International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 04, 2020
ISSN: 1475-7192

Pharmacist Led Assessment of Drug Related Problems in Type 2 Diabetes Mellitus Patients

[1]Syed Zia Inamdar, [2]Raghavendra V Kulkarni, [3]VuyyuruAkhila

***ABSTRACT**--Patients with Type-2 diabetes mellitus are known to be at risk of drug related problems as they receive multiple medications due to co-morbidities associated with the condition. A Drug related problem is defined as any event involving drug treatment that potentially interferes with the patient achieving an optimum outcome of medical care. Thisstudy tends to evaluate the prevalence of drug related problems and related factors among the study population. An interventional study in adults with Type 2 diabetes was conducted in a tertiary care hospital. The study subjects were reviewed to collect relevant data and analyzed to report the prevalence of drug related problems (DRPs) occurred during the management of diabetic patients. A total of 107 Study population were finally reviewed with a reporting incidence 278 DRP's and were grouped under the following; drug without indication 25(8.99%), indication without drug 27(9.71%), drug not appropriate for therapy 12(4.32%), supra and sub therapeutic dose 03(1.08%), additive toxicity 03(1.08%), drug duplication 07(2.52%), adverse drug reaction 08(2.88%) drug interactions 193 (69.42%). Majority of the drug related problems were appropriately intervened. Age, polypharmacy, multiple co morbidities were the factors associated with DRP's in diabetic patients. The study revealed a substantial incidence of drug related problems associated with drug therapy in management of diabetes.*

***Keywords**--type 2 diabetes mellitus, drug related problems, adverse drug reaction, drug interaction, pharmacist interventions.*

I INTRODUCTION

Diabetes Mellitus is a common condition in which pancreas reduces the production of insulin or cells stop responding to the insulin that is produced, so that glucose in the blood does not get absorbed into the system [1]. Uncontrolled diabetes is the major cause of microvascular complications and death. Type-2 diabetes mellitus (T2DM) treatment focuses on treatment with oral antidiabetic agents such as hypoglycemic agents.Patients with T2DM receive a wide range of pharmacotherapeutic agents due to the presence of co-morbidities and are at high risk of experiencing drug related problems (DRPs) [1]. "A drug related problem (DRP) is defined as any event involving drug treatment that potentially interferes with the patient achieving an optimum outcome of medical care". Various DRP's classifications and definition were reported, among which Pharmaceutical Care Network Europe (PCNE) system is used globally to analyze the DRP's and classify them under major categories asadverse reaction(s), drug choice problem, dosing problem, drug use/administration problem, interactions and others. Treatment for diabetes is complex, inconvenient and factors like sex, age, duration of diseases, associatedcomorbidities,disabilities, polypharmacy, complexity of treatment directly or indirectly influences diseases and medication management which leads todrug related problems [4].

[1] *Department of Pharmacy Practice, BLDEAs SSM College of pharmacy and Research Center, syedzia.inamdar@gmail.com,*
[2] *Department of Pharmacy Practice, BLDEAs SSM College of Pharmacy and Research Center*
[3] *Student, BLDEAs SSM College of Pharmacy and Research Center, akhila1357@gmail.com.*

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

II METHODOLOGY

A prospective interventional study was conductedfor 6 months in a teaching hospital in Bijapur district, North Karnataka. The study was performed on inpatients with Type 2DM meeting the inclusive criteria of the study after the approval from institute's ethical committee. A total of 107 study inpatients were finally reviewed from general medicine department. The study patients were reviewed on day to day basis to intercept any DRPs. Analysis of data for DRPs was based on the process of classification, identification and evaluation of DRP. We first categorized DRPs using the established system developed by The Pharmaceutical Care Network Europe (PCNE).Adult patients of either gender from 18 – 60 years of age and diagnosed with Type 2DM and receiving at least one anti-diabetic drug were included.Type 1 Diabetic and all OPD patients, and diabetic patients other than the above said departments, Patient with insufficient data, non- consenting and patients with ER admission were excluded.Relevant data from patient's prescriptions, case files, progress notes, clinical findings and drug therapy were collected and documented on a standard data collection form prepared for effective data segregation and analysis.

III RESULTS

A Total of 107 subjects were included in the study, 64(59.81%) were male and 43(40.21%) were female shown in table.1, of the total subjects included, maximum number of patients affected with type 2 diabetes mellitus werebetween 40 – 59 years of age (86.92%) shown in table.1. Duration and history of diabetes in the enrolled was observed highest 75(50.36%)from 0 – 5 years shown in table.1. The study population were investigated for associated co-morbidities and found to be having CVS disorders 86 (71.67%) as highest shown in table.2. The study population was highly prescribed with metformin 31 (64.5%) as oral hypoglycemic agent shown in table.3 and highly prescribed combination therapy of oral hypoglycemic agents are Glibenclamide + metformin 09 (36%) shown in table.4and highly prescribed insulin was actrapid 35(47.29%) shown in table.5.

Drug Related Problems (DRPs)

A Total of 278 DRP's was identified and was categorized as Drug without Indication (DWI) 25(8.99%)shown in table.6,Indication without Drug (IWD) 27(9.71%)shown in table.7, Drug not appropriate for therapy 12(4.32%)shown in table.8, supra and sub therapeutic dose 03(1.08%) shown in table.9, Additive toxicity 03(1.08%)shown in table.10,Therapeutic Duplication 07(2.52%) shown in table.11, Adverse Drug Reaction (ADRs) 08(2.88%) shown in table.12, Drug Interaction (DI) 193(69.42%)shown in table.13. In the total of 278 DRP's, indirect interventions are recommended by clinical pharmacist of which, 101(36.33%) were implemented, 128(46.04%) were apprehended and 49(17.62%) were unknown for their outcomes shown in table.14.

Table 1: shows the demographic and clinical characteristics of the patient population studied.

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

The study analyzed a total of 107 patient records, consisting of 64 (59.81%) males and 43 (40.21%) females (Table 1). The majority of the patients (86.91%) fell within 40 -59 years. Mean duration of treatment was 0- 5 years (50.36%) per patient.

Table 1: Demographic and clinical data n=107

Associated co morbidities:

Characteristics	**Number of patients**	**Percentage (%)**
Sex		
Male	64	59.81%
Female	43	40.21%
Age (years)		
18 -19	01	0.93%
20 -39	13	12.14%
40 -59	93	86.91%
Duration of disease		
0 -5	75	50.36%
6 -10	17	20.22%
11 -15	07	11.39%
16 – 20	08	18.01%

Table 2: Co-morbidities associated with type 2DM, where n = 120

This lists the common co-existing conditions associated with Type 2DM, shows that CVS disorders was the highest co-morbidity, existing in 71.67% of the patients.

Table 2: Co-morbidities associated with type 2DM n =120

Co morbidities	**No of patients**	**Percentage**
CVS disorders	86	71.67%
Respiratory disorders	14	11.67%
Anemia	10	8.33%
Gastroenteritis	02	1.66%
Renal failure	05	4.17%

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

CNS	03	2.50%

CVS: cardiovascular system, CNS: central nervous system.

Table: 3 percentage of oral hypoglycemic agents used as mono therapy, where n= 48

This lists the common oral hypoglycemic agents used as monotherapy in which metformin 64.5% washighly prescribed drug.

Table 3:percentage of oral hypoglycemic agents used as mono therapy, where n= 48

Name of drug	**No of prescriptions**	**Percentage**
Metformin	31	64.5%
Gliclazide	06	12.5%
Voglibose	03	6.25%
Glimepiride	03	6.25%
Pioglitazone	04	8.33%
Repaglinide	01	2.08%

Table 4: combination therapy of OHA's where n = 25

This lists the commonly prescribed combination therapy of OHA's in which Glimepiride + Metformin was highly prescribed drug with 28%.

Table 4: combination therapy of OHA'swhere n = 25

Name of drugs	**No of prescriptions**	**Percentage**
Glimepiride +Metformin	07	28%
Glipizide + Metformin	03	12%
Pioglitazone + Metformin	01	4%
Gliclazide + Metformin	01	4%
Glibenclamide +Metformin	09	36%
Nateglinide + Metformin	01	4%
Glimepiride + Pioglitazone + Metformin	03	12%

OHA's – oral hypoglycemic agents

Table 5: Insulin used for the treatment of type 2 DM, where n = 74

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

This lists the commonly prescribed insulin used for treatment of type 2 DM in which actrapid was highly prescribed drug with 47.29%.

Table 5: Insulin used for the treatment of type 2 DM, where n = 74

Name of the drug	**No of Prescriptions**	**Percentage**
Insulin mono therapy		
Actrapid	35	47.29%
Recosulin	21	28.37%
Lupisulin	01	1.35%
Insugen	06	8.10%
Huminsulin	04	5.40%
Combination therapy		
Mixtard	07	9.45%

Table 6: Drug without indication, where n= 25

Drug related problems

Table 7: indication without drug, where n = 27

Drugs	**Frequency**	**Percentage**
Furosemide	07	28.0%
Enoxaparin	02	8.0%
Phenytoin	01	4.0%
Fluconazole	02	8.0%
Metronidazole	02	8.0%
Ramipril	01	4.0%
Bro-zedex	01	4.0%
Atorvastatin	02	8.0%
Metformin	01	4.0%
Efcorlin	01	4.0%
Furosemide + spironolactone	01	4.0%
Acetazolamide	01	4.0%
Amikacin	01	4.0%
Thrombophob	01	4.0%
Methyldopa	01	4.0%

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

Indication	Frequency	Percentage
Hypertension	05	18.52%
Anemia	07	25.93%
Fever	03	11.11%
DKA	01	3.70%
IHD	01	3.70%
Pain	02	7.41%
Hyperlipidemia	01	3.70%
Hysteria	01	3.70%
Diabetic foot	01	3.70%
Cough	02	7.41%
Breathlessness	01	3.70%
Acute bronchitis	01	3.70%
Hyperglycemias	01	3.70%

DKA: *Diabetic ketoacidosis, IHD: Ischemic heart disease.*

Table 8: Drug not appropriate for therapy, where n = 12

Drugs	Frequency	Percentage
Ceftriaxone	04	33.33%
Metoprolol	03	25%
Mefloquine	01	8.33%
Tramadol	01	8.33%
Enoxaparin	01	8.33%
Spironolactone	01	8.33%
Ofloxacin + Ornidazole	01	8.33%

Table 9: Supra and Sub therapeutic therapy n = 3

Drug	Frequency	Percentage
Supra therapeutic n = 1		
Atorvastatin	01	100%
Sub therapeutic n = 2		
Piperacillin + Tazobactam	01	50%
Metoprolol	01	50%

Table 10: Additive toxicity, n = 3

Drug	Frequency	Percentage
Aceclofenac + Tramadol	02	66.67%
Ramipril + Amlodipine	01	33.33%

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

Table 11: Therapeutic duplication, where n = 7

Drug	Frequency	Percentage
Rabeprazole	01	14.29%
Midazolam	01	14.29%
Furosemide	01	14.29%
Spironolactone	01	14.29%
Diclofenac	01	14.29%
Hydrochlorothiazide	01	14.29%
Metformin	01	14.29%

Table 12: Adverse drug reactions observed n = 8

Drug	Effect	Frequency	Percentage
Glimepiride	Hypoglycemia	02	25%
Cefoperazone	Fever	02	25%
ISMN	Headache	01	12.5%
Insulin	Hypoglycemia	01	12.5%
Ranitidine	Constipation	01	12.5%
Warfarin	Vomiting	01	12.5%

ISMN: Isosorbide mononitrate

Table 13: Most common drug interactions observed n = 193

Interacting drug	Effect	Severity	Frequency
Furosemide + Amikacin	Increase risk of renal damage	Major	19(9.84%)
Clopidogrel + Enoxaparin	Increase risk of bleeding	Major	14(7.25%)
Metformin + Metoprolol	Hypoglycemia/ hyperglycemia	Moderate	64(33.16%)
Metformin + Ranitidine	Hypoglycemia	Moderate	51(26.42%)
Rabeprazole +Furosemide	Hypomagnesemia	Moderate	25(12.95%)
Insulin + Metformin	Hypoglycemia	Moderate	20(10.36%)

Table 14: Outcomes of pharmacist indirect interventions for identified DRP's

DRP categories	No of DRP'S	Implemented	Apprehended	Not known
Drug without indication	25	13	10	02

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

Indication without drug	27	15	11	01
Drug not appropriate	12	05	06	01
Supra and sub therapeutic dose	03	02	01	00
Additive toxicity	03	03	00	00
Therapeutic duplication	07	04	03	00
Suspected ADR	08	04	04	00
Drug interactions	193	55	93	45
Total	278	101	128	49

IV DISCUSSION

Results suggest that diabetes is more prevalent among the age group of 40 -59 years (86.91%)in our study and the malediabetics with 64 (59.81%) were more compared to females. A total of 278 drug related problems (DRP) were reported.The DRP was categorized intoDrug without indication 25(8.99%), Indication without drug 27(9.71%), drug not appropriate for therapy 12(4.32%), supra and sub therapeutic therapy 3(1.08%), additive toxicity 03(1.08%), drug or therapeutic duplication 07(2.52%), adverse drug reaction 08(2.88%), drug interaction 193(69.42%).

Drug without indication

The presence of a drug prescribed by the physician, but there will be no specific indication of that drug for which it was indicated. The study observed 25(8.99 %) drug without indication of total DRP's, shown in table.6.Around 25 Drug without indication episodes were reported found to associated with the following class of medications; furosemide 7(28.0%), enoxaparin 2 (8.0%), phenytoin 1 (4.0%), fluconazole 2 (8.0%), metronidazole2 (8.0%), ramipril 1 (4.0%), Bro-zedex 1 (4.0%), atorvastatin 2 (8.0%), Metformin 1 (4.0%), Efcorlin 1 (4.0%), acetazolamide 1(4.0%), amikacin 1 (4.0%), methyldopa 1 (4.0%), thrombophob 1(4.0%). The study observed incidence of DWI occurrence at every 4.28 patients.

Indication without drug

It indicates no drug in the therapeutic regimen prescribed by the physician for a particular indication. Thestudy observed indication for whichdrugs werenot prescribed, comprising of 27(9.71%) of total reported DRP's shown in table.7, Around 27 indication without drugs are obtained which are hypertension 05(18.52%), anemia 07(25.93%), fever03(11.11%), DKA 01(3.70%), IHD 01(3.70%), pain 02(7.41%), hyperlipidemia 01(3.70%), hysteria 01(3.70%),diabetic foot 01(3.70%), Cough 02(7.41%), breathlessness 01(3.70%), acute bronchitis 01(3.70%), hyperglycemias 01(3.70%). The prescribers while reviewing the patient might not consider treating some secondary symptoms which would be easily dismissed once the primary ailment subsides. The probable assessment of which revealed physician's lack of time due to his/her busy schedules, increase patient

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

load, patients were admit with a severe co morbid conditions. The study observed an incidence of IWD occurring at every 3.96 patients.

Drug Not Appropriate for Therapy

It is an inappropriateselection or choosing of a drug in order to treat a specific indication. The study observed drug not appropriate for therapy contributing 12(4.32%) of total DRP's with an occurrence rate at every 8.92 patients shown in table.8. Around 12 incidences of Drug not appropriate for indication were reported comprising of ceftriaxone 04(33.33%), Metoprolol03(25%), mefloquine 01(8.33%), tramadol 01(8.33%), enoxaparin 01(8.33%), spironolactone 01 (8.33%), ofloxacin+ ornidazole 1 (8.33%).These drugs were not appropriate for therapy as reported and observed in literatures surveys, but there are chances by which they may have prescribed basis of evidencebase medicine practice.

Supra and sub Therapeutic Dose

It indicates prescribing high level of doses for the treatment for an indication, then the required, supra and sub therapeutic dose contributing 03(1.08%)of total DRP, as shown in table.9.Around 3 supra and sub therapeutic dose were reported comprising of atorvastatin 01(100%), piperacillin + tazobactam 01(50%) and metoprolol 01(50%) due to prescribing negligence for incorrect dose possibly due to lack of dosage regimen information.

Additive toxicity

It is a toxic effect caused by a drug when it is prescribed in a higher dose. The study observed 03(1.08%) of total DRP as episode of additive toxicity shown in table.10, with drugs comprising of Aceclofenac + tramadol 2(66.67%), Ramipril + amlodipine 1(33.33%) and assessment reveals due to the evidence based therapy where the patient condition demands the situation for a higher dose. such conditions are common in critical clinical situations where risk and benefit ratio have to be thoroughly evaluated before initiating drug therapy.

Therapeutic Duplication

The study observed 07(2.52%) therapeutic duplication of medications in study population, contributing to total DRP's reported shown in table.11. Around 7 cases of drug duplication or therapeutic duplication observed among study population related the following drug categoriesrabeprazole 01(14.29%),midazolam 01(14.29%), furosemide 01(14.29%), spironolactone 01(14.29%), diclofenac 01(14.29%), hydrochlorothiazide 01(14.29%), metformin 01(14.29%). Duplication could arise due to many reasons such as inadequate time during reviewing of the patient is one of the prominent causes of this issue.

Suspected Adverse Drug Reactions

These are prominently known as acceptable, appreciable harmful effects caused by drug when prescribed with in a normal dose. In the present study 08(2.88%) Adverse drug reactions were observed of total DRP's.They are unwanted effects occurring from drugs when administered in normal safety dose to treat the considering conditions. These are highly unavoidable. Around 08 adverse drug reactions were reported comprising of

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

Glimepiride 02(25%), Isosorbide mononitrate01(12.5%), Cefoperazone02(25%), Insulin 01(12.5%), Ranitidine 01(12.5%), Warfarin 1(12.5%), shown in table.12. The adverse effects identified for the above drugs areHypoglycemia,Headache, fever, Hyperglycemia, constipation and vomiting respectively.

Drug interaction

These are the type of interactions which modifies the effect of a drug when administered with another drug. The effect may be an increase or decrease in the action of either substance, or it may be an adverse effect that is not normally associated with either drug. The study reported around 193 drug interactions (69.42%) of total DRPs. The drug interactions observed among study population related the following drug categories; drugs is seen pertaining to furosemide + amikacin 19(9.84%), clopidogrel + enoxaparin14(7.25%), metformin + metoprolol 64(33.16%), metformin + ranitidine 51(26.42%), rabeprazole +furosemide 25(12.95%), insulin +metformin 20(10.36%) shown in table.13. The study reveals possible reasons of inappropriate timing of administration or dosing intervals, multiple medications or polypharmacy, multiple diagnosis or associated co-morbidity, potential drug incompatibility characteristics, and lack of appropriate information and knowledge about the drug pharmacokinetics.

Pharmacist intervention for DRP and outcome

All the identified 278 DRP's are intervened by the pharmacist indirectly. A majority of recommendations made by clinical pharmacists were accepted, in which 101(36%) were implemented, 128(46%) were apprehended, 49(17%) were unknown, shown in table.14.By this study it gives an opportunity to the clinical pharmacist to optimize patient care by identifying, resolving and preventing drug related problems in the study population and a challenge to clinical pharmacist to carefully assess the medication profile, for safest, efficacious and simplest medication regimen possible to meet patient requirement.

V CONCLUSION

There is substantial incidence of drugs related problems in the treatment of diabetes in the tertiary hospital. These problems occur mostly in thepatients due to co-morbidities, polypharmacy, and inappropriate use of drugs associated with Type 2DM.A total of 278 drug related problems (DRP) were reported after assessing 107 study with a prevalence of 2.60 DRP per study patient.The majority of DRPs identified is of drug-drug interactions type (69.42%). The identified DRP'S were intervened and majority of recommendations made by the clinical pharmacist were accepted. Early identification and prevention of DRPs in T2DM and rational use of drugs are necessary to prevent complications and unnecessary hospitalization and deaths among diabetic patients.

REFERENCES

1. Ogbonna B. O., Ezenduka C. C., Opara C. A., Ahara L. G., "Drug therapy problems in patients with type-2 Diabetes in aTertiary Hospital in Nigeria," International Journal of innovative research and development, vol. 3, no. 1, pp.494 – 502, January 2014.

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020

2. Bereket MollaTigabu, Daniel Daba and Belete Habte, “Drug‐related problems among medical ward patients in Jimma university specialized hospital, Southwest Ethiopia”, Journal of Research in Pharmacy Practice, vol. 3, no. 1, pp.1 -5, Jan-Mar 2014.
3. Mohammed Yimama, HabtemuJarso and Tigestu Alemu Desse, “Determinants of drug- related problems among ambulatory type 2 diabetes patients with hypertension comorbiditiy in southwest Ethiopia: a prospective cross-sectional study”, BMC research notes, vol.11, article no. 679 September 2018.
4. S.Z. Inamdar, R. V. Kulkarni, “Drug related problems in elderly patients with type 2 diabetes mellitus”, Journal of Diabetology, vol. 1, no. 1, February 2016.
5. Hasniza Zaman Huri and Lee Chai Ling, “Drug –related problems in type 2 diabetes mellitus patients with dyslipidemia”, BMC Public Health, vol. 13, article no. 1192, 2013.
6. POOJITHA.S, RAGURAAM.S, VENKATESH.M. "SOLDIER HEALTH MONITORING AND TRACKING SYSTEM." International Journal of Communication and Computer Technologies 7 (2019), 24-26. doi:10.31838/ijccts/07.SP01.05
7. Grandpierre, A. Biological extension of the action principle: Endpoint determination beyond the quantum level and the ultimate physical roots of consciousness (2007) NeuroQuantology, 5 (4), pp. 346-362.
8. Sorli, A. Bijective analysis of physical equations and physical models (2018) NeuroQuantology, 16 (7), pp. 30-38.

DOI: 10.37200/IJPR/V24I4/PR201059
Received: 22 Oct 2019 | Revised: 13 Sep 2019 | Accepted: 15 Jan 2020