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

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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 ± 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± 4.3 years and 7.94 ± 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.
independent chronic diseases in the same person, a fact that is almost always accompanied by multiple drug use. Concerns about polypharmacy include increased adverse drug reactions, drug interactions, prescribing cascade, and higher costs. Polypharmacy is often associated with a decreased quality of life, including decreased mobility and cognition especially in the elderly. 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 ± 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 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 ± 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± 4.66 years.

Duration of hypertension

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

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%), Gliclazide (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         |

### 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, and other co-morbidities.

| 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        |

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

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

**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. Many studies have demonstrated

| Table 5. Duration of hypertension in years |
|-------------------------------------------|
| Duration of Hypertension in years | Number of patients | % of patients |
|--------------------------------------|--------------------|---------------|
| 1-5 years                             | 104                | 43.3          |
| 6-10 years                            | 86                 | 35.8          |
| 11-15 years                           | 38                 | 15.8          |
| >15 years                             | 12                 | 5             |
| Total                                 | 240                | 100.0         |

| Table 6. Antidiabetic drugs prescribed |
|----------------------------------------|
| Antidiabetic drugs | Number of patients | % of patients |
|---------------------|--------------------|---------------|
| 1. Metformin         | 186                | 77.5          |
| 2. Glimepiride      | 69                 | 32.1          |
| 3. Gliclazide        | 34                 | 14.1          |
| 4. Glipizide        | 24                 | 10            |
| 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. 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. 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. 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. 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. Another study done by Agrawal and Nagpur revealed that ≤4 number of

**Antihypertensive drugs prescribed**

| 12. Hydrochlorothiazide | 11. Amlodipine | 10. Nifedipine | 9. Olmesartan | 8. Telmisartan | 7. Losartan | 6. Ramipril | 5. Enalapril | 4. Nebivolol | 3. Metoprolol | 2. Atenolol | 1. Prazosin |
|------------------------|-------------|--------------|-------------|--------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| % of patients          |             |              |             |              |             |             |             |             |              |             |              |
| Number of patients     |             |              |             |              |             |             |             |             |              |             |              |
| (n=240)                |             |              |             |              |             |             |             |             |              |             |              |

**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 ≤4 drugs were prescribed to 66.25% of the study population and 5–9 drugs were prescribed to 33.75% of the study population. 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 ≤7.5%). The authors concluded that the aggressive treatment of cardiovascular risk factors raises the risk of polypharmacy, especially in frail patients. 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. It has also been reported to be associated with other important adverse health outcomes such as the increased risk of hospitalization and mortality. 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. Based on a 2018 Cochrane review, it is unclear if interventions to reduce inappropriate polypharmacy improve patient-oriented outcomes.

**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  |

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

- Miscellaneous
- Vitamins (Neutraceuticals)
- H2 blockers/PPI
- Antibiotics
- Hypolipidemics
- Antiplatelets

% Number of patients (n=240)
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.18-19 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.19 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.20 Distinguishing between appropriate and inappropriate polypharmacy is necessary and more studies are needed to apply this approach.

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