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Research Article

PHARMACOECONOMICS AND CHRONIC COST-EFFECTIVE STUDY OF ANTIBIOTICS IN IN-PATIENTS OF OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Background According to world health organization (WHO) Chronic Obstructive Pulmonary Disease (COPD) is a 3rd leading cause of death and budget consuming illness worldwide. It is the chronic and progressive disease, which has an enormous financial burden on living standards of patients. **Objective** The present study was under taken to reduce the socio-economic burden on patients with improved quality of life. **Settings** The study was carried out in Shri B M. Patil Medical College and Research Center, Vijayapura. **Methods** A prospective and observational study was conducted in COPD patients, to assess the efficacy of antibiotics and it's cost effective. **Outcome** Clarithromycin was found to be cost effective and high efficacious antibiotic in COPD. **Results** The total numbers of patients selected for the present study was 100, among 63 were males and 37 were females. Initially the patients were categorized based on GOLD guidelines for their severity of the disease and prescribed with different antibiotics such as Ceftriaxone, Levofloxacin, Clarithromycin, Piperacillin/Tazobactam and Amoxicillin/Clavulanic acid. The efficacies of the antibiotics were measured in terms of reduction in the rate of symptoms of COPD and cost effectiveness was calculated by using the ICER formula.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a respiratory disorder that is characterized by progressive, partially reversible airway obstruction, systemic manifestations, and increasing frequency and severity of exacerbations [1]. COPD is responsible for early mortality, high death rates and significant cost to health systems. The majority of studies (62%) concerned patients over 40 years of age, in particular those aged between 40 and 64 years. The prevalence of COPD increases with age; with a five fold increased risk for those aged over 65 years compared with patients aged less than 40 years. The prevalence of COPD was estimated to be 7.6% (95% CI 6-9.2%) independent of the defined diagnostic criteria. According to WHO, with approximately 2.75 million deaths per annum, or 4.8% of deaths. Mortality from COPD is higher in males and also increases with severity of disease [2].

Antibiotics are one of the pillars of modern health care and have an inevitable role in the treatment of infectious disease [3]. Antibacterial drugs are very costly; therefore, searching for effective strategies for treatment by using methods of

pharmaco-economical analysis becomes very important. Antibiotic resistance is a serious and growing phenomenon in contemporary medicine and has emerged as one of the pre-eminent public health concerns of the 21st century, in particular as it pertains to pathogenic organisms [4]. Between 50-70% of COPD exacerbations have an infectious etiology, and current guidelines base their recommendations about antibiotic prescription mainly on the study by Anthonisen and colleagues, which was performed in patients with moderate to very severe COPD [5]. Up to 5% of COPD people have a deficiency in a protein called alpha-1-antitrypsin [6]. Selection of empiric antimicrobial therapy should be based on the most likely organisms: Haemophilus influenza, Moraxella catarrhalis, Streptococcus pneumonia, and Haemophilus Para influenza. Irrational use of antibiotics leads to the growth of antibiotic resistance and to an increase in costs of treatment [7].

The goals of prescription treatment for COPD are to improve symptoms, reduce future exacerbations, and improve health status [8]. Recently there has been growing interest in the economic assessment of health and health care programmes as well as in performing a pharmaco-economical analysis. The

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current global initiative for chronic obstructive lung disease (GOLD) strategy provides recommendations for a multiple-component evaluation of patient with COPD, including symptom assessment with the CAT or the modified Medical Research Council (Mmrc) questionnaire, and the patient's history of exacerbations as a risk factor for future exacerbations. The CAT is a validated and reliable 8-item, patient-completed questionnaire that measures a wide range of COPD symptoms (chronic cough, phlegm, chest tightness, breathlessness, activities, confidence, sleep and energy), with a severity score ranging from 0 to 40 (higher score indicating worse health status). The CAT is a simpler and requires less time to complete to assess health status in everyday clinical practice.

Cost-effectiveness studies evaluate incremental costs in currency units, while expressing clinical benefits in non-monetary terms, such as clinical success, avoided deaths, life years gained or quality adjusted life years (QALYS) etc..., The concept of the cost-effectiveness plane has attracted much attention. The results of any cost-effectiveness analysis can easily be displayed in this manner, directly showing the incremental cost-effectiveness ratio (ICER) of the new over the old treatment option, with a quick overview of additional costs and effects of the new treatment [9]. The clinical response, based on clinical outcome, was either success or failure. Clinical feature at the end of therapy was carried forward to follow-up as failure [10]. This review focuses on three specific aspects: first, the level and distribution of costs associated with exacerbations; second, the economic value of antibiotics in the management of COPD exacerbations and third, factors influencing the economic value of antibiotics [11]. The primary goal of antibiotic treatment here is to cure infection, thereby improving disease condition and quality of life [12].

The aim of this study is to evaluate cost-effectiveness of antimicrobial used for inpatient treatment of AECOPD, this results of this study will provide us data and useful information, which antibiotic will give best expected outcomes, with least produced costs.

Aim of the study

To investigate the antibiotics that reduces severity of exacerbations, length of hospital stay with least produced costs and shows better efficacy in patients suffering from COPD.

Ethics approval

Ethics approval (Ref: IEC/BLDE COP/2018/05) was obtained from BLDEA's, S.S.M. College of Pharmacy & Research Centre, Vijayapura.

MATERIALS AND METHODS

Study design and settings: A prospective and observational study was conducted for a period of six months from November 2017 to April 2018 in the department of medicine of Shri B M. Patil Medical College and Research Center, Vijaypur after obtaining the IEC clearance (Ref: IEC/BLDE COP/2018/05) from Institution. The study hospital provides primary and secondary health care facilities to the people in and around the Vijayapur district. The patients admitted to medicine ward were screened according to inclusion and

exclusion criteria and 100 patients were selected for the present study.

Inclusion Criteria

- All patients willing to participate.
- Patients prescribed with antibiotics are included.
- All patients admitted to ICU and General medical wards.
- Both the genders, of ages above 40yrs are included.

Exclusion Criteria

- Out patients are excluded from the study.
- Incomplete case files are excluded.
- Patients prescribed with no antibiotics are excluded
- Pediatrics, pregnancy and lactating women are excluded from the study.

Source of data

- Patient case files (Consists of demographic details, clinical characteristics, social history, blood pressure readings, brand name of drugs, drug, dosages and duration of the patient's treatment).
- Truven Micromedex online drug data base.
- Stockley's Drug-Drug interaction book.
- Standard Text, Journals, Research articles and Newsletters.

Data collection and assessment

The status of COPD such mild, moderate, severe and very severe were categorized by GOLD guidelines. All COPD patient's prescribed with antibiotics were selected for the study and assessed for choice of antibiotics, efficacy of antibiotics and cost effective analysis. The cost effective study of antibiotics were calculated by ICER formula.

$$\text{ICER} = \frac{(\text{Cost of drug A} - \text{Cost of drug B})}{(\text{Effect of drug A} - \text{Effect of drug B})} \quad (1)$$

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables. The difference of the means of analysis variables between more than two independent groups was tested by ANOVA. If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

Sample size calculation

Sample size of 81(~100) subjects will allow the study to determine the cost and their efficacy of antibiotics given to the patient with 95% confidence level and margin of error +/-5% with finite population correction.

RESULTS

Gender Distribution: In gender distribution totally 100 patient out of which 63 were male patients and 37 were female

patients. Males were more in number when compared to females. Hence majority of study subjects were males (figure 2).

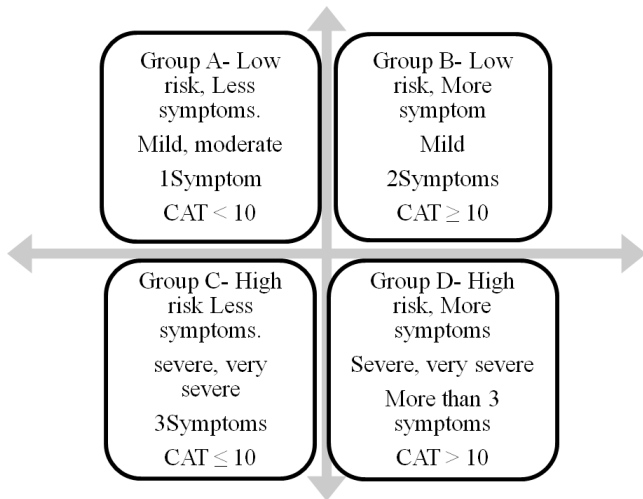


Fig 1 GOLD Classification of COPD

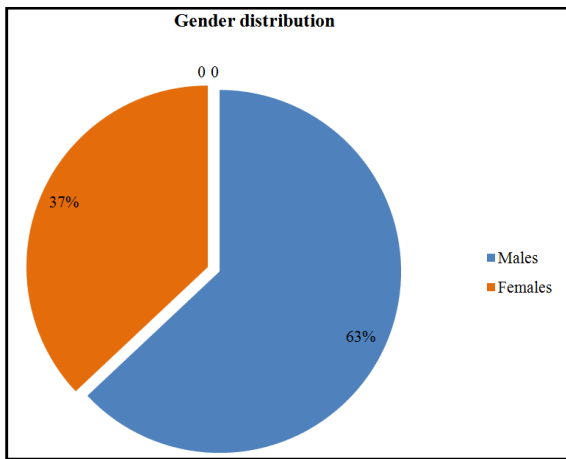


Fig 2 Gender Distribution

Age distribution: The minimum and maximum age was 40 and above 90 years respectively. Accordingly the age groups were formed. Among all age groups maximum subjects 1 were found between 51-60 in which males were 60 and females were 13. The maximum subjects were found in the age group of greater than 90 years in which 1 male and no female patient (figure 3). Distribution of cases according to age (years)

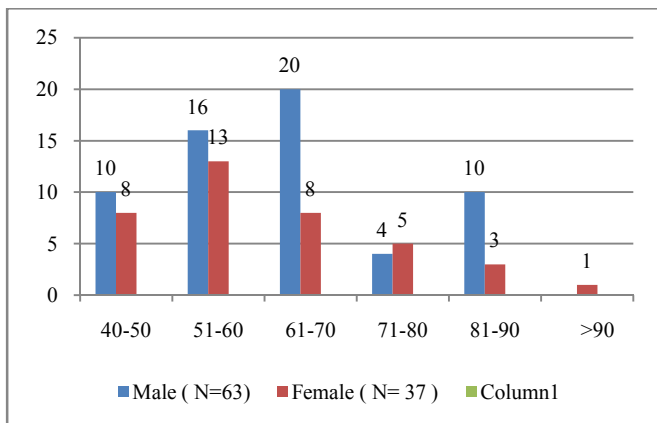


Fig 3 Age Distribution

Socio-economic status: In socio – economic status distribution totally 100 patients out of which 62 patients were low, 48 patients were middle and no patients were under high category (figure 4).

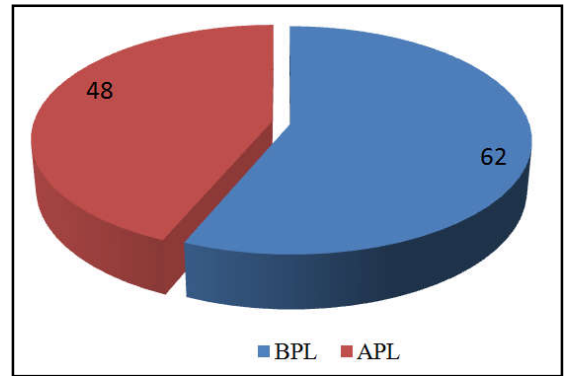


Fig 4 Socio-economic status

Social habits: Among 100 patients 37 patients were having smoking habit, two patients were alcoholics, 7 patients were smokers & alcoholics and 17 were none (figure 5).

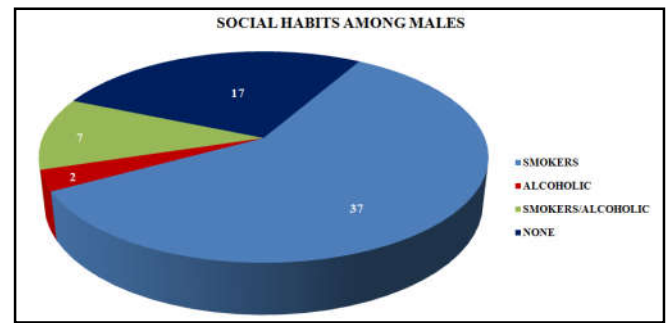


Fig 5 social habits

Types of antibiotics in prescription: Out of 100 prescriptions 5 antibiotics are commonly prescribed in which most of them accounted for Levofloxacin (23%), Ceftriaxone (23%), Clarithromycin (20%), Piperacillin / Tazobactam(17%) and Amoxicillin/Clavulanic acid (17%) (figure 6).

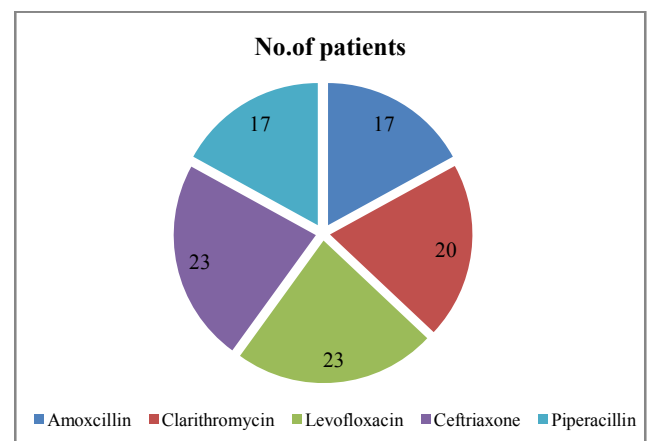


Fig 6 Types of antibiotics in prescription

Cost of antibiotic per dose and per day: Among 5 Antibiotics, the cost of Amoxicillin/ Clavulanic acid is 254; Clarithromycin (56.88); Levofloxacin (110); Ceftriaxone (109.58); Piperacillin / Tazobactam (431.8) (figure 7) (table 2).

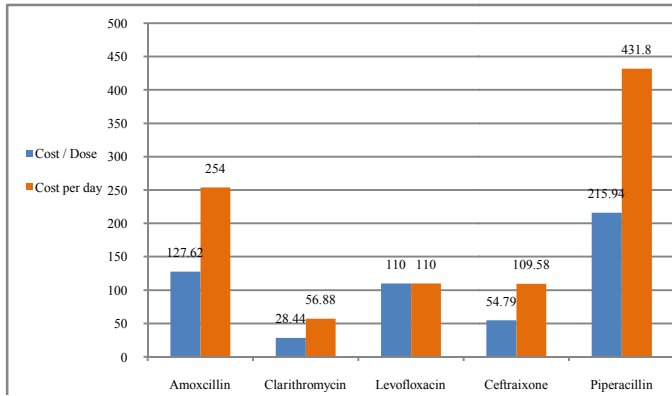


Fig 7 Cost of antibiotics per dose & per day

Chi square p value= 0.380

Table 2 Cost of antibiotics per dose & per day

Antibiotics	Dose	Cost / Dose(INR)	Frequency	Cost / Day(INR)
Amoxicillin/Clavulanic acid	12 gm	127.62	2 times/day	254
Clarithromycin	250mg	28.44	2 times/day	56.88
Levofloxacin	100 ml	110	1 time/day	110
Ceftriaxone	1gm	54.79	2 times/day	109.58
Piperacillin/Tazobactam	4.5gm	215.94	2 times/day	431.8

Hospital stay of patients: Out of 100 patients average days spend by patients for each antibiotic Amoxicillin (16.8%), Clarithromycin (20.45%), Levofloxacin (31.64%), Ceftriaxone (15.49%), Piperacillin / Tazobactam (15.65%) (Figure 8)

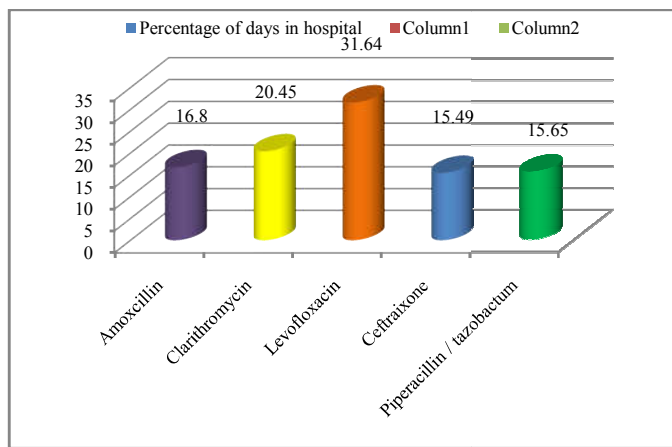


Fig 8 Hospital stay of patients

Calculation of ICER: ICER ratio for each antibiotic is Amoxicillin/clavulanic acid (143.17), Clarithromycin (-3117.5), Levofloxacin (2496.6), Ceftriaxone (-4107), Piperacillin / Tazobactam (10206.2) (figure 9) (table 3)

Table 3 Calculation of ICER

Antibiotic	C	E	Δ C	Δ E	ICER
Amoxicillin/Clavulanic acid	1371.6	9.58	1371.6	9.58	143.17
Clarithromycin	374	9.9	-997.6	0.23	-3117.5
Levofloxacin	1123	10.2	749	0.3	2496.6
Ceftriaxone	547.9	10.34	-575.1	0.14	-4107
Piperacillin/Tazobactam	2108	10.5	1633	0.16	10106.2
ANOVA p value	<0.001*	<0.001*	-	-	-

Note: * significant at 5% level of significance (p<0.05).

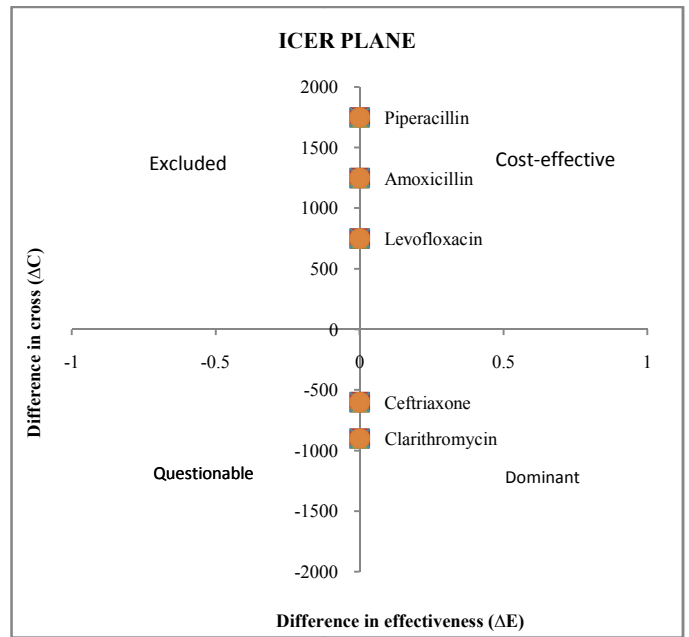


Fig 9 ICER plane

DISCUSSION

COPD is a common, preventable, and treatable disease usually caused by significant exposure to noxious particles or gases. Cost effectiveness of anti-microbials used for the treatment of AECOPD, the results of this study will give best expected outcomes with least produced costs. Total 100 are included in this study.

Based on GOLD classification distribution out of 100 patients 7 were mild with 1 symptom, CAT score < 10, 35 were moderate with 2 symptoms, CAT score ≥10, 38 were severe with 3 symptoms, CAT score ≤ 10, 20 were very severe with more than 3 symptoms, CAT score >10 (figure 1) (table 1).

In our study out of 100 patients males 63 were dominant than females 37 because most of the males have smoking habit as it is a trigger for COPD flare-ups, which was similar to study conducted by Asha ann joseph *et.al* where males are more (11).

Most of the patients were between the age groups of 51-60 and 61-70 with subjects 29 and 28 following 40-50, 81-90, 71-80, >90.

Out of 100 patients 62% patients were with low socio-economic status and 48% were with middle socio-economic status. Which closely correlates with the study conducted by Asha ann joseph *et.al*, where people with low (77%) socio-economic status are high than middle class (23%) (11).

Out of 100 patients 37 patients were having smoking habit, 2 patients were having alcohol habit and 7 patients were having both smoking and alcohol habits were seen among males only (figure 5).

Among 5 iv antibiotics (Ceftriaxone, Levofloxacin, Clarithromycin, Piperacillin/Tazobactam, Amoxicillin/Clavulanic acid) the costliest one is piperacillin/tazobactam which is 215.94/dose and 431.8/day, followed by Amoxicillin which is 127.62/dose and 254/day, levofloxacin was 110/dose and 110/day, ceftriaxone was 54.79/dose and 109.58/day, Clarithromycin was 28.44/dose and 56.88/day. After application of pharmacoeconomic analysis clarithromycin is

cost –effective compared to other 4 antibiotics. Which is contrast to study conducted by Acevski stevche *et.al*, Cefuroxime and Amoxicillin/Clavulanic acid are cost-effective (3).

Out of 5 antibiotics, most commonly prescribed are levofloxacin and ceftriaxone in 23 patients followed by clarithromycin in 20 patients, amoxicillin and piperacillin/tazobactam in 17 patients.

Out of 100 patient's average days spend by patients for each antibiotic were levofloxacin-10.21 days (31.64%), Clarithromycin-6.6 days (20.45%), Amoxicillin-5.4 days (16.8%), Piperacillin/Tazobactam- 5.05 days (15.65%), ceftriaxone - 5 days (15.49%). Acevski stevche *et.al*, study showed that average days of treatment spent by patients for Clarithromycin are 6.1 days which closely correlates with this study (3). But differs from Asha ann joseph *et.al*, study where the average days of therapy for Amoxicillin and Levofloxacin were 7 and 5 days (11).

ICER ratio for each antibiotic is amoxicillin (143.17), Levofloxacin (2496.6), Piperacillin/Tazobactam (10206.2), clarithromycin (-3117.5), ceftriaxone (-4107). Negative ICER score for clarithromycin and Ceftriaxone means that these two antibiotics have improvement to the effectiveness with reduction in costs and are dominant alternatives over other antibiotics. But differs from Acevski stevche *et.al* study which shows Amoxicillin/Clavulanic acid is dominant.

CONCLUSION

As hospital is located in interior area mostly middle class and lower class people visits. Hence effective use of antibiotics play important role and usage of antibiotics cost-effectively may be reduces financial burden on patients with same safety, efficacy and better clinical outcome of health. COPD is major problem concerning a lot of patients, huge amount of time and resources are invested in preventing, diagnosing and cure patients with this life threatening disease. Treatment of acute bacterial exacerbations of COPD is often acute treatment where good treatment decisions must be made fast and prompt to decrease hospital stay. Acute bacterial exacerbations require fast interventions since every exacerbation leads to severe illness, and causes death to the patient. To conclude, we believe that cost-effectiveness analysis will continue to grow in importance, as scientific and clinical researches develop new technologies and medicines.

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Conflict of Interest Authors do not have any conflict of interest.

Abbreviations:

ICER	: Incremental cost effectiveness ratio
CAT	: COPD Assessment test
GOLD	: Global initiative of chronic obstructive lung disease
QUALY	: Quality-adjusted life year
AECOPD	: Acute exacerbations of chronic obstructive pulmonary disease
IEC	: Institutional ethics committee
APL	: Above poverty line
BPL	: Below poverty line
C	: Cost
E	: Efficacy
ΔC	: Difference in costs
ΔE	: Difference in efficacy

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