% for onset at ≥ 14 days and efficacy 85.4% for onset at ≥ 28 days) [21]. Besides, after the pooling of four randomized controlled trials (RCTs), 80.2% of efficacy was reported for adenovirus vectored covid-19 vaccines, e.g., Oxford-AstraZeneca, Gamaleya (Sputnik V), and CanSino [22]. When individually assessed Astra-Zeneca showed 100% efficacy against hospitalizations, with only 0.9% having serious adverse events after the second dose. The efficacy is higher in the participants who received the second dose ≥ 12 weeks after primary injection (81.3%) when compared to those who received the second dose < 6 weeks after the primary injection (55.1%) [23]. Whilst, according to the interim analysis of phase 3 trial held in Russia, Sputnik was found to be 91.6% effective [24]. In May 2021, the phase 3 trials in the United Arab Emirates (UAE) and Bahrain showed that BBIBP-CorV (Sinopharm) was 78.1% effective against symptomatic cases and 100% against severe cases [25]. Conversely, phase 3 results from Brazil showed a 50.7% efficacy of Sinovac at preventing symptomatic infections; however, efficacy against symptomatic infections increased to 62.3% with an interval of 21 days or more between the doses [26]. Based on phase 3 trials in Turkey, 14 days or more after the second dose, Sinovac vaccine efficacy was 83.5% with only 18.9% adverse events and no fatality [27].

A study among health care personnel in the U.S shows that two doses of mRNA vaccines (Pfizer-BioNTech's BNT162b2 and Moderna's mRNA-1273) were 90% effective against SARS-CoV-2 infections at 14 days after full vaccination with the mRNA vaccines and 80% (≥ 14 days after the first dose but before the second dose) [28, 29]. A study in Israel found that the real-world effectiveness of BNT162b2 at seven days or more after the second dose were 95.3% effective against SARS-CoV-2 infection, 91.5% against asymptomatic SARS-CoV-2 infection, 97.0% against symptomatic COVID-19, 97.2% against COVID-19-related hospitalization, 97.5% against severe or critical COVID-19-related hospitalization, and 96.7% against COVID-19-related death [30]. The estimated BNT162b2 vaccine effectiveness at seven or more days after the second dose among 596,618 persons was 94% against symptomatic COVID-19, 87% against hospitalization, and 92% against severe disease [31].

Safety and adverse events of vaccines

A meta-analysis found that mRNA-based vaccines are associated with the highest number of side effects such as pain, redness, swelling, and induration on injection site as well as systematic adverse events such as fever, arthralgia, myalgia, fatigue, vomiting, and headache [22]. Reports of lymphadenopathy and Bell's palsy were also found in very low frequency of those who received the Pfizer vaccine [32]. Oxford-AstraZeneca vaccine had a good safety profile; however, different serious adverse events such as a case of hemolytic anemia, and three cases of transverse myelitis were observed out of 168 participants in Brazil, South Africa, and UK trials [33]. BBIBP-CorV (Sinopharm) and CoronaVac (Sinovac) in phases 1 and 2 of its clinical trial reported well-tolerated adverse reactions, mainly related to the injection site, including pain, itching, and induration along with systemic side effects such as fever, nausea, and constipation [33-35].

COVID-19 vaccine acceptance

Several studies have been conducted to assess the acceptance of COVID-19 around the globe. In Indonesia, a recent cross-sectional study reported 93% and 67% acceptance rates for two vaccines with 95% and 50% effectiveness, respectively [36]. In the United States, the acceptance

rate ranged between 67% and 69% [11, 37]. In China, a study found that vaccine acceptance was 90.6% in the population of high and medium income [38]. Another study found a 91.3% vaccine acceptance rate in the Chinese population mainly due to the effect of the pandemic on their daily lives coupled with the fear of being infected [39]. Studies conducted in different countries revealed acceptance rates of 69% in Turkey [40], 86% in the UK [40], and between 59%-86.1% in Italy [41, 42]. A global survey in 19 countries (Brazil, Canada, China, Ecuador, France, Germany, India, Italy, Mexico, Nigeria, Poland, Russia, Singapore, South Africa, South Korea, Spain, Sweden, UK, and the US) found that Brazil had the highest acceptance rate (85.3%) while Russia had the lowest (54.8%) [43]. The rates of vaccine acceptance in some countries are presented in **Table 1**.

Several studies have revealed some factors associated with COVID-19 vaccine acceptance. A study found that anxiety, risk perception, government satisfaction, and believing in the natural origin of the virus played a key role in the acceptance of vaccines amongst the population of the UK and Turkey [40]. In Italy, age, gender, and different socioeconomic variables were associated with vaccine acceptance [41, 42]. A global survey in 19 countries found that the pandemic situation in the country (case numbers and mortality per million population) and trust in government had significant influence on vaccine acceptance, which resulted in a 71.5% acceptance rate [43]. A complete list of the factors associated with vaccine acceptance is listed in **Table 1**.

COVID-19 vaccine hesitancy

According to the WHO, vaccine hesitancy is one of the top ten global threats to health [44]. A study found that people hesitant to COVID-19 vaccine belonging to low socioeconomic groups, Asian and black ethnic groups, Muslims, Buddhists, and younger female age groups [45]. Lack of awareness and conflicting beliefs were related to COVID-19 vaccine effectiveness, side effects, and objectives, eventually led to a global package of myths and false beliefs [46-49]. The Understanding Society UK Household Longitudinal survey reported 42.7% of participants indicating future unknown effects as the key reason for hesitancy as well worries about side effects and the lack of trust in vaccines [50]. In addition to the people's concerns, media has been playing a significant role in potentiating vaccine-related myths and controversies through headlines, talk shows, and newspapers; thus, upsurging global hostile conduct towards the COVID-19 vaccine [51].

A study in the UK reported that some of the reasons for vaccine rejection are: concerns on vaccine safety and effectiveness, low perceived risk of COVID-19, had infection with COVID-19, no transparency on vaccine development, efficacy, safety, and lack trust in vaccination, science or healthcare workers [52]. A study in Bangladesh showed that vaccine acceptance was influenced by perceived social norms, perceived safety of COVID-19 vaccine, perceived efficacy, perceived risk and severity of getting COVID-19, and trust in the COVID-19 vaccine itself [53]. Among healthcare workers (HCW) in Pakistan, the reasons for COVID-19 vaccine rejection varied based on gender; females HCW had religious concerns and doubts about vaccine effectiveness, while males HCW rejected the vaccine due to prior COVID-19 infection and the side effects of the vaccine [54].

Furthermore, the haram notion is one of the main reasons for the rejection among Muslims and this has fueled negative religious beliefs on COVID-19 vaccine [55]. The haram notion is further intensified by the anti-vaccine propaganda in 2011, resulting in people believing that vaccine is a western intrigue to sterilize Muslim girls [51]. Moreover, it can also be said that certain myths questioning the existence of COVID-19 are emerging to be one of the causes for the hesitancy towards vaccine acceptance [56]. Subsequently, the belief in such myths can result in the unwillingness of people to get the vaccine, predominantly because according to them COVID-19 is nothing more than normal flu or an illness, and not a life-threatening disease, which requires urgency to be vaccinated.

Table 1. COVID-19 vaccine acceptance rate and its associated factors

Country	Design	Sample	COVID-19 vaccine acceptance rate (%)	Factor associated with acceptance/rejection	Reference
China	Cross - sectional	2,058	91.3	Education City of resident Family income Suspected risk of COVID-19 Impact of the pandemic on daily life Vaccination history	[57]
Indonesia	Cross-sectional	1,359	93.3 (95% efficacy)	Perceived risk Healthcare related job Type of occupation Age	[36]
Indonesia	Cross-sectional	1,359	67.0 (50% efficacy)	Healthcare related job	[36]
United States	Cross - sectional	672	67.0	Education Race Risk perception score	[11]
Saudi Arabia	Cross - sectional	992	64.7	Education Occupation City of resident	[58]
Denmark, France, Germany, Italy, Portugal, the Netherlands, and the UK	Cross - sectional	7664	73.9	Concern about potential side effects	[59]
Chile	Cross-sectional	566	90.6 (Willing to pay vaccine)	Income Education Employment Health system Chronic disease Suspected risk of COVID-19	[38]
Israel	Cross-sectional	1,112	75.0	Gender Age Geographic locations Region of residence Marital status Parenthood Status	[60]
Israel	Cross-sectional	829 (healthcare staffs)	69.5	Gender Age Geographic locations Region of residence Marital status Parenthood status	[60]
United States	Cross-sectional	2,006	69.0	Type of health insurance Underlying medical condition Personal history of COVID-19 diagnosis	[37]

France	Cross-sectional	3,259	77.6	Recommendation from the health care provider Gender Age Health care worker Chronic medical condition Vaccine hesitancy Fears about COVID-19 Consideration at risk of COVID-19	[61]
United Kingdom Turkey	Cross-sectional	1,088 (UK) 3,936 (Turkey)	83.0 (UK) 76.0 (Turkey)	Anxiety Risk perception Government satisfaction Gender Believe in the natural origin of the virus	[40]
Italy	Cross-sectional	735 (College students)	86.1	Age Gender Healthcare and non-healthcare curricula	[41]
Ecuador	Cross-sectional	1,050 Households	85.0	Age Household size Income Gender Education Health insurance Employment status Location of residence Region of residence	[62]
Italy	Cross-sectional	1,004	59.0	Age Gender Smoking status Socio-economic variables	[42]
England	cross-sectional survey and semi-structured interviews	1252 parents and guardians	55.8	Household income Employment Ethnicity	[52]
China, Brazil, South Africa, South Korea, Mexico, United States, India, Spain, Ecuador, United Kingdom, Italy, Canada, Germany, Singapore, Sweden, Nigeria, France, Poland, and Russia	Cross-sectional	13,426	71.5	Age Sex Income Education Cases per million population Mortality per million populations Trust in Government	[43]
Uganda	Cross-sectional	1,067	53.6	Age Sex Education Religion Employment	[63]

Jordan	Cross-sectional	3,100	37.4	Marital status Location of residence Age Sex Received influenza vaccine this year The trusted information source of COVID-19 Concern about COVID-19 as conspiracy The safety of the vaccine	[64]
Libya	Cross-sectional	12,006	79.6	Age Have a family member or friend infected with COVID-19 Have a family member or friends died due to COVID-19	[65]
Germany	Cross-sectional	1,037	57.2	Marital status Having chronic illness Perceptions of becoming infected Perceptions of the severity of the potential long-term effects The efficacy of the COVID-19 vaccine The benefits of vaccination	[66]
Jordan	Cross-sectional	1,144	36.8	Sex Marital status Having children Education Concerns regarding the use of vaccines Lack of trust of COVID-19 vaccine	[67]
US, India, Brazil, Russia, Spain, Argentina, Colombia, UK, Mexico, Peru, South Africa, Italy, Chile, Australia, New Zealand, and the Philippines	Cross-sectional	17,871 (Pregnant women and mothers)	52.0 (pregnant women) 73.4 (mothers)	Age Income Education level Marital status Health insurance Confidence in COVID-19 vaccine safety and efficacy Belief in the importance of vaccines/mass vaccination to their own country Confidence in routine childhood vaccines Trust of public health agencies/health science Compliance to mask guidelines	[68]
Malaysia	Cross-sectional	735 (March 2020) 758 (March 2020)	77 (March 2020) 89 (June 2020)	Gender Race Economic disruptions during pandemic Personal experience with COVID-19 Friends experience with COVID-19 Family members' experience with COVID-19 Media experience of a COVID-19 case	[69]
Bangladesh, India, Iran, Pakistan, Egypt, Nigeria, Sudan, Tunisia, Brazil, and Chile	Cross-sectional	1337	74.0 (95% vaccine efficacy and 20% side effect)	Country Monthly household income Religion Having comorbidity	[70]

Bangladesh, India, Iran, Pakistan, Egypt, Nigeria, Sudan, Tunisia, Brazil, and Chile	Cross-sectional	1337	80.1 (75% vaccine efficacy and 5% side effect)	Change of salary as a result of the COVID-19 pandemic Believe or not that social distancing can protect the child or children from COVID-19 Believe or not vaccines are important for health Believe or not that the new vaccines carry more risks Believe or not that all routine recommended vaccines are beneficial Believe or not that information about vaccines from the government is reliable and trustworthy Having flu vaccination during the past 12 months Country Urbanicity Religion Monthly household income Vaccines are important for my health Believe or not that the new vaccines carry more risks Believe or not that all routine recommended vaccines are beneficial Believe or not that information about vaccines from the government is reliable and trustworthy Having flu vaccination during the past 12 months	[70]
Bangladesh, India, Iran, Pakistan, Egypt, Nigeria, Sudan, Tunisia, Brazil, and Chile	Cross-sectional	1337	55.6 (75% vaccine efficacy and 20% side effect)	Country Religion Monthly household income Having comorbidity Change of salary as a result of the COVID-19 pandemic Believe or not vaccines are important for health Believe or not that the new vaccines carry more risks Believe or not that all routine recommended vaccines are beneficial Believe or not that information about vaccines from the government is reliable and trustworthy Having flu vaccination during the past 12 months	[70]
Bangladesh, India, Iran, Pakistan, Egypt, Nigeria, Sudan, Tunisia, Brazil, and Chile	Cross-sectional	1337	58.3 (50% vaccine efficacy and 5% side effect)	Country Religion Monthly household income Believe or not vaccines are important for health Believe or not that the new vaccines carry more risks Believe or not that all routine recommended vaccines are beneficial Believe or not that information about vaccines from the government is reliable and trustworthy Having flu vaccination during the past 12 months	[70]

Conclusion

The surge in COVID-19 vaccine hesitancy could possibly remain a crucial barrier in combatting COVID-19 until researchers, health care professionals, and public health educators take vital steps in diminishing myths and anti-vaccine conspiracies circulating throughout social media. Studies are therefore important to develop contextualized advertising and information exchange, which will lead to trust and uptake of COVID-19 vaccine.

Ethics approval

Not required.

Acknowledgments

The authors would like to thank the institutions for their support.

Conflict of interest

The authors declare that they have no competing interests.

Funding

This study received no external funding.

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

How to cite

Hassan W, Kazmi SK, Tahir MJ, *et al.* Global acceptance and hesitancy of COVID-19 vaccination: A narrative review. *Hassan et al. Narra J* 2021; 1 (3): e57 - <http://doi.org/10.52225/narra.vii3.57>.

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