

**PHARMACO-ECONOMIC ANALYSIS OF MACROLIDE
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Corresponding Author*Dr. Sujay Patil**Department of
Pharmacology, DYPUSM,
Navi Mumbai, India.**ABSTRACT**

Macrolides contain macrocyclic lactone ring and used in various infectious diseases. Macrolides inhibit protein synthesis and have excellent tissue penetration properties. Pharmaco-economic studies are important as the prescriptions by doctors usually contain brand names and less of generic names. Five macrolides were selected – Azithromycin, Clarithromycin, Erythromycin, Roxithromycin & Spiramycin which are available in Indian market. The cost of all these Macrolides was collected from Current Index of Medical Specialties (CIMS). In our study, we evident that many drugs have wide cost

range especially those drugs that are available in market under various brand names but also similar aspect found with lesser brand names. Both had significant price difference. Cost effective therapies should be emphasized for the benefit of patients by the Pharma companies and by the Government.

KEYWORDS: Macrolides, pharmaco-economic, price, generic, brand.**INTRODUCTION**

Macrolides are a class of drugs which contain a macrocyclic lactone ring of 12 or more elements in its structure. Lactone rings are usually 14, 15 or 16 membered^[1] Macrolides group of drugs are primarily used in treatment of various infectious diseases. They inhibit protein synthesis and bacterial growth followed by death of pathogen. Anti-inflammatory and anti-viral properties have been reported by some of the studies.^[2, 3] They are also called bioactive agents possessing antibiotic, antifungal, prokinetic and immunomodulatory

properties. Macrolides are widely used everywhere, as they harbor excellent tissue penetration and antimicrobial properties against gram positive and atypical bacteria.^[4]

Erythromycin was successfully used till for more than 50 years to treat various respiratory infections but due to marked instability, poor bioavailability, resistance and gastro-intestinal side effects has limited its usage worldwide. Erythromycin analogs like azithromycin and clarithromycin are stable macrolide antibiotics which are more commonly used now.^[5]

Discovery of chronic erythromycin treatment in patients of chronic inflammatory pulmonary disease called diffuse panbronchiolitis (DPB) was benefitted by improved 5 year survival rates. DPB is a chronic obstructive pulmonary disease found in Japanese people with symptoms of dyspnea on exertion, productive cough, wheezing, and weight loss. Sputum culture was positive with one or more pathogens preferably *P.aeruginosa*. Many other inflammatory pulmonary conditions are benefitted with help of macrolides including asthma, bronchiectasis, bronchiolitis, obliterans syndrome and cystic fibrosis.^[6]

Clarithromycin's intracellular cidal activity is dependent on the type of organism involved and its concentration at the target site. It is more acid stable than erythromycin and higher tissue plus plasma concentrations are achieved specially in the lung.^[7] Inhibition of leukocyte degranulation, reduction of eosinophilic inflammation, increased macrophage phagocytic activity and increase mucociliary transport, reducing mucus production in both vivo and vitro is done by macrolides.^[8]

In India, expense on health sciences spent by government is less than 1% according to the recent budget report. Pharmaco-economic studies are important as the prescriptions by doctors usually contain brand names and less of generic names. The present study aims towards survey of every drug cost by calculating cost range and cost ratio. The study would help to find out cost –effective treatments with respect to Macrolides, upgrading patient compliance and impact on national gross productivity.

MATERIALS AND METHODS

Five macrolides were selected – Azithromycin, Clarithromycin, Erythromycin, Roxithromycin & Spiramycin which are available in Indian market. The cost of all these Macrolides was collected from Current Index of Medical Specialties (CIMS). Cost has been expressed in terms of Indian National Rupees depending on the number of tablets in a packet. Generic drug cost, Cost range, Cost ratio were calculated.

Minimum and maximum costs are expressed depending on the number of tablets and cost per tablet in the packet. Quotient of maximum cost over minimum cost is been noted down for the calculation of cost ratio. Mean cost of generic drug was calculated as sum of cost of all its brand names divided by total number of brands available for the same generic drug.

OBSERVATIONS AND RESULTS

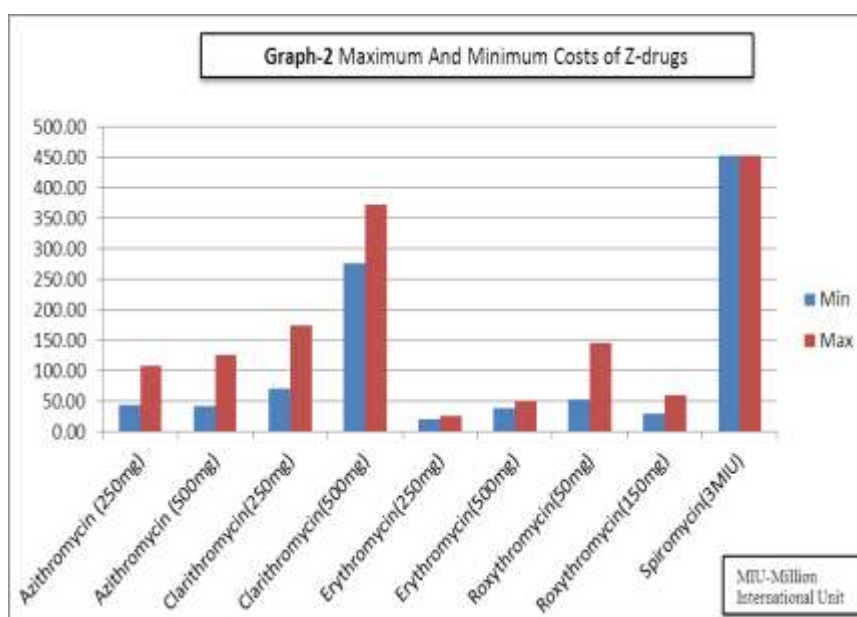
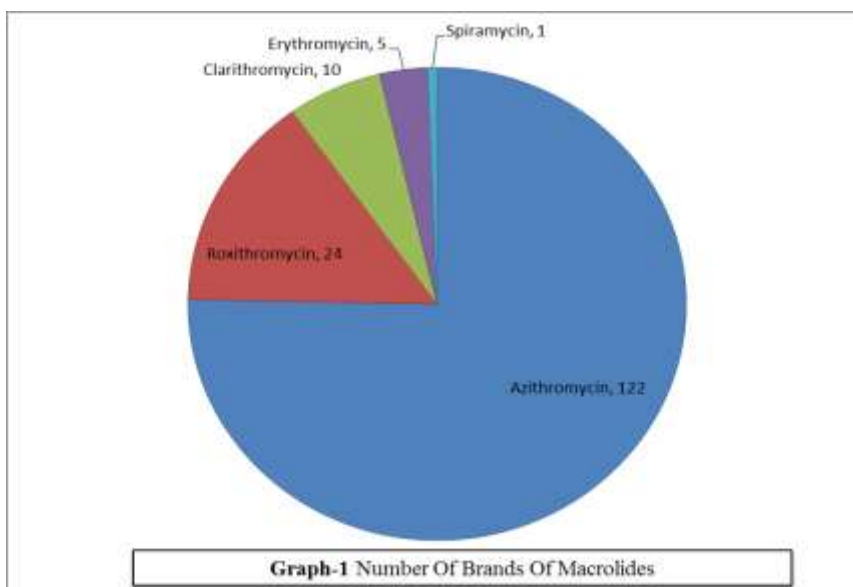
After observation, total number of brands for Azithromycin available is 122, Roxithromycin 24, Clarithromycin 10, Erythromycin 5 and Spiramycin is 1. [Graph 1]

Out of 5 macrolides mentioned, 4 drugs have 2 dose variants except Spiramycin. Azithromycin has dose variants of (250 mg, 500 mg), Clarithromycin (250 mg, 500 mg), Erythromycin (250 mg, 500 mg), Roxithromycin (50 mg, 150 mg) and Spiramycin (3 MIU-Million International Unit).

Wide cost range (INR) was noted down between many of these drugs which might be attributed to the number of brands available in the Indian market. For example – highest number of brands were available for Azithromycin with the following cost range – 250 mg: INR 63.9, 500 mg: INR 83.1. Clarithromycin has cost range of – 250 mg: INR 103.3, 500 mg: INR 97.3. Erythromycin has cost range of – 250 mg: INR 6.47, 500 mg: INR 13.05. Roxithromycin shows cost range of – 50 mg: INR 93, 150 mg: INR 29.78. No cost range for Spiramycin was noted down, as only single brand is available in the market. [Graph 2]

An idea about how many times is the costlier brand expensive than the cheapest one of the same drug is been provided by the Cost ratio chart. For example, cost ratio of Azithromycin 250 mg is INR 2.46 which indicates that costliest brand of Azithromycin is 2.46 times higher than its cheapest alternative.

Table 1 enlists data about Minimum cost, Maximum cost, Cost range, Cost ratio, Mean cost, noted against each dose variant of the drug. Number of brands available in Indian market under each particular dose is enlisted in the table.



DISCUSSION

Worldwide, about 85–88 % of ARI episodes are Acute Upper Respiratory Infections (AURI) while the remaining is Acute Lower Respiratory Infections (ALRI).^[9-11] Short term macrolide therapies have shown positive clinical outcomes for patients suffering from Community Associated Pneumonia (CAP) owing due to their anti-inflammatory action. Pronounced effect on cytokines and immune cells and less damage to the tissue is being observed.^[6]

Azithromycin 250 mg usage in lung transplant or greater bronchiolitis obliterans syndrome (BOS) showed a significant improvement of 17% in FEV1 as compared to baseline.^[12] Clarithromycin usage in mild to moderate asthma patients for a defined dosing period

decreases serum and sputum eosinophil counts, eosinophilic cationic protein and incidence of asthma attacks.^[13] Macrolides like erythromycin and Roxithromycin have been used in bronchiectasis patients with the idea of improving airway responsiveness.^[14]

Improvement in PFT and reduction in incidence of exacerbations was noted in patients of cystic fibrosis taking azithromycin therapy.^[15-17] Macrolides are usually recommended with third generation Cephalosporin's as first line empirical therapy in patients suffering from serious infections and CAP, as they might overcome pneumococcal resistance.^[18-20]

Many beneficial effects exerted by macrolides are known to collectively limit tissue damage by neutrophils, chemo-attractants, inhibition of their oxidation bursts, granulation impairment and improves rate of neutrophil apoptosis. Stimulation of production of beta-defensin-1 and beta-defensin-2 having antimicrobial properties is done by epithelial cells. Expression of mannose receptors and phagocytic activity of macrophages is stimulated by macrolides which help in rapid elimination of bacterial pathogens. COPD patients show better clinical improvement due to such aspect of macrolides. Long-term treatment with azithromycin, erythromycin or clarithromycin in COPD patients is in generally safe and effective reducing exacerbations and related hospitalizations.^[21]

In our study it is evident that many drugs have wide cost range especially those drugs that are available in market under various brand names but also seen with lesser brand names. Both had significant price difference.

During consultancy, doctors need to take in account the drug cost as well the economic status of the patient. Economic analysis, if carried out among different subgroups in society would help the physician in decision making formulary decision making, drug policy decision, medico marketing and treatment guidelines. India is a developing country, so cost effective therapies should be emphasized for the benefit of patients. Generic names should be used while writing prescription by the doctor.

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