Assessment of Comorbidities, Polypharmacy and Drug Therapy Problems Among Hypertensive Patients at a Tertiary Care Teaching Hospital

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ABSTRACT
The treatment of hypertension requires special attention because of comorbid conditions and polypharmacy. A previous study found that polypharmacy was associated with a high risk of drug therapy problems (DTPs). The study aimed to analyse the correlation between comorbidity, polypharmacy and drug therapy problems in hypertensive patients. A prospective observational study was conducted among 100 hypertensive patients in Navodaya medical college hospital, Raichur for a period of three months. Classification of DTPs were done using Pharmaceutical Care Network Europe V6.02. The data obtained were analyzed using univariate descriptive analysis. The result revealed that a total of 87 DTP were identified in 70 patients out of 100 study subjects. From the patients studied 53 (76%) had at least one DTP. Unnecessary drugs 30 (43%) followed by potential interactions 23 (33%) and need additional drug therapy 20 (26%) were the most common DTP identified. Similarly comorbidity was found in 69 study subjects. Independent factors which predicted the occurrence of DTPs in the study population were presence of comorbidity in 69% and polypharmacy in 75% of hypertensive patients. A significant percentage of patients being treated for hypertension experienced DTP. These DTPs were associated with poor blood pressure control. The implementation of clinical pharmacy services for all patients with hypertension is strongly recommended. The role of clinical pharmacist and physicians in monitoring drug therapy needs to be prioritized to prevent and resolve DTPs in patients with hypertension. Thus efforts that could boost compliance and minimizes substance use should be adopted.

Keywords: Co-morbidity, Polypharmacy, Drug therapy problem, Hypertension, World health organization.
INTRODUCTION
Hypertension, also known as high or raised blood pressure, is a global public health issue. It contributes to the burden of heart disease, stroke, kidney failure, premature mortality and disability. It disproportionately affects populations in low- and middle-income countries where health systems are weak.\(^1\) Currently, high BP is considered a real global epidemic, with the latest estimates showing that around 1.13 billion people suffer from this disease globally, with its overall prevalence being around 30–45%. Ultimately, a worrying aspect regarding hypertension is the population’s awareness of this subject. Although, according to the latest estimates, approximately 59% of patients receive correct antihypertensive treatment (compared to 31% in previous years), only 34% have controlled BP (lower than 140/90 mmHg), and over 30% of patients are not aware that they have high BP.\(^2\) In 2019, it was reported that in India, approximately 29.8% of people suffered from increased blood pressure.\(^3\) As it is a multifactorial disease, this increase in cases could be attributed to both genetic as well as environmental risk factors.\(^4\)

Hypertension is usually associated with other co-morbid conditions. Modern medicine has heralded a slew of medical innovations that have revolutionized disease treatment in patients, not only in the treatment of hypertension but other conditions as well. The increasing number of developed drug classes has benefited mankind immensely, but when faced with the problem of multimorbidity, has also increased the chances of inappropriate polypharmacy. The guidelines of pharmacy were initially framed for only single morbidities and, in the wake of multi-morbidity, they are having to be reassessed.\(^5\) Patients with hypertension often receive multiple medications and have different comorbid chronic diseases that can lead to the occurrence of drug related problems.\(^6\) These co-morbidities encompass the common ones such as stroke, coronary artery disease, heart failure, chronic kidney disease, and chronic obstructive pulmonary disease, while the uncommon ones include rheumatic and psychiatric ailments. Diabetes is also common among elderly patients suffering from hypertension and requires careful monitoring by the physician to ensure adequate care is given to the patient. Ultimately, these ailments need to be treated as well as hypertension, and hence arises the problem of polypharmacy.

Polypharmacy is a complex phenomenon that has experienced an important increase in recent decades, determined mainly by the increase in life expectancy of the population and, at the same time, by a higher number of comorbidities that require the administration of a specific therapy.\(^7\) The effects of polypharmacy are numerous and should concern physicians and policy makers both in terms of finances (due to significant health costs) and medical consequences (due to multiple drug interactions).\(^8\) There is no single definition of polypharmacy as it is still debatable. The World Health Organization (WHO) defines polypharmacy as “the administration of many drugs at the same time or the administration of an excessive number of drugs.”\(^9\) In some literature, taking 2–4 drugs at the same time is classified as minor polypharmacy, whereas taking 5 or more drugs is classified as major polypharmacy. On the contrary, other sources defined the use of 10 or more drugs daily as a major polypharmacy, whereas others still termed it hyper polypharmacy. Moreover, polypharmacy may result in drug-drug interactions, potential duplication of drug therapy, decreased adherence, adverse drug events, increase in the costs to the drug therapy, hospitalizations, decreased quality of life and additional surgical or medical interventions.

Drug therapy problem (DTP) is a term describing an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.\(^10\) DTPs are classified into seven categories these including unnecessary drug therapy, need for additional drug therapy, ineffective
drug, dosage too high, dosage too low, adverse drug reaction and noncompliance. Pharmacist can play an important role in identifying, resolving and preventing potential DTP through careful pharmaceutical practice.[11] Clearly interventions to improve drug therapy problems are needed to overcome the harms imposed by the problem. If such interventions are to be successfully designed, targeted, and cost effective, it is critical to understand the complex reasons for drug therapy problem and to identify those that are modifiable in hypertensive patients. Drug therapy problems can be prevented by avoiding medication errors by the usage of computerized physician order entry tools, the interpretation, transcription, prescription errors can be reduced. Few other measures to prevent drug therapy problems are the education of individuals concerned with the process of, prevention of look-a-like products, distribution of drugs, and creating systems for early identification of adverse drug events. A potential DTP is not yet manifested, but if left unresolved, it may harm the patient. However, an actual DTP has resulted in clinical manifestations like adverse drug reactions. DTPs may arise at any stage of the medication use process from prescription to follow-up of the treatment Early identification is important for avoiding adverse drug reactions and therefore every hospital should have a system for the recognition of adverse drug reactions.[10] The study will try to estimate the correlation between polypharmacy, co-morbidities and drug therapy problems in hypertensive patients.

MATERIALS AND METHODS
This prospective observational study was conducted for a period of three months from February 2023 to April 2023 in Navodaya Medical College Hospital & Research Centre (NMCH & RC) Raichur. Permission was obtained from Institutional Ethics Committee of Navodaya Medical College Hospital and Research Centre. The study was approved by the committee by issuing ethical clearance certificate.

Data Collection: Data was collected using data entry form, case sheet and PCNE classification was used to access drug therapy problems in hypertensive patients.

Inclusion Criteria:
- Hospitalized hypertensive patients with or without co-morbidities.
- Patients above the age of 18 years.
- Prescriptions with drugs prescribed throughout hospitalization has been only decided for the study.

Exclusion Criteria:
- Participants who were not willing to participate in the study and in those were enough medical records are not available are excluded from the study.
- Patients who were pregnant and lactating/nursing a child.
- Outpatients at the time of study.
- Alternative system (Ayurveda, Siddha) of medicine.

A specially designed structured data entry format was used to enter all patient details. Provision is given in the format to enter investigations like diagnosis, drug therapy problems, comorbidities, drugs prescribed, drug interactions and any interventions.

The information obtained from case files about study participants were kept confidential and only the collected data was processed. Based on the responses obtained, data were analysed.

The collected data were analyzed and monitored for the following variables

- Socio-demographic data
- Drug therapy problems associated with comorbidities
- Polypharmacy in prescription
The data from the study were analyzed using descriptive statistics namely total numbers, percentage and mean. Microsoft excel and word were used to generate graphs, tables and results etc.

RESULTS AND DISCUSSION
The present study “Assessment of co-morbidities, polypharmacy and drug therapy problems among hypertensive patients at a tertiary care teaching hospital” was the first attempt to assess the correlation between comorbidities, polypharmacy and drug therapy problem in hypertensive patients of Navodaya Medical College Hospital & Research Centre (NMCH & RC) Raichur. It provides information on socio demographic details, comorbidities associated with drug therapy problem and polypharmacy. In this study, total 100 participants were selected, sample size was calculated based on recorded prevalence of hypertension in Raichur. Taking 95% confidence interval, the required sample size for the study was minimum of 100 study subjects. The result of this study clearly indicate that comorbidities plays a considerable role in polypharmacy associated with drug therapy problems.

![Figure 1: Age distribution of study subjects](image)

A total of 100 patients who met the inclusion criteria were recruited into the study. Out of the 100 patients in the study 35% of them were in the age group of 60-70 yrs, followed by 30% of patients in the age group of 40-50 yrs. This is depicted in Figure 1. Age is a big risk factor for hypertension. Hypertension really start to spike in middle age. The rate for developing hypertension in age group of 40-50 yrs is five times more when compared to 18-40 years.
On categorizing the study population based on gender group it was evident that most of the study population were male i.e., 57% and 43% were females. The results are shown in Figure 2. Previous studies have shown that for men, the bad news is they are more likely to be found hypertensive than females. One of the main reasons include drinking too much alcohol and smoking.

Figure 3 represent duration of hypertension. It was found that about 36% of the patients were diagnosed with hypertension in a period of between 1 to 5 yrs followed by 25% of study population who were diagnosed with hypertension in less than 5 yrs.
Among the total 100 samples collected, about 52% of the study participants comes under stage I category i.e. (SBP: 140-159 and DBP: 90-99), followed by 25% of study participants in prehypertensive stage i.e. (SBP: 120-139 and DBP: 80-89).

### Table 1: Comorbidities in hypertensive subjects

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>No of participants (n=100)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>69</td>
<td>69%</td>
</tr>
<tr>
<td>NO</td>
<td>31</td>
<td>31%</td>
</tr>
</tbody>
</table>

Table 2 depicts that among 100 hypertensive patients, 69% of the subjects have comorbidities. Hypertension is a severe threat to human being’s health due to its association with many comorbidities. The identification and management of these risk factors is an important part of the overall management of hypertensive patients because patients are more predisposed to target organ damage (TOD). There is a particular need for effective 24-hour BP control in these patients, due to the increased likelihood of non-dipping status, which is a risk factor for TOD and mortality.

### Table 2: Types of comorbidities

<table>
<thead>
<tr>
<th>Types of comorbidities</th>
<th>No of participants</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>19</td>
<td>27%</td>
</tr>
<tr>
<td>DM</td>
<td>25</td>
<td>36%</td>
</tr>
<tr>
<td>CVD</td>
<td>5</td>
<td>7%</td>
</tr>
<tr>
<td>Stroke</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>URTI</td>
<td>3</td>
<td>4%</td>
</tr>
<tr>
<td>CKD</td>
<td>11</td>
<td>16%</td>
</tr>
<tr>
<td>COPD</td>
<td>8</td>
<td>11%</td>
</tr>
<tr>
<td>UTI</td>
<td>5</td>
<td>7%</td>
</tr>
<tr>
<td>GERD</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>4</td>
<td>6%</td>
</tr>
</tbody>
</table>
Table 2: Types of comorbidities

Table 2 shows the distribution of important comorbidities. The numbers of patients in each group of each risk factor category were presented. The summary of above result shows that majority of hypertensive patients i.e. 36% are suffering from diabetes mellitus, followed by 27% of study subjects have tuberculosis and 16% of the study subjects have chronic kidney disease (CKD). Regarding the relationship between diabetes mellitus (DM) and hypertension, according to study high BP values are found in two-thirds of patients diagnosed with DM. Our study validates the close relationship between high BP and DM. Thus, approximately one-third of hypertensive patients (~36%) had associated DM. The association of these two diseases increases the risk of other cardiovascular diseases. Treatment of hypertension in diabetic patients is more difficult, with resistant hypertension being more common among these patients. Usually, for the control of BP values in patients who have associated DM, it is necessary to combine two or more antihypertensive drugs. The results from the study also showed that male hypertensive patients have comorbidities more when compared to female hypertensive patients.

Table 3: Level of Polypharmacy

As it is depicted in Table 3, the overall level of polypharmacy was 75%. Of these, a total of 25% prescriptions containing 2 to 4 drugs per prescription constitute minor polypharmacy, whereas 67% prescriptions containing 5 or more drugs constitute major polypharmacy and 8% prescriptions containing 9 or more drugs constitute hyper polypharmacy.
Table 4: Frequency of medicines taken by respondents according to age group
The present study revealed that majority of the participants i.e. 19% were prescribed below 4 medicines, 69% more than 4 drugs and 8% were using more than 10 medicines. Mean number of medications used by patients was 6.4 ± 1.25 in the current study, which showed similarity with other studies in a Tertiary Care Hospital in Puducherry, the mean number of drugs were found as 5.48±2.46 (Kartik et al, 2016).

<table>
<thead>
<tr>
<th>Age Group</th>
<th>No. of Patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-60</td>
<td>4</td>
<td>19%</td>
</tr>
<tr>
<td>60-70</td>
<td>9</td>
<td>69%</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>8%</td>
</tr>
</tbody>
</table>

Table 5: Drug therapy problem in hypertensive subjects
Table 5 depict that among 100 study subjects, 70% of them have drug therapy problem. From the patients having DTP, most of the patients 53 (76%) had at least one DTP and 17 (24%) patients had identified with two DTPs.

<table>
<thead>
<tr>
<th>DTP</th>
<th>No of Patients</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>70</td>
<td>70%</td>
</tr>
<tr>
<td>No</td>
<td>30</td>
<td>30%</td>
</tr>
</tbody>
</table>

Table 6: Category of drug therapy problem
Table 6 depicts distribution of drug therapy problem in hypertensive subjects. In 30 (43%) of cases unnecessary drugs were included in the prescription. In 20 (26%) cases showed that additional drug should be included in the prescription followed by 23 (33%) cases were found to have potential drug interactions.
Table 7: Multivariate analysis of characteristics for DRP among HTN patients

Table 7 multivariate analysis of characteristics for DRP among HTN patients. It showed that 61 hypertensive patients with comorbidities found to have DTP and 8 hypertensive patients don’t have DTP, while 9 patients without comorbidities have DTP and 22 Patients without comorbidities don’t have DTP. Similarly 50 patients with polypharmacy have DTP and 25 patients with polypharmacy don’t have DTP, while 20 patients without polypharmacy have DTP.

Recommendations

Based on the findings of this study the following recommendations are made:

➢ Special attention should be given to hypertensive patients with comorbidity and should be closely monitored for DTPs.
➢ To effectively establish and develop pharmaceutical care services in hospitals since the current findings have important implications on practice, particularly pertaining to the implementation of pharmaceutical care services.
➢ To strengthen pharmaceutical care services since early identification and prevention of drug therapy problem in hypertensive patients are necessary to prevent complication.
➢ Special attention should be given to counselling which is important to increase the awareness and knowledge of this patient.
➢ To Researchers to investigate the impact of DTP on health outcome

CONCLUSION

This study showed managing patients with hypertension is prone to different DTP for different reasons including presence of comorbidity, polypharmacy and concurrent medication. In this study, relatively higher prevalence of DTPs was identified and the most common were need of additional therapy and unnecessarily prescribed medication. This study also showed that comorbidity is highly prevalent in hypertensive patients of Raichur district. The independent predictor found to be associated with drug therapy problem were presence of comorbidity, number of medication (Polypharmacy) and uncontrolled blood pressure. The number of DTPs among patients with hypertension is relatively high in both patients with controlled and uncontrolled blood pressure. These DTPs were associated with poor blood pressure control. A more valid design is needed to investigate how and how much resolving identified DTPs will impact blood pressure control. Pharmaceutical care services are strongly recommended for all patients with hypertension, even those with controlled blood pressure who suffer from several DTPs. Effectiveness, adherence and monitoring DTPs should be given the highest priority.
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CONFLICT OF INTEREST
The author declare no conflict of interest.

REFERENCE