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Evaluation of Antibiotics Used for Lower Respiratory Tract Infections in a Tertiary Care Hospital

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Abstract **Original Research Article**

Objective: The main objective of the study was to evaluate patterns of antibiotics prescribed for Lower respiratory tract infections (LRTIs) in a tertiary care hospital. Methodology: A prospective observational study was conducted in the pulmonology and general medicine departments of a tertiary care hospital. The data was collected from the in- patient department after considering inclusion and exclusion criteria for a period of 6 months. Antibiotics prescribed were compared with the guidelines mentioned in the European respiratory society guidelines (ERS), Indian respiratory guidelines, IDSA guidelines, and NICE guidelines to determine the appropriateness of therapy. Statistical tools like Chi-square test were applied to the data by using SPSS software. ***Result***: A total of 284 patients diagnosed with various LRTIs, male 55% patients predominated over female patients of 45%. The majority of the patients were under age group of 61-70 years (24%), literates (71.84%), and symptoms of SOB (88.73%), Cough (69.01%), generalized weakness/body pains (54.92%), fever (50.70%), wheeze (11.26%) and chest pain (9.85%). Among all cases of LRTI, most of the patients 56.4% were diagnosed with viral pneumonia (COVID-19). Higher number of patients was treated with beta-lactam antibiotics. Inj.Piperacillin/tazobactum (38%), Tab.Cefpodoxime proxetil/Clavulanic acid (41%), Inj.Cefaperazone/Sulbactum (35%) and Inj.Amoxicillin/Clavulanic acid (23%) were frequently used. ***Conclusion***: Lower respiratory tract infections are mostly seen in males, elder age groups and in literate patients. Present study showed that the antibiotics were used taking into consideration various clinical and diagnostic evidences like radiology, bio-markers, patient condition and severity of the disease. However the establishment of antibiotic stewardship program is necessary to ensure safe and appropriate use of antibiotics and to prevent antibiotic resistance in patients.

Keywords: LRTIs, Viral pneumonia (COVID-19), Beta-lactams, Broad-spectrum antibiotics.

INTRODUCTION

The respiratory system is a network of tissues, organs and blood vessels that function together to help us carryout breathing normally. This coordinated function helps to remove carbon dioxide and transports oxygen throughout the body [1]. The respiratory tract is divided into upper and lower parts: the upper respiratory tract consists of the sinuses, middle ear, pharynx, epiglottis and larynx, while the lower respiratory tract consists of the structures below the larynx, the bronchi, bronchioles and alveoli [2].

LOWER RESPIRATORY TRACT INFECTIONS (LRTIs):

The lower respiratory tract infection is a terminology that includes bronchitis, bronchiolitis, pneumonia, chronic obstructive pulmonary disease (COPD), acute exacerbations of COPD and bronchiectasis [3]. The lower respiratory tract infections are among the leading infectious disease cause of death across the world. 95% of all deaths from acute lower respiratory infections occur in countries with a low income rate [4].

Among the lower respiratory tract infections, the chronic obstructive pulmonary disease and acute

exacerbations of COPD were the leading causes of LRTI cases followed by Pnuemonia and other lung infections [5]. But the recent outbreak of COVID-19 in December 2019 has led to global crisis and the World Health Organisation (WHO) declared the disease as pandemic on 11 March 2020 [6]. According to Global overview data published by the WHO as of 6th June 2021 the Global case and death incidences decreased by 15% and 8% respectively in European, Sout-East Asia and Africa [7].

Due to higher incidence of respiratory infections and increased rate of hospital admissions Hospital acquired pneumonia (HAP) and Ventilator associated pneumonia (VAP) are on a rapid growing trend [8]. Bronchitis is an illness which does not involve chronic lung disease and is seen with symptoms including productive cough and other features suggestive of LRTI and is not associated with alternative sinusitis or asthma [9]. Bronchiolitis is characterized by inflammatory changes in the smaller bronchi and bronchioles, but not by consolidation [10]. It is presented by fever and coryzal symptoms which progresses to wheezing, respiratory distress and hypoxia. Bronchiectasis is a condition defined by the presence of permanent and pathological dilation of the bronchi. This usually occurs in response to a chronic respiratory infection causing inflammation [11]. Pneumonia may be defined as an infection of the lung characteristically involving the alveolar space. It is an inflammation of the lung parenchyma. It involves alveoli rather than the bronchi or bronchioles, of infective origin and is characterized by consolidation. Consolidation is a pathological process in which the alveoli are filled with a mixture of inflammatory exudate, bacteria and WBC that on chest X-ray appear as an opaque shadow in the normally clear lungs [12]. COMMUNITY-ACQUIRED PNEUMONIA (CAP): Infection acquired in the community [13] HOSPITAL-ACQUIRED PNEUMOMMIA (HAP): Infection acquired following more than 2 days stay in hospital or in someone recently discharged from hospital within 7 days [14]. VENTILATOR-ASSOCIATED PNEUMONIA (VAP): Infection acquired by patient on ICU and is mechanically ventilated for more than 2 days [15]. LOBAR PNEUMONIA: Lobar pneumonia is the term used when there is diffuse consolidation of the lung involving the entire lobe [16]. BRONCHOPNEUMONIA: Bronchopneumonia is a condition in which localised inflammation is seen as patches around the bronchi. These inflammatory patches may or may not be localised to a single lobe of the lung [17]. EMPHYSEMA: When an infection spreads to the pleural space forming a fibrinopurulent exudate that fills the entire pleural space the condition is called as Emphysema [18]. LUNG ABSCESS: Lung abscess occurs when there is complete damage of the lung and fluid-filled pockets are formed around the focal area of the lung [19].

COVID-19 is an extremely contagious disease caused by severe acute respiratory syndrome coronavirus-2 (SAR-CoV-2) one of the family members of Coronaviridae family In the past, two members of this viral family namely SARS-CoV-1 and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) have caused a global epidemic [20]. Aspiration pneumonia is a condition that may occur either in a community or a hospital. It is caused by inhalation of stomach contents that are contaminated by bacterial pathogens by the mouth [21]. Causes include the use of hypnotic drugs, alcohol or general anaesthesia, all of these might cause the patient to vomit while unconscious [22]. Aspiration pneumonia is usually managed with Metronidazole and Amoxicillin+Clavulanic acid, but the use of other broad-spectrum antibiotics may be necessary if the patient has been hospitalized [23, 24].

Management of Community acquired pneumonia involves the estimation of initial risk and to make a decision of whether to manage the patient on an out-patient basis, or in a hospital setting in a general medicine/pulmonology ward or an intensive care unit (ICU).Out-patient management [25]. The patients are treated with Fluoroquinolones or Beta-lactams and macrolide antibiotics if the patient is associated with other respiratory illness and with macrolides or doxycycline is the patient does not have any comorbidities [26]. If the patient presents with severe onset of symptoms with other clinically significant conditions like higher respiratory rate (>30), Blood urea nitrogen (BUN) greater than 20mg/dL, low blood pressure (usually <100/70mm/Hg) and age > 65 years, he/she may be admitted and managed in a general medicine ward [27]. The first line of antibiotics to be used is fluoroquinolones or macrolides and beta-lactams. Sustained worsening of symptoms associated with radiological and clinical evidence the patient should be admitted and managed in an ICU. The antibiotic regimen in this category should be between fluoroquinolones and beta-lacatams or beta-lactams and macrolides [28]. The management of Hospital acquired pneumonia and Ventilator associated pneumonia is much more complicated and involves the use of broad-spectrum antibiotics much more when compared to the management of community acquired pneumonia [29]. The management approach should involve the identification and separation of patients with Multi drug resistant (MDR) risk factors. The regimen generally involves the use of Piperacillin/Tazobactum+third generation cephalosporin+levofloxacin for patients without MDR risk factors and for patients with MDR risk factors the antibiotic regimen involves aminoglycoside with any one of imipenem, meropenem, piperacillin/tazobactum or a third generation cephalosporin [30].

- The main objective of the study is to study and evaluate the patterns of antibiotics prescribed for Lower respiratory tract infections (LRTIs) and classify various

types of LRTIs. study the most common respiratory tract infections, their clinical presentation and effective treatment in a tertiary care hospital.

MATERIALS AND METHODS

The present study is a prospective observational study conducted in Pulmonology and General Medicine departments in a Tertiary care hospital for duration of 6 months. Sample size for the study was 284 subjects and data was collected from the out-patient and in-patient departments by interviewing the patients and their prescriptions and case-sheets. The data collection format was verified and authenticated by the hospital preceptors for the study. In-patients and out-patients of Pulmonology and General medicine department diagnosed with lower respiratory tract infections (LRTIs), Patients of all ages who have received/are receiving antibiotics for lower respiratory tract infections. Antibiotics prescribed were compared with the guidelines mentioned in the European respiratory society guidelines (ERS), Indian respiratory guidelines, IDSA guidelines, and NICE guidelines to determine the appropriateness of therapy.

Descriptive statistics was done by using SPSS software to determine mean and standard deviation of collected data. The statistical tool Chi square test was performed to determine P-Value between the different collected data like age vs gender, social history vs gender, past medical history vs gender, symptoms vs gender, gender vs duration of symptoms, gender vs duration of hospital stay, gender vs diagnosis and gender vs antibiotics prescribed. The P-value is used to determine the statistical significance with in statistical hypothesis significance for the evaluation of antibiotics used for lower respiratory tract infections. The P-value was set at < 0.05 and confidence interval was 95%

RESULTS

In present study 284 cases were included as per our criteria. Table 1 indicates mean, standard deviation and P-value of various parameters considered in our study. Figure 1 describes the Gender Wise Distribution, were percentage of males diagnosed with lower respiratory tract infections was more in number (55%) than females (45%). While Figure 2 expresses the Age Wise Distribution, here, among different age groups 61-70yrs were highest (24%) and 90-100yrs were least (5%). As per educational status concern, the percentage of patients affected with LRTIs is comparatively high in case of literates (71.84%) than illiterates (28.16%). Data regarding social history shows smokers-8%, alcoholic-6%, both alcoholic and smoker-12%, tobacco chewers 2%. Whereas data of past medical history states HTN (21%), DM (28%), COPD (16%), other respiratory disorders (18%) as mentioned in Figure 3.

Table 1: Mean, Standard deviation and P-value of variables

Characteristics	N	Mean	Standard Deviation	P-Value
Age	284	56.87	17.087	0.002
Gender	284	1.45	0.498	0.004
SYMPTOMS				
SOB	284	1.10	0.299	0.003
Cough	284	1.32	0.469	0.004
Expectoration	284	1.80	0.399	0.006
Wheeze	284	1.89	0.317	0.006
Fever	284	1.49	0.501	0.005
Chest pain	284	1.90	0.299	0.006
Generalized weakness/body pains	284	1.48	0.500	0.005
Diagnosis	284	6.59	3.006	0.02
ANTIBIOTIC THERAPY				
Inj.Piperacillin+Tazobactum	284	1.61	0.490	0.005
Inj.Amoxicillin+Clavulanic acid	284	1.79	0.409	0.006
Inj.Cefaperazone+Sulbactum	284	1.65	0.478	0.005
Inj.Ceftriaxone	284	1.90	0.299	0.006
In.jClindamycin	284	1.94	0.231	0.006
T.Levofloxacin	284	1.83	0.375	0.006
T.Clarithromycin	284	1.75	0.436	0.006
T.Cefpodoxime proxetil+Clavulanic acid	284	1.59	0.492	0.005
T.Faropenem	284	1.97	0.166	0.006
T.Doxycycline	284	1.99	0.118	0.007
T.Metronidazole	284	1.99	0.118	0.007
T.Linezolid	284	1.99	0.118	0.007
Inj.Meropenem	284	1.99	0.118	0.007

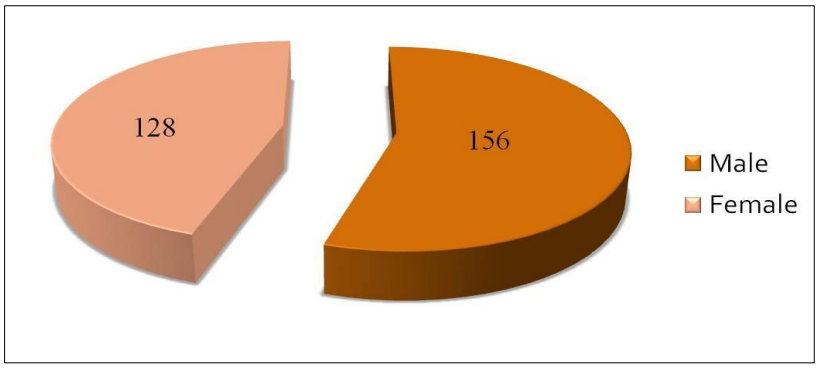

Figure 1: Gender Distribution of Subjects

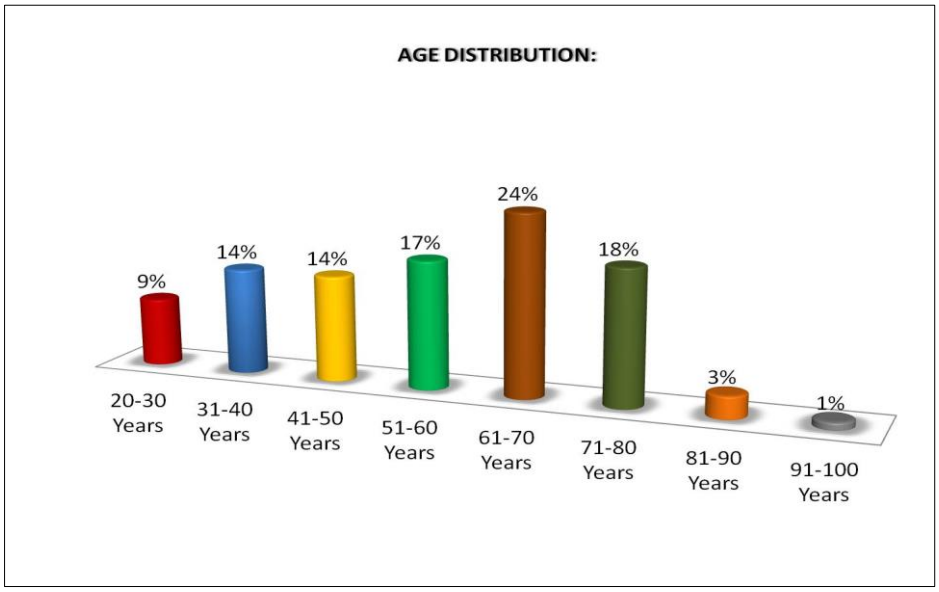

Figure 2: Age Distribution of Subjects

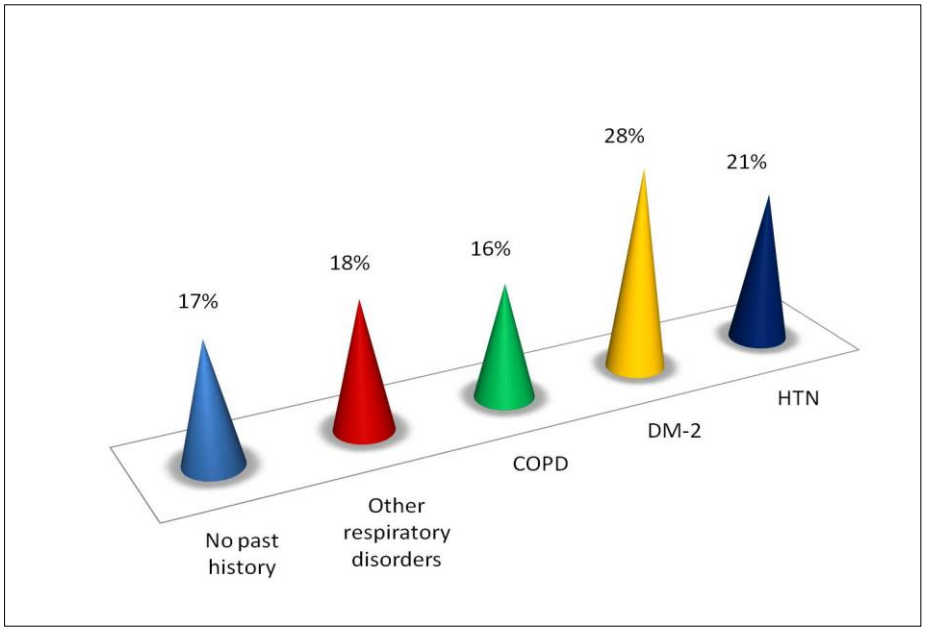

Figure 3: Past Medical History of Subjects

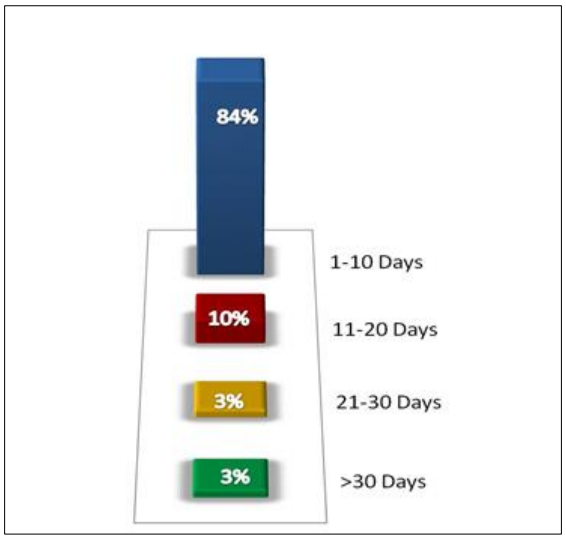

Figure 4: Duration of Symptoms

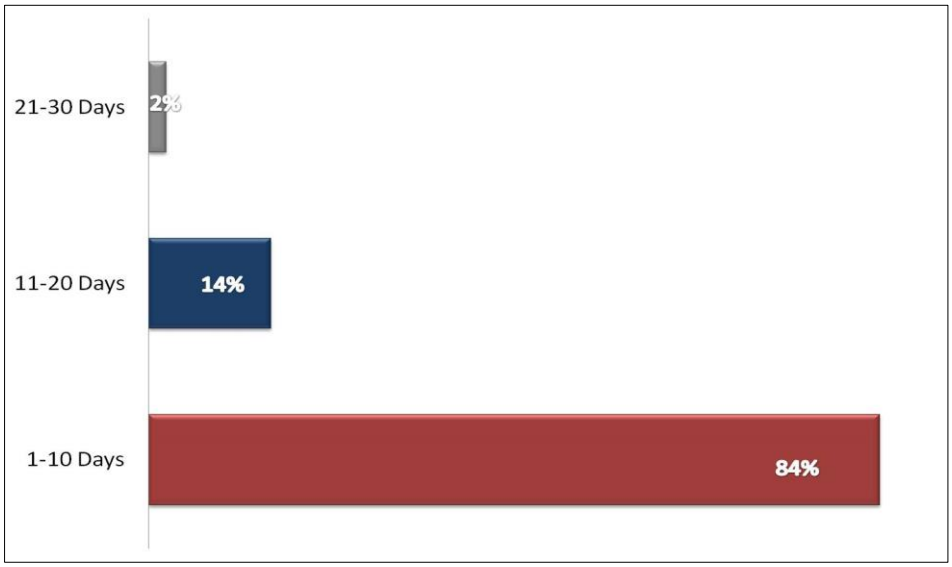

Figure 5: Duration of hospital stay

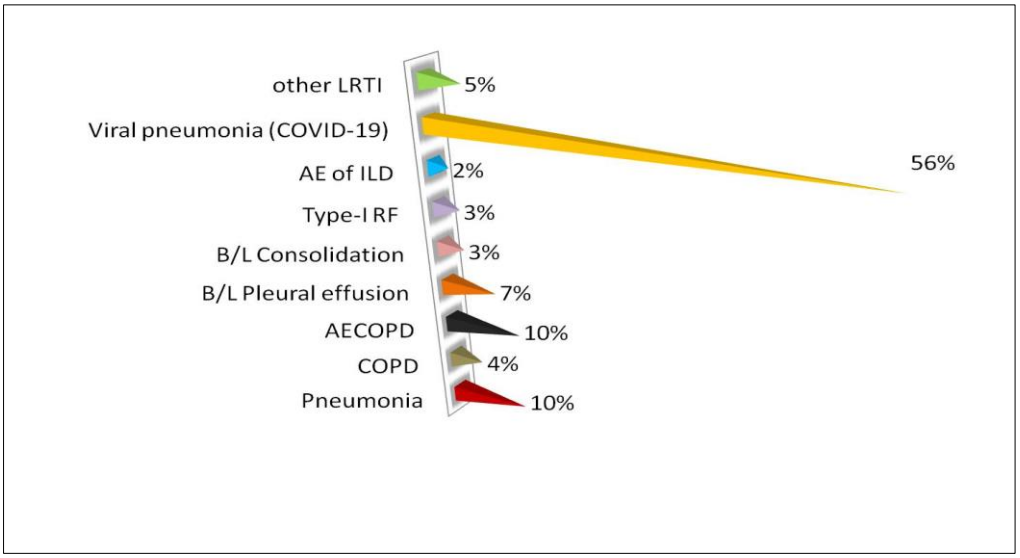

Figure 6: Diagnosis of Subjects

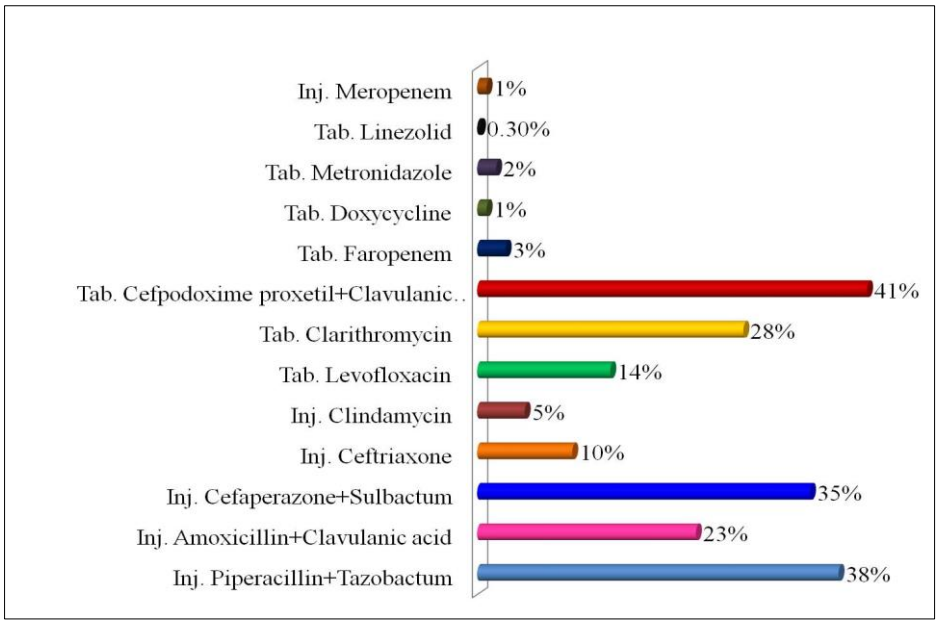

Figure 7: Antibiotics Prescribed To Subjects

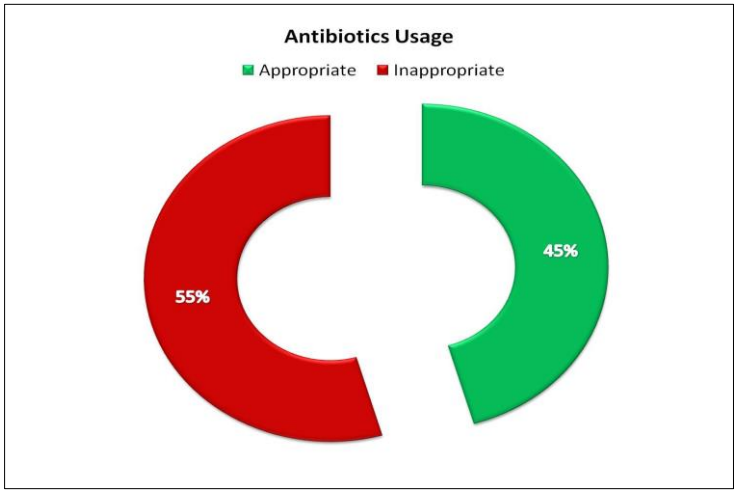

Figure 8: Antibiotics Usage Evaluation

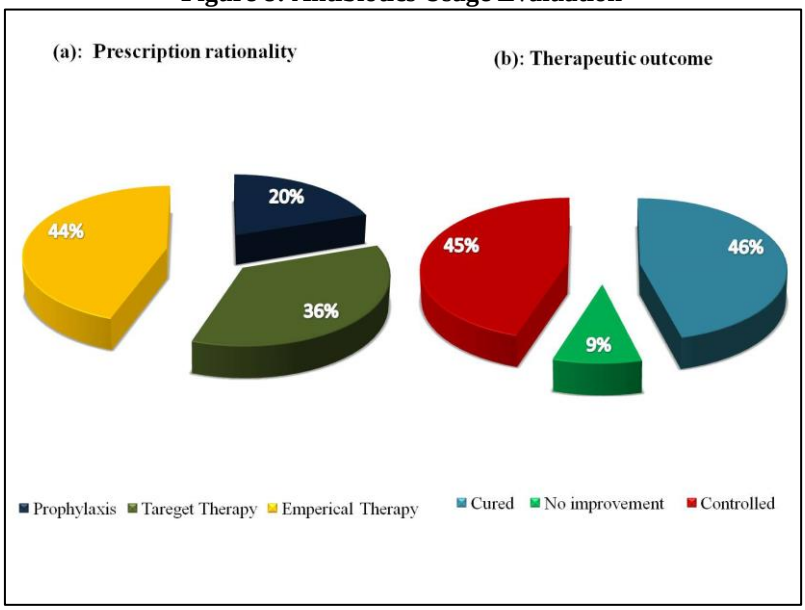

Figure 9: (a) Prescription rationality, (b) Therapeutic Outcome

In case of symptoms it was observed that, most cases had more than one (or two in some cases) symptom appeared simultaneously with SOB (88%) and cough (70%) predominantly followed by fever (50.7%) and Body Pains & Generalized Weakness (64%). Moreover Figure 4 indicates the duration of symptoms presented by the patient. It is observed that in the majority of cases, symptoms persisted for a period of 1-10 days as seen in (84%) patients followed by 11-20 days in (10%) patients. However Duration of Hospital Stay expresses the number of days the patient was admitted in the hospital which can be observed in Figure 5 where, it is categorized into 3 divisions, in which 84% patients were admitted for 1-10 days, 14% were admitted for 11-20 days and 2% for 21-30 days.

Above all Figure 6 states various diagnosis of LRTI, here 56% patients were diagnosed with viral pneumonia (COVID-19), 10%-AECOPD, 10%-Pneumonia, 4%-COPD, 7%-B/L pleural effusion, 3%-B/L Consolidation, 3%-Type-I Respiratory Failure, and 2%-AE of ILD. When it comes to therapy the frequency of combined and individual antibiotic therapy prescribed to the patients is Monotherapy 9.1% and combinationtheray 90.9%. However Figure 7 explains the types of antibiotic prescribed for subjects, where Inj Pipercillin+ tazobactam and Tab cefpodoxime+clavulinic acid are most commonly used and Inj Meropenem and Tab Linezolid least used respectively. In the end Figure 8 states the antibiotics usage with respect to the guidelines mentioned in the European respiratory society guidelines (ERS), Indian respiratory guidelines, IDSA guidelines, and NICE guidelines to determine the appropriateness of therapy for which appropriateness was found to be 45% for the antibiotics prescribed.

Last but not least, Figure 9 has two diagrams 9(a) regarding the subject's prescription rationality. 20% of patients receive prophylactic antibiotics, 44% of patients receive empiric antibiotic therapy (often for nonbacterial infections), and 36% of patients receive targeted antibiotic therapy (for bacterial infections). 9(b) displays the therapeutic outcome in subjects, showing that 46% of patients were successfully treated with antibiotics, 45% of patients' signs and symptoms were under control, and 9% of patients showed no change.

Chi-square test was performed using SPSS software between the variables, such as AGE VS GENDER (0.002), SOCIAL HISTORY VS GENDER (0.007), PAST MEDICAL HISTORY VS GENDER (0.002), GENDER VS SYMPTOMS: SOB (0.006), COUGH(0.002), FEVER(0.002), GENERALISED WEAKNESS/BODY PAINS(0.001), GENDER VS DURATION OF SYMPTOMS(0.001), DURATION OF HOSPITAL STAY VS GENDER (0.001), ENDER VS DIAGNOSIS (0.001), GENDER VS ANTIBIOTICS PRESCRIBED: Inj. Piperacillin+ Tazobactum (0.007), Inj. Amoxicillin+ Clavulanic acid (0.009), Inj. Cefaperazone+Sulbactum (0.001), Inj. Meropenem (0.006), T.Cefpodoximeproxetil + Clavulanicacid (0.002), T.Doxycycline (0.006), T.Metronidazole (0.006), T.Linezolid (0.006). The p-value was clinically significant (<0.05) for all the above mentioned variables.

DISCUSSION

A prospective observational study, "EVALUATION OF ANTIBIOTICS USED FOR LOWER RESPIRATORY TRACT INFECTIONS IN A TERTIARY CARE HOSPITAL" was conducted in a tertiary care hospital in both out-patient and in-patient departments. The data was collected for 284 patients using data collection forms.

As per our study among 284 patients admitted in a tertiary care hospital for 1-10 days (84%), 11-20 days (14%) and 21-30 days (2%), 45% patients were females and 55% were males as similar to the study of, Meena DK and Jayanthi M [31]. Our study included a relatively higher number of patients of age group 65+ years about 41% than other age groups as observed in study done by Giarratano A *et al*., [32].

Data of comorbities showed that 21% HTN, 28% Type-2 DM, 16% COPD and 18% patients had a history of other respiratory disorders, stating the PMHx in order to assess the risk of the patient in present condition and need to provide a optimized therapy. Whereas a study performed by Lisspers K, *et al*., [33] had commorbidites to risk assessment.

Among LRTIs, Viral pneumonia (COVID-19) is the most common infection diagnosed (56%) and Acute exacerbation of ILD (2%) being least even article by Biscevic-Tokic J *et al*., [34] states pneomunia is the common LRTI but here the corresponds to bacterial and in our case Viral.

Patients were commonly treated with an intravenous betalactam antibiotic during their hospital stay which was between 1-10 days in most patients as similar to study of A Schreiner [35]. Upon discharge, an oral cephalosporin or macrolide or fluoroquinolone was prescribed for <10 days. Among betalactam antibiotics Inj. Piperacillin+Tazobactum and Inj. Cefaperazone x+ Sulbactum were mostly preferred. Inj. Amoxicilln+ Clavulanic acid and Inj. Ceftriaxone were less commonly prescribed.

In patients with viral pneumonia (COVID-19), Inj. Cefaperazone+Sulbactum was mostly prescribed followed by an oral macrolides and Tab.Cefpodoxime proxetil+Clavulanic acid were chosen upon discharge.Patients an abit similar pattern canbe observed through report by Hui Tian *et al*., with other LRTIs were treated with intravenous betalactams like

Inj. Piperacillin+Tazobactum and Inj. Amoxicillin+ Clavulanic acid and an oral fluoroquinolone, Tab. Levofloxacin was preferred.

Patients with severe LRTI along with co morbidities with a hospital stay of >10 days were treated with combination of broad spectrum antibiotics like Tab.Doxycycline, Tab.Meropenem along with Inj.Piperacillin+Tazobactum or Inj, Amoxicillin+ Clavulanic acid. In the study it is observed that antibiotics were prescribed taking into consideration the severity of the LRTI, onset of symptoms, radiological evidences like high resolution computerized tomography (HRCT) and biomarkers such as C - reactive protein (CRP) and Procalcitonin (PCT).

Chi-square test performed in our study showed that P-value was clinically significant for all socio-demographic details, symptoms, diagnosis, duration of symptoms, duration of hospital stay and antibiotic therapy.

CONCLUSION

Lower respiratory tract infections are the sixth most common cause of mortality globally and the primary cause of infectious illness deaths.

The numerous viral infections of the lower respiratory system are not treated by antibiotics. Acute exacerbations of chronic bronchitis can be treated with antibiotics, even though acute bronchitis frequently does not require antibiotic therapy. Increased dyspnea and a rise in the volume or purulence of the sputum are signs that treatment is necessary. The patient's age, the severity of the illness, and the presence of underlying diseases are taken into account while choosing the best course of treatment for bacterial pneumonia. Many lower respiratory tract infections found in general practice

It's crucial to keep in mind that when it comes to antibiotic use, these substances are potentially life-saving resources that must be utilised sensibly in terms of the precise agent, duration, and dose as well as under the appropriate conditions to get the best therapeutic response, the right antibiotic needs to be prescribed. The prescribed antibiotics have the adequate range of effectiveness in the various conditions specified. When more than one drug has been noted, the drug with the least amount of adverse reactions, cost effective and best probability of being taken by the patient should be prioritised.

However, as per the Indian Chest Society and National College of Chest Physicians (ICS/NCCP-I) and Infectious Diseases Society of America and American Thoracic Society (IDSA/ATS) guidelines, establishment of an antibiotic stewardship program is essential to ensure rational and appropriate use of antibiotics thus, minimizing antibiotic resistance which is a rapid growing threat in the modern world.

SUMMARY

To sum up this research **"EVALUATION OF ANTIBIOTICS USED FOR LOWER RESPIRATORY TRACT INFECTIONS IN A TERTIARY CARE HOSPITAL"** we had explained the results on whole despite the fact that most of our figures state gender wise as graph. Thus here we end with short note on gender perception of evaluation on this research. First and foremost Age Above/Below 50 males are most affected with LRTI. Additionally males are even affected with LRTI irrespective of being literate or illiterate. As a matter of fact 91% of males developed LRTI have social history (Smokers and Alcoholics). Furthermore longer duration of symptoms was observed in males than female's as a result longer duration of hospital stay. When it comes to diagnosis females were diagnosed with COPD, AECOPD and other LRTI besides males mostly diagnosed with COVID19. More combination therapies of antibiotics where given to females than males .Inj Amoxicillin+Clavulanic acid, Inj Ceftriaxone, Tab Cefpodoximeproxetil+Clavulanicacid and Tab Levofloxacin are mostly prescribed in females on the other hand Inj Piperacillin+Tazobactum, Inj Cefaperazone+Sulbactum, Tab Cefpodoximeproxetil+Clavulanicacid and Tab Clarithromycin are mostly prescribed in Males.

Conflict of Interest: None

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It is a moment of gratification and pride to look back with a sense of contentment at the long travelled path to be able to recapture some of the fine moments, to be able to thank infinite number of people, some who were with me from the beginning some who joined us at some stage during the journey, whose kindness, love and blessing has brought this day. I wish to thank each one of them from the core of my heart. First of all, lam very much grateful to the Almighty & my beloved Parents for their blessings upon me at each and every stage of my life. I wish to sincerely thank our Chairman Sri. A.V. Ramana Reddy garu, and Secretary Sri M. Rajendra Krishna Garu, for providing fully equipped and sophisticated labs. Principal. Dr. D.Venkataramana, M.Pharm., Ph.D. Samskruti College of Pharmacy, for providing adequate facilities for the successful completion of our work successfully It gives me a great pleasure to thank my esteemed supervisor and teacher Dr. Nikhilesh Andhi. For the enthusiasm with which he guided us to carry out this work. He has shown tremendous patience and understanding without which this project would not have been succeeded. I wish to express my sincere thanks to our Faculty members and non-teaching staff of our college for their well cooperation, and timely help. lam thankful to my Classmates for their constant help. suggestions and

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ABBREVATIONS

RTI: Respiratory Tract Infection
URTI: Upper Respiratory Tract Infection
LRTI: Lower Respiratory Tract Infection
COPD: Chronic Obstructive Pulmonary Disease
AECOPD: Acute Exacerbation of Chronic Obstructive Pulmonary Disease
ILD: Interstitial Lung Diseases
COVID-19: Corona Virus Disease-2019
SARS: Severe Acute Respiratory Syndrome
WHO: World Health Organization
HAP: Hospital-Acquired Pneumonia
VAP: Ventilator-Associated Pneumonia
MRSA: Methicillin Resistant Staphylococcus Aureus
SPSS: Statistical Package for the Social Sciences
MERS-CoV: Middle East Respiratory Syndrome Corona virus
SOB: Shortness of Breath
BUN: Blood Urea Nitrogen
MDR: Multi-Drug Resistance
CAP: Community-Acquired Pneumonia

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