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Review Article

Unraveling COVID-19: A Global Health Crisis and Ongoing Research

Osama Alam[1*], Muhammad Ahmad[2], Munib Qureshi[1], Marina Gul[3], Naveed Khan[4], Abdul Samad[5], Zewran Khan[1], Syed Atiq[6], Arsalan Iqbal[1] and Asim Ullah[4]

[1]Department of Biotechnology, University of Science & Technology, Bannu, Pakistan
[2]Department of Zoology, Quaid-E- Azam University, Islamabad, Pakistan
[3]Department of Botany, University of Science & Technology, Bannu, Pakistan
[4]Department of Zoology, Govt. Post Graduate College, Bannu, Pakistan
[5]Department of Biotechnology and Genetic Engineering, Kohat University of Science and Technology, Kohat, Pakistan
[6]Department of Chemistry, University of Science & Technology, Bannu, Pakistan

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***Corresponding Author:**
Osama Alam
Department of Biotechnology, University of Science & Technology, Bannu, Pakistan
osamaalam9988@gmail.com

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ABSTRACT

The COVID-19 pandemic, sparked by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has triggered an unparalleled global health crisis with far-reaching consequences. SARS-CoV-2 primarily spreads through respiratory droplets, utilizing angiotensin-converting enzyme 2 (ACE2) receptors in the respiratory system for cellular entry and replication, underscoring the critical need for preventive measures. The emergence of worrisome mutations has led to the development of more transmissible variants, heightening the virus's potential impact. Diagnostic testing, including reverse-transcriptase polymerase chain reaction (RT-PCR), antigen detection, and serology, plays a pivotal role in identifying. COVID-19 diagnostic tests include the ABBOTT ID NOW™ COVID-19 test (95% sensitivity and 100% specificity), the COBAS® SARS-CoV-2 test (98.8% sensitivity and 99% specificity), the SOFIA® 2 SARS ANTIGEN FIA test (91.7% sensitivity and 100% specificity), the XPERT® XPRESS SARS-CoV-2 test (95.4% sensitivity and 97% specificity), and the ACCULA SARS-CoV-2 test (98% sensitivity and 100% specificity). While vaccines include the Pfizer-BioNTech vaccine (95% efficacy), Moderna vaccine (94.10% efficacy), Johnson & Johnson vaccine (66% efficacy), Oxford-AstraZeneca vaccine (76% efficacy), Sinovac vaccine (50.38% efficacy), Sinopharm vaccine (79% efficacy), Bharat Biotech (Covaxin) vaccine (81% efficacy), Sputnik V vaccine (91.60% efficacy), Novavax vaccine (96.4% efficacy), and Covovax vaccine (100% efficacy). The COVID-19 pandemic underscores the ongoing necessity for global cooperation among scientific and medical communities to understand this emerging pathogen, mitigate health impacts, and advance long-term solutions through continuous therapeutic and vaccine research.

INTRODUCTION

Coronaviruses are a group of positive-sense single-stranded RNA viruses, belonging to the family Coronaviridae [1]. These pathogens have been present in various animal species like bats, mice, and birds for millions of years. Within the coronaviruses, four distinct genera exist: Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus. SARS-CoV-2 falls under the Betacoronavirus genus and is closely related to other significant human coronaviruses - severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Bats are recognized as a natural reservoir for several coronaviruses, including those responsible for SARS, MERS, and COVID-19. Genetic similarities between SARS-CoV-2 and the bat coronavirus RaTG13 underscore their connection. However, it's hypothesized that disease transmission from bats to humans is more likely to occur through intermediary hosts, such as pangolins or other mammals [2, 3]. The coronavirus possesses an outer lipid membrane consisting of three key structural proteins: spike (S), membrane (M), and envelope (E). The spike protein is crucial for infecting host cells by binding to the

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ACE2 receptor, leading to fusion of viral and host cell membranes [4]. The M protein provides structural stability, influences virus assembly, and guards the viral RNA genome. The E protein plays a less obvious but vital role in virus assembly, release, and membrane manipulation, affecting overall virulence [5]. The N protein safeguards the viral RNA genome, forming the ribonucleoprotein (RNP) complex, ensuring the virus's persistence. These proteins orchestrate the complex life cycle of the coronavirus. COVID-19's genetic structure is intricate, led by ORF1a and ORF1b genes that produce 16 non-structural proteins [5]. The S protein, with S1 and S2 subunits and various domains, plays a central role. The S protein contains specific domains like CP, FP, HR, RBD, SP, and TM, each significant in the virus's story [5]. Cleavage sites in S1/S2 highlight proteolytic processes shaping the protein. The Spike (S) protein takes center stage in coronaviruses, facilitating their entry into host cells by binding to the ACE2 receptor. This connection initiates membrane fusion and endocytosis, allowing the virus's genetic material to be released into the cell's cytoplasm. Viral proteins are then synthesized, leading to the creation of new viral particles. Coronaviruses are adept at evading the immune system, sidestepping interferon responses, natural killer cells, and adaptive immune mechanisms, enabling them to multiply and thrive within the host [6]. Vaccines and immunization are pivotal in the battle against the COVID-19 pandemic. Various vaccines, such as mRNA-based (Pfizer-BioNTech, Moderna), viral vector-based (Oxford-AstraZeneca, Johnson & Johnson), and protein subunit vaccines, have been authorized for widespread use [7]. They work by stimulating the body's immune response against the SARS-CoV-2 virus. mRNA-based vaccines carry the genetic instructions for the spike protein, leading to its production on cell surfaces. Viral vector-based vaccines use a harmless virus to deliver the spike protein gene, initiating an immune response involving dendritic cells, B cells, and T cells. B cells produce spike protein-specific antibodies that neutralize the virus, while T cells eliminate infected cells, providing lasting immunity [8]. The ABBOTT ID NOW™ COVID-19 test by Abbott Laboratories utilizes isothermal amplification, producing results in 5-13 minutes with a sensitivity of 95% and specificity of 100%, using nasal-pharyngeal swabs as the sample [9, 10]. The COBAS® SARS-CoV-2 test by Roche Diagnostics is based on RT-PCR, taking 210 minutes for results, with a sensitivity of 98.8% and specificity of 99%, also using nasal-pharyngeal swabs [11]. The SOFIA® 2 SARS ANTIGEN FIA test by Quidel Corporation is a rapid antigen detection method with a 15-minute result turnaround time, a sensitivity of 91.7%, and specificity of 100%, also employing nasal-pharyngeal swabs [12]. The XPERT® XPRESS SARS-CoV-2 test by Cepheid is another RT-PCR test, providing results in 45 minutes, with a sensitivity of 95.4% and specificity of 97%, using nasal-pharyngeal swabs [13]. Lastly, the ACCULA SARS-CoV-2 test by Mesa Biotech uses RT-LAMP technology, delivering results in 30 minutes, with a sensitivity of 98% and specificity of 100%, and it also relies on nasal-pharyngeal swabs [13]. These tests vary in their detection methods, result times, and diagnostic accuracy, offering healthcare professionals essential options for COVID-19 diagnosis. The Pfizer-BioNTech and Moderna vaccines, both mRNA-based, demonstrate efficacies of 95% and 94.10%, respectively, with two doses administered 21 and 28 days apart via intramuscular injection, and approvals from the FDA, EMA, and WHO [13, 14]. Johnson & Johnson's viral vector vaccine exhibits a 66% efficacy, requiring a single dose via IM injection, and holds approvals from the same regulatory bodies [15]. The Oxford-AstraZeneca vaccine, another viral vector option, offers a 76% efficacy, necessitating two doses given 4-12 weeks apart through IM injection, with approvals from the EMA and WHO [16]. Inactivated virus vaccines include Sinovac (50.38% efficacy, two doses 14-28 days apart, IM, WHO-approved) [17], Sinopharm (79% efficacy, two doses 3-4 weeks apart, IM, WHO-approved) [18], and Bharat Biotech's Covaxin (81% efficacy, two doses 4-6 weeks apart, IM, WHO-approved) [19]. The viral vector-based Sputnik V boasts a 91.60% efficacy, with two doses administered 21 days apart via IM injection and WHO approval [20]. Novavax offers a protein subunit vaccine with 96.4% efficacy, requiring two doses 21 days apart via IM injection, and WHO approval [20]. Covovax, also a protein subunit vaccine, stands out with 100% efficacy, administered in two doses 21 days apart via IM injection and WHO approval [21]. These vaccines represent diverse approaches to combat COVID-19 and have gained approval from esteemed regulatory bodies, attesting to their safety and efficacy in preventing COVID-19 infections.

Coronavirus

The term "coronavirus" draws its inspiration from the Latin word "corona," evoking images of crowns and halos that mirror the distinctive appearance of the virus particles when viewed under a microscope. Another alias for this entity is SARS-CoV-2, recognized for inducing respiratory and gastrointestinal infections in both human and animal populations. Encased in an envelope and characterized by a single-stranded RNA with positive polarity, this virus finds its place within the esteemed Coronaviridae family [22]. Carving its path through history, this viral agent has become the driving force behind the global stage known as the COVID-19 pandemic. The narrative commenced in December 2019, unfolding a tale that continues to resonate globally, reshaping lives and landscapes. The architectural

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intricacies of the virus become central players, dictating its interactions with host cells and orchestrating its journey of transmission [23]. From its evocative name to its captivating biology, the virus emerges as a multifaceted character, transcending the microscopic realm to become a profound player in the ongoing human narrative [24]. Some of the latest studies conducted on COVID-19 are discussed in Table 1.

Table 1: Various types of research conducted on SARS-CoV-2 with methodology, findings and references

Study title	Research topic	Methodology	Findings	References
Characterization of SARS-CoV-2 variants	Genomic analysis of SARS-CoV-2 variants	Next-generation sequencing analysis	Identification of multiple variants with distinct mutations	[25]
Antiviral activity of remdesivir against SARS-CoV-2	Evaluation of Remdesivir's efficacy against SARS-CoV-2	In vitro cell culture experiments	Remdesivir showed antiviral activity against SARS-CoV-2	[26]
Effectiveness of COVID-19 vaccines in real-world settings	Assessment of COVID-19 vaccine effectiveness in real-world scenarios	Observational study using population data	COVID-19 vaccines demonstrated high effectiveness	[27]
Structural analysis of SARS-CoV-2 spike protein	Structural analysis of the spike protein of SARS-CoV-2	Cryo-electron microscopy and X-ray crystallography	Detailed understanding of spike protein structure	[28]
COVID-19 transmission dynamics in child	Investigation of COVID-19 . transmission dynamics in school . settings	Epidemiological analysis and contact tracing	Limited transmission observed within schools	[29]
"Innate immune response to SARS-CoV-2 infection"	Study of innate immune response to SARS-CoV-2 infection in humans	Immune cell profiling and cytokine analysis	Dysregulated immune response observed in severe cases	[30]
"Impact of non-pharmaceutical interventions on COVID-19"	Evaluation of the effectiveness of non-pharmaceutical interventions	Mathematical modeling and epidemiological analysis	NPIs played a crucial role in controlling COVID-19 spread	[31]

The coronavirus has an outer lipid membrane derived from host cell materials during replication, containing three key structural proteins: S protein, M protein, and E protein. Among these, the spike protein, prominently projecting from the virus's surface, plays a central role by binding to the ACE2 receptor on host cell surfaces, facilitating infection (Figure 1) [32]. Upon binding to the ACE2 receptor, the spike protein undergoes a transformative shift, facilitating the fusion of viral and host cell membranes, allowing the viral genome to enter the host cell. The M protein takes a leading role in this intricate process, providing structural stability to the viral envelope and influencing virus assembly, ultimately determining the virus's shape. Additionally, the M protein orchestrates the inclusion of the N protein, responsible for safeguarding the viral RNA genome. In this intricate dance, E protein also plays a vital, albeit more understated, role in the virus's lifecycle [33]. E protein's role extends beyond its less conspicuous presence, as it orchestrates crucial aspects of the virus's life cycle, including assembly, release, and membrane curvature manipulation. Despite its understated role, the E protein significantly influences the virus's overall virulence, contributing to the creation and maturation of new viral particles. Meanwhile, the N protein, nestled within the protective envelope, takes on the responsibility of safeguarding the viral RNA genome. This protein intertwines with the genome, forming the ribonucleoprotein (RNP) complex. As the viral symphony reaches its crescendo, this complex becomes an integral part of the viral envelope, thus solidifying the coronavirus's enduring legacy [34].

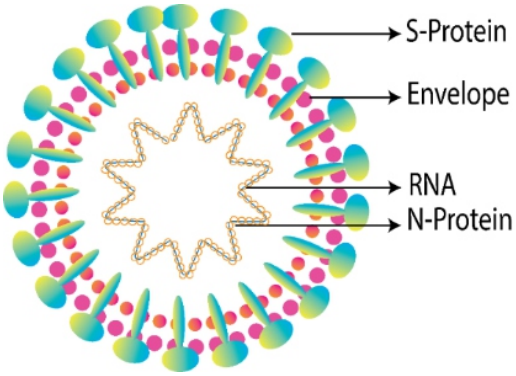

Figure 1: Structure of Corona virus. The outer boundary is S-Protein and inner part contain RNA and N-Protein illustrated in Adobe illustrator

The intricate machinery of COVID-19's S protein unfolds visually in a graphic representation, seamlessly interwoven with its genomic architecture. Standing as substantial foundations, the ORF1a and ORF1b genes command the stage, conjuring 16 non-structural proteins (nsp1-nsp16) that orchestrate the virus's multifaceted maneuvers (Figure 2). These genetic architects are encoded within the single-stranded RNA genome, choreographing a symphony of functionality [35]. As the symphony deepens, the spotlight shifts to the structure-related genes that craft the virus's tangible presence-the artistry of S protein, the elegance of E, the strength of M protein, and the resilience of Nucleocapsid (N) [36]. Amid this genetic tableau, a verdant aura signifies the auxiliary genes, lending an ensemble of supporting roles. Beneath this genetic tapestry lies the beguiling S protein, a tale of two halves, represented as S1 and S2 subunits, striving for equilibrium within the whole. Within the S-protein realm, distinct

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domains emerge - the enigma of the cytoplasm domain (CP), the poetic fusion peptide (FP), the echoing heptad repeat (HR), the strategic receptor-binding domain (RBD), the heralding signal peptide (SP), and the enduring transmembrane domain (TM), each carrying its significance within the viral narrative [30]. As if painted with dotted brushstrokes, the locations of S1/S2 cleavage draw attention, a reminder of the proteolytic processes that shape the protein's essence. In this intricate genetic ballet, each element performs its role, weaving a story that spans the invisible world of RNA and the tangible realm of viral structure, as the symphony of COVID-19 continues to unfold.

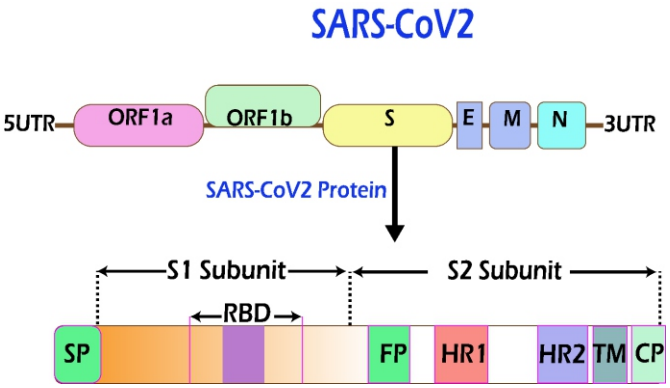

Figure 2: Structural features of the SARS-CoV-2 virus genome. It has four main structural proteins: S protein, E protein, M protein, and nucleocapsid (N) redrawn from reference [37]

Mode of Action

Stepping into the limelight is the Spike (S) protein, a central figure in the world of coronaviruses, leading their dramatic entry into host cells. This protein forms a meticulous bond, embracing the angiotensin-converting enzyme 2 (ACE2) receptor present on human cell surfaces, particularly in the respiratory realm. This encounter serves as the gateway for the virus, unlocking the cell's interior through a meticulously orchestrated process known as membrane fusion–a dance of molecular interactions that echoes far beyond the physical embrace. Once this connection is sealed, the virus embarks on a journey within the host cell, an act known as endocytosis. A symphony of collaboration begins as the virus's genetic script is released into the cell's interior, the cytoplasm. Here, the cell's machinery is commandeered to interpret this script, guiding the synthesis of a medley of viral proteins (Table 2). As these proteins harmonize and assemble, new viral entities are born. Released from the cell's grasp, these creations set the stage for their voyage of cellular colonization [38]. Yet, the narrative doesn't conclude here. Coronaviruses, masters of adaptation, wield a strategic playbook to elude the immune system's vigilant gaze. By orchestrating interactions that sidestep the interferon response, natural killer cells, and adaptive immune mechanisms, these viruses elude detection. This tactical prowess grants them the space to multiply and flourish within their host, a saga of molecular intrigue that shapes their path towards pathogenesis. This duality of invasion and evasion intertwines to unfold the gripping tale of the coronavirus's cellular odyssey [39].

Table 2: List of SARS-CoV-2 proteins that are involved in the infections with references

SARS-CoV Protein	Human Host Protein	The function of Host Protein	Implication in SARS-CoV Life Cycle
Spike S	ACE2	Angiotensin-con enzyme 2	Entry into host cells
Nucleocapsid N	hnRNPA1	Heterogeneous nuclear ribonucleo protein A1	RNA replication and translation
ORF3a	VDAC1	Voltage-dependent anion channel 1	Apoptosis regulation
ORF9b	TOM70	Mitochondrial import receptor subunit TOM70	Virus-induced apoptosis and immune response regulation
Nsp13	DHX9	DExH-box helicase 9	Innate immune response evasion
Nsp1	RPL13A	Ribosomal protein L13a	Host translation shutoff
Nsp7-Nsp8	RPA1	Replication protein A1	Viral RNA replication and evasion of host DNA repair machinery
Nsp9	HSPA5	Heat shock 70kDa protein 5 GRP78	Virus-induced stress response and morphogenesis
Nsp10-Nsp14	EXOSC5	Exosome component 5	Viral RNA degradation and modification
Nsp15	SQSTM1/p62	Sequestosome 1/p62	Virus-induced autophagy and immune response regulation

Transmission through contaminated surfaces, such as doorknobs, phones, and tables, is another potential mode. A study by found that SARS-CoV-2 could remain viable on surfaces for extended periods. Some studies have also suggested the possibility of fecal-oral transmission of the virus, as SARS-CoV-2 RNA has been detected in the feces of infected individuals. It is essential to practice good hygiene, and social distancing, and follow local health guidelines to minimize the risk of viral transmission [40].

Immunization of COVID-19

In the ongoing narrative of the COVID-19 pandemic, vaccines and immunization emerge as crucial protagonists, wielding a powerful force against the relentless advance of the virus. A spectrum of vaccines has taken the spotlight, gaining emergency authorization or approval for widespread use [41]. Their collective mission revolves around rallying the body's defenses against the

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SARS-CoV-2 virus, orchestrating a harmonious dance of immunity [42]. This choreography showcases various approaches, encompassing mRNA-based vaccines, viral vector- based vaccines, and protein subunit vaccines. In the realm of mRNA-based vaccines, exemplified by Pfizer-BioNTech and Moderna, the spotlight shines on messenger RNA (mRNA) which carries the genetic blueprint for the spike protein. Within the body, this script is executed within cells, leading to the graceful production of the spike protein on cell surfaces. In the parallel stage of viral vector-based vaccines, Oxford-AstraZeneca and Johnson & Johnson take the lead [43]. Here, a benign virus delivers the spike protein gene, initiating its production. This event becomes a catalyst for a captivating immune performance, with key players like dendritic cells presenting the spike protein to other immune components. This presentation sets off a symphony of immune response, engaging B cells and T cells in harmony. In this orchestrated spectacle, B cells assume the role of artists, crafting antibodies tailor-made to bind to the spike protein. These antibodies emerge as a shield, neutralizing the virus's intrusion by blocking its entry into human cells. In parallel, T cells undertake the task of vigilant guardians, discerning infected cells through spike protein fragments displayed on their surface. Their intervention culminates in the elimination of infected cells, crafting a canvas of long-lasting immunity [44]. In this grand tale of science and resilience, vaccines and the immune system converge as champions, illustrating humanity's prowess in the face of adversity through innovation and unity (Figure 3).

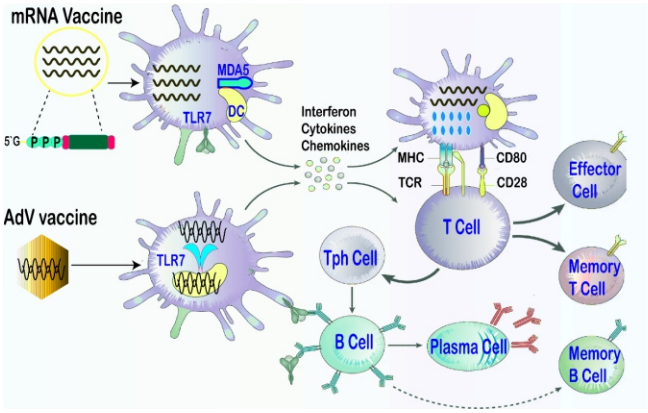

Figure 3: Immunization of Corona virus under the action of mRNA vaccine (Single-stranded RNA) and Adenovirus vaccine (Double-stranded vaccine) redrawn from reference [45]

Various techniques have been employed for the detection of COVID-19, the disease caused by the novel coronavirus SARS-CoV-2. These techniques can be broadly categorized into three main approaches: molecular-based tests, serological tests, and imaging techniques. Each of these approaches has its own performance characteristics, limitations, and associated challenges (Table 3).

Table 3: Various techniques used for COVID-19 detection with its performance, limitations, and challenges with references

Testing Techniques	Performance	Limitations	Challenges
Rt-PCR	Highly specific	Requires expertise	Supply chain issues, longer turnaround time
Rapid antigen	Quick results	Lower sensitivity than RT-PCR	Higher false-positive rate
Antibody serology	Detects past I nfections	Delayed seroconversion	IgM/IgG cross-reactivity
CRISPR-based assays	High sensitivity	Specialized equipment	Limited availability
Loop-mediated isothermal amplification (lamp)	Rapid results	Limited data on sensitivity	Challenges in implementation
Saliva-based testing	Non-invasive	Variable sensitivity and specificity	Contamination risk
Ct scans	Imaging of abnormalities	Lower specificity	Radiation exposure
Breathalyzer	Potentially rapid	Limited data on sensitivity and specificity	Standardization
Digital PCR	High specificity	Expensive equipment and reagents	Limited availability
Next-generation sequencing (NGS)	Comprehensive detection and genotyping	High cost	limited capacity

Emergency Use Authorization (EUA) Kits used for COVID test

Various types of testing kits are utilized to diagnose COVID-19, and they employ different techniques to detect the presence of the SARS-CoV-2 virus, the causative agent of the disease (Table 4). These testing kits play a critical role in the identification of individuals who are infected with the virus. By identifying infected individuals, authorities can isolate them and implement appropriate measures to control the spread of the virus within communities and populations. These tests are essential tools in the fight against the COVID-19 pandemic, aiding in early detection, timely treatment, and the prevention of further transmission of the virus [46].

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Table 4: Various types of kits used for COVID test with high sensitivity and specificities

Test kit name	Manufacturer	Detection method	Time to results(min)	Type of sample	Sensitivity (%)	Specificity (%)
Abbott ID Now™ COVID-19	Abbott Laboratories	Isothermal amplification	5-13	NPS	95	100
Cobas® SARS-CoV-2	Roche Diagnostics	RT-PCR	210	NPS	98.8	99
Sofia® 2 SARS Antigen FIA	Quidel Corporation	Rapid antigen detection	15	NPS	91.7	100
Xpert® Xpress SARS-CoV-2	Cepheid	RT-PCR	45	NPS	95.4	97
Accula SARS-CoV-2	Mesa Biotech	RT-LAMP	30	NPS	98	100

NPS: Nasal-pharyngeal swab

Vaccines used for COVID test

Vaccines' play a crucial role in controlling of Corona virus. Different types of vaccines such as DNA vaccine, mRNA vaccine or viral vectors are used. mRNA vaccine directly translates the RNA in the ribosome that form various viral parts quicks. While, DNA vaccine firstly transcribe and then translate in the cell. Same as viral vectors or parts of virus induced immunity against corona viruses(Table 5)[47].

Table 5: Different types of vaccines used for COVID-19 with its efficiency, dosage and its administration route

Vaccine name	Manufacturer	Type	Efficiency (%)	Dosage doses/days	Administration route	Approved
Pfizer-biontech	Pfizer, BioNTech	mRNA	95	2/21	IM	FDA, EMA, WHO
Moderna	Moderna, NIAID	mRNA	94.10	2/28	IM	FDA, EMA, WHO
Johnson &johnson	Janssen, Johnson & Johnson	Viral vector	66	Single dose	IM	FDA, EMA, WHO
Oxford-astrazeneca	AstraZeneca, University of Oxford	Viral vector	76	2/ 4-12 weeks	IM	EMA, WHO
Sinovac	Sinovac Biotech	Inactivated virus	50.38	2 /14-28	IM	WHO
Sinopharm	Sinopharm, Beijing Institute of Biological Products	Inactivated virus	79	2/3-4 weeks	IM	WHO
Bharat biotech (covaxin)	Bharat Biotech, Indian Council of Medical Research	Inactivated virus	81	2/ 4-6 weeks	IM	WHO
Sputnik v	Gamaleya Research Institute	Viral vector	91.60	2/21	IM	WHO
Novavax	Novavax	Protein subunit	96.4	2/21	IM	WHO
Covovax	Novavax, Serum Institute of India	Protein subunit	100	2/21	IM	WHO

IM: Intramuscular injection

Future Perspective

The ever-evolving landscape of SARS-CoV-2 variants promises to keep us on our toes. This dynamic challenge necessitates an unwavering commitment to vigilant observation and in-depth analysis. Delving into the intricacies of these variants becomes our compass in understanding their implications on transmission, severity, and the effectiveness of our vaccines. In this intricate dance, our best moves lie in public health measures that mirror our adaptability. Genomic surveillance, swift testing mechanisms, and targeted interventions emerge as our allies in navigating the terrain of future outbreaks, sculpted by new variants. COVID-19, like a seasoned traveler, might find a home in populations at a lower hum, leading to periodic eruptions akin to seasonal flu. To tame this rhythm, our playbook embraces flexibility. A symphony of strategies encompasses robust vaccination campaigns, pinpointed tests, the art of tracing contacts, and the timeless refrain of hygiene practices. These harmonies aim to mitigate the impact of future flare-ups. In this global theater, unity shines as the spotlight. Nations and organizations, bound by shared concern, continue to script a story of collaboration. The script is familiar: sharing knowledge, pooling resources, and exchanging expertise. This script, however, carries an extraordinary weight, for it cultivates strategies that guard against the virus's advance. A universal truth arises: access knows no boundaries. The act of ensuring widespread access to vaccines and healthcare stands as the guardian of global health security. This truth is our guiding star, reminding us that our journey to surmount this crisis is bound not just by borders. The COVID-19 pandemic has highlighted the importance of preparedness for future outbreaks. Investments in public health infrastructure, surveillance systems, and research capabilities will be essential to detect and respond rapidly to emerging infectious diseases. Lessons learned from COVID-19 will inform future pandemic response plans and policies.

Authors Contribution

Conceptualization: OA

Writing-review and editing: OA, MA, MQ, MG, NK, ST, AS, ZK, AA, AI, AU

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Al-Kuraishy HM, Al-Gareeb AI. From SARS-CoV to nCoV-2019: Ruction and argument. Archives of Clinical Infectious Diseases. 2020 Apr; 15: e102624. doi: 10.5812/archcid.102624.

[2] Boni MF, Lemey P, Jiang X, Lam TT, Perry BW, Castoe TA, *et al.* Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic. Nature Microbiology. 2020 Nov; 5(11): 1408-17. doi: 10.1038/s41564-020-0771-4.

[3] Jackson CB, Farzan M, Chen B, Choe H. Mechanisms of SARS-CoV-2 entry into cells. Nature reviews Molecular Cell Biology. 2022 Jan; 23(1): 3-20. doi: 10.1038/s41580-021-00418-x.

[4] Belouzard S, Millet JK, Licitra BN, Whittaker GR. Mechanisms of coronavirus cell entry mediated by the viral spike protein. Viruses. 2012 Jun; 4(6): 1011-33. doi: 10.3390/v4061011.

[5] Nieto-Torres JL, DeDiego ML, Verdiá-Báguena C, Jimenez-Guardeño JM, Regla-Nava JA, Fernandez-Delgado R, *et al*. Severe acute respiratory syndrome coronavirus envelope protein ion channel activity promotes virus fitness and pathogenesis. PLoS Pathogens. 2014 May; 10(5): e1004077. doi: 10.1371/journal.ppat.1004077.

[6] Sandhu R and Kaur M. Recombinant ACE2-opportunities and challenges in COVID 19 treatment. Authorea Preprints. 2020 May: 1-4. doi: 10.22541/au.158880140.09169536.

[7] Rudan I, Adeloye D, Sheikh A. COVID-19: vaccines, efficacy and effects on variants. Current Opinion in Pulmonary Medicine. 2022 May; 28(3): 180-91. doi: 10.1097/MCP.0000000000000868.

[8] Simnani FZ, Singh D, Kaur R. COVID-19 phase 4 vaccine candidates, effectiveness on SARS-CoV-2 variants, neutralizing antibody, rare side effects, traditional and nano-based vaccine platforms: a review. 3 Biotech. 2022 Jan; 12(1): 15. doi: 10.1007/s13205-021-03076-0.

[9] Guaman-Bautista LP, Moreta-Urbano E, Oña-Arias CG, Torres-Arias M, Kyriakidis NC, Malcı K, *et al.* Tracking SARS-CoV-2: Novel trends and diagnostic strategies. Diagnostics. 2021 Oct; 11(11): 1981. doi: 10.3390/diagnostics11111981.

[10] Stokes W, Berenger BM, Singh T, Adeghe I, Schneider A, Portnoy D, *et al.* Acceptable performance of the Abbott ID NOW among symptomatic individuals with confirmed COVID-19. Journal of Medical Microbiology. 2021 Jul; 70(7): 001372. doi: 10.1099/jmm.0.001372.

[11] Poljak M, Korva M, Knap Gašper N, Fujs Komloš K, Sagadin M, Uršič T, *et al.* Clinical evaluation of the cobas SARS-CoV-2 test and a diagnostic platform switch during 48 hours in the midst of the COVID-19 pandemic. Journal of Clinical Microbiology. 2020 May; 58(6): 10-128. doi: 10.1128/JCM.00599-20.

[12] Bornemann L, Kaup O, Kleideiter J, Panning M, Ruprecht B, Wehmeier M. Real-life evaluation of the Sofia SARS-CoV-2 antigen assay in a large tertiary care hospital. Journal of Clinical Virology. 2021 Jul; 140: 104854. doi: 10.1016/j.jcv.2021.104854.

[13] Moran A, Beavis KG, Matushek SM, Ciaglia C, Francois N, Tesic V, *et al.* Detection of SARS-CoV-2 by use of the Cepheid Xpert Xpress SARS-CoV-2 and Roche cobas SARS-CoV-2 assays. Journal of Clinical Microbiology. 2020 Jul; 58(8): 10-128. doi: 10.1128/jcm. 00772-20.

[14] Meo SA, Bukhari IA, Akram J, Meo AS, Klonoff DC. COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna Vaccines. European Review for Medical and Pharmacological Sciences. 2021 Feb; 25(3): 1663-9.

[15] Beleche T, Ruhter J, Kolbe A, Marus J, Bush L, Sommers B. COVID-19 vaccine hesitancy: demographic factors, geographic patterns, and changes over time. ASPE Issue Brief. 2021 May; 27: 1-27.

[16] Sønderskov KM, Dinesen PT, Østergaard SD. Sustained COVID-19 vaccine willingness after safety concerns over the Oxford-AstraZeneca vaccine. Danish Medical Journal. 2021 Mar; 68(5): A03210292.

[17] Serap BA, Burucu R, Cantekin I, Dönmez H. Determining the side effects of COVID-19 (Sinovac) vaccination on nurses; an independent descriptive study. Konuralp Medical Journal. 2021 Aug; 13(S1): 479-87. doi: 10.18521/ktd.981790.

[18] Ghiasi N, Valizadeh R, Arabsorkhi M, Hoseyni TS, Esfandiari K, Sadighpour T, *et al.* Efficacy and side effects of Sputnik V, Sinopharm and AstraZeneca vaccines to stop COVID-19; a review and discussion. Immunopathologia Persa. 2021 Jun; 7(2): e31. doi: 10.34172/ipp.2021.31.

[19] Darbar S, Agarwal S, Saha S. COVID19 vaccine: COVAXIN®-India's first indigenous effective weapon to fight against coronavirus (A Review). Parana Journal of Science and Education. 2021 Apr; 7(3): 1-9.

[20] McDonald I, Murray SM, Reynolds CJ, Altmann DM, Boyton RJ. Comparative systematic review and meta-analysis of reactogenicity, immunogenicity and efficacy of vaccines against SARS-CoV-2. NPJ Vaccines. 2021 May; 6(1): 74. doi: 10.1038/s41541-021-00336-1.

[21] Kanokudom S, Chansaenroj J, Suntronwong N,

DOI: https://doi.org/10.54393/fbt.v3i02.47

Assawakosri S, Yorsaeng R, Nilyanimit P, *et al*. Safety and immunogenicity of a third dose of COVID-19 protein subunit vaccine (CovovaxTM) after homologous and heterologous two-dose regimens. International Journal of Infectious Diseases. 2023 Jan; 126: 64-72. doi: 10.1016/j.ijid.2022.11.022.

[22] Semwal DK, Chauhan A, Semwal RB, Sircar D, Roy P, Lehmann J. Natural molecules having anti-SARS-CoV activity–cannot they be effective against SARS-CoV-2. Current Science. 2020 Sep; 119: 757-70. doi: 10.18520/cs/v119/i5/757-770.

[23] Onyeaka H, Anumudu CK, Al-Sharify ZT, Egele-Godswill E, Mbaegbu P. COVID-19 pandemic: A review of the global lockdown and its far-reaching effects. Science Progress. 2021 May; 104(2): 00368504211019854. doi: 10.1177/00368504211019854.

[24] de Kloet J. COVID-19 in China: Imagination and deep mediatization. China Information. 2021 Nov; 35(3): 265-73. doi: 10.1177/0920203X211051057.

[25] Sahin E, Bozdayi G, Yigit S, Muftah H, Dizbay M, Tunccan OG, *et al*. Genomic characterization of SARS-CoV-2 isolates from patients in Turkey reveals the presence of novel mutations in spike and nsp12 proteins. Journal of Medical Virology. 2021 Oct; 93(10): 6016-26. doi: 10.1002/jmv.27188.

[26] Frediansyah A, Nainu F, Dhama K, Mudatsir M, Harapan H. Remdesivir and its antiviral activity against COVID-19: A systematic review. Clinical Epidemiology and Global Health. 2021 Jan; 9: 123-7. doi: 10.1016/j.cegh.2020.07.011.

[27] Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. International Journal of Infectious Diseases. 2022 Jan; 114: 252-60. doi: 10.1016/j.ijid.2021.11.009.

[28] Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, *et al.* Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature. 2020 May; 581(7807): 215-20. doi: 10.1038/s41586-020-2180-5.

[29] Lopez AS, Hill M, Antezano J, Vilven D, Rutner T, Bogdanow L, *et al.* Transmission dynamics of COVID-19 outbreaks associated with child care facilities—Salt Lake City, Utah, April–July 2020. Morbidity and Mortality Weekly Report. 2020 Sep; 69(37): 1319. doi: 10.15585/mmwr.mm6937e3.

[30] Ricci D, Etna MP, Rizzo F, Sandini S, Severa M, Coccia EM. Innate immune response to SARS-CoV-2 infection: From cells to soluble mediators. International Journal of Molecular Sciences. 2021 Jun; 22(13): 7017. doi: 10.3390/ijms22137017.

[31] Mendez-Brito A, El Bcheraoui C, Pozo-Martin F. Systematic review of empirical studies comparing the effectiveness of non-pharmaceutical interventions against COVID-19. Journal of Infection. 2021 Sep; 83(3): 281-93. doi: 10.1016/j.jinf.2021.06.018.

[32] Curti F, Fortunati S, Knoll W, Giannetto M, Corradini R, Bertucci A, *et al.* A folding-based electrochemical aptasensor for the single-step detection of the SARS-CoV-2 spike protein. ACS Applied Materials & Interfaces. 2022 Apr; 14(17): 19204-11. doi: 10.1021/acsami.2c02405.

[33] Satarker S and Nampoothiri M. Structural proteins in severe acute respiratory syndrome coronavirus-2. Archives of Medical Research. 2020 Aug; 51(6): 482-91. doi: 10.1016/j.arcmed.2020.05.012.

[34] Narayanan K, Chen CJ, Maeda J, Makino S. Nucleocapsid-independent specific viral RNA packaging via viral envelope protein and viral RNA signal. Journal of Virology. 2003 Mar; 77(5): 2922-7. doi: 10.1128/JVI.77.5.2922-2927.2003.

[35] Li X, Geng M, Peng Y, Meng L, Lu S. Molecular immune pathogenesis and diagnosis of COVID-19. Journal of Pharmaceutical Analysis. 2020 Apr; 10(2): 102-8. doi: 10.1016/j.jpha.2020.03.001.

[36] Pandey P, Rane JS, Chatterjee A, Kumar A, Khan R, Prakash A, *et al*. Targeting SARS-CoV-2 spike protein of COVID-19 with naturally occurring phytochemicals: an in silico study for drug development. Journal of Biomolecular Structure and Dynamics. 2021 Nov; 39(16): 6306-16. doi: 10.1080/07391102.2020.1796811.

[37] Zeyaullah M, AlShahrani AM, Muzammil K, Ahmad I, Alam S, Khan WH, *et al.* COVID-19 and SARS-CoV-2 variants: current challenges and health concern. Frontiers in Genetics. 2021 Jun; 12: 693916. doi: 10.3389/fgene.2021.693916.

[38] Mannar D. Structure, function, and neutralization of SARS-CoV-2 spike glycoproteins (Doctoral dissertation, University of British Columbia). 2023. Available at: https://open.library.ubc.ca/soa/clRcle/collections/ubctheses/24/items/1.0434137.

[39] Chen X, Li R, Pan Z, Qian C, Yang Y, You R, *et al.* Human monoclonal antibodies block the binding of SARS-CoV-2 spike protein to angiotensin converting enzyme 2 receptor. Cellular & Molecular Immunology. 2020 Jun; 17(6): 647-9. doi: 10.1038/s41423-020-0426-7.

[40] Coroiu A, Moran C, Campbell T, Geller AC. Barriers and facilitators of adherence to social distancing recommendations during COVID-19 among a large international sample of adults. PloS One. 2020 Oct; 15(10): e0239795. doi: 10.1371/journal.pone.0239795.

[41] Dinleyici EC, Borrow R, Safadi MA, van Damme P,

DOI: https://doi.org/10.54393/fbt.v3i02.47

Munoz FM. Vaccines and routine immunization strategies during the COVID-19 pandemic. Human Vaccines & Immunotherapeutics. 2021 Feb; 17(2): 400-7. doi: 10.1080/21645515.2020.1804776.

[42] Pastorino R, Villani L, Mariani M, Ricciardi W, Graffigna G, Boccia S. Impact of COVID-19 pandemic on flu and COVID-19 vaccination intentions among university students. Vaccines. 2021 Jan; 9(2): 70. doi: 10.3390/vaccines9020070.

[43] Vanaparthy R, Mohan G, Vasireddy D, Atluri P. Review of COVID-19 viral vector-based vaccines and COVID-19 variants. Le Infezioni in Medicina. 2021 Sep; 29(3): 328. doi: 10.53854/liim-2903-3.

[44] Lemley MA and Sherkow JS. The antibody patent paradox. Yale LJ. 2022; 132: 994. doi: 10.2139/ssrn.4032912.

[45] Teijaro JR and Farber DL. COVID-19 vaccines: modes of immune activation and future challenges. Nature Reviews Immunology. 2021 Apr; 21(4): 195-7. doi: 10.1038/s41577-021-00526-x.

[46] Weinberg CR. Making the best use of test kits for COVID-19. American Journal of Epidemiology. 2020 May; 189(5): 363-4. doi: 10.1093/aje/kwaa080.

[47] Chavda VP, Bezbaruah R, Athalye M, Parikh PK, Chhipa AS, Patel S, *et al*. Replicating viral vector-based vaccines for COVID-19: potential avenue in vaccination arena. Viruses. 2022 Apr; 14(4): 759. doi: 10.3390/v14040759.