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Post Marketing Surveillance and Safety Evaluation of Covishield Vaccine: A Comprehensive Review

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ABSTRACT:

The rapid development and deployment of COVID-19 vaccines have played a critical role in mitigating the global pandemic. Covishield, the Indian-manufactured version of the Oxford-Astra Zeneca vaccine, has been widely administered as part of mass immunization programs. Post-marketing surveillance (PMS) serves as a vital pharmacovigilance tool to assess the real-world safety and effectiveness of vaccines beyond controlled clinical trials. This review comprehensively examines PMS data on Covishield, focusing on adverse events following immunization (AEFIs), rare adverse reactions such as thrombosis with thrombocytopenia syndrome (TTS), and overall benefit-risk assessment. Data from national and international pharmacovigilance databases, peer-reviewed literature, and regulatory reports were analyzed to provide insights into the frequency, severity, and management of reported adverse events. Findings indicate that while Covishield is associated with common mild-to-moderate side effects like fever, injection site pain, and fatigue, serious adverse events remain rare and manageable under current medical guidelines. Continuous post-marketing monitoring has enhanced vaccine safety through updated recommendations, risk communication strategies, and clinical guidance. The review concludes that Covishield maintains a favorable safety profile, reinforcing its role in achieving herd immunity, while highlighting the importance of robust pharmacovigilance systems for early detection and mitigation of vaccine-related risks.

Keywords: Covishield, post-marketing surveillance, pharmacovigilance, COVID-19 vaccine, adverse events, safety profile, adverse reactions, development of vaccine.

INTRODUCTION :

The World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) a global pandemic due to its worldwide impact, affecting more than 220 countries [1,2]. COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that first emerged in late 2019 when a cluster of severe pneumonia cases of unknown cause was reported in Wuhan, Hubei Province, China, and soon became a global threat [3,4]. Based on WHO dashboards, there are 500 million confirmed cases globally as of April 2022, and death counts exceed 6.2 million worldwide [5]. All regulatory authorities worked collaboratively by adopting various responsive measures, such as lockdowns, social distancing, the use of masks, and subsequent sanitization procedures, to prevent the spread of COVID-19 infection [6]. Pharmacological agents such as prophylactic anticoagulants, hydroxychloroquine, oxygen supplements, parenteral steroids, and other antiviral drugs, such as remdesivir, lopinavir/ritonavir, favipiravir, and oseltamivir, were used in the management of this pandemic, but none of these agents were 100% effective in seriously ill patients with high mortality [7].This finding emphasized the need for the development and authorization of specific antivirals against SARS-CoV-2 to control the pandemic. Many pharmaceutical companies have developed vaccines against COVID-19 using preexisting and novel strategies, such as virus-vector vaccines, inactivated virus vaccines, messenger RNA (mRNA) vaccines, live attenuated virus vaccines, and protein subunit vaccines, to control the transmission of SARS-CoV-2 infection and reduce mortality [8]. Regulatory authorities in many countries approved the AstraZeneca vaccine from Oxford University, the mRNA vaccine from Moderna, and the mRNA-based BNT162b2 from Pfizer for emergency use [9]. In India, two vaccines were authorized by the Indian Drug Regulatory-Central Drug Standard Control Organization (CDSCO) for emergency use, namely Covishield from the Serum Institute of India (SII) and Covaxin from Bharat Biotech.

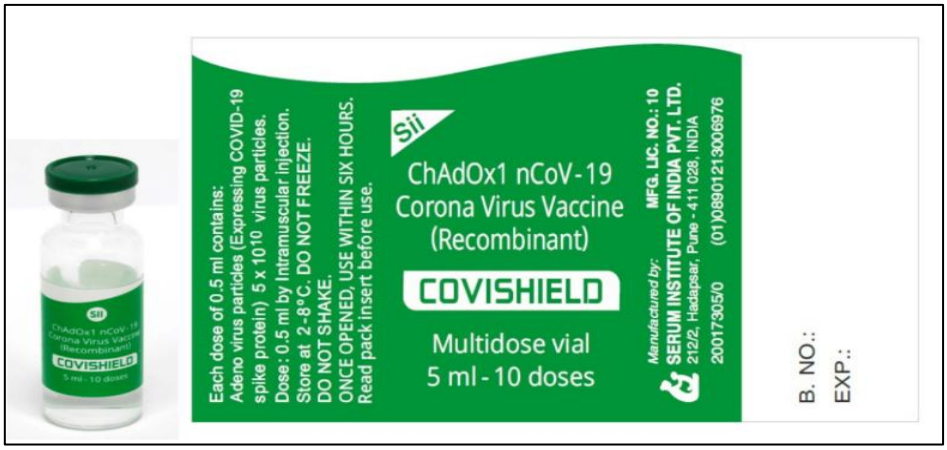
Covishield (ChAdOx1-nCOV) is a genetically engineered, recombinant, replication-deficient chimpanzee adenovirus vector strain, whereas Covaxin consists of an inactivated SARS-CoV-2 viral particle. On January 16, 2021, India started vaccinating against SARS-CoV-2, first involving healthcare workers (HCWs) and other frontline workers, then extending to elderly people with different comorbidities, and finally to all age groups [10]. The Covishield vaccine, which is similar to the Oxford AstraZeneca

vaccine concerning safety and immunogenicity, has accounted for almost 88% of all doses administered in the country and is the only vaccine available in our area [11]. Data from four clinical trials demonstrated that the Covishield vaccine has an efficacy of 67% (95% confidence interval) in preventing symptomatic COVID-19 infection and approximately 72%-100% in preventing hospitalization and severe infection beginning 21 days after receiving the second dose [12].Current evidence on the safety profiles of COVID-19 vaccines relies mainly on data available from controlled trials and vaccine safety surveillance systems. According to a phase 2/3 clinical study conducted in India, the frequency of adverse events due to the Covishield vaccine was greater than 1%, including injection-site pain, pyrexia, body ache, headache, myalgia, malaise, asthenia, and fatigue [13]. The safety surveillance data for certain age groups, such as children, pregnant women, and individuals with comorbid conditions, have not been well studied. Although adverse events reported in clinical trials after post-marketing approval are common or uncommon ADRs, delayed-onset drug reactions will require extended pharmacovigilance studies [14]. Many more clinical studies will be required to justify the benefit-risk analysis of the vaccine over time. Therefore, this study is concerned with the safety surveillance of the Covishield vaccine (either first or second dose) by determining the number of adverse events and their association with related factors such as age, gender, category, severity (serious or non-serious), duration of the event, causality, and outcome in the North Indian population

Ingredients	Use
ChAdOx1	API
Polysorbate 80	Emulsifier
L-Histidine	Buffer
Ethanol	Solvent
Magnesium Chloride	Maintain Isotonicity

- Dose – 0.5 ml each dose
- The Indian govt . has recommended that the time interval between the 1st and 2nd dose should be between 12-16 weeks.
- Side effects or adverse reactions have been reported with COVISHIELDTM vaccine.
- Direction – As per the physicians
- Storage – Store in cool and dry place,

Keep away from sun light.



1. Background :

Covishield is the Indian name for the Oxford–AstraZeneca COVID-19 vaccine (ChAdOx1 n CoV-19, later named AZD1222).It is developed by the University of Oxford in collaboration with AstraZeneca, and manufactured in India by the Serum Institute of India (SII). It uses a non-replicating chimpanzee adenovirus vector to deliver the SARS-CoV-2 spike protein gene, prompting an immune response.

2. Phases of Clinical Trials:

Phase I/II (UK - April–May 2020):

Trial Name: COV001 Participants: ~ 1,077 healthy adults (aged 18–55) Design: Randomized, single-blind, controlled trial Findings: Safe and well tolerated Strong humoral and cellular immune response Mild side effects: fever, headache, and muscle pain.

• Phase II/III (UK - May–August 2020):

Trial Name: COV002.

Participants: ~10,000 adults, including elderly (>70 years).

Findings: Good immune response across age groups

Two standard doses (SD/SD) vs. low dose followed by standard dose (LD/SD) tested.

LD/SD regimen showed up to 90% efficacy; SD/SD showed around 62% efficacy.

Phase III (Brazil and South Africa - mid-2020):

Trial Names: COV003 (Brazil), COV005 (South Africa).

Participants: Tens of thousands

Outcomes: Efficacy confirmed across geographies

light reduction in effectiveness against Beta variant in South Africa Serious adverse events were rare.

Phase III (Brazil and South Africa - mid-2020):

Trial Names: COV003 (Brazil), COV005 (South Africa) Participants: Tens of thousands

Outcomes: Efficacy confirmed across geographies

Slight reduction in effectiveness against Beta variant in South Africa

Serious adverse events were rare

3. Indian Clinical Trials Bridging Trial in India (Phase II/III):

Conducted by: Serum Institute of India (SII)

Timeframe: August to November 2020

Participants: ~1,600 adults across 17 sites in India

Design: Observer-blind, randomized, controlled

Key Findings: Immunogenicity comparable to UK data No major safety concerns

Allowed fast-track emergency use authorization (EUA) in India in January 2021

4. Safety Profile:

Common mild side effects:

Pain at injection site Fever, chills, muscle ache

Rare but reported:

VITT (Vaccine-Induced Immune Thrombotic Thrombocytopenia)

Extremely rare: ~4 cases per million

Led to age-restrictions in some countries

No deaths linked directly to the vaccine in trials

5. Global Use & Approvals:

Approved in over 100 countries

Used extensively in:

India under the name Covishield UK, EU, Africa, South America as AstraZeneca

vaccine Included in COVAX distribution for global equity

6. Variants & Booster Research:

Initial efficacy reduced against Beta and Omicron variants

Booster studies (both homologous and heterologous) showed:

Improved protection with a third dose

Good cross-variant immunity, especially when mixed with mRNA boosters

7. Timeline Summary:

Date Milestone Apr 2020 - Phase I trials begin in UK

Aug 2020 - Phase II/III trials expand globally

Nov 2020 - Indian bridging trials conclude

Jan 2021 - Emergency Use Approval in India

Mid-2021 - Mass rollout in India and COVAX nations.

Effectiveness Against Variants

Covishield (Oxford-AstraZeneca vaccine) is a viral vector-based COVID-19 vaccine developed by AstraZeneca and Oxford University, manufactured by the Serum Institute of India.

1. Mechanism of Action

Covishield uses a weakened adenovirus (from chimpanzees) to deliver genetic material coding for the SARS-CoV-2 spike protein.

- It stimulates the immune system to produce neutralizing antibodies and T-cell response, providing protection against COVID-19.

2. Efficacy in Clinical Trials

• Initial Trials: Demonstrated 70.4% average efficacy in preventing symptomatic COVID-19 infection (ranging from 62–90% based on dosing interval).

Protection from Severe Disease: Over 90% effectiveness in preventing hospitalization and death.

Works effectively across different age groups, including elderly populations.

3. Effective ness Against Variants

Alpha & Delta Variants: Provided strong protection (~67% against Delta for symptomatic infection).

Omicron Variant: Reduced protection against mild infection but maintained significant protection against severe disease and death when combined with a booster dose.

4. Real-World Studies

Multiple studies from the UK, India, and Brazil confirmed its real-world effectiveness

India (ICMR data): Two doses reduced the risk of hospitalization by 80–90% during the Delta wave.

UK data: 92% effective in preventing hospitalization from Delta after two doses.

5. Duration of Protection

Antibody levels decline over time (~6 months), but T-cell immunity persists longer.

Booster doses significantly enhance protection, particularly against newer variants.

6. Global Usage: Widely used in over 170 countries.

Approved by WHO for emergency use.

Contributed significantly to global vaccination coverage during the pandemic.

Would you like me to also create an infographic summarizing the effectiveness of Covishield for presentations or reports?

Adverse effects of vaccine

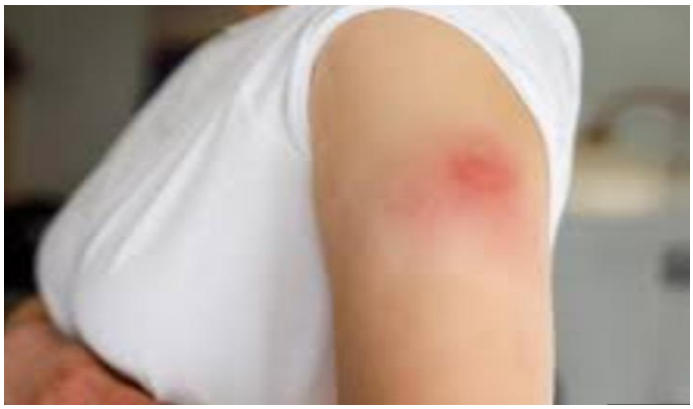
Common adverse effects:

A: Local reactions

Pain: Localised pain, tenderness, or soreness at the site of injection (usually upper arm). Typically begins within a few hours post-vaccination. Usually lasts 24-48 hours, sometimes up to3 day.

Redness and swelling: Visible redness or discoloration of the skin around the injection site. Reported in 10-20% of recipient. Typically appears within 24 hours of vaccination. Usually resolves within 2-3 days.

Swelling-Mild puffiness or localised swelling near the injection site. Occurs in up to 15% of recipients. Uaually within the first 48 hours after vaccination. Subsides within 2-4 days without treatment.



B: Systemic reaction:

Fever: Fever is one of the most frequently reported systemic side effects of covishield. It indicates that the body's immune is actively responding to the vaccine and developing protection against COVID-19.

Usually occurs within 6-24 hours after vaccination. Typically lasts 1-2days and resolves on its own without complications.

Fist dose: ~30-40% of recipients experience fever.

Second dose:Lower frequency(~15-20%).

Fever is generally low to moderate.

High or prolonged fever is rare and may require medical evaluation.

Mechanism: caused by the release of cytokines and other immune mediators as the body recognizes the vaccines spike protein. Represents a normal immune activation process.

Management- Paracetamol, adequate hydration and rest,seek medical attention if fever lasts >3 days, is very high, or accompanied by rash, severe headache, or breathing difficulty.

• **Headache :** Headache is one of the most commonly reported adverse effects following administration of the Covishield vaccine (AstraZeneca's ChAdOx1 nCoV-19). Here's a detailed explanation:

1. Occurrence and Frequency

Headache is classified as a very common side effect, affecting more than 1 in 10 vaccinated individuals.

It typically appears within a few hours to 2 days after vaccination.

2. Mechanism Immune Response: The vaccine triggers an immune reaction, causing the release of inflammatory mediators (e.g., cytokines), which can lead to headache .Fever and Inflammation: Often accompanied by fever and malaise, which may intensify headache severity .Blood Vessel Dilation: Minor transient changes in blood vessel tone due to immune activation can also contribute.

3. Characteristics of Headache Usually mild to moderate in intensity. May present as pressure-like pain, often affecting both sides of the head. Duration: Typically resolves within 1–3 days without treatment.

4. Management Over-the-counter pain relievers such as paracetamol (acetaminophen) or ibuprofen can effectively reduce discomfort .Staying hydrated and resting also helps alleviate symptoms.

5. Rare but Serious Consideration. In rare cases, severe and persistent headache (especially accompanied by blurred vision, confusion, or weakness) occurring 4–30 days after vaccination could indicate thrombosis with thrombocytopenia syndrome (TTS), a very rare adverse event .Immediate medical evaluation is recommended if these symptoms occur .References World Health Organization (WHO). COVID-19 subunit, viral vector vaccines safety update .European Medicines Agency (EMA) – Safety of

Vaxzevria (AstraZeneca COVID-19 vaccine).Would you like me to also create a table summarizing Covishield's common neurological adverse effects (headache, dizziness, etc.).

Fatigue : Fatigue is one of the commonly reported adverse effects after receiving the Covishield vaccine, which is the Indian-manufactured version of the Oxford-AstraZeneca COVID-19 vaccine (ChAdOx1 nCoV-19).

Fatigue after vaccination is typically a sign that the body is responding to the vaccine as it is supposed to. Here's a breakdown of the underlying mechanism:1. Immune System Activation Covishield introduces a harmless version of a virus (a chimpanzee adenovirus vector) that carries the genetic instructions for making the SARS-CoV-2 spike protein.Your immune system recognizes this spike protein as foreign and starts producing antibodies and training immune cells. This process releases inflammatory mediators (like cytokines), which are part of the immune response.2. Systemic Inflammatory Response The release of cytokines and other immune substances can affect the central nervous system, leading to symptoms like fatigue, headache, and muscle aches. This is similar to how your body reacts when fighting an actual infection.

Muscle pain (myalgia) is one of the commonly reported adverse effects of the Covishield vaccine (ChAdOx1 nCoV-19). Here's a detailed explanation:

1. Occurrence and Frequency Muscle pain occurs in 20–40% of individuals, typically appearing within 24 hours of vaccination. It is more common after the first dose but may also occur after subsequent doses.

2. Mechanism Immune Response: Activation of the immune system releases inflammatory mediators (cytokines, prostaglandins) that can cause muscle soreness. Local Reaction: Minor irritation and inflammation at the injection site may spread to surrounding muscles. Systemic Effect: Often accompanies other systemic symptoms like fever and fatigue as part of the body's immune reaction.

3. Characteristics of Muscle Pain Usually mild to moderate and generalized, affecting arms, shoulders, or other muscle groups. May feel like aching, tenderness, or stiffness, similar to post-exercise soreness .Typically resolves within 1–3 days without complications.

4. Management Pain Relievers: Paracetamol or NSAIDs (e.g., ibuprofen) can reduce muscle soreness .Rest & Hydration: Adequate rest and fluid intake aid recovery .Warm Compress: Applying a warm cloth to sore muscles may provide relief.

Joint pain : Joint pain (arthralgia) is another frequently reported musculoskeletal adverse effect of the Covishield vaccine (ChAdOx1 nCoV-19). Here's a detailed explanation:

1. Occurrence and Frequency Joint pain occurs in 10–20% of vaccinated individuals, based on clinical trial and post-marketing data. Usually appears within 24–48 hours after vaccination and is more common after the first dose.

2. Mechanism Immune Activation: The body's immune response to the vaccine produces inflammatory mediators (cytokines), which may temporarily affect joints .Systemic Inflammation: Mild, transient inflammation can lead to discomfort or stiffness in joints .Post-vaccine Reaction: Often occurs alongside other systemic reactions like fever, fatigue, and muscle pain.

3. Characteristics of Joint Pain Typically mild to moderate in intensity. May involve knees, elbows, wrists, or smaller joints and can be symmetrical or isolated. Feels like aching or stiffness, similar to viral flu-related joint pain. Usually resolves spontaneously within 1–3 days.

4. Management Analgesics: Paracetamol or NSAIDs (ibuprofen) can alleviate pain and inflammation. Rest: Avoiding strenuous activity during the first 24–48 hours post-vaccination. Hydration: Helps reduce systemic inflammatory effects.

5. Rare but Serious Concerns Persistent or severe joint pain lasting more than a week is uncommon. If accompanied by swelling, redness, or reduced mobility, medical assessment is recommended to rule out rare immune-mediated conditions (e.g., reactive arthritis).

Mild nausea is a less common but documented adverse effect following administration of the Covishield vaccine (ChAdOx1 nCoV-19). Here's a detailed explanation:

1. Occurrence and Frequency Reported in 5–10% of individuals during clinical trials and post-marketing surveillance. Often occurs within 24 hours after vaccination and usually subsides quickly.

2. Mechanism Immune System Activation: The body's immune response can temporarily affect the gastrointestinal (GI) system, leading to mild nausea. Cytokine Release: Inflammatory mediators released during immune activation may impact the stomach lining or vagal nerve signaling, causing discomfort. Associated Symptoms: May occur alongside fever, headache, or fatigue as part of a systemic reaction.).

3. Characteristics of Nausea Usually mild and transient, without vomiting. May feel like queasiness or stomach unease, sometimes with reduced appetite. Typically resolves within 1–2 days without treatment.

4. Management Hydration: Drinking clear fluids (water, oral rehydration solutions).Light Meals: Eating small, bland meals (e.g., crackers, toast).Anti-nausea Medication: Over-the-counter remedies (like domperidone) can be used under medical advice if symptoms are bothersome. Rest: Helps the body recover faster.

5. Rare but Serious Concerns Persistent nausea accompanied by vomiting, abdominal pain, or jaundice is rare and requires medical evaluation to rule out allergic or immune-mediated reactions.

2. Uncommon to rare adverse effect :

Hypersensitivity : reactions to the Covishield vaccine (ChAdOx1 nCoV-19, Oxford-AstraZeneca) are immune-mediated adverse effects that occur when the body's immune system overreacts to one or more vaccine components.

1. Mechanism of Hypersensitivity.

a.Vaccine composition and immune activation Covishield contains: Recombinant chimpanzee adenovirus vector (carrying the SARS-CoV-2 spike protein gene)Excipients: polysorbate 80, ethanol, sucrose, amino acids, EDTA, etc .After injection, the adenovirus vector enters cells → expresses spike protein → stimulates the immune system to produce antibodies and T-cell responses.

b. Hypersensitivity trigger In certain individuals, immune cells recognize some excipients (e.g., polysorbate 80) or spike protein antigens as harmful, leading to Type I or Type IV hypersensitivity reactions: Type I (Immediate): IgE antibodies bind to allergens → mast cells release histamine → causes allergic symptoms (rash, urticaria, anaphylaxis).Type IV (Delayed): T-cell–mediated reaction occurring hours to days later → causes localized skin reactions or contact dermatitis.

2. Clinical Manifestations

Mild hypersensitivity: Rash, itching, redness at injection site Swelling or mild hives

Severe (rare): Anaphylaxis (difficulty breathing, drop in blood pressure, swelling of face/throat) Systemic urticaria Serum sickness–like reaction.

3. Role of Polysorbate 80Polysorbate 80 (a stabilizer in Covishield) is structurally similar to polyethylene glycol (PEG) used in mRNA vaccines. Individuals allergic to PEG may cross-react with polysorbate 80, increasing risk of hypersensitivity. This is one of the primary suspects in vaccine-associated allergic responses.

4. Incidence Hypersensitivity reactions to Covishield are very rare. UK's Medicines and Healthcare products Regulatory Agency (MHRA) reported : Anaphylaxis rate: ~4–5 cases per million doses Most reactions are mild and resolve with antihistamines.

5. Management and Prevention Pre-vaccination screening: Individuals with known PEG or polysorbate allergies should consult healthcare providers. Observation period: Recipients are monitored for 30 minutes post-vaccination for early detection. Treatment: Immediate administration of epinephrine, antihistamines, corticosteroids in case of severe reactions.

4. **Lymphadenopathy (Swelling of lymph nods) :** is a recognized but uncommon adverse effect of the Covishield (ChAdOx1 nCoV-19) vaccine.

1. Abnormal enlargement of lymph nodes, usually due to immune system activation. Typical presentation: Swelling in lymph nodes (commonly in the armpit or neck, near the injection site) May be tender or painless Usually self-limited and resolves without treatment.

2. Mechanism in Covishield Vaccination

Covishield uses a non-replicating adenoviral vector carrying the SARS-CoV-2 spike protein gene. After injection: a. The immune system recognizes the spike protein as an antigen. b. Lymph nodes become activated as they produce:B cells and T cells to fight the perceived infection. Antibodies against the spike protein.

3.Clinical Features

Onset: Typically appears within 2–7 days post-vaccination. Location : Ipsilateral (same side as injection site) axillary lymph nodes (most common) Cervical or supraclavicular nodes (less common) Symptoms : Localized swelling Mild pain or tenderness Occasionally redness or warmth over the area Duration: Usually resolves within 7–14 days, rarely longer.

4. Incidence

Reported as uncommon (≤1% of recipients) in Covishield post-marketing surveillance. Lower incidence compared to mRNA vaccines (Pfizer, Modern), but still documented in: MHRA Yellow Card reports Indian AEFI data (as part of local immune reactions).

5. Differentiating from Serious Conditions

Benign lymphadenopathy: Small, mobile, resolves quickly. Red flags: Persistent, very large, hard, or accompanied by fever or systemic symptoms → may require medical evaluation to rule out infection or other causes.

6. Management

Typically no treatment needed. Supportive care: Cold compress Analgesics (paracetamol, NSAIDs) for discomfort Patients are advised to not confuse it with cancerous lymph node swelling; it's a temporary immune response.

Dizziness : is a recognized but generally mild and transient adverse effect of the Covishield (ChAdOx1 nCoV-19) vaccine**.**

1. Mechanism of Dizziness After Covishield

a. Immune and inflammatory response After vaccination, the immune system mounts a response against the spike protein. This can cause fever, fatigue, low blood pressure, and dehydration, all of which may contribute to dizziness.

b. Vasovagal reaction

Some individuals experience vasovagal syncope (fainting episode) due to: Needle anxiety or pain during injection Sudden drop in heart rate and blood pressure Leads to brief dizziness or fainting, usually resolving within minutes.

c. Neurological effects In rare cases, dizziness may be associated with neurological adverse events (e.g., Guillain-Barre syndrome or thrombosis-related complications), but these are extremely uncommon.

2. Clinical Presentation

Timing: Usually occurs within minutes to hours post-vaccination.

Symptoms: Lightheadedness, Feeling of imbalance, Vertigo (rare)

May be accompanied by nausea or sweating

Duration: Most cases resolve within a few hours to 1–2 days.

3. Incidence

Reported as a common side effect in : MHRA (UK) Yellow Card data WHO safety reports Occurs in approximately 1–10% of recipients, usually mild and non-serious.

4. Management

Observation: Vaccine centers monitor recipients for 15–30 minutes post-dose.

Supportive care: Sit or lie down if dizzy Hydration and rest Slow position changes to avoid orthostatic hypotension Medical attention: Seek help if dizziness persists, worsens, or is accompanied by: Severe headache Vision changes Limb weakness (to rule out rare clotting events).

5. Prognosis: Typically benign and self-limited.

Indicates normal immune response or mild stress reaction. Does not usually predict serious neurological complications.

Abdominal pain is reported as a less common adverse effect of the Covishield (Oxford-AstraZeneca) COVID-19 vaccine.

1. Occurrence

Abdominal pain is generally mild to moderate and tends to appear within 1–3 days after vaccination .It occurs less frequently compared to systemic effects like fever, fatigue, or headache.

2. Possible Mechanisms

Immune response: The vaccine triggers the body's immune system to produce antibodies, which may cause temporary inflammation affecting the gastrointestinal tract .Mild allergic reactions: Some people may have a minor allergic reaction leading to stomach discomfort .Fever or systemic inflammation: Fever and body aches after vaccination can also indirectly cause abdominal pain .Rare events: In very rare cases, abdominal pain can be an early sign of thrombosis with thrombocytopenia syndrome (TTS), a serious but rare clotting disorder.

3. Associated Symptoms

Nausea, Mild vomiting ,Loss of appetite, Diarrhea (in some cases)

4. Duration and Management

Typically resolves within 24–48 hours without treatment .Drinking fluids, resting, and using mild analgesics (if prescribed) can help .If pain is severe, persistent, or accompanied by symptoms like swelling of the abdomen, shortness of breath, severe headache, or vision changes, immediate medical attention is required to rule out serious reactions like TTS.

5. Reported Frequency

According to pharmacovigilance data and post-marketing surveillance, abdominal pain is reported in less than 1 in 100 vaccine recipients, making it an uncommon side effect.

Hyperhidrosis (Excessive sweating) refers to abnormally increased sweating not necessarily related to heat or exercise. While not among the most commonly reported side effects of the Covishield vaccine, some recipients have experienced episodes of excessive sweating post-vaccination.

2. Possible Mechanisms

Immune system activation: The vaccine stimulates the body's immune response, which can temporarily activate the sympathetic nervous system, leading to increased sweat production. Fever-related sweating: Post-vaccination fever or elevated body temperature often triggers sweating as a cooling mechanism. Stress or anxiety response: Anticipation or stress surrounding vaccination can also activate sweat glands. Autonomic imbalance: Rarely, immune responses may cause temporary dysregulation of autonomic nervous control of sweat glands.

3. Timing and Duration

Typically appears within 24 hours after vaccination. Usually resolves within 1–3 days without treatment.

4. Associated Symptoms

Fever and chills, Fatigue or malaise, Mild tachycardia (fast heart beat), Headache or body aches

5. Management

Maintain hydration and wear breathable clothing. Over-the-counter antipyretics (like paracetamol) can help if sweating is linked to fever. Persistent or excessive sweating lasting more than 3–4 days should be reported to a healthcare provider.

6. Frequency

Classified as rare or uncommon (less than 1% of recipients) in pharmacovigilance reports. Often self-limiting and not associated with serious complications.

3. Rare but serious adverse effects :

Thrombosis with thrombocytopenia syndrome (TTS) :

Thrombosis with Thrombocytopenia Syndrome (TTS) is a rare but serious condition involving : Thrombosis: blood clots forming in unusual sites (e.g. cerebral venous sinuses, abdominal veins),Thrombocytopenia : low platelet count, often with anti-PF4 antibodies This immune-mediated reaction resembles heparin-induced thrombocytopenia but occurs without exposure to heparin.

WHO Expert Review & Risk Assessment

In a 19 March 2021 meeting, WHO's Global Advisory Committee on Vaccine Safety (GACVS) reviewed data across Europe, UK, India and WHO's Vigi Base. They concluded the overall benefits of Covishield far outweigh the very rare risk of TTS .A follow-up statement on 16 April 2021 described TTS as "very rare", estimating about 4 cases per million doses in the UK and 1 per 100 000 in the EU after the first dose. They highlighted the importance of surveillance and caution around the 4–20-day window post-vaccination.

Time Frame & Clinical Features

Onset typically occurs 4–20 days after vaccination, often after the first dose.

Symptoms may include: Severe persistent headache, Abdominal pain, Shortness of breath, Leg swelling or chest pain, Neurological signs (e.g. blurred vision),Unusual bruising or bleeding.

Mechanism & Diagnosis

Thought to be caused by the production of anti-platelet factor 4 (PF4) antibodies, triggering clot formation and platelet consumption without heparin exposure .Diagnosis involves lab tests showing low platelets, elevated D-dimer, and anti-PF4 antibodies, along with imaging studies confirming thrombosis.

Treatment

WHO recommends avoiding heparin or related anticoagulants due to potential exacerbation. Effective treatments include: Intravenous immunoglobulin (IVIG). Non-heparin anticoagulants (e.g. direct oral Xa – inhibitor fonAdaparinux)

Aspect	Details
Frequency	1 in 250,000 to 1 in 1000000 doses (varies by region)
Onset window	4-20 days post-vaccination
Affected sites	Brain()CVST), abdorr (splanchnic veins), others unusual thromboses
Diagnostic markers	Low platelets, high D-dimer, anti-PF4 antibodies
Treatment	IVIG + non-heparin anticoagulants; avoi heparin

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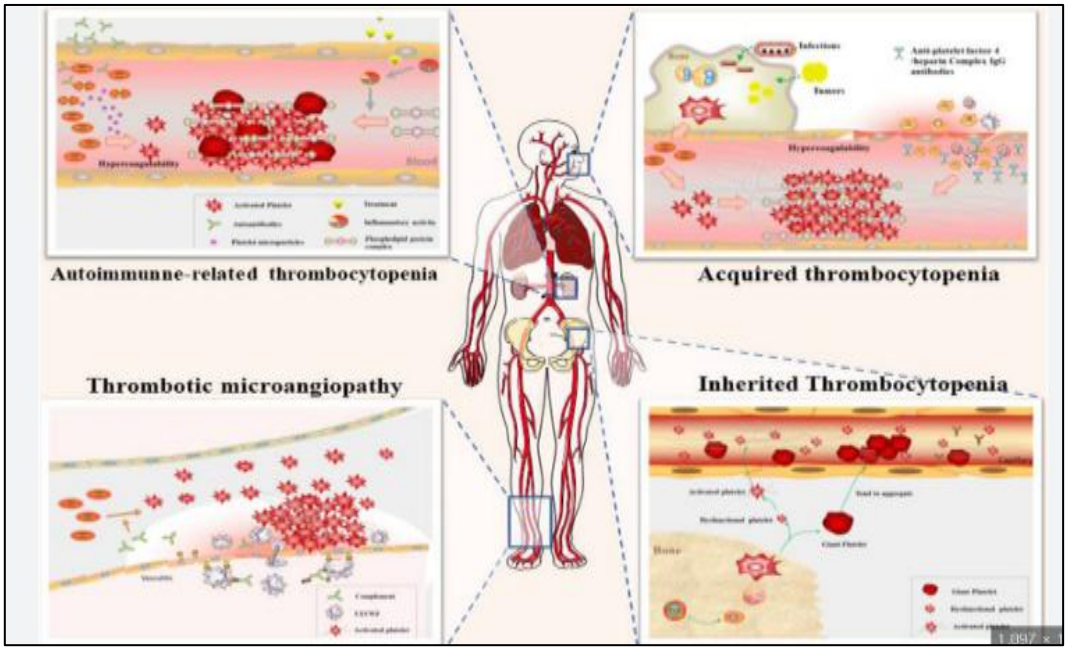

Mechanism: How Thrombocytopenia Leads to Thrombosis:

1. Abnormal Immune Response: In rare cases (e.g., after COVID-19 adenovirus-based vaccines), the immune system mistakenly produces antibodies against platelet factor 4 (PF4).These antibodies bind to PF4 and form immune complexes on platelet surfaces.

2. Platelet Activation The immune complexes activate platelets instead of destroying them directly .Activated platelets release pro-coagulant substances, which accelerate clot formation.

3. Massive Clot Formation Activated platelets aggregate and cause abnormal clotting in veins or arteries (thrombosis).Common sites: cerebral venous sinuses, pulmonary veins, deep veins of the legs, and splanchnic veins.

4. Consumption of Platelets As clots form excessively, platelets are consumed rapidly. This lowers the overall platelet count, leading to thrombocytopenia.

5. Paradoxical Condition Normally, low platelets → bleeding .In VITT/HIT, autoimmune activation causes both clotting and low platelets simultaneously. This is why patients may have life-threatening clots despite having very few platelets.

Clinical Implications:

Patients can develop stroke, pulmonary embolism, or deep vein thrombosis. Symptoms include severe headache, abdominal pain, chest pain, or leg swelling within 5–30 days post-vaccination. Treatment involves IVIG and non-heparin anticoagulants to stop antibody-mediated platelet activation.

Guillain – Barre Syndrome (GBS):

Guillain- Barré Syndrome (GBS) is a rare but reported adverse effect associated with certain COVID-19 vaccines, including Covishield (Oxford-AstraZeneca). It is a neurological disorder where the body's immune system mistakenly attacks peripheral nerves, leading to muscle weakness and, in severe cases, paralysis.

Overview of GBS

Type: Autoimmune neuropathy

Onset: Usually within days to weeks after vaccination or infection

Incidence: Very rare (a few cases per million doses administered)

Mechanism: How Covishield May Trigger GBS

1. Immune Activation: The vaccine stimulates the immune system to produce antibodies against SARS-CoV-2.

2. Molecular Mimicry: In some individuals, these antibodies may cross-react with nerve cell components (e.g., myelin or axonal structures).

3. Nerve Damage: This immune attack damages the myelin sheath or nerve fibers, impairing nerve signaling.

4. Inflammation: Leads to progressive weakness and sensory disturbances.

Symptoms of GBS:

Tingling or numbness in feet and hands

Progressive muscle weakness (starting in legs, spreading upward) Difficulty walking or climbing stairs

Facial weakness or difficulty swallowing (in severe cases)

Breathing difficulties if respiratory muscles are affected

Diagnosis

Neurological exam (muscle strength, reflexes)

Electromyography (EMG): Detects nerve conduction abnormalities

Lumbar puncture: Increased protein levels in cerebrospinal fluid

Treatment ;

Hospitalization: Early monitoring is essential

Intravenous immunoglobulin (IVIG) or Plasmapheresis: Removes harmful antibodies

Supportive care: Physical therapy and respiratory support if needed.

Regulatory and WHO Findings

WHO and other regulatory agencies have noted rare reports of GBS following Covishield vaccination.

The condition remains very uncommon, and benefits of vaccination outweigh the risk.

Ongoing post-marketing surveillance monitors such neurological side effects globally.

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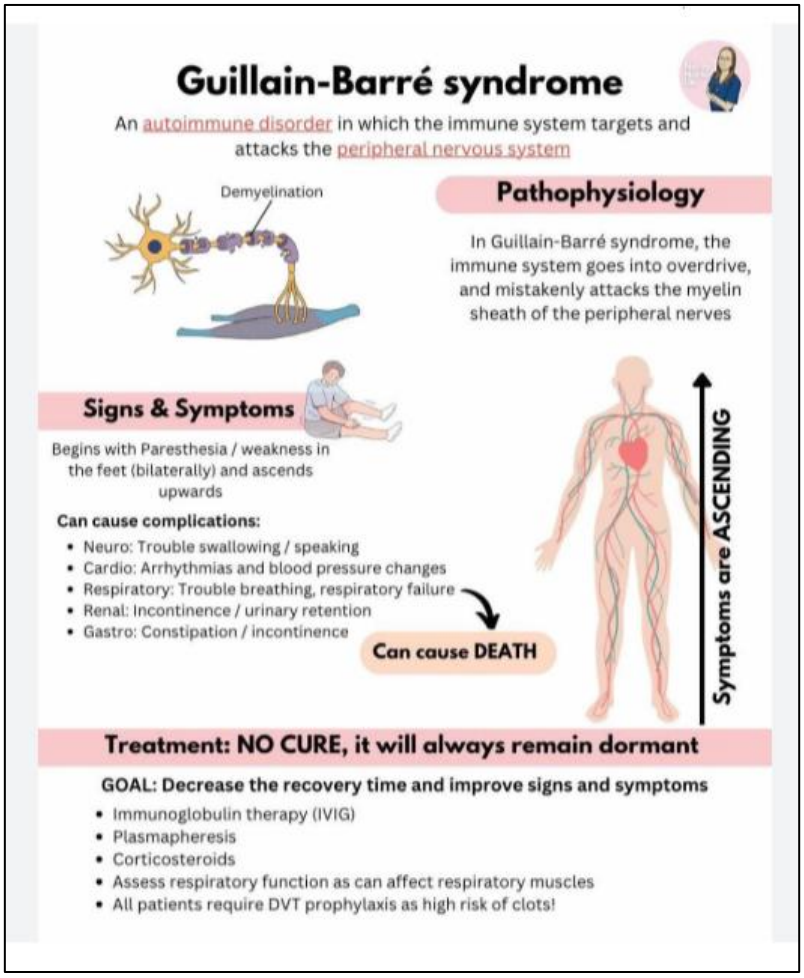

Capillary Leak Syndrome : (CLS) is a rare but serious adverse effect that has been reported in some individuals after receiving the Covishield (ChAdOx1 nCoV-19) COVID-19 vaccine.

CLS is a medical condition characterized by sudden and severe leakage of plasma (fluid and proteins) from small blood vessels (capillaries) into surrounding tissues, leading to :

Hypotension (low blood pressure),Edema (swelling, mainly in limbs), Hemoconcentration (increased blood thickness), Hypoalbuminemia (low blood protein levels).

Mechanism (Possible Cause):

The exact mechanism of CLS after Covishield is not fully understood, but it is believed to involve : Immune dysregulation: The vaccine may trigger an abnormal immune response in susceptible individuals. Endothelial dysfunction: Inflammatory mediators can damage the inner lining of capillaries, causing them to leak. Pre-existing susceptibility: Individuals with a history of CLS are at higher risk of recurrence after vaccination.

Reported Cases & Incidence:

CLS has been reported extremely rarely post-vaccination (less than 1 case per million doses).Regulatory bodies like the European Medicines Agency (EMA) and WHO have listed CLS as a possible side effect of Covishield.

Symptoms to Watch For Rapid onset of :

Swelling in arms or legs, Sudden weight gain ,Low blood pressure (dizziness, fainting), Nausea or fatigue. Severe cases can lead to shock, organ failure, or death if untreated.

Anaphylaxis is a rare but potentially life-threatening adverse effect reported after administration of the Covishield (ChAdOx1 nCoV-19) COVID-19 vaccine.

A severe, rapid-onset allergic reaction triggered by exposure to a specific allergen.It can involve multiple organ systems (skin, respiratory, cardiovascular, gastrointestinal).

Mechanism (Cause):

Hypersensitivity reaction primarily mediated by IgE antibodies. After vaccination, immune cells may release histamine and other mediators, causing systemic allergic symptoms .

Possible triggers:

Polysorbate 80, an excipient in Covishield that can cross-react with polyethylene glycol (PEG).Pre-existing severe allergies to vaccine components.

Frequency & Regulatory Findings :

Extremely rare (estimated ~1–2 cases per million doses).Reported globally and listed by WHO, EMA, and MHRA as a recognized risk.

Symptoms (usually within minutes to hours post-vaccination)

Skin: Rash, itching, hives, Respiratory: Swelling of lips/tongue/throat, difficulty breathing, wheezing, Cardiovascular: Drop in blood pressure, dizziness, fainting, Gastrointestinal: Nausea, vomiting, abdominal pain. Severe cases: Anaphylactic shock → requires emergency intervention

Emergency Management:

Immediate treatment: Intramuscular epinephrine (adrenaline)Supportive care with oxygen, antihistamines, corticosteroids Patients monitored for ≥30 minutes after vaccination.

Stroke is a rare but serious adverse effect that has been observed following vaccination with Covishield (ChAdOx1 nCoV-19). Most reported cases are linked to a specific condition known as Thrombosis with Thrombocytopenia Syndrome (TTS).

A stroke occurs when the blood supply to part of the brain is interrupted or reduced, leading to brain cell damage.

Can be :Ischemic stroke: Caused by a blood clot blocking a vessel

.Hemorrhagic stroke: Caused by bleeding in the brain.

Association with Covishield :

Post-vaccination, some individuals have developed unusual blood clots, often in combination with low platelet counts .This syndrome is termed Thrombosis with Thrombocytopenia Syndrome (TTS) or Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT).

Clots may occur in:

Cerebral venous sinuses → leading to Cerebral Venous Sinus Thrombosis (CVST), which can cause a stroke .Arteries → causing ischemic stroke.

Mechanism:

Immune-mediated reaction: Vaccine may rarely trigger antibodies against platelet factor 4 (PF4).These antibodies activate platelets, leading to clot formation despite low platelet counts .The mechanism is similar to heparin-induced thrombocytopenia (HIT).

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Incidence

Extremely rare: Estimated 4–6 cases per million doses. Most cases occur within 4–28 days after vaccination .Higher risk observed in younger adults (<60 years), especially women, but overall risk remains very low compared to benefits of vaccination.

Symptoms (seek urgent care if within 3–4 weeks post-vaccination):

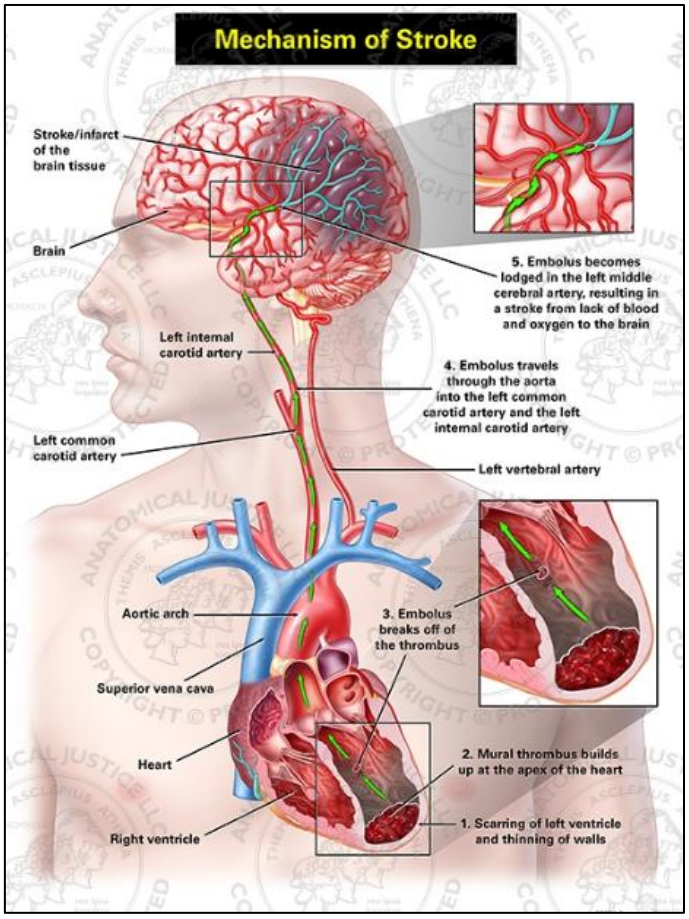
Severe or persistent headache ,Blurred vision Seizures ,Weakness or numbness on one side of the body ,Difficulty speaking ,Shortness of breath or chest pain.

Treatment :

Immediate hospital care with: Non-heparin anticoagulants Intravenous immunoglobulins (IVIG) Supportive management for stroke Early diagnosis improves recovery chances.---

✅ Safety Guidance :

Regulatory agencies (WHO, EMA, MHRA) have confirmed stroke risk is very rare and vaccine benefits outweigh risks. Ongoing post-marketing surveillance continues to monitor and manage these cases.



Strokes occur when blood supply to the brain is interrupted, leading to brain cell damage due to oxygen and nutrient deprivation. The two main types are ischemic (caused by a blockage) and hemorrhagic (caused by bleeding). Ischemic strokes are further classified into thrombotic (clot forms locally), embolic (clot travels from elsewhere), and hypoperfusion (general reduction in blood flow). Hemorrhagic strokes involve bleeding within the brain, either from a ruptured blood vessel or from blood leaking into brain tissue.

Ischemic Stroke Mechanisms:

A blood clot (thrombus) forms within a brain artery, often at the site of a narrowed artery due to atherosclerosis (plaque buildup). Embolism :A clot or other material (like a blood clot, air bubble, or fat globule) forms elsewhere in the body and travels to the brain, blocking a smaller artery. Hypoperfusion: A general decrease in blood flow to the brain, possibly due to heart problems or severe blood loss, can lead to tissue damage, particularly in smaller vessels.

Hemorrhagic Stroke

Mechanisms:

Intracerebral Hemorrhage: Bleeding directly into the brain tissue, often due to a ruptured blood vessel weakened by high blood pressure or other factors. Subarachnoid Hemorrhage: Bleeding into the space between the brain and the skull, often caused by a ruptured aneurysm (weakened blood vessel).

Cellular Mechanisms: Excitotoxicity: Deprived of oxygen, brain cells release excessive amounts of excitatory neurotransmitters, which can damage nearby cells. Edema: Swelling of brain cells due to fluid accumulation, further compressing blood vessels and worsening damage. Inflammation: The body's immune response to injury can contribute to further damage and cell death. Cell Death Depending on the severity and duration of the oxygen deprivation, brain cells may die through various mechanisms, including apoptosis (programmed cell death) and necrosis (uncontrolled cell death).

Hypertension (high blood pressure) has been reported as a less common but notable adverse effect following administration of the Covishield (Oxford-AstraZeneca) COVID-19 vaccine.

1. Occurrence

Clinical trial data and post-marketing surveillance indicate that mild to moderate increases in blood pressure may occur in some individuals within hours to a few days after vaccination. Most cases are transient and resolve spontaneously or with routine antihypertensive therapy .Incidence is lower than common side effects (e.g., fever, injection site pain), but it has been observed in susceptible populations such as those with pre-existing hypertension.

2. Possible Mechanisms

Stress Response: Vaccination can trigger a transient stress response leading to elevated blood pressure. Immune Activation: The immune response and release of cytokines post-vaccination may temporarily increase vascular resistance. Corticosteroid Surge: Some studies suggest temporary sympathetic nervous system activation and cortisol release. Underlying Conditions: Patients with undiagnosed or poorly controlled hypertension may experience noticeable BP spikes.

3. Clinical Presentation

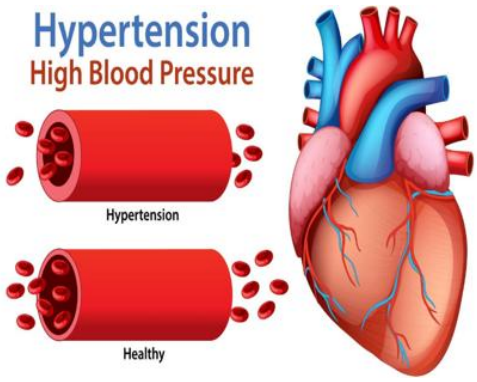
Patients may report headache, dizziness, palpitations, or flushing shortly after receiving Covishield .Blood pressure readings can show moderate to severe elevation, sometimes requiring monitoring.

4. Management :

Monitoring blood pressure before and after vaccination, particularly in hypertensive patients.Use of antihypertensive medication if needed.Most cases do not progress to hypertensive crisis and subside within a few days.

5. Regulatory Observations :

The European Medicines Agency (EMA) and World Health Organization (WHO) pharmacovigilance data mention hypertension as a reported adverse event but not as a major safety signal .Reported cases are relatively rare compared to the large number of administered doses, suggesting no strong causal relationship but a potential transient reaction.



Conclusion :

Post – marketing surveillance has been critical in continuously assessing the safety and efficacy of covishield in real – world settings. The data confirm that covishield maintains a strong protective effect against COVID-19 , significantly reducing severe disease and mortality . While rare adverse event such as TTS and Guillain-Barre syndrome have been identified, their incidence remains extremely low compared to the benefits of vaccination. Ongoing pharmacovigilance, prompt adverse event reporting, and transplant risk communication are essential to maintain public trust and guide future vaccination policies. Overall, covishield remains a safe and effective component of global COVID-19 immunization strategies.

Result :

Post-marketing surveillance of covishield has included dada from national pharmacovigilance systems, WHO vigibase report, and published observational studies covering over 1 billion administration dosese globally. The majority of adverse events reported were mild to moderate, including injection site pain (60-70%),fever (40-50%), fatigue (30-40%) and headache (20-30%).serious adverse events were rare, with thrombosis with thrombocytopenia syndrome (TTS) occuring in approximately 1 per 100,000 doses, Guillain-barre syndrome in 1-2 per million doses, and anaphylaxis in <0.01% of recipients. Real-world effectiveness studies showed 70-90% protection against severe COVID-19 and hospitalization. No unexpected safety concerns emerged beyond those identified in clinical trials, confirming a favorable benefit-risk profile.

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