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Review Article

Comprehensive analysis of COVID-19 vaccines: safety characteristics, and post-immunization adverse events based on contemporary global evidence

Ali Adel Dawood[1]* ORCID: https://orcid.org/0000-0001-8988-5957
Zeyad Thonoon Al-Rrassam[2] ORCID: https://orcid.org/0000-0002-9014-976X
Mahmood Abduljabbar Al-Tobje[3] ORCID: https://orcid.org/0009-0007-1402-0749

[1]Department of Anatomy, Al-Batool College of Medicine, University of Mosul, Mosul, Iraq.
[2]Department of Medical Physics, College of Science, University of Mosul, Mosul, Iraq.
[3]Department of Biology, College of Science, University of Mosul, Mosul, Iraq.

Corresponding author: aad@uomosul.edu.iq.

A solution to the COVID-19 vaccine production and rapid deployment is an unparalleled step in medical history. This review has examined evidence of the effectiveness and safety of COVID-19 vaccines in vaccine platforms including mRNA (Pfizer-BioNTech, Moderna), adenoviral vector (AstraZeneca, Johnson and Johnson), whole inactivated virus (Sinovac, Sinopharm), recombinant protein subunit (Novavax), and Cuban developed vaccines, conjugate and recombinant protein subunit platforms (Soberana, Abdala), which are important contributors to vaccine diversity and equity. These vaccines show high effectiveness in preventing severe diseases, hospitalization, and death in different groups of people. However, they are associated with a spectrum of adverse reactions ranging in severity from mild to serious. Common expected reactions include local injection site pain, erythema, and swelling, accompanied by systemic symptoms such as fever, fatigue, myalgia, and headache, which are generally transient and self-limited. Rare but serious complications have been identified and characterized, most notably myocarditis and pericarditis predominantly in young males after mRNA vaccination, thrombosis with thrombocytopenia syndrome after adenoviral vector vaccines, Guillain-Barré syndrome, and various autoimmune manifestations. Reproductive health concerns, including transient menstrual irregularities, have also been reported, though fertility and pregnancy outcomes data are reassuring. Global pharmacovigilance systems have consistently demonstrated that serious adverse events are rare compared to the substantial protective benefits of vaccination. This review also discusses long-term safety considerations, special population profiles, and the critical role of transparent risk communication in maintaining public confidence in vaccination programs.

Keywords: vaccine safety; adverse event; immunization; pharmacovigilance.

Introduction

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), appeared at the end of 2019 and rapidly evolved into a global pandemic of unprecedented scale, profoundly affecting human society, healthcare systems, and the trajectory of scientific research.(1) According to the latest figures as of 2024, more than 777 million confirmed cases and over 7 million deaths have been reported worldwide; however, given widespread underreporting and limited testing capacity in many regions, actual statistics are expected to be substantially higher.(2)

The traditional vaccine development cycle normally takes 10 to 15 years between inception research up to regulatory approval including preclinical trials, multiple phases of clinical trials, scale-up manufacturing and regulatory processes.(3,4) Nevertheless, the catastrophic toll of the COVID-19 pandemic necessitated unprecedented acceleration. This was achieved through parallel rather than sequential development phases, massive public and private financial investment exceeding 100 billion dollars worldwide, elimination of financial risk for the pharmaceutical industry, and expedited regulatory evaluation without compromising

* Department of Anatomy, Al-Batool College of Medicine, University of Mosul, Mosul, Iraq.

scientific rigor.[4] The result was emergency use authorization of the first COVID-19 vaccines within eleven months of the release of the viral genetic sequence an extraordinary accomplishment demonstrating the capacity of modern vaccine science and international scientific cooperation.

Several distinct vaccine platforms were designed and implemented. The Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1273) vaccines are mRNA-based, delivering synthetic messenger RNA encoding the spike protein via lipid nanoparticles.[5,6] The Oxford-AstraZeneca (ChAdOx1 nCoV-19), Johnson & Johnson (Ad26.COV2. S), and Sputnik V vaccines use non-replicating adenoviral vectors to deliver genetic instructions for spike protein production.[7] Inovac (CoronaVac) and Sinopharm (BBIBP-CorV) are developed based on well-established and established platforms of chemically inactivated whole virus particles respectively; Novavax (NVX-CoV2373) is based on a platform of recombinant purified spike protein and the Matrix-M adjuvant. Cuba also created vaccines of its own, such as Soberana and Abdala, which were extensively used in the country and thus are significant in the global diversity and equity of vaccines.[8,9]

As of December 2024, more than 13.5 billion vaccine doses have been administered worldwide, but enormous coverage disparities exist between countries and regions. High-income nations achieved vaccination rates exceeding 80% of their populations, while most low-resource nations were unable to vaccinate more than 20% of their populations due to supply chain constraints, infrastructure limitations, vaccine hesitancy, and geopolitical factors.[9]

The rapid development and widespread deployment of COVID-19 vaccines, while constituting a landmark achievement in public health, generated significant controversy regarding safety, efficacy, and adverse effects. This discussion emerged against the background of unparalleled information saturation and misinformation via social media platforms, politicization of individual health, historical distrust of medical services by some groups, and reasonable scientific skepticism about the safety of new vaccine technology in the long term.[10]

As a counter to this, the healthcare system across the globe has developed extensive pharmacovigilance programs that entail the collaboration between passive surveillance programmes, including the U.S. Vaccine Adverse Event Reporting System (VAERS), and active surveillance programmes, including the Vaccine Safety Datalink (VSD), and the multilateral efforts in this context through the WHO Global Advisory Committee on Vaccine Safety.[11] These systems allowed quick recognizing of safety signals and prompt changes in recommendations on vaccinations.

The present review is a synthesis of the available evidence regarding COVID-19 vaccine adverse events that have been reported in peer-reviewed literature since 2022 that includes real-world safety information on first-generation vaccines and variant-specific vaccine modifications and maturation of global pharmacovigilance systems. It aims at equipping clinicians, public health practitioners, and policymakers with a holistic, evidence-based profile of the benefits and risks of available COVID-19 vaccines.[11]

Methods

Literature search strategy

The search of the literature was systematic in PubMed, Scopus, Web of Science, and Cochrane Library concerning the articles published between January 2022 and December 2024. The search terms were the following: COVID-19 vaccines, SARS-CoV-2 immunization, vaccine adverse events, vaccine safety, mRNA vaccines, viral vectors vaccines, and the names of individual adverse events such as myocarditis, thrombosis, thrombocytopenia, neurological complications, and autoimmune reactions.[12]

Inclusion and exclusion criteria

The inclusion criteria included peer-reviewed original research articles, systematic reviews, and meta-analyses; publications that reported adverse events following the COVID-19 vaccination; large-scale population-based surveillance studies; randomized controlled trials containing safety data; literature published in English in 2022 to 2024.

The exclusion criteria included case reports of less than five patients, preprint articles that had not undergone peer review, and commentaries and editorials that did not include original data and studies that included an ambiguous methodology or inadequate data reporting.[5,13]

Data extraction and synthesis

Information was obtained regarding type of vaccine, type and frequency of adverse events, demographics of patient, level of severity, and time association with the vaccination. Since study designs and the populations of the studies under analysis are highly heterogeneous, the narrative synthesis approach was chosen rather than formal meta-analysis.[13] The Cochrane Risk of Bias tool of randomized studies and Newcastle-Ottawa Scale of observational studies were used to determine the quality of studies.

Common and expected adverse events

Local reactions at the injection site

Local reactions at the injection site are the most frequently reported adverse events following COVID-19 vaccination, affecting between 50% and 90% of vaccine recipients depending on the specific vaccine and dose number. Patients who receive mRNA vaccines typically experience pain at the injection site after receiving the vaccine, with 70-90% reporting such pain, and the pain being more often and more severe after the second dose of a two-dose primary vaccine.[14] The pain typically peaks within 24-48 hours' post-vaccination and resolves within 3-5 days without specific treatment.

Erythema and swelling at the injection site occur less frequently, affecting approximately 10-20% of recipients. In a subset of cases, delayed large local reactions have been documented, characterized by redness and swelling exceeding 10 cm in diameter, sometimes termed "COVID arm" or "Moderna arm" due to their higher frequency with the Moderna vaccine.[15] These delayed reactions typically appear 4-11 days after vaccination and resolve spontaneously; they are not indicative of bacterial cellulitis and do not require antibiotic treatment.[15]

Axillary or cervical lymphadenopathy ipsilateral to the vaccination site has been reported in approximately 10-15% of mRNA vaccine recipients, typically appearing 1-4 days' post-vaccination and resolving within 1-2 weeks. Importantly, this reactive lymphadenopathy may be misinterpreted as malignant involvement on breast imaging and other radiological examinations. Current evidence-based guidance recommends deferring routine mammography or lymph node imaging by 4-6 weeks following vaccination whenever clinically feasible to avoid false-positive findings.[16]

Systemic reactions

Post-vaccination systemic symptoms are common and reflect the normal immunological activation triggered by vaccine administration. The most frequently reported systemic symptom is fatigue, occurring in 40-70% of recipients, with higher frequency following the second dose of two-dose regimens.[17] This is a mild to moderate fatigue which usually ends in 2-4 days. Common vaccine side effects are headache, fatigue, myalgia and fever. Around 30-60% of recipients experience a headache, which generally resolves within 2-3 days, whereas 40-70% have fatigue and 30-50% experience myalgia, both of which are generally short-lived and self-limited, and fever is seen in 10-40% of the recipients, and is generally short-lived and self-limited.[17]

Myalgia and arthralgia are experienced by 30-50% of vaccine recipients, and it is associated with general muscle pains or joint pain that may occur up to 24 hours after the vaccine, and may end in 2-4 days. Although there is much variation in the presence of fever depending on the vaccine platform, dose number and age group, fever is reported by 10-40% of vaccine recipients and is more common with mRNA vaccines than with viral vectors or inactivated virus vaccines and second doses than first doses.[18] Younger adults (ages 18-55) tend to have a higher rate of fever after vaccination than older adults (≥65 years). This age difference is attributed to the increased reactogenicity of immunity response in younger populations versus the less reactogenic response in the older population which is associated with lower rates of post-vaccination fever.[19]

Cardiovascular complications

Myocarditis and pericarditis

After mRNA COVID-19 vaccination, an important vaccine safety signal was identified as myocarditis (inflammation of the myocardium) and pericarditis (inflammation of the pericardium) in adolescent and young adult males.[20] A series of population-based studies in various countries showed that there were regularly high rates of myocarditis after an mRNA vaccination compared with prior background rates, and that the most significant rate occurred after the second dose in the initial series.

The VAERS and the VSD showed a range of 12-30 per 1,000,000 second doses of mRNA vaccine in males aged 12-29 years, many times more than background rates. The rates of 50-70 cases per million second doses were recorded among the most at risk population in males aged 16-19 years, and the most critical period was 3-5 days after the vaccination. In females, risk was significantly reduced at about 2-4 cases/million doses. The risk level went down significantly with age, and people above 40 years had only slightly higher rates than the baseline.[21,22] Figure 1 shows a more detailed age and sex-stratified incidence of myocarditis after mRNA vaccination, which clearly shows that the risk is significantly higher in young males but decreases with age. The data for Figure 1 were gathered from the publicly available surveillance reports from the VAERS and the VSD.[23,24] The Figure 1 was compiled by the authors based on aggregated incidence figures, by age and sex.

The Moderna vaccine (mRNA-1273) was associated with a higher incidence of myocarditis compared to the

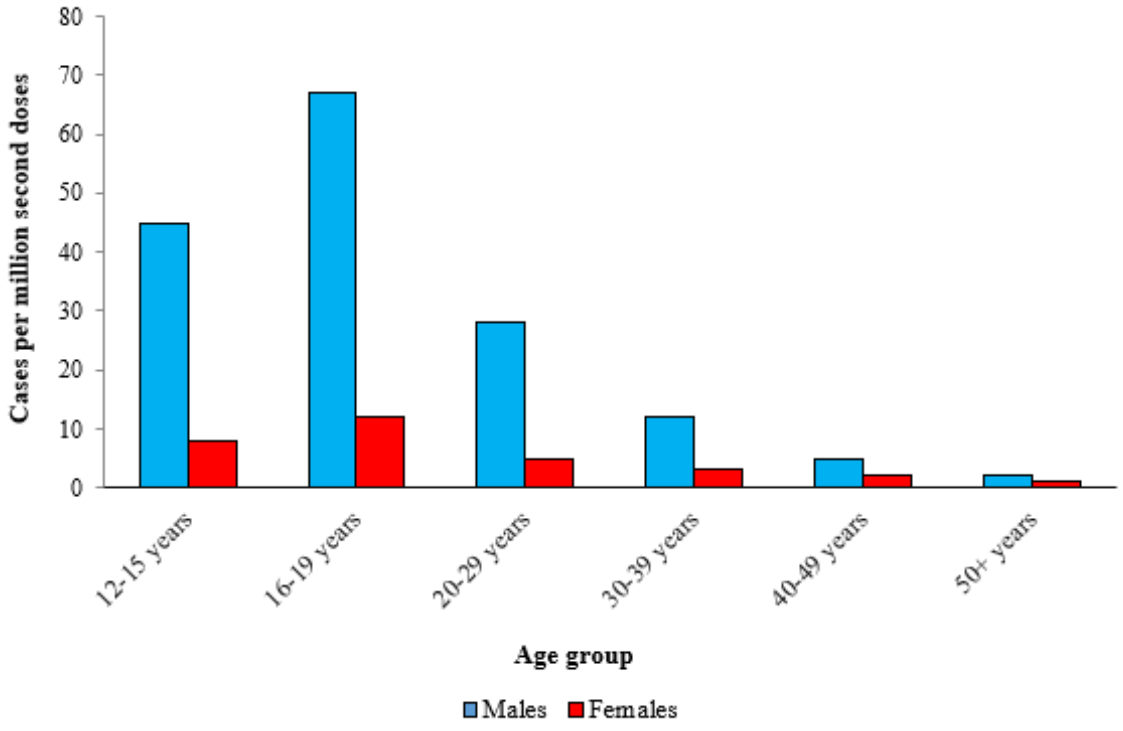


Fig. 1. Age and sex-stratified myocarditis risk following mRNA vaccination.

Pfizer-BioNTech vaccine (BNT162b2), which may be related to the larger mRNA dose (100 µg versus 30 µg) or differences in lipid nanoparticle composition.[25] The clinical picture of vaccine-associated myocarditis is usually characterized by chest pain that appears 2-5 days after the vaccination that is sometimes characterized as sharp or pressure-like. Most cases do have electrocardiographic abnormalities most frequently ST-segment elevations implying acute myocardial injury. Most of the diagnosed cases show a high level of cardiac troponin levels, which are biomarkers of myocardial injury.[20,26]

The mechanisms proposed to cause vaccine-associated myocarditis are not fully characterized but probably an immune-mediated injury as SARS-CoV-2 virus or vaccine mRNA has not been identified in cardiac biopsies. The suggested mechanisms are molecular mimicry of spike protein epitopes with cardiac proteins, overproduction of inflammatory cytokines after vaccination, and direct action of lipid nanoparticle components on toll-like receptors.[26]

The vaccine-associated myocarditis prognosis is typically positive as compared to viral myocarditis or COVID-19 infection-related myocarditis. Most of the cases are mild and moderate in nature and it is only to monitor and not to give aggressive treatment that patients have to be hospitalized. Subsequent studies have shown that the majority of patients experience complete or almost complete resolution of both cardiac abnormalities and symptoms in 3-6 months. Comparative studies have shown that, in all age groups, the risk of myocarditis after SARS-CoV-2 infection is significantly higher than after vaccination. Furthermore, infection-related myocarditis has been correlated with the more serious clinical symptoms and poor prognosis.[27]

Thrombosis with thrombocytopenia syndrome (TTS)

Adenoviral vaccine COVID-19 vaccines, most commonly the AstraZeneca (ChAdOx1 nCoV-19) and Johnson and Johnson (Ad26.COV2. S) vaccines, were found to cause a rare but clinically significant adverse effect called thrombosis with thrombocytopenia syndrome (TITS), also known as vaccine induced immune thrombotic thrombocytopenia (VITT).[28,29] Incidences differ by age and sex with rates estimated to be 1-2 cases in every 100,000 AstraZeneca doses and 1-3 cases in every million J&J doses. The risk is significantly greater in younger persons and women who are less than 50 years old specifically where the risks of about 10-15 cases per million doses have been reported and the risk is relatively low in older populations.[30]

TTS normally occurs 7-14 days after the vaccination with extreme persistent headache, visual or localized neurological disorders, stomach pains, and swelling of limbs.[31] Among the findings in the laboratory, there is marked thrombocytopenia, increased D-dimer (>4,000 ng/mL), and positive platelet factor 4 (PF4) antibodies-pathognomonic of vaccine-associated TTS in patients who had no previous exposure to heparin. The mechanism pathophysiology entails the anti-PF4 antibody-mediated immunologic complexes interacting platelets through Fc-receptors, which stimulates platelet aggregation and thrombocytopenia and is paradoxical, as it induces a prothrombotic condition.[30] This is a pathological process, with important therapeutic implications, particularly avoiding the use of heparin. Intravenous immunoglobulin and non-heparin anticoagulants (argatroban or fondaparinux) are recommended; plasma exchange should be used in refractory cases.[32] The mortality rate of TTS is approximately 2-4% and highest in the cerebral venous sinus thrombosis. This has led to several countries substantially changing their vaccine policies.[30]

Neurological complications

Guillain - Barré syndrome

Guillain-Barré syndrome (GBS) is a rare acute inflammatory demyelinating polyneuropathy which has been reported at a slightly increased rate after COVID-19 adenoviral vector vaccines, primarily the Johnson & Johnson Ad26.COV2.S vaccine. Population-based surveillance studies identified a small rise in the incidence of GBS, around 1-2 per million doses, over and above the background rate.[33] These clinical features are progressive ascending weakness that starts in the lower extremities, sensory, and areflexia, and in some cases, respiratory muscle impairment leading to the need of mechanical ventilation. Therapy is by intravenous

immunoglobulin or therapeutic plasma exchange and most patients show great improvements in their neurological recovery but some deficits may be left behind.[34]

An equally significant contextual fact is that comparative epidemiological research has always revealed that the risk of GBS due to COVID-19 itself is significantly greater than that due to vaccination, and the rates related to infections are always 5-10 times higher than those related to vaccination. Such a risk-benefit orientation is crucial to clinical counseling and health education to the population.[35]

Cerebral venous sinus thrombosis

The development of cerebral venous sinus thrombosis (CVST), which is a rare type of stroke that occurs in response to thrombosis of the cerebral venous drainage system, was identified as a very worrying presentation of TTS, following adenoviral vectors vaccination. CVST is characterized by acute and unremitting headache, optical and neurological disturbances, seizures, local cerebral impairments, and confusion.[29] CVST and thrombocytopenia combined should immediately raise the question of TTS. Specialized non-heparin anticoagulation and neurocritical care support and extensive attention to clinical deterioration are required in the management.

Neurological manifestations other than neuropathy

Other neurological side effects reported following COVID-19 vaccination include Bell's palsy (facial nerve paralysis), transverse myelitis (inflammation of the spinal cord) and sensory disturbances. There was a slight increase in the number of cases of Bell's palsy in early clinical trials compared to placebo. Later, large-scale surveillance studies, however, did not support this finding, with the overall rates being similar to those of the unvaccinated population.[36]

Autoimmune and inflammatory complications

Immune thrombocytopenia

Immune thrombocytopenia (ITP), also referred to as isolated thrombocytopenia, is an autoimmune condition characterized by antibody-mediated platelet destruction. Rare cases have been reported following COVID-19 vaccination across different platforms. Unlike TTS, the ITP manifests as isolated thrombocytopenia without thrombotic complications. The estimated incidence is approximately 1-2 cases per 100,000 vaccinations, which is broadly consistent with background population rates. Management strategies include observation in mild cases, while corticosteroids, intravenous immunoglobulin, and thrombopoietin receptor agonists are recommended for more severe presentations. With appropriate treatment, clinical outcomes are generally favorable.[37]

Autoimmune hepatitis

Rare adverse effects that have been described after COVID-19 vaccination, specifically after adenoviral vectors vaccine include autoimmune hepatitis, which presents itself as hepatocellular injury with increased liver enzymes and autoantibodies. Jaundice, fatigue and biochemical hepatitis evidence were clinical manifestations. Immunosuppressive therapy using corticosteroids was usually effective in cases, and majority of the patients had biochemical remission. The pathophysiology suggested is autoimmune reactivity of immune dysregulation caused by the vaccine to hepatic antigens.[38,39]

Thyroid disorders

COVID-19 vaccination is related to thyroid dysfunction but a number of published case series and surveillance reports describe it as either subacute thyroiditis or exacerbations of underlying autoimmune thyroid disease, including Graves' disease and Hashimoto's thyroiditis.[40] Subacute thyroiditis has symptoms of anterior neck pain, fever and biphasic thyroid functional abnormalities, first hyperthyroidism, then transient hypothyroidism and the subsequent euthyroidism in most instances. There are mild cases where the management involves the use of non-steroidal anti-inflammatory drugs or moderate to severe disease where corticosteroids are used and most cases are self-limiting and resolved in a few months.[41]

Reproductive health concerns

Menstrual irregularities

There has been reports that a large percentage of women experienced changes in their menstrual cycle after COVID-19 vaccination, such as a change in the length of the cycle, flow changes, and increased dysmenorrhea. Large cohort studies have found that 25-40% of menstruating women reported some type of menstrual problem, including: starting menstruation earlier than usual; starting menstruation later than usual; having heavier periods; having lighter periods; or having more menstrual pain. Importantly, these changes tended to be temporary, with most women experiencing the return of their pre-vaccination periods within 1-2 cycles.[42]

These menstrual changes are believed to be due to the transient immune activation that occurs in the hypothalamic-pituitary-ovarian axis, an endocrine control system that controls the menstrual cycle. Notably, these changes seem to be reversible and have not been linked to any long-term reproductive impairment.[43]

Fertility and pregnancy outcomes

In the strict sense of the word, it should be noted that fertility and pregnancy outcomes are not considered an adverse event; however, they have been a significant concern of the public, the source of vaccine hesitancy, and of clinical interest when counseling pregnant women about immunizations.

There has been no scientific evidence that vaccines against COVID-19 will affect fertility. The first report of cross-reactivity between SARS-CoV-2 spike protein and syncytin-1 has been definitively rejected. The results of large prospective cohort studies have shown that there are no differences in fertility indicators between vaccinated and unvaccinated people. Research on in-vitro fertilization (IVF) outcomes has shown that there is no effect on ovarian reserve, fertilization rates, embryo quality or implantation.[44] The male fertility parameters (sperm count, motility and morphology) were also not affected. In addition, hundreds of thousands of women were followed and there was no higher risk of miscarriage, stillbirth, premature delivery or birth defects among women who were vaccinated during pregnancy than among those who were not. Important, vaccination during pregnancy has been proven to generate protective antibodies that pass on to the fetus and newborn, and all major medical bodies recommend vaccination against COVID-19 in pregnancy.[45]

Long-term safety considerations

Duration of safety monitoring

Unlike conventional vaccine development during which long-term safety data accumulate over years before mass deployment, COVID-19 vaccines were authorized under emergency conditions.[21] Nevertheless, several observations provide reassurance: mRNA degrades within days without genetic modification; immune responses mirror those from natural infection; historical vaccine data consistently show serious adverse events appear within weeks-to-months post-vaccination rather than years; and ongoing surveillance now encompasses billions of vaccinated individuals with follow-up periods extending to 2-3 years, without identifying systematic increases in serious adverse events beyond those already characterized.[21]

Risk of immune system dysregulation

Theoretical concerns about potential long-term immune system dysregulation following COVID-19 vaccination including increased susceptibility to infectious diseases or autoimmune conditions have been systematically investigated. Available evidence does not demonstrate any signs of generalized immune suppression, elevated infection rates, or compromised vaccine responses to other pathogens in vaccinated populations. Ongoing surveillance of autoimmune disease development has not revealed systematic increases in autoimmune disease incidence beyond expected baseline levels.[18]

Cancer risk considerations

Circulating claims about potential carcinogenic effects of COVID-19 vaccines lacked any biological plausibility and have been extensively investigated and refuted. mRNA vaccines do not carry out any biological processes associated with carcinogenesis, as the mRNA does not integrate into the genome, does not encode

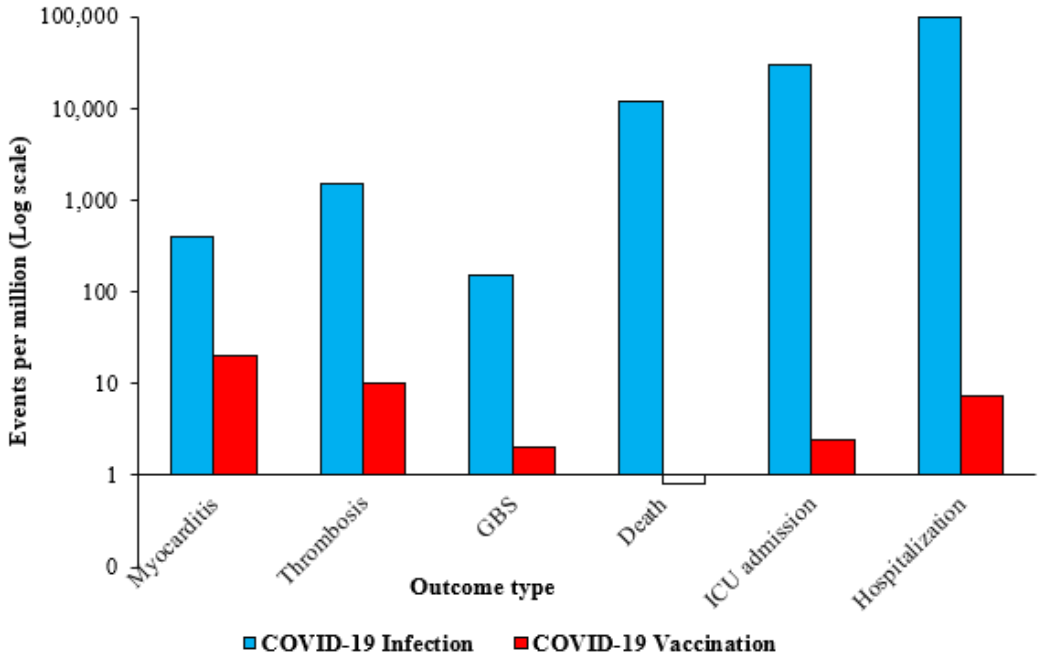


Fig. 2. Risk-benefit analysis: COVID-19 disease and vaccination complications.

oncoproteins, and does not persist beyond days in cells. Large-scale pharmacovigilance data have not identified any evidence of increased cancer incidence rates in vaccinated populations compared to unvaccinated controls or expected baseline rates.[46]

The overall results of a quantitative comparison between major adverse outcomes rates with COVID-19 infection and vaccination per million individuals exposed shows the overwhelming advantage of vaccination in all major categories of complications using a logarithmic scale to show the vast range of values (Fig. 2). The data for Figure 2 were obtained from published population-based comparisons of adverse event rates after COVID-19 infection and vaccination.[25,28,47,48,49]

Special populations

Pediatric populations

Vaccination of children and adolescents against COVID-19 generated substantial public debate, reflecting the generally milder clinical course of COVID-19 in this age group and concerns particularly about myocarditis risk with mRNA vaccines. Extensive clinical trials and post-authorization surveillance data demonstrated that vaccines are both safe and immunogenic across pediatric age groups, though adverse event profiles vary by age.[50] Children aged 5-11 years exhibited reduced reactogenicity and substantially lower myocarditis rates compared to adolescents, attributable in part to use of a lower vaccine dose (10 μg for the Pfizer vaccine). Male adolescents aged 12-17 years represent the highest-risk demographic for vaccine-associated myocarditis, necessitating individualized benefit-risk assessment considering local COVID-19 epidemiology and individual health factors.[49,50]

Immunocompromised individuals

Immunocompromised individuals including solid organ transplant recipients, patients with hematological malignancies, and individuals receiving immunosuppressive therapy are among those at greatest risk for severe COVID-19 outcomes and therefore stand to derive considerable benefit from vaccination. COVID-19 vaccination in these populations is generally safe, with adverse event rates comparable to or lower than those observed in immunocompetent individuals and no evidence of increased serious complications.[21] However, vaccine-induced immune responses may be

attenuated due to underlying immune dysfunction or the effects of immunosuppressive medications, often necessitating additional primary series doses and earlier booster vaccination.[51]

Elderly populations

Elderly populations bear the greatest burden of severe COVID-19 disease and represent the highest-priority group for vaccination. The safety profile of COVID-19 vaccines in older adults is favorable, characterized by reduced reactogenicity compared to younger recipients, likely reflecting age-related immunosenescence with attenuated innate immune activation following vaccination. Common adverse events such as injection site pain, fatigue, and fever occur less frequently and with lesser severity in older adults. The benefit-risk calculation for COVID-19 vaccination is overwhelmingly favorable in elderly populations, given their disproportionate risk for hospitalization, intensive care admission, and mortality from COVID-19 infection.[23]

Global pharmacovigilance systems

The world-wide distribution of COVID-19 vaccines demanded unprecedented collaboration of safety surveillance in the varied healthcare systems. Several complementary surveillance methods were put in place: passive surveillance (VAERS, in the US, Yellow Card in the UK), active surveillance (VSD, Clinical Immunization Safety Assessment project), and the international coordination (the WHO Global Vaccine Safety Initiative). These platforms showed a very high level of responsiveness; regulatory agencies have changed recommendations within weeks of identifying safety signals, such as age-based restrictions on adenoviral vectors vaccines because of TTS risk, bias in mRNA vaccine recommendations in younger males because of concerns about myocarditis, and clinical guidance on how to identify and manage rare vaccine-associated conditions. The pharmacovigilance of COVID-19 vaccines has produced insights and infrastructure gains that can advance the future of safety monitoring of vaccines.[21,46]

Comparative risk-benefit analysis

Quantitative risk comparisons

The related risks of COVID-19 infection significantly and uniformly significantly outweigh the risks related to vaccination in the case of virtually adverse events related to COVID-19 vaccines. Compared to vaccination, myocarditis is much higher after COVID-19 infection in all ages and both sexes, and myocarditis due to infection is generally more severe in clinical presentation and poorer prognosis than myocarditis due to vaccination. Likewise, thrombotic events such as CVST, deep vein thrombosis, and pulmonary embolism are more frequently observed as a result of COVID-19 infection compared to vaccination.[52]

Neurological events, including GBS, encephalitis, and stroke, and autoimmune events such as ITP, myocarditis and multisystem inflammatory syndromes, occur far more frequently in people who have contracted the virus COVID-19. Infection is more likely to cause these conditions than vaccination. Most importantly, the risks associated with COVID-19 infection are high; however, the risks associated with vaccination are very small, and most benefits of vaccination are found in older adults and those at higher risk.[35,52]

Population-level benefits

The COVID-19 vaccination programs avoided the occurrence of millions of hospitalizations and deaths around the world. Studies on epidemiological modeling estimated that COVID-19 vaccination averted approximately 2.5 million deaths worldwide during 2020-2024 (sensitivity range 1.4-4.0 million), corresponding to about 15 million life-years saved. The benefits of vaccination to society were far more than direct effects on health, and involved significant economic benefits in terms of health burden saved to the healthcare system, workforce productivity, and the ability to resume educational, social, and economic activities that had been devastated by the pandemic.[53]

Future directions

The current development of vaccines is expected to enhance resistance against new variants, minimize reactogenicity, and ease their delivery. Newer strategies

involve modified mRNA preparations with less inflammatory reactions, pan-coronavirus vaccines that provide wider cross-variant coverage, and intranasal preparations of the mucosa. Insight into the underlying mechanism of the current adverse events will provide a direct input to the development of safer new generation vaccines.[54] Innovations in pharmacogenomics could potentially provide an opportunity to adopt a more individual approach to vaccination, determining which individuals are at a high risk due to genetic or immunological factors to certain adverse events and personalizing selection of vaccines or changing monitoring regimens. The continued safety of both existing and future vaccines will require strengthening the pharmacovigilance infrastructure across the whole world with uniformity in the definition of adverse events, enhancing integration of electronic health records to facilitate automated detection of signals, and increasing the range of data sharing by countries worldwide.[55]

Conclusions

This overview shows that the benefit-risk ratio is clearly positive for all the approved COVID-19 vaccines in most of the populations. The benefits of preventing severe illness, hospitalization and death far outweigh the reported risks. Common side effects include local injection site reactions, mild fever, fatigue and myalgia, which are all transient immune reactions and disappear within days. Although a small number of rare and more severe adverse events have been described, such as myocarditis, TTS, GBS, and autoimmune problems, there is no evidence of the incidences of these events being significantly higher than they are when COVID-19 itself occurs. The unprecedented evidence of real-world safety that has been obtained during rollout of vaccines across the world underscores the need for ongoing pharmacovigilance. Future objectives are to better understand the mechanisms underlying rare complications, establish predictive markers for risk stratification, refine vaccine formulation and achieve equitable global access.

Conflict of interest

The authors declare that there is no conflict of interest.

Author's contributions

Ali Adel Dawood: conceptualization, methodology, writing original draft, writing review and editing, supervision.

Zeyad Thonoon Al-Rrassam: data curation, writing review and editing.

Abduljabbar Al-Tobje: data curation, writing review and editing.

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

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Análisis detallado de las vacunas contra la COVID-19: características de seguridad y efectos adversos tras la vacunación según la evidencia mundial actual

Resumen

La solución para la producción y el rápido despliegue de las vacunas contra la COVID-19 fue un hito sin precedentes en la historia de la medicina. En esta revisión se ha analizado la eficacia y la seguridad de las vacunas contra la COVID-19 en diversas plataformas, entre las que se incluyen las de ARNm (Pfizer-BioNTech, Moderna), las de vector adenoviral (AstraZeneca, Johnson & Johnson), las de virus inactivado completo (Sinovac, Sinopharm), las de subunidades proteicas recombinantes (Novavax), y las vacunas desarrolladas en Cuba —plataformas de conjugado y de subunidades proteicas recombinantes (Soberana, Abdala)—, que han contribuido de manera importante a la diversidad y la equidad en materia de vacunas. Estas vacunas han demostrado una alta eficacia a la hora de prevenir la enfermedad grave, la hospitalización y la muerte en diferentes grupos de población. Sin embargo, se han asociado a una serie de reacciones adversas, cuya gravedad varía de leve a grave. Entre las reacciones comunes esperadas se incluyen dolor local, eritema e hinchazón en el lugar de la inyección, acompañados de síntomas sistémicos como fiebre, fatiga, mialgia y cefalea, que suelen ser transitorios y autolimitados. Se han identificado y caracterizado complicaciones poco frecuentes, pero graves, entre las que destacan la miocarditis y la pericarditis —predominantemente en hombres jóvenes tras la vacunación con ARNm—, el síndrome de trombosis con trombocitopenia tras las vacunas con vector adenoviral, el síndrome de Guillain-Barré y diversas manifestaciones autoinmunes. También se han notificado problemas de salud reproductiva, incluidas irregularidades menstruales transitorias, aunque los datos sobre la fertilidad y los resultados del embarazo son tranquilizadores. Los sistemas mundiales de farmacovigilancia han demostrado de forma sistemática que los efectos adversos graves son poco frecuentes en comparación con los importantes beneficios protectores de la vacunación. En esta revisión también se analizan las consideraciones relativas a la seguridad a largo plazo, los perfiles de poblaciones especiales y el papel fundamental que desempeña la comunicación transparente de los riesgos a la hora de mantener la confianza del público en los programas de vacunación.

Palabras clave: seguridad de las vacunas; evento adverso; inmunización; farmacovigilancia.

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