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Full Length Research Paper

Frequency of lower respiratory tract infections in Karachi and comparison of different antibiotic agents used for the treatment

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The objective of this study is to compare the use of different antibiotics in lower respiratory tract infections at Jinnah postgraduate Medical Centre (JPMC), Karachi, Pakistan. A non blind randomized study design was used to for this study which was carried out in JPMC, for a period of four months. A total of 137 patients infected with various infections were selected and their prescribed treatments were compared with the recommended treatments. Rate of occurrence of different lower respiratory tract infections and drugs recommended at JPMC were statistically evaluated with P value <0.05. Two way ANOVA was used to determine the significance of the hypothesis. It is observed that there are a significant number of patients suffering from TB (42%), MDR-TB (18%) and pneumonia (11.6%), and there are also patients suffering from the fourth most common infection known as Pneumothorax (7.3%). The guidelines for treatment of these patients used in JPMC were analyzed by student-t test and ANOVA, and it was found that the modes of treatment are more or less same with the standard recommended therapies for these infections. It was concluded that the treatment which is being prescribed in JPMC is more or less similar with the recommended therapy but if the difference is observed, the reason may involve several factors like geographical region, ethnicity, tolerance and resistance, no availability of recommended medicine, and cost (government hospital for poor people).

Key words: Lower respiratory tract infections (LRTIs), antibiotics, comparison, evaluation, Jinnah Postgradute Medical Centre (JPMC).

INTRODUCTION

Lower respiratory tract infections (LRTIs) are amongst the most wide spread and serious infections, accountings for over 50 million deaths globally each year. In developing countries, infants under 4 years of age are at greatest risk of lower respiratory tract infections, whereas in developed counties the severity of infection and rate of mortality are greater in elderly (WHO Report, 2005). LRITs also are the most common reason for physician visits and prescription of antibiotics. The objective of this project was to determine the statistical evaluation and comparison of different antibiotic agents for the treatment of LTRI (Shann et al., 1984).

Infections of lower respiratory include pneumonia, tuberculosis, chronic obstructive pulmonary disorder (COPD), bronchiectasis pnuemothorax, pleural effusion, empyema (Mogyoros, 2001; Sieger et al., 1997).

In Pakistan, most LRTIs are treated empirically, perhaps due to higher cost of laboratory services or non availability of standardized laboratories. Surveillance studies are important tool for defining regional patterns of antibiotics resistance, guiding empirical therapy and establishment of guidelines. Therefore, this study was conducted to determine susceptibility patterns of common respiratory tract diseases and their treatment by antibiotics seen in Karachi (Sieger et al., 1997).

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MATERIALS AND METHODS

The study was performed at JPMC and 137 patients suffering from various lower respiratory tract infections were selected for comparing the prescribed treatment with the recommended therapy. The study was conducted for a period of one month. All adult patients who were admitted into the hospital, JPMC, were included in this study for a one month period in the year 2011 (Chan et al., 1995).

Statistical analysis

Student t-distribution test and ANOVA were used for analysis of data; the values were considered significant which were having $P<0.05$.

Hypothesis

H_0: All the drugs are equally effective.
H_a: At least there is difference between two drugs.
H_0: There is no difference in patient's disease groups.
H_b: At least there is difference between two patients groups.

LRTIs and their recommended therapy

1. Bronchiectasis (Robbins, 1991; Corey et al., 2010): Permanent dilation of bronchi and bronchioles due to destruction of muscle".
Treatment: Postural drainage, antibiotics like amoxicillin or amoxicillin clavulanate or tetracycline or trimethoprim-sulfamethoxazole (Lawrence et al., 2001).

2. Tuberculosis: Chronic granulomatous, communicable disease usually involves the lung".
Treatment: Anti tuberculosis drugs for example, INH, Rifampicin, ethambutol, pza and other antibiotics (Kumar et al., 2010).

3. Chronic obstructive pulmonary disorder (COPD): (Barbara et al., 2003): It is a group of disease characterized by features of chronic obstruction to air flow in the lungs and includes chronic bronchitis and emphysema.

- Chronic bronchitis: Persistent productive cough is observed for at least three consecutive months in at least two consecutive years.
Treatment (Lawrence et al., 2001): The treatments are as follows:

a. Oxygen supply by liquid oxygen system (LOX), compressed gas cylinders, oxygen concentrators by nasal or transtracheal delivery.
b. Ipratropium Bromide.
c. Trimethoprim-sulfamethoxazole.
d. Amoxicillin or Amoxicillin-calvulanate.

4. Pneumonia (Barbara et al., 2003): It is an acute inflammation of the lung parenchyma resulting from infection of alveoli and respiratory bronchioles, or pathologically by consolidation (solidification) of lung parenchyma and clinically by fever, cough, dyspnea and chest pain.
Treatment: Third generation betalactam such as cefotaxime or ceftriazone or ampicillin for allergic with penicillin, fuoroquinolones with or without clindamycin (Lawrence et al., 2001).

5. Empyema (Gabriel et al., 1991): An empyema is a collection of pus within a naturally existing anatomical cavity, such as the lung pleura. It must be differentiated from an abscess, which is a collection of pus in a newly formed cavity.
Treatment: The goal of this treatment is to cure the infection and remove the collection of pus from the lung. Antibiotics are prescribed to control the infection. The health care provider will place a chest tube to completely drain the pus. A surgeon may need to perform a procedure to peel away the lining of the lung (decortications) if the lung does not expand properly.

6. Pleural effusion (Gabriel et al., 1991): Pleural effusion is excess fluid that accumulates in the pleural cavity, the fluid-filled space that surrounds the lungs. Excessive amounts of such fluid can impair breathing by limiting the expansion of the lungs during inhalation.
Treatment: Treatment of pleural effusion may be directed at removing the fluid, preventing it from accumulating again, or addressing the underlying cause of the fluid buildup. Therapeutic thoracentesis may be carried out if the fluid collection is large thereby causing pressure, shortness of breath, or other breathing problems, such as low oxygen levels. Removing the fluid allows the lung to expand, making breathing easier. Treating the underlying cause of the effusion then becomes the goal. Chemotherapy, radiation therapy, surgery, or instilling medication into the chest that prevents re-accumulation of fluid after drainage may be used in some cases.

7. Pnuemothorax (Corey et al., 2010): A collapsed lung, or pneumothorax, is the collection of air in the space around the lungs. This buildup of air puts pressure on the lung, so it cannot expand as much as it normally does when you take a breath.
Treatment: The following treatments can be administered:

(a) Pneumothoraces which are too small to require tube thoracostomy and too large to be left untreated, may be aspirated with a small catheter.
(b) Lung surgery may be needed to treat pneumothorax or to prevent future episodes. The area where the leak occurred may be repaired.

RESULTS

The results are summarized in Table 1 showing comparison of prescribed drugs versus recommended therapy and in Table 2 showing frequency of occurrence of different LRTIs. Table 3 and Figure 3 exhibit the number of patients using different antibiotics at JPMC for treatment of LRTIs.

1. If the calculated value is $f_1 = 3.34$, then it means it is greater than the p-value of the table which is $f_1 = 1.94$. So if $p \leq$ '0.05', we therefore reject the null hypothesis which shows that there is difference between the two drugs used for treatment.
2. Calculated value that is $f_2 = 0.57$, is smaller than table p value that is $f_2 = 1.67$. So, $p >$ '0.05' therefore we accept null hypothesis so there is no difference in patients diseases groups.

On the basis of statistical evaluation (ANOVA) of results, it is found that the treatments which are being prescribed in JPMC are more or less similar with the recommended therapy but if the difference is observed, the reason may involve several factors like geographical region, ethnicity, tolerance and resistance, non availability of recommended medicine, and its cost (government hospital for poor people). As such, there is a need to screen the reason for resistance in different patients (if

Table 1. Comparison of prescribed drugs In JPMC versus recommended medications used for the treatment of LRTIs.

LRTIs	Drugs used in JMPC	Most appropriate drugs[5],[6]
Pleural effusion	Metronidazole Cefotaxime	Bleomycin Tetracycline Doxycycline
Pulmonary tuberculosis	Isoniazid Ethambutol Pyrazinamide Rifampin Amikacin Streptomycin	Isoniazid Ethambutol Pyrazinamide Rifampin Streptomycin
COPD	Cefotaxime Amikacin Levofloxacin	Ipratropium salmetrol/formatrol corticosteroid eg:prednisone etc Theophylline
Pneumonia	Metronidazole Amoxicillin Cefotaxim Ceftazidime Nystatin	Cephalosporins Carbapenems Quinolones Aminoglycosides Vancomycins
Cystic fibrosis	Levofloxacin Ofloxacin Ciprofloxacin Cefotaxim Kanamycin Ethionamide	N-Acetylcystine Albuterol Ipratropium Vancomycin Tobramycin Meropenem Ciprofloxacin Piperacillin Aztreonam Azithromycin
Bronchitis	Ciprofloxacin Cefotaxime	Amoxicillin Doxycycline Bronchodialators eg: ipratropium Chorticosteriod
MDR-TB	Kanamycin Ethionamide Cycloserine Metronidazole Ceftazidime Kanamycin Levofloxacin P.A.Salicylic Acid	Amikacin Kanamycin Capeomycin Moxifloxacin Ciprofloxacin Rifabutin Cycloserine Ethionamide Clarithromycin

Table 1. Cont.

		high dose INH interferon-Y Thiozine
Empyema	Cefotaxime	1. Drainage of the infected pleural fluid. 2. Intravenous antibiotics are given. 3. Surgical debridement of the pleural space may be required.
Pneumothorax	Cefotaxime Metronidazole Amoxicillin Levofloxacin	

Table 2. Number of patients suffering from different LRTIs coming to JPMC in one month period.

S/N	Disease	Number of patients
1	Pneumothorax	10
2	Bronchitis	04
3	TB	58
4	MDR-TB	25
5	COPD	08
6	Pneumonia	16
7	Pleural effusion	07
8	Cystic fibrosis	08
9	Empyema	01
10	Total	137

occurring) by culture sensitivity tests at JPMC.

Occurrence of LRTIs in patients shows that there is a significant number of patients suffering from TB (42%) and MDR-TB (18%) and pneumonia (11.6%) and there are also patients suffering from fourth most common infection, Pneumothorax (7.3%) (Figures 1 and 2).

DISCUSSION

The results reveal that the occurrence of LRTIs is found to be highest for TB and secondly for MDR-TB. This deadly strain of the disease can emerge as a result of low quality health systems, poor quality drugs, lack of accessibility to treatment, and when a patient intermittently takes his medicine or fails to complete his treatment. The poor structure of health care system, poverty and poor hygiene are the factors responsible to make the country more vulnerable to the emerging TB crisis.

In essence, TB patients are left on their own to deal with the consequences of being infected with a contagious disease they knew very little about. Over the past 10 years, the country has begun to implement new programs focusing on TB, but there is still very little education about the disease and even fewer resources to help treat and prevent it. TB seems to take a back seat to other social and health issues, evidenced by the fact that there are only four organizations in the country that work on tuberculosis. While the overall TB numbers have dropped or stayed stagnant in recent years, the number of MDR-TB patients has also dropped down, showing that our country needs more vigorous awareness program dealing with the complex problems that TB treatment and prevention present.

Multiply resistant organisms render therapy more precarious and costly and sometimes unsuccessful. Individuals may succumb to MDR infections because all available drugs have failed, especially in the developing world (Levy, 2002). Notable global examples include hospital and community (ROAR, GAARD) MDR strains of *Mycobacterium tuberculosis*, *Enterococcus faecium*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Acinetobacter baumanii* and *Pseudomonas aeruginosa* (Levy, 1998; Walsh and Amyyes, 2004; Weinstein, 2001; World Health

Table 3. Number of patients using antibiotics for various LRTIs.

Diseases	Drugs	No of Pts. using drugs
T.B.	Isoniazid+Rifampin+Ethambutol+Pyrazinamide	53
	Isoniazid+Rifampin+Ethambutol+Pyrazinamide +Amikacin	3
	Isoniazid+Rifampin+Ethambutol+Pyrazinamide +Streptomycin	2
	Total	58
Pneumothorax	Cefotaxime	5
	Metronidazole	3
	Amoxicillin	1
	Levofloxacin	1
	Total	10
Pleural effusion	Metronidazole	3
	Cefotaxime	4
	Total	7
Empyema.	Cefotaxime	1
Cystic Fibrosis	Levofloxacin	2
	Ofloxacin	2
	Ciprofloxacin	1
	Cefotaxim	1
	Kanamycin	1
	Ethionamide	1
	Total	8
Pneumonia	Metronidazole	4
	Amoxicillin	4
	Cefotaxim	2
	Ceftazidime	3
	Nystatin	3
Total		16
MDR T.B.	Kanamycin	5
	Ethionamide	5
	Cycloserine	5
	Metronidazole	4
	Ceftazidime	1
	Levofloxacin	1
	P.A.Salicylic Acid	4
Total		25
COPD	Cefotaxime	2
	Amikacin	5
	Levofloxacin	1
		8
Bronchitis	Ciprofloxacin	1
	Cefotaxime	3
Total		4

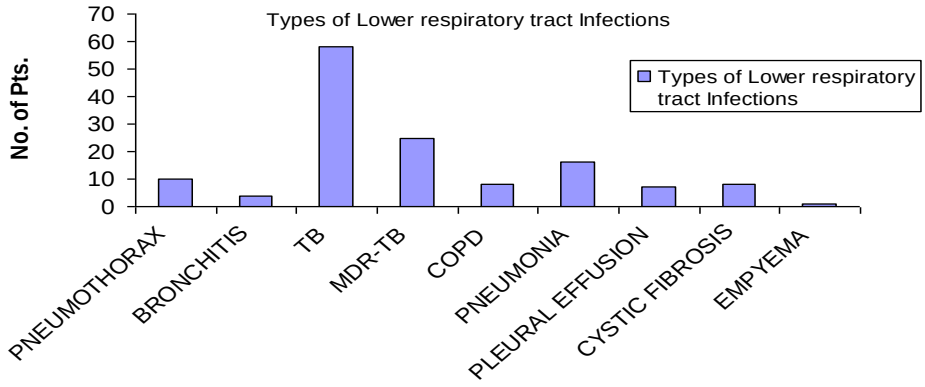

Figure 1. Number of patients suffering from different LRTIs coming to JPMC in one month period.

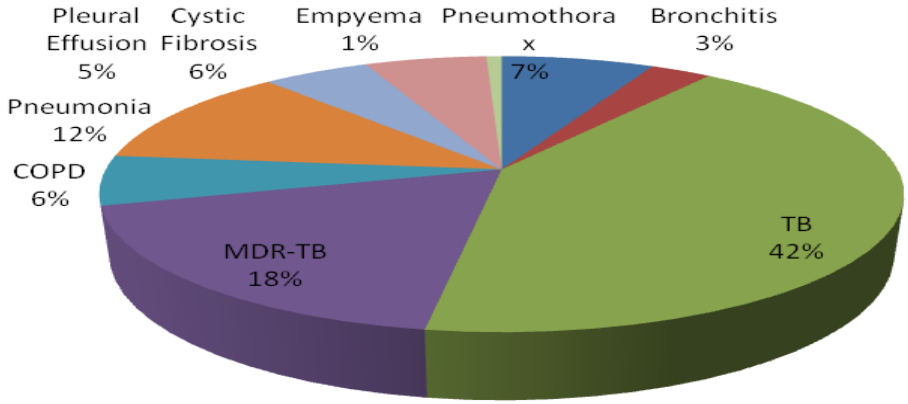

Figure 2. Percentage of patients suffering from various LRTIs hospitalized in JPMC in one month period.

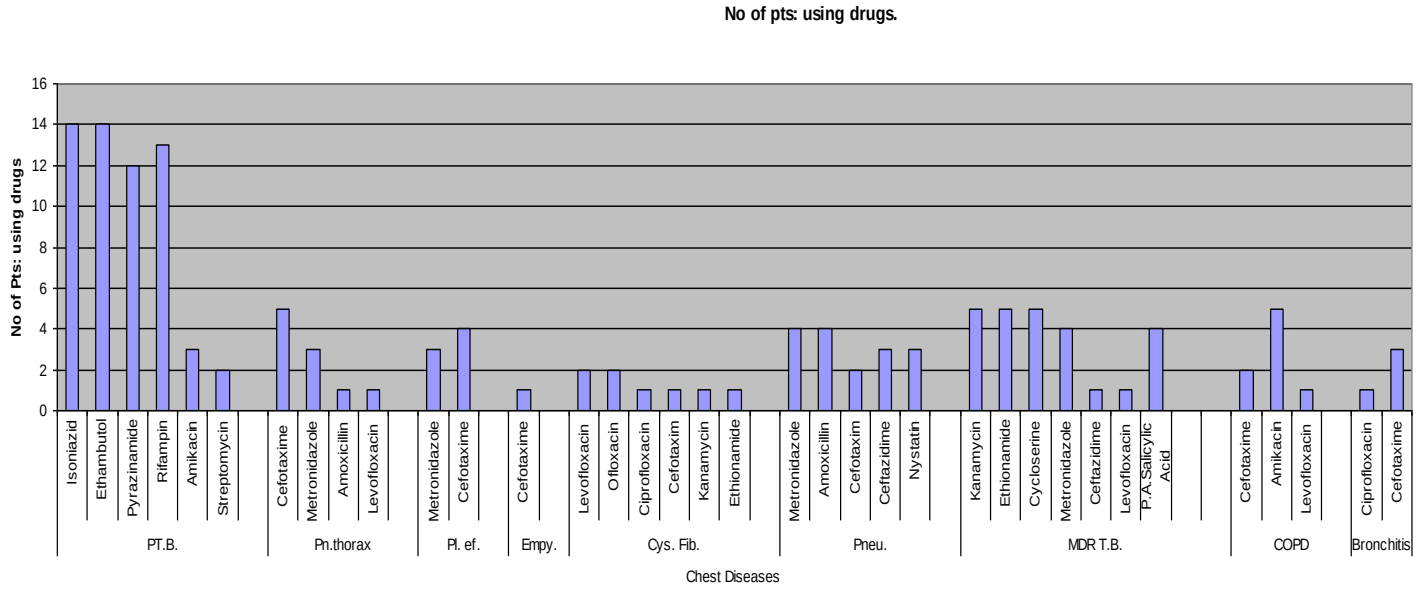

Figure 3. Frequency of use of different antibiotics in patients affected with LRTIs.

Organization website).

Among the Gram-negative bacteria, hospital infections caused by *P. aeruginosa* and *A. baumanii* are sometimes resistant to all, but one, antibiotics, which seriously challenges the treatment of immune-compromised individuals and can result in death. The extended spectrum β-lactamases, carried among Enterobacteriaceae such as *Enterobacter* and *Klebsiella*, destroy even the latest generations of penicillin and cephalosporins (Bush, 2001; Paterson et al., 2004; Bradford, 2001). Of particular note, is the increase in strains bearing metallo-β-lactamases that inactivate carbapenems drugs that are often the 'last resort' in serious infections of Gram-negative bacteria (Nordmann, and Poirel 2002; Livermore and Woodfurt, 2000; Wang, et al., 2001).

The community has become similarly encumbered with MDR organisms. Some strains of *E. coli*, a common cause of urinary tract infection, resist members of six drug families including the more recently recommended fluoroquinolones. Resistance in pneumococci continues to be an ever-increasing global threat that curtails treatment of pneumonias and ear infections, particularly in children. Having started with penicillin resistance, the organisms now tout resistance to macrolides and tetracyclines in many areas (Schrag et al., 2004). One study has predicted that multidrug resistance will override single-drug resistance in the present decade (McCormick et al., 2003).

Strains of *Neisseria gonorrhoeae* confront clinicians worldwide with triple resistance to penicillins, tetracyclines and fluoroquinolones (Tanaka et al., 2000). Because of the need to provide a single-dose therapy to this highly noncompliant population of infected individuals, a parenteral cephalosporin is the only treatment remaining. Today, MRSA strains that differ from the hospital strains and possess a new virulence toxin (Panton-Valentine leukocidin) have emerged in communities of industrialized countries (Wang et al., 2003; Vandenesch et al., 2003; Herold et al., 1998).

The so called 'community-acquired MRSA' is resistant to the β-lactam antibiotics, requiring physicians to commence alternative therapies when MRSA is suspected. Children were found to succumb to community acquired MRSA infection because the disease had become too far advanced by the time that another effective therapy was initiated. *M. tuberculosis*, particularly in some endemic areas, bears resistance to as many as eight drugs, making some individuals with tuberculosis incurable (Bloom and Murray, 1992). Previously (inadequately), treated individuals are at greatest risk; in some areas, more than 50% of such individuals have MDR tuberculosis. The frequency of drug resistance in the community has extended the resistance problem beyond the confines of the hospital. Resistant strains can be traced from the community to the hospital and vice versa, indicating that drug resistance is no longer localized.

The resistance problem can be seen simplistically as an equation with two main components: the antibiotic or antimicrobial drug, which inhibits susceptible organisms and selects the resistant ones; and the genetic resistance determinant in microorganisms selected by the antimicrobial drug (Levy, 1994, 2002). Millions of kilograms of antimicrobials are used each year in the prophylaxis and treatment of people, animals and agriculture globally, (Mellon et al., 2001; Barza and Gorbach 2002), driving the resistance problem by killing susceptible strains and selecting those that are resistant.

Conclusion

This study will definitely help to reduce the unnecessary use of antibiotics and steroid side by side their adverse effects, however the recommended treatment should be followed for good health care services. Resistance findings by culture sensitivity test can lead to reduction in complication, duration and cost of treatment.

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