

# A Study of Polypharmacy in Patients with Co-Existing Diabetes Mellitus Type II and Hypertension in a Tertiary Care Center

Shaima Zafer Khan

Department of Basic Medical sciences, Lecturer in Pharmacology,  
Dar Al Uloom University, Riyadh, KSA.

<https://dx.doi.org/10.13005/bpj/2282>

(Received: 15 August 2021; accepted: 27 September 2021)

Polypharmacy is most commonly defined as the use of five or more medications daily by an individual. In India, the prevalence of polypharmacy varies from 5.82 % to 93.14% in different states. Concerns about polypharmacy include increased adverse drug reactions, drug interactions, prescribing cascade, and higher costs. The present study is a non-interventional, observational, descriptive study carried out in 240 patients attending the medicine outpatient department of a tertiary care hospital, over one-and-a-half-year duration. The mean age of the study population was  $53.97 \pm 7.62$  years, out of which 52.5% were male and 47.5% were female. 62% of the study population were from low socioeconomic status and 38 % were from the middle class. The mean duration in years for hypertension and diabetes was  $7.1 \pm 4.3$  years and  $7.94 \pm 4.66$  years respectively. Apart from various antihypertensive and antidiabetic medicines prescribed the study population was also prescribed Vitamins (51.6%), Hypolipidemics (42.5%), Miscellaneous (41.6%), Antiplatelets (40%), H2 blockers/PPI (35.8%), and Antibiotics (22.5%). Polypharmacy (5 or more than 5 drugs) was seen in 33.75% of the study population. Polypharmacy with is integral in patients suffering from hypertension with coexisting diabetes mellitus and other comorbidities. It is essential to practice judicious prescribing especially in patients with multiple conditions.

**Keywords:** Adverse effects; Comorbidities; Drug prescription; Multiple drugs.

Polypharmacy is most commonly defined as the use of five or more medications daily by an individual. Some studies also generally define polypharmacy as the use of multiple concurrent medications or simultaneous long-term use of different drugs by the same individual.<sup>1</sup> In India, the prevalence of polypharmacy varies from 5.82 % to 93.14% in different states, the highest being in Uttaranchal and least in West Bengal.<sup>2</sup> India bearing the dubious distinction of being the diabetes capital of the world according to the Diabetes Foundation of India, the number of people with diabetes mellitus in India are 62 million, which is set to rise to 79.4 million by 2030.<sup>3</sup> Globally

50 % of the population with diabetes mellitus have co-existing hypertension. The co-existence of diabetes mellitus and hypertension is also important as they are multiplicative risk factors for macro and microvascular diseases, resulting in increased risks of cardiac death, coronary artery disease, congestive cardiac failure, cerebrovascular disease, and peripheral vascular disease. To tackle the complications of diabetes mellitus type II and hypertension, additional drugs are being prescribed leading, to polypharmacy. Between the determinants of polypharmacy increased age was highlighted as a major one, as aging is characterized by the presence of multiple

independent chronic diseases in the same person, a fact that is almost always accompanied by multiple drug use.<sup>4</sup> Concerns about polypharmacy include increased adverse drug reactions, drug interactions, prescribing cascade, and higher costs.<sup>5</sup> Polypharmacy is often associated with a decreased quality of life, including decreased mobility and cognition especially in the elderly.<sup>6</sup> Periodic evaluation of polypharmacy studies needs to be carried out to enable suitable modifications in the prescription of drugs to increase the therapeutic benefit and decrease the adverse effects of adverse effects of the prescribed concoction of medicines. This study aims to analyze the polypharmacy in patients with co-existing diabetes mellitus type II and hypertension in a tertiary care center.

## MATERIAL AND METHODS

### Source of data

Patients with co-existing hypertension and diabetes mellitus attending the medicine department of Owaisi Hospital and Research center. (OHRC) Hyderabad.

### Inclusion Criteria

1. Patients with co-existing hypertension and diabetes mellitus type II (with or without associated chronic complications).
2. Patient who gave informed consent.
3. Patients of 40-70 years age group of either sex.

### Exclusion Criteria

1. Patients with type-1 diabetes mellitus.
2. Patients who did not give informed consent.
3. Patients aged less than 40 years and more than 70 years.
4. Gestational diabetes mellitus.
5. Acute complications like diabetic ketoacidosis and infection.

### Methods of collection of data

- A. Study design - Non-interventional, observational, descriptive study
- B. Study duration - 1 year 6 months (January 2015 – June 2016)
- C. Sample size - 240 patients
- D. Place of study - Owaisi Hospital and Research Centre, Telangana.
- E. Statistical analysis - Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean  $\pm$  SD (Min-Max) and results

on categorical measurements are presented in Number (%).

### Statistical Software

The Statistical software namely SPSS 22.0, and R Environment Ver.2.11.1 were used for the analysis of the data, and Microsoft Word and Excel have been used to generate graphs, tables, etc.

## METHODOLOGY

After obtaining clearance and approval from the institutional ethical committee, 240 cases of hypertension and co-existing diabetes mellitus (with or without associated chronic complications) as diagnosed by a physician, fulfilling the above-mentioned criteria and who gave informed consent were included in the study. Details from the case records were noted using study proforma.

The results obtained were analyzed under the following headings:

1. Age and gender-wise distribution of patients with hypertension and co-existing diabetes mellitus
2. Duration of diabetes mellitus and hypertension.
3. Class-wise distribution of antidiabetic agents and antihypertensive agents prescribed.
4. Percentage of drugs prescribed for other co-morbid conditions.
5. Percentage of patients with polypharmacy (5 or >5 drugs/prescription)

## RESULTS

The present non-interventional, prospective, observational study was carried out for 1 year 6 months and a total of 240 case records were collected and were analyzed and arranged in appropriate tables.

**Table 1.** Age distribution of patients studied

Age in years	Number of patients	% of patients
40-45	40	16.6
46-50	54	22.5
51-55	26	10.3
56-60	66	27.5
61-65	43	17.9
66-70	11	4.5
Total	240	100

**Epidemiological profile****Age distribution**

Table I shows the age wise distribution of hypertension with co-existing diabetes mellitus patients. The mean age of the study population was  $53.97 \pm 7.62$  years.

**Gender-wise distribution**

Table II shows the gender wise distribution in the study population. Out of 240 patients studied, 52.5% were male and 47.5% were female.

**Socio-economic status**

Table III shows the socio-economic status of patients studied. In the study population 62% were from low socio-economic status and 38 % were from middle class.

**Duration of type-2 diabetes mellitus in years**

Table IV shows the duration of type-2 diabetes mellitus in the study population with mean duration being  $7.94 \pm 4.66$  years.

**Duration of hypertension**

Table V shows the duration of hypertension in the study population with mean duration being  $7.1 \pm 4.3$  years.

**Drug data****Prescription of antidiabetic drugs**

Table VI shows the individual antidiabetic drugs prescribed in the study population in the descending order, Metformin (77.5%), Glimepiride (32.1%), Insulin (29.1%), Glibenclamide (24.2%), Glucalazide (14.1%), Voglibose and Pioglitazone (16.25% each) and least common prescribed was Acarbose (3%).

**Prescription of antihypertensive drugs**

Table VII shows the antihypertensive drugs prescribed in the study population in the following descending order, Amlodipine (42.5%), Enalapril (32.5%), Ramipril (22.9%), Atenolol (18.75%), Metoprolol (12%), Losartan (10.4 %), Hydrochlorothiazide (10%), Telmisartan (8.7%), Olmesartan (2%), Nebivolol and Prazosin (1.25% each) and Nifedipine (0.8%).

**Drugs prescribed for comorbid conditions**

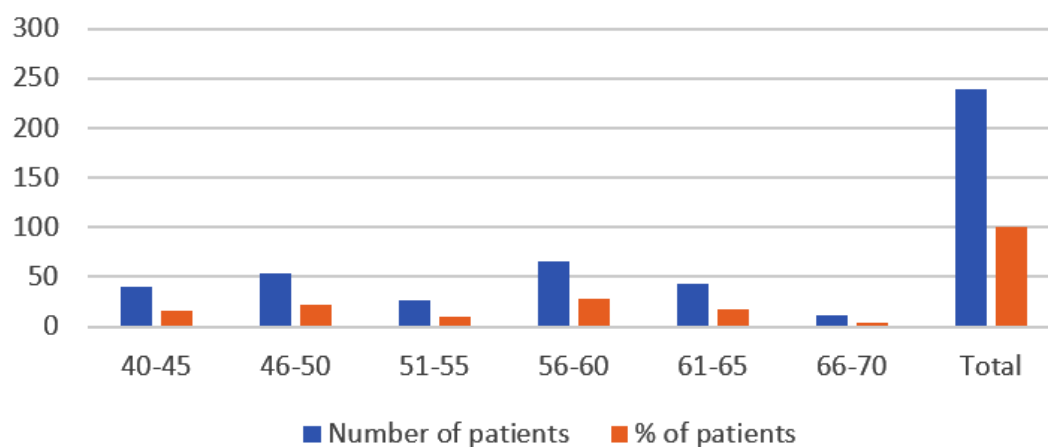
Table VIII shows the drugs prescribed for other co-morbid conditions in the study

**Table 2.** Gender distribution of patients studied

Gender	Number of patients	% of patients
Male	126	52.5
Female	114	47.5
Total	240	100.0

**Table 3.** Socio-economic status of patients studied. (According to Prasad classification)

Socio-economic status	Number of patients	% of patients
Low	148	62
Middle	92	38
High	0	0.0
Total	240	100.0

**Age distribution****Graph 1.** Age-wise distribution of study population

population. Drugs for other co-morbid conditions were prescribed in the following descending order: Vitamins (51.6%), Hypolipidemics (42.5%), Miscellaneous (41.6%), Antiplatelets (40%), H2 blockers/PPI (35.8%), and Antibiotics (22.5%).

#### Number of drugs prescribed per encounter

Table IX shows the number of drugs prescribed/ patient/encounter. Polypharmacy (5 or more than 5 drugs) was seen in 33.75% of study population.

### DISCUSSION

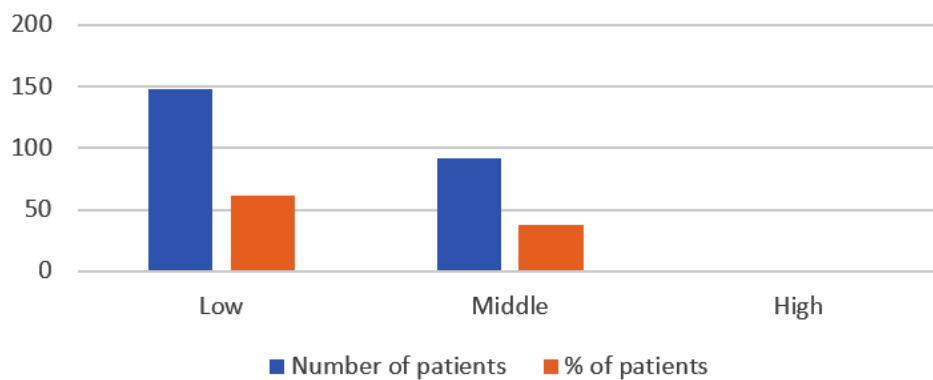
In the present study, polypharmacy was observed in 33.75% of the study population.

The probable reason for prescribing more drugs in diabetic hypertensive patients is that these are chronic diseases, in which hypertension is usually associated with other co-morbidities like cardiovascular, cerebrovascular, renal morbidity,

**Table 4.** Duration of type-2 diabetes mellitus in years

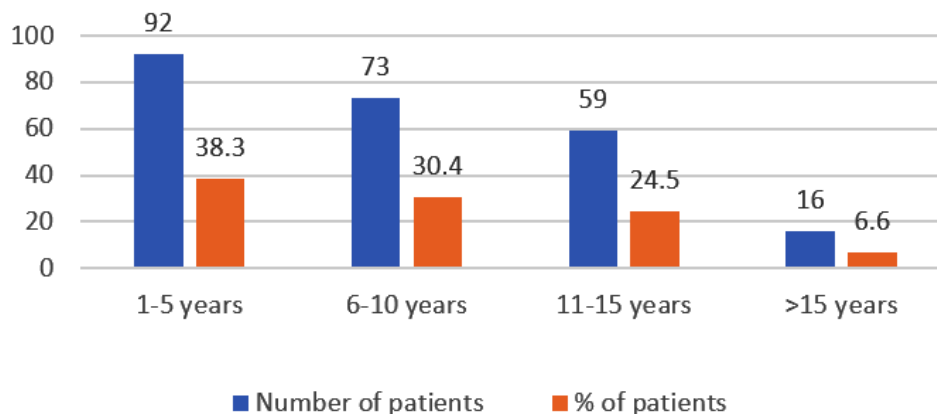
Duration of DM in years	Number of patients	% of patients
1-5 years	92	38.3
6-10 years	73	30.4
11-15 years	59	24.5
>15 years	16	6.6
Total	240	100.0

#### Socio-economic status



**Graph 2.** Socio-economic status of patients studied

#### Duration of Diabetes mellitus in years



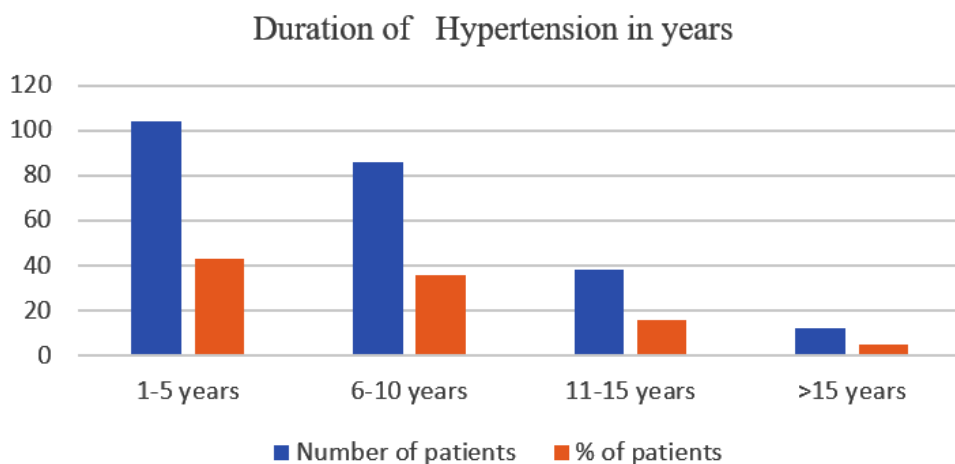
**Graph 3.** Duration of type-2 diabetes mellitus in years

and mortality whereas diabetic complications cause heart attack, stroke, blindness, and kidney disease. These serious and chronic metabolic disorders have a significant impact on the health, quality of life, and life expectancy of patients,

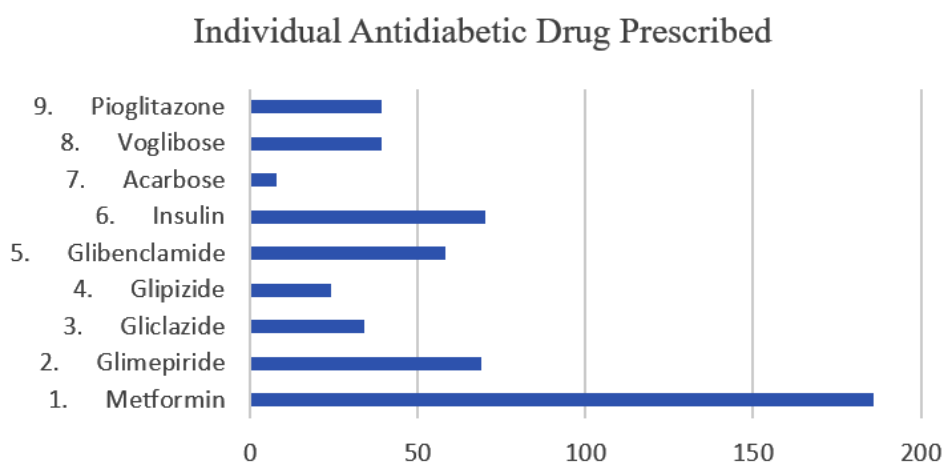
as well as on the health care systems and for the better management of these conditions more drugs are prescribed.<sup>7</sup> Many studies have demonstrated

**Table 6.** Antidiabetic drugs prescribed

<b>Table 5.</b> Duration of hypertension in years					
Duration of Hypertension in years	Number of patients	% of patients	Antidiabetic drugs	Number of patients	% of patients
1-5 years	104	43.3	1. Metformin	186	77.5
6-10 years	86	35.8	2. Glimepiride	69	32.1
11-15 years	38	15.8	3. Gliclazide	34	14.1
>15 years	12	5	4. Glipizide	24	10
Total	240	100.0	5. Glibenclamide	58	24.2
			6. Insulin	70	29.1
			7. Acarbose	8	3
			8. Voglibose	39	16.25
			9. Pioglitazone	39	16.25



**Graph 4.** Duration of hypertension in years

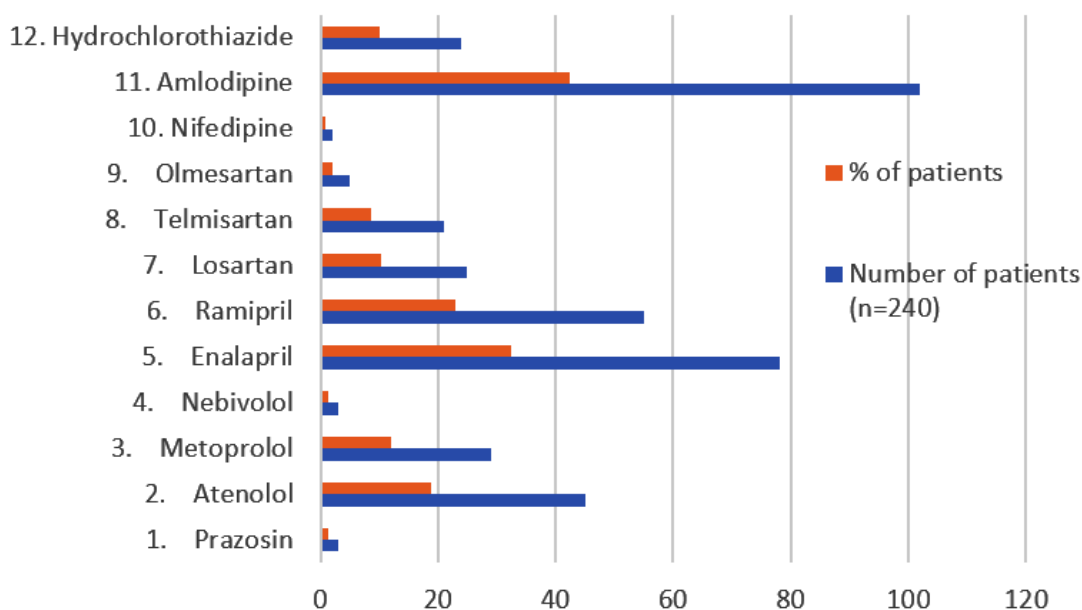


**Graph 5.** Antidiabetic drugs prescribed

the need to prevent complications of hypertension with coexisting diabetes mellitus not just with tight glycemic and blood pressure control, but also control of other factors associated with increased risk of cardiovascular complications like Coronary artery disease and Hyperlipidemia. In the present study, Lipid-lowering drugs were prescribed to 42.5% of the study population. Evidence now exists about the benefits of statins in reducing cardiovascular events in diabetic patients independent of lipid levels.<sup>8</sup> H2 blockers/ PPI were prescribed to 35.8% of the study population which indicates the high incidence of acid peptic disease in the study population.<sup>9</sup> Antiplatelets were prescribed to 40% of the study subjects. This shows the presumed high risk of cardiovascular complications like Ischemic heart disease in diabetic hypertensive patients. 5000 patients were followed for 12 years in the MRFIT trial and it was found that the occurrence of cardiovascular disease (CVD) was up to three times more in diabetic men than nondiabetic controls, irrespective of systolic pressure, age, cholesterol, ethnic group, or use of tobacco. The same study also confirmed that systolic HTN, elevated cholesterol, and cigarette

smoking were independent predictors of mortality and that the presence of at least one of these risk factors had a greater impact on increasing CVD mortality in patients with diabetes than in those without diabetes.<sup>10</sup> Overuse of vitamins (51.6%) was also observed in this study. Several reasons can be attributed to the upsurge in the use of dietary supplements for the management of diseases. Diabetes and hypertension represent a huge financial cost to the government and affected individuals, which is predicted to increase over the next 20 years. Not everyone can afford the latest technology and advancements in the treatment of these diseases, dietary supplements and pharmacological interventions are therefore necessary.<sup>11</sup> In this study polypharmacy is about 33.75%, which is similar to a cross-sectional analysis of the Survey of Health, Ageing, and Retirement in Europe (SHARE) database which showed that the prevalence of polypharmacy, defined as taking five or more medications concurrently in older adults aged 65 years or more, was between 26.3% and 39.9% among 17 European countries and Israel.<sup>12</sup> Another study done by Agrawal and Nagpur revealed that  $\leq 4$  number of

### Antihypertensive drugs prescribed



Graph 6. Antihypertensive drugs prescribed

drugs were prescribed to 74% population, 5–9 number of drugs were prescribed to 25% population which is similar to this study in which  $\leq 4$  drugs were prescribed to 66.25% of the study population and 5-9 drugs were prescribed to 33.75% of the study population.<sup>13</sup> One Canadian study, which enrolled nursing home residents, reported polypharmacy employment in 214 patients with type 2 diabetes mellitus and arterial hypertension, with 48% of these patients having been prescribed at least nine drugs. More non-antidiabetic drugs were prescribed in patients with overtreated diabetes (those receiving at least one antidiabetic drug, with an HbA1c  $\leq 7.5\%$ ). The authors concluded that the aggressive treatment of cardiovascular

risk factors raises the risk of polypharmacy, especially in frail patients.<sup>14</sup> Observational studies have shown that polypharmacy is associated with increased side effects, harmful drug interactions, medication non-adherence, and functional and cognitive decline, and frailty.<sup>15</sup> It has also been reported to be associated with other important adverse health outcomes such as the increased risk of hospitalization and mortality.<sup>16</sup> However, no validated tool or strategy has been proven superior in improving polypharmacy-related patient outcomes. Also, no one validated tool assesses all aspects of potentially inappropriate medication use or polypharmacy.<sup>17</sup> Based on a 2018 Cochrane review, it is unclear if interventions to reduce inappropriate polypharmacy improve patient-oriented outcomes.<sup>17</sup>

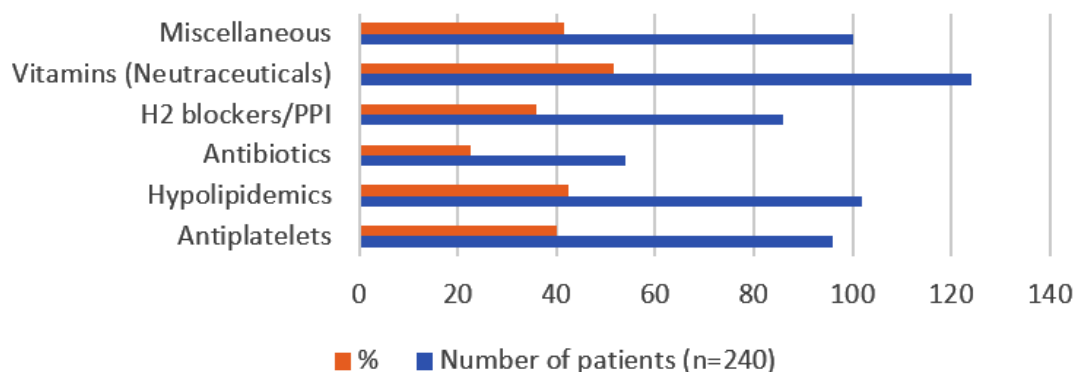
**Table 7.** Antihypertensive drugs prescribed

Antihypertensive Drugs	Number of patients(n=240)	% of patients
1. Prazosin	3	1.25
2. Atenolol	45	18.75
3. Metoprolol	29	12.0
4. Nebivolol	3	1.25
5. Enalapril	78	32.5
6. Ramipril	55	22.9
7. Losartan	25	10.4
8. Telmisartan	21	8.7
9. Olmesartan	5	2
10. Nifedipine	2	0.8
11. Amlodipine	102	42.5
12. Hydrochlorothiazide	24	10

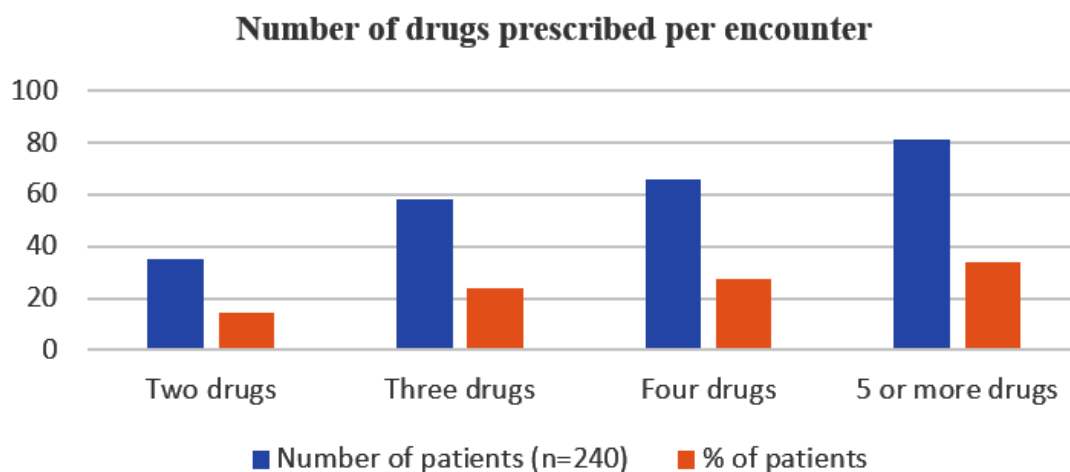
**Table 8.** Patients prescribed with drugs for other co-morbid conditions

Drug category	Number of patients (n=240)	%
1. Antiplatelets	96	40
2. Hypolipidemics	102	42.5
3. Antibiotics	54	22.5
4. H2 blockers/PPI	86	35.8
5. Vitamins (Neutraceuticals)	124	51.6
6. Miscellaneous	100	41.6

### Patients prescribed with drugs for other co-morbid conditions



**Graph 7.** Patients prescribed with drugs for other co-morbid conditions

**Graph 8.** Number of drugs prescribed per encounter**Table 9.** Number of drugs prescribed per encounter

Number of Drugs Prescribed per Encounter	Number of patients (n=240)	% of Patients
Two drugs	35	14.5
Three drugs	58	24.1
Four drugs	66	27.5
5 or more drugs	81	33.75

## CONCLUSION

Polypharmacy has been found to be integral in patients with coexisting hypertension, diabetes mellitus type II, and other comorbidities. It is essential to practice judicious prescribing especially in patients with multiple conditions. Moreover, the physicians should identify and prioritize medications to discontinue and discuss potential deprescribing with the patient.<sup>18-19</sup> Three professional organizations in the American Board of Internal Medicine Foundation's Choosing Wisely campaign (American Geriatrics Society, American Society of Health-System Pharmacists, and American Psychiatric Association) specifically mention polypharmacy and the need to review medications regularly, question the utility of adding new medications, and deprescribe when appropriate.<sup>19</sup> The necessity for immediate and effective polypharmacy management has been prioritized to decrease the risks and costs of prescriptions, especially in developing

countries. There is a need for larger studies that follow patients throughout life to improve understanding of factors predicting polypharmacy and allow detection of vulnerable people at earlier stages.<sup>20</sup> Distinguishing between appropriate and inappropriate polypharmacy is necessary and more studies are needed to apply this approach.

## ACKNOWLEDGMENT

I would like to thank Professor and Head of the Medicine department, Owaisi hospital and research center, Dr. Siraj and Dr. Mohammed Mohsin, Professor and Head of the Department of Pharmacology, Deccan college of medical sciences for their support.

## Conflict of interest

Nil

## Funding

Nil

## REFERENCES

- Masnoon, Nashwa; Shakib, Sepehr; Kalisch-Ellett, Lisa; Caughey, Gillian E. "What is polypharmacy? A systematic review of definitions". *BMC Geriatrics*. 17(1):230 (2017). doi:10.1186/s12877-017-0621-2. ISSN 1471-2318. PMC 5635569. PMID 29017448
- Sharma P, Gupta N L, Chauhan H S. Prevalence of Polypharmacy: Comparing the status of Indian states. *Indian j Community Fam Med* [serial online] 2019;5:4-9. Available from: <https://www.icfm.org/text.asp?2019/5/1/4/262114>



3. Seema Abhijeet, Cowall. The current status of diabetes mellitus in India – NCBI. *Australasian medical journal*, **7**(1) 45-48 (2014).
4. T. Linjakumpu, S. Hartikainen, T. Klaukka, J. Veijola, S.-L. Kivelä, and R. Isoaho, "Use of medications and polypharmacy are increasing among the elderly," *Journal of Clinical Epidemiology*, **55**(8): 809–817 (2002). View at: Publisher Site | Google Scholar
5. Haider SI, Johnell K, Weitoft GR, Thorslund M, Fastbom J. "The influence of educational level on polypharmacy and inappropriate drug use: a register-based study of more than 600,000 older people". *Journal of the American Geriatrics Society*. **57**(1): 62–9 (2009). doi:10.1111/j.1532-5415.2008.02040.x. PMID 19054196. S2CID 205703844
6. "Polypharmacy in Elderly Patients" (PDF). Vumc.nl. Archived from the original (PDF) on 22 January 2016. Retrieved 16 January 2015.
7. Afolayan AJ, Wintola OA. Dietary supplements in the management of hypertension and diabetes - a review. *Afr J Tradit Complement Altern Med*. **11**(3):248-258 (2014). Published 2014 Apr 3. doi:10.4314/ajtcam.v11i3.35
8. Bishnu H. Subedi, MD, Rajesh Tota-Maharaj, et al. The Role of Statins in Diabetes Treatment. *Diabetes Spectrum*; **26**(3): 156164 (2013). <https://doi.org/10.2337/diaspect.26.3.156>
9. Xiong X, Chen J, He M, Wu T, Yang H. Helicobacter pylori infection and the prevalence of hypertension in Chinese adults: The Dongfeng-Tongji cohort. *J Clin Hypertens*; **22**:1389-1395 (2020).
10. Multiple risk factor intervention trial. Risk factor changes and mortality results. Multiple Risk Factor Intervention Trial Research Group. *JAMA*; **248**:1465–1477. (1982) [PubMed] [Google Scholar]
11. Bastaki S. Review: Diabetes mellitus and its treatments. *Int J Dia Metabol*; **13**:111–134 (2005). [Google Scholar] [Ref list]
12. Midão L, Giardini A, Menditto E, et al. Polypharmacy prevalence among older adults based on the survey of health, ageing and retirement in Europe. *Arch Gerontol Geriatr*; **78**: 213–220 (2018). [PubMed] [Google Scholar]
13. Agrawal RK, Nagpure S. A study on polypharmacy and drug interactions among elderly hypertensive patients admitted in a tertiary care hospital. *Int J Health Allied Sci*; **7**:222 (2018). [Full text]
14. McCracken R., McCormack J., McGregor M.J., Wong S.T., Garrison S. Associations between polypharmacy and treatment intensity for hypertension and diabetes: A cross-sectional study of nursing home patients in British Columbia, Canada. *BMJ Open*; **7**:e017430 (2017). doi: 10.1136/bmjopen-2017-017430. [PMC frearticle] [PubMed] [CrossRef] [Google Scholar]
15. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf*; **13**: 57–65. (2014) [PMC free article] [PubMed] [Google Scholar]
16. Leelakanok N, Holcombe AL, Lund BC, et al. Association between polypharmacy and death: a systematic review and meta-analysis. *J Am Pharm Assoc* (2003) ; **57**: 729–738.e10 (2017). [PubMed] [Google Scholar]
17. Rankin A, Cadogan CA, Patterson SM, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev*. **9**: CD008165 (2018).
18. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med*; **175**(5):827–834 (2015).
19. Choosing Wisely. An initiative of the ABIM Foundation. <http://www.choosingwisely.org>. Accessed May, 2021.
20. Khezrian M, McNeil CJ, Murray AD, Myint PK. An overview of prevalence, determinants and health outcomes of polypharmacy. *Ther Adv Drug Saf*. 2020; **11**: 2042098620933741. Published 2020 Jun 12. doi:10.1177/2042098620933741