Pharmacoeconomic evaluation of Levothyroxine in the treatment of Hypothyroidism in Nepal

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INTRODUCTION

Hypothyroidism is a disorder of endocrine system in which the thyroid gland does not produce enough thyroid hormone [1]. Worldwide, too little iodine in the diet is the most common cause of hypothyroidism [2]. The symptoms include tiredness, unexplained weight gain, muscle cramps, slow heart rate, sensitivity to cold temperatures, constipation, depressed mood and memory difficulty [3]. In population-based studies, women were more likely to develop hypothyroidism, and seven times more likely than men to have TSH levels above 10 mU/L [4]. The prevalence of thyroid disorders in general population of 5 districts of Nepal, was 4.32% as of 2019 [5]. Hypothyroidism was also found to be prevalent in all age group of female residents of western region of Nepal [6]. Most people with hypothyroidism symptoms and confirmed thyroxine deficiency are treated by thyroid hormone replacement therapy with a synthetic long-acting form of thyroxine, known as levothyroxine (L-thyroxine) [4,7]. Medical professionals adjust the dose according to symptoms and normalization of the thyroxine and TSH levels [1].

Pharmacoeconomics is the branch of health economics that focuses on weighing the costs and benefits of a particular intervention in comparison with an analogous alternative [8]. Levothyroxine that is commercially available in Nepal, is manufactured by many pharmaceutical companies of India. Despite the yearly rise in incidence of hypothyroidism, our nation lacks manufacturing potential of levothyroxine for its general population with hypothyroidism, as there is only 1 company named Pharmonics Life Sciences Pvt. Ltd. Budhari-12, Sunsari, Nepal, which has been manufacturing it [9]. In a developing country like ours, where cost is one of the major limiting factor for seeking medical help, cost can largely affect the treatment seeking behavior of hypothyroid patients, with levothyroxine, which generally has to be consumed life long.

Since, cost of drugs is an important factor influencing compliance with treatment [10]. The maximum retail price of levothyroxine for different strengths and quantity varies between the companies manufacturing it in India, as well as it also varies with that of levothyroxine manufactured in Nepal. The variation in cost of levothyroxine under different brand names, makes it difficult to select a particular brand drug for a patient, and also the selection of a personal drug (P-drug) as per the WHO guide to good prescribing, becomes difficult, as the selection is largely influenced by the cost of drug [11]. Hence, it is very important for the prescribers to be updated on the cost of drugs available in the practicing area / country.

Though, levothyroxine is the mainstay of treatment of hypothyroidism, no pharmacoeconomic studies have been carried out for it in Nepal, thus this study was conducted.
to evaluate the cost ratio and percentage cost variation, of different brands of levothyroxine, available in the Nepali market. The findings of this study can be used by a treating physician for prescribing an alternative cheaper brand of levothyroxine for better compliance and for reducing the total health-care cost.

**MATERIALS AND METHODS**

**Study design and setting:**

This observational pharmacoeconomic study, was carried out at Department of Pharmacology of Janaki Medical College, Janakpurdham, Nepal from 5 April to 30 May, 2023.

**Data collection procedure and study variables:**

Maximum retail price (Cost) in Nepalese currency (NPR), of levothyroxine available in Nepali market, of same dosage form but different strength and quantity manufactured by various pharmaceutical companies of Nepal and India was obtained from different pharmacy shops, drug suppliers of Nepal and also, the Current Index of Medical Specialities (CIMS, 44th Year, Jan-Apr. 2023, India) was reviewed for the cost of levothyroxine manufactured by Indian pharmaceutical companies. The difference of maximum and minimum cost of levothyroxine, manufactured by different pharmaceutical companies, but having the same strength, number and dosage form were calculated and compared to find out the cost ratio and percentage (%) cost variation by using the formulas [12]:

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

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

**Statistical analysis and data management:**

The collected data was checked for completeness and correctness. Data was entered into MS Excel 2010. The data was analyzed and results were calculated in terms of frequency and percentages.

**Ethical consideration:**

The ethical approval for the study was taken from Janaki Medical College (IRC/23/2079-080), before the commencement of the study.

**RESULTS**

The cost of levothyroxine available in different strengths in microgram (mcg) and quantity as manufactured by pharmaceutical companies of Nepal and India were analyzed. For 120 tablets of levothyroxine, maximum cost ratio of 1.37 and percentage cost variation of 37.14% was observed with 50 mcg of levothyroxine while minimum cost ratio of 1.02 and percentage cost variation of 2.72% was observed with 12.5 mcg of levothyroxine (Table 1).

For 100 tablets of levothyroxine, maximum cost ratio of 1.65 and percentage cost variation of 65.44% was observed with 50 mcg of levothyroxine. Minimum cost ratio of 1.13 was observed with 75 mcg and 125 mcg of levothyroxine while the minimum percentage cost variation of 13.09 was observed with 125 mcg of levothyroxine (Table 2).

**DISCUSSION**

Levothyroxine is the main stay of treatment for hypothyroidism, but except for Pharmonics life sciences Pvt Ltd. Bugdari-12, Sunsari, Nepal, the major supply of levothyroxine is from Indian Pharmaceutical companies, for treatment of hypothyroidism in Nepal.

Cost ratio, which indicates the number of times an expensive drug is costlier than its cheapest counterpart, of levothyroxine of different strengths and quantity is not too much as seen in results. However, the percentage cost variation was highest (37.14%) with 50mcg of 120 levothyroxine tablets followed by 13.19% for 25mcg of 100 levothyroxine tablets packaging, which suggest that, the prescribing physician can reduce the cost of treatment by

<table>
<thead>
<tr>
<th>Doses (mcg)</th>
<th>No. of Manufacturing Pharmaceutical companies</th>
<th>Minimum retail price in NPR (Brand name/ Pharmaceutical company)</th>
<th>Maximum retail price in NPR (Brand name/ Pharmaceutical company)</th>
<th>Cost Ratio</th>
<th>Percentage cost variation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5</td>
<td>2</td>
<td>282 (Thyronics / Pharmonics Life Sciences)</td>
<td>289.68 (Thyronorm / Abbott)</td>
<td>1.02</td>
<td>2.72</td>
</tr>
<tr>
<td>25</td>
<td>4</td>
<td>275 (Thyronics / Pharmonics Life Sciences)</td>
<td>311.28 (Thyrox / Macleods)</td>
<td>1.13</td>
<td>13.19</td>
</tr>
<tr>
<td>37.5</td>
<td>2</td>
<td>281.05 (Thyronorm / Abbott)</td>
<td>310 (Thyronics / Pharmonics Life Sciences)</td>
<td>1.10</td>
<td>10.30</td>
</tr>
<tr>
<td>50</td>
<td>4</td>
<td>154.03 (Eltroxin / GSK)</td>
<td>211.24 (Thyronorm / Abbott)</td>
<td>1.37</td>
<td>37.14</td>
</tr>
<tr>
<td>75</td>
<td>4</td>
<td>257.40 (Thyrox / Macleods)</td>
<td>280 (Thyronics / Pharmonics Life Sciences)</td>
<td>1.08</td>
<td>8.78</td>
</tr>
<tr>
<td>100</td>
<td>4</td>
<td>255 (Thyronics / Pharmonics Life Sciences)</td>
<td>284.94 (Thyrox / Macleods)</td>
<td>1.11</td>
<td>11.74</td>
</tr>
</tbody>
</table>
prescribing the lowest cost levothyroxine (Eltroxin 50 mcg, GSK), unlike for other doses of levothyroxine which do not have higher cost variation percentage. Also, Thyronics (levothyroxine, 120 tablets) manufactured by Pharmonics Life Sciences Pvt. Ltd., Bugdari-12, Sunsari, Nepal, can be a better option for reducing the cost of hypothyroidism treatment for 12.5 mcg, 25 mcg and 100 mcg of 120 levothyroxine tablets, compared to that manufactured by Indian pharmaceutical companies. The low price could be due to less of manufacturing cost, transportation cost and promotional costs.

There are no Nepali pharmaceutical companies which manufacture 100 tablets of levothyroxine packaging, so the cost ratio and percentage cost variation has been calculated for the different brand drugs manufactured by Indian pharmaceutical companies only. The cost ratio is not significantly different for different doses of levothyroxine. However, the percentage cost variation was highest (65.44%) with 50mcg of 100 levothyroxine tablets followed by 35.06% for 12.5mcg of 100 levothyroxine tablets, which suggest that, the treatment cost can be reduced for patients consuming 50mcg of levothyroxine by prescribing, Eltroxin 50mcg tablets manufactured by GSK. The difference in the cost ratio and percentage of cost variation, also suggest that the Government of Nepal, should form a policy for the various brands of levothyroxine, so as to have a uniform minimum cost of levothyroxine, which will increase the affordability and reduce the cost related noncompliance.

**CONCLUSIONS**

Wide variation in percentage cost variation was seen with levothyroxine manufactured by few pharmaceutical companies, which, suggest that, further study is needed to explore the reason of such variation for those pharmaceutical companies. Continuous pharmacoeconomic analysis, if carried out at government level, can greatly minimize the cost variation as well as reduce the overall treatment cost for hypothyroid patients in Nepal.

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**ADDITIONAL INFORMATION AND DECLARATIONS**

**Acknowledgements:** Authors would like like to acknowledge all the drug suppliers and pharmacy shop owners for providing the maximum retail prices of various brands of levothyroxine.

**Competing Interests:** The authors declare no competing interests.

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**Author Contributions:** Concept and design: L.C, Statistical analysis: L.C, R.S, R.C.S, and S.D., Writing of the manuscript: L.C, R.S, R.C.S, and S.D., R.S., Data collection: L.C, R.S, R.C.S, and S.D., Revision and editing: L.C, R.S, R.C.S, S.D. and R.S.. All authors have contributed equally for the concept and design, statistical analysis, writing of the manuscript, data collection, revision and editing. All authors have read and agreed with the contents of the final manuscript towards publication.

**Data Availability:** Data will be available upon request to corresponding authors after valid reason.

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<th>Percentage cost variation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5</td>
<td>3</td>
<td>168.81 (Thyrorich / Primus Remedies)</td>
<td>228 (Thyrox / Macleods)</td>
<td>1.35</td>
<td>35.06</td>
</tr>
<tr>
<td>25</td>
<td>6</td>
<td>182.40 (Thyrosain / Sain Medicaments)</td>
<td>234.20 (Thyrox / Macleods)</td>
<td>1.28</td>
<td>28.39</td>
</tr>
<tr>
<td>50</td>
<td>8</td>
<td>127.68 (Eltroxin / GSK)</td>
<td>211.24 (Thyronorm / Abbott)</td>
<td>1.65</td>
<td>65.44</td>
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<tr>
<td>75</td>
<td>4</td>
<td>196.72 (Thyrozyte / Aamorb)</td>
<td>222.60 (Thyrorich / Primus Remedies)</td>
<td>1.13</td>
<td>13.15</td>
</tr>
<tr>
<td>100</td>
<td>7</td>
<td>186.32 (Thyrozyte / Aamorb)</td>
<td>232 (Thycora / Corazon)</td>
<td>1.24</td>
<td>24.51</td>
</tr>
<tr>
<td>125</td>
<td>3</td>
<td>237.68 (Thyrorich / Primus Remedies)</td>
<td>268.80 (Thyrox / Macleods)</td>
<td>1.13</td>
<td>13.09</td>
</tr>
</tbody>
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REFERENCES


