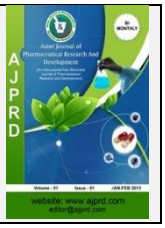
Available online on 15.8.2025 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research



Open Access

Research Article

Evaluation of suspected adverse drug reactions of Anti-Diabetic Drugs in a Tertiary Care Hospital for Type II Diabetes Mellitus

Jiji K[1], Hemalatha A[2], N Rekha[2], Sowmya D[2]

[1]Assistant Professor, Spurthy College of Pharmacy, Banglore, Karnatak

[2]Students, Spurthy College of Pharmacy, Banglore, Karnatak

A B S T R A C T

Background and Objective: The objective of the study was to evaluate and analyze ADRs in type II diabetic patients and to determine the causality, severity and preventability of reactions.

Methods: 150 diabetic patients on anti-diabetic drugs were evaluated prospectively over a period of three months. All patients were observed for ADRs which were then evaluated for its incidence, frequency, severity and causality. Causality was categorized according to the scores obtained from WHO-UMC scale and Naranjo scale.

Results and Discussion: A total of 22 ADRs were reported from 150 patients during the study period with female predominance over male. The biguanides class of drugs was responsible for causing the majority of ADRs while the GI system was the most affected organ system. Among the outcomes of 22 ADRs 17 were recovered 5 reactions still continued and there were no fatal evidence. The suspected ADRs were assessed for their causality, it was revealed that 19 were probable and 3 were possible and as per Naranjo scale 20 were probable and 2 possible.

Conclusion: These study results provide insight to the healthcare providers on the importance of monitoring and reporting ADR associated with the drug.

Keywords: Anti-diabetic drugs, type II diabetic patients, predominance, ADRs

A R T I C L E I N F O: Received 11 Jan 2025; Review Complete 05 March 2025; Accepted 15 July 2025. ; Available online 15 August. 2025

Cite this article as:

Jiji K, Hemalatha A, N Rekha, Sowmya D, Evaluation of suspected adverse drug reactions of Anti-Diabetic Drugs In A Tertiary Care Hospital For Type II Diabetes Mellitus Asian Journal of Pharmaceutical Research and Development. 2025; 13(4):178-188,

DOI: http://dx.doi.org/10.22270/ajprd.v13i4.1614

*Address for Correspondence:

Jiji K, Assistant Professor, Spurthy College of Pharmacy

INTRODUCTION

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose due to defects in insulin secretion, insulin action or both. It may lead over time to serious damage, dysfunction and failure of the heart, blood vessels, eyes, kidneys, nerves and other organs.[1] The most common is Type-2 diabetes, a grave problem worldwide usually seen in adults which occurs due to insulin resistance or insufficient insulin secretion whose major sources are genetic or environmental factors.

In India, the burden of diabetes has been increasing steadily since 1990 and leaps at a faster pace from the year 2000. The occurance of diabetes in India has increased from 7.1% in 2009 to 8.9% in 2019. At present, about 25.2 million adults are estimated to have IGT, which is estimated to further increase to35.7 million by the year 2045. India stands second after China in the diabetes epidemic with 77 million people with diabeat global level. Of these12.1 million are aged

>65years, which is estimated to increase to 27.5 millioninthe year 2045.[2]

The management principles of diabetes focus on disease prevention, correct diagnosis, treatment, self-monitoring, basic requirements essential to practice self-care, record keeping and screening high risk individuals in the pre-diabetic state.[3] Pharmacological treatment remains the best choice for most of these patients.

The key elements of the treatment of diabetes mellitus are:

1. Diet (along with exercise if possible)

2. Oral hypoglycaemic drugs
3. Insulin treatment[4]

The most common anti-diabetic drugs used in Type 2 diabetes mellitus are Biguanides, Sulfonylureas (SU), Alpha-glucosidase inhibitors, Meglitinides, Thiazolidinedione (TZD), Dipeptidyl Peptidase-4 inhibitors and Sodium Glucose Co-transport 2 inhibitors.[3]

Treatment with insulin is one aspect of management in which adequate education of the patient cannot be over emphasized. Achieving good control by mimicking physiological insulin secretion as much as possible and minimizing the risk of hypoglycemia is the main aim of insulin therapy.[5]

Drugs and insulin supplements are the commonest medical interventions used to alleviate sufferings but drugs themselves can prove lethal and can result in adverse drug reactions (ADR) which can be mild to serious.[3] Some of the ADRs as associated with anti-diabetic drugs are gastro-intestinal problems, metabolic disorders, central nervous system disorders (CNS), muscoskeletal disorders,genito-urinarydisorders,peripheraloedema,nasopharyngitis,weightlos setcwhilethe long term complications are eye complications, nephropathy, neuropathy, foot care, cardiovascular disease and hypertension.[5]

World Health Organiation (WHO) defines adverse drug reactions as any response to a drug which is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis or treatment of a disease or for the alteration of the physiological functions. Thus, this definition excludes overdose (either accidental or intentional), drug abuse, failure of treatment and errors of drug administration.[6-7]

One-third of the people with diabetes experience at least one ADR. However, there is remarkable inter individual heterogeneity resulting in patient harm and unnecessary medical costs.[8] Since diabetes is a chronic disease the use of certain drugs for longer time may also show ADRs. Due to lack of knowledge and early detection of ADRs the reactions may become severe. Therefore, the medications must be personalized for each patient with a goal of reduction in blood glucose levels and with a long term benefit by considering side effects, ease of use, long term adherence, expense etc.[9,10]

The detection of Adverse Drug Reaction is crucial in the management of any patient's health. Specific investigations can assist in the diagnosis of an ADR by providing objective evidence of the reaction and confirming a drug induced disease.[11] The most familiar method to detect ADRs is relying on spontaneous reports. Unfortunately, the low reporting rate of spontaneous reports is a serious limitation of pharmacovigilance.[12] Attention should be given in identifying the patient populations at danger and the drugs most commonly responsible for the ADRs. Adverse Drug Reactions can result in loose of patient confidence leading to negative emotions towards the physicians treatment and engage in self treatment options, which may consequently precipitate additional ADRs.[10,13]

Importance of hospital-based ADR monitoring is identifying and minimizing preventable ADRs and enhance the ability of prescribers to manage the ADRs more effectively.[14] WHO has seriously considered this matter by establishing an international adverse drug reactions monitoring centre at Uppsala, Sweden in 1978. It is collaborating with national monitoring centers in around 70 countries. The first ADR monitoring programme started with 12 regional centers in 1986 and India joined the WHO monitoring program Uppsala, Sweden in 1997.[15-18] Recognizing the need for improved ADR monitoring in the country, in July 2010, a nation-wide revised ADR monitoring programme was launched and named as Pharmacovigilance Programme of India (PvPI) under the aegis of Health Ministry. In India, there are very few ADR monitoring centers and efforts are required to be put in collecting ADR data for generating safety surveillance of drugs.[19-21]

MATERIALS AND METHODS

Study Site

The study was conducted in in-patients of endocrinology department of Oxford Medical College and Hospital, Bangalore.

Study Design

The prospective observational study was carried out in150 diabetic patients attending in-patient endocrinology department to evaluate the incidence, frequency, severity and causality.

Study population

Patients taking treatment for Type-II Diabetes Mellitus.

Study duration

The study was carried out for a period of 2 months (September 2023– October2023)

Study criteria Inclusion criteria

In-patients of endocrinology department taking oral hypoglycemic agents and insulin for type-II diabetes, patients of both sex

Exclusion criteria Out-patients

Adverse drug reaction due to over dosing, diabetic nephropathic patients, intensive are patients, Type I diabetic patients and gestational diabetic patients are excluded.

Study procedure

Data were collected from patients undergoing treatment of diabetes mellitus in endocrinology department in Oxford medical college and hospital and were selected, interviewed and recorded. All relevant data including various demographics, drugs received by patients, their dosage and duration of disease were collected.

RESULTS

Drug Utilization Pattern of Anti-Diabetic Drugs

Table 1: Drug Utilization Pattern of Anti-Diabetic Drugs

Class of Drugs	Number of Drugs Prescribed	Percentage of Drugs Prescribed
Sulfonylureas	36	24%
Biguanides	57	38%
Thiazolidinediones	11	7.3%
DPP-4 inhibitors	33	22%
α–glucosidase inhibitors	5	3.3%
Insulin	25	16.6%

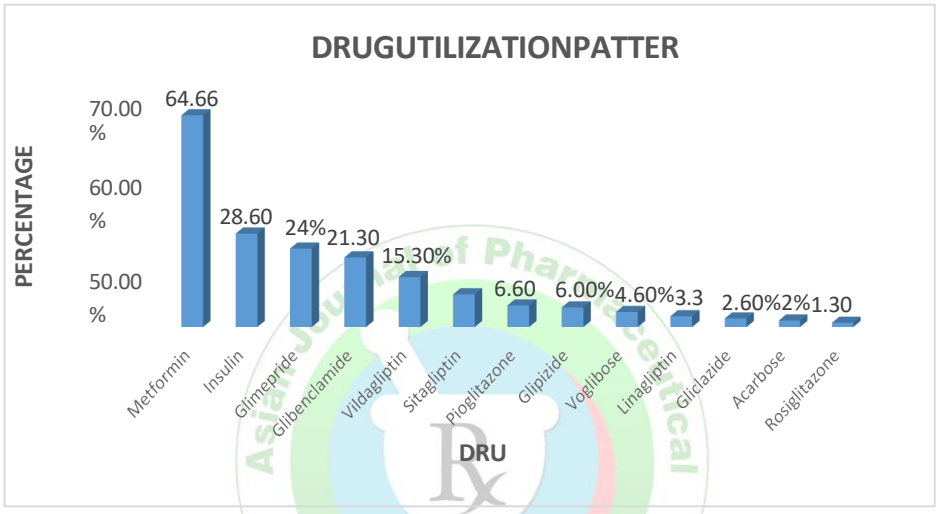


Figure1: Drug utilization pattern of anti-diabetic

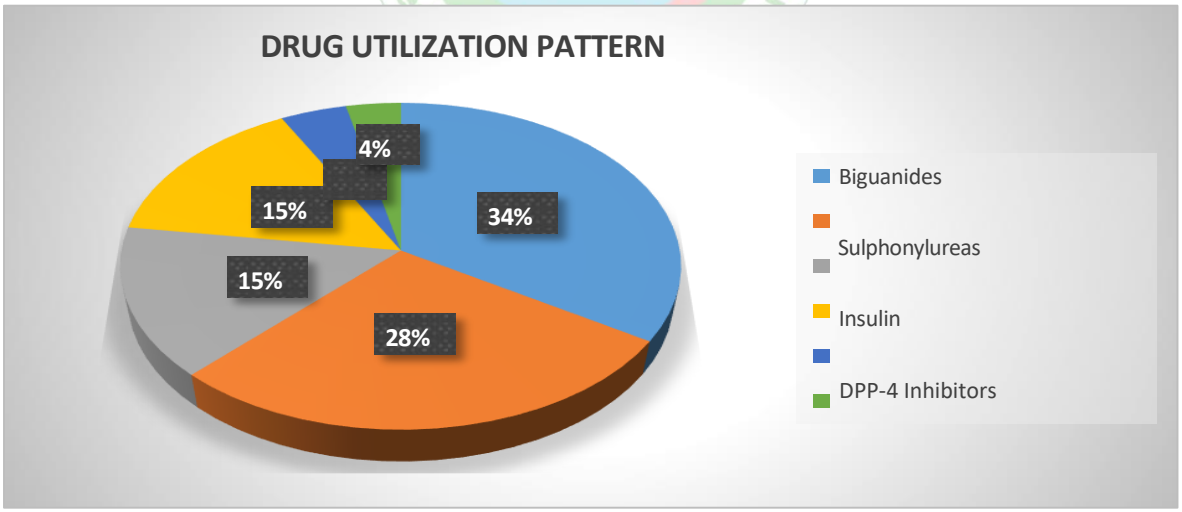


Figure 2: Drug utilization pattern of class of anti-diabetic drugs

Gender wise distribution of ADR

Table 2: Gender wise distribution of ADR

GENDER	**FREQUENCY**	**PERCENTAGE**
Female	92	61.3%
Male	58	38.7%
Total	150	100%

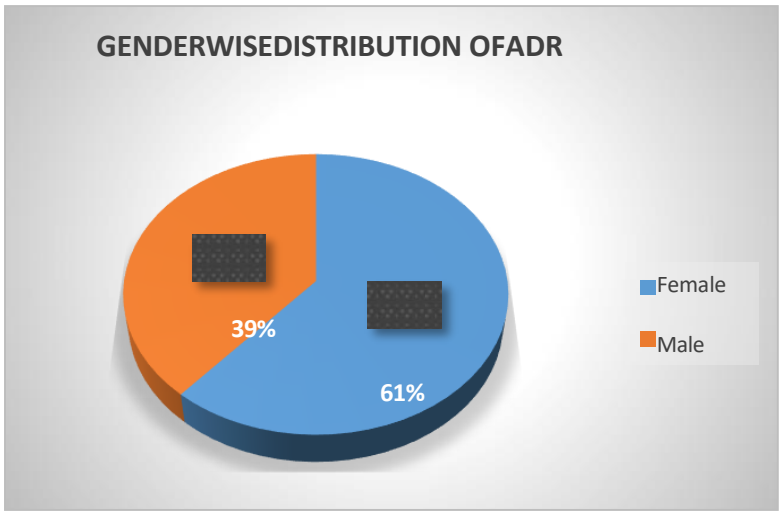


Figure 3: Gender wise distribution of ADR

Age wise distribution of ADR

Table 3: Age wise distribution of ADR

Age Group	Frequency	Percentage
<40	12	8%
40-49	35	23.3%
50-59	45	30%
60-69	41	27.3%
>=70	17	11.3%
Total	150	100%

Figure 4: Age wise distribution of ADR

ADR associated with anti-diabetics

Table 4: ADRs associated with anti-diabetics

Class of Drugs	Name of Drug	No. of ADRs	ADRs
Sulfonylureas	Glimepride	3	Hypoglycaemia, Weight gain, Dizziness, Gastric irritation
	Glibenclamide	1	Hypoglycaemia,Weight gain
	Gliclazide	1	Vomiting,Weightgain, Gastric irritation
DPP-4 inhibitors	Teneligliptine	1	Hypoglycaemia,Weight gain, Oedema
Thiazolidinediones	Pioglitazone	2	Weightgain, Oedema
α–glucosidase inhibitors	Voglibose	1	Bloating, Dyspepsia, Gastric irritation, Diarrhoea
Biguanides	Metformin	11	Gastricirritation, Dizziness, Decreased appetite, Tiredness, Metformin intolerance, Vomiting, Dyspepsia
Insulin	Insulin	2	Hypoglycaemia, Hypokalemia

ADR associated with anti-diabetics

Table 4: ADRs associated with anti-diabetics

CLASSOFDRUGS	NAMEOF DRUG	NO.OFADRs	ADRs
Sulfonylureas	Glimepride	3	Hypoglycaemia,Weight gain, Dizziness,Gastric irritation
	Glibenclamide	1	Hypoglycaemia,Weight gain
	Gliclazide	1	Vomiting,Weightgain, Gastric irritation
DPP-4inhibitors	Teneligliptine	1	Hypoglycaemia,Weight gain, Oedema
Thiazolidinediones	Pioglitazone	2	Weightgain, Oedema
α–glucosidase inhibitors	Voglibose	1	Bloating, Dyspepsia, Gastric irritation, Diarrhoea
Biguanides	Metformin	11	Gastricirritation, Dizziness, Decreased appetite, Tiredness, Metformin intolerance, Vomiting, Dyspepsia
Insulin	Insulin	2	Hypoglycaemia, Hypokalemia

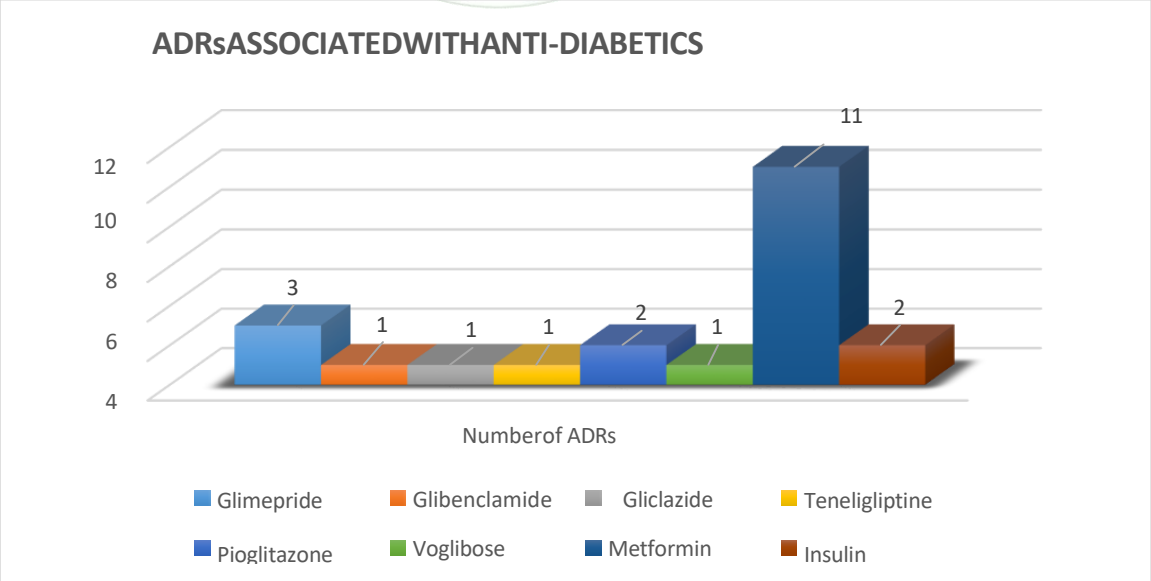


Figure 5: ADRs Associated with anti-diabetics

Organ system affected

Table 5: Organ system affected due to ADR

Organ system Affected	ADRs	Total number of ADRs
GI system disorders	Dyspepsia	11
	Diarrhoea	
	Constipation	
	Metforminintolerance	
	Gastricirritation	
	Bloating	
	Vomiting	
	Decreasedappetite	
Metabolic disorders	Hypoglycaemia	5
	Hypokalemia	
CNS Disorders	Dizziness	1
Others	Oedema	5
	Tiredness	
	Weight Gain	

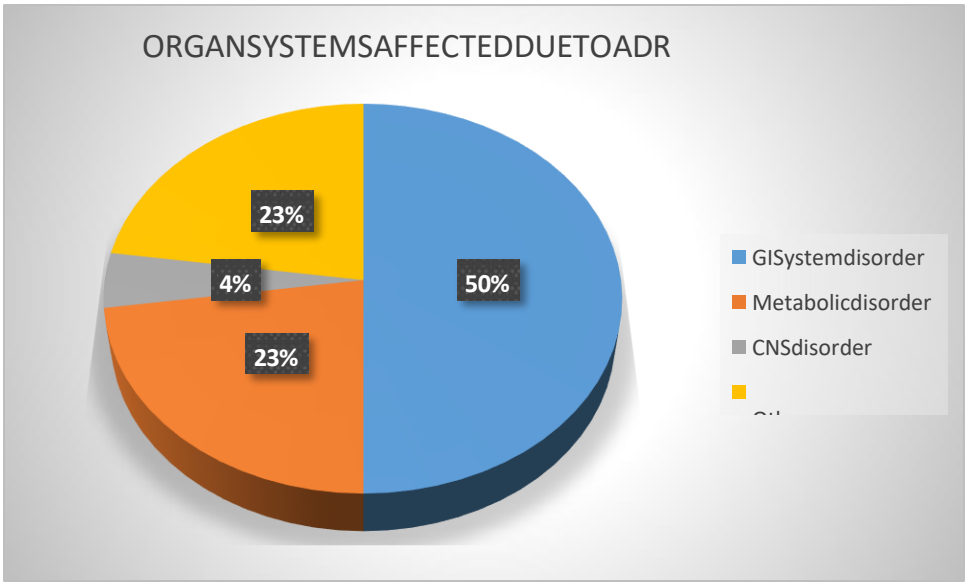


Figure 6: Organ system affected due to ADR

Incidence of ADR with drugs prescribed

Table 6: Incidence rate of ADR with drugs prescribed

Class of Drugs	Number of Drugs Prescribed	Percentage of Drugs Prescribed	ADR Reported	Percentage of Drug Prescribed With ADR (%)
Sulfonylureas	36	24%	5	13.9%
Biguanides	57	38%	11	19.3%
Thiazolidinediones	11	7.3%	2	18.2%
DPP-4 inhibitors	33	22%	1	3%
A–Glucosidase Inhibitors	5	3.3%	1	3%
Insulin	25	16.6%	2	18.2%

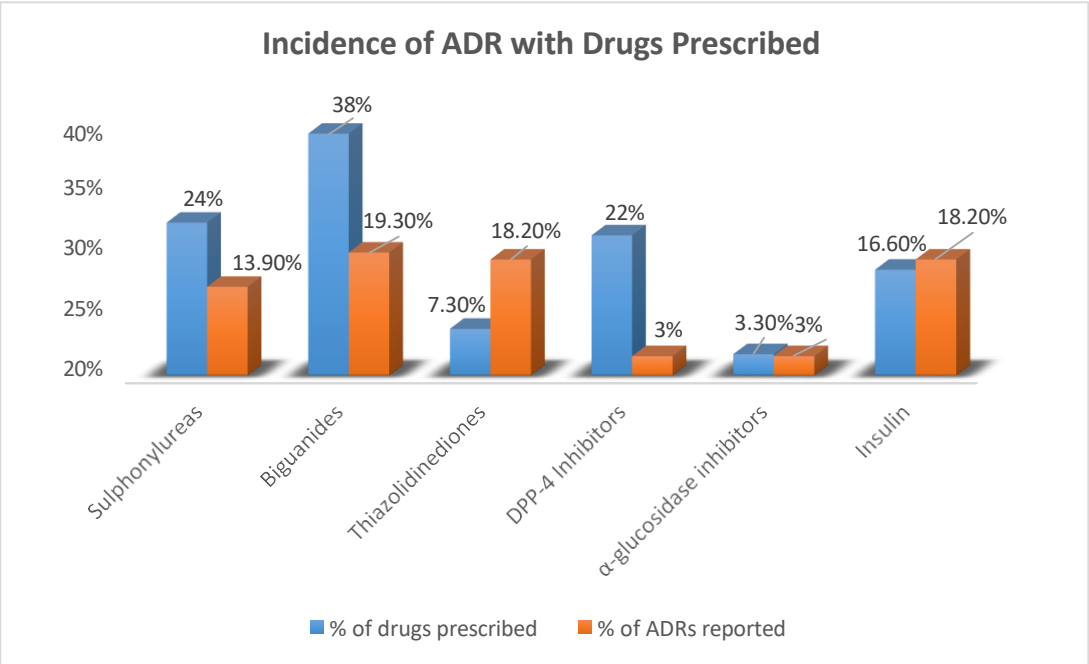


Figure 7: Incidence of ADR with drugs prescribed

Management

Table7: Management carried out

Management	Number of patients
Drug with drawn	16
Dose altered	1
No change	4
Symptomatic treatment	1

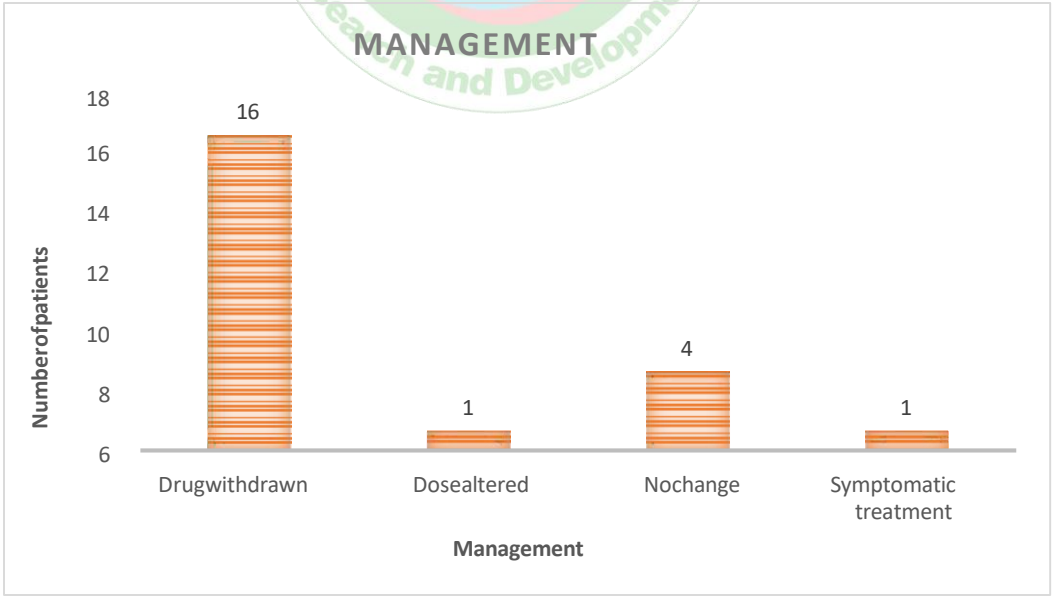


Figure 8: Management carried out

Outcome of ADR

Table 8: Outcome of ADR

Conditions	Number of ADRs
Recovered	17
Continues	5
Fatal	0

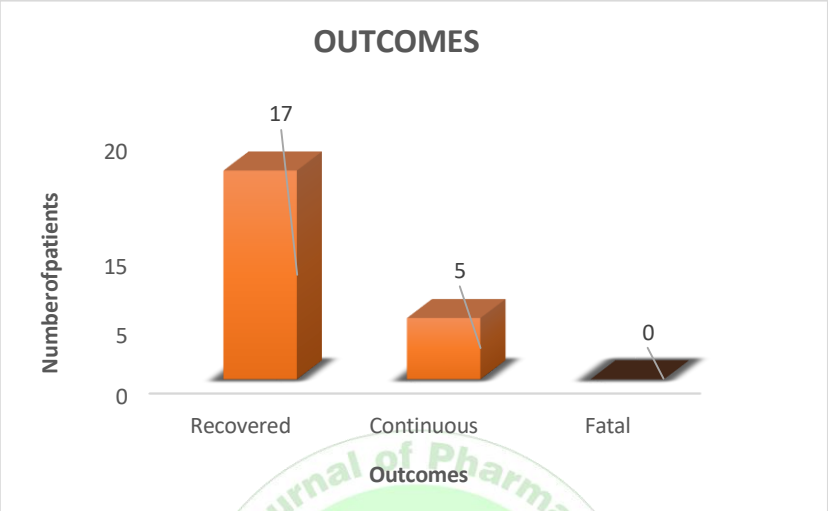


Figure 9: Outcome of ADR ADRs associated with different therapies

Table 9: ADRs associated with different therapies

Treatement	Number of Patients	Number of Patients Showing ADRs	Percentage
Monotherapy	86	12	14.6%
Combination therapy	64	10	15.6%

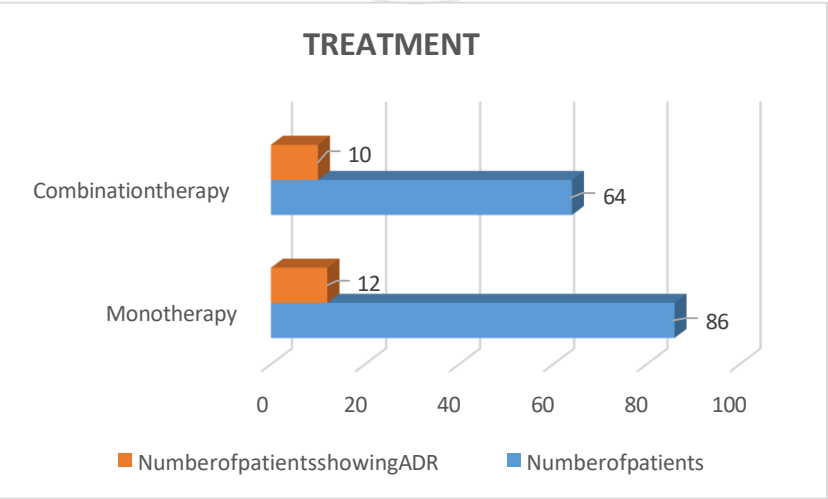


Figure 10: ADRs associated with different therapies

WHO causality assessment scale

Table 10: WHO causality assessment scale

Conditions	Number of ADRs
Certain	0
Probable	19
Possible	3
Unlikely	0
Unclassified	0

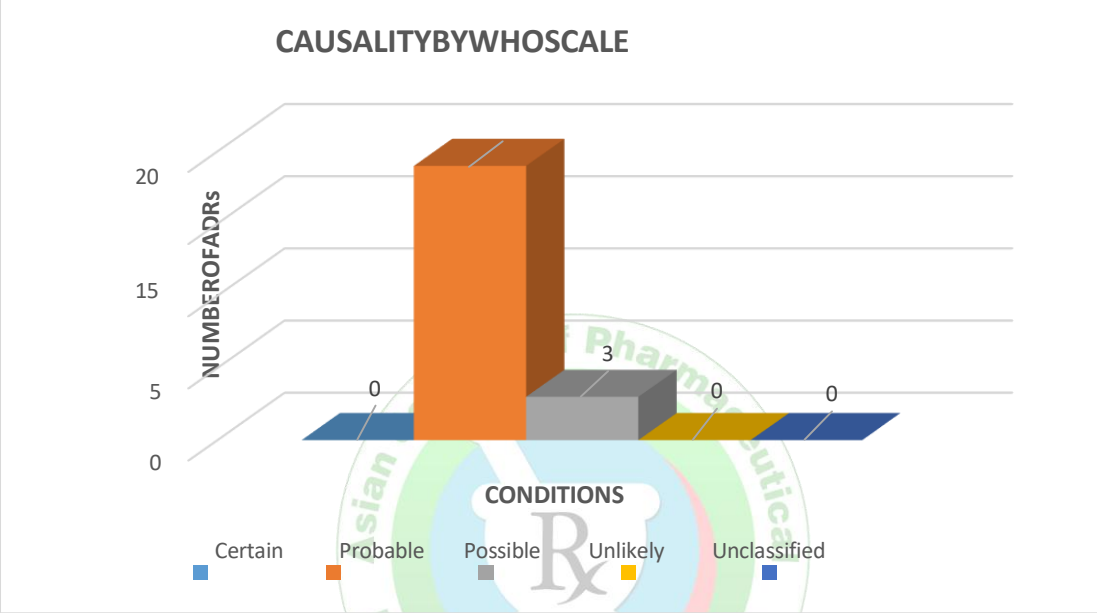


Figure 11: WHO causality assessment scale

Naranjo causality assessment scale

Table11: Naranjo causality assessment scale

Conditions	Number of ADRs
Definite	0
Probable	20
Possible	2
Doubtfull	0

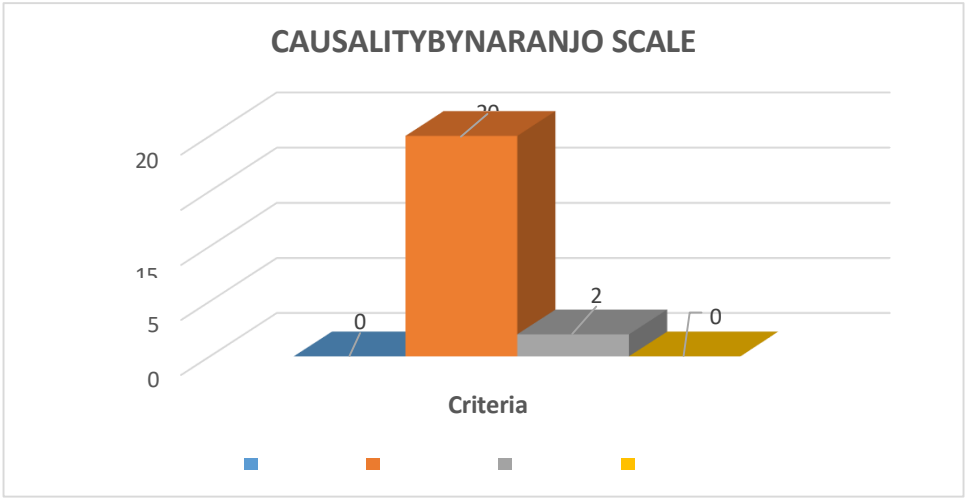


Figure 12: Naranjo causality assessment scale

RESULTS

Patient Demographics

Drug utilization pattern of anti-diabetic drugs

From this study around 64.66% of the patients were taking biguanides, followed by insulin (28.6%), glimipride (24%), glibenclamide (21.3%) and rest of the drugs having lesser percentage as shown in Figure 1 & 2.

Gender Distribution

Table 2 shows that among 150 patients, 92 (61.3%) were females and 58 (38.7%) were males.

Age Distribution

Age wise distribution geriatric patients weremore table 2 shows that 30% of the patients werein the age group of 50-59 and less percentage were seen in age group of less than 40.

ADR Occurence

Among 150 patients 17 patients (10.9%) experienced ADR and out of that 3 patients had more than 1 ADR. The most commonly identified ADRs were with Biguanides followed by Sulphonylureas, Insulin, Thiazolidinediones, DPP-4 inhibitors and α- glucosidase inhibitors.

Organ system affected due to ADR

Organ system most commonly affected was gastro-intestinal system, followed by metabolic disorders, CNS disorders and others.

Incidence of ADR with drugs prescribed

When we are comparing the number of drugs prescribed with the ADRs observed, it is found that the incidence rate of ADR is comparatively less in most commonly prescribed drugs indicated in Figure 7 and Table 6. From the data obtained more number of ADRs was seen with Biguanide

But when comparing it with the total number of drugs prescribed the incidence rate of ADRs with respect to biguanide (19.3%) is less.

Management

Methods carried out in managing the ADRs were as follows, drugs were directly withdrawn in16 cases, in 4 cases no changes were done, dose was alteredin1caseand symptomatic treatment was provided in 1 case as shown in Figure 8 and Table 7.

Outcome of ADR

Table 8 and Figure 9 indicates that 17 of the ADRs were recovered and 5 reactions still continued and there were no fatal evidence.

ADRs associated with different therapies

From the data in Table 9 and Figure 10 with a total of 150 patients, 86 patients under monotherapy have shown 12 ADRs while 64 patients under combination therapy showed 10 ADRs.

WHO causality assessment scales

According to WHO causality assessment scale, out of 22AD Rs19 ADRs were identified to be probable and 3 were possible as shown in Table 10 and Figure 11.

Naranjo causality assessment scale

According to Naranjo causality assessment scale it is indicated that majority of the ADRs were probable and 2 were possible as shown in Table 11 and Figure 12.

DISCUSSION

In the study a total of 150 diabetic patients were encountered and 22 ADRs were detected from 17patients(10.9%). Majority of the patients in the study were females (61.3%) while males were 38.7%. Patients in the age group of 50-59 years experienced maximum ADRs (45) which shows that the incidence of ADRs is more in geriatric population.

The most commonly utilized anti-diabetic medication was metformin which was also responsible for causing more number of ADRs. Insulin being a parenteral anti-diabetic medication has also shown a significant number of ADRs.

Gastro-intestinal system was mostly affected due to anti-diabetic drugs. Metabolic disorders also affected the organ systems with hypoglycaemic conditions and hypokalemia in Insulin administration.

As a part of management, in 16 cases the drug was withdrawn while no changes were done in 4 cases. Doses were altered in1caseandsymptomatic treatment was providedin 1case. In case of hypoglycemia in diabetic patients with insulin administration the doses were altered to maintain the blood glucose levels while hypokalemia with such patients was treated symptomatically with potassium supplements.

The adverse drug reactions observed were treated and the final outcomes were measured. About 17 ADRs were found to be recovered and 5 were continuing.

Majority of the ADRs encountered were seen in patients taking monotherapy. However, patients taking insulin under combination therapy showed more ADRs than those taking insulin as monotherapy.

While examining the safety of drugs, in this study more number of ADRs were reported with biguanides similarly most commonly prescribed drugs was also metformin. Therefore, the incidence rate of ADR with the drug is comparatively less i.e., 19.3%, whereas in case of sulphonylureas 5 ADRs were reported from 36 prescriptions and the incidence rate of ADRs with sulphonylureas was 13.9%. In Insulin 2 ADRs were reported from 25 prescription with the incidence rate of ADR 18.2%. In case of α-glucosidase inhibitors 1 ADR was reported from 5 prescriptions and the incidence rate of ADR with α-glucosidase inhibitors is 3%. Therefore, metformin is considered as the safest drug compared to newer classes of drugs.

In order to strengthen and further emphasize the validity of the study, causality assessment was done usingWHO scale and Naranjo scale. The assessment showed that out of 22 ADRs, 19were probable and 3 were possible as per WHO

scale and Naranjo scale indicated that majority of ADRs [20] were probable and 2 were possible.

CONCLUSION

ADRs are the noxious and unintended reactions to drugs which is considered as an important drawback for drug safety. The spontaneous reporting is a familiar method used to detect and attribute the ADRs. The aim of the present study was to provide information regarding the occurrence of ADRs and their distribution among different genders, age groups, organ system affected and therapeutic classes of medicines. The present study is useful in considerable ADR monitoring and in rational use of drugs.

Monitoring of adverse drug reactions is a continuous process. As newer and newer drugs are being introduced in the market, ADR occurance has also increased gradually making the pharmacovigilance an important aspect of drug safety. Monitoring of ADRs in patients taking oral anti-diabetic drugs plays an important role due to the long-term usage of drugs which is the major cause of the ADRs therefore very essential to monitor those drugs. It is also important to prevail on healthcare professionals to understand their responsibilities in identifying, management, recording and reporting of ADRs for maximizing drug safety. Proficient prescribing helps in reducing avoidable ARDs. Promoting education and providing awareness of ADRs reporting by the healthcare professionals would increase the reporting among medical practitioners and the reporting rates of ADRs. This study concludes that hospital-based ADR monitoring is a good method to detect and report the known and unknown links between drug exposure and ADRs. Pharmacovigilance centers and doctors should have a good relationship so that ADR reporting is considered as an integral part of clinical activities. Doctors should be aware regarding the importance of identifying ADRs, recording them and reporting them to the concerned authority. This practice is very valuable in making the drug therapy rational and safer. In future an all-inclusive programmed is necessary at each level of health care system including doctors, nurses, paramedics and drug dispensing pharmacist in order to ensure safer and effective pharmacotherapy and improve conformity among patients.

REFERENCES

1. Harrison T, Kasper D. Harrison's principles of internal medicine.18thed.NewYork: McGraw-Hill Medical Publ. Division. 2012; 2968-3002.
2. Rajendra P, V is wanathan M. Epidemiology of type2 diabetes in India. Indian J Ophthalmol. 2021; 69(11):2932-2938.
3. Jiji K. Evaluation of Suspected Adverse Drug Reactions of Oral Anti-diabetic Drugs in a Tertiary Care Hospital for Type II Diabetes Mellitus. IJPP. 2019; 12(2).
4. Ebnezer AN,Terri WJ. Management of type 2diabetes; evolving strategies for the treatment of patients with type 2 diabetes. J. Metabol. 2011; 60(1): 1-23.
5. Parthasarathi G, Nyfort-Hansen K,Milap CN.A text book of clinical pharmacy practice. 2nd ed. Universities Press Private Limited, India. 2012; 104-10.
6. Raschetti R, Morgutti M, Menniti-Ippolito F, Belisari A, Rossignoli A, Longhini P,*etal.* Suspected adverse drug events requiring emergency department visits or hospital admissions. European Journal of Clinical Pharmacology. 1999; 54(12):959-63.
7. Sowmya MA, Sreelekshmi BS, Smitha S, Jiji KN, Arun SM, Uma D.Drug utilization pattern of anti-diabetic drugs among diabetic patients in a tertiary care hospital. Asian Journal of Pharmaceutical and Clinical Research. 2015; 8(2):144-6.
8. Aseefa MB, Teferi GF, Moneeza KS, Adem YD.The Genetics of Adverse Drug Outcomes in Type 2 Diabetes: A Systematic Review. Front. Genet. 2021; 12.
9. IDFDiabetesAtlas.Idf.org.2013.[cited31January].Available from:https://idf.org/e-library/epidemiology-research/diabetes-atlas/atlas-6th edition.html
10. Ramachandran A, Snehalatha C. Currents cenario of diabetes in India. J Diabetes. 2009;1(1):18-28.
11. Jamie JC, Sarah K P. Adverse drug reactions. Clin Med. 2016; 16(5):481-485.
12. Chi-Shiang W, Pei-Ju L, Ching-Lan C, Shu-Hua T, Yea-Huei K Y, Jung-Hse in C. Detecting Potential Adverse Drug Reactions Usinga Deep Neural Network Model.J Med Internet Res. 2019;21(2).
13. Patidar D, Rajput M, Nirmal N, Savitri W. Implementation and evaluation of adverse drug reaction monitoring system in a tertiary care teaching hospital in Mumbai, India. Interdisciplinary Toxicology. 2013; 6(1):41-6.
14. Marcia G A, Sandra M B P, Jose G D, Valeria G M, Maria-Cristina S P. Adverse drug reaction monitoring : support for pharmacovigilance a tatertiary care hospital in Northern Brazil. BMC Pharmacol Toxicol. 2013; 14(5).
15. King H, Aubert R, Herman W. Global Burden of Diabetes,1995-2025:Prevalence, numerical estimates and projections. Diabetes Care. 1998; 21(9):1414-31.
16. World Health Organisation. WHO-UMC causality assessment system. Available from: http://www.who-umc.org/pdfs/causality.pdf.
17. Hane feld M.A carbose reduces the risk of myocardial infarction in type 2 diabetic patients; meta-analysis of seven long-term studies. European Heart Journal. 2004; 25(1); 10-6.
18. Arun C, Chitharanjan D, Vijaya SRD, Shashank K, Aditya C, Rahul R, *et al.* Clinical Review of Antidiabetic Drugs: Implications forType2 Diabetes Mellitus Management. Frontiers in Endocrinology. 2017; 8:6.
19. Singh H, Dulhani N, Kumar BN, Singh P, Tewari P, Nayal K. A Pharmacovigilance Study in Medicine Department of Tertiary Care Hospitalin Chattisgarh, India. J Young Pharm. 2010;2(1):95-100.
20. Tirthankar D, Abhik C, Abhishek G.Adverse drug reactions in type 2 diabetes mellitus patients on oral antidiabetic drugs in a diabetes outpatient department of atertiary care teaching hospital in the Eastern India. International Journal of Medical Science and Public Health.2016; 6(3):554-7.
21. Allu H, Prasanna kumar N, Hemanth kumar MC. Adverse Drug Reaction Monitoring and Reporting at H.S.K Hospital and Research Centre-Bagalkot. Journal of Hospital and Clinical Pharmacy. 2016; 2(2):54-62.