INTRODUCTION

Benign prostatic hyperplasia (BPH) is a noncancerous condition in which there is multiplication of prostatic stromal and epithelial cells which lead to enlargement of prostatic gland [1]. It is the most common medical condition affecting elderly males and its prevalence increases from 25% in the age group of 40–49 years to 80% in 70–79 years age [2]. The risk factors of BPH are divided into non-modifiable factors such as age, genetic, and modifiable factors such as testosterone, obesity, diabetes, diet, physical activity, and inflammation [3]. Symptoms of BPH include frequent urination, inability to urinate, weak stream, trouble starting to urinate, and if untreated may lead to complications such as frequent urinary tract infections, bladder damage, and kidney damage [4,5].

The medical management of BPH includes alpha-blockers such as prazosin, alfuzosin, doxazosin, silodosin, tamsulosin, and terazosin. These drugs act by blocking the alpha receptors present in the prostate gland thus relaxes the muscles of the prostate and urethra but they do not reduce the size of the prostate and are associated with side effects such as headache and dizziness. The second group of drugs is the 5 alpha-reductase inhibitors, which includes finasteride and dutasteride. These drugs act by blocking the production of dihydrotestosterone, a male sex hormone, thereby shrinking the prostate gland and their side effects include fatigue and retrograde ejaculation [6].

India is a hub of branded generic market, which means that the doctors, instead of prescribing underlying formulation of drugs, prescribe the brand name of the drugs. Doctors many times prescribe leading brands though there is the availability of affordable brands and patients are ignorant about cheaper substitutes of drugs, they sometimes buy the expensive drug brands recommended by their doctors. This will have a direct effect on patient’s finance adversely if the costly brand is prescribed, especially in conditions like BPH, in which patients need treatment for prolonged duration. These reasons have enabled the government to take a step forward to make essential drugs accessible to patients at reasonable prices [7]. In India, National Pharmaceutical Pricing Authority (NPPA) controls and regulates the prices of pharmaceutical drugs in India and it has limited authority to fix, review and justify pharmaceutical prices under the Drug Prices Control Order (DPCO), 1995 [8].

In developing countries like India, pharmacoeconomic analysis of drugs plays a key role for policy-makers in analyzing the affordability and also access to the rational use of drugs. Cost variation analysis of drugs is a type of pharmacoeconomic evaluation method, which compares the costs of two or more drugs without regard to outcome. By this evaluation method, one can understand different brands of the same drug, inter-brand cost variation, the best cost-effective drug available which will guide doctors in selecting the right drug for a particular disease condition [9].

The present study was aimed at investigating the cost differences in various brands of drugs used in the treatment of BPH, following which a cheaper effective brand can be prescribed, which will ensure better patient adherence to drugs, good compliance and will also reduce total healthcare expenditure. Medical management is the main modality of treatment in BPH and also as it is more common in the aging population who also suffer from other co-morbidities such as hypertension and diabetes, thus requiring multiple daily medications. There are no studies in Indian scenario, which compare the cost of different drugs used in the management of BPH. The study has the following objectives: (1) To evaluate cost variation of different brands of the drugs used in the treatment of BPH and (2) to assess cost ratio of the drugs used in the treatment of BPH.
METHODS
The cost of alpha-blockers—prazosin, terazosin, doxazosin, alfuzosin, tamsulosin, silodosin, and 5 alpha-reductase inhibitors—finasteride and dutasteride which are used in the treatment of BPH and available in the Indian market was noted from CIMS (Oct 2019–Jan 2020), Drugs Update, and Medline. The cost of the drugs in the same strength and form which are manufactured by different pharmaceutical companies was noted. For oral forms of the drug, price was calculated per 10 tablets. All the prices were calculated in Indian rupees. Drugs with fixed-dose combinations, two or more drugs manufactured by the same company in the same strength or form were excluded from the study.

The cost ratio was calculated using the formula:

\[ \text{Cost ratio} = \frac{\text{Cost of most expensive brand}}{\text{Cost of the least expensive brand}} \]

This will tell how many times the costliest brand costs more than the cheapest one in each group.

The difference in the maximum and minimum price of the same drug formulation was calculated.

The percentage variation in cost was calculated using the formula:

\[ \text{Cost variation (\%)} = \left( \frac{\text{Cost of the least expensive brand} - \text{Cost of the most expensive brand}}{\text{Cost of the least expensive brand}} \right) \times 100 \]

Based on percentage variation, the cost of all the drugs was divided into four groups as follows:

Group 1: <24.99%
Group 2: 25-49.99%
Group 3: 50-99.99%
Group 4: 100-499.99%

RESULTS
All the drugs used in the management of BPH are only available in two oral forms—tablet and capsule. These drugs are available in 10 different dosages and 242 different brand names. Table 1 shows cost variation of various drugs used in benign prostatic hypertrophy.

Prazosin is available only in tablet form, in 4 different dosages, with 29 different brands. Furthermore, terazosin is available in 3 different dosage forms, with 26 different brands. There are 3 dosage forms with 11 brands of doxazosin, while alfuzosin is available in 2 dosages with 32 brands. Tamsulosin is available in both tablet and capsule form, of which tablet is available in 51 different brands and capsule in 25 brands. Silodosin is available in both tablet and capsule forms with 12 brands each. Finasteride is available in 3 different dosages in tablet form with 32 different brands, while dutasteride is available in 2 dosages, in both tablet and capsule form with 4 brands each. Alphuzosin is available in 10 mg and 2.5 mg tablet form. Finasteride is only available in tablet form in 3 different dosages and dutasteride is available in both tablet and capsule form with 4 brands each. Of all the drugs in this group, 10 mg alfuzosin and 2.5 mg finasteride have the highest and lowest percentage of cost variation, while 0.4 mg tablet form of tamsulosin is available in the maximum number of brands. Table 2 shows the classification of drugs based on the percentage of cost variation of drugs and it was highest in group 3 with 15 formulations. Mean cost of alpha-blockers and 5 alpha-reductase inhibitors used in BPH is shown in Graphs 1 and 2, respectively.

DISCUSSION
The main objective of the study was to identify the cost variation and cost ratio of different brands of drugs used in the medical management of BPH in India and this study reveals that there is huge cost variation among various formulations of these drugs. Further more, similar studies done in the past with anti-hypertensive drugs [10], anxiolytic drugs [11], drugs used in thromboembolic disorders [12], and anticancer drugs [13] have also given conclusion on huge cost variation of drugs. The results of the study indicate that despite the measures of cost control of drugs in India, under Drug Price Control Order (DPCO) initiative by the Government of India, significant inter-brand cost variations still exist in the Indian pharmaceutical market. The main objective of DPCO was to bring down or even remove such inter-brand cost variations, but the results of the study clearly indicate that to date it has not yet achieved its objectives completely [14].

Table 1: Cost variation of various drugs used in benign prostatic hypertrophy

| Drugs        | Forms | Dose (mg) | No. of brands | Minimum price (INR)* | Maximum price (INR)* | Cost ratio | Cost variation (%) |
|--------------|-------|-----------|---------------|-----------------------|-----------------------|------------|-------------------|
| Prazosin     | Tablet | 1         | 3             | 60-114                | 2.8-2.2               | 185        |                   |
|              | Tablet | 2         | 1             | 97                    | 125                   | 1.6        | 100               |
|              | Tablet | 2.5       | 11            | 50                    |                        |            |                   |
|              | Tablet | 5         | 14            | 75                    |                        |            |                   |
| Terazosin    | Tablet | 1         | 14            | 182                   | 4.5                   | 355        |                   |
|              | Tablet | 2         | 9             | 107                   | 2.5                   | 152        |                   |
|              | Tablet | 5         | 3             | 161                   | 3.3                   | 235        |                   |
| Doxazosin    | Tablet | 1         | 5             | 39                    | 2.1                   | 116        |                   |
|              | Tablet | 2         | 4             | 74                    | 2.9                   | 196        |                   |
|              | Tablet | 4         | 2             | 87                    | 1.1                   | 15         |                   |
| Alphuzosin   | Tablet | 5         | 2             | 89                    | 1.5                   | 51         |                   |
|              | Tablet | 10        | 30            | 451                   | 6.1                   | 518        |                   |
| Tamsulosin   | Tablet | 0.2       | 10            | 40                    | 2.6                   | 168        |                   |
|              | Capsule| 0.4       | 41            | 225                   | 5.7                   | 477        |                   |
|              | Capsule| 0.2       | 10            | 94                    | 2.7                   | 176        |                   |
|              | Capsule| 0.4       | 15            | 225                   | 5.6                   | 463        |                   |
| Silodosin    | Tablet | 4         | 2             | 180                   | 1.3                   | 33         |                   |
|              | Capsule| 8         | 2             | 259                   | 1.2                   | 23         |                   |
|              | Capsule| 4         | 6             | 128                   | 1.3                   | 36         |                   |
|              | Capsule| 8         | 18            | 185                   | 2.2                   | 105        |                   |
| Finasteride  | Tablet | 1         | 16            | 29                    | 3.7                   | 279        |                   |
|              | Tablet | 2.5       | 3             | 63                    | 1.1                   | 14         |                   |
|              | Tablet | 5         | 13            | 60                    | 3.1                   | 217        |                   |
| Dutasteride  | Tablet | 0.5       | 4             | 107                   | 1.6                   | 62         |                   |
|              | Capsule| 0.5       | 4             | 166                   | 1.5                   | 57         |                   |
Therefore, there is an urgent need of controlling cost of various drugs of which high cost of drugs is found to be the main reason [16]. The huge doctor fees, and high cost of drugs are the reasons for OOP expenses from the patients. Unnecessary operations, poor quality of care, and expensive drugs belong to low socioeconomic class leading to an increase in Out of Pocket expenditure from the patients. Some patients are burdened with huge cost variation, due to high prices of branded drugs from different pharmaceutical companies has resulted in huge cost variation among the drugs [15]. All these factors lead to huge economic burden on patients, especially those belonging to low socioeconomic class leading to an increase in Out of Pocket expenditure from the patients. In many cases, doctors have to write rational prescriptions and need to adhere to the rules and regulations before prescribing. Furthermore, given the magnitude of inter-brand variations observed among the drugs in this study, it is strongly recommended that the government authorities need to revise their pricing policies on drugs, ensure regulatory checks on pharmaceutical companies to bring all brand prices within ceiling prices, thus reducing economic burden on patients and health care system. Prescribing doctors have to write rational prescriptions and need to adhere to the World Health Organization (WHO) standards for prescriptions. This will definitely make quality health care accessible to India’s present and future generations.

CONCLUSION

This study shows that there is a wide variation in the cost of most of the drugs used in BPH which are available in India. Health care providers must be aware of the availability of low-cost brands or generics and they also need to have a moral responsibility to consider drug prices before prescribing. Furthermore, given the magnitude of inter-brand variations observed among the drugs in this study, it is strongly recommended that the government authorities need to revise their pricing policies on drugs, ensure regulatory checks on pharmaceutical companies to bring all brand prices within ceiling prices, thus reducing economic burden on patients and health care system. Prescribing doctors have to write rational prescriptions and need to adhere to the World Health Organization (WHO) standards for prescriptions. This will definitely make quality health care accessible to India’s present and future generations.

AUTHORS’ CONTRIBUTIONS

Dr. Vibha Rani: Concept and design of the study, extensive literature search, data analysis, statistical analysis, manuscript preparation, manuscript editing, and reviewing the manuscript. Dr. Sailaxmi Venepally: Extensive literature search, data analysis, statistical analysis, manuscript preparation, manuscript editing, and reviewing the manuscript.

CONFLICTS OF INTEREST

Nil.

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