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Original Research Article

Cost variation analysis of various brands of anti-retroviral agents currently available in Indian market: an economic perspective study

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ABSTRACT

Background: The aim was to analyze the percentage cost variations among different brands of the commonly prescribed anti-retroviral agents in the treatment of human immunodeficiency virus.

Methods: The cost of different brands of commonly used Anti-Retroviral agents was sorted out by referring latest Indian drug index online, drug today, current index of medical specialties, Indian drug review.

Results: The percentage variation in the cost was above 100% with most of the commonly used anti-retroviral agents. Overall sequinafir 500 mg shows maximum cost variation of 1490.3%, while nelfinavir (625 mg) shows minimum cost variation of 6.1% in single drug therapy. Lamivudine 300 mg and tenofovir 300 mg combination shows maximum cost variation of 14055% whereas, lamivudine 150 mg, zidovudine 300 mg and efavirenz 600 mg shows minimum cost variation of 10% in combination drug therapy.

Conclusions: HIV is the most common infectious, life-threatening disease and drugs are to be prescribed for life-long period. If a costly brand is prescribed, the patients cannot afford to pay more money for their treatment. This also leads to poor patient compliance, dissatisfaction and failure of the treatment. Ideally, therefore, the drugs should be prescribed in such a way, to save the patient's economic burden and enhance the compliance of the treatment.

Keywords: Human immune deficiency virus, Anti-retroviral agents, Drug price control order, Pharmaco-economics, Cost variation

INTRODUCTION

Human immunodeficiency viruses (HIV) are lentiviruses belong to a family of retroviruses, is a chronic persistent infection that attacks the body's immune system, specifically the CD4 cells (white blood cells) with gradual onset of clinical symptoms.^{1,2} The prevalence of HIV infection in India is estimated to be 0.22% accounting for, the third largest number of people living with HIV.³ It is most commonly found among the age group of 15-45 years. HIV being one of the most prevalent causes of death which requires a lifelong therapy.⁴

It is shown that introduction of anti-retroviral treatment (ART) for people with HIV infection had led to decline in morbidity and mortality with significant improvement on the quality of life.^{5,6} Anti-retroviral agents (ARVs) has shown to be the most promising line of therapy in the management of HIV infections.² The pharmacotherapy of HIV infection is a rapidly moving field. The current minimum standard of care includes three drug combinations. So available agents and formulations constitute several thousand possible regimens.¹ HIV being an incurable disease and require a lifelong therapy, it is associated with significant and long-lasting health, social and financial burdens, for both patients and the caregivers.⁴ In limited resource countries like India,

health sector has been affected, leading to increase in the cost of medicines.^{4,7}

In a developing country like India pharmaco-economics plays an important role. Cost of the drug is an essential factor influencing patient compliance with the treatment of disease. There are many branded formulations of the same drug supplied by the pharmaceutical industries with large difference in selling price. This may affect the patient's finance adversely if costly brand is prescribed specially in diseases like HIV which need treatment for lifetime.⁸ Increasing cost of medicines may be one of the reason for people not accessing health care.⁴ Insufficient knowledge about the cost of ARVs can be difficult for physician to decide and prescribe economical treatment regime.⁴ Sparsity of studies comparing cost of various brands of ARVs available in the Indian market led us to carry out the study which compares the cost of different brands of ARVs. Hence, the study was designed to evaluate the variation of cost of ARVs belonged to different classification.¹ Drugs belonging to different brand names available in Indian market used for the treatment of HIV are also included in the study. The study here focuses on cost variation analysis on different brands of ARVs available in the Indian market. This will help physicians to prescribe economical drugs which will improve patient compliance.

METHODS

This study was conducted in the department of pharmacology, Bangalore medical college and research institute. The study was exempted from ethical committee review because it did not involve any human or animal subjects. Data were obtained from the following sources; current index of medical specialties (CIMS) December-March 2022, drug today January to April 2022 Vol. No. I, Indian drug review (IDR) 2022, Indian drug index (IDI) 2020 online.

This study had an analytical study design, the maximum and minimum costs of various ARVs for ten tablets/capsules used in the treatment of HIV were obtained. Cost in INR (₹) of various ARVs being manufactured by different companies in the same strength and dosage form were compared. The study includes both single drug therapy and combination drug therapy. Cost ratio and percentage cost variation were derived from the below data. Cost ratio is defined as the ratio of the cost of highest priced to the lowest priced branded formulations of the same drug, in same strength, same dosage form, for the unit containing same number of tablets. Cost ratio gives valuable information on how many times is the cost of the most expensive brand more than the least expensive brand, for the drug considered for evaluation.⁹

Cost ratio between the maximum and minimum cost of the same drug manufactured by different pharmaceutical companies was calculated as follows,

$$\text{Cost ratio} = \frac{\text{maximum cost}}{\text{minimum cost}}$$

Percentage cost variation (%) was calculated as follows: (Highest branded price of a particular drug Formulation-Lowest branded price of the same drug formulation)/Lowest branded price of the same drug formulation $\times 100$ ⁹

$$\% \text{ Cost variation} = \frac{\text{maximum cost} - \text{minimum cost} \times 100}{\text{minimum cost}}$$

The drug formulation being manufactured by only one company was excluded. Data obtained were analyzed using descriptive statistics.

RESULTS

The prices of commonly used ARVs (22 single and 16 combination preparations) manufactured by different pharmaceutical companies were analyzed. The percentage cost variation of 22 commonly used ARVs, used as a single drug therapy is depicted in (Table 1).

Overall Sequinafir 500 mg shows maximum price variation of 1490.3%, while Nelfinavir (625 mg) shows minimum variation of 6.1%. The maximum and minimum percentage price variation respectively for each group is as follows. Nucleoside reverse transcriptase inhibitors: Lamivudine 150 mg is 1023.2% and Tenofovir 25 mg is 33%. Non-nucleoside reverse transcriptase inhibitors: Nevirapine 200 mg 557.9% and Efavirenz 200 mg 71.9%. Protease inhibitors: Sequinavir 500 mg 1490.3% and Nelfinavir 625 mg 6.1%. Integrase Inhibitors: Dolutegravir 50 mg 42.6% and Raltegravir 400 mg 1%. Percentage cost variation of 16 commonly used ARVs combination is depicted in (Table 2). Lamivudine 300 mg and Tenofovir 300 mg combination shows maximum variation of 14055% whereas, Lamivudine 150 mg, Zidovudine 300 mg and Efavirenz 600 mg shows minimum variation of 10%.

DISCUSSION

Anti-Retroviral agents (ARVs) is highly recommended in the treatment for HIV patients. It has seen to suppress the HIV infection by targeting different stages in the life cycle of HIV replication. It is efficient in suppressing the viral load below the level of detection in plasma, which helps in drastic improvement in survival of patients because long-term HIV infection causes selective reduction of T lymphocytes that express CD4 molecules, which leads to an extreme immunosuppression. Hence early combined ART may be more favourable in HIV.² Our study findings showed a very high fluctuation in the minimum and maximum price of ARVs (Figure 1-4) which is being manufactured by several companies across the different brands. The cost ratio was also observed to be very high (Figure 2-5). The percentage variation in the cost was above 100% with most of the commonly used

ARVs (Figure 3) and also with combination of ARVs (Figure 6).

A similar study done by Panchal et al at Mumbai also showed significant higher price variations in different

brands of the same anti-retroviral drugs.⁴ More than one pharmaceutical company sells a particular drug under different brand names in India. Over 100,000 formulations are there in Indian market.

Table 1: Minimum and maximum cost, cost ratio and percentage cost variation of single drug therapy as anti-retroviral agents.

| Drug | Minimum cost (Per 10 tablets) | Maximum cost (Per 10 tablets) | Cost ratio | Percentage of cost variation |
|--|-------------------------------|-------------------------------|------------|------------------------------|
| Single drug therapy | | | | |
| Nucleoside reverse transcriptase inhibitors (in mg) | | | | |
| Zidovudine 100 | 37.14 | 204 | 5.49273 | 449.3 |
| Zidovudine 300 | 90.46 | 600 | 6.632766 | 563.3 |
| Tenofovir 300 | 389 | 833.33 | 2.142237 | 114.3 |
| Stavudine 30 | 35.31 | 225 | 6.372133 | 537.3 |
| Stavudine 40 | 37.7 | 90 | 2.387268 | 138.8 |
| Lamivudine 100 | 76 | 535 | 7.039474 | 604 |
| Lamivudine 150 | 92.65 | 1040.56 | 11.23108 | 1023.2 |
| Didanosine 250 | 233 | 745 | 3.197425 | 219.8 |
| Didanosine 400 | 377 | 984 | 2.61008 | 161.1 |
| Abacavir 300 | 470 | 1466 | 3.119149 | 212 |
| Tenofovir alfenamide 25 | 389 | 517.19 | 1.329537 | 33 |
| Non-nucleoside reverse transcriptase inhibitors (in mg) | | | | |
| Nevirapine 200 | 142.5 | 937.5 | 6.578947 | 557.9 |
| Efavirenz 200 | 232.74 | 400 | 1.718656 | 71.9 |
| Efavirenz 600 | 644.47 | 2000 | 3.103325 | 210.4 |
| Protease inhibitors (in mg) | | | | |
| Indinavir 400 | 26.43 | 400 | 15.13432 | 1413.5 |
| Nelfinavir 250 | 230.76 | 400 | 1.733403 | 73.4 |
| Nelfinavir 625 | 509 | 540 | 1.060904 | 6.1 |
| Sequinavir 200 | 38.43 | 246 | 6.401249 | 540.2 |
| sequinavir 500 | 54.5 | 866.66 | 15.90202 | 1490.3 |
| Atazanavir 300 | 525 | 766 | 1.459048 | 46 |
| Darunavir 300 | 761.91 | 879.15 | 1.153876 | 15.4 |
| Darunavir 600 | 1569.93 | 1833.33 | 1.167778 | 16.8 |
| Integrase Inhibitors | | | | |
| Dolutegravir 50 | 833.33 | 1187.66 | 1.425198 | 42.6 |
| Raltegravir 400 | 1448.1 | 1462.12 | 1.009682 | 1 |
| CCR5 receptor inhibitors (in mg) | | | | |
| Maraviroc 150 | 1746.03 | 1833.33 | 1.049999 | 5 |

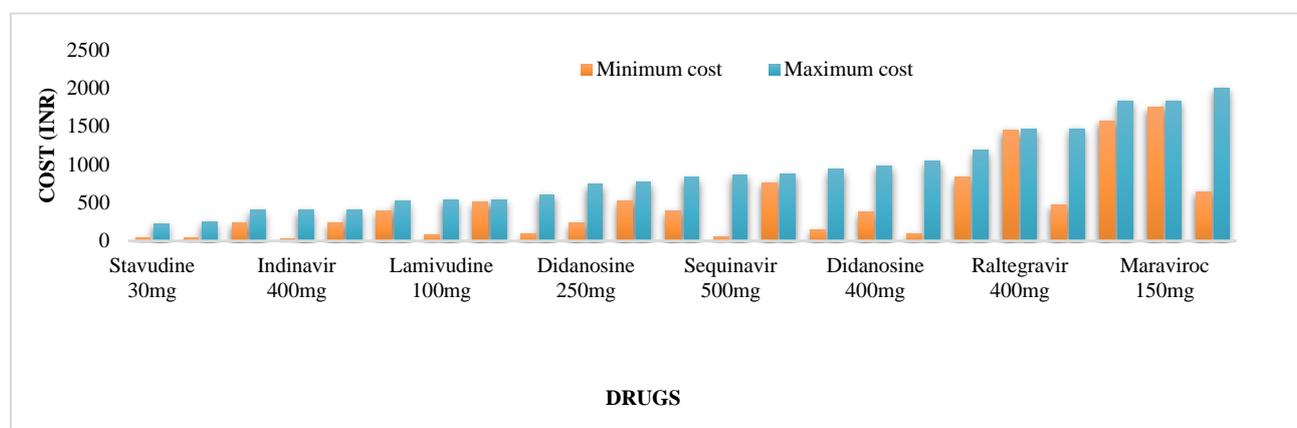


Figure 1: Cost difference (minimum and maximum) commonly used antiretroviral drugs used as a single drug therapy.

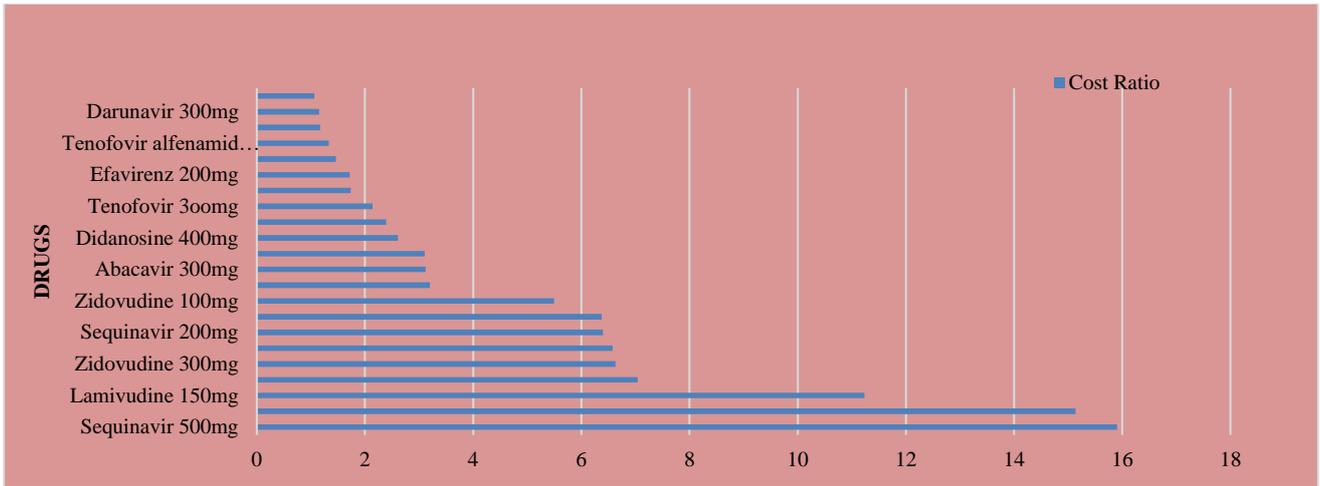


Figure 2: Cost ratio of commonly used antiretroviral drugs used as a single drug therapy.

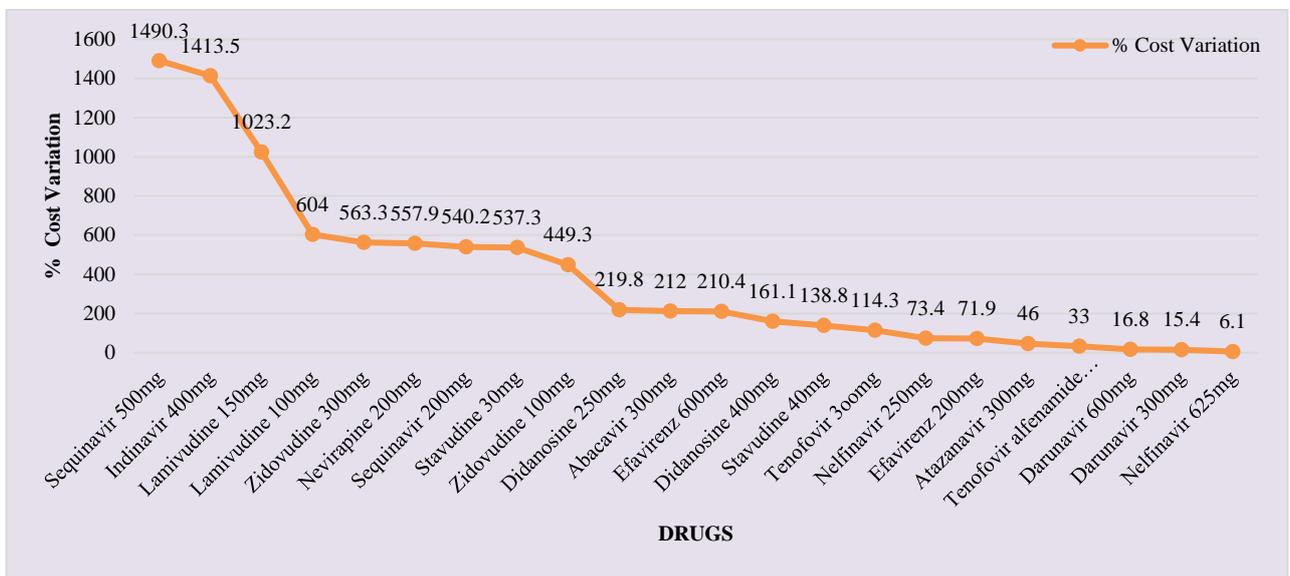


Figure 3: Percentage cost variation of commonly used antiretroviral drugs used as a single drug therapy.

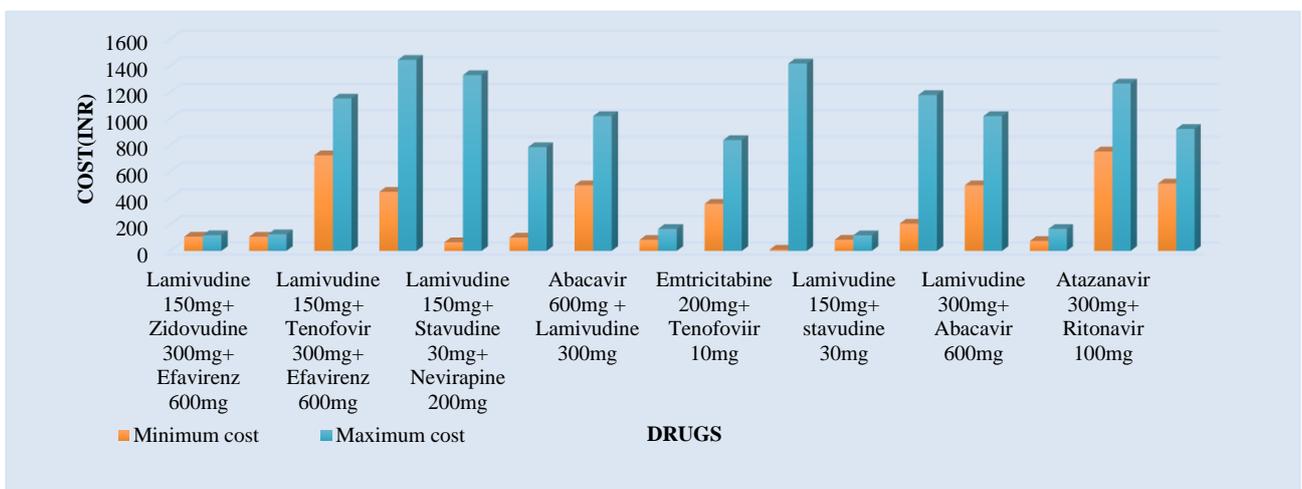


Figure 4: Cost difference (minimum and maximum) commonly used antiretroviral drugs used as a combination drug therapy.

Table 2: Minimum and maximum cost, cost ratio and percentage cost variation of combination drug therapy as anti-retro viral agents.

| Drug | Minimum cost (Per 10 tablets) | Maximum cost (Per 10 tablets) | Cost ratio | Percentage of cost variation |
|--|-------------------------------|-------------------------------|------------|------------------------------|
| Combination drug therapy | | | | |
| Lamivudine 150 mg+Zidovudine 300 mg+Efavirenz 600 mg | 107.51 | 118.2 | 1.099433 | 10 |
| Lamivudine 150 mg+Didanosine 250 mg+Efavirenz 600 mg | 107 | 125.19 | 1.17 | 17 |
| Lamivudine 150 mg+Tenofovir 300 mg+Efavirenz 600 mg | 721.66 | 1150.94 | 1.594851 | 59.5 |
| Emtricitabine 200 mg+Tenofovir 300 mg+Efavirenz 600 mg | 445.51 | 1443.55 | 3.240219 | 224.1 |
| Lamivudine 150 mg+Stavudine 30 mg+Nevirapine 200 mg | 65.38 | 1328 | 20.31202 | 1931.3 |
| Lamivudine 150 mg+Zidovudine 300 mg+Nevirapine 200 mg | 100 | 783.19 | 7.8319 | 683.2 |
| Abacavir 600 mg +Lamivudine 300 mg | 495.33 | 1017.6 | 2.054388 | 105.5 |
| Tenofovir 300 mg+Emtricitabine 200 mg+Atazanavir 300 mg+Ritonavir 100 mg | 83.33 | 166 | 1.99208 | 99.3 |
| Emtricitabine 200 mg+Tenofovir 10 mg | 355.56 | 836.66 | 2.353077 | 135.4 |
| Lamivudine 300 mg+Tenofovir 300 mg | 10 | 1415.5 | 141.55 | 14055 |
| Lamivudine 150 mg+ Stavudine 30 mg | 84.45 | 117.75 | 1.394316 | 39.5 |
| Lamivudine 150 mg+ zidovudine 300 mg | 206 | 1177.71 | 5.717039 | 471.8 |
| Lamivudine 300 mg+ Abacavir 600 mg | 495.3 | 1017.6 | 2.054512 | 105.5 |
| Tenofovir 300 mg+ Lamivudine 300 mg+ Atazanavir 300 mg+ Ritonavir 100 mg | 75 | 166 | 2.213333 | 121.4 |
| Atazanavir 300 mg+Ritonavir 100 mg | 750 | 1263.65 | 1.684867 | 68.5 |
| Lopinavir 200 mg+Ritonavir 50 mg | 508.8 | 920.63 | 1.809414 | 81 |

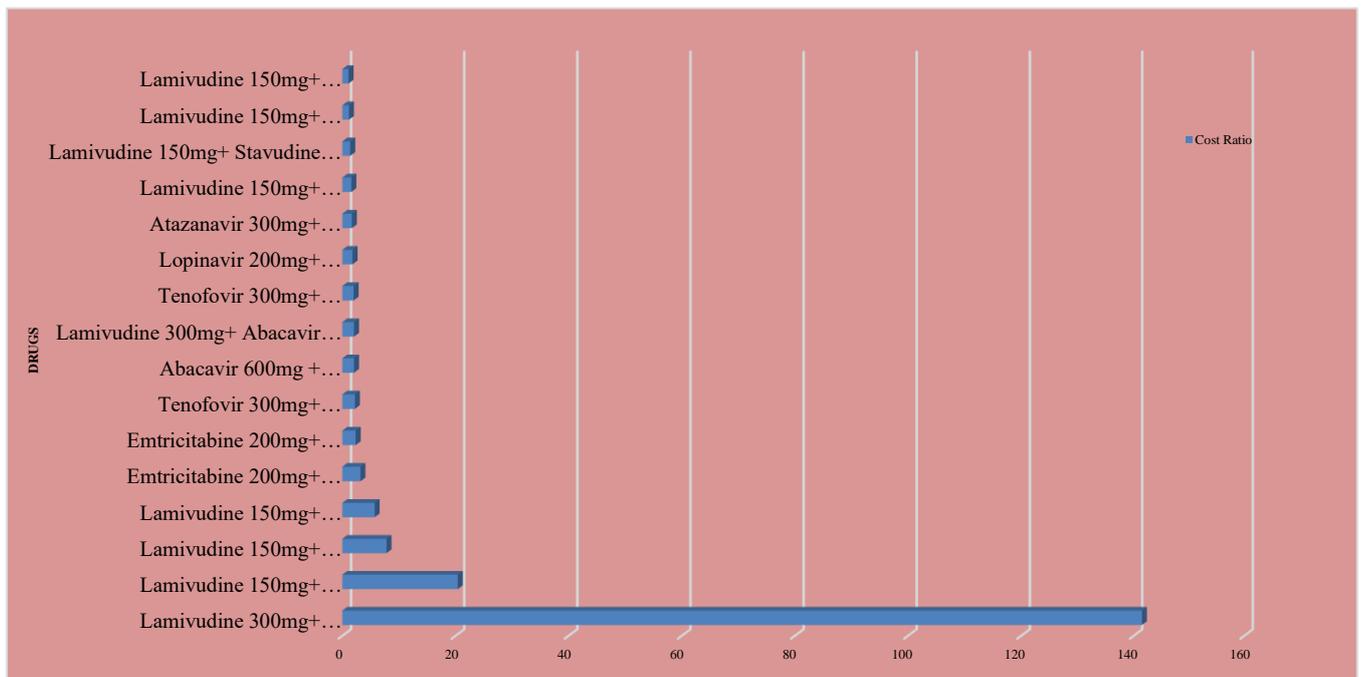


Figure 5: Cost ratio of commonly used antiretroviral drugs used as a combination drug therapy.

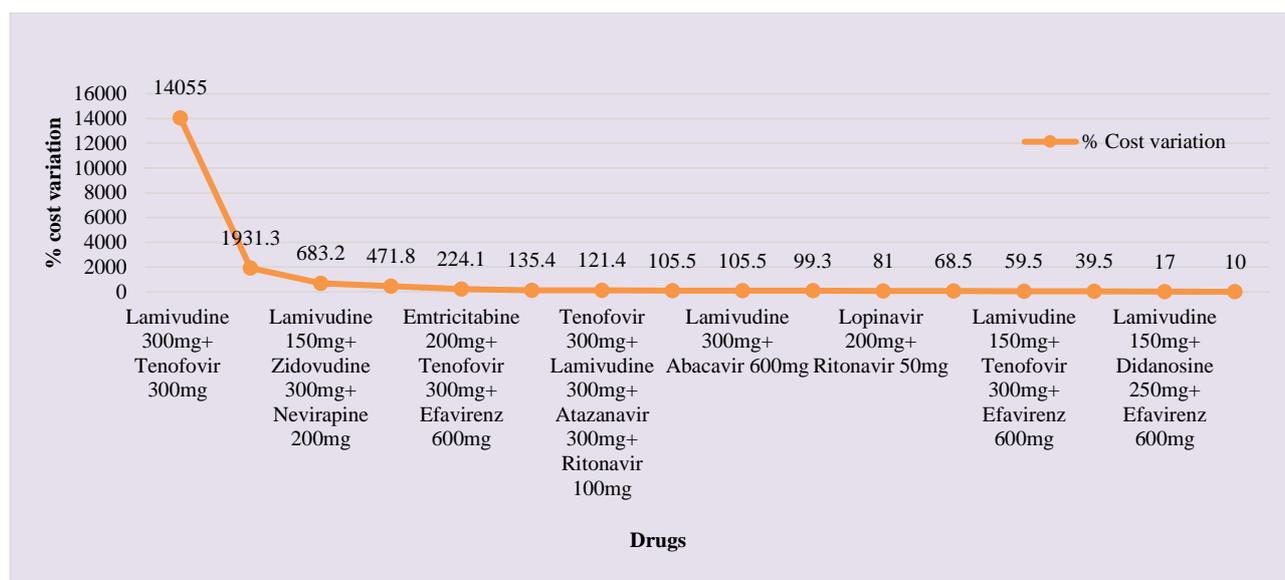


Figure 6: Percentage cost variation of commonly used antiretroviral drugs used as a combination drug therapy.

There is no system of registration of medicines.⁸ Because of this there is a greater price variation among drugs marketed. This situation with wide variations of drug formulations of same drug has led to severe economic drawback in India. An order is issued by the Indian government to fix prices of drugs called Drug price control order (DPCO).^{4,8,9} Under DPCO once the medicine is bought it cannot be sold at higher price than that fixed by the government. Very few drugs under ARVs are listed under DPCO updated in 2022. Many combinations available outside are not listed under DPCO.¹⁰ Over the years' drugs under DPCO is decreased, this has increased the cost of medicines and in turn has become an economic burden for the unaffordable patients. Hence, it is desired that the Government should bring all lifesaving drugs and combinations under price control. The combination of ART has significantly shown prognosis in HIV patients. So it is preferred over single drug therapy.¹¹ But the combination of ARVs is expensive compared to single drug therapy. Since in India most of the patients are not covered under medical insurance and also not all diseases are covered under the same, so it is very difficult for patients with low socio-economic status to pay for the medicines. This is leading to poor compliance of the treatment, because patients are not affordable to the medicines.⁴ Since there is absence of information on prices and quality of drugs along with the combinations, it is difficult for the doctors to prescribe most effective and economical treatment to the patients.⁴ Also Government of India, sells generic medicines manufactured by public sector companies under generic drug stores.⁸ Government should increase the number of combinations under these generic stores at cheaper rates. The disability and cost of care associated with HIV can potentially impose considerable economic burden on the family. Our current study only measures the price of the drug. Several other direct and indirect costs are not

included in our study. Also, inherent to this methodological design, there is a lack of relevant comparison on drug efficacy and safety. Further studies in the same direction are needed.

CONCLUSION

This study finding provides a wide variation in the prices of different brands of same anti-retroviral agents available in India, used in the treatment of HIV. This wide variation can cause poor compliance, economic burden among patients and dissatisfaction. A strong awareness to be created among government, general public, healthcare workers, pharmacists and policy makers to reduce the economic burden on patients as well as health care system. This will encourage the usage of drugs with low cost among the general population and healthcare providers. Results of our study make the prescriber informed about various brands and their price variations. So the prescriber can choose the cost effective Anti-Retroviral agents for a patient with HIV, in order to achieve rational prescribing.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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