ISSN: 0975-5160

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2021; 11(4); 75-85

Original Research Article

A Cross-sectional Retrospective Study to Determine the Pattern of Reported Adverse Drug Reactions with Reference to Specific Drug Class and Organ System

Sachida Nand Sachit[1], Swetabh Verma[2], Asha Kumari[3], V K Mishra[4]

[1]Tutor, Department of Pharmacology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India.

[2]Tutor, Department of Pharmacology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India.

[3]Assistant Professor, Department. of Pharmacology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India.

[4]Professor, Department of Pharmacology, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India.

Received: 10-08-2021 / Revised: 15-09-2021 / Accepted: 21-10-2021
Corresponding author: Dr. Swetabh Verma
Conflict of interest: Nil

Abstract

Aim: The pattern of reported adverse drug reactions with reference to specific drug class and organ system. **Methods:** A cross-sectional retrospective study was conducted in the Department of Pharmacology Darbhanga Medical College, Darbhanga Bihar India for 10 months (1 October 2020 - 30 July 2021). The department of pharmacology, of our college has been a recognized ADR monitoring centre (AMC) under the PvPI. **Results:** The highest percentage of ADRs 21.46% were reported among the age group of 40-49 years followed by 17.54% of ADRs among the age group of 50-59 years. The most common therapeutic class of drugs causing ADRs, were antimicrobial agents (36.07%) followed by drugs acting on the central and peripheral nervous systems including the NSAIDS (7.49%), anti- epileptics (4.08%) and anti-depressants (2.72%). 12.92% of ADRs are caused by hormones like the corticosteroids and anti-diabetic drugs. 8.16% of ADRs were reported by the CVS drugs like the antihypertensive drugs and anti- angina drugs. 6.80% of ADRs were reported with anticoagulants, anti-platelets and statins. A total 9.52% of ADRs were reported with other classes of drugs like drugs acting on the respiratory system, diuretics, anti-emetics, antacids and antihistaminic. Also, vaccines, immuno suppressants, vitamins and herbal medicines have been reported to cause ADRs. The clinical presentation of affected system shows that, the skin is the most common affected organ system (n=97; 25.39%) and gastrointestinal tract system (n=74; 19.37%). Other organ systems involved are the central and peripheral nervous system, elevated liver and renal function tests and electrolyte disturbances. **Conclusion:** The skin and subcutaneous is the most commonly affected specific organ class. 104 ADRs were reported under the seriousness criteria. The outcome of reported ADRs was recovering in 52.10 and 81% of ADRs were probable as per WHO causality assessment scale.

Keywords: ADRs, immuno suppressants, skin

Introduction:

Adverse drug reaction (ADR) has been defined by the World Health Organization (WHO) as "any response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function"[1]. A meta analysis of 39 epidemiological studies by Lazarou et al., found that ADRs ranked fourth and sixth leading causes of deaths in USA[2]. Considering the importance of monitoring ADRs to improve public health, Pharmacovigilance programme of India (PvPI) was started in 2010[3]. As per this program, ADR monitoring centers have been started in many medical institutions all over the country to estimate the frequency of ADRs occurring with various drugs among the Indians. It has been reported that ADRs account for 5% of all hospital admissions and occur in 10-20% of hospitalized patients[4]. An overall incidence of serious and fatal ADR among the hospitalized patients is 6.7 and 0.32% respectively[4,5]. The overall ADR rate is estimated to be 6.5 and 28% of these are preventable[5]. ADR incidence in Indian population ranges between 1.8-25 with 8% resulting in hospitalization[6]. The recent epidemiological studies have estimated that adverse drug reactions are the fourth to sixth leading causes of death[7,4]. Identification and reporting of these ADRs is extremely crucial as it may possibly help the treating physicians on being vigilant while prescribing those drugs and achieving substantial reduction in health care cost[8]. The pharmacovigilance programme of India (PvPI) is an initiative to address this issue. Activities under PvPI include collection, reporting and follow up of ADRs occurring in the patients[9]. The spontaneous reporting system has resulted in many marketed drugs being withdrawn for safety concerns[10,11]. It is important to identify the risks for ADRs, henceforth the common drugs causing ADRs, their therapeutic class and concomitant drugs used should be known. Also, ADR specific data such as type of reaction, system affected and probable causes will be of great help to minimize the ADRs[12]. Hence, the present study was undertaken to study the pattern of reported ADRs with reference to specific drug class and organ system in a tertiary care hospital.

Materials and methods

A cross-sectional retrospective study was conducted in the Department of Pharmacology Darbhanga medical college Darbhanga Bihar India for 10 months (1 October 2020 – 30 July 2021) after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

The department of pharmacology, of our college has been a recognized ADR monitoring centre (AMC) under the PvPI. A patient safety pharmacovigilance associate was appointed by the PvPI, Indian pharmacopoeia commission (IPC), bihar. The AMC also spreads awareness about the need and importance of the pharmacovigilance. This is achieved by regular sharing of drug safety alerts in the in-patient and out-patient departments and also by emphasizing the need for reporting ADRs and conducting sensitization sessions to health care professionals (HCPs) and the para-medical staff. In parallel to pharmacovigilance,

hemovigilance and adverse event following immunization (AEFI) surveillance is also conducted at AMC.

Individual case safety reports (ICSRs) of all patients of suspected adverse drug reactions seen in various out- patient departments and admitted in the wards of the hospital were included in the study. The central drug standard control organization (CDSCO) ADR reporting forms were used for collection of the data. The ADRs identified and reported by the physicians of the hospital were collected and reported to the AMC. The collected information included patients initials, age, gender, reporting department of the hospital, details of the suspected adverse drug reaction, duration of the reaction, suspected drug history, temporal correlation with the drug and concomitant medications. Relevant lab investigations and relevant medical history were recorded in the ADR form. The ICSRs were analysed for patient demography, causality and severity. Causality assessment of the ADR were done by the causality assessment committee by using the WHO-UMC causality assessment scale. The seriousness criteria of the reaction and the outcome of the patient were monitored by using guidance document for spontaneous adverse drug reaction reporting version: 1.0 IPC, NCC– PvPI[13]. The anatomical therapeutic chemical classification (ATC) and the medical dictionary for regulatory activities (MedDRA) version-23.0 are used to code active principles and reactions respectively. The different types of reported ADRs were classified according to the medical dictionary for regulatory activities (MedDRA) and system organ class (SOC)[14]. The ADR reports were analysed for the above data using descriptive statistics.

Results

Total number of ADRs reported during the study period were 382. Among them, 191 ADRs were reported in male patients and 191 ADRs in female patients (Table 1).

Table 1: Gender wise distribution of the ADRs

Gender	No. of patients (n=382)	Percentage (%)
Male	191	50
Female	191	50

The highest percentage of ADRs 21.46% were reported among the age group of 40-49 years followed by 17.54% of ADRs among the age group of 50-59 years (Table 2).

Table 2: Age wise distribution of the ADRs

Age (Years)	No. of patients (n=382)	Percentage (%)
0-9	28	7.32
10-19	18	4.72
20-29	53	13.88
30-39	61	15.96
40-49	82	21.46
50-59	67	17.54
60-69	45	11.78
70-79	22	5.76
80-89	6	1.58

The seriousness criteria include hospitalization, life- threatening, disability, congenital anomaly and required intervention, of the 382 ADRs reported, 104 ADRs were

reported as serious accounting for 27.2% of the ADRs. 89% of serious reports required hospitalization, 4% reported were life-threatening and 4% required intervention, 2% were of congenital anomaly and 1% showed disability (Table 3).

Table 3: Classification of seriousness criteria

Seriousness criteria	No. of patients (n=104; 27.2%)
Hospitalization	93 (89)
Life-threatening	4 (4)
Required intervention	4 (4)
Congenital anomaly	2 (2)
Disability	1 (1)

The outcome of the reported ADRs were grouped as recovered, recovering, recovered with sequelae, fatal, not recovered and unknown. Out of 382 ADRs reported, 52.10% patients were recovering and 44.5% patients have recovered (Table 4).

Table 4: Outcome parameters of reported ICSRs

Outcome	No. of patients (n=382)	Percentage (%)
Recovering	199	52.10
Recovered	170	44.5
Recovered with sequelae	6	1.58
Unknown	4	1.04
Not recovered	2	0.52
Fatal	1	0.26

The WHO-UMC causality assessment scale has grouped ADRs as certain, probable, possible, unlikely, unclassified and unclassifiable. Majority of the reports were rated as probable (n=310; 81%) and 72 (19%) ICSRs were possible
(Table 5).

Table 5: WHO causality assessment

Causality	No. of ICSRs (n=382)	Percentage (%)
Probable	310	81
Possible	72	19

The most common therapeutic class of drugs causing ADRs (Table 6) were antimicrobial agents (36.07%) followed by drugs acting on the central and peripheral nervous systems including the NSAIDS (7.49%), anti-epileptics (4.08%) and anti-depressants (2.72%). 12.92% of ADRs are caused by hormones like the corticosteroids and anti-diabetic drugs. 8.16% of ADRs were reported by the CVS drugs like the antihypertensive drugs and anti- angina drugs. 6.80% of ADRs were reported with anticoagulants, anti-platelets and statins.

A total 9.52% of ADRs were reported with other classes of drugs like drugs acting on the respiratory system, diuretics, anti-emetics, antacids and antihistaminic. Also, vaccines, immuno suppressants, vitamins and herbal medicines have been reported to cause ADRs.
The clinical presentation of affected system (Table 7) shows that, the skin is the most common affected organ system (n=97;

25.39%) and gastrointestinal tract system (n=74; 19.37%). Other organ systems involved are the central and peripheral nervous system, elevated liver and renal function tests and electrolyte disturbances.

Table 6: Most common therapeutic class of drugs causing ADRs

Class of drug	Number of cases	Percentage of cases (%)
Anti-microbial agents	53	36.07
Antibiotics	37	25.19
Anti-retroviral	9	6.12
Anti-tubercular	3	2.04
Anti-amoebic	2	1.36
Anti-viral	2	1.36
Drugs acting on central nervous system	21	14.29
NSAIDS	11	7.49
Anti-epileptics	6	4.08
Anti-depressants	4	2.72
Hormones	19	12.92
Anti-diabetics	8	5.44
Corticosteroids	7	4.76
Other hormones	4	2.72
Others	14	9.52
Respiratory system	4	2.72
Anti-emetics	3	2.04
Antacids	3	2.04
Diuretics	2	1.36
Anti-histaminic	2	1.36
Drugs acting on cardiovascular system	12	8.16
Anti-hypertensives	7	4.76
Cardiac glycosides	3	2.04
Anti-anginal	2	1.36
Drugs acting on blood and blood forming organs	10	6.80
Anti-coagulants	6	4.08
Anti-platelets	2	1.36
Statins	2	1.36
Immuno pharmacology	10	6.80
Immuno suppressants	6	4.08
Vaccines	4	2.72
Miscellaneous	8	5.44
Vitamins and minerals	6	4.08
Herbal medicines	2	1.36
Total	147	100

The major clinical presentation of skin and subcutaneous tissue is the generalized rash, itching, urticaria, lichenoid rash, exfoliative dermatitis and hyperpigmentation of the skin. Diarrhea, nausea, constipation, abdominal pain and vomiting are the common ADRs reported in the gastrointestinal system. In the central and peripheral nervous system, headache, dizziness, involuntary movements, burning sensation of the feet and seizures are the commonly reported ADRs. The liver function tests showed increased triglycerides, increased total cholesterol and increased bilirubin levels. Blood and the lymphatic system reported anemia, pancytopenia and thrombocytopenia. Renal and urinary systems have reported acute kidney injury, hematuria and renal failure. The immune system has reported anaphylactic reactions, facial edema and red man syndrome.

Table 7: Details of affected body system and clinical presentation of the adverse drug reactions

Body system affected as per SOC	Clinical presentation of the affected system (number of ADRs)	Number ADRs	Percentage of ADRs (%)
Skin and subcutaneous system	Generalized rash (33), Itching (24), Urticaria (12), Maculopapular rash (10), Lichenoid rash (9), Exfoliative dermatitis (3), Erythematous rash (2), Sweating (2), Steven Johnson syndrome (1), Hyperpigmentation of skin (1).	97	25.39
Gastrointestinal system	Diarrhoea (18), Nausea (14), Constipation (10), Abdominal pain (7), Vomiting (5), Oral ulcer (5), Upper gastrointestinal bleed (4), Gum bleed (3), Gastritis (3), Flatulence (2), Rectal bleed (1), Hematemesis (1), Esophagitis (1).	74	19.37
Central and peripheral nervous system	Headache (14), Dizziness (7), Involuntary movements (6), Burning sensation of feet (5), Seizure (4), Peripheral neuropathy (2), Intracranial bleed (1).	39	10.21
Investigations (serum electrolytes, LFT, RFT)	Increased triglycerides (18), Hyponatremia (5), Hypokalaemia (4), Increased total cholesterol (4), Increased serum creatinine (3), Increased serum bilirubin (2), Hyperkalaemia (1).	37	9.68
Blood and lymphatic system	Anaemia (17), Pancytopenia (6), Thrombocytopenia (1), Lymphadenopathy (1).	25	6.54
General disorders and administration site conditions	Fever (7), Injection site pain (5), Fatigue (4), Injection site swelling (3), Injection site irritation (2), Chills (2), Pedal oedema (1).	24	6.28
Endocrine system	Hypoglycaemia (11), Hyperglycinemia (6), Hypothyroidism (1), Cushing syndrome (1)	19	4.98
Immune system	Anaphylactic reaction (8), Facial oedema (5), Fixed drug eruption (1), Red man syndrome (1)	15	3.93
Renal and urinary system	Acute kidney injury (9), Haematuria (2), Renal failure (2).	13	3.41
Cardiovascular system	Hypotension (3), Bradycardia (2), Palpitations (2), Prolonged QT interval (2), Chest pain (1).	10	2.62
Musculoskeletal and connective tissue disorders	Arthralgia (3), Myalgia (3), Back pain (2), Neck stiffness (1).	9	2.36
Hepatobiliary system	Jaundice (5), Hepatitis (3).	8	2.09

Respiratory system	Epistaxis (3), Haemoptysis (1), Cough (1).	5	1.30
Psychiatric disorders	Insomnia (3).	3	0.79
Eye disorders	Blurred Vision (2), Cataract (1).	3	0.79
Reproductive system	Vaginal itching (1)	1	0.26
Total		382	100

Discussion

ADRs are common causes of mortality and morbidity worldwide, and represent a fundamental economic burden on any given health system, ADRs that occur in medical practice cannot always be predicted by premarket data owing to intrinsic limitations of clinical trials such as inadequate number of patients and limited follow-up time. Therefore, post-marketing surveillance is a necessary tool for early detection of severe and unexpected ADRs.

Spontaneous ADR reporting activity is important to monitor known and unknown adverse effects of medicines. It has played an important role in the detection of serious and unusual ADRs after marketing, when the drug is actually being prescribed by the clinicians. This activity of continuous vigil on the drug related ADRs has resulted in withdrawal of quite a few drugs in the past such as refecoxib, cisapride, terfenadine etc. ADRs have to be considered as one of the major causes of iatrogenic disease with detrimental effect on patient wellbeing and overall health care system[15].

The present study was done to analyze the ICSR forms (n=382) collected from various departments, shows equal distribution of ADRs among both the genders. This was a comparable finding to that reported by Jose and Belhekar et al.[15,16] However, the spontaneous reporting studies in our country had observed high percentage of ADRs in females[17-22]. The various factors influence the drug metabolism and response of individuals which include differences in body mass index, genetic constitution and differences in levels of various enzymes responsible for drug metabolism[23].

In present study, 21.46% of ADRs were reported in age group of 40-49 years, 17.54% of ADRs were reported in age group 50-59 years and 19.12% of ADRs were reported in the elderly group. Since previous studies have stated that advanced age increases the risk of ADR due to pharmacokinetic and pharmacodynamics changes, the present study was comparable to the findings reported by Scheneiderjk, Belhekar, David, Ramesh, and Arulmani et al.[6,16-19,24,25]

The seriousness criteria as observed in the present study is 27.2% (n=382). The present study reports of seriousness criteria were different from the studies reported by Singh, Venkatasubbaiah and Sneha et al which was 14.93% (n=154); 5.12% (n=254) and 39% (n=177) respectively[21,26,27].

The outcome parameter of the reported ICSRs showed 52.10% as recovering and 44.50% as recovered which were comparable with studies done by Sneha et.al, which reported cases with recovering outcome parameter as 79% and recovered as 13%, Hemavathy et al reported cases with recovering outcome parameter as 63.28% and recovered as 19.53%[27,28].

According to WHO causality assessment of the ICSRs showing the relatedness or the likelihood of the drugs with reactions is probable (81%), in most of the cases. Where the earlier studies report by Badyal, Sood and Shrivastava et al showed probable (83.5, 55 and 55.89% respectively) were more[12,29,30]. However, compared with other studies, the study reported by Venkatasubbaiah and Hemavathy et al showed more possible (48.82 and 71.09%) followed by

probable (27.17 and 28.12%) and none of the ICSRs of present study were reported as certain[26,27].

In the present study, the most common therapeutic class of drug implicated in ADRs were the antimicrobial agents (36.07%) which included the antibiotics, anti-retroviral and anti-tubercular agents followed by other class of drugs like NSAIDS, anti-epileptics and hormones. Earlier studies have also reported ADRs due to same class of drugs[15,31].

The ADRs due to anti-retroviral and anti-tubercular are immunologically mediated hypersensitivity reactions and are mostly dose dependent in nature. This indicates, that a dose monitoring and follow up of patients is essential in the initial month for early detection and prevention of serious ADRs. This information should help the clinicians to remain vigilant during this period and also educate the consumers[32].

Kanjanarat et al noted cardiovascular drugs to be causative in 17.9% of ADRs, while Lakshmanan et al in a study of hospital admissions due to iatrogenic illness found antihypertensive agents to be responsible for most of the iatrogenic admissions[33,34]. Bates et al reported 30% ADRs to be due to analgesics, 24% due to antibiotics[35]. In present study, 8.16% of ADRs were due to cardiovascular drugs, 4.76% of ADRs were due to anti hypertensives drugs, 7.49% of ADRs were due to NSAIDs and 25.19% of ADRs were due to antibiotics. Davies et al in UK have found the most frequent ADR causative drugs relative to usage to be opioid analgesics, anticoagulants, fibrinolytics, systemic glucocorticoids, diuretics and antibiotics[36]. Above studies are consistent with the present study with regard to therapeutic class of drugs implicated in ADRs. However, these differences seen in different places could also be due to variation in drug usage and disease prevalence in different places[37].

As regard to the body system affected as per SOC in the present study, 25.39% ADRs have involved skin and subcutaneous system, 19.37% of ADRs involved the gastrointestinal system, 10.21% of ADRs involved the central and peripheral nervous system, 9.68% of ADRs are the deranged serum electrolytes, LFT and RFT. 6.54% of ADRs involving the blood and lymphatic system, 6.28% of ADRs are of general disorders and administration site conditions, 3.93% of ADRs involving the immune system and 3.41% of ADRs involving the renal and urinary system. Other systems included are the cardiovascular system, hepatobiliary system, respiratory, psychiatric disorders, eye disorders, endocrine and the reproductive system. The involvement of skin, GI system, central and peripheral nervous system in that order in our study was similar to that of other previous studies Belhekar and Lihite et al also reported skin is the most commonly affected organ system.[4,6,12, 16,18,20]

Conclusion

A total of 382 ADRs were reported during the study period. The antimicrobial agents were implicated as the most common cause of ADRs. The skin and subcutaneous is the most commonly affected specific organ class. 104 ADRs were reported under the seriousness criteria. The outcome of reported ADRs was recovering in 52.10 and 81% of ADRs were probable as per WHO causality assessment scale. A coordinated system of identifying the ADRs early in the course of treatment and recognizing the preventable ADRs is required by the health care system. The sensitization programs are being conducted at our Gandhi hospital and medical college, coordination of prescribing physicians and pharmacovigilance personnel can produce better trend of reporting the ADRs.

Reference

1. The use of the WHO-UMC system for standardised case causality assessment. [Internet] [Cited 2019July 4]. Available from: http://who-umc.org/Graphics/24734.pdf.
2. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. J Am Med Assoc. 1998;15:1200-05.
3. Pharmacovigilance programme of India. [Internet]. 2013 April [Cited 2019 July 4]. Available from: http://ipc.nic.in/writereaddata/linkimages/April-2013,%20PvPI-IPC%20News%20Letter,%20Volume-3,%20Issue-5-4537494506.pdf.
4. Lihite RJ, Lahkar M, Das S, Hazarika D, Kotni M, Maqbool M et al. A study on adverse drug reactions in a tertiary care hospital of Northeast India. Alexandria J Med. 2017;53(2):151-6.
5. Raut LA, Patel P, Patel C, Pawar A. Preventability, predictability and seriousness of adverse drug reactions amongst medicine inpatients in a teaching hospital: a prospective observational study. Int J Chem Pharmac Sci. 2012;1(3):1293-9.
6. Gaur S, Paramjeet S, Srivastava B, Bhardwaj R, Ahuja S, Gunjita B. Evaluation of Adverse Drug Reactions in teaching hospital in Kumoun Region. J Med Sci Clin Res. 2016;4(8):12139-45.
7. Srinivasan R, Ramya G. Adverse drug reaction causality assessment. Int J Res Pharmacy Chem. 2011;1(3):606-11.
8. Doshi MS, Patel PP, Shah SP, Dikshit RK. Intensive monitoring of adverse drug reactions in hospitalized patients of two medical units at a tertiary care teaching hospital. J Pharmacol Pharmacotherap. 2012;3(4):308-13.
9. Sharma PK, Misra AK, Gupta N, Khera D, Gupta A, Khera P et al. Pediatric pharmacovigilance in an institute of national importance: Journey has just begun. Indian J Pharmacol. 2017;49(5):390-5.
10. Mann RD, Andrews EB. Introduction. In: Mann RD, Andrews EB, eds. Pharmacovigilance. 2nd Edition. England: John Wiley and Sons, Ltd. 2007:3-11.
11. Brown JS, Landry FJ. Recognizing, reporting, and reducing adverse drug reactions. Southern Med J. 2001;94(4):370-3.
12. Shrivastava M, Uchit G, Chakravarti A, Joshi G, Mahatme M, Chaudhari H. Adverse drug reactions reported in Indira Gandhi Government Medical College and Hospital, Nagpur. J Assoc Physicians India. 2011;59:296-9.
13. Guidance Document for Spontaneous Adverse Drug Reaction Reporting Version: 1.0. Indian Pharmacopoeia Commission, National Coordination Centre-Pharmacovigilance Programme of India, Ministry of Health and Family Welfare, Governemnt of India. 2014-12.
14. Medical Dictionary for Regulatory Activities Maintance and Support Services Organization (MedDRA MSSO). Available from URL: http:// www.meddramsso.com. Accessed 17 Jun 2010.
15. Jose J, Rao PG. Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. Pharmacol Res. 2006;54(3):226-33.
16. Belhekar MN et al. A prospective study on causality, severity and preventability assessment of adverse drug reactions in a tertiary care hospital in India. Int J Basic Clin Pharmacol. 2019;8(1):104-10.
17. David P, Devinder Mohan T. Adverse cutaneous drug reactions: Clinical pattern and causative agents in a tertiary care center in South India. Indian J Dermatol Venereol Leprol. 2004;70(1):20.

18. Ramesh M, Pandit J, Parthasarathi G. Adverse drug reactions in a south Indian hospital-their severity and cost involved. Pharmacoepidemiol Drug Safety. 2003;12(8):687-92.
19. Arulmani R, Rajendran SD, Suresh B. Adverse drug reaction monitoring in a secondary care hospital in South India. British J Clin Pharmacol. 2008;65(2):210-6.
20. Rao PG, Archana B, Jose J. Implementation and results of an adverse drug reaction reporting programme at an Indian teaching hospital. Indian J Pharmacol. 2006;38(4):293.
21. Singh H, Dulhani N, Kumar BN, Singh P, Tewari P, Nayak K. A pharmacovigilance study in medicine department of tertiary care hospital in Chhattisgarh (Jagdalpur), India. J Young Pharmacists. 2010;2(1):95-100.
22. Bhuvaneshwari E, Chakradhar T, Sravani M. Analysis of spontaneous individual case safety reports reported at adverse drug reaction monitoring centre: tertiary care teaching hospital in South India. Int J Basic Clin Pharmacol. 2019;8(11):2541-7.
23. Adhikari A, Bhattacharjee N, Bhattacharya S, Indu R, Ray M. Evaluation of adverse drug reports from a tertiary care hospital of Kolkata, West Bengal, India. J Young Pharmacists. 2017;9(3):311-4.
24. Routledge P, O'Mahony M, Woodhouse K. Adverse drug reactions in elderly patients. Bri J Clin Pharmacol. 2004;57:121-6.
25. Davies EC, Green CF, Mottram DR, Green CF. Adverse drug reactions in hospitals: a narrative review. Curr Drug Safety. 2007;2(1):79-87.
26. Venkatasubbaiah MP, Reddy D, Satyanarayana SV. Analysis and reporting of adverse drug reactions at a tertiary care teaching hospital. Alexandria J Med. 2018;54(4):597-603.
27. Sneha G, Sowmya N, Goka P, Rao N, Prasanthi N, Nadendia R et al. An observational prospective study on prevalence and monitoring of adverse drug reactions in tertiary care teaching hospital. Bri J Pharmac Res. 2016;11:1-9.
28. Hemavathy G, Rathinam J, Preethi A, Divakar R. A retrospective analysis of adverse drug reactions reported at a tertiary care hospital in South India. Int J Basic Cli Pharmacol. 2018;7:1257-62.
29. Badyal DK, Kanish B, Gulrez G. Causality assessment and pattern of adverse drug reactions in a tertiary care hospital. Int J Basic Clin Pharmacol. 2018;7:210-4.
30. Sood A, Sood V, Prajapati H, Sharma A, Bansal R, Mahajan V. Pharmacovigilance analysis in a rural tertiary care hospital in North India: a retrospective study. Int J Basic Clin Pharmacol. 2016;5:1425-31.
31. Akshaya SS, Srihitha. An Epidemiological Study on Adverse Drug Reactions in Indian Population: Meta- Analysis. Int J Pharmac Clin Res. 2017;9(10):654-9.
32. Prajapati K, Desai M, Shah S, Panchal J, Kapadia J, Dikshit R. An analysis of serious adverse drug reactions at a tertiary care teaching hospital. Perspectives Clin Res. 2016;7:181-6.
33. Kanjanarat P, Winetrstein AG, Johns TE, Hatton RC. Nature of preventable adverse drug events in hospitals: a literature review. Am J Health-System Pharmacy. 2003;60(17):1750-59.
34. Lakshmanan MC, Hershey Co, Brealan D. Hospital admission caused by iatrogenic disease. Arch Internal Med. 1986;146(10):1931-4.
35. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D et al. Incidence of adverse drug events and potential adverse drug events. Adverse drug event prevention study group. J Am Med Asso. 1995;274:29-34.
36. Davies E, Green C, Taylor S, Williamson P, Mottram D, Pirmohamed M. Adverse

drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes. Public Library Sci One. 2009;4:e4439.

37. Padmaja U, Adhikari P, Pereira P. A Prospective Analysis of Adverse Drug Reactions in a South Indian Hospital. Online J Health Allied Sci. 2009;8(3):12.