



## A review on vaccine pharmacovigilance during covid-19

Jyothi K. Navya<sup>1\*</sup>, Jaka Archana<sup>1</sup>, Velpula Padma Sujaya<sup>1</sup>, Rupavath Pallavi Nayak<sup>1</sup>, Randeep Raj C Vaddadi<sup>2</sup>

<sup>1</sup> Clinical Research Intern, Clinosol Research Private Limited, Hyderabad, India

<sup>2</sup> Clinical SAS Trainer, Clinosol Research Private Limited, Hyderabad, India

### Article History

Received: 11-05-2021

Revised: 29-06-2021

Accepted: 06-08-2021



**Keywords:** Vaccine, covid-19, virus, immunization, pharmacovigilance, clinical trials, ISOP

### Abstract

Pharmacovigilance is important for collecting, detecting, monitoring adverse events which is the main objective. The adverse events reported should be assessed in order to know the casual relationship and avoid unnecessary effects on the recipient. Many people are vaccinating in a short period, so it is becoming much burden to the pharmacovigilance centers. The international society of pharmacovigilance (ISOP), the French national agency for medicines and health products safety (ANSM), and many others were in continuous collaboration and taking many initiatives to identify the safety and efficacy of vaccines and to provide answers to the raised questions respectively. Through pharmacovigilance, signals were detected, and many adverse events were identified. Pharmacovigilance of BioNTech/Pfizer-m-RNA, Moderna-mRNA vaccine, Covishield, Johnson and Johnson, Vaxzevria, Sputnik V, Convidecia are addressed. With BioNTech/Pfizer-m-RNA 12,249 ADRs, with Moderna-mRNA vaccine 577 ADRs, with Covishield 447 ADRs, with Johnson and Johnson 653 ADRs, with Vaxzevria 743 ADRs were reported. These vaccines resulted in immune thrombocytopenic purpura, cerebrovascular events, thrombosis, thrombocytopenia, facial paralysis, deaths, and many other reactions which may be fatal. But the events reported were less compared to the safety of the patients. All these events were maintained by the Uppsala monitoring center.

This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Copyright © 2021 Author(s) retain the copyright of this article.



### \*Corresponding Author

Jyothi k. Navya

Clinical Research Intern,

Clinosol Research Private Limited,

Hyderabad, India

Email: [naviyahjyouthi24@gmail.com](mailto:naviyahjyouthi24@gmail.com)



<https://doi.org/10.37022/jiaps.v6i2.226>

Production and Hosted by

[www.saap.org.in](http://www.saap.org.in)

### Introduction

The pandemic which is predicted long earlier by experts has arrived and created a huge impact on society. However, there must be a continuous need for experts which is evident from the first wave of pandemic [1]. Vaccine development helps in the prevention of spread of novel coronavirus infection. As many vaccines of different types are under development [2], and the participants were receiving the first dose of vaccines.

Vaccine pharmacovigilance plays an important role when once vaccine is released into the market. The main objective of vaccine pharmacovigilance is the detection and monitoring of adverse events associated with vaccination. As a large number of people are vaccinating against COVID-19, it is very difficult for the pharmacovigilance centers to assess suspected adverse events in a short period of time. The understandings between patients, caregivers, private portioners, government doctors, field-level health care workers, personnel involved in the AEFI program, and pharmacovigilance program is more important than ever.

The information about adverse reactions is imperative and should be reported immediately so that action can be taken, thus safeguard the vaccine recipients and avoid unnecessary reactions [3]. The adverse events reported will reach Vigibase, which is the database of individual case reports maintained by the Uppsala monitoring center. Spontaneous reporting by health care professionals is the main backbone of pharmacovigilance.

The National passive surveillance (e.g., spontaneous reporting of suspected adverse drug reaction) is used most widely to detect vaccine-related signals, in cooperation with healthcare professionals (HCPs) or patients to spontaneously report the occurrence of safety and/or effectiveness. The Active surveillance method involves the collection of organized data at a particular point in time from vaccinated individuals who are participating in a study. Figure 1 shows the study flow of COVID-19 active surveillance and post-marketing study in the UK [3].

Collaborations with international societies will help to obtain information regarding the suspected adverse reactions which help in reducing unnecessary reactions in a large population. The available real-life data is used for making treatment decisions. Continuous review of real-life data and events provides information to the health care professionals regarding the safety of vaccines. Thus, the collection of data from adverse drug reactions is also the objective of pharmacovigilance [1,4].

#### **Role of ISOP (international society of pharmacovigilance) during COVID-19**

The international society of pharmacovigilance (ISOP) along with the special interest group (SIG) were been working together to identify the safety and efficacy of medicines and vaccines in the prevention or treatment of coronavirus. Some of the ISOP initiatives are:

1. Monitoring medicine and vaccine publications related to Novel coronavirus
2. Provide support to regional pharmacovigilance societies
3. Developing infographics and provide pharmacovigilance updates to health care professionals and patients all over the world
4. Conducting webinars in collaboration with drug safety
5. Encouraging ISOP chapters and SIGs members to work and share their outputs with other team members

The executive ISOP committee came in touch with individual ISOP members to provide help to the first-line workers. The main objective of ISOP is to provide professional and personal support. The support, in low-income countries, is to manage challenges with limited resources. Communicating gained knowledge to regional pharmacovigilance centers will help to decrease the burden of the people through campaigns and communication tools. Electronic health records and big data networks provide evidence to raised issues about medicines and vaccines [1].

#### **French organisation for the pharmacovigilance of COVID-19**

The collaboration of ANSM (French national agency for medicines and health products safety) with the French pharmacovigilance network is effective to answer possible questions in this pandemic situation. French

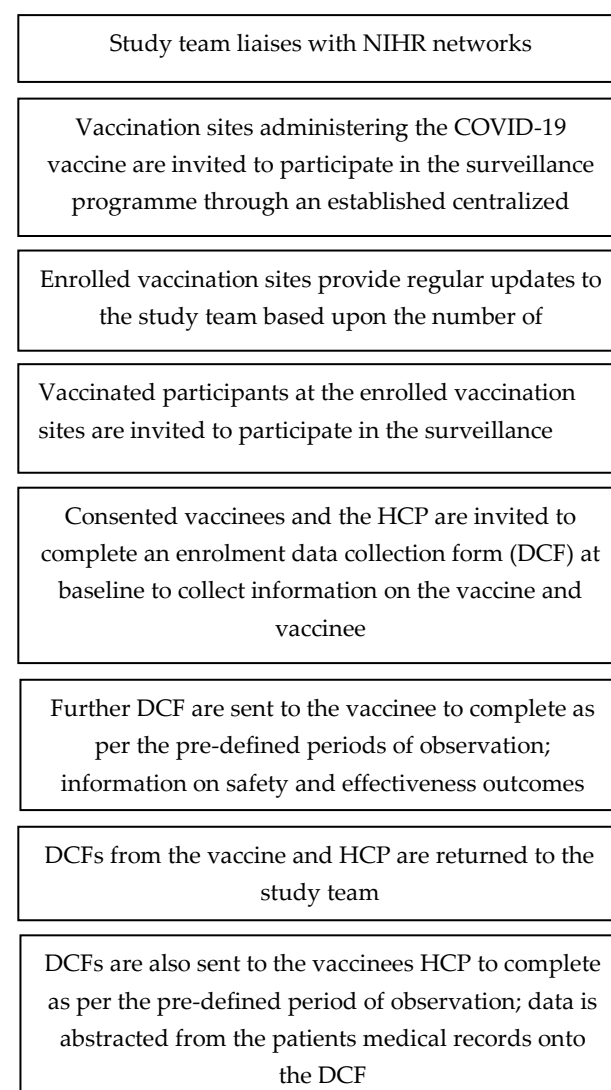
Pharmacovigilance organization for COVID-19 vaccines surveillance is shown in figure 2. The pharmacovigilance of COVID-19 vaccine according to French organization is based on two dimensions: [5,6,7]

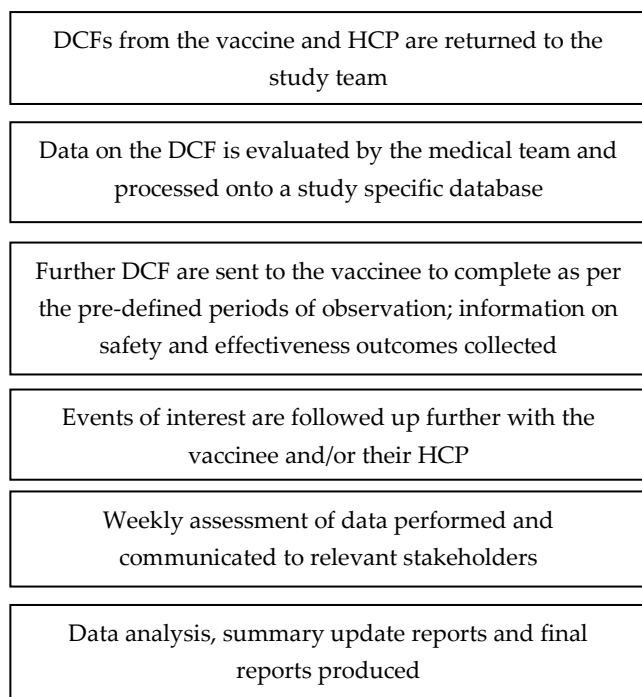
1. Individual analysis of all real-time ADRs by regional pharmacovigilance centers (RPVc)
2. Scientific analysis of all ANSM and RPVc experts

The main objectives of French organization in COVID-19 are: [8]

1. Detection of signals fastly
2. Transparency in the safety of COVID-19 vaccine
3. Weekly reports by experts made available on the French national agency for medicines and health products safety (ANSM) website
4. Health care professionals provide a response to patient queries about adverse effects of vaccines
5. Responsibility within the territories in relation with the general public, health care professionals, hospitals, medical social establishments

**Fig 01: Shows the study flow of COVID-19 active surveillance and post-marketing study in the UK**





#### Workflow at French network [9]

One pair of RPVCs completely analyze all ADRs reported daily after vaccination



For a complete analysis, RPVCs will provide specific organ expertise



Every Tuesday these reports are transmitted to ANSM



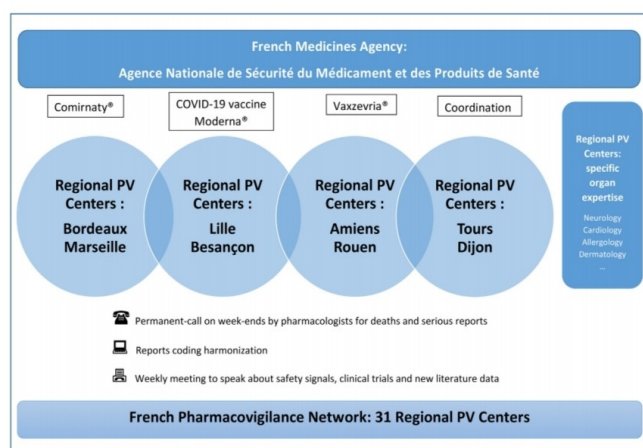
Gather data about exposed population, qualitative and quantitative analysis of ADRs



Experts discuss every Thursday about PV report in case reports



For safety signal, risk minimization strategies will be implemented by EMA



**Fig 02: French Pharmacovigilance organization for COVID-19 vaccines surveillance**

#### Vigilance of COVID-19 Vaccines (table 01)

With BioNtech/Pfizer COVID-19 vaccine, 74% of women and 43% of 50-64 years age group patients were reported with arterial hypertension, cardiac arrhythmias, Herpes zoster infection, thrombocytopenia, spontaneous hematomas, diabetes imbalance. 5 cases of severe hypersensitivity reactions were reported immediately. The above ADRs are rare but ADRs like fatigue, headache, nausea, fever, vomiting occurs due to the second dose in young adults from clinical trial data [10]. 313 cases of severe arterial hypertension were reported immediately or within a few hours or days after vaccination with or without the history of hypertension, can be treated with anti-hypertensives or increasing dosage of pre-existing antihypertensive agents [8]. With the Moderna COVID-19 vaccine, 74% of women and 49% of 75-84 years age group patients are mainly concerned with ADRs. ADRs like reactions at the vaccination site (pain, inflammation, cutaneous eruption), influenza-like syndrome (fever, chills, myalgia, arthralgia, asthenia), lymphadenopathy, digestive disorders and, hypersensitivity reactions. Delayed local reactions were reported 5- 10 days after vaccination [11].

With the Vaxzevria COVID-19 vaccine, 74% of women and 72% of 16-49 years age group patients are mainly concerned with ADRs of Vaxzevria. Influenza-like syndrome association with dyspnea and asthma was reported. These cases are reported within 24 hours after the first dose. 12 cases of thrombosis of a large vein associated with Thrombocytopenia and disseminated intravascular coagulation were reported [8].

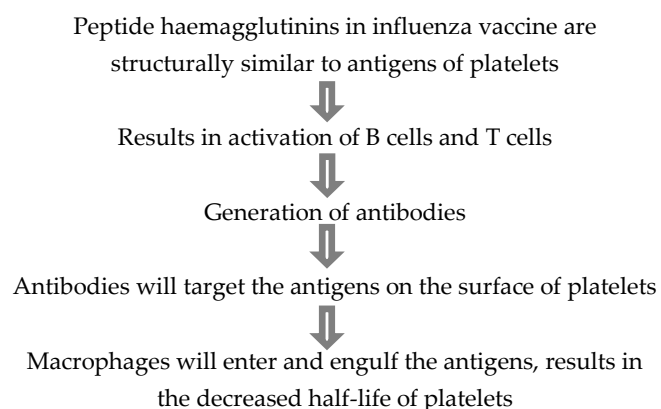
With AstraZeneca/ Oxford COVID-19 vaccine group, Medicine and healthcare regulatory (MHRA) authority on 18th March 2021 confirmed that there is no evidence which suggests blood clots are caused by vaccine and benefits outweigh thrombotic risks. MHRA also stated that sinus vein thrombosis associated with thrombocytopenia has been reported in less than one in a million people vaccinated so far in the UK, and a causal association with the vaccine could not be established [12].

Table 01: vigilance of COVID-19 vaccines

SL.no	Vaccine	No. Of doses	ADRs Reported	Signals
1.	Cominarty BioNTech/Pfizer-m-RNA	2	12,249 (25 <sup>th</sup> march 2021)	Arterial hypertension, cardiac arrhythmias, herpes zoster infection, thrombocytopenia/ spontaneous hematomas, diabetes imbalances
2.	Moderna-mRNA vaccine	2	577 (25 <sup>th</sup> march 2021)	Delayed local reactions
3.	AstraZeneca-Oxford vaccine group Covishield	2	447 (17 <sup>th</sup> Jan 2021)	Deaths with possible temporal relationship, 1 death associated with thrombocytopenia and stroke
4.	Janssen (Johnson and Johnson)	1	653 , 35( 11 <sup>th</sup> june 2021)	Fainting events, Cerebral venous thrombosis
5.	AstraZeneca-Oxford vaccine group Vaxzevria	2	743 (25 <sup>th</sup> march 2021)	Influenza like symptoms, large venous thrombosis (cerebral, digestive), with thrombocytopenia or coagulation disorders, CVA, MI, PE, monoplegia, DVT, Ischemic stroke
6.	Sputnik V	2		Deep vein thrombosis, cerebral circulatory failure, transient ischemic attack, vascular encephalopathy
7.	Convidecia	1		Non reported from phase 3 clinical trials

### Vigilance of immune thrombocytopenia purpura after COVID-19 vaccine

Immune Thrombocytopenic Purpura (ITP) is an immune-mediated disease that resulted in decreased platelet count caused by abnormal platelet production and destruction of platelets in the circulatory system. This results in bleeding, bruise, petechiae, bleeding gums, or life-threatening bleeding. This usually preceded by infection about 7-10 days before the onset of symptoms [13-15]. The pathogenesis of ITP is unclear but it may be due to molecular mimicry, as described in the flow chart below.



These antibodies will also decrease platelet production. Risk factors of ITP are influenza, measles, mumps-rubella (MMR), hepatitis B, human papillomavirus, varicella, and diphtheria-tetanus-pertussis (DPT) vaccines in children and adolescents, other constituents of vaccines like yeast proteins, adjuvants, and preservative diluents. Additives like aluminum

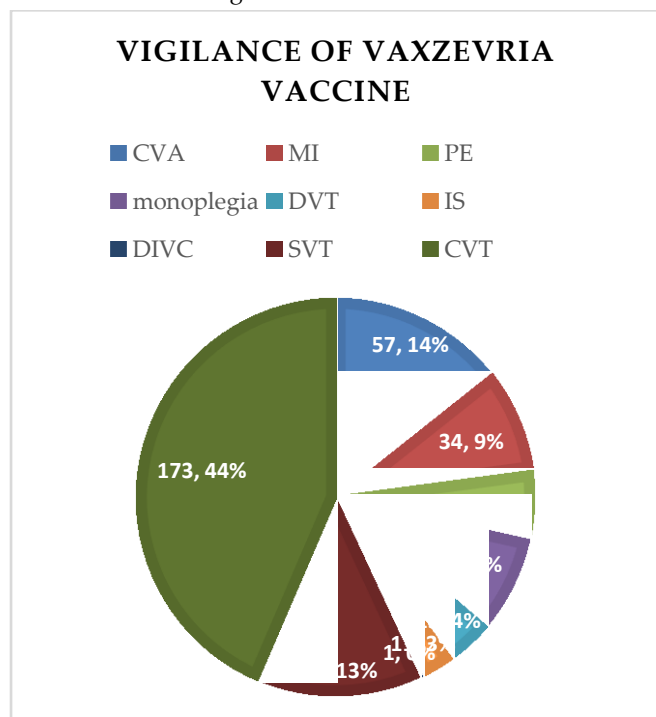
hydroxide and phosphate used in vaccines to enhance immunogenicity will result in autoimmune inflammatory syndrome induced by adjuvants [5,13-16].

After Pfizer/BioNtech and Moderna COVID-19 vaccines, 36 cases of immune thrombocytopenic Purpura were recorded to Vaccine adverse events reporting system [17]. 150 cases of immune thrombocytopenic Purpura were reported post-vaccination in the pharmacovigilance database stated by BMJ [18]. According to USFDA and CDC, the cases of ITP were few compared to the general population can be treated with corticosteroids and immunoglobulins [19]. Increased risk of ITP after COVID-19 vaccine administration, and response to treatment with standard ITP therapy, states that there is a possibility of an association between ITP and COVID-19 vaccine [20].

### Vigilance of thrombosis and thrombocytopenia after COVID-19 vaccine

After the Janssen's COVID- 19 vaccination 6 cases of cerebral vein thrombosis (CVT) associated with thrombocytopenia in women of age group 18-48 years after 6-13 days of vaccination were reported [21]. This suspended its use in the European Union, South Africa, USA [22]. With the Vaxzevria vaccine, 269 thromboembolic cases were reported to Eudravigilance. 57 cases of cerebrovascular accident, 34 cases of myocardial infarction, 22 cases of pulmonary embolism, 31 cases of monoplegia, 15 cases of deep vein thrombosis, 11 cases of ischemic stroke, 1 case of dissemination intravenous coagulation, 53 cases of splanchnic vein thrombosis, 173 cases of cerebral vein thrombosis were reported [23]. Most

commonly these events have occurred in females. the Vaxzevria was suspended in Denmark and is recommended in the older age group in UK, Belgium, Italy, Spain, Germany, France, Netherland, Finland, Sweden. The pharmacovigilance Risk assessment committee concluded that benefits overweigh the risk.



In India with the Covishield vaccine, 3 death were reported with possible temporal relationships, and 1 death is associated with thrombocytopenia and stroke [24]. With Sputnik Vaccine 1 case of deep vein thrombosis, 1 case of cerebral circulatory failure, 1 case of transient ischemic attack, 1 case of vascular encephalopathy were reported. This is Approved for emergency use in 62 countries, Rolling review in the EU. Currently in use in Russia, Armenia, Belarus, Guinea, Hungary, Iran, Kazakhstan, Kenya, Laos, Lebanon, Nicaragua, Pakistan, Paraguay, Serbia, Syria, Tunisia, UAE, Venezuela [25]. With Convidecia no reports of thrombosis were reported in phase 3 clinical trials [26].

#### The vigilance of facial paralysis related events after COVID-19

Facial paralysis cases were reported with mRNA Covid-19 vaccines (Pfizer/BioNTech and Moderna) in pivotal phase 3 clinical trials. 7 out of 35654 cases were reported facial paralysis events with the vaccine group compared with 1 out of 35611 cases who received the placebo group [10,27]. A causal relationship could not be established so far. 133883 cases of adverse drug reactions are reported with mRNA Covid-19 vaccines in the World Health Organization Pharmacovigilance database as of 9th March 2021. A total of 844 facial paralysis-related events are reported. Of which 683 cases are facial paralysis, 168 cases are facial paresis, 25 cases

are facial spasms, 13 cases are facial nerve disorders (figure 04) With Pfizer-BioNtech mRNA Covid-19 vaccine 749 cases of facial paralysis-related events were reported and 95 cases of facial paralysis-related events were reported with Moderna mRNA Covid-19 vaccine as of 9th March 2021. Of the total 844 cases, 572 patients were females, the median age was 49 (39-63) years, time of onset is 2 days [28].

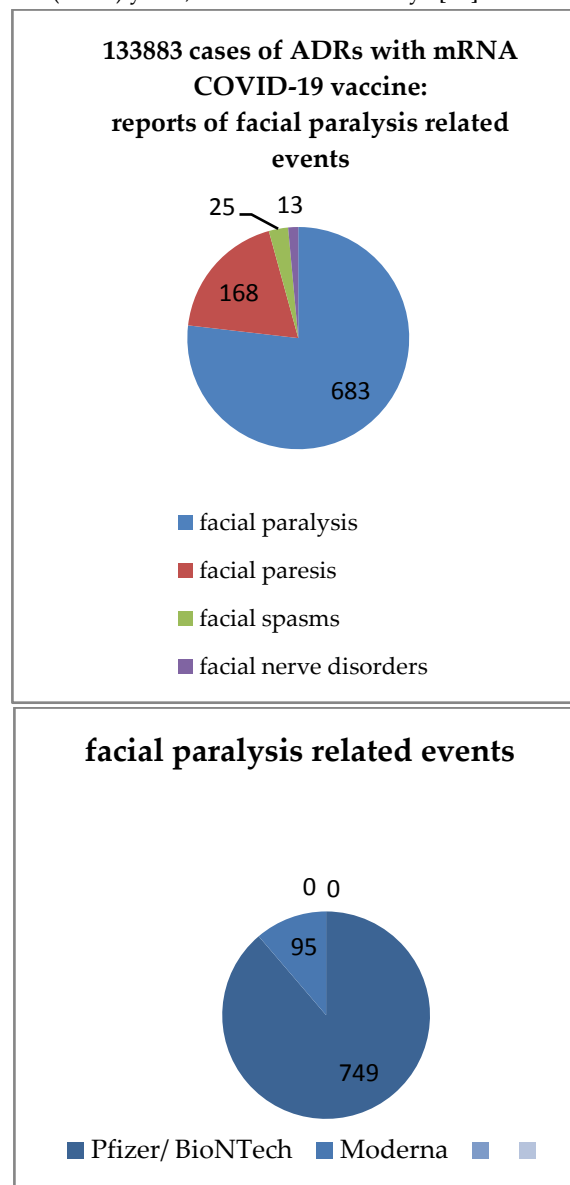
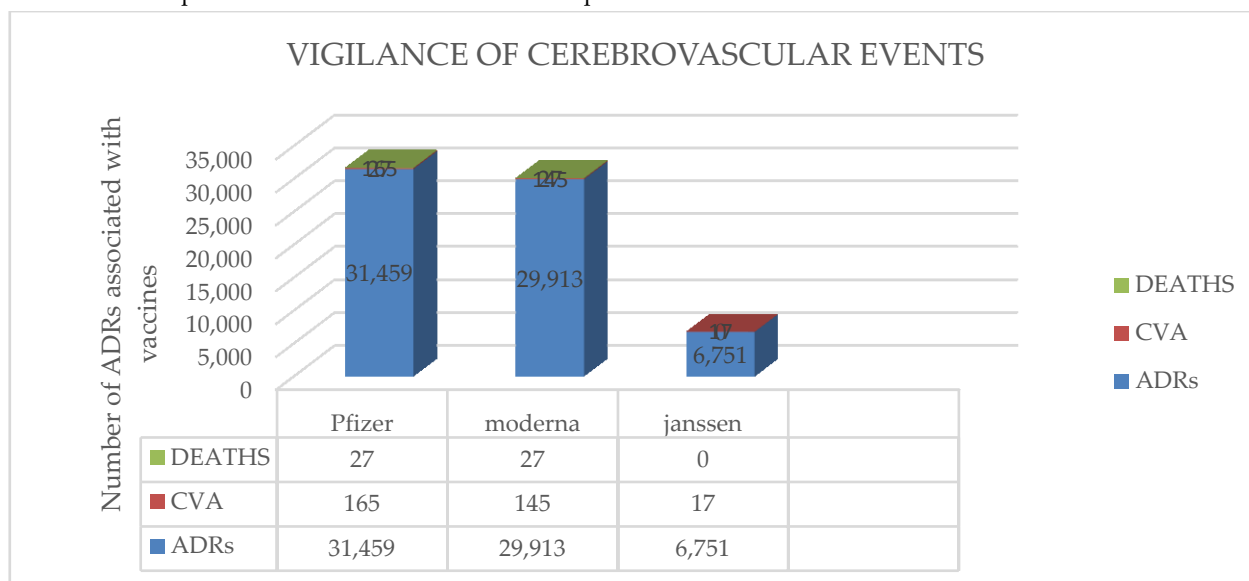


Fig 04: ADRs with m-RNA vaccines related to facial events and comparison between Pfizer and Moderna vaccines

#### Vigilance of cerebrovascular accident(cva) events after COVID-19 fig 05

With the Pfizer/BioNtech COVID-19 vaccine, a total of 31,459 cases of adverse events were reported in the vaccine adverse event reporting system database (VAERS).165 cases of CVA were reported, of which 27 reports resulted in death. With the Moderna COVID-19 vaccine, a total of 29,913 cases of Adverse events were reported. 145 cases of CVA event were reported, of which 27 reports resulted in death. With Janssen's anti-COVID vaccine, a total of 6,751 cases of

adverse events were reported. 17 cases of CVA event were reported with 0 deaths.



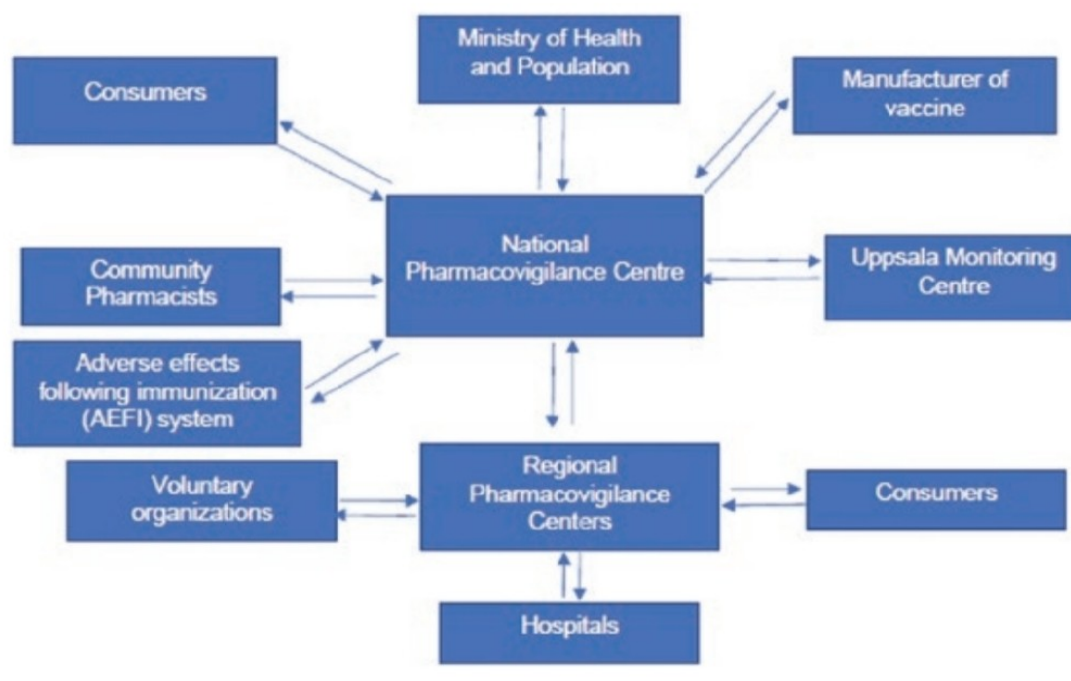
**Fig 05: Vigilance of Cerebrovascular events**

Females are more prone to ADRs like CVA, life-threatening CVA events, and permanent disability than males. Females had more reports of death with CVA associated with the Pfizer/BioNtech vaccine and Moderna vaccine. The majority of deaths occurred in the age group 65 or older. 111 CVA reports out of 165 with Pfizer-BioNtech vaccine, 114 CVA reports out of 145 with Moderna vaccine and, 9 CVA reports out of 17 with Janssen's vaccine were in the age group 65 or older [29].

#### Pharmacovigilance of COVID-19 in Nepal

Oxford/AstraZeneca COVID-19 AZD1222 (Covishield) is vaccination is going on in Nepal to the frontline healthcare professionals, sanitary and security workers. The reports of these individual recipients were transmitted to a regional pharmacovigilance center (KIST medical college) as shown in figure 6. Casualty and severity were analyzed using the Naranjo algorithm and Modified Hartwig and Siegel scales, respectively to improve the safety of the COVID-19 vaccine. Five ADRs reported to RPVCs are fever, myalgia, urticaria, diarrhea, sudden rise in blood pressure [30].

During preliminary trials, at least 1 ADR was observed in greater than 75% of recipients within 7 days of administration. The commonest ADR was injection site pain (58%) and Fever (46%) according to one study [31]. In another study, injection site pain (58%) and Fever (50%) were observed [32].



**Fig 06: Pharmacovigilance programme in Nepal**



# Deaths After COVID-19 Vaccination

As of January 8th, 2021, 6,688,231 individuals received COVID-19 Vaccines and 55 deaths were reported, mortality rate is 8.2 per million population. When 6,93,246 residents of long-term care facilities were vaccinated, 37 deaths were reported with a mortality rate of 53.4 per million population. Among them, half of the reported 25 deaths is in the age group above 85 years. 14 individuals died immediately within a day and, 45 individuals died within 1 week after vaccination. Comorbidities associated with deaths are hypertension, dementia, chronic obstructive pulmonary disease (COPD), diabetes, and heart failure. Medications associated with this are pain killers, fever reducers, and anti-hypertensives [33].

# Conclusion

Vaccines help to protect against infections by developing antibodies, similarly, COVID-19 vaccines help to develop immunity against COVID-19. After getting approval from the national immunization technical advisory group, vaccines are released into the market. Thus, pharmacovigilance helps in the detection, assessment, understanding, prevention of adverse events following immunization. This is used to protect from developing unnecessary reactions and reduce the burden on the public health.

# References

1. Chandler R, McCarthy D, Delumeau J, Harrison-Woolrych M. The Role of Pharmacovigilance and ISO P During the Global COVID-19 Pandemic. *Drug Safety*. 2020;43(6):511-512.
2. Le T, Cramer J, Chen R, Mayhew S. Evolution of the COVID-19 vaccine development landscape. *Nature Reviews Drug Discovery*. 2020;19(10):667-668.
3. Meher B. Need of vibrant vaccine pharmacovigilance during current global COVID-19 pandemic: More than ever. *Journal of Pharmacy And Bioallied Sciences*. 2021;13(1):1.
4. Dhanda S, Osborne V, Lynn E, Shakir S. Postmarketing studies: can they provide a safety net for COVID-19 vaccines in the UK?. *BMJ Evidence-Based Medicine*. 2020;:bmjebm-2020-111507.
5. Olivier P, Montastruc J. The nature of the scientific evidence leading to drug withdrawals for pharmacovigilance reasons in France. *Pharmacoepidemiology and Drug Safety*. 2006;15(11):808-812.
6. Abou Taam M, Jacquot B, Ferard C, Thery A, Mounier C, Grandvuillemin A et al. The French pharmacovigilance surveys: A French distinctiveness, a real input. *Therapies*. 2020;.

7. Soeiro T, Lacroix C, Micallef J. Adverse drug reaction monitoring: Doing it the French way – Act II. *Therapies*. 2020;.
8. Lacroix C, Salvo F, Gras-Champel V, Gautier S, Massy N, Valnet-Rabier M et al. French organization for the pharmacovigilance of COVID-19 vaccines: A major challenge. *Therapies*. 2021;.
9. Agence nationale de sécurité du médicament et des produits de santé. *Journal de Pédiatrie et de Puériculture*. 2021;26(1):67-72.
10. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine*. 2021;384(16):1576-1578.
11. McMahon D, Amerson E, Rosenbach M, Lipoff J, Moustafa D, Tyagi A et al. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. *Journal of the American Academy of Dermatology*. 2021;85(1):46-55.
12. Merchant H. CoViD vaccines and thrombotic events: EMA issued warning to patients and healthcare professionals. *Journal of Pharmaceutical Policy and Practice*. 2021;14(1).
13. Mantadakis E, Farmaki E, Thomaidis S, Tsalkidis A, Chatzimichael A. A Case of Immune Thrombocytopenic Purpura After Influenza Vaccination. *Journal of Pediatric Hematology/Oncology*. 2010;32(6):e227-e229.
14. Hamiel U, Kventzel I, Youngster I. Recurrent Immune Thrombocytopenia After Influenza Vaccination: A Case Report. *PEDIATRICS*. 2016;138(6):e20160124-e20160124.
15. Rinaldi, M., Perricone, C., Ortega-Hernandez, O., Perricone, R. and Shoenfeld, Y., 2014. Immune thrombocytopaenic purpura: an autoimmune cross-link between infections and vaccines. *Lupus*, 23(6), pp.554-567.
16. Pellegrino P, Clementi E, Radice S. On vaccine's adjuvants and autoimmunity: Current evidence and future perspectives. *Autoimmunity Reviews*. 2015;14(10):880-888.
17. [Internet]. 2021 [cited 12 June 2021]. Available from: <https://www.jwatch.org/fw117502/2021/02/08/officials-investigatingreportsthrombocytopeniaafter>
18. Wise J. Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots. *BMJ*. 2021;:n699.
19. Lee E, Cines D, Gernsheimer T, Kessler C, Michel M, Tarantino M et al. Thrombocytopenia following Pfizer and Moderna SARS-CoV -2 vaccination.

- American Journal of Hematology. 2021;96(5):534-537.
20. Saudagar V, Patil S, Goh S, Pothiwala S. Vigilance regarding immune thrombocytopenic purpura after COVID-19 vaccine. Irish Journal of Medical Science (1971 -). 2021;.
21. [Internet]. 2021 [cited 12 June 2021]. Available from: <https://www.fda.gov/news-events/press-announcements/joint-cdc-and-fda-statement-johnson-johnson-covid-19-vaccine-2021>
22. Gupta A, Sardar P, Cash M, Milani R, Lavie C. Covid-19 vaccine- induced thrombosis and thrombocytopenia-a commentary on an important and practical clinical dilemma. Progress in Cardiovascular Diseases. 2021;.
23. EMA. European Medicines Agency AstraZeneca's COVID-19 Vaccine Analysis. Available at: <https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood> 2021.
24. Request Rejected [Internet]. Main.mohfw.gov.in. 2021 [cited 12 June 2021]. Available from: <https://main.mohfw.gov.in/Organisation/Departments-of-Health-andFamily-Welfare/immunization/aefi-reports> 2021
25. Logunov D, Dolzhikova I, Shcheblyakov D, Tukhvatulin A, Zubkova O, Dzharullaeva A et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. The Lancet. 2021;397(10275):671-681.
26. [Internet]. 2021 [cited 12 June 2021]. Available from: <https://clinicaltrials.gov/ct2/show/NCT04526990> 2021.
27. Alimehmeti I. Efficacy and Safety of AZD1222, BNT162b2 and mRNA-1273 vaccines against SARS-CoV-2. Albanian Journal of Trauma and Emergency Surgery. 2021;5(1):791-796.
28. Association of Facial Paralysis With mRNA COVID-19 Vaccines: A Disproportionality Analysis Using the World Health Organization Pharmacovigilance Database. american medical association. 2021;.
29. Lt. Pushkar a. Pharmacovigilance analysis on cerebrovascular accidents and Corona virus disease 2019 vaccines. 2021;.
30. Jha N, Palaian S, Shankar P, Dangal G. Pharmacovigilance of COVID-19 vaccines in the context of Nepal: an assessment based on early adverse drug reaction reports. Journal of Pharmaceutical Health Services Research. 2021;.
- Logunov, D., Dolzhikova, I., Tukhvatullin, A. and Shcheblyakov, D., 2020. Safety and efficacy of the Russian COVID-19 vaccine: more information needed – Authors' reply. *The Lancet*, 396(10256), pp.e54-e55.
31. Zhu F, Li Y, Guan X, Hou L, Wang W, Li J et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. The Lancet. 2020;395(10240):1845-1854.
32. Lv G, Yuan J, Xiong X, Li M. Mortality Rate and Characteristics of Deaths Following COVID-19 Vaccination. *Frontiers in Medicine*. 2021;8.