ROLE OF CLINICAL PHARMACIST IN PROMOTING RATIONAL USE OF ANTIMICROBIALS IN THE MANAGEMENT OF PEDIATRIC LOWER RESPIRATORY TRACT INFECTIONS IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT
Antimicrobials are commonly prescribed drugs in pediatrics with Respiratory Tract Infections. Monitoring and control of antimicrobial usage is important these days. The main objective of this study is to analyze and assess the prescription pattern in the management of pediatric Lower Respiratory Tract Infection (LRTI) and to promote the rational use of antimicrobials. Among 86 cases included in the study, it was observed that wheeze associated lower respiratory tract infections (WALRI) were more common in neonates. Bronchopneumonia cases were more common in the age group between 1 year and 12 years. Combination of two antibiotics were more frequently prescribed. Broad spectrum antibiotics are frequently used for viral respiratory illnesses which are generally self-limiting, adding to the threat of antibiotic resistance.

Various study reports suggest that involvement of clinical pharmacist in a health setup have results in improvement in medicine use like reduction in the cost of therapy, minimizing practice of polypharmacy, reduction in unnecessary prescribing of antimicrobials and improving rational use. Close monitoring of prescriptions helped us to find 47 medication errors and 8 adverse drug reactions. From this study it can be concluded that it is important to have guidelines for antibiotic prescription to avoid unnecessary prescribing of multiple drugs.

Keywords: Pediatrics, LRTI, Rational use, Antimicrobials.

INTRODUCTION
Worldwide, infants and children represent a higher proportion of the population. Twenty Eight percentage of the world’s total population is accounted by Children younger than 15 years of age. Across the globe this category has higher than average risk of developing infectious disease. Respiratory tract infection (RTI) is considered as one of the major public health problems in developing countries. It occurs both among children and adults. It is recognized as the leading cause of morbidity and mortality in many developing countries. In developing countries 30% of all patients consultation and 25% of all pediatric admission are due to acute respiratory tract infections and which ultimately causes death of 3.5 million children each year. While antimicrobial drugs are responsible for some of the most dramatic improvements in medical therapy in history, these medicines are also the only class of drug whose efficacy diminishes with their wide-scale use in hospital-based and outpatient settings. The increased use of antimicrobial drugs has coincided with the emergence of antimicrobial resistance, which constitutes an important clinical, economic, and public
health problem\textsuperscript{[1-3]} . Resistant pathogens increase healthcare associated expenses, complicate therapy and make treatment failure more often. Therefore, there has been a growing attentiveness to the rational use of antimicrobials since 1990s\textsuperscript{[4]} . The use of antibiotics has become a routine practice for the treatment of pediatric illnesses\textsuperscript{[5,6]} . Thus children and infants are subjected to innumerous discrepancies in antibiotic medications. There are various reports of irrational use of antibiotics in pediatrics\textsuperscript{[7,8,9]} . Drug resistance is the reduction in effectiveness of a drug in curing a disease or improving a patient's symptoms and it is an important factor in the development of antibiotic resistance\textsuperscript{[10]} . Broad spectrum antibiotic refers to an antibiotic with activity against a wide range of disease causing bacteria. A global perspective of safe and effective antibiotic therapy has become a necessity these days. Several professional societies have issued guidelines designed to reduce the use of antibiotics world-wide by means of various control strategies\textsuperscript{[11,12]} . Most infections are limited to the upper respiratory tract and only 5% involve the lower respiratory tract. Recent studies showed that \textit{Streptococcus pneumoniae}, \textit{Haemophilus influenzae} and respiratory syncytial virus are the main causes of RTI in children. With effective management and appropriate drug RTI can be managed successfully. Antibiotics are commonly prescribed in treating common respiratory tract infections even with viral aetiology. As there is difficulty in establishing bacterial aetiology at the time of prescription, antibacterial therapy of RTIs is usually empirical considering the risk factors and severity of disease. Such use of antibiotics has led to the development of antibiotic resistant bacteria. Nowadays, antimicrobial resistance is a recognized problem throughout the world. Excessive use of antibiotics in the outpatient setting has contributed to the increase in antimicrobial resistance. The main objective of this study is to analyze and assess the prescribing pattern in pediatrics in a tertiary care teaching hospital and to promote rational use of antimicrobials in the management of pediatric LRTI.

Principles for rational use of antibiotics in LRTIs
1) The diagnosis of pneumonia needs to be considered.
2) Many children with pneumonia and no significant co-morbidities can be treated at home.
3) The principle guide to antibiotic choice for community management of pneumonia is the age of the child.
4) Bronchiolitis is a viral infection (usually respiratory syncytial virus) and does not respond to antibiotics.
5) Antibiotics do not prevent pneumonia in children with URTIs.
6) Steroids or beta-agonists are not indicated in the community management of bronchiolitis.

Principles for rational antibiotics use for acute bronchitis
1) Systematic reviews indicate antibiotics have marginal benefits.
2) The presence of mucopurulent sputum is not an indication for antibiotic use.
3) Patient leaflets can reduce antibiotics use.

Principles for rational antibiotics use in acute exacerbation of COPD
1) Approximately 50% bacterial. Antibiotics not indicated in absence of purulent or mucopurulent sputum.
2) Prophylactic antibiotic therapy is not recommended in the management of stable COPD.
3) Amoxicillin or doxycycline are valuable in increased purulent sputum.
4) In penicillin allergy use erythromycin.

Principles for rational antibiotics use in Community Acquired Pneumonia (CAP)
1) Only a small range of pathogens cause CAP, the commonest is \textit{S.pneumoniae}.
2) People with non severe community acquired pneumonia can be given empirical antibiotic treatment at home without the need for microbiological and radiological investigations.
3) People with severe CAP need hospital admission and empirical antibiotics may be started if a delay to admission of more than 2 hours will occur.
4) In severely ill give parenteral benzyl penicillin before admission and seek risk factors for Legionella.

5) Amoxicillin at higher dosage remains the preferred agent for community managed CAP with erythromycin for those who are allergic to penicillin.

6) A combination of these two agents may be appropriate in localities with high prevalence of legionella.

Cystic fibrosis
It is an inherited autosomal recessive disease which at the cellular level is due to a defect in the transport of ions in and out of cells. This leads to changes in the consistency and chemical composition of exocrine secretions, which in the lungs is manifest by the production of very sticky, tenacious mucus which is difficult to clear by mucociliary action. The production of such mucus leads to airway obstruction with resulting infection.

Treatment
- Diet with increased fat and sodium or salt supplements
- Pancreatic enzyme replacement
- Breathing exercises, chest percussion, and postural drainage
- Inhaled bronchodilators
- Antibiotics such as azithromycin
- Transplantation of heart or lungs
- Mucus-thinning drugs such as dornase alfa
- Positive expiratory pressure devices
- Flutter valves
- High-frequency chest compression vest

Severe acute respiratory syndrome
Severe acute respiratory syndrome (SARS) is a serious form of pneumonia, resulting in acute respiratory distress and, in some cases, death. In February 2003, the World Health Organization (WHO) identified SARS as a global health threat and issued an unprecedented travel advisory. Over the next few months, the illness spread to more than two dozen countries in North America, South America, Europe, and Asia before the outbreak was contained.

Causes
New member of the Coronaviridae family (the same family causing the common cold)

Treatment
- Antiviral drugs
- Steroids
- Supplemental oxygen
- Mechanical ventilation
- Chest physiotherapy

MATERIALS
1. Patient standard data collection form.
2. Prescriptions of patients.

METHODOLOGY
A non invasive prospective observational study was undertaken in the Pediatric department of Rajah Muthiah Medical College and Hospital (RMMC and H), a tertiary care teaching hospital, Annamalai Nagar, Tamil Nadu. The study was approved by Institutional Human Ethics Committee (IHEC). The study was carried out during November 2010 - April 2011. Patient data collection form was prepared based on study objectives. Clinicians and nursing staff were also consulted for further details. Pediatric prescriptions dealing with antimicrobial usage were analyzed. Patients below 12 years of age were included in this study. We analyzed 86 prescriptions during the study period. The exclusion criteria were
- Age above 12 years
- Whose parents unwilling to participate
- Patients with significant Hepatic and Renal diseases.
- Those with congenital anomalies
- Children with major illness

Patient characteristics like age, sex, body weight, cases with previous drug history, duration of hospitalization were noted. Admission, discharge diagnosis, the condition of the patients on admission, discharge, Dosage regimen (form, route, frequency and duration), type of drugs and quantity prescribed were also recorded.

RESULTS
Gender categorization(TableNo.1,Fig. 1)
Out of 86 patients enrolled in our study 63.95% were male and 36.04% were female.
Age group categorization based on gender (Table No. 2, Fig. 2)
The prevalence of LRTI was more pronounced among the age group of 1 month to 1 year [45.34% (24.41% male and 20.93% female)] followed by the age group of 1yr to 12yrs [38.36% (29.06% male and 9.3% female)].

Commonly occurring symptoms in LRTI (Table No. 3, Fig. 3)
The common symptom in the study group was found to be cough [62.79%] followed by breathlessness, cough + fever and cough + expectoration.

Diagnosis (Table No. 4, Fig. 4)
Among the 86 pediatric patients enrolled in the study 30.23% were diagnosed with WALRI being highest in the incidence followed by Bronchopneumonia [26.74%].

Antibiotics use pattern in the management of pediatric LRTI (Table no. 5, Fig. 5)
Two drug combination of antimicrobials were mostly prescribed [51.16%] than monotherapy [26.74%] and three drug combination [22.09%].

Poly pharmacy prescriptions (Table no. 6, Fig. 6)
Poly pharmacy prescriptions indicated the wide use of antibiotics + bronchodilators [70.93%] followed by antibiotics + NSAIDs [39.53%].

Prescribing pattern of antibiotics in the management of pediatric LRTI (Table No. 7, Fig. 7)
All the prescriptions contained one or more antibiotic/s
Majority of the prescriptions included broad spectrum antibiotics [57%] followed by narrow spectrum antibiotics [26%] and broad + narrow spectrum antibiotics [17%].

Incidence of disease based on age (Table No. 8, Fig. 8)
From our study we have observed that WALRI is more common in neonates (first 4 weeks of life). Prevalence of WALRI, Acute bronchitis and Bronchiolitis is more common at the age group 1month to 1 year. Bronchopneumonia is more common at the age group 1year-12years.

Out of 86 patients, (8, 9.3%) of patients were found to have Adverse Drug Reactions (ADR).

Type of medication errors
Out of 47 medication errors identified, inappropriate interval of drug administration (53.19%) was found to be the most commonly occurring error followed by drug-drug interactions (23.40%), over dose (14.89%) and incomplete prescription (8.51%).

DISCUSSION
Escorihuela Esteban R et al., 2000, studied Antibiotic prescribing patterns for pediatric in patients with acute respiratory tract infection where 58% were male; this found to be little less than our study where males were 63.95%. Upper respiratory tract infection was found in 54% patients, Bronchitis in 18%, Bronchiolitis in 15% and pneumonia in 10% whereas our study focused mainly on Lower respiratory tract infection; WALRI in 30.23%, Bronchopneumonia in 26.74%, Acute Bronchitis in 24.41% and Bronchiolitis in 18.6%.

The prevalence of LRTI was more pronounced among the age group of 1 month to 1 year [45.34% (24.41% male and 20.93% female)] followed by the age group of 1yr to 12yrs [38.36% (29.06% male and 9.3% female)].

Sharma R, Chopra V S, et al., 2009, studied Use of Antibiotics for Respiratory Illnesses in Rural India. Cephalosporins were the most frequently prescribed antibiotics in all the age groups of patients. In our study also majority of the prescriptions included broad spectrum antibiotics [57%] followed by narrow spectrum antibiotics [26%] and broad + narrow spectrum antibiotics [17%].

M. Ceyhan et al., 2010, studied inappropriate antimicrobial use in Turkish pediatric hospitals: A multicenter point prevalence survey. Of the 1302 patients surveyed, 711 (54.6%) were receiving antimicrobial drugs. Among patients receiving antimicrobials, 39.8% were receiving one drug, 42.8% two drugs,
12.1% three drugs, 3.5% four drugs, 1.4% five drugs, and 0.4% six different drugs. In our study also two drug combination of antimicrobials were mostly prescribed [51.16%] than monotherapy [26.74%] and three drug combination [22.09%].

Vidya Viswanad et al., 2010, studied confrontational use of antibiotics in pediatric prescriptions. The Antibiotic usage by the patients was examined and a high incidence of polypharmacy was reported. In our study also Poly pharmacy prescriptions were reported and indicated the wide use of antibiotics + bronchodilators [70.93%] followed by antibiotics + NSAIDs [39.53%].

Ann-Christine Nyquist et al., 2005, evaluated antibiotic-prescribing practices for children younger than 18 years who had received a diagnosis of cold, upper respiratory tract infection (URI), or bronchitis. From this study they concluded that antibiotic prescribing for children diagnosed as having colds, URIs, and bronchitis, conditions that typically do not benefit from antibiotics, represents a substantial proportion of total antibiotic prescriptions to children. In our study also broad spectrum antibiotics are frequently used for viral respiratory illnesses which are generally self limiting, further adding to the threat of antibiotic resistance.

During the study period of six months, 8 ADRs (9.3%) were reported.

- The inappropriate interval was found to be the leading type of medication error. Delayed administration of drugs can result in undesirable outcomes. Drug – Drug interactions were found to be the second most common type of error, leading to varied therapeutic outcomes. Overdose was the third most medication error resulting in toxic levels of drug and followed by incomplete prescription. For example in some patients, the height and weight were not documented. These parameters are essential in dose calculation particularly in pediatric patients.

CONCLUSION
Two drug combination of antibiotics were more prescribed than monotherapy and three drug combination. Broad spectrum antibiotics are frequently used for viral respiratory illnesses which are generally self limiting, adding to the threat of antibiotic resistance. Because antibiotic prescribing rates are particularly high for children aged 0-6 years, it is the role of clinical pharmacist to take a special effort to reach the parents of young children with information about appropriate use.

As per Standard Treatment Guidelines for the treatment of Bronchiolitis, the priority is antiviral therapy but in practice antibacterial therapy is following for treating secondary infections. Monitoring medication errors, unnecessary use of antimicrobials and reporting ADRs suggests the need to appoint clinical pharmacists at various levels in a health setup to analyze the prescriptions of doctors and to provide them feedback to improve their prescribing skills.

From this study it can be concluded that it is important to have guidelines for antibiotic prescription and use appropriate drugs for the disease to avoid unnecessary prescribing of multiple drugs.

ACKNOWLEDGEMENT
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### Table 1: Gender Categorization

<table>
<thead>
<tr>
<th>S. No</th>
<th>Sex</th>
<th>No. of patients</th>
<th>% of patients</th>
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<tr>
<td>1</td>
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<td>2</td>
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<td>Table 2: Age Group Categorization Based on Gender</td>
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</tr>
<tr>
<td>Age</td>
<td>Male</td>
<td>%</td>
<td>Female</td>
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<tr>
<td>First 4 wks of life</td>
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<td>10.46</td>
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<tr>
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<td>18</td>
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<td>1 yr-12yrs</td>
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| Table 3: Commonly Occurring Symptoms in LRTI |
|-----------------|--------|--------|--------|--------|
| Age             | Cough | Cough + Fever | Breathlessness | Cough + Expectoration | Hemoptysis |
| First 4 wks of life | 5     | 8          | 8      | 6      | 0         |
| 1 month-1year    | 27    | 16         | 18     | 13     | 1         |
| 1 yr-12yrs       | 22    | 12         | 10     | 17     | 3         |

| Table 4: Diagnosis |
|-------------------|--------|--------|
| Diagnosis         | No. of patients | % of patients |
| Acute bronchitis  | 21     | 24.41  |
| WALRTI            | 26     | 30.23  |
| Bronchopneumonia  | 23     | 26.74  |
| Bronchiolitis     | 16     | 18.6   |

| Table 5: Antibiotics Use Pattern |
|-----------------|--------|
| Prescribing pattern | % of prescriptions |
| Monotherapy      | 26.74  |
| Two drug combination | 51.16 |
| Three drug combination | 22.09 |

| Table 6: Poly Pharmacy Prescriptions |
|----------------|--------|--------|
| Type of prescription | No. of prescriptions | % of prescriptions |
| Combination         | 16     | 18.6   |
| Antibiotics+ Bronchodilators | 61 | 70.93 |
| Antibiotics+ Nasal drops | 18 | 20.93 |
| Antibiotics+ Vitamins | 5      | 5.81   |
| Antibiotics+ NSAIDs  | 34     | 39.53  |

| Table 7: Prescribing Pattern of Antibiotics |
|----------------|--------|--------|
| Type of antibiotics prescribed | No. of prescriptions | % of prescriptions |
| Broad spectrum antibiotics     | 49     | 57     |
| Narrow spectrum antibiotics   | 22     | 26     |
| Broad + Narrow spectrum antibiotics | 15 | 17     |
Table 8: Incidence of Disease Based on Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Acute bronchitis</th>
<th>WALRI</th>
<th>Broncho pneumonia</th>
<th>Bronchiolitis</th>
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<td>First 4 wks life</td>
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<td>1yr-12 yrs</td>
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Fig. 1: Gender categorization

Fig. 2: Age group categorization based on gender
Fig. 3: Commonly occurring symptoms in LRTI

Fig. 4: Diagnosis
Fig. 5: Antibiotics use pattern

Fig. 6: Poly pharmacy prescriptions
Fig. 7: Prescribing pattern of antibiotics

Fig. 8: Incidence of disease based on age
REFERENCES