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# Study Of Adverse Event Following Immunization Against SARS-CoV-2

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**ABSTRACT**
This study investigates the safety profile of COVID-19 vaccines administered under emergency use authorization, focusing on the occurrence and management of adverse events following immunization (AEFIs). Results indicate that the majority of AEFIs were mild to moderate, consistent with findings from phase III clinical trials. Notably, adverse events were more frequent after the first dose, highlighting the importance of robust post-vaccination monitoring. Gender-based differences revealed a higher prevalence of AEFIs in males, suggesting a potential link to sex-specific immune responses influenced by hormones such as testosterone. Comparative analysis showed a slightly higher incidence of AEFIs with Covishield, an adenoviral vector vaccine, compared to Covaxin, an inactivated virus vaccine. The use of over-the-counter medications like Dolo 625 mg and PCM 500 mg was effective in managing symptoms, though a significant portion of participants did not seek treatment. These findings underscore the need for public health campaigns to raise awareness about AEFIs and their management. While limited by its observational design and self-reported data, this study emphasizes the importance of future research, including long-term follow-up and studies involving diverse populations, to further understand vaccine safety and efficacy.

**Keywords:** COVID-19 Vaccines, Adverse Events Following Immunization (AEFIs), Vaccine Safety, Gender-Based Differences, Covishield, Covaxin, Post-Vaccination Monitoring, Reactogenicity, Public Health Awareness, Emergency Use Authorization, Immune Response.

## INTRODUCTION

The global health crisis caused by the coronavirus disease 2019 (COVID-19) outbreak necessitated a swift and comprehensive response, resulting in the accelerated development and distribution of vaccines. The pandemic began in Wuhan City, Hubei Province, China, where, on December 31, 2019, the China Health Authority informed the World Health Organization (WHO) about cases of pneumonia of unknown origin. The pathogen, initially named 2019-nCoV and later classified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) y the Coronavirus Study Group, was declared a Public Health Emergency of International Concern (PHEIC) by the WHO on January 30, 20201,2.SARS-CoV-2 is a positive-sense single-stranded RNA (+ssRNA) virus belonging to the Beta-coronavirus genus of the Coronaviridae family. It shares its lineage with other highly pathogenic viruses, including SARS-CoV and Middle Eastern respiratory syndrome coronavirus (MERS-CoV)3. The virus's rapid global spread led to significant morbidity and mortality, particularly among older adults and individuals with underlying health conditions4. Its ability to exploit host cell entry receptors, such as angiotensin-converting enzyme 2 (ACE2), highlighted the urgency of implementing public health interventions5,6

Table 1 explains various pathophysiological pathways by which SARS-CoV-2 exploits a person's immunity and

the clinical manifestations caused by such pathways.27

**Table 1. Pathophysiology and clinical manifestations of SARS-CoV-2**

| Category | Mechanism | Pathophysiology | Clinical Manifestations |
|---|---|---|---|
| **Immediate Hypersensitivity** | IgE-mediated degranulation of mast cells and basophils due to components like polyethylene glycol (PEG). | Allergens bind to IgE on mast cells, leading to histamine release, vasodilation, smooth muscle contraction, and increased vascular permeability. | Urticaria, angioedema, bronchospasm, hypotension, anaphylaxis. |
| **Autoimmune Activation** | Molecular mimicry and cross-reactivity between vaccine antigens and host tissues. | **Guillain-Barré Syndrome (GBS):** Autoreactive T cells and macrophages attack peripheral myelin or axons. **Immune Thrombocytopenia (ITP):** Autoantibodies target platelets, causing splenic destruction. | Progressive muscle weakness, thrombocytopenia, easy bruising, bleeding complications. |
| **Inflammatory Response** | Excessive activation of innate and adaptive immune pathways with cytokine overproduction. | Overproduction of IL-6, TNF-α, and interferons leads to systemic inflammation. Rarely, a cytokine storm may result in multi-organ dysfunction. | Fever, myalgia, fatigue, systemic inflammatory symptoms. |
| **Myocarditis & Pericarditis** | Combination of molecular mimicry and immune cell infiltration in cardiac tissue. | T cells and macrophages infiltrate the myocardium, causing inflammation, injury to cardiac myocytes, and release of cardiac biomarkers (e.g., troponin). | Chest pain, palpitations, dyspnea, elevated troponin levels. |
| **Thromboembolic Events (VITT)** | Formation of anti-platelet factor 4 (PF4) antibodies triggers platelet activation and | Immune complexes form between anti-PF4 antibodies and platelets, activating coagulation pathways and leading to thrombosis in unusual | Cerebral venous thrombosis, pulmonary embolism, low platelet count. |

| | | | |
|---|---|---|---|
| | thrombus formation. | sites like cerebral veins and pulmonary vasculature. | |
| **Neurological Complications** | Neuroinflammation and immune-mediated disruption of the blood-brain barrier. | Pro-inflammatory cytokines and immune cells infiltrate the central nervous system, leading to neuronal inflammation. | Headache, Bell's palsy, encephalomyelitis, or other focal neurological symptoms. |
| **Exacerbation of Pre-existing Conditions** | Individuals with autoimmune diseases or genetic predispositions experience heightened immune reactions. | Dysregulated immune checkpoints, toll-like receptor (TLR) overactivation, or complement pathway dysfunction amplify inflammation and autoimmune responses. | Flare-ups of autoimmune conditions or severe inflammatory responses. |

The table below enlists the various variants of concern (VOC) of SARS-CoV-2.29

**Table 2. Variants of SARS-CoV-2.**

| Variant | Pango Lineage | WHO Label | Origin | Key characteristics | Date identified |
|---|---|---|---|---|---|
| Alpha | B.1.1.7 | Alpha | United Kingdom | Increased transmissibility (50% more) | September 2020 |
| Beta | B.1.351 | Beta | South Africa | Immune evasion; reduced vaccine efficacy | May 2020 |
| Gamma | P.1 | Gamma | Brazil | Increased transmissibility; potential for reinfection | November 2020 |
| Delta | B.1.617.2 | Delta | India | Highly transmissible (60% more than Alpha) | October 2020 |
| Omicron | B.1.1.529 | Omicron | South Africa | Very high transmissibility; significant immune escape | November 2021 |

Efforts to mitigate the pandemic's impact resulted in the development of over 48 vaccine candidates undergoing clinical trials by 20207. Vaccination programs have played a crucial role in reducing disease severity, preventing hospitalizations, and curbing virus transmission. However, COVID-19 vaccines have been associated with adverse events following immunization (AEFI), ranging from mild and self-limiting reactions to rare but severe complications such as myocarditis, Guillain-Barré syndrome, and anaphylaxis8,9.

The widespread reliance on emergency use authorizations (EUA) for vaccine deployment has heightened the need for robust pharmacovigilance systems and transparent reporting 10. Post-marketing surveillance systems, such as the Vaccine Adverse Event Reporting System (VAERS) in the United States, have been instrumental in identifying rare but significant adverse effects 11. The table below enlists few vaccines which were developed and administered in population of various sects to counter the virus transmissibility and infection.28

**Table 3. List of vaccines used for SARS-CoV-2**

| Vaccine Name | Type of Vaccine | Common Adverse Events | Severe Adverse Events |
|---|---|---|---|
| Pfizer-BioNTech (BNT162b2) | mRNA | Injection site pain, fever, fatigue | Myocarditis, anaphylaxis, Bell's palsy |
| Moderna (mRNA-1273) | mRNA | Chills, headache, localized swelling | Myocarditis, thrombosis |
| AstraZeneca (ChAdOx1-S) | Adenoviral vector | Fever, myalgia, nausea | Vaccine-induced immune thrombotic thrombocytopenia (VITT), Guillain-Barré Syndrome (GBS) |
| Johnson & Johnson (Ad26.COV2.S) | Adenoviral vector | Pain at injection site, fatigue, headache | Thrombosis with thrombocytopenia syndrome (TTS), rare neurological events |
| Sinovac (CoronaVac) | Inactivated virus | Pain at injection site, low-grade fever | Rare hypersensitivity reactions |
| Covaxin (BBV152) | Inactivated virus | Mild fever, swelling, redness | Rare cases of severe allergic reactions |
| Sputnik V (Gam-COVID-Vac) | Adenoviral vector | Muscle pain, mild fever | VITT, myocarditis |

SARS-CoV-2 primarily spreads through respiratory droplets, but transmission also occurs via direct contact with contaminated surfaces. While initial human-to-human transmission was linked to the Huanan Seafood Wholesale Market, subsequent studies revealed earlier transmissions in other locations, prompting urgent public health measures and vaccine development 12,13.

Although vaccination efforts have been critical in managing the pandemic, concerns regarding AEFI have emerged from both clinical trials and real-world data. Documented adverse events include neurological complications like cerebral venous sinus thrombosis and ischemic stroke, cardiovascular events such as myocarditis, and dermatological manifestations like urticaria 14,15. Investigating the mechanisms underlying these events has focused on immune-mediated pathways and host genetic predispositions 16.

Systematic reviews indicate that the incidence of adverse effects associated with COVID-19 vaccines is comparable to that of other vaccines, with most reactions being mild and transient. Nonetheless, rare severe reactions underscore the necessity for ongoing safety monitoring. The emergence of novel vaccine platforms, such as mRNA and vector-based vaccines, presents unique challenges and opportunities in understanding AEFI 17,18. Healthcare professionals are pivotal in identifying, reporting, and managing AEFI to maintain public trust and ensure the success of immunization campaigns. Public health education programs have also been essential in addressing vaccine hesitancy, promoting equitable access, and fostering community-wide immunity 19,20.

Both direct clinical observations and data from vaccinated individuals through surveys have enriched the understanding of AEFI. Large-scale observational studies conducted in countries such as Israel and the United

Kingdom have provided valuable insights into the safety and efficacy of various vaccine formulations 21,22.

This study aims to investigate the incidence, nature, and determinants of AEFI following COVID-19 vaccination among diverse populations, including adults, pregnant women, and geriatric groups. By analysing data from healthcare and community settings, this research seeks to enhance vaccine safety profiles, offer evidence-based recommendations, and strengthen public confidence in vaccination programs 23,24.

In conclusion, the study of AEFI is essential for the continued success of COVID-19 vaccination campaigns. By identifying and characterizing these events, healthcare systems can optimize vaccination strategies, improve patient outcomes, and bridge critical knowledge gaps regarding vaccine safety for diverse populations 25,26.

## METHODOLOGY

### *Study Design*

This was a prospective observational study conducted to evaluate adverse events following immunization (AEFI) in patients who received at least one dose of the COVID-19 vaccine.

### *Sample Size*

The study aimed to include approximately 3,000–4,000 participants.

### *Study Criteria*

**Inclusion Criteria:** Adult patients who had received at least one dose of a COVID-19 vaccine.

Post-vaccinated cases of pregnant women and geriatric populations., Participants aged 18 years and older.

**Exclusion Criteria:** Patients who had not taken any COVID-19 vaccine., Patients who tested positive for COVID-19., Pediatric patients (under 18 years of age).

### *Study Sites*

**The study was conducted at the following locations: Parul Sevashram Hospital**

Parul Sevashram Vaccination Center

Community Health Center, Padra

Online surveys were also used to collect data from eligible participants.

### *Materials Required*

**The following materials were utilized during the study:** Data Collection Form: For capturing demographic and clinical data.

**Patient Information Sheet:** To provide study details and ensure transparency with participants.

**Informed Consent Form:** For obtaining informed consent from study participants.

**Online Data Collection Form:** To gather data remotely from participants who were unable to visit the study sites.

### *Data Collection Procedure:*

Participants were recruited based on the inclusion and exclusion criteria. Data were collected through face-to-face interactions, physical examinations at the study sites, and online surveys. Each participant provided informed consent before participating in the study. Information such as demographics, vaccine details, adverse reactions, and subsequent medical treatments were systematically recorded using the data collection forms.

## RESULTS

### *1. Graphical Analysis*

**Table 4. Demographic distribution of patients.**

| GENDER | COVISHEILD | COVAXIN |
|---|---|---|
| Male | 1073 | 512 |
| Female | 549 | 234 |

The study included a total of 2,368 participants, categorized based on vaccine type and gender. Among males, 1,073 received Covishield and 512 received Covaxin. Similarly, among females, 549 received Covishield and 234

received Covaxin. These figures indicate a higher preference for Covishield across both genders. The inclusion of diverse demographic groups, such as pregnant women and geriatric populations, enhances the study's generalizability to broader populations.

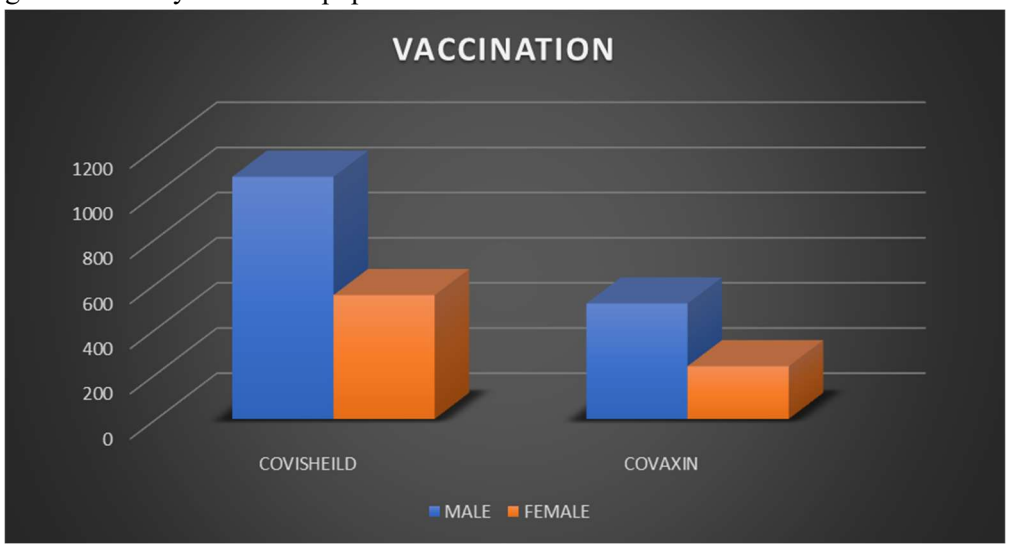


**Fig 1. Demographic distribution of patients.**

**Table 5. Distribution of Adverse effects following immunization after 1st and 2nd dose.**

| ADVERSE EFFECTS | AFTER 1st DOSE | AFTER 2nd DOSE |
|---|---|---|
| Pain at site of injection | 1613 | 1193 |
| Headache | 335 | 353 |
| Cough | 104 | 90 |
| Constipation | 37 | 23 |
| Gastric disturbance | 78 | 48 |
| Fever | 1531 | 1031 |
| Diarrhea | 62 | 104 |
| Allergic reaction | 78 | 50 |
| Joint pain | 138 | 113 |
| Body pain | 1049 | 722 |
| Arrythmia | 2 | 4 |
| Congestive heart failure | 1 | 0 |
| Myocardial infarction | 1 | 1 |
| Atherosclerosis | 4 | 2 |
| Cardiac arrest | 1 | 1 |

Adverse effects were reported more frequently following the first dose compared to the second dose, irrespective of the vaccine type. The findings suggest that initial immunization triggers a stronger immune response, as expected in primary vaccination. Mild symptoms such as fever, body ache, and pain at site of injection were the most commonly reported side effects. Severe adverse events, though rare, were more likely to occur after the first dose and required medical attention. Most adverse events occurred within 24 hours of vaccination, aligning with existing literature on reactogenicity conducted by Habot Wilner et al. 9

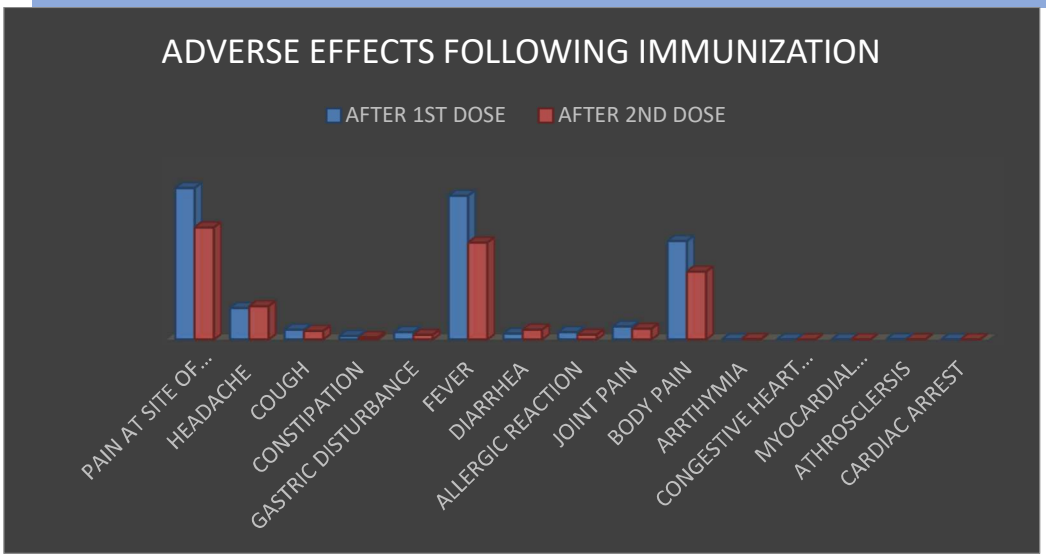


**Fig 2. Distribution of Adverse effects following immunization.**

**Table 6. Gender-Based Analysis of adverse effects following immunization.**

| GENDER | 1ST DOSE ADVERSE EFFECT | TOTAL PARTICIPANTS | 2ND DOSE ADVERSE EFFECT | TOTAL PARTICIPANTS |
|---|---|---|---|---|
| MALE | 1559 | 1587 | 1536 | 1587 |
| FEMALE | 766 | 783 | 748 | 783 |

The prevalence of AEFIs was notably higher in males compared to females across both doses. This trend was consistent for both Covishield and Covaxin, highlighting potential differences in immunological or physiological responses between genders.

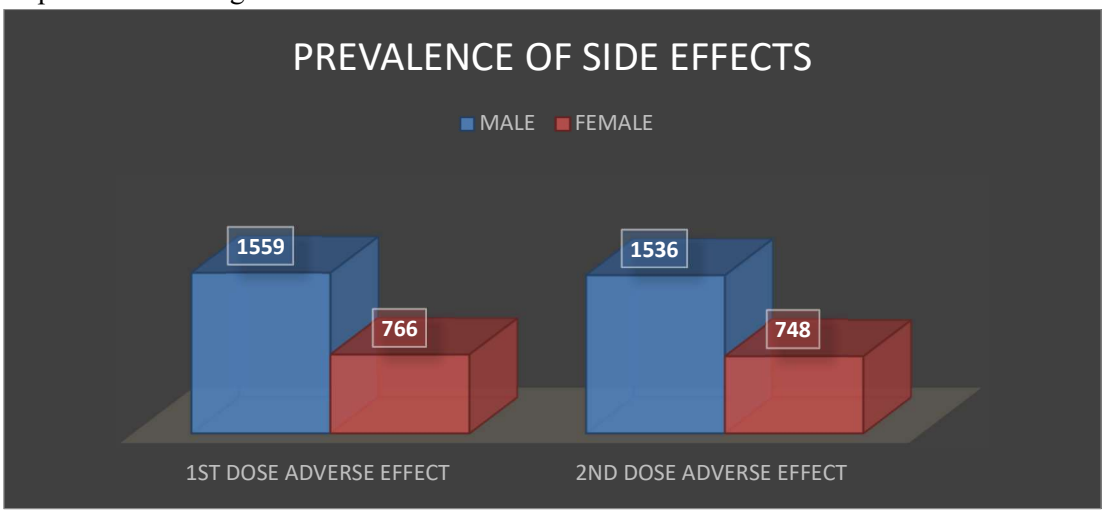


**Fig 3. Gender-Based Analysis of adverse effects following immunization.**

**Table 7. Distribution of patients as per the necessity of drug intake after immunization.**

| CRITERIA | NUMBER OF PATIENTS | PERCENTAGE |
|---|---|---|
| Treatment Taken After Vaccination | 1547 | 65% |

| | | |
|---|---|---|
| Treatment Not Taken After Vaccination | 815 | 35% |

Among the participants who experienced adverse effects, 65% sought medical intervention, while 35% managed their symptoms without treatment.

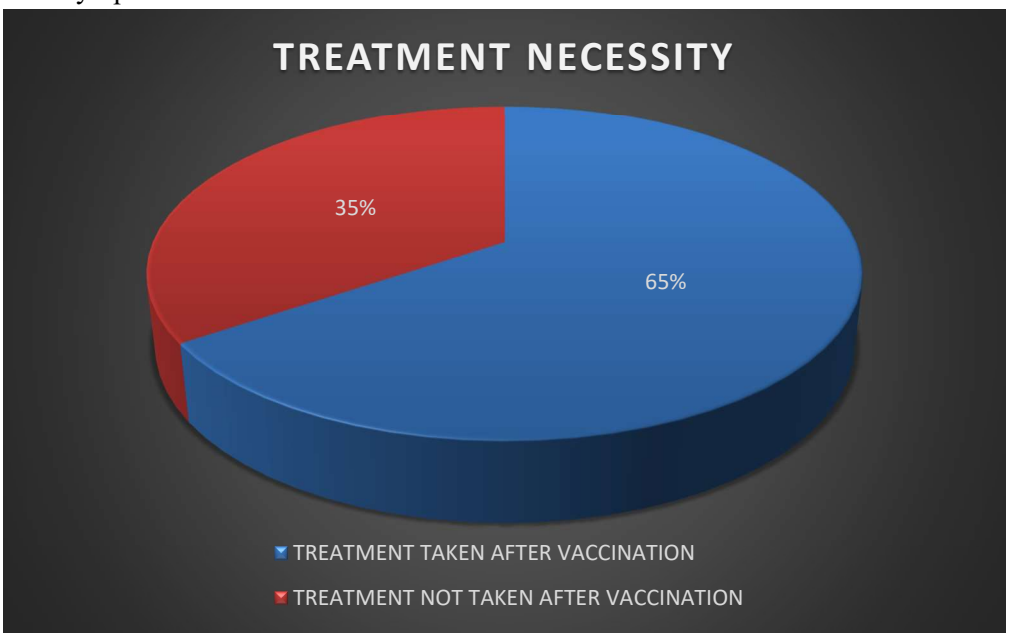


**Fig 4. Distribution of patients as per the necessity of drug intake after immunization.**

**Table 8. Distribution of drugs used in the Management of AEFIs.**

| MEDICATION | NUMBER OF PATIENTS |
|---|---|
| Dolo 650 | 929 |
| Loperamide | 82 |
| Pan D | 179 |
| PCM 500 | 470 |
| Azithromycin | 9 |
| Levocitrizine | 18 |
| Syrup DMR | 17 |
| Nimison P | 4 |
| Disprin | 4 |
| Crocin | 1 |

Among the participants who experienced adverse effects, 65% sought medical intervention, while 35% managed their symptoms without treatment. The most used medications included Dolo 650 mg and PCM 500 mg, emphasizing the role of analgesics and antipyretics in managing post-vaccination symptoms.

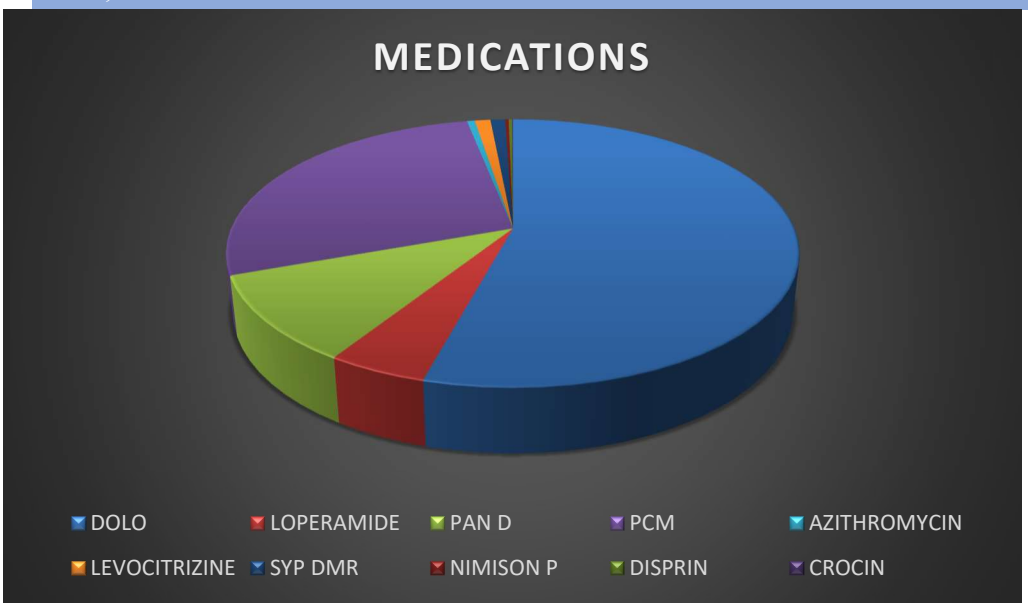


**Fig 5. Distribution of drugs used in the Management of AEFIs**

**Statistical Analysis**

***1. Chi-Square Test for finding association between Gender and Adverse Events***

The Chi-Square Test is used to determine whether there is a significant association between two categorical variables – gender and the occurrence of adverse effects following vaccination.

| | Male (n = 1587) | Female (n = 783) |
|---|---|---|
| Adverse effects reported | 1559 | 766 |
| No adverse effects reported | 28 | 17 |

***Results***

- Chi-Square Statistic: 0.273
- p-value: 0.601
- Degrees of Freedom: 1

***Interpretation***

- Since the p-value (0.601) is greater than 0.05, there is no statistically significant association between gender and the occurrence of adverse effects.
- This suggests that while males reported more adverse effects numerically, this difference is not significant when accounting for sample size.
- The expected frequencies in each cell were reasonably close to the observed values, supporting the conclusion that the distribution of adverse effects is similar across genders.

***2. Standard Deviation – Comparing Adverse Effects Between 1st and 2nd Dose***

The SD Test is used to compare the means of two independent groups—in this case, the number of adverse effects reported after the 1st and 2nd vaccine doses.

| ADVERSE EFFECTS | AFTER 1st DOSE | AFTER 2nd DOSE |
|---|---|---|
| **Pain at site of injection** | 1613 | 1193 |
| **Headache** | 335 | 353 |
| **Cough** | 104 | 90 |
| **Constipation** | 37 | 23 |
| **Gastric disturbance** | 78 | 48 |
| **Fever** | 1531 | 1031 |
| **Diarrhea** | 62 | 104 |
| **Allergic reaction** | 78 | 50 |
| **Joint pain** | 138 | 113 |
| **Body pain** | 1049 | 722 |
| **Arrythmia** | 2 | 4 |
| **Congestive heart failure** | 1 | 0 |
| **Myocardial infarction** | 1 | 1 |
| **Atherosclerosis** | 4 | 2 |
| **Cardiac arrest** | 1 | 1 |

***Standard Deviations Calculated***

1. 1st Dose Adverse Effects SD: 567.97
2. 2nd Dose Adverse Effects SD: 399.92

***Interpretation***

The higher standard deviation for 1st dose adverse effects (567.97) compared to the 2nd dose (399.92) indicates greater variability in the number of adverse effects reported after the 1st dose.

***3. T-Test Comparing Adverse Effects Between 1st and 2nd Dose***

The T-Test is used to compare the means of two independent groups—in this case, the number of adverse effects reported after the 1st and 2nd vaccine doses.

**Table 7. Data Used (Number of Adverse Effects)**

| ADVERSE EFFECTS | AFTER 1st DOSE | AFTER 2nd DOSE |
|---|---|---|
| **Pain at site of injection** | 1613 | 1193 |
| **Headache** | 335 | 353 |
| **Cough** | 104 | 90 |
| **Constipation** | 37 | 23 |
| **Gastric disturbance** | 78 | 48 |
| **Fever** | 1531 | 1031 |
| **Diarrhea** | 62 | 104 |
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| **Joint pain** | 138 | 113 |
| **Body pain** | 1049 | 722 |
| **Arrythmia** | 2 | 4 |

| | | |
|---|---|---|
| **Congestive heart failure** | 1 | 0 |
| **Myocardial infarction** | 1 | 1 |
| **Atherosclerosis** | 4 | 2 |
| **Cardiac arrest** | 1 | 1 |

***Results***

- T-statistic: 0.483
- p-value: 0.633

***Interpretation***

- Since the p-value (0.633) is greater than 0.05, there is no statistically significant difference in the number of adverse effects between the 1st dose and the 2nd dose.
- Although adverse effects were more frequent after the 1st dose, the variation is within a range that can occur by chance.
- This indicates that the immune response to the 1st and 2nd doses of the vaccine is not significantly different regarding the frequency of reported adverse effects.

***Summary of Insights:***

- Chi-Square Test: No significant relationship between gender and adverse events.
- Standard Deviation: Indicates greater variability in the number of adverse effects reported after the 1st dose.
- T-Test: No significant difference between the frequency of adverse effects after the 1st and 2nd doses.
- These statistical tests suggest that while numerical differences exist in the data, they do not provide strong evidence of significant patterns or associations.

**DISCUSSION**

The results provide critical insights into the safety profile of COVID-19 vaccines administered under emergency use authorization. The predominance of mild to moderate AEFIs confirms the vaccines' safety and aligns with global findings from phase III clinical trials. However, the higher occurrence of adverse events following the first dose underscores the need for robust post-vaccination monitoring systems.

Implications of Gender-Based Differences – The observed higher prevalence of AEFIs in males raises important questions about gender-specific immune responses. Existing studies suggest that sex hormones, such as testosterone, may modulate immune activity, potentially leading to heightened reactogenicity in males. This finding underscores the need for further research to explore sex-based differences in vaccine responses, which could inform personalized vaccination strategies.

Importance of Timely Management – The reliance on over-the-counter medications like Dolo 625 mg and PCM 500 mg demonstrates their effectiveness in managing post-vaccination symptoms. However, the 35% of participants who did not seek treatment highlight the importance of public health campaigns to improve awareness of AEFIs and available management options.

Comparative Analysis of Vaccines – The slightly higher incidence of AEFIs with Covishield is consistent with its adenoviral vector platform, known for inducing robust immune responses. Covaxin, an inactivated virus vaccine, appears to elicit a milder reactogenicity profile, making it a viable option for individuals at higher risk of adverse reactions.

Broader Public Health Implications – This study reinforces the importance of mass vaccination campaigns in mitigating the COVID-19 pandemic. The findings highlight the need for clear communication about vaccine safety, emphasizing the rarity of severe adverse events. Additionally, healthcare providers should be equipped to manage AEFIs effectively, ensuring public trust in vaccination programs.

Limitations and Future Directions – While the study provides valuable data, it is limited by its observational design

and reliance on self-reported outcomes. Future research should include long-term follow-up to assess the persistence of AEFIs and their impact on vaccine efficacy. Expanding the study to include diverse populations, such as paediatric and immunocompromised individuals, would further enhance its applicability.

## CONCLUSION

This study highlights key insights into the safety of COVID-19 vaccines administered under emergency use authorization. The predominance of mild to moderate adverse events following immunization (AEFIs) aligns with findings from phase III clinical trials, confirming the overall safety of these vaccines. The higher frequency of AEFIs after the first dose emphasizes the importance of post-vaccination monitoring systems. Gender-based differences, particularly the higher rate of AEFIs in males, point to the need for further investigation into sex-specific immune responses to inform more personalized vaccination approaches.

The differences in AEFI rates between Covishield and Covaxin reflect their distinct platforms, suggesting that vaccine choice could be tailored based on individual risk factors. Public health initiatives should improve awareness of AEFIs and promote effective symptom management strategies to ensure timely care. While the study is limited by its observational nature and self-reported data, future research with long-term follow-up and diverse populations, including children and immunocompromised individuals, will enhance the understanding of vaccine safety and efficacy. These insights are essential for strengthening vaccination campaigns and maintaining public confidence.

## REFERENCES

1. Marsden J, Stevenson V, Jarrett L. Treatment of spasticity. Handb Clin Neurol. 2023;196:497–521. doi: 10.1016/B978-0-323-98817-9.00010-7. PMID: 37620087.
2. Taberlet P, Coissac E, Hajibabaei M, Rieseberg LH, others. Environmental DNA: for biodiversity research and monitoring. Oxford: Oxford Academic; 2018. doi: 10.1093/oso/9780198767220.001.0001. Accessed 2024 Dec 6.
3. Li X, Mi Z, Liu Z, Rong P. SARS-CoV-2: pathogenesis, therapeutics, variants, and vaccines. Front Microbiol. 2024;15:1334152. doi: 10.3389/fmicb.2024.1334152.
4. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020;579(7798):270–3. doi: 10.1038/s41586-020-2012-7.
5. Manfrini N, Notarbartolo S, Grifantini R, Pesce E. SARS-CoV-2: a glance at the innate immune response elicited by infection and vaccination. Antibodies (Basel). 2024;13(1):13. doi: 10.3390/antib13010013. PMID: 38390874; PMCID: PMC10885122.
6. Chung C, Irudayaraj P, Lallow E, et al. An overview of SARS-CoV-2 viral proteins with relevance to improved diagnostic and therapeutic platforms. Front Virol. 2024;4:1399993. doi: 10.3389/fviro.2024.1399993.
7. Marschalek R. SARS-CoV-2: the virus, its biology and COVID-19 disease-counteracting possibilities. Front Biosci (Landmark Ed). 2023;28(10):273. doi: 10.31083/j.fbl2810273. PMID: 37919074.
8. Eslait-Olaciregui S, Llinás-Caballero K, Patiño-Manjarrés D, et al. Serious neurological adverse events following immunization against SARS-CoV-2: a narrative review of the literature. Ther Adv Drug Saf. 2023;14:20420986231165674. doi: 10.1177/20420986231165674. PMID: 37223456; PMCID: PMC10201278.
9. Habot-Wilner Z, Neri P, Okada AA, et al. COVID vaccine-associated uveitis. Ocul Immunol Inflamm. 2023;31(6):1198–205. doi: 10.1080/09273948.2023.2200858. PMID: 37145198.
10. Hodel KVS, Fiuza BSD, Conceição RS, et al. Pharmacovigilance in vaccines: importance, main aspects, perspectives, and challenges—A narrative review. Pharmaceuticals (Basel). 2024;17(6):807. doi: 10.3390/ph17060807. PMID: 38931474; PMCID: PMC11206969.
11. Gee J, Shimabukuro TT, Su JR, et al. Overview of U.S. COVID-19 vaccine safety surveillance systems.

Vaccine. 2024;42(Suppl 3):125748. doi: 10.1016/j.vaccine.2024.02.065. PMID: 38631952.
12. Halma M. Towards robust pharmacovigilance surveillance systems. Open Health. 2024;5(1):20230033. doi: 10.1515/ohe-2023-0033.
13. Saeed MA, Marzook F, Saeed MR, et al. Unveiling the emergency use authorization of COVID-19 vaccines: safety, efficacy, and public trust. Preprints. 2024. doi: 10.20944/preprints202409.1204.v1.
14. Faksova K, Walsh D, Jiang Y, et al. COVID-19 vaccines and adverse events of special interest: a multinational global vaccine data network (GVDN) cohort study of 99 million vaccinated individuals. Vaccine. 2024;42(9):2200–11. doi: 10.1016/j.vaccine.2024.01.100. PMID: 38350768.
15. Wise J. Covid-19: two rare vaccine side effects detected in large global study. BMJ. 2024;384:q488. doi: 10.1136/bmj.q488. PMID: 38408769.
16. Panos LD, Bargiotas P, Hadjigeorgiou G, Panos GD. Neurovascular adverse effects of SARS-CoV-2 vaccination. Drug Des Devel Ther. 2024;18:1891–905. doi: 10.2147/DDDT.S464394. PMID: 38836116; PMCID: PMC11147783.
17. Hosseini R, Askari N. A review of neurological side effects of COVID-19 vaccination. Eur J Med Res. 2023;28:102. doi: 10.1186/s40001-023-00992-0.
18. Singh M. Cardiovascular side effects of COVID-19 vaccination. J Res Pharm Sci. 2024;10:27–34. doi: 10.35629/2995-10082734.
19. Lo Moro G, Ferrara M, Langiano E, et al. Countering vaccine hesitancy: a systematic review of interventions to strengthen healthcare professionals' action. Eur J Public Health. 2023;33(5):905–15. doi: 10.1093/eurpub/ckad134. PMID: 37581903; PMCID: PMC10567238.
20. Loftus R, Sahm LJ, Fleming A. A qualitative study of the views of healthcare professionals on providing vaccines information to patients. Int J Clin Pharm. 2021;43(6):1683–92. doi: 10.1007/s11096-021-01299-y. PMID: 34155584; PMCID: PMC8216584.
21. Ghare F, Meckawy R, Moore M, Lomazzi M. Determinants of acceptance of COVID-19 vaccination in healthcare and public health professionals: a review. Vaccines (Basel). 2023;11(2):311. doi: 10.3390/vaccines11020311. PMID: 36851189; PMCID: PMC9961323.
22. Pavlovic D, Sahoo P, Larson HJ, Karafillakis E. Factors influencing healthcare professionals' confidence in vaccination in Europe: a literature review. Hum Vaccin Immunother. 2022;18(1):2041360. doi: 10.1080/21645515.2022.2041360. PMID: 35290160; PMCID: PMC9009961.
23. Boyce TG, McClure DL, Hanson KE, et al. Lack of evidence for vaccine-associated enhanced disease from COVID-19 vaccines among adults in the vaccine safety datalink. Pharmacoepidemiol Drug Saf. 2024;33(8):e5863. doi: 10.1002/pds.5863. PMID: 39155049; PMCID: PMC11377022.
24. Karam R, Iskandar K, Watfa M, Zeitoun A. Serious adverse events following immunization with COVID-19 vaccines in Lebanon: a retrospective analysis of the National Pharmacovigilance Database. BMC Public Health. 2024;24:2905. doi: 10.1186/s12889-024-20297-z. PMID: 39434043; PMCID: PMC11495130.
25. Riad A, Schünemann H, Attia S, et al. COVID-19 vaccines safety tracking (CoVaST): protocol of a multi-center prospective cohort study for active surveillance of COVID-19 vaccines' side effects. Int J Environ Res Public Health. 2021;18(15):7859. doi: 10.3390/ijerph18157859. PMID: 34360156; PMCID: PMC8345554.
26. Soe P, Wong H, Naus M, et al. mRNA COVID-19 vaccine safety among older adults from the Canadian National Vaccine Safety Network. Vaccine. 2024;42(18):3819–29. doi: 10.1016/j.vaccine.2024.04.096. PMID: 38714447.
27. Anant Parasher, COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment, Postgraduate Medical Journal, Volume 97, Issue 1147, May 2021, Pages 312–320, https://doi.org/10.1136/postgradmedj-2020-138577

28. World Health Organisation official website.
29. Harvey, W. T., Carabelli, A. M., Jackson, B., et al. (2021). SARS-CoV-2 variants, spike mutations, and immune escape. Nature Reviews Microbiology, 19(7), 409-424.