ejpmr, 2022,9(7), 383-389

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

ANALYSIS OR INVESTIGATION & REPORTING OF ADVERSE DRUG REACTIONS REVIEW OF THE CURRENT SCENARIO, OBSTACLES AND POSSIBLE SOLUTIONS.

Vandna Dewangan[1]*, Saraswati Sahu[2], Ram Sahu[3] and Trilochan Satapathy[4]

[1]Department of Pharmacology, All India Institute of Medical Sciences, Tatibandh, G.E. Road, Raipur 492099 (C.G.).
[2]Department of Pharmacology, Columbia Institute of Pharmacy Near Vidhansabha, Village Tekari Raipur, (C.G.) India-493111.

***Corresponding Author: Vandna Dewangan**

Department of Pharmacology, All India Institute of Medical Sciences, Tatibandh, G.E. Road, Raipur 492099 (C.G.).

Article Received on 26/04/2022 **Article Revised on 17/05/2022** **Article Accepted on 07/06/2022**

ABSTRACT

Medication-related adverse events or adverse drug reactions (ADRs) are harmful events caused by medication. Adverse drug reactions (ADRs) could have profound effects on the patients' quality of life, as well as creating an increased burden on the healthcare system. Adverse drug reactions are one of the rising causes of morbidity and mortality internationally, and will continue to be a significant public health issue with the increased complexity in medication, to treat various diseases in an aging society. identified that the most causes of ADRs were drug related and due to allergies and This scoping review aims to provide a detailed map of the most common adverse drug reactions experienced in primary healthcare setting, the drug classes that are most commonly associated with different levels or types of adverse drug reactions, causes of adverse drug reactions, their prevalence and consequences of experiencing adverse drug reactions. The most common adverse drug reactions (ADRs) reported in the studies included in this review were those that are associated with the central nervous system (CNS), gastrointestinal system (GI) and cardiovascular system (CVS). Several classes of medications were reported to be associated with adverse drug reactions (ADRs).

KEYWORD: Adverse drug reactions, Pharmacovigilance, World health organization, Fatigue, blood cell count, Nerve injury, Dizziness, cardiovascular system (CVS), nervous system, gastrointestinal, Drug-related side effects.

HISTORY: The Pharmacovigilance and World health organization has put the definition of adverse drug reaction (ADR) as since 2002; the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problem.

Adverse reaction world health organization, since 1972; A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modifications of physiological function'.

Adverse event; Medical occurrence temporally associated with the use of a medicinal product, but not necessarily causally related.

The first remarkable adverse drug reaction (ADR) reported in Japan was anaphylactic shock caused by penicillin. Although intradermal testing for antibiotics had been exercised as prediction method of anaphylactic shock for a long time, it was discontinued in 2004 because of no evidence for prediction. The malformation of limbs, etc. caused by thalidomide was a global problem, and thalidomide was withdrawn from the market.

A careful medication history can assist a prescriber in understanding the patient's previous experiences with drug treatment, particularly in identifying previous ADRs that may preclude re-exposure to the drug And Preventing ADRs depends on avoiding treatment in cohorts of patients who are at increased susceptibility or providing treatment under a therapeutic plan that reduces the risk of an adverse effect (eg co-administration of other drugs, monitoring blood test results). Spontaneous reporting (using the Yellow Card Scheme in the UK) based on the suspicion of an ADR is an important part of Pharmacovigilance but, overall, ADRs are vastly underreported across healthcare settings and sectors. If in doubt, it is best to submit a report.

AIM AND OBJECTS

Analysis or Investigation & Reporting Of Adverse Drug Reactions Review of the Current Scenario, Obstacles and Possible Solutions.

- **PRIMARY OBJECT**
- The observation & Analysis of adverse drug reactions in primary care and profound effects on the patients.
- Adverse drug reactions (ADRs) – unintended, harmful events attributed to the use of medicines – occur as a cause of and during a significant proportion of unscheduled hospital admissions.
- **SECONDARY OBJECT**: - The severity & investigation of adverse drug reactions and their influencing factors or seriousness based on the ADR monitoring.

INTRODUCTION OF ADVERSE REACTION: - ADR In pharmacology, any unexpected harmful or dangerous reaction to a drug and unwanted effect caused by the administration of a drug. It can be defined as 'an appreciably harmful or unpleasant reaction resulting from an intervention related to the use of a medicinal product; adverse effects usually predict hazard from future administration and warrant prevention, or specific treatment, or alteration of the dosage regimen, or withdrawal of the product. The onset of the adverse reaction may be sudden or develop over time.[1] Also called an adverse drug event (ADE), adverse drug reaction (ADR), adverse effect or adverse event. The most common adverse drug reaction (ADR) constipation is nausea, vomiting, fatigue, alopecia, drowsiness, myelosuppression, skin reactions, anorexia, mucositis, diarrhoea and Medicines that have been particularly implicated in adverse drug reaction-related hospital admissions include anti-platelets, anticoagulants, cytotoxics, immunosuppressant's, diuretics, anti-diabetics and antibiotics.[1,2] Fatal ADRs, when they occur, are often attributable to hemorrhage, the most common suspected cause being an antithrombotic/anticoagulant co-administered with a non-steroidal anti-inflammatory drug (NSAID).[3]

The actual incidence of adverse drug reaction (ADRs) is impossible to assess, there is no doubt that adverse drug reaction (ADRs) have a significant impact on both the healthcare delivery and the drug development industries.[3,5,6] The impact of adverse drug reaction is to realize that approximately 5% of all hospital admissions are a direct result of adverse drug reaction, and unfortunately incidence has not changed over the past 30 years.[1,2,6,5]

Examples: - such adverse drug reactions (ADR) include rashes, jaundice, and anemia, a decrease in the white blood cell count, kidney damage, and nerve injury that may impair vision or hearing. These reactions tend to be more serious but typically occur in a very small number of people.

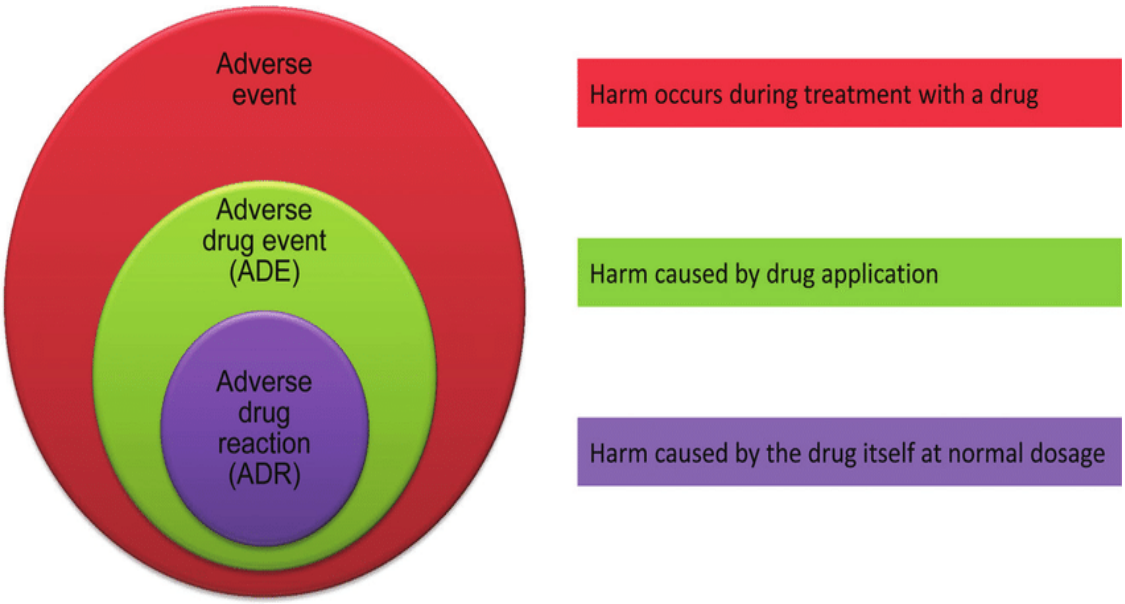

FIG: - ADVERSE DRUG REACTION (ADE/ADR).

CLASSIFICATION OF ADVERSE DRUG REACTION: - adverse drug reaction (ADRs) event occurs during drug therapy but does not necessarily have any causal relationship with the drug, whereas an adverse drug reaction is directly related to the drug and occurs in the course of its appropriate use. Drug reactions may be classified as.

- **Type A: - DOSE-RELATED REACTIONS** adverse effects at either normal dose or overdose.
  Examples: - Serotonin syndrome or anti-cholinergic effects of tricyclics**.**
- **Type B: - NON-DOSE-RELATED REACTIONS** any exposure is enough to trigger such a reaction.

Examples: - allergic or anaphylaxis reactions.

- **Type C: - DOSE AND TIME-RELATED REACTIONS** due to dose accumulation, or with prolonged use.
  Examples: - adrenal suppression with corticosteroids.
- **Type D: - TIME RELATED REACTIONS** due to prolonged use in a drug which doesn't tend to accumulate.
  Examples: - Tardive dyskinesia from antipsychotics.
- **Type E: - WITHDRAWAL REACTIONS** the undesired effects of ceasing the drug.
  Examples: - opiate withdrawal.
- **Type F: - UNEXPECTED FAILURE OF THERAPY** where a drug undesirably increases or decreases in efficacy.

Examples: - the decreased clearance of a drug by dialysis, or the decreased effect of antibiotics due to resistance.

ADVERSE INCIDENT: - An adverse incident is defined as an unexpected occurrence that led to, and could have led to, serious unintended, unexpected harm, loss, and damage.[8,9] Any incident which has occurred during use of the medical device which might lead to or might have led to death of a patient, or user or of other persons or to a serious deterioration in their state of health. Adverse effects can result from non-compliance, or non-adherence and incidents result in unintended harm to the patient by an act of commission, rather than by the underlying disease and condition.[5,6,8]

Examples

- A psychological event; for example, altered cognition.
- A laboratory event; for example, elevated creatinine.
- Ensure the treatment plan mitigates any possible adverse effects.

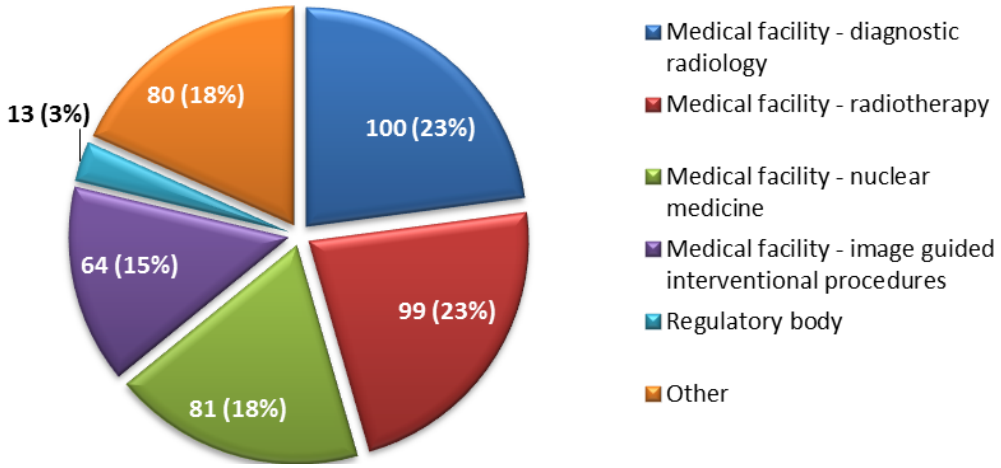

FIG: - DRUG ADVERSE INCIDENT.

REPORT ON ADVERSE INCIDENTS: - incident report is a formal recording of the facts related to a workplace accident, injury. Its primary purpose is to uncover the circumstances and conditions that led to the event in order to prevent future incidents.[9,10,8] Every incident report you file should contain a minimum of the following.

- Death.
- Abuse/neglect/exploitation.
- Major medication incident.
- Altercation requiring medical intervention.
- Involvement with law enforcement.
- Member elopement/missing.
- Member major injury, near miss, property damage, or theft.
- Member major illness.

Here are some of the vital elements to include in your description of the incident.

- Type of incident (injury, near miss, property damage, or theft).
- Location (Address).
- Date/time of incident.
- Name or family details.
- Name of supervisor.
- Description of the incident, including specific job site location, the sequence of events, and the results of the event.
- Whether or not proper PPE was being used.
- The root cause(s) of the incident.
- Associated hazards raised and resolved following the event.
- The affected individual's version of the events.
- Actions taken by concerned individuals after the incident.
- Description of injuries.

- How the decision was made to call (or not to call) emergency services.
- Treatment required.
- Witness name(s).
- Witness statements.
- Photographs of the scene.

CAUSES EFFECT ON ADVERSE DRUG REACTIONS: - The most common cause of adverse drug reactions (ADR); among older adults, oral anticoagulants are leading to emergency room visits and emergent hospitalizations.[5,8,9] They increase the possibility of the occurrence of adverse drug reactions include; extremes of age, gender, multiple drugs, disease state, drug doses, past history of adverse drug reactions and allergy, genetic factors, large doses, lack of patients' education and patients' co-morbidities and many other factors.[5,7,9] Adverse effects usually causes effect on predict hazard from future administration and warrant prevention, or specific treatment, or alteration of the dosage regimen.[1]

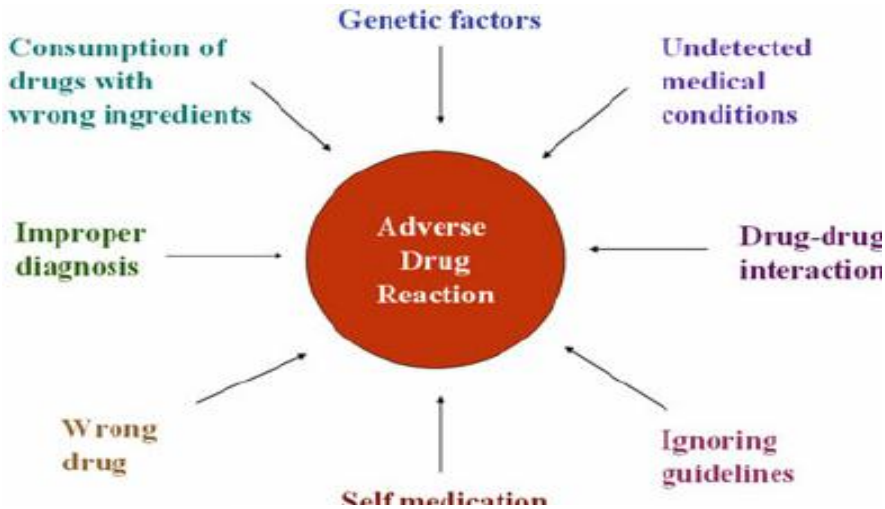

FIG: - CAUSES EFFECT ON ADRs.

COMMON SIDE EFFECT OF ADVERSE DRUG REACTIONS:- side effect is considered serious if the result is: death; life-threatening; hospitalization; disability or permanent damage; or exposure prior to conception or (Congenital anomaly)during pregnancy caused birth defect and increase or decrease the dose (amount) of a drug that to be take and Intervention required to prevent permanent impairment or damage. Common side effects by drug type.

SR. NO.	DRUG TYPE	COMMON SIDE EFFECT
1	Antibiotics	Nausea, diarrhea, rash, yeast infection, fever
2	Antihistamines, allergy medications	Drowsiness, insomnia, weakness
3	Diabetes medications	Nausea, heartburn, fatigue, dizziness
4	Asthma medications	Nervousness, sweating, nausea, vomiting
5	Heart and blood pressure medications	Dizziness, drowsiness, chest pain, loss of appetite, leg pain
6	Pain relievers	Stomach upset, tinnitus, nausea
7	Antidepressants	Weight gain, insomnia, nervousness

SERIOUSNESS ADVERSE EVENT: - seriousness of Adverse Drug Reaction is any event or reaction that results in death, a life threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions and adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the investigator or sponsor, A harmful or abnormal result.[11,13] An adverse effect may be caused by administration of a medication or by exposure to a chemical and be indicated by an untoward result its occurrence places the patient or subject at immediate risk of death.[13,14,16,17] Their seriousness adverse event function like.

- Death.
- Life-threatening.
- Hospitalization (initial or prolonged).
- Disability or Permanent Damage.
- Congenital Anomaly/Birth Defect.
- Required Intervention to Prevent Permanent Impairment or Damage (Devices).
- Other Serious (Important Medical Events).

REDUCE ADVERSE DRUG REACTIONS: - Adverse drug reaction occur in 15% or more of older patients presenting to offices, hospitals, and extended

care facilities.[15,16,20] These events are potentially preventable up to 85% of the time.[15] Common serious manifestations include falls, orthostatic hypotension, heart failure, and delirium. The most common causes of death are gastrointestinal or intracranial bleeding and renal failure.[21,25] Antithrombotic and anti-diabetic medications, diuretics, and non steroidal anti-inflammatory drugs cause most of the preventable hospital admissions due to adverse drug events.[26] Strategies to reduce the risk of adverse drug events include discontinuing medications, prescribing new medications sparingly, reducing the number of prescribers, and frequently reconciling medications. Screening tool of older persons' potentially inappropriate prescriptions and screening tool to alert doctors to right treatment criteria can help identify medications causing adverse drug events.[28,29,5] Not all potentially inappropriate medications can be avoided. Clinicians should involve patients in shared decision making and individualize prescribing decisions based on medical, functional, and social conditions; quality of life; and prognosis.[29,30,32]

- Avoid and be vigilant of high-risk drugs.
- Discontinue unnecessary drugs.
- Consider drugs as a cause of any new symptom.
- Avoid treating side effects with another drug.
- Avoid drug-drug interactions.
- Adjust dosing based on age and creatinine clearance.
- Address non-adherence.

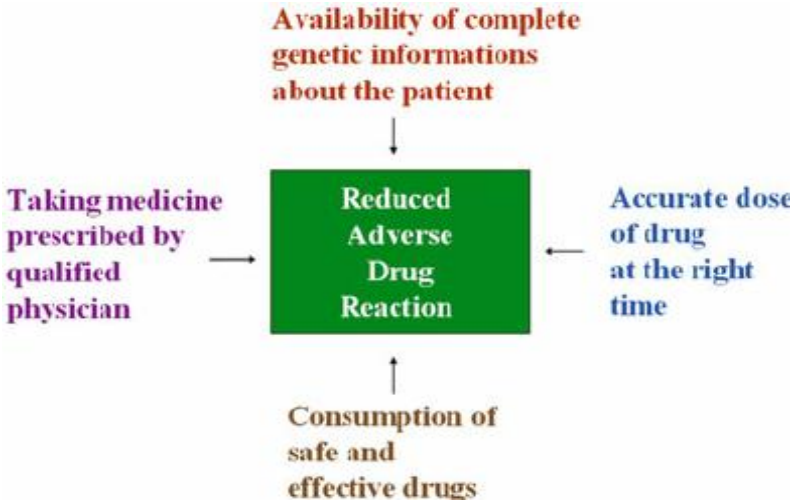

FIG: - REDUCE ADVERSE DRUG REACTIONS.

RESULT

The final search yielded a total of 29 citations for inclusion published over a 14-year period that primarily focused on investigating the different types of adverse drug reactions in primary healthcare. The incidence of adverse drug reaction reported in the studies ranged between 16% and up to 90% in cases. Idiosyncratic adverse reactions were not very commonly reported in the literature.[5,8,12] This is mainly because it is hard to predict and these reactions are not associated with drug doses or routes of administration.[28] The most causes of adverse events were related to drug related and allergies. Idiosyncratic adverse reactions were not very commonly reported. The most common adverse drug reactions reported in the studies included in this review were those that are associated with the central nervous system, gastrointestinal system and cardiovascular system. Several classes of medications were reported to be associated with adverse events.[28,29,30,31]

CONCLUSION

This scoping review considered quantitative study designs including experimental, descriptive and observational studies reporting any quantitative data that can be included in the review and the concept of interest for the scoping review was the type of adverse drug reactions experienced by patients and the classes of medications associated with these adverse drug events and the study has reported that as high as 85% of all aged care residents had medication discrepancies after the transition from hospital to primary care setting.[25] Most of the adverse medication events are associated with prescription errors in general practice. Medication errors in general practice had a prevalence rate of 15% in hospital according to a large retrospective case review study.[26] With the incorporation of technology in healthcare system, the implementation of computerized prescribing systems also has a range of medication error rates that may lead to mild or severe adverse drug events. Drug complication of the patients taking prescription drugs, 395 (20%) reported having had a drug complication, defined as a problem or symptom in the last year related to their prescription medications and adverse effect of a drug produced by an exaggeration of the effect that produces the therapeutic response. The considered participants of any age and any condition treated or managed from any primary care services.[31,32,35]

DISCUSSION

The causes and nature of adverse drug events are often complex and multifactorial. The types of adverse

reactions are classified into the following categories: dose or drug related, allergic or idiosyncratic reactions.[24] Dose-related and drug related adverse drug reactions are usually related to the dose of the medication and are usually predictable but sometimes unavoidable. The allergic drug reaction is when the patients develop an inappropriate reaction to the medication, which mostly could be avoided with a skin test prior to or through effective consultation and communication between primary care facilities and patients. The context of the review was the primary care setting.[28] These include; primary health care organizations, general practitioner clinics, pharmacies, outpatient clinics and any other clinics that do not classify patients as inpatients. We only excluded hospital patients.[26]

A total of 12 studies out of the 29 included studies addressed specific classes of medications such as; anti-tuberculosis drugs (ATD), antipsychotics, anti-epileptics, antidepressants and mood stabilizers, antibiotics, insulin and oral diabetic medications (ODM), biological, and anti-Cholinergic drugs including dementia medications.[15] The remainder of the studies covered other classes of medications such as beta blockers, analgesics, benzodiazepines, lipid modifying agents, musculoskeletal drugs, stimulants, anti-platelets, selective serotonin reuptake inhibitors and skin preparations. The classes of drugs that were associated with the highest ADRs reported in the included studies were drugs used for the cardiovascular system (beta-adrenergic blocking agents, diuretics, Angiotensin converting enzyme inhibitors "ACE") warfarin, opioids analgesics and antipsychotic agents.[20,24,25]

ACKNOWLEDGED

I am very thankful to Principal (Dr Amit Roy), & Columbia Institute of pharmacy tekari Raipur Chhattisgarh and my teachers for their valuable guidance. I would like to thank all monitors who participated in data collection for this study and structures involved into the project: Himanshu pandey, Ramu Singh, Saraswati Sahu, Dr.Trilochan Sathpathy (HOD- Pharmacology), Dr.Aashish Dewangan, Dr.Ram Sahu, Rajani Yadav, and Mogesh Dewangan.

I am also thankful to my friends, school teacher and colleagues for their time to time support. Especially thanks to my family and also all India institutes of medical sciences, Raipur (C.G.) hospital staff for informatics support and help for collecting of adverse drugs reaction (ADRs) reports at hospitalized patients.

REFERENCE

1. Van Der Hooft CS, Sturkenboom MC, van Grootheest K, Kingma HJ, Stricker BH. Adverse drug reaction-related hospitalizations. Drug safety, 2006 Feb; 29(2): 161-8.
2. McLernon DJ, Bond CM, Hannaford PC, Watson MC, Lee AJ, Hazell L, Avery A. Adverse drug reaction reporting in the UK. Drug safety, 2010 Sep; 33(9): 775-88.
3. van Hunsel F, Härmark L, Pal S, Olsson S, van Grootheest K. Experiences with adverse drug reaction reporting by patients. Drug safety, 2012 Jan; 35(1): 45-60.
4. Faich GA. US adverse drug reaction surveillance 1989–1994. Pharmacoepidemiology and drug safety, 1996 Nov; 5(6): 393-8.
5. Van Grootheest K, de Graaf L, de Jong-van den Berg L. Consumer adverse drug reaction reporting. Drug safety, 2003 Apr; 26(4): 211-7.
6. Herdeiro MT, Figueiras A, Polónia J, Gestal-Otero JJ. Physicians' attitudes and adverse drug reaction reporting. Drug safety, 2005 Sep; 28(9): 825-33.
7. Hajjar ER, Hanlon JT, Artz MB, Lindblad CI, Pieper CF, Sloane RJ, Ruby CM, Schmader KE. Adverse drug reaction risk factors in older outpatients. The American journal of geriatric pharmacotherapy, 2003 Dec 1; 1(2): 82-9.
8. de Langen J, van Hunsel F, Passier A, de Jong-van den Berg L, van Grootheest K. Adverse drug reaction reporting by patients in The Netherlands three years of experience. Drug Safety, 2008 Jun; 31(6): 515-24.
9. Bateman DN, Sanders GL, Rawlins MD. Attitudes to adverse drug reaction reporting in the Northern Region. British journal of clinical pharmacology, 1992 Nov; 34(5): 421.
10. Doherty MJ. Algorithms for assessing the probability of an adverse drug reaction. Respiratory Medicine CME, 2009 Jan 1; 2(2): 63-7.
11. Belton KJ, Lewis SC, Payne S, Rawlins MD, Wood SM. Attitudinal survey of adverse drug reaction reporting by medical practitioners in the United Kingdom [see comments]. British journal of clinical pharmacology, 1995 Mar; 39(3): 223-6.
12. Huynh T, He Y, Willis A, Rüger S. Adverse drug reaction classification with deep neural networks. Coling.
13. Bate A, Lindquist M, Edwards IR, Olsson S, Orre R, Lansner A, De Freitas RM. A Bayesian neural network method for adverse drug reaction signal generation. European journal of clinical pharmacology, 1998 Jul; 54(4): 315-21.
14. Oshikoya KA, Awobusuyi JO. Perceptions of doctors to adverse drug reaction reporting in a teaching hospital in Lagos, Nigeria. BMC clinical pharmacology, 2009 Dec; 9(1): 1-8.
15. Green CF, Mottram DR, Rowe PH, Pirmohamed M. Attitudes and knowledge of hospital pharmacists to adverse drug reaction reporting. British journal of clinical pharmacology, 2001 Jan; 51(1): 81-6.
16. Baniasadi S, Fahimi F, Shalviri G. Developing an adverse drug reaction reporting system at a teaching hospital. Basic & clinical pharmacology & toxicology, 2008 Apr; 102(4): 408-11.
17. Muehlberger N, Schneeweiss S, Hasford J. Adverse drug reaction monitoring—cost and benefit considerations. Part I: frequency of adverse drug

reactions causing hospital admissions. Pharmacoepidemiology and drug safety, 1997 Oct; 6(S3): S71-7.
18. Kardaun SH, Sekula P, Valeyrie- Allanore L, Liss Y, Chu CY, Creamer D, Sidoroff A, Naldi L, Mockenhaupt M, Roujeau JC, RegiSCAR Study Group. Drug reaction with eosinophilia and systemic symptoms (DRESS): an original multisystem adverse drug reaction. Results from the prospective R egi SCAR study. British Journal of Dermatology, 2013 Nov; 169(5): 1071-80.
19. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. British journal of clinical pharmacology, 2008 Feb; 65(2): 210-6.
20. Margraff F, Bertram D. Adverse drug reaction reporting by patients: an overview of fifty countries. Drug safety, 2014 Jun; 37(6): 409-19.
21. Bigby M, Stern RS. Adverse reactions to isotretinoin: a report from the Adverse Drug Reaction Reporting System. Journal of the American Academy of Dermatology, 1988 Mar 1; 18(3): 543-52.
22. Van der Linden CM, Kerskes MC, Bijl AM, Maas HA, Egberts AC, Jansen PA. Represcription after adverse drug reaction in the elderly: a descriptive study. Archives of internal medicine, 2006 Aug 14; 166(15): 1666-7.
23. Choi NK, Park BJ. Adverse drug reaction surveillance system in Korea. Journal of preventive medicine and public health, 2007; 40(4): 278-84.
24. Angamo MT, Chalmers L, Curtain CM, Bereznicki LR. Adverse-drug-reaction-related hospitalizations in developed and developing countries: a review of prevalence and contributing factors. Drug safety, 2016 Sep; 39(9): 847-57.
25. Zaki S. Adverse drug reaction and causality assessment scales. Lung India, 2011 Apr 1; 28(2): 152.
26. Bäckström M, Ekman E, Mjörndal T. Adverse drug reaction reporting by nurses in Sweden. European journal of clinical pharmacology, 2007 Jun; 63(6): 613-8.
27. Lardon J, Abdellaoui R, Bellet F, Asfari H, Souvignet J, Texier N, Jaulent MC, Beyens MN, Burgun A, Bousquet C. Adverse drug reaction identification and extraction in social media: a scoping review. Journal of medical Internet research, 2015; 17(7): e171.
28. Gony M, Badie K, Sommet A, Jacquot J, Baudrin D, Gauthier P, Montastruc JL, Bagheri H. Improving adverse drug reaction reporting in hospitals. Drug safety, 2010 May; 33(5): 409-16.
29. Tan WC, Ong CK, Kang SL, Razak MA. Two years review of cutaneous adverse drug reaction from first line anti-tuberculous drugs. Medical Journal of Malaysia, 2007 Jun 1; 62(2): 143.
30. Gedde- Dahl A, Harg P, Stenberg- Nilsen H, Buajordet M, Granas AG, Horn AM. Characteristics and quality of adverse drug reaction reports by pharmacists in Norway. Pharmacoepidemiology and drug safety, 2007 Sep; 16(9): 999-1005.
31. Montastruc F, Bagheri H, Lacroix I, Damase-Michel C, Chebane L, Rousseau V, Jouanjus E, Lapeyre-Mestre M, Durrieu G, Montastruc JL. Adverse drug reaction reports received through the mobile app, VigiBIP®: a comparison with classical methods of reporting. Drug safety, 2018 May; 41(5): 511-4.
32. de Araújo Lobo MG, Pinheiro SM, Castro JG, Momenté VG, Pranchevicius MC. Adverse drug reaction monitoring: support for pharmacovigilance at a tertiary care hospital in Northern Brazil. BMC Pharmacology and Toxicology, 2013 Dec; 14(1): 1-7.
33. Mannesse CK, Van Puijenbroek EP, Jansen PA, Van Marum RJ, Souverein PC, Egberts TC. Hyponatraemia as an adverse drug reaction of antipsychotic drugs. Drug safety, 2010 Jul; 33(7): 569-78.
34. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. The lancet, 2000 Oct 7; 356(9237): 1255-9.
35. Pirmohamed M, Breckenridge AM, Kitteringham NR, Park BK. Adverse drug reactions. Bmj. 1998 Apr 25; 316(7140):1295-8.
36. Mannesse CK, Derkx FH, De Ridder MA, Man In't Veld AJ, Van der Cammen TJ. Contribution of adverse drug reactions to hospital admission of older patients. Age and ageing, 2000 Jan 1; 29(1): 35-9.
37. Chowta MN, Kamath P, Ramapuram JT, Shenoy KA, Hadigal S. Evaluation of adverse drug reaction profile of drugs used as first-line antiretroviral therapy. Interdisciplinary perspectives on infectious diseases, 2018 Aug 2; 2018.