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# A PROSPECTIVE OBSERVATIONAL STUDY ON ANTIBIOTIC PRESCRIBING IN RESPIRATORY TRACT INFECTION IN A TERTIARY CARE TEACHING HOSPITAL

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## ABSTRACT

**Background:** Inappropriate use of antibiotics specifically, the broad spectrum antibiotics in respiratory tract infections results in resistance to antibiotics. The common use of antibiotics is the prime reason for the spread of drug resistant bacterial strains which not only results in costly treatment, but also high rate of morbidity and mortality. Hence, the present study was aimed at evaluating the prescribing pattern of antibiotics, disease conditions for which they were prescribed in the departments of General medicine. **Aims and Objectives:** The aim of present study is to describe different types of Respiratory tract infections and antibiotics used to treat such infections, to quantify the changes or adjustments made to the initial therapy and to determine appropriateness of antibiotic use, using standardized quality indicators.

- To identify commonly used antibiotics prescribed for the treatment of respiratory tract infections and to improve the appropriateness of antibiotic therapy.
- To recognize appropriate use of blood cultures, sputum cultures, chest x-ray and other investigations used in respiratory tract infections .
- To identify the drug resistance in hospitalized patients.

**Methodology:** A prospective observational study was carried out involving in-patients of respiratory medicine, general medicine, 750 bedded tertiary teaching hospital for six months. The data of two hundered patients were collected for the study in predefined forms from the medical case records and drug charts. The enrolled patients were observed from admission till discharge. **Results and Conclusions:** The most commonly diagnosed disease among respiratory tract infection in the in-patient department of Respiratory medicine, general

medicine was found to be LRTI. The most commonly prescribed antibiotics for LRTI respiratory tract infections were cephalosporin, macrolides, penicillin's. The most commonly prescribed antibiotics for URTI respiratory tract infections were cephalosporins. From this study, it is concluded that cautious and judicious use of antibiotics enables better patient management limiting the resultant morbidity and mortality arising from respiratory tract infections.

## INTRODUCTION

Based on alarming accumulated facts in the previous few years, antimicrobial resistance is an increasingly important patient safety and public health issue. As per the different studies undertaken in the previous year, antibiotics were the most common drug categories associated with both prescribing and administration errors. Antibiotic therapy is considered adequate if spectrum, dose application modus, and duration of therapy were appropriate according to local recommendations or published guidelines.

## URTI DISEASES

### PHARYNGITIS

Pharyngitis is inflammation of the back of the throat, known as the pharynx. It typically results in a sore throat and fever. Other symptoms may include a runny nose, cough, headache, and a hoarse voice. Symptoms usually last three to five days. Complications can include sinusitis and acute otitis media. Pharyngitis is a type of upper respiratory tract infection.

### LARYNGITIS

Laryngitis is inflammation of the larynx (voice box). Symptoms often include a hoarse voice and may include fever, cough, pain in the front of the neck, and trouble swallowing. Typically, these last under two weeks.

### TONSILITIS

Tonsillitis is inflammation of the tonsils, typically of rapid onset. It is a type of pharyngitis. Symptoms may include sore throat, fever, enlargement of the tonsils, trouble swallowing, and large lymph nodes around the neck.

**LRTI DISEASES**

**ASTHMA**

Asthma is a common long-term inflammatory disease of the airways of the lungs. It is characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. Symptoms include episodes of wheezing, coughing, chest tightness, and shortness of breath. These may occur a few times a day or a few times per week. Depending on the person, they may become worse at night or with exercise.

**PNEUMONIA**

**Pneumonia** is an infection that inflames the air sacs in one or both lungs. The air sacs may fill with fluid or pus (purulent material), causing cough with phlegm or pus, fever, chills, and difficulty breathing. A variety of organisms, including bacteria, viruses and fungi, can cause pneumonia.

**Chronic Obstructive Pulmonary Disease**

**Chronic obstructive pulmonary disease** (**COPD**) is a type of obstructive lung disease characterized by long-term breathing problems and poor airflow. The main symptoms include shortness of breath and cough with sputum production. COPD is a progressive disease, meaning it typically worsens over time. Eventually everyday activities, such as walking or getting dressed, become difficult. Chronic bronchitis and emphysema are older terms used for different types of COPD. The term "chronic bronchitis" is still used to define a productive cough that is present for at least three months each year for two years.

**METHODS**

RESEARCH DESIGN: A Prospective observational study.

INCLUSION CRITERIA: All in –patients (18-60years) admitted in the general medicine wards, diagnosed with respiratory tract infections during the study period were included in the study.

EXCLUSION CRITERIA: Pregnant, lactating women, Pediatric patients,Patients above 60 years.

SAMPLE SIZE: 200 Patients.

STUDY PERIOD: The study was conducted over a period of 6 months.

## METHODOLOGY

A prospective observational study will be conducted for 6 months. All adult patients who are diagnosed with respiratory tract infection and who receives an antibiotic therapy within 24hrs of admission are included.

Data on demographic characteristics, diagnosis, comorbidities, microbiological tests and administered antibiotics will be collected prospectively.

## RESULTS

In our current study, to focus on prescribing pattern of antibiotics, out of all the patients attending the general medicine inpatient department were included, among them 200 patients with respiratory tract infections receiving antibiotics were considered.

**Table 1: Sex Wise Distribution of Patients.**

| Sex | No. Of patients | Percent |
|---|---|---|
| FEMALE | 90 | 45 |
| MALE | 110 | 55 |
| TOTAL | 200 | 100 |

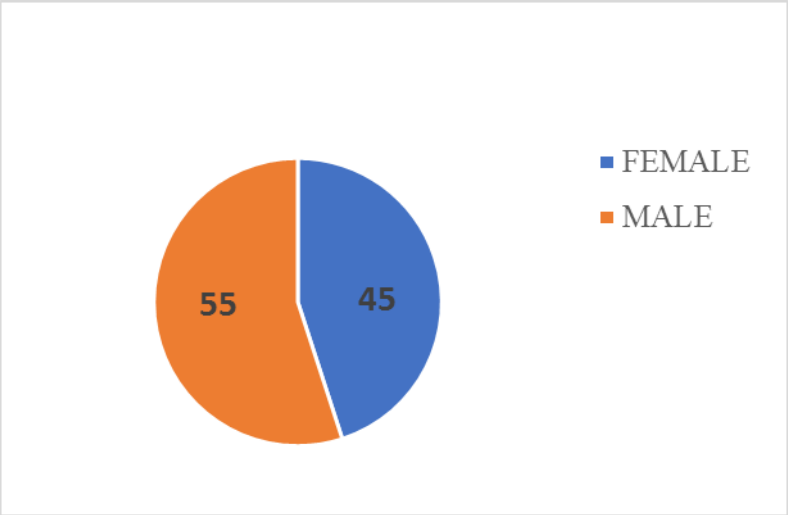


**Fig 1: Graphical Representation on Sexwise Distribution.**

Table 1; Fig :1 reported that male patients (55%) are more effected by respiratory tract infections than female patients (45%).

**Table 2: Number Of Patients Based On Their Age Groups.**

| AGE GROUPS | NUMBER OF PATIENTS | PERCENTAGE |
|---|---|---|
| 16-30 Years | 17 | 8.5 |
| 30-49 Years | 62 | 31 |
| 50-60 Years | 121 | 60.5 |
| TOTAL | 200 | 100 |

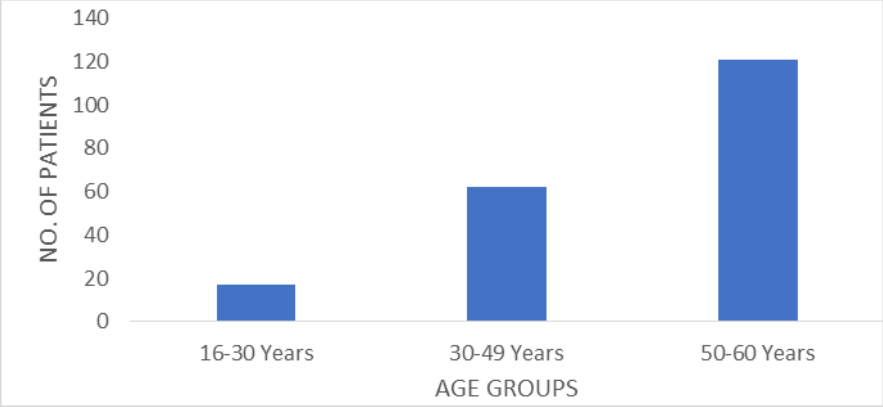


**Fig 2: Graphical Representation Agewise Distribution.**

Table :2; Fig :2; reported that the patients with age group 50-60 years (60.5%) are mostly effected by respiratory tract infections and patients below 30 years age group are less effected(17%).

**Table 3: Classification Based On Diseases.**

| CLASSIFICATION | NO. OF PATIENTS | PERCENTAGE |
|---|---|---|
| LRTI | 128 | 64 |
| URTI | 72 | 36 |
| TOTAL | 200 | 100 |

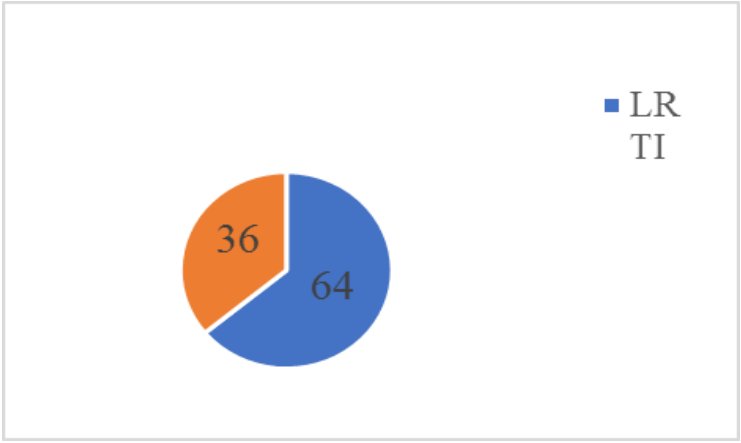


**Fig:3 Graphical Representation Of Classification Based On Diseases.**

Table :3; Fig :3; reported that the patients are most commonly affected with lower respiratory tract infections(64%) than upper respiratory tract infections(36%).

**Table 4: Disease Wise Distribution of Patients.**

| Number Of Diseases | No. Of Patients | Percent |
|---|---|---|
| PNEUMONIA | 43 | 21.5 |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | 56 | 28 |
| ASTHMA | 19 | 9.5 |
| PLEURAL EFFUSION | 10 | 5 |
| TUBERCULOSIS | 17 | 8.5 |
| BRONCHITIS | 17 | 8.5 |
| ACUTE PHARYNGITIS | 1 | 0.5 |
| OTHER RESPIRATORY TRACT INFECTIONS | 37 | 18.5 |
| TOTAL | 200 | 100 |

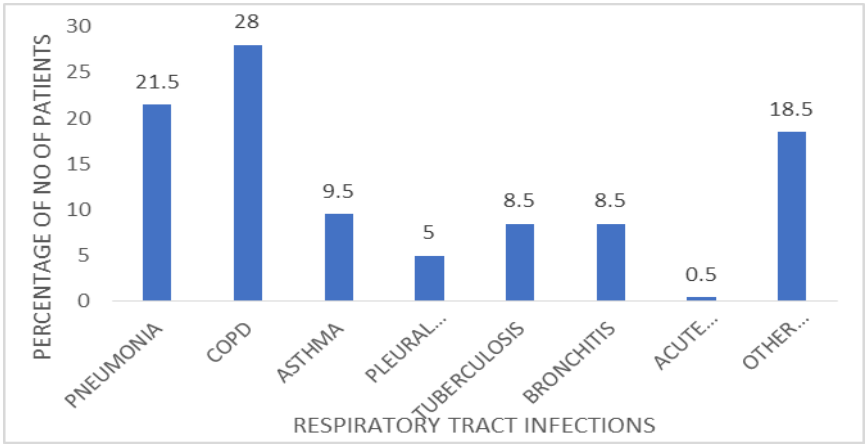


**Fig 4: Graphical representation disease wise distribution.**

Table :4; Fig :4; reported that the patients with chronic obstructive pulmonary disease (28%) are most affected and patients with acute pharyngitis are least affected (0.5%).

**Table 5: Disease Wise Distribution of Patients According To Gender.**

| Number Of Diseases | Male Percentage | Female Percentage |
|---|---|---|
| Pneumonia | 12 | 9.5 |
| Copd | 23 | 6.5 |
| Asthama | 2.5 | 7 |
| Pleural Effusion | 2 | 3 |
| Tuberculosis | 5 | 4 |
| Bronchitis | 3.5 | 5 |
| Acute Pharyngitis | 0.5 | 0.5 |
| Others | 6 | 11 |
| Total | 54.5 | 46.5 |

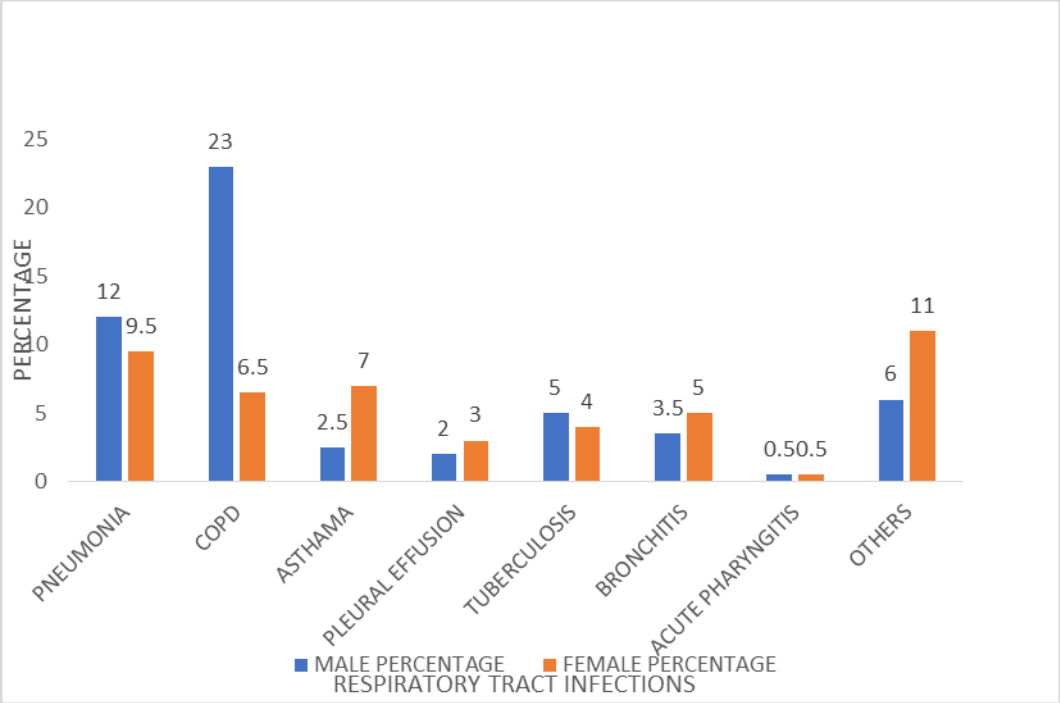


**Fig 5: Graphical Representation of Disease Wise Distribution of Patients According to Gender.**

Table 5: Fig :5; reported that the male patients with chronic obstructive pulmonary disease (23%) are most affected and least affected with acute pharyngitis (0.5%).

Female patients with pneumonia (9.5%) are most affected and least affected with acute pharyngitis (0.5%).

**Table 6: Prescribing Pattern of Antibiotics in LRTI.**

| Antibiotics prescribed in LRTI | Number of antibiotics | Percentage% |
|---|---|---|
| Ampicillin+amikacin+metronidazole | 18 | 9 |
| Amoxicillin | 5 | 3 |
| Ceftriaxone | 54 | 25 |
| Azithromycin | 42 | 19 |
| Cefperazone | 27 | 13 |
| Amoxicillin +clavulanic acid | 36 | 16 |
| Cefotaxime | 24 | 11 |
| Ceftriaxone+sulbactum | 5 | 2 |
| Levofloxacin | 1 | 0.5 |
| Doxycycline | 1 | 0.5 |
| Metronidazole | 2 | 1 |

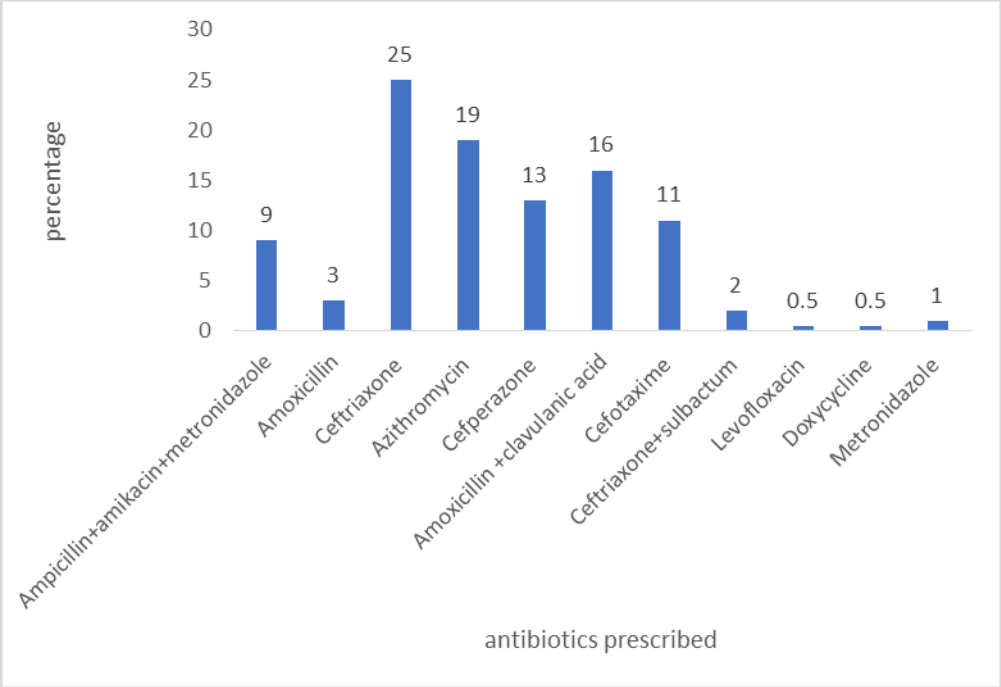


**Fig 6: Graphical Representation on Prescribing Pattern of Antibiotics in LRTI.**

Table 6; fig 6 reported that out of 215 antibiotics prescribed in LRTI, were ceftriaxone 54(25%), azithromycin42(19%), amoxicillin+ clavulanic acid 36(16%), cefperazone 27(13%), cefotaxime 24(11%), ampicillin+amikacin+metronidazole 18(9%), amoxicillin 5(3%), ceftriaxone+sulbactum 5(2%), metronidazole 2(1%) levofloxacin 1(0.5%), doxycycline 1(0.5%). Ceftraiaxone was the most commonly prescribed antibiotic in LRTI.

**Table 7: Prescribing Pattern of Antibiotics in URTI.**

| Antibiotics Prescribed In URTI | Number Of Antibiotics | Percentage% |
|---|---|---|
| Ampicillin+amikacin +metronidazole | 2 | 9 |
| Amoxicillin | 1 | 4 |
| Ceftriaxone | 3 | 13 |
| Azithromycin | 2 | 9 |
| Cefperazone | 9 | 39 |
| Amoxicillin +clavlunic acid | 3 | 13 |
| Cefotaxime | 2 | 9 |
| Metronidazole | 1 | 4 |

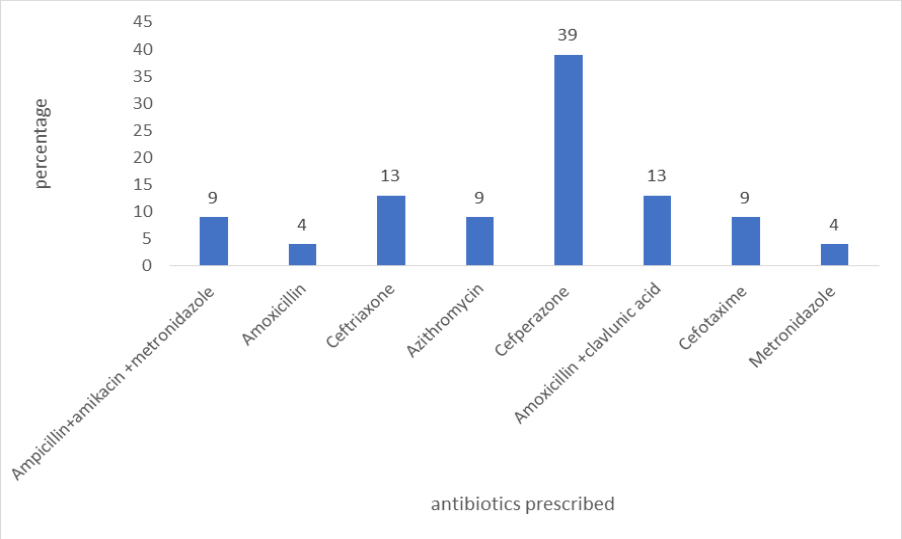


**Fig 7: Graphical Representation on Prescribing Pattern of Antibiotics in URTI.**

Table 7; Fig 7 reported that out of 23 antibiotics prescribed in URTI; cefperazone 9(39%), ceftriaxone& amoxicillin + clavulanicacid 3(13%), ampicillin+amikacin+metronidazole &azithromycin & cefotaxime 2(9%), amoxicillin& metronidazole1(4%).

**Table 8: Patients distribution based on diagnostic parameters.**

| Diagnostic Tests | Percentage |
|---|---|
| Sputum Culture | 7 |
| Chest Xray | 53.5 |
| Sputum +X Ray | 32 |
| Others | 7.5 |
| Total | 100 |

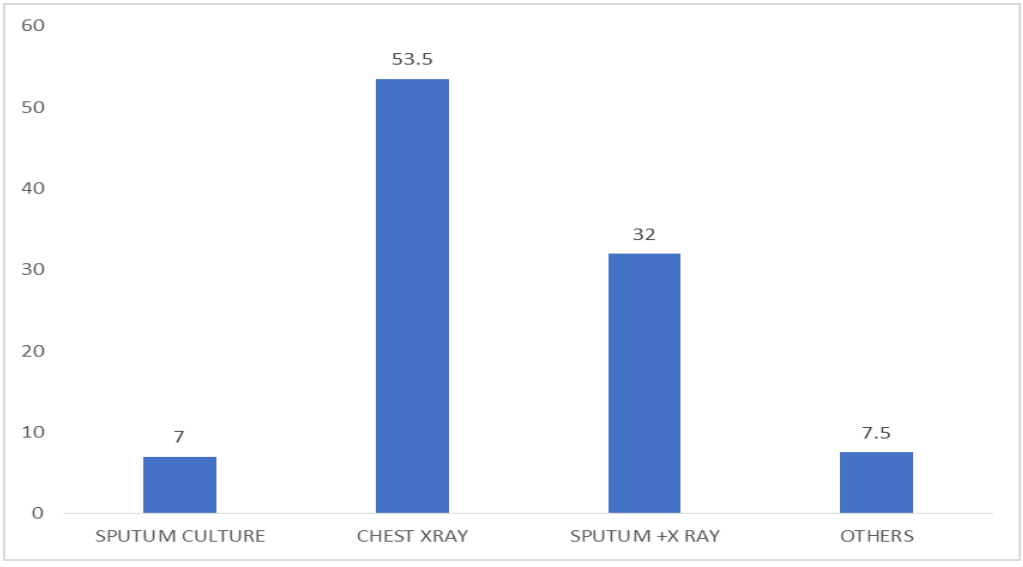


**Fig 8: Graphical Representation of Patients Distribution Based on Diagnostic Parameters.**

Table 8; Fig 8; reported that the Chest X-ray and sputum and chest x-ray are the most commonly used diagnostic tools.

**Table 9: Most Commonly Prsescribed Antibiotics Before Culture Test.**

| Drugs | Percentage |
|---|---|
| Twibact | 25.8 |
| Augmentin | 20.5 |
| Azithromycin | 10.2 |
| Monocef | 20.5 |
| Taxim | 17.9 |
| Ampicillin+amikacin+metronidazole | 0 |
| Metrogyl | 5.1 |

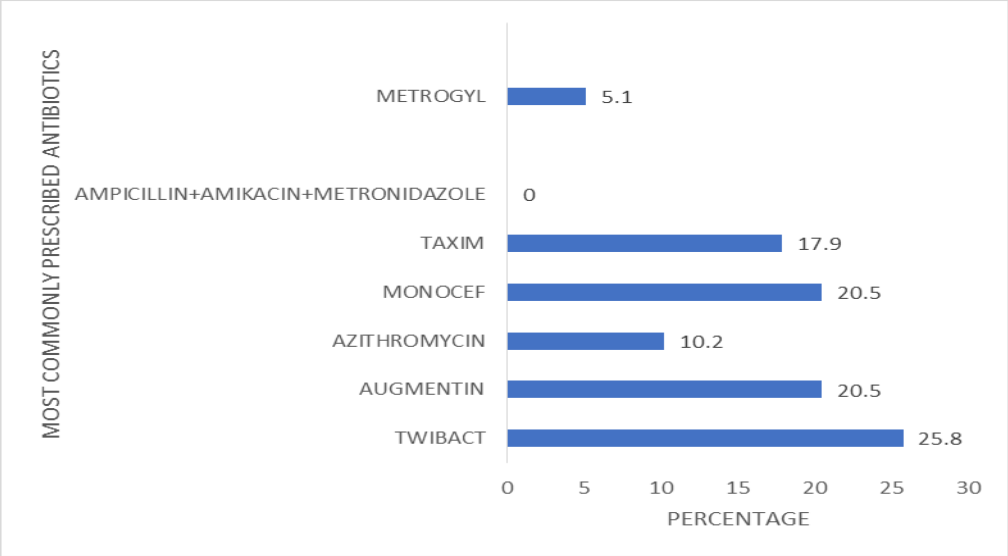


**Fig 9: Graphical Representation of Most Commonly Prsescribed Antibiotics Before Culture Test.**

Table :9; fig :9 reported that twibact(25.8%)is the most prescribed antibiotic and ampicillin+ amikacin+ metronidazole is least prescribed antibiotic before culture sensitivity test.

**Table 10: Most Prsescribed Type of Antibiotics After Culture Test.**

| Drugs | Percentage |
|---|---|
| Twibact | 0 |
| Augmentin | 17.8 |
| Azithromycin | 21.4 |
| Monocef | 14.28 |
| Taxim | 7.14 |
| Ampicillin+amikacin+metronidazole | 14.2 |
| Metrogyl | 25.18 |

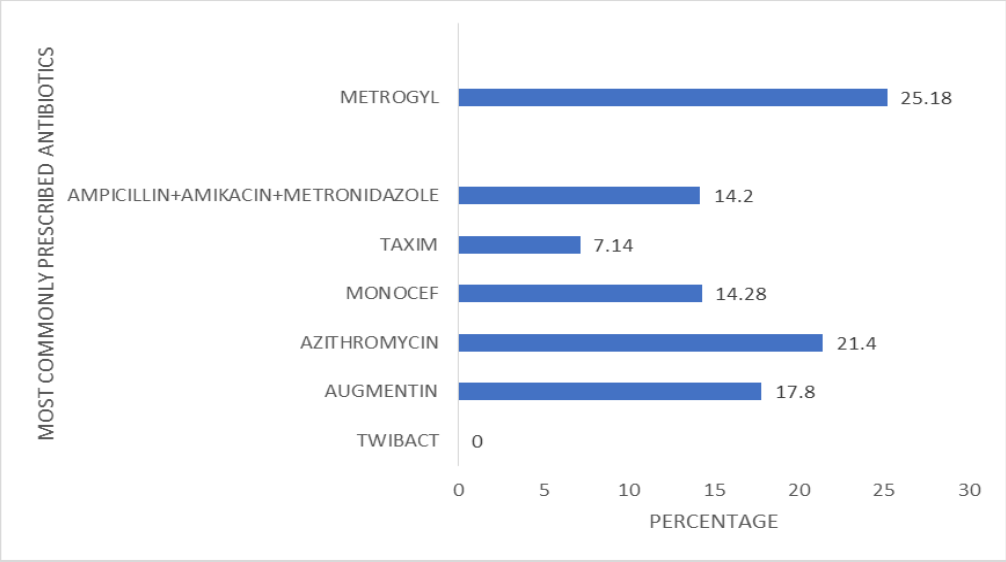


**Fig.10 Graphical Representation of Most Commonly Prescribed Antibiotics After Culture Test.**

Table :10;fig :10 reported that metronidazole is the most prescribed antibiotic and twibact(2) is the least prescribed antibiotic after the culture sensitivity test.

**Table 11: Type of Antibiotic Class Prescribed.**

| Class of Drugs | Percentage |
|---|---|
| Cephalosporins | 16.5 |
| Penciliins | 38 |
| Aminoglycosides | 10.5 |
| Macrolides | 31 |
| Antiamoebics | 13.5 |

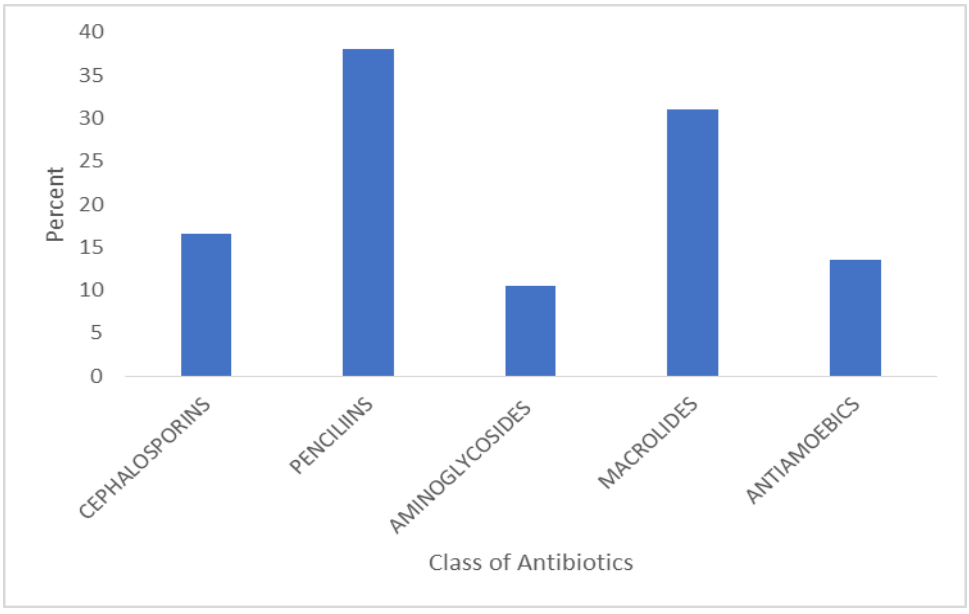


**Fig 11: Graphical Presentation on Type of Antibiotic Class Prescribed.**

Table :11; Fig :11; reported that the 38% of patients were prescribed with pencillin class of antibiotics and 11% of patients were prescribed with aminoglycoside class of antibiotics.

**Table 12: Type of Antibiotic Drugs Prescribed.**

| Drugs | Percentage |
|---|---|
| Azithromycin | 31.5 |
| Augmentin | 24.5 |
| Monocef | 28 |
| Taxim | 16.5 |
| Twibact | 21 |

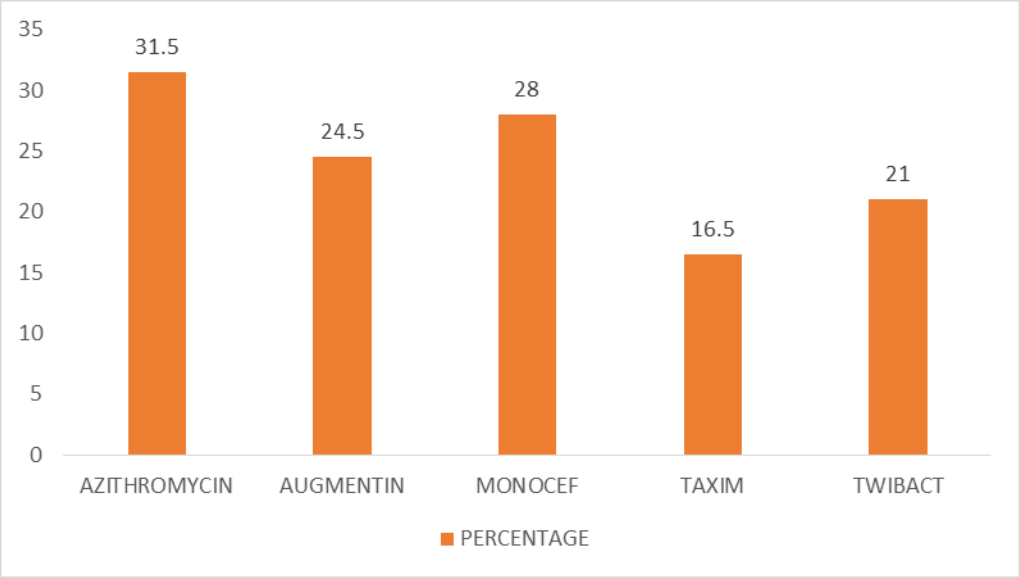


**Fig 12: Graphical Representation on Type of Antibiotic Drugs Prescribed.**

Table :12; Fig :12; reported that the most of the patients were prescribed with azithromycin (31.5) drug and least prescribed with taxim (16.5) drug.

**Table 13: Number of Days of Hospitalization.**

| Days | Frequency |
|---|---|
| BELOW 7 | 4O |
| 7 | 98 |
| 8 - 9 DAYS | 52 |
| ABOVE 10 | 10 |

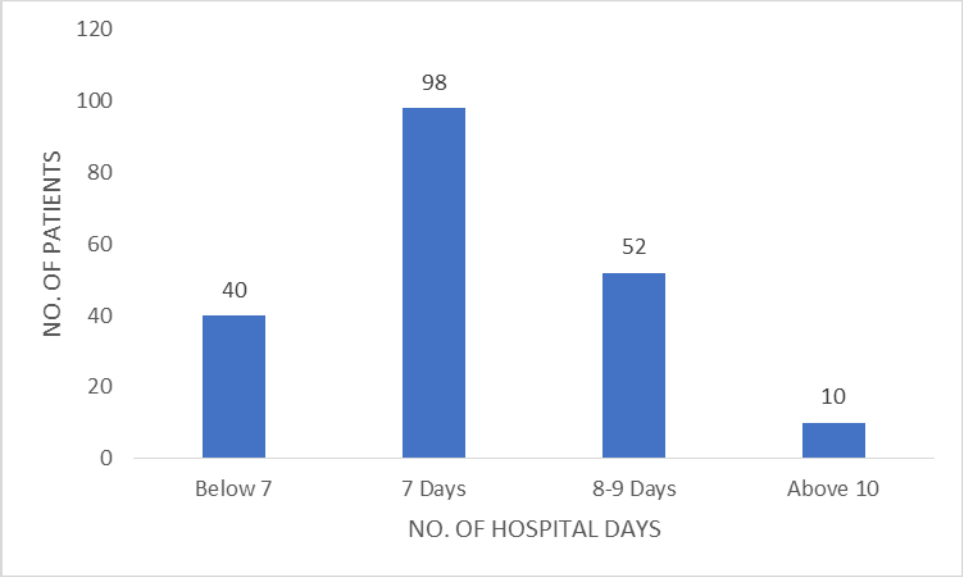


**Fig 13: Graphical Representation on Number of Days of Hospitalization.**

Table:13; fig:13 reported that most of the patients hospitalization is 7 days.

## DISCUSSION

The emerging problem of antibiotic resistance has become a major threat to the medical field. There is currently no national clinical guideline relating to antibiotic prescribing for RTIs. Hence, management of RTIs has been a challenge to the physician, mostly due to emergence of multi drug resistance. A study of prescribing pattern of antibiotics is an effective way of reflecting appropriateness of antibiotic use. In addition, it can also help in reduction in the cost of therapy, minimizing practice of polypharmacy and improving rational use of antibiotics.

The issues related to antibiotic resistance can be solved by making the practitioners aware of the treatment for respiratory tract infection. There are many studies related to antibiotic use in hospitals The information regarding antibiotics use provide a constructive approach in solving problems arising from multiple antibiotic use(Remesh et al., 2013).

Out of all the in patients analysed in the study who were having lower respiratory tract infections and upper respiratory tract infections 55% of patients were males and 45% of patients were females. This is accordance with previous surveys and studies which already revealed that incidence of respiratory tract infections are almost equal in females and males. When the demographic profiles of the patients were done it was found that as large as 60% of patients are of range 50-60 years and 31% of patients are of range 30-49 years and 8% of

patients are of range 16-30 years. In our study it can be said that respiratory tract infections are more common in old age group than middle age group.

In the present study majority of the study population, i.e. 64% of the patients were diagnosed with LRTI and 36% were diagnosed with URTI. When analysed 28% of patients were with COPD, 21% of patients with pneumonia, 9.5% of patients with asthma, 8.5% of patients with TB, and 8.5%of patients with bronchitis, 5% of patients with pleural effusion, 0.5% of patients with acute pharyngitis and 18.5% of patients with other respiratory tract infections.

Our study stated that the male patients with COPD (23%) were most affected and least affected with acute pharyngitis(0.5%) female patients with pneumonia (9.5%) were most affected and least affected with acute pharyngitis .

Bacteriological analysis in RTIs helps in providing accurate antibiotic therapy to the patient in turn leading to better patient outcome and decreased emergence of drug resistance.

In the current study, out of total 200 patients that were enrolled only 53.5% of patients are diagnosed with chest x-ray, 32% of patients are diagnosed with both sputum and x-ray .only 7% of patients were diagnosed with sputum culture. 7.5% of patients are diagnosed with other diagnostic tools.

The most commonly prescribed antibiotics for URTI were Cephalosporins. Our study reported that out of 23 antibiotics prescribed in URTI; cefperazone 9(39%), ceftriaxone 3 (13%) & amoxicillin & clavulanicacid were 3(13%), ampicillin+amikacin+metronidazole 2(9%) & azithromycin were 2(9%), cefotaxime 2(9%), amoxicillin 1 (4%) & metronidazole 1(4%).

In the current study all the study patients diagnosed with LRTI were prescribed with antibiotics. Out of 215 antibiotics prescribed in LRTI, were ceftriaxone 54(25%), azithromycin42(19%), amoxicillin + clavulanic acid 36 (16%), cefperazone 27 (13%), cefotaxime 24 (11%), ampicillin + amikacin + metronidazole 18 (9%), amoxicillin 5(3%), ceftriaxone + sulbactum5 (2%), metronidazole 2 (1%) levofloxacin 1 (0.5%), doxycycline 1(0.5%). Ceftraiaxone was the most commonly prescribed antibiotic in LRTI.

Our study states that Twibact(25.6%) was the most commonly prescribed antibiotic before culture test, followed by augmentin (20.5%)and monocef (20.5%). the most commonly

prescribed antibiotic after culture test were metronidazole(25.18%) followed by azithromycin (21.4%) augmentin (17.8%) taxim (7.14%) an least prescribed twibact.

Our study states that pencillins (16.5%) class of antibiotics are the mostly prescribed and aminoglycoside(10.5%) class of antibiotics are least prescribed.

Our study states that azithromycin(31.5%) antibiotic drug was most commonly prescribed and taxim(16.5%) antibiotic drug was leastly prescribed.

Our study reported that most of the patients hospitalisation is 7days (98%)

**CONCLUSION**

The most commonly diagnosed disease among respiratory tract infection in the inpatient department of Respiratory medicine, general medicine was found to be LRTI.

The most commonly prescribed antibiotics for LRTI respiratory tract infections were cephalosporin, macrolides, penicillin's.

The most commonly prescribed antibiotics for URTI respiratory tract infections were cephalosporins.

Our study concludes that the use of broad spectrum antibiotics before diagnostic tests should be reduced.

From this study, it is concluded that cautious and judicious use of antibiotics will reduce the burden of multi-drug resistance and thereby enabling better patient management and limiting the resultant morbidity and mortality arising from respiratory tract infections.

Clinical pharmacists play a major role in early detection and prevention of medication errors and thus can improve the quality of care to the patients.

Involvement of clinical pharmacist in prescription analysis and prescribing pattern studies can help provide feedback to the physicians on the current prescribing practices. This can further contribute in reducing the incidence of emergence of drug resistance and promote rational prescribing of antibiotics.

**REFERENCES**

1. Eccles MP, Grimshaw JM, Johnston M, et al. "Applying psychological theories to evidence-based clinical practice: identifying factors predictive of managing upper respiratory tract infections without antibiotics". (2007). Implement Sci, 2: 26. doi:10.1186/1748-5908-2-26. PMC 2042498. PMID 17683558.
2. Robert Beaglehole...; et al. The World Health Report 2004 - Changing History (PDF). World Health Organization, (2004). pp. 120–4. ISBN 92-4-156265-X.
3. Antibiotic Expert Group. Therapeutic guidelines: Antibiotic. 13th ed. North Melbourne: Therapeutic Guidelines, 2006.
4. van Riel D, Munster VJ, de Wit E, et al. "H5N1 Virus Attachment to Lower Respiratory Tract". Science, April 2006; 312(5772): 399. doi:10.1126/science.1125548. PMID 16556800.
5. Jump up to:a b c Doan, Quynh; Enarson, Paul; Kissoon, Niranjan; Klassen, Terry P.; Johnson, David W. "Rapid viral diagnosis for acute febrile respiratory illness in children in the Emergency Department". The Cochrane Database of Systematic Reviews (2014-09-15).
6. "Breath Test Could Sniff Out Infections in Minutes". Scientific American. 11 January 2013. Retrieved 5 February 2013.
7. Zhu, Jiangjiang; Bean, Heather D; Wargo, Matthew J; Leclair, Laurie W; Hill, Jane E . "Detecting bacterial lung infections:in vivoevaluation ofin vitrovolatile fingerprints". Journal of Breath Research, (2013).
8. Smith, JD; MacDougall, CC; Johnstone, J; Copes, RA; Schwartz, B; Garber. "Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis". CMAJ: Canadian Medical Association Journal, (17 May 2016); 188(8): 567–74. doi:10.1503/cmaj.150835. PMC 4868605. PMID 26952529.
9. Barlam TF, Morgan JR, Wetzler LM, et al. Antibiotics for respiratory tract infections: a comparison of prescribing in an outpatient setting. Infect Control Hosp Epidemiol, 2015 Feb; 36(2): 153–9. [PubMed]
10. Gonzales R, Bartlett JG, Besser RE, et al. Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults: background, specific aims, and methods. Ann Intern Med, 2001 Mar 20; 134(6): 479–86. [PubMed]

11. Scott JG, Cohen D, DiCicco-Bloom B, et al. Antibiotic use in acute respiratory infections and the ways patients pressure physicians for a prescription. J Fam Pract, 2001 Oct; 50(10): 853–8. [PubMed]
12. Kronman MP, Zhou C, Mangione-Smith R. Bacterial prevalence and antimicrobial prescribing trends for acute respiratory tract infections. Pediatrics, 2014 Oct; 134(4): e956–65. [PubMed]
13. Smith M. Antibiotics Early, Often Linked to Childhood Obesity. MedPage Today. 2014.
14. Altiner A., Brockmann S., Sielk M., Wilm S., Wegscheider K., Abholz H. Reducing antibiotic prescriptions for acute cough by motivating GPs to change their attitudes to communication and empowering patients: A cluster-randomized intervention study. (2007). J Antimicrob Chemother, 60: 638–644. [PubMed]
15. Arnold S., Straus S.Interventions to improve antibiotic prescribing practices in ambulatory care. (2005).Cochrane Database Syst Rev, 4: CD003539. [PubMed]
16. Ashworth M., Charlton J., Ballard K., Latinovic R., Gulliford M. (2005) Variations in antibiotic prescribing and consultation rates for acute respiratory infection in UK practices 1995–2000. Br J Gen Pract, 55: 603–608. [PMC free article] [PubMed]
17. Ayanruoh S., Waseem M., Quee F., Humphrey A., Reynolds T. Impact of rapid streptococcal test on antibiotic use in a pediatric emergency department. (2009); Pediatr Emerg Care, 25: 748–750. [PubMed]
18. Bergman M., Huikko S., Pihlajamäki M., Laippala P., Palva E., Huovinen P., et al. Effect of macrolide consumption on erythromycin resistance in Streptococcus pyogenes in Finland in 1997–2001. (2004); Clin Infect Dis, 38: 1251–1256. [PubMed]
19. Bjerrum L., Gahrn-Hansen B., Munck A.C-reactive protein measurement in general practice may lead to lower antibiotic prescribing for sinusitis. (2004). Br J Gen Pract, 54: 659–662. [PMC free article][PubMed]
20. Bjerrum L., Munck A., Gahrn-Hansen B., Hansen M., Jarbol D., Cordoba G., et al.Health Alliance for prudent antibiotic prescribing in patients with respiratory tract infections (HAPPY AUDIT) -impact of a non-randomised multifaceted intervention programme. (2011); BMC Fam Pract 12: 52. [PMC free article][PubMed]
21. Borg M., Sciclunca E. Over-the-counter acquisition of antibiotics in the Maltese general population.(2002). Int J Antimicrob Agents, 20: 253–257. [PubMed]
22. Boucher H., Talbot G., Benjamin D., Jr, Bradley J., Guidos R., Jones R., et al. (2013) 10 × ′20 progress—development of new drugs active against Gram-negative bacilli: an

update from the Infectious Diseases Society of America. Clin Infect Dis, 56: 1685–1694. [PMC free article] [PubMed]

23. Butler C., Rollnick S., Pill R., Maggs-Rapport F., Stott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats.(1998). BMJ, 317: 637–642. [PMC free article] [PubMed]
24. Butler C., Simpson S., Dunstan F., Rollnick S., Cohen D., Gillespie D., et al. Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. (2012). BMJ, 344: d8173. [PMC free article] [PubMed]
25. Cals J.W., Scheppers N.A., Hopstaken R.M., Hood K., Dinant G.J., Goettsch H., et al. Evidence based management of acute bronchitis; sustained competence of enhanced communication skills acquisition in general practice. (2007). Patient Educ Couns, 68: 270–278. [PubMed]
26. Cals J., Butler C., Hopstaken R., Hood K., Severens J., Dinant G. Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial. (2009). BMJ, 338: b1374. [PMC free article] [PubMed]
27. Cals J., de Bock L., Beckers P., Francis N., Hopstaken R., Hood K., et al. Enhanced communication skills and C-reactive protein point-of-care testing for respiratory tract infection: 3.5-year follow-up of a cluster randomized trial. (2013); Ann Fam Med, 11: 157–164. [PMC free article] [PubMed]
28. Cals J., Schot M., de Jong S., Dinant G., Hopstaken R. Point-of-care C-reactive protein testing and antibiotic prescribing for respiratory tract infections: a randomized controlled trial. (2010); Ann Fam Med, 8: 124–133. [PMC free article] [PubMed]
29. Cals J., van Weert H. Point-of-care tests in general practice: hope or hype? (2013); Eur J Gen Pract, 19: 251–256. [PubMed]
30. Carrasco-Garrido P., Jiménez-García R., Barrera V., Gil de Miguel A. Predictive factors of self-medicated drug use among the Spanish adult population. (2008); Pharmacoepidemiol Drug Saf, 17: 193–199. [PubMed]
31. Centers for Disease Control and Prevention (2012) Diseases/pathogens associated with antimicrobial resistance. Available at: http://www.cdc.gov/drugresistance/DiseasesConnectedAR.html (Accessed: 24 August 2014).

32. Chang C., Schiano T. Review article: drug hepatotoxicity. (2007); Aliment Pharmacol Ther, 25: 1135–1151. [PubMed]
33. Chen L., Chopra T., Kaye K. Pathogens resistant to antibacterial agents. (2009) ; Infect Dis Clin North Am, 23: 817–845. [PubMed]
34. Coenen S., Francis N., Kelly M., Hood K., Nuttall J., Little P., et al. Are patient views about antibiotics related to clinician perceptions, management and outcome? A multi-country study in outpatients with acute cough, (2013); PLoS One, 8: e76691. [PMC free article] [PubMed]
35. Cole A. GPs feel pressurised to prescribe unnecessary antibiotics, survey finds. (2014); BMJ, 349: g5238. [PubMed]
36. Costelloe C., Metcalfe C., Lovering A., Mant D., Hay A. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: Systematic review and meta-analysis. (2010); BMJ, 340: c2096. [PubMed]
37. Davies S., Grant J., Catchpole M. (2013) The drugs don't work. A Global Threat. London: Penguin Specials.
38. Department of Health (2012) Chief Medical Officer Annual Report 2011: Volume 2. Available at: http://www.gov.uk/government/publications/chief-medical-officer-annual-report-volume-2 (Accessed: 24 August 2014).
39. Deschepper R., Vander Stichele R. Differences in use of antibiotics in Europe: the role of cultural aspects. (2001); Pharm Weekbl, 136: 794–797.
40. Dingle T., Abbott A., Fang F. Reflexive culture in adolescents and adults with group A streptococcal pharyngitis. (2014); Clin Infect Dis, 59: 643–650. [PubMed]
41. Ebell M.H., Lundgren J., Youngpairoj S. How long does a cough last? Comparing patients' expectations with data from a systematic review of the literature. (2013); Ann Fam Med, 11: 5–13. [PMC free article] [PubMed]
42. European Commission Eurobarometer 338. Antimicrobial resistance. Survey carried out by TNS Opinion & Social at the request of the Directorate-General for Health and Consumers. (2010); Available at: http://ec.europa.eu/health/antimicrobial_resistance/docs/ebs_338_en.pdf (Accessed: 24 August 2014).
43. European Centre for Disease Prevention and Control (2010) Surveillance report. Surveillance of antimicrobial consumption in Europe. 2010. Available at: http://www.ecdc.europa.eu/en/publications/Publications/antimicrobial-antibiotic-consumption-ESAC-report-2010-data.pdf (Accessed: 24 August 2014).

44. European Centre for Disease Prevention and Control (2011) Antimicrobial resistance surveillance in Europe. Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Available at: http://www.ecdc.europa.eu/en/publications/Publications/antimicrobial-resistance-surveillance-europe-2011.pdf (Accessed: 24 August 2014).
45. European Centre for Disease Prevention and Control Key messages for primary care prescribers. Available at: http://ecdc.europa.eu/en/eaad/antibiotics/pages/messagesforprescribers.aspx (Accessed: 24 August 2014)
46. Falagas M., Rafailidis P., Matthaiou D., Virtzili S., Nikita D., Michalopoulos A. Pandrug-resistant Klebsiella pneumoniae, Pseudomonas aeruginosa and Acinetobacter baumannii infections: Characteristics and outcome in a series of 28 patients. (2008); Int J Antimicrob Agents, 32: 450–454. [PubMed]
47. Flanders S., Stein J., Shochat G., Sellers K., Holland M., Maselli J., et al. Performance of a bedside C-reactive protein test in the diagnosis of community-acquired pneumonia in adults with acute cough, (2004); Am J Med, 116: 529–535. [PubMed]
48. Francis N., Butler C., Hood K., Simpson S., Wood F., Nuttall J. Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: A cluster-randomised controlled trial, (2009); BMJ, 339: b2885. [PMC free article][PubMed]
49. Gonzales R., Anderer T., McCulloch C., Maselli J., Bloom F., Jr, Graf T., et al. A cluster randomized trial of decision support strategies for reducing antibiotic use in acute bronchitis, (2013); JAMA Intern Med, 173: 267–273. [PMC free article] [PubMed]
50. Goossens H., Ferech M., Vander Stichele R., Elseviers M. and ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: A cross-national database study, (2005); Lancet, 365: 579–587. [PubMed].
51. Harbart S., Samore M. Antimicrobial resistance determinants and future control. (2005); Emerg Infect Dis, 11: 794–801. [PMC free article] [PubMed]
52. Hay A., Tilling K.Can 88% of patients with acute lower respiratory infection all be special? (2014); Br J Gen Pract, 64: 60–62. [PMC free article] [PubMed]
53. Ho J., Tambyah P., Paterson D. Multiresistant gram-negative infections: A global perspective, (2010); Curr Opin Infect Dis, 23: 546–553. [PubMed]
54. Hollis A., Ahmed Z. Preserving antibiotics, rationally, (2013); N Engl J Med, 369: 2474–2476. [PubMed]

55. Hopstaken R., Muris J., Knottnerus J., Kester A., Rinkens P., DinantG. Contributions of symptoms, signs, erythrocyte sedimentation rate, and C-reactive protein to a diagnosis of pneumonia in acute lower respiratory tract infection. (2003); Br J Gen Pract, 53: 358–364. [PMC free article] [PubMed]
56. Høye S., Gjelstad S., Lindbæk M. Effects on antibiotic dispensing rates of interventions to promote delayed prescribing for respiratory tract infections in primary care. (2013); Br J Gen Pract, 63: e777–e786. [PMC free article] [PubMed]
57. Huang Y., Chen R., Wu T., Wei X., Guo A. Association between point-of-care CRP testing and antibiotic prescribing in respiratory tract infections: a systematic review and meta-analysis of primary care studies. (2013) ; Br J Gen Pract, 63: e787–e794. [PMC free article] [PubMed]
58. Hulscher M., Grol R., van der Meer J. Antibiotic prescribing in hospitals: a social and behavioural scientific approach. (2010); Lancet Infect Dis, 10: 167–175. [PubMed]
59. Humair J., Revaz S., Bovier P., Stalder H. Management of acute pharyngitis in adults: reliability of rapid streptococcal tests and clinical findings. (2006); Arch Intern Med, 166: 640–644. [PubMed]
60. Huttner B., Goossens H., Verheij T., Harbarth S. Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries. (2010); Lancet Infect Dis, 10: 17–31. [PubMed]
61. Infectious Diseases Society of America, Spellberg B., Blaser M., Guidos R., Boucher H., Bradley J., et al. Combating antimicrobial resistance: policy recommendations to save lives. (2011);Clin Infect Dis, 52(Suppl. 5): S397–S428. [PMC free article] [PubMed]
62. Kenealy T., Arroll B. Antibiotics for the common cold and acute purulent rhinitis. (2013); Cochrane Database Syst Rev, 6: CD000247. [PubMed].
63. Kirby A., Herbert A. Correlations between income inequality and antimicrobial resistance, (2013); PLoS One, 8: e73115. [PMC free article] [PubMed]
64. Kollef M.Broad-spectrum antimicrobials and the treatment of serious bacterial infections: Getting it right up front. (2008); Clin Infect Dis, 47: S3–S13. [PubMed]
65. Kumar S., Little P., Britten N. Why do general practitioners prescribe antibiotics for sore throat? Grounded theory interview study, (2003). BMJ, 326: 138. [PMC free article] [PubMed]