



# Review Article On Pharmacovigilance

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## Abstract

Pharmacovigilance is defined by the World Health Organization (WHO) as the science and activities related to the detection, assessment, understanding, and prevention of adverse drug reactions (ADRs) and other medicine-related problems. It plays a critical role in ensuring drug safety throughout a drug's lifecycle. Despite its importance, under-reporting of ADRs remains a significant global challenge due to factors such as lack of time and awareness among healthcare professionals. The WHO has initiated programs to promote ADR reporting and enhance drug safety monitoring.

The history of pharmacovigilance highlights its evolution, including the thalidomide tragedy of the 1960s, which underscored the necessity of stringent drug safety protocols. In India, pharmacovigilance began formally in 1986 and has since developed into a robust system supported by WHO and the National Pharmacovigilance Program. Pharmacovigilance is essential to identify rare and long-term adverse effects, especially in vulnerable populations like children, pregnant women, and the elderly.

The primary goals of pharmacovigilance include early detection of ADRs, risk-benefit analysis, and educating healthcare professionals and patients about safe drug use. Addressing ADRs requires systematic documentation, reporting, and monitoring to ensure safer medicines and improve patient care. While challenges such as under-reporting persist, the collective efforts of healthcare providers and regulators can strengthen pharmacovigilance systems worldwide.

This abstract emphasizes the importance of pharmacovigilance in safeguarding public health and highlights its impact on enhancing drug safety through effective ADR monitoring and reporting.

**Keywords:** - Pharmacovigilance, Adverse Drug Reactions (ADRs), Drug Safety Monitoring, WHO Pharmacovigilance Program, National Pharmacovigilance System

## Introduction of Pharmacovigilance-

WHO characterizes pharmacovigilance as “the science and exercises relating to the discovery, appraisal, understanding and Avoidance of unfavorable impacts or any other medicine-related Problem” (WHO 2004, 1). Terms related to the science of Pharmacovigilance are characterized in an unexpected way in numerous settings and by diverse organizations.

The under-reporting of unfavourable sedate responses is The major mishap around the world which may be Ascribed to the need of time and report shapes. It Has been known that world wellbeing organization (WHO) has started the program of announcing all Antagonistic responses had by the drugs.

Pharmacovigilance is the science and exercises related to the location, evaluation, understanding and anticipation of antagonistic impacts or any other conceivable drug-related issues. Unconstrained announcing of antagonistic occasions and unfavourable medicate responses is the commonest strategy utilized for creating security information. A few modern drugs are being launched in India nearly at the same time as within the world advertise. Consequently, hone of pharmacovigilance has ended up a need

The by and large rate of ADRs in hospitalized patients is evaluated to be 6.7% (extend 1.2-24.1%) which of deadly ADRs 0.32% (0.1 0.85%).[2] Information demonstrates that in patients who encounter ADRs, passing Rates are 19.18% higher and the length of clinic remain is 8.25% higher. Add up to therapeutic fetched for patients with ADRs are expanded by a normal of 19.86%.

## History of Pharmacovigilance: -

History Amid the twentieth century medicate improvement as an industry begun to require off. With the Disclosure of affront, penicillin and sulphonamides it was conceivable to treat illnesses which Had already been dangerous, saving millions of lives. Within the early days of sedate improvement there were no directions with respect to a drug's quality, viability and security .

**A thalidomide catastrophe:** The thalidomide occasion is happened in Europe in 1956. In spite of the fact that Thalidomide was broadly acclaimed to be a secure antiemetic and narcotic sedate indeed for pregnant moms at first, it was watched that a expansive number of distorted babies were born , essentially in Germany, amid 1959 to 1961.

The hone as well as the science of pharmacovigilance has been created and Nowadays pharmacovigilance is characterized by the WHO as 'the science and exercises relating to the Location, evaluation, understanding and avoidance of adverse impacts or any other sedate Related issue.

Sr No.	Year	Event
1	1938	Sulphanilamide liquid, with a sweet raspberry taste containing diethylene glycol caused kidney damage (USA).
2	1951	The Durham-Humphrey Amendment required certain drugs to be available only through prescription from a licensed physician (USA).
3	1952	In France, sudden deaths after diethyl tin diiodide were mistakenly used in a skin preparation.
4	1961	In Germany, Thalidomide birth defect tragedy
5	1962	Kefauver-Harris amendment of Federal Food, Drug and Cosmetic Act 1938 (USA) introduced following Thalidomide tragedy. The amendment required drug companies to register with FDA.
6	1966	USFDA released guidelines for reproduction studies.
7	1968	WHO Programme for International Drug Monitoring, now coordinated by Uppsala Monitoring Centre (UMC).
8	1974	National Research Act of 1974 (45CFR46): The National Commission for the Protection of Human, the protection of human subjects in Biomedical and subjects in Biomedical: Investigational Review Board/Ethics Committee.
9	1978	First German Medicines Act with reform of public health including pharmacovigilance.

## History of Pharmacovigilance in India –

Pharmacovigilance in India begun from 1986. A formal Adverse Drug Reactions (ADR) checking framework was started with 12 territorial centres, each covering a populace of 50 million. Be that as it may, no essential development was made. A short time later in 1997, India joined the World Health Organization (WHO) Adverse Drug Reaction (ADR) scrutinizing program Based at Uppsala, Sweden but got fall flat. Subsequently, after 2005 WHO backed and World Bank – Financed National Pharmacovigilance Program (NPPV) of India was made operational

### Need of pharmacovigilance:

It is broadly acknowledged that clinical improvement of Solutions may be a complex prepare which require colossal sum of time for its completion. Once a Sedate is showcased, it takes off the secure and secured logical environment of clinical trials and is free for utilization by the common open. At this point, most solutions will as it was had been Tried for short-term security and viability on a Restricted number of carefully chosen people. Consequently, require of pharmacovigilance emerges which Incorporate, securing the early location of unused Unfavourable responses or patients subgroups of Uncommon affectability; and presenting certain Measures in arrange to oversee such dangers. Moreover, it is basic that modern and therapeutically Still advancing medicines are observed for their Adequacy and security beneath genuine life Conditions after being showcased. Besides, More data is by and large required approximately utilize In particular populace bunches like children, Pregnant ladies and the elderly, around the Viability and security of unremitting utilize in combination With other drugs. Numbers of antagonistic Impacts, drug-interactions and hazard components have Been detailed afterward within the a long time of sedate discharge.

### Aims of Pharmacovigilance: Major aims of pharmacovigilance are:

1. Early location of until now obscure unfavourable responses and intuitive.
2. Discovery of increment in recurrence of (known) unfavorable responses.
3. Distinguishing proof of hazard components and conceivable components fundamental antagonistic responses.
4. Estimation of quantitative perspectives of benefit/risk investigation and dispersal of data required to progress medicate endorsing and direction.

The extreme objectives of pharmacovigilance are:

The sound and secure utilize of restorative drugs.

The appraisal and communication of the dangers and benefits of drugs on the showcase. Teaching and educating the patients.

### Pharmacovigilance in India

1. India has more than half a million qualified specialists and 15,000 healing centers having a bed Quality of 6,24,000. It is the fourth biggest maker of pharmaceuticals within the world. It is Rising as an important trial center within the world. Numerous new drugs are presented in our Nation. Subsequently, there's a require for a dynamic pharmacovigilance framework within the nation to Ensure the populace from the potential hurt that will be caused by a few of these modern Drugs. Clearly mindful of the tremendousness of errand the Central Drugs Standard Control Organization (CDSCO) has started a well organized and exceedingly participative National pharmacovigilance Program. It is to a great extent based on the proposals the WHO report titled “safety Observing of restorative items-Rules for setting up and running a pharmacovigilance Centre”.<sup>[13]</sup>The particular points of pharmacovigilance software engineers are to:
  - Contribute to the administrative evaluation of advantage, hurt, adequacy empowering their Secure, sound and successful utilize (counting taken a toll compelling utilize).
  - Move forward quiet care and in connection to utilize medication and all restorative and Para therapeutic Mediations.
  - Improve public health and safety in relation to use of medicines
    - Promote understanding, education and clinical training in pharmacovigilance and its Effective communication to the public.

## Objective of pharmacovigilance

Advancement of persistent care and security in Connection to the utilize of drugs with restorative and Paramedical intercessions remains to be an Critical parameter. The most goals of Pharmacovigilance include showing the adequacy Of drugs by checking their antagonistic impact Profile for numerous a long time from the lab to the Drug store; following any extreme impacts of drugs Making strides open wellbeing and security in connection to The utilize of drugs; empowering the secure, Levelheaded and cost-effective utilize of drugs; Advancing understanding, instruction and clinical Preparing in pharmacovigilance; and viable Communication to the non specific open. In Expansion, giving data to buyers, Professionals and controllers on the effective use Of drugs beside planning programs and Strategies for collecting and dissecting reports From patients and clinicians conclude to the Destinations of pharmacovigilance thinks about.

## Adverse Drug Reaction: -

Antagonistic Sedate Responses Antagonistic Sedate Responses (ADRs) are the hindering or truly undesirable impacts of medicate which comes about at restorative, prophylactic or symptomatic dosage level. ADR comes about to call for diminished within the measurements or withdrawal of the medicate from future utilize. The frequencies of ADRs are due to accessibility of numerous powerful drugs.

### ADR can be characterized as following:

-ADR could be a harm state which can be result from restorative inclusion related to a medicate. -As per WHO, antagonistic sedate responses are characterized as any harmful and undesirable impact of sedate that happens at measurements given to human being for prophylaxis, conclusion or treatment.

## TYPE of unfavourable medicate responses:

ADRs are classified as Sort A or Sort B responses. Both Sort A and B responses have a few subcategories. In spite of the fact that signs, side effects, and onset time can offer assistance separate between these sorts of responses, a few clinical cover may exist. Sort A –

ADRs that happen as the result of known pharmacological properties of the medicate are called Sort A reactions. They can happen in any person given a adequate measurements. Sort A responses are common and constitute 85% to 90% of ADRs. These responses incorporate the taking after categories:

1. Excessive pharmacological effect.
2. Side effects.
3. Toxic effects.
4. Secondary pharmacological effect.
5. Rebound response after discontinuation

### 1 Excessive Pharmacological Effect:

It creates in all patients in case intemperate measurement is given result in intemperate pharmacological impact. It is seen in cardio dynamic operators, CNS depressant, hypoglycaemic specialists and hypotensive specialists.

It is common in neonates, newborn children and elderly persistent too in patients with kidney infections, who have misplaced more than 70% of their kidney work with typical measurements. It is additionally common in quiet with lower egg whites level due to liver or kidney harm. Illustration:

At intemperate dose of Digoxin produces bradycardia; Morphine and bradycardia produces respiratory sadness in bronchitis patients.

## 2 Side Effect:

Side impacts are a few expansion of pharmacological impacts which created at restorative dosages. It is dosage related and minor in nature.

Side impact of most of the drugs misused for a restorative utilize. The illustrations of such side impacts of medicate that utilized as sign are as takes after:

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Codeine (antitussive) has constipating side impacts which is utilized in treatment of the runs.

-Sulfonylureas (tried as anti-bacterials) are found to diminish blood glucose level. Prazosin produces postural hypotension.

Hypokalemia created by Furosemide. – Nitrates produces cerebral pain.

## 3 Toxic effect:

The impacts deliver at overdose or delayed utilize of the medicate. Taking after are a few illustrations of poisonous impacts:

Paracetamol causes hepatic rot. Barbiturates cause coma.

Morphine causes respiratory disappointment.

## 4 Secondary Pharmacological effect:

A few of the drugs having other numerous pharmacological activities at commonly managed measurement. The impact delivered by the sedate is distinctive than medicate managed at first for avoidance or treatment implies it is an backhanded result of a essential medicate activity.

Taking after are a few cases of auxiliary pharmacological impact:

Understanding accepting antihistaminic medicate for the avoidance of movement ailment or within the unfavorably susceptible skin response may ended up lazy.

Vitamin insufficiency or astute diseases happen in patients whose typical bowel greenery has been modified by anti-microbials like tetracyclines.

## 5 Rebound Response after Discontinuation/Drug Withdrawal Reactions:

Utilize of long term of numerous drugs deliver resilience at cellular level. Sudden withdrawal of such medicine may allow rise to extreme antagonistic impacts. These responses happen in nonattendance of sedate causing it. These sorts of responses are

common with drugs which acting on CNS. For case:

opiates, analgesics, hypnotics, ethanol, etc. It can moreover result with a few antihypertensive drugs and corticosteroids. The withdrawal impacts can be minimizing by progressive withdrawal of medicate.

Taking after are the cases of medicate withdrawal reaction:

Clonidine is antihypertensive specialist which causes extreme bounce back hypertension in case its utilize ceases abruptly. The long-term utilize of CNS-depressants like; benzodiazepines, barbiturates and liquor after sudden withdrawal result in disarray, incoherence, tachycardia and writhing.

Anti-epileptic sedate withdrawal may increment seizures.

### Type B:

ADRs that happen when the known pharmacological properties of the sedate don't foresee the response are called Sort B reactions. These responses incorporate the taking after categories:

Extreme touchiness responses

The immunologic or incendiary impacts of a medicate cause extreme touchiness responses.

These responses constitute 6% to 10% of all ADRs. Extreme touchiness responses are categorized into the taking after sorts:

1. **Type I** responses are intervened by immunoglobulin E (IgE), pole cells, and basophils and are prompt in onset. With beginning introduction, drug-specific IgE is shaped and involves the surface receptors of pole cells and basophils. In the event that reexposure happens, the medicate is bound by the preformed IgE antibodies, which comes about within the discharge of vasoactive and PR incendiary arbiters from pole cells and basophils. This discharge can cause indications such as urticarial hasty, pruritus, and flushing. In extreme cases, the discharge can result in angioedema, hypotension, and anaphylaxis. Drugs commonly embroiled in Sort I touchiness responses incorporate beta-lactams, quinolones, and platinum-containing chemotherapeutic agents.
2. Type II extreme touchiness responses happen when IgG or IgM ties cellular or extracellular network antigens. The resultant response can lead to cellular pulverization and harm to tissues. Sort II touchiness responses are late in onset, and side effects ordinarily show up 5 to 8 days after sedate introduction. Cases of these responses incorporate drug-induced hemolytic frailty (cephalosporin, penicillin), medicate initiated thrombocytopenia (heparin, apixaban, quinidine, sulphonamides), and drug-induced neutropenia (propylthiouracil, flecainide).
3. Type III extreme touchiness responses are intervened by resistant complexes and the enactment of complement. Comparable to sort II responses, they are deferred in onset. In any case, it can take weeks for side effects to seem. In Sort III responses, a sedate shapes an safe complex by authoritative to drug-specific IgG, which actuates complement. These responses happen in different tissues, counting joints, kidneys, and blood vessels. Examples of sort III extreme touchiness responses incorporate serum affliction with equine-antitoxins and monoclonal antibodies, vasculitis with penicillin, cephalosporin, and phenytoin, and Arthurs responses with diphtheria and lockjaw vaccines.
4. Type IV touchiness responses are interceded by T cells and are postponed in onset. Depending on what cells are in this way enacted to discharge cytokines, sort IV responses are assist separated into a few subtypes, counting Iva (macrophages), IVb (eosinophils), IVc (T cells), and IVd (neutrophils). Illustrations of Sort IV responses incorporate contact dermatitis, intense generalized exanthemata's pustulosis, Stevens-Johnson disorder (SJS), drug-induced extreme touchiness disorder (DiHS), and sedate response with eosinophilia and systemic disorder (DRESS).

### Other immunological responses

1. Drug-induced autoimmunity may happen after sedate presentation and lead to immune system diseases. For case, lupus-like infection can create after presentation to isoniazid, phenytoin, procainamide, or hydralazine. Also, IgA bullous dermatosis can create after presentation to vancomycin or ceftriaxone, and a pemphigus-like clutter can create with presentation to penicillamine.
2. Settled sedate ejections are characterized by drug-induced injuries repeating at the same anatomical location. Regularly, these injuries are erythematous plaques with a dim canter that happen on the lips, tongue, genitalia, confront, and sacral zones. Intraepidermal CD8+ T cells are embroiled in these reactions. These T cells stay tranquil within the mended injuries; be that as it may, upon challenging with the offender sedate, they are enacted and discharge interferon-gamma and cytotoxic granules, accelerating another eruption. Sulfonamides and anticoagulants can cause settled sedate eruptions.

### Idiosyncratic Reactions

Type B reactions not mediated by immunological or inflammatory mechanisms are called idiosyncratic drug reactions. These reactions can arise because of genetic anomalies (eg, dapsone-induced hemolysis in a patient with G6PD deficiency) or exaggerated sensitivity at low doses (eg, tinnitus after a single dose of aspirin).

## Pseudoallergic Responses

Pseudoallergic medicate responses take after unfavourably susceptible medicate responses; in any case, they are not started by immunologic instruments. Regularly alluded to as “nonimmune touchiness reactions,” pseudoallergic responses emerge due to the coordinate actuation of fiery cells. Particularly, the Mas-Related G-Protein Coupled Receptor Part X2 is embroiled in coordinate pole cell incitement without requiring IgE interceded activation. A few drugs, such as fluoroquinolones and neuromuscular blocking specialists, can tie to these receptors and cause nonimmunogenic anaphylaxis. A commonly experienced illustration of a pseudoallergic response within the inpatient setting is vancomycin flushing disorder. Vancomycin specifically actuates the degranulation of basophils and pole cells, driving to histamine discharge and flushing. Interests, this response may be dodged by abating the mixture rate of vancomycin, which controls the discharge rate of histamine.

## Documentation of ADRs

The pharmacovigilance educational modules passed on around the world spur that all suspected drug-Related unfavorable occasions ought to be laid out. It takes interface on reports of the taking after:

(A) Each unfavorable impact suspected or happened by unused drugs and drugs of current issue

(B) Documentation of different drugs that cause ADRs, which incorporate passing, life-threatening Conditions, inability, hospitalization and inherent variations from the norm.

The noteworthy unfavorable response of any medicate ought to be informed inside seven days. The other Realities related to unfavorable occasions ought to be educated inside eight days. (Bates et al. 1995;

Classed et al 1997). The ADR shape can be collected through any pharmacovigilance middle. After looking into the frame, the middle advances it to the territorial middle and after that, it is Impelled to the zonal middle (Goldman 1998: Palaian et al. 2006:

Ravi Shankar et al. 2010). The points of interest are at that point factually assessed and sent to WHO-Uppsala Observing Committee.

## Benefits of ADR monitoring: -

An ADR checking and announcing program can outfit taking after benefits:

1. It caters data around quality and security of pharmaceutical items.
2. It starts risk-management plans.
3. It anticipates the unsurprising unfavorable impacts and makes a difference in measuring ADR adherence.
4. It instrument wellbeing care group i.e., patients, drug specialists and medical caretakers approximately antagonistic medicate Impacts and makes mindfulness with respect to ADRs. The fundamental objective of ADR observing is to reveal the quality and recurrence of ADRs and To distinguish the chance components that can cause the unfavorable reactions.

## CONCLUSION

Pharmacovigilance is the as it were way to guarantee the security of the sedate all through the life cycle. It is exceptionally much vital as the clinical trials have confinement to distinguish the uncommon and exceptionally uncommon ADRs. The information and data accessible with respect to security of any sedate is exceptionally much Critical to require suitable choice by medicate controllers to secure watch open wellbeing. Health Care experts are the most columnists of the ADRs. Be that as it may there are tall rates of Under-reporting detailed all inclusive. It is the major challenge of nowadays. In show disdain toward of those Restrictions, unconstrained detailing framework remains as a most broadly utilized strategy to report ADRs and is able to create flag of uncommon and exceptionally uncommon sorts of ADRs. On the off chance that all the wellbeing care Experts take ADR announcing as an ethical commitment and a major duty, we are able Make our world more secure than what is nowadays. Each detailing by wellbeing care experts is Vital, indeed in spite of the fact that center on the genuine unlabelled sorts of ADRs is more vital. There are critical impacts on the pharmacovigilance to create it more

utilitarian after the Concept has developed and day by day we are getting closer to the predetermination. It is our Obligation to guarantee well working of pharmacovigilance framework. ADR detailing ought to Be taken as a really vital obligation not as an additional clinical burden by wellbeing care experts To guarantee the more secure drugs utilize all through the world.

Reference:-

1. WHO Policy Perspectives on Medicines. Geneva: WHO; 2004. Geneva: World Health Organization. Looking at the Pharmacovigilance: ensuring the Safe use of medicines.
2. Dr.S.B.BHISE and Dr.S.B.BHISE : pharmacovigilance Book , Nirali Prakashan , page No – (1.1)
3. Lazaro, Pomeranz BH, Corey PN; Incidence of Adverse Drug Reactions in Hospitalized patients. JAMA, 198; 279: 1200-1205.
4. Board CA, Ranchi CL; Adverse Drug Reactions in United States Hospitals. Pharmacotherapy, 2006; 26(5): 601-08
5. Heath G, Colburn WA. An evolution of drug development and clinical pharmacology during the 20th century. Clinical Pharmacology 2000; 40:918-29.
6. The Importance of Pharmacovigilance. WHO 2002. Available via <http://apps.who.int/medicinedocs/en/d/Js4893e/1.html> Accessed Jan 20, 2012.
7. Shukla SS, Gidwani Bina, Pandey R, Rao SP, Singh V and Vyas Amber, “Importance of Pharmacovigilance in Indian Pharmaceutical Industry”, Asian Journal of Research in Pharmaceutical Science, 2, 2012, 04-08.
8. Jadhav Sudhakar and Chakraborty Guano, “Pharmacovigilance in India: Need of Hour”, Journal of Advances in Pharmacy and Healthcare Research (JAPHR), 1, 2011, 01-03.
9. The importance of pharmacovigilance. Geneva: World Health Organization; 2002.
10. Shukla SS, Gidwani Bina, Pandey R, Rao SP, Singh V and Vyas Amber, “Importance of Pharmacovigilance in Indian Pharmaceutical Industry”, Asian Journal of Research in Pharmaceutical Science, 2, 2012, 04-08.
11. Jadhav Sudhakar and Chakraborty Guano, “Pharmacovigilance in India: Need of Hour”, Journal of Advances in Pharmacy and Healthcare Research (JAPHR), 1, 2011, 01-03.
12. The importance of pharmacovigilance. Geneva: World Health Organization; 2002.
13. Joshi SR, Sapatnekar SM. Pharmacovigilance in India: how safe are the new drugs? How sure are We?. J Asoka Physicians In 2008;56:933-4.
14. Olsson S. Pharmacovigilance training with focus On India. In J Pharmacology 2008;40: S28-S30.
15. Biswas, A. K. Biswas setting standards for proactive pharmacovigilance in India: the Way forward. Indian Journal of pharmacology, 2007; 39: 124-128.
16. Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: a clinician’s guide to terminology, documentation, and reporting. Ann Intern Med. 2004 May 18;140(10):795-801.
17. Coleman JJ, Pontefract SK. Adverse drug reactions. Clin Med (Lond). 2016 Oct;16(5):481-485. [PMC free article] [PubMed]
18. Abbas M, Moussa M, Akel H. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 17, 2023. Type I Hypersensitivity. Reaction. [PubMed]
19. Bajwa SF, Mohammed RH. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 4, 2023. Type II Hypersensitivity Reaction. [PubMed]
20. Usman N, Annamaraju P. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 22, 2023. Type III Hypersensitivity Reaction. [PubMed]
21. Marwa K, Kondamudi NP. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Aug 12, 2023. Type IV

Hypersensitivity Reaction. [PubMed]

22. Uetrecht J. Current trends in drug-induced autoimmunity. *Autoimmun Rev.* 2005 Jun;4(5):309-14. [PubMed]
23. Shiohara T, Mizukawa Y. Fixed drug eruption: a disease mediated by self-inflicted responses of Intraepidermal T cells. *Eur J Dermatol.* 2007 May-Jun;17(3):201-8. [PubMed]
24. Mizukawa Y, Shiohara T. Fixed drug eruption: a prototypic disorder mediated by effector memory T cells. *Curr Allergy Asthma Rep.* 2009 Jan;9(1):71-7. [PubMed]
25. Ozkaya E. Fixed drug eruption: state of the art. *J Dtsch Dermatol Ges.* 2008 Mar;6(3):181-8. [PubMed]
26. McNeil BD, Pundir P, Meeker S, Han L, Undem BJ, Kulka M, Dong X. Identification of a mast-cell-specific receptor crucial for pseudo- allergic drug reactions. *Nature.* 2015 Mar 12;519(7542):237-41. [PMC free article] [PubMed]
27. Martel TJ, Jamil RT, King KC. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jan 25, 2023. Vancomycin Flushing Syndrome. [PubMed]
28. Moore N (2001). The role of clinical pharmacologist in management of ADRs. *Drug Safety*, 21(1): 1-7.

