Clinical Outcomes and Its Associated Factors of Community Acquired Acute Respiratory Infections Among Admitted Pediatric Patients in Jimma Medical Center: Concurrent Observational Study



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A Research Thesis Submitted to Jimma University, Institute of Health Sciences, School of Pharmacy, in Partial Fulfillment for the Requirement for Master of Sciences in Clinical Pharmacy

February, 2020

Jimma, Ethiopia

# Jimma University

# Institute of Health Sciences

School of Pharmacy

Clinical Outcomes and Its Associated Factors of Community Acquired Acute Respiratory Infections Among Admitted Pediatric Patients in Jimma Medical Center

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January, 2020 Jimma, Ethiopia

#### Abstract

**Background:** acute respiratory infections are infections of the air ways and are classified as upper respiratory tract infections and lower respiratory tract infections. They are the most common illnesses in childhood, comprising as many as 50% of all illnesses in children less than 5 years old and 30% in children aged 5 - 12 years. Despite the availability of antibiotics, acute respiratory infections bear high morbidity and mortality burden worldwide, just the largest share taken by developing nations including Ethiopia.

**Objective:** to assess clinical outcome (s) and its predictors of community acquired acute respiratory infections in pediatric patients admitted to Jimma medical center.

**Method and Participants:** prospective observational study was conducted starting from April – September 2019 on patients admitted to pediatric wards of Jimma medical center with a diagnosis of any of the acute respiratory infections to determine in-patient clinical outcomes. These outcomes were designed as good or poor for this study. Multivariate logistic regression was conducted to identify independent predictors of poor outcome.

**Results:** overall, 212 pediatric population was enrolled in this study with a male: female ratio of 1.12:1 and the average age of the participants was  $38.66 \pm 17.36$  months. Almost all (99.5%) of the participants had been provided with at least one antibiotic. Seventy eight (36.8%) of the cases had "poor outcome" and the outcome was fatal in 1.4% of the participants. Independent predictors of poor outcome were cyanosis [AOR = 11.911(95% CI, 4.354-32.587)], wasted body weight [AOR = 5.492(95% CI, 1.729-17.445)], initial ceftriaxone plus gentamicine administration [AOR = 3.166 (95% CI, 1.114-8.996)], antibiotic use within 3 months prior to admission [AOR = 2.961(95% CI, 1.087-8.069)], co morbidity [AOR = 2.116(95% CI, 1.468-3.654)] and duration of symptoms [AOR = 1.046(95% CI, 1.001-1.092)] in order of their relative importance.

**Conclusion and Recommendation:** both the burden of acute respiratory infections and its poor outcome were high in our setting. Factors including cyanosis, wasted body weight, initial ceftriaxone plus gentamicine administration, antibiotic use of 3 months prior to admission, co morbidity and duration of symptoms were independent predictors of poor outcome and hence practitioners should never contempt these factors to give priority for those cases coming with them.

Key words: Acute respiratory infections, Clinical outcomes, Pediatric, Jimma Medical Center

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# Acknowledgment

I would like to express my special thanks to Jimma University Institute of Health Sciences, Department of Pharmacy for its formal permission on the study and all over support.

Again, I would like to express my deepest gratitude to my research advisor **Dr. Legese Chelkeba (Ph.D, Associate Professor)** for his unreserved encouragements and provision of guidance while preparing this research paper. He sacrifices his golden time and donates me his knowledge and experience for the overall success of the work. I don't have an adjective to express my thanks even though I know what is feeling to me actually.

My thanks also gone to my colleague and friend Mr Mengist Aweke (B.pharm, MSc in Clinical pharmacy) for his constructive comments and unreserved support.

My acknowledgment also gone to the care givers of the participants for their genuine responses and data collectors for their commitment to involve during the study period. Physicians working at pediatric ward of Jimma medical center are greatly thanked for overall support during this research process.

# Abbreviations and Acronyms

| AGE- Acute Gastroenteritis        | LOS- Length of Hospital Stay         |
|-----------------------------------|--------------------------------------|
| AOM- Acute Otitis Media           | LRIs-Lower Respiratory Infections    |
| AOR- Adjusted Odds Ratio          | Mg- mili gram                        |
| ARI- Acute Respiratory Infection  | PO-Per Oral                          |
| CAP- Community Acquired Pneumonia | SAM- Severe Acute Mulnutrition       |
| CI- Confidence Interval           | SPSS- Statistical Package for Social |
|                                   | Sciences                             |
| COR- Crude Odds Ratio             | URIs- Upper Respiratory Infections   |
| EBF- Exclusive Breast Feeding     | USA – United States of America       |
| HIV- Human Immune Virus           | USA – United States of America       |
|                                   | WFA- Weight for Age                  |
| IV- Intra Venous                  |                                      |
| 17 1 1                            | WFH- Weight for Height               |
| Kg- kilo gram                     | WHO- World Health Organization       |

## 1. Introduction

# 1.1 Back ground

Air is drawn into the body via the nose and sometimes via the mouth, and passes through a series of airways to reach the lungs. This series of airways is referred to as the respiratory tract and anatomically can be divided into two main parts. The upper respiratory tract which includes the nose, nasal cavity, mouth, middle ear, pharynx and larynx and the lower respiratory tract consist of the trachea, bronchi and lungs (1).

Acute respiratory infections (ARIs) are infections of the air ways and are classified as upper respiratory tract infections (URIs) or lower respiratory tract infections (LRIs). ARIs are not confined to the respiratory tract and have systemic effects because of possible extension of infection or microbial toxins, inflammation, and reduced lung function (2)

URIs are the most common infectious diseases and includes rhinitis, sinusitis, ear infections, acute pharyngitis or tonsillopharyngitis, epiglottitis, and laryngitis. The vast majority of URIs have a viral etiology, rhinoviruses account for 25%-30%, while Acute Otitis Media (AOM), and pharyngitis are bacterial URIs (3).

The most common clinical features for URIs include rhinorrhea, sneezing, fever, exudative tonsillitis, sore throat, cough, hoarseness of voice and more (4). Earache, red and bulging tympanic membrane, ear discharge, irritability, restlessness, crying and sometimes pulling at the ear may be the symptoms of AOM (5)

As mentioned above, the majority of URIs are caused by viruses and are self-limiting, which makes their complications (if any) to be more important than the infections (2, 6, 7). Hence antibiotics are not usually necessary for URIs except AOM and pharyngitis (4).

On the other hand, acute LRIs are relatively severe forms of respiratory infections with pneumonia and bronchiolitis being the most common ones. Differences between these two conditions can be particularly difficult in young children (8, 9).

Pneumonia can be classified, based on the origin, as either 'Community Acquired Pneumonia (CAP)' (when the presumed pathogen is acquired outside the health facility), or 'healthcare associated' when the antecedents of the disease can be traced to a health facility of any level (10).

Several microorganisms mainly viruses and bacteria cause acute LRIs in infants and youngsters. Group B streptococcus and gram-negative enteric bacteria are the most common pathogens in neonates while streptococcus pneumonia is the most common pathogen in infants aged three weeks to three months (11). In infants older than four months and in preschool-aged children, viruses are the most frequent cause of CAP with respiratory synctial virus being the most common (11). Mycoplasma pneumonia, chlamydophila pneumonia, and streptococcus pneumonia are the predominant etiologies of CAP in school age and adolescents (12).

The wide spectrum of clinical manifestations of pneumonia often makes it difficult to distinguish from other acute LRI clinical syndromes like bronchitis and bronchiolitis. In general, the clinical presentation of childhood pneumonia varies with the age of the child and the causative agent; the younger the infant, the less specific the clinical presentation. Young infants below 3 months with pneumonia may present with poor feeding, vomiting, irritability or cough (10) while older infants and pre-school children with a bacterial etiology can present with the strongest predictors of pneumonia like fever, cyanosis, tachypnea and cough (11). Intracellular pathogens are frequent causes of pneumonia cases and the clinical presentation is "atypical", characterized by sub–acute symptoms, non-productive cough, low fever and normal white blood cells count (13).

Where the facilities exist, radiological, microbiological and hematological investigations are explored to sort out confusing clinical presentations, identify the extent and severity of the disease, the presence of complications, exclude other diagnostic considerations (like foreign body aspiration, pulmonary tuberculosis and congenital heart diseases), and frequently, to follow the appropriateness of therapeutic interventions for LRIs (10).

The initial antibiotic treatment of CAP is empiric because the pathogen is rarely known at the time of diagnosis (12). For pneumonia, give oral (PO) amoxicillin at least 40 mg/kg per dose

twice a day for 5 days in settings with high HIV infection rate, while for 3 days in areas with low HIV prevalence. On the other hand, children with severe pneumonia should get ampicillin 50 mg/kg or benzyl penicillin 50 000 units/kg every 6 hours with gentamicin 7.5 mg/kg once a day all intramuscular or Intra-Venous (IV) for at least 5 days (5)

Macrolide antibiotics may be added if mycoplasma pneumonia or chlamydophila pneumonia are suspected when the child is not improving after 24 - 48 hours or in very severe cases (14). Clindamycin 40mg/kg/day IV or vancomycin 60mg/kg/day IV both divided every 8 hours should be consider if methicillin-resistant staphylococcus aureus infection is suspected (15).

Despite an increasing availability of specific antiviral agents which are of potential value for treating viral pneumonias, the current recommendation is that of 'watchful waiting', while pursuing supportive care (10)

Bronchiolitis occurs predominantly in the first year of life and with decreasing frequency in the second and third years. Inflammatory obstruction of the small airways, which leads to hyper-inflation of the lungs, and collapse of segments of the lung occur (2). Respiratory synctial virus is the most common virus causing bronchiolitis and often starts with rhinorrhoea and fever, thereafter gradually increasing with signs of LRIs including tachypnoea, wheezing and cough (16).

Management of acute bronchiolitis is generally supportive, as no medical treatment has shown to improve important clinical outcomes, such as length of hospital stay, use of supportive care or transfer to an intensive care unit (16). Antibiotics are not indicated unless evidence of bacterial infection and even though the use of bronchodilators is controversial, it may be beneficial in some patients but should be driven by oxygen (if oxyhemoglobin saturation falls persistently below 90%) (17)

#### **1.2 Statement of the Problem**

Acute respiratory infections (ARIs) are one of the leading causes of child morbidity and mortality globally and are responsible for an estimated 3.9 million childhood deaths every year worldwide (18). Even other report indicated that ARIs in young children are responsible for over 15 million hospital admissions which resulted in about 0.3 million in-hospitals deaths (19).

In 2016, LRIs caused about 0.6 million deaths in children younger than 5 years, 1. 08 million deaths in adults older than 70 years, and 2.38 million deaths in people of all ages, worldwide (20) while pneumonia alone killed around 0.9 million children under the age of 5, accounting for 15% of all deaths of children under five years old in 2015(13).

In developing countries, ARIs are not only more prevalent but more severe also, with 10-15 times higher morbidity and mortality in these nations (8, 9). It carries 30-50% of death in young children in low income countries (21), accounting for almost 1.4-2 million annual deaths (22, 23). Moreover, it remains the major cause of child mortality in Sub-Saharan Africa with various factors associated with its occurrence and varies by context (24).

It has been reported that there are links between environmental risk factors (such as overcrowding, indoor and outdoor air pollution) and risk factors in the child (such as breast feeding, low birth weight, malnutrition, and vitamin A deficiency) with ARIs (18).

In Ethiopia, most of the population is distributed in rural areas(25), has low income and highly linked with the aforementioned potential risk factors (26, 27), one can normally anticipate high burden of ARIs and their overall consequences in the country and then the problem of these infections in terms of morbidity and/or mortality has to be sufficiently described to health planners . In fact the available, but limited in number, studies done at different sites of the country, including the most recent Ethiopia demographic and health survey (27) actually reflect this presumed trend. Likewise, the overall prevalence of illness was 5.8% among under-five children in Butajira district and ARIs alone contributed to over 48% of this total perceived illness and accounted for more than a third of infant and more than a fifth of child deaths (28).

Moreover, despite Ethiopia is one of the countries that are on a "fast track" in terms of progress made in reducing child mortality, the country still bears a high child mortality burden (24). It is estimated that 3.4- 4 million children encounter pneumonia annually in Ethiopia that contributes to 20-28 percent of all causes of deaths (23, 29) which pushes the country to be fifth (62 deaths in 1000) among 15 countries having the highest death rate of under five years from clinical pneumonia in the world (30, 31).

In general, there is paucity of study based information on the burden of ARIs and its contribution to the existing high child mortality rate in Ethiopia both at community level and health care settings. As said elsewhere above, studies on this topic are few in the literature and confined themselves only to severe pneumonia (23, 29). Moreover, even though a series of both institutional and community based studies assured the high burden of childhood non-pneumonic ARIs including AOM and remains a public health problem, especially in low-income countries (32-34), there is no inclusive and well established study, to our knowledge, about it in Ethiopia in terms of burden or treatment outcome. To add, the locally relevant factors that highly determine clinical outcomes of the disease are yet mysterious. Therefore, there is a need to have figure about burden of the infection, to get due attention, and hence preventive strategy may be employed as needed. Again, knowledge about the pattern for the clinical outcome of children hospitalized with ARIs is equally important so as to intensify the level of care based on need as much as possible.

Antibiotics are powerful and effective drugs in the fight against infectious diseases caused by bacteria including ARI and are among the most frequently prescribed drugs for pediatric patients (35, 36). Because of an overall rise in health care costs, lack of uniformity in drug prescribing and the emergence of antibiotic resistance, monitoring and control of antibiotic use are of growing concern (35).

Even though there are a series of standard guidelines about the use of antibiotics including in pediatric population, there is significant deviation from these guidelines while prescribing these drugs which may potentially lead to antibiotic resistance, a major health threat in the  $21^{st}$  century. For instance, a literature review by Dona D *et al* showed a global heterogeneity in the antibiotics prescription for pediatric CAP, with application of guidelines varying from 0% to more than 91% and with important differences even within the same country (37). To add more,

half of all viral URIs received antibiotics inappropriately while only 70% of all pneumonia cases, which warrant antibiotic treatment, receive antibiotics in developing countries (38).

In fact there are few in-state studies and reviews in the literature about pediatric antibiotic utilization patterns (35, 39), but these were highly generalized for the whole pediatric population which makes it vague to interpret in terms of ARI treatment pattern and hence there is a need of specific evaluation about it.

Hence, this study which is wide scope in its kind is designed with a contemplation to deal and bring knowledge about the hospital burden, treatment pattern with its degree of adherence towards WHO recommendations and clinical outcome of ARIs. Further, it will define the elements that determine in-patient treatment clinical outcomes of these infections.

#### 1.3 Significance of the Study

The other vow of this study was to present with clinical treatment outcomes of ARIs that will have paramount importance with its own contribution for national and/or local guideline developers to design effective management protocols for the disease and dictates practitioners to provide more comprehensive and harmonized care accordingly.

Additionally, the early identification of risk factors for a poor outcome among ARI patients could help health professionals prioritize the management of those patients and perhaps increase their likelihood of surviving from complication or death.

Our study tried to address antibiotic use patterns and its degree of adherence to WHO recommendations which in turn helps to prevent antibiotic resistance and associated consequences.

More studies are needed on this issue, to be compiled, and hence this research could serve as bench mark for some or supportive for other studies of similar intention.

# 2. Literature Review

## 2.1 Burden of Pediatric Acute Respiratory Infections

A longitudinal cohort study was conducted by Vinod K.R *et al.* on 400 under 5 children in India and found the burden ARIs to be 27.25% and URIs was found among 19.25% and LRIs among 8% (40).

A cross-sectional study conducted by Alexis A. *et al.* at Bamenda regional hospital, Cameroon, on 512 children under 5 years to evaluate hospital burden of pediatric ARIs found it to be 54.7% and AOM alone accounts 14% (41).

A community based cross-sectional study aimed to assess prevalence of middle ear infections and associated factors in 810children under 5 years in Kigali city, Rwanda, by Mukara KB *et al.* indicated this prevalence to be 1.8% (33).

The national prevalence of under-five ARIs is 7% (24, 42) and approximately 3.37 - 4 million childhood pneumonia cases are occurring in Ethiopia annually which contributes for 20% - 28% of all deaths in children aged less than 5 years (23).

Institutional based cross sectional study was employed at Wondo Genet district, Ethiopia, by Abuka T *et al.* in 206 under five children aimed to determine the prevalence and factors associated with pneumonia and found this prevalence to be 33.5% (42).

Prospective cross-sectional study was conducted by Bayisa *et al.* on 222 hospitalized pediatric patients at Nekemte referral hospital, Ethiopia, targeted on clinical treatment outcomes of pneumonia and the hospital prevalence of pneumonia was routinely reported to be 36% (29).

#### 2.2 Antibiotic Use Patterns of Pediatric Acute Respiratory Infections

A retrospective chart review study conducted in two Chinese hospitals, Guangdong provincial hospital (3,046 patients) and Peking university people's hospital (1,112 patients) by Wen *et al.* (43) revealed that, the majority of hospitalizations, 82.9% and 95.5%, received antibiotic therapy respectively in hospital order and ceftriaxone was the most common antibiotic used in both hospitals. Among these hospitalizations, medication was modified in 62.2% patients from Peking university people's hospital and 24.7% from Guangdong provincial hospital.

A prospective study done by Han L *et al.* (44) at Jining No.1 people's hospital over 140 patients noted that third generation cephalosporin antibiotics (cefotaxime) were the most common antimicrobials used for pediatric pneumonia and average length of treatment was 18.80±4.57 days.

Another hospital based case series study conducted on 200 children by Kumar A *et al.* (45) at Hanagal Shri Kumareshwara hospital and research centre, India, which aimed to assess clinical outcomes of pediatric acute LRIs routinely found that 28.5% of these patients treated with antibiotics have encountered regimen modification.

A multicenter retrospective cohort study by Brogan *et al.* (46) at Seattle children's hospital, USA, on 21213 patients found that cephalosporins used as single-agent therapy were the most common antibiotic regimen and specifically the most common antibiotics from this class used were ceftriaxone (56%), cefuroxime (22%) and cefotaxime (19%). It also notified that, combination antibiotic therapy was usual and co-administration of cephalosporin with a macrolide antibiotic was the most frequent (21%) combination. Antimicrobial agents with expected activity against methicillin-resistant staphylococcus aureus (vancomycin/clindamycin) were administered in combination with cephalosporins or macrolides to approximately 20% of children.

A university hospital based retrospective cohort study by Simbalista R *et al.* (47) in Salvador, focused on outcome of 154 children hospitalized with CAP observed that the median duration of penicillin G administration was 3.5 days (mean  $4\pm 2$ ) and this drug was substituted by other

antibiotics in 28 (18.2%) patients. The subsequent antimicrobial agents were oxacillin plus ceftriaxone (7.1%), ceftriaxone (7.1%), erythromycin and oxacillin (1.9%).

A longitudinal study performed by Ciommo VD *et al.* (48) on 165 patients to explore the appropriateness of antibiotic prescriptions among children with LRIs admitted to the Italian pediatric hospital 'Bambino Gesù' revealed all children received antibiotic therapy and 64.6% of cases were administered by the IV route. Cephalosporines (83.2% of parenteral antibiotics and 68.7% of oral antibiotics) were antibiotics prescribed commonly. More specifically, the most frequently prescribed antibiotic for parenteral therapy was ceftriaxone (58.3%), and for oral therapy cefprozil (58.1%). It also found that switch therapy was performed in 43.4% of cases.

A retrospective study conducted by Zec SL *et al.* (49) on 104 cases to determine the most commonly used antibiotics at the pediatric clinic in Sarajevo shown that cefazolin, ceftazidime generation and penicillin with 40.4%, 31.7% & 26.68% of pneumonia cases respectively were the most widely used parenteral antimicrobials, and total duration of antibiotic therapy was averaged  $4.5 \pm 1.9$  days and ranged from 1 to 11 days.

A prospective cross-sectional study conducted by Bayisa *et al.* (29) at Nekemte referral hospital on 222 cases reported ceftriaxone as the most frequently used antibiotic which accounted in 50.5% of cases. Initial treatment regimens were replaced by other treatment agents in 61.7% of cases with ceftriaxone being the most frequently substituted (17%) antibiotic followed by cephalexin (16.2%) and cotrimoxazole (10.8%). The study also indicated that among 57 patients who had initiated treatment by crystalline penicillin, 73.7% were switched to another antibiotic.

#### 2.3 Clinical Outcomes and Its Predictors of Pediatric Acute Respiratory Infections

A retrospective chart review study conducted in Peking university people's hospital, to describe treatment patterns, and clinical outcomes of pediatric pneumonia patients, found a 0.5% death rate which was considered attributable to the pneumonia infection. The same study reported a mean Length of Hospital Stay (LOS) of  $17.4 \pm 19.9$  days and a median length of stay of 11 days. Different but simultaneous study by the same investigator at Guangdong Provincial hospital found a mean and a median LOS of  $5.8 \pm 3$  and 5 days respectively (43).

A prospective study conducted by Han *et al.* at Jining No.1 People's Hospital, China, found a case fatality rate of 22.86% after treatment of severe pediatric pneumonia and average LOS was 26.50±3.21 days (44).

Hospital based case series study conducted at Hanagal Shri Kumareshwara hospital and research centre, India, reported sepsis was the most frequent complication occurred in 6% cases followed by empyema in 4% cases, 1% developed meningitis and 0.5% were complicated by pneumothorax. Around 44.5% had LOS of more than 7 days. The study also assured that 92% improved and 3% got discharged against advice while mortality was 3% (45).

Another multicenter observational study in Bangladesh conducted by Naheed A *et al.* on 6856 patients found a case fatality rate of 3.6% and death in female children was 4 times higher than that reported in males. As per to the study, duration of hospital stay was  $5\pm3.5$  days and 14.1% of cases left the hospital against the medical advice of clinician while 0.6% were referred (50).

A multi-center case series study on 5054 hospitalized children with pneumonia in Philippines, designed to assess mortality and associated factors of the disease revealed a case fatality rate of 4.7%. The risk factors significantly associated with death included age of 2–5 months, severe malnutrition, grunting, central cyanosis, tachypnoea, fever and saturation of peripheral oxygen less than 90% (51).

A longitudinal observational study on children affected by acute LRIs and admitted to the Italian pediatric hospital 'Bambino Gesù' to define clinical and economic outcomes of pneumonia in

this population revealed that hospital management of pneumonia required a median LOS of 3 days with a cure rate of 99% (48).

A multi-center retrospective cohort study at Seattle children's hospital reported overall median LOS of 2 days. Twenty five percent of children aged < 12 years had LOS of  $\geq$  3 days, and 25% of children aged 13–18 years had LOS of  $\geq$  4 days (46).

A retrospective cohort study at Cincinnati children's hospital, USA, found a median LOS of pediatric pneumonia cases to be 1.3 days for the total cohort (50).

A university hospital based 13-months prospective study on 689 children admitted to Ho<sup>p</sup>ital d'Enfants de Raba, Morocco, intended to identify risk factors for a poor outcome among children admitted with clinically severe pneumonia reported the rate of poor prognosis as 27.2% including 4% mortality. As per to this study, history of prematurity, fever, living in a house with smokers, impaired consciousness, cyanosis and pallor were all independent risk factors for poor prognosis, whereas a history of asthma was the only independent risk factor for a positive outcome (22).

A prospective study on children admitted at University of Maiduguri teaching hospital, Nigeria, on 98 cases to evaluate complications of CAP shown that this complication was detected in 51.7% of the children studied. Dehydration (30.3%) and congestive cardiac failure (20.2%) were the most prevalent complications occurred. While 91% of the patients recovered and were discharged home, the outcome was fatal in 9% of them. The prevalence of complications didn't significantly differ in the different age groups(52).

A prospective cohort study by Kelly MS *et al.* in Botswana on 310 patients to address clinical treatment outcomes of severe childhood pneumonia reported that 34% of children failed treatment and 5.8% died. It also revealed that the median LOS for the survivors was 3.8 days (53).

R. Nantanda *et al.* in his cross-sectional study among 157 children in Uganda reported a case fatality rate of 15.5% with independent predictors of death including very severe pneumonia,

hypoxemia and severe malnutrition. Three children (1.9%) developed complications, two had empyema and one had pneumothorax, and the remaining 82.8% showed clinical improvement. Twenty-three (14.6%) children stayed in hospital for more than 7 days (54).

A retrospective cohort study was conducted among children aged 2-59 months admitted in six Kenyan hospitals and found mortality rate of 1.2%. Children aged 2-11 months were more than four times more likely to die than those aged 12-59 months. More deaths were also observed among children who reported duration of symptoms of 3 or more days compared to children with shorter durations of illness while mortality did not vary by sex (55).

Prospective cross-sectional study by Bayisa *et al.* identified the treatment outcome of patients as 69.4% cured without development of any complications. Fifty seven patients (25.7%) were cured with one or more complications among which the major ones being pleural effusion in 30%, pharyngeal abscess in 21%, laryngeal edema in 15.8%, lung abscess in 14%, septic shock in 10.5% and pneumothorax in 10.5%. The study also reported that 3.6% of the participants who had pneumonia and other co morbidity were died while only 2.3% patients died were attributable to pneumonia. While 48% of cases were discharged after twenty four to seventy two hours, the remaining 41% had stayed in the hospital for more than 3 days (29).

A cross sectional study on 107 admitted children done by Bekele F *et al.* studied treatment outcomes and associated factors among 107 under 5 children visited Jimma university specialized hospital, currently Jimma medical center, pediatrics ward and found that 87.9% were discharged in improved conditions, 4.7% of cases died during hospitalization and 3.7% left hospital against medical advice. Duration of hospital stay was less than 4 days for the majority of participants. The study also said that there is significant associations between factors like nutritional status of the children and smoker in the house with outcomes including duration of hospital stay and status of discharge observed. Status of discharge also tends to be affected by previous history of pneumonia too (23).

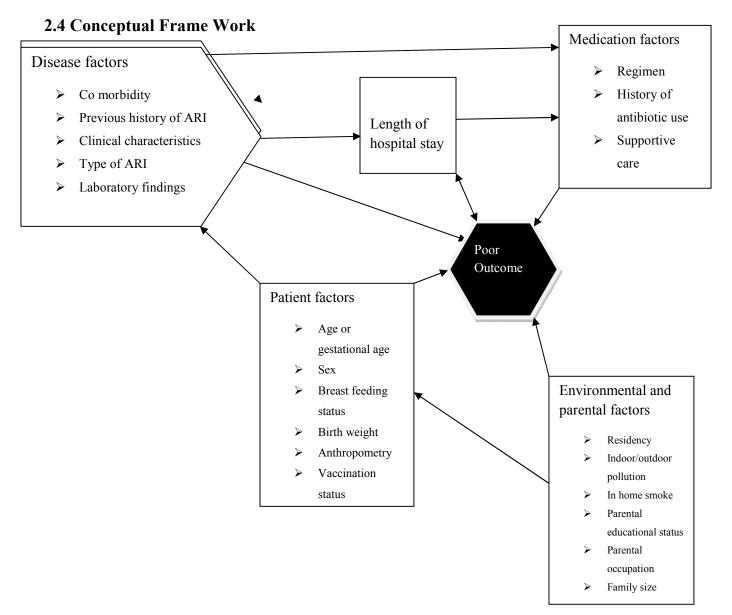


Figure -1: Conceptual frame work of the study

# 3. Objectives

## **3.1 General Objective**

To assess clinical outcome (s) and its predictors (s) of community acquired pediatric acute respiratory infections in pediatric patients admitted to Jimma medical center.

#### **3.2 Specific Objectives**

To assess burden of ARIs among children admitted to Jimma medical center.

To determine the antibiotic use pattern for ARIs and its adherence to WHO recommendations in Jimma medical center.

To determine inpatient clinical outcome (s) of pediatric patients admitted to Jimma medical center with ARIs.

To assess LOS of pediatric patients admitted to Jimma medical center with ARIs.

To identify associated factors for poor outcome among pediatric patients admitted to Jimma medical center with ARIs.

## 4. Methods and Participants

#### 4.1 Study Area and Period

The study was conducted at Jimma medical center which is found in Jimma university, Jimma town, Oromia region, south west Ethiopia. Geographically, it is located in Jimma city 346 km southwest of Addis Ababa. Currently it is the only teaching and referral hospital in the southwestern part of the country,with1448 health professionals of all teams, providing services for approximately 15,000 inpatient, 160,000 outpatient attendants, 11,000 emergency cases and 4500 deliveries in a year coming to the hospital from the catchment population of about 15 million people. Pediatric ward of this hospital has 11 rooms each occupied with 8 beds in average. The study was conducted starting from April – September 2019.

#### 4.3 Study Design

Hospital based prospective observational study was applied for this study.

#### 4.4 Population

#### 4.4.1 Source Population

All patients under 15 years old admitted to Jimma medical center, pediatric ward, during the study period.

#### 4.4.2 Study Population

Members of the source population who fulfilled the pre specified inclusion criteria were the study population

#### 4.5 Eligibility Criteria

#### 4.5.1 Inclusion Criteria

- Child diagnosed with ARIs who were taking medication or supportive care for at least 48 hours.
- > Child guards who gave assent to participate in the study.

#### 4.5.2 Exclusion Criteria

- Child guards who are unable to hear and/or speak
- Children who have no guard
- ARIs child whose pertinent information cannot be fully retrieved either from the patient guard or from his/her chart.
- Already complicated ARI cases

#### 4.6 Sample Size

Sample size (n) for the study was determined using Cochran's formula with assumption of maximum variability, i.e. complication and/or death proportion (p) among ARIs patients in the ward is 0.5 and taking 95% confidence level ( $\alpha$ = 5%) with ±5% precision (d).

n = 
$$(\underline{Z_{\alpha/2}})^2 \underline{p(1-p)}$$
  
d<sup>2</sup>  
n =  $\frac{(1.96)^2(0.5)(0.5)}{(0.05)^2} = 384$ 

The average 5 months ARIs admission load of the ward from April-September 2018 was 408 patients and assuming this admission load don not differ significantly in the next similar season, it is considered that the same number of ARI patients (N) were admitted during this study period. But in this case, the sample size (384) exceeds 5% of the population size (408) or N is less than 10,000, and it is rational to use the correction formula to calculate the final sample size ( $n_f$ ).

Hence: 
$$n_f = \frac{n}{1+n-1/N} = \frac{384}{1+383/4\ 0} = 198$$

An additional 10% of  $n_f$  (20) patients were included to substitute missed individuals and the ultimate sample is 218 patients.

#### 4.7 Sampling Technique

All patients admitted to pediatric ward of Jimma medical center, were attended and then consecutive sampling technique was used to collect data from study subjects who were available at the time of the study and fulfilled the inclusion criteria.

#### 4.8 Study Variables

#### 4.8.1 Outcome Variables

#### 4.8.1.1 Primary Outcome

Inpatient occurrence of complication and/or death

#### 4.8.1.2 Secondary Outcomes

Burden of ARIs, pattern of antibiotic use and length of hospital stay.

#### 4.8.1.2 Ascertainment Measures for Primary Outcome

For the purpose of this specific study, two treatment clinical outcome groups were designed. The first was "good outcome" which included patients achieved *cure without complication* and this cure was ascertained using clinical parameters listed in annex-I. The other was "poor outcome" which comprised all patients *developed complication (s) or died*, which are assumed to be the worst events, happened during pharmacologic and non-pharmacologic intervention (s) periods while the patient was inpatient and both ascertained by respective physician. In the same fashion, variables that affect the occurrence of the later outcome were sought in to "*associated facto* 

#### 4.8.2 Independent Variables

Socio demographic characteristics

- ✓ Age
- ✓ Sex

Environmental factors

- ✓ Presence of cigarette smoker in the house
- ✓ Indoor or outdoor pollution

- ✓ Residence
- ✓ Family size
- ✓ Parental educational status
- ✓ Parental occupational

Nutritional and immunity factors

- ✓ Breast feeding status
- ✓ Birth weight

Disease and drug related factors

- ✓ Co morbidity
- ✓ Previous history of ARIs
- ✓ Clinical and laboratory findings

- ✓ Gestational age
- ✓ Vaccination status
- ✓ Anthropometric measurements
- ✓ Type of ARI
- ✓ Duration of symptoms
- ✓ Previous history of antibiotic
- ✓ Supportive care
- ✓ Type of antibiotic

#### 4.9 Data Collection Procedure

Semi-structured questionnaire had been developed from different literatures (22, 23, 45, 50, 51, 55) and patient chart and was provided to the three (2 pharmacists and 1 nurse) data collector arms to recruit data on the important parameters after training. Child guard were interviewed for information regarding parental occupation, parental educational status, family size, residence, pollution, breast feeding and vaccination status of child while data including age, sex, anthropometry, investigations, diagnosis, interventions and outcomes were taken from patient's chart. Patients were strictly followed until self-discharge, discharged officially, referred or get died during the study period.

#### 4.10 Data Quality Assurance

All possible measures were employed to maintain the quality of the data for this research. Before conducting the research, three days training were given for data collectors on the overall purpose of the study and items of the questioners and then pretest had been done on 11 patients to ensure the validity, reliability and internal consistency of the instrument and revised accordingly. Some items of the questionnaire were translated from English to Amharic and Affan Oromo to make easy for respondents. During the actual data collection process, supervisor assigned cross checked the data collectors on the field randomly every day for filled questionnaires consistency and completeness. Filled questionnaires were again checked finally by the principal investigator.

#### 4.11 Data Analysis

The collected data had been cleaned, entered into Epi Data version 3.1 and then exported for analysis to SPSS version 21.0. The data was cleaned for inconsistencies and missed values of vital variables.

Simple frequencies were ran to see the overall distribution of the study subjects with the categorical variables under study while mean and median were used for continuous variables. Bivariate analysis was employed to determine the association between different factors and the primary outcome variable and multivariate logistic regression was progressed for those variables that have p-value of < 0.25 after binary logistic regression to identify independent variables predicting these outcomes. Confidence interval of 95% was used to see the precision of the study and the level of significance was taken at  $\alpha < 0.05$ . Finally the findings are either tabulated, presented in graphics or phrases with the quantitative result during write up.

#### **4.12 Ethical Clearance**

Ethical clearance was obtained from Research and Ethics committee (IRB) of the Institute of Health Sciences of Jimma University. During data collection, each of the child guard was informed about the purpose, scope, and significance of the research, and appropriate informed verbal consent were taken from them. Anyone who refused to participate was simply excluded from the study or who want discontinue the interview were allowed to do so. In order to establish anonymous linkage, only codes were registered on the questionnaire. Moreover, during the training of data collectors and supervisor, ethical issues had been addressed as important component of the research.

#### **4.13 Dissemination of Results**

After the study is accomplished, it was presented to Jimma University, institute of health sciences, school of pharmacy. Subsequently, attempts will be made to present it on the annual meetings of Oromia heath bureau and other meetings in the region concerned with child health. Moreover, attempts will also be made to present it on scientific conferences and publish it on known scientific journals.

# 4.14 Definition of Terms

| Term                | Definition   |
|---------------------|--|
| АОМ                 | Case with history of ear pain and pus draining from the ear for $< 2$                |
|                     | weeks(5)   |
| Tonsilopharyngitis  | Sore throat and fever of sudden onset with/ without red pharynx and                  |
|                     | enlarged tonsils (56)  |
| Pneumonia           | A diagnosis for a patient presented with cough or difficult breathing plus           |
|                     | fast breathing of $\geq$ 60 / min for under 2 months, $\geq$ 50/min for age 2–11     |
|                     | months, $\geq$ 40/min for age 1–5 years, $\geq$ 30/min for over 5 year-olds or lower |
|                     | chest wall in drawing (5)  |
| Sever pneumonia     | A case with cough or difficulty in breathing plus oxygen saturation $<90\%$          |
|                     | or severe respiratory distress (grunting, very severe chest in drawing).             |
| Pertussis           | A diagnosis for a patient with paroxysmal coughing followed by a whoop               |
|                     | when breathing in with/ without subconjunctival hemorrhages (5)                      |
| Bronchiolitis       | Diagnosis of patients with wheezing that is not relieved by up to three              |
|                     | doses of a rapid-acting bronchodilator plus lower chest wall indrawing or            |
|                     | hyperinflation of the chest or difficulty in feeding (5)                             |
| <b>Co-morbidity</b> | Presence of additional findings with ARIs just during admission                      |
| Fully vaccinated    | A child who received all the vaccines indicated for his/her age(57)                  |
| Partially           | A child who received some of the vaccines indicated for his/her age(57)              |
| vaccinated          |  |
| Not vaccinated      | A child who never received vaccines indicated for his/her age(57)                    |

# 4.15 Operational Definitions

| Term      | Definition  |
|-----------|---|
| Pediatric | Patients admitted to Jimma medical center, pediatric ward who are $\leq 15$ |
|           | years old   |
| Inpatient | While the patient is admitted   |
| Burden    | Proportion of patients with ARI against the whole admission during study    |
|           | period (period prevalence)  |

| Treatment     | Complication (s), death, cure and LOS after treatment is commenced          |
|---------------|---|
| Good outcome  | Achievement of cure without complication after treatment is given           |
| Poor outcome  | ARI case who developed complication (s) <i>or died</i> during pharmacologic |
| 1 oor outcome | and non-pharmacologic intervention (s) periods while the patient is         |
|               | inpatient   |
| LOS           | Period from admission to self-discharge, official discharge or death        |
| Cured         | A patient fulfilled cure ascertainment criteria for ARIs                    |

Phenomenon where patient initially diagnosed with one or more of the<br/>ARIs develop either additional ARI or another physician confirmedComplicationdisease including pleural effusion or empyema, lung abscess,<br/>pneumothorax, acute rheumatic fever, sepsis and septic shock, meningitis<br/>and other new infectious disease (s) or ARI related non-infectious events<br/>after treatment started provided that no other cause is justified for it.

| Alive | A patient discharged, referred to another health institution or self-     |
|-------|---|
|       | discharged while in life.   |
| Died  | A patient declared as passed away in hospital by respective physician     |
|       | provided that no other reason beyond ARI or its complication is justified |
|       | for death   |

# 5. Results

# **5.1 Patient Enrollment Processes**

We observed 1489 children admitted to Jimma medical center, pediatric ward during study period and 412 were diagnosed with ARIs.

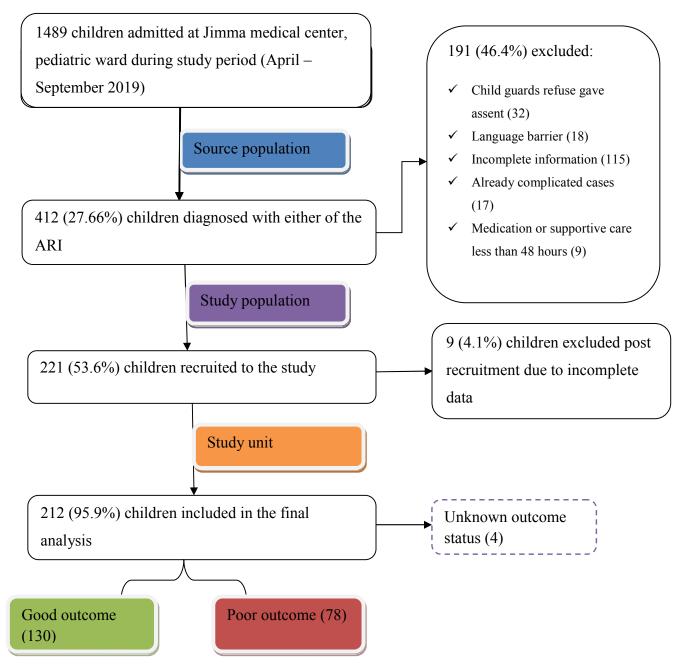


Figure- 2: Participants enrolment flow chart (N= 212), April – September 2019

#### 5.2 Socio-demographic Characteristics

Overall, 212 pediatric population was enrolled into the study with male participants accounted 112 from total and male: female ratio of 1.12:1.Children under 60 months old were the dominant age group in number 175 (82.5%) and the median for age of the participants was 18.5 months. Of these enrolled, 135 (63.7%) were rural residents. One hundred twelve (77.8%) of the study participants came from a family of not more than 4 members and 14.2% of them had cigarette smoker co residents or were exposed to air pollution. Eighty three (39.2%) patients were referred cases after they had visited another health facility.

Seventy seven (43.9%) and 59 (36.8%) of participants' mothers and fathers respectively completed grade 8. At the same time 167 (76.9%) of the mothers were house wives while more than half (55.7%) of the fathers were farmers.

One hundred twenty nine (60.8%) of the participants were fully vaccinated for their age as per WHO guidelines and conversely 16.5% were not vaccinated at all. Seventy six (of which 47 are less than 6 months old) patients had EBF only for less than 6 months (table-1).

| Characteristic                               |                            |              | P-value      |                    |      |                            |
|--|----------------------------|--------------|--------------|--------------------|------|----------------------------|
|  |                            | Poor outcome | Good outcome | Total <sup>y</sup> |      |                            |
|  | Male                       | 41 (36.6)    | 69 (61.6)    | 112 (52.8)         |      | -                          |
| Sex  | Female                     | 37 (37)      | 61 (61)      | 100 (47.2)         | .943 |                            |
| -  | 5 years old or less        | 68 (38.9)    | 103 (58.9)   | 175 (82.5)         |      |                            |
| Age group                                    | Older than 5 years old     | 10 (27)      | 27 (73)      | 37 (17.5)          | .000 |                            |
|  | Rural                      | 49 (36.3)    | 83 (61.5)    | 135 (63.7)         |      |                            |
| Residency                                    | Urban                      | 29 (37.7)    | 47 (61)      | 77 (36.3)          | .882 | Keys                       |
| ÿ  | Less than 4                | 37 (33)      | 72 (64.3)    | 112 (52.8)         |      |                            |
| Family size                                  | Four or more               | 41 (41)      | 58 (58)      | 100 (47.2)         | .267 | $x \rightarrow$ Merchant,  |
|  | Can't read or write        | 26 (33.8)    | 50 (64.9)    | 77 (36.3)          |      | ,                          |
| Mother educational level                     | Grade 1-8                  | 34 (36.6)    | 57 (61.3)    | 93 (43.9)          | _    | daily laborer,             |
|  | Grade 9-12                 | 14 (43.8)    | 17 (53.1)    | 32 (15.1)          | .673 | student                    |
|  | College or University      | 4 (40)       | 6 (60)       | 10 (4.7)           |      |                            |
| Father educational level                     | Can't read or write        | 21 (35.6)    | 37 (62.7)    | 59 (27.8)          |      |                            |
|  | Grade 1-8                  | 26 (33.3)    | 51 (65.4)    | 78 (36.8)          |      | $y \rightarrow Over$       |
|  | Grade 9-12                 | 26 (44.1)    | 31 (52.5)    | 59 (27.8)          | .713 | frequency come             |
|  | College or University      | 5 (31.2)     | 11 (68.8)    | 16 (7.5)           |      | from unknown               |
| Mother occupation                            | House wife                 | 57 (35)      | 103 (63.2)   | 163 (76.9)         |      |                            |
| 1  | Government employed        | 8 (53.3)     | 7 (46.7)     | 15 (7.1)           |      | outcome                    |
|  | Farmer                     | 4 (26.7)     | 11 (73.3)    | 15 (7.1)           | .299 | belonged to eac            |
|  | Others <sup><i>x</i></sup> | 9 (47.4)     | 9 (47.4)     | 18 (8.4)           |      | variable                   |
| Father occupation                            | Government employed        | 8 (42.1)     | 11 (57.9)    | 19 (8.9)           |      |                            |
| •  | Private employed           | 6 (35.3)     | 10 (58.8)    | 17 (8.0)           |      | $EBF \rightarrow exclusiv$ |
|  | Daily laborer              | 10 (45.5)    | 11 (50)      | 22 (10.4)          | .393 |                            |
|  | Farmer                     | 43 (36.4)    | 73 (61.9)    | 118 (55.7)         |      | breast feeding             |
|  | Merchants                  | 11 (30.6)    | 25 (69.4)    | 36 (16.9)          |      |                            |
| Cigarette smoker co residents or indoor /out | Yes                        | 16 (53.3)    | 14 (46.7)    | 30 (14.2)          |      |                            |
| door pollution                               | No                         | 62 (34.1)    | 116 (63.7)   | 4 (85.4)           | .056 |                            |
|  | < 6 months                 | 33 (42.9)    | 43 (55.8)    | 77 (36.7)          |      |                            |
| EBF  | $\geq$ 6 months            | 45 (33.3)    | 87 (64.4)    | 135 (63.7)         | .182 |                            |
| Vaccination status                           | Fully vaccinated           | 47 (36.4)    | 80 (62)      | 129 (60.8)         |      | 1                          |
|  | Partially vaccinated       | 21 (43.8)    | 25 (52.1)    | 48 (22.6)          | .120 | N                          |
|  | Not vaccinated             | 10 (28.6)    | 25 (71.4)    | 35 (16.5)          |      | -                          |
| Gestational age                              | Term                       | 72 (37.7)    | 115 (60.2)   | 191 (90.1)         |      |                            |
|  | Pre-term                   | 4 (26.7)     | 11 (73.3)    | 15 (7.1)           | .760 |                            |
|  | Unknown                    | 2 (33.3)     | 4 (66.7)     | 6 (2.8)            |      |                            |
| Birth weight                                 | Normal                     | 37 (43.5)    | 47 (55.3)    | 85 (40.1)          |      |                            |
| -  | Under weight               | 9 (36)       | 15 (60)      | 25 (11.8)          | .094 |                            |
|  | Unknown                    | 32 (31.4)    | 68 (66.7)    | 102 (48.1)         |      |                            |

# Table -1: Socio-demographic characteristics of patient/guardian of study participants (N= 212), April – September 2019.

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#### 5.3 Clinical Characteristics and Laboratory Findings of Participants

Cough, fever and fast breathing were the most common clinical presentations with 89.6%, 81.1% and 58% respectively. Objectively, 154 (72.6%) were found to be tachypnic while 99 (46.7%) and 83 (39.2%) of participants have elevated axial temperature and MUAC measurements below the reference index respectively. It was interesting to see that about 25.9% of the children have previous history of ARI. Gram stain was performed in 5 cases where the result was gram positive in 2 cases and gram negative in 3 cases. Similarly, culture was done in 3 cases where 2 were reported to be Escherichia coli and the other was staphylococcus aureus.

# Table -2: Clinical characteristics and laboratory findings of study participants (N= 212), April – September 2019.

| Clinical or             |             | F            | requency (%) |                    |         |
|-------------------------|-------------|--------------|--------------|--------------------|---------|
| laboratory              | Values      |              |              |                    |         |
| findings                |             | Poor outcome | Good outcome | Total <sup>x</sup> | P-value |
| Canab                   | Yes         | 73 (38.4)    | 113 (59.5)   | 190 (89.6)         | .138    |
| Cough                   | No          | 5 (22.7)     | 17 (77.3)    | 22 (10.4)          | .138    |
| COD                     | Yes         | 14 (36.8)    | 23 (60.5)    | 38 (17.9)          | 0(2     |
| SOB                     | No          | 64 (36.8)    | 107 (61.5)   | 174 (82.1)         | .963    |
|                         | Yes         | 14 (30.4)    | 32 (69.6)    | 46 (21.7)          | 264     |
| Grunting                | No          | 64 (38.6)    | 98 (59)      | 166 (78.3)         | .264    |
| A                       | Yes         | 28 (41.2)    | 40 (58.8)    | 68 (32.1)          | 115     |
| Appetite loss           | No          | 50 (34.7)    | 90 (62.5)    | 144 (67.9)         | .446    |
| F                       | Yes         | 49 (39.8)    | 71 (57.7)    | 123 (58.0)         | .247    |
| Fast breathing          | No          | 29 (32.6)    | 59 (66.3)    | 89 (41.9)          |         |
| F                       | Yes         | 67 (39)      | 101 (58.7)   | 172 (81.3)         | .149    |
| Fever                   | No          | 11 (27.5)    | 29 (72.5)    | 40 (18.9)          |         |
|                         | Normal      | 57 (35.2)    | 103 (63.6)   | 162 (76.4)         | .276    |
| Pulse rate              | Tachycardia | 21 (42.9)    | 26 (53.1)    | 49 (23.1)          |         |
|                         | Bradycardia |              | 1 (100)      | 1                  |         |
|                         | Normal      | 16 (30.2)    | 36 (67.9)    | 53 (25.0)          |         |
| <b>Respiratory rate</b> | Tachypnea   | 61 (39.6)    | 90 (58.4)    | 154 (72.6)         | .194    |
|                         | Bradypnea   | 1 (20)       | 4 (80)       | 5(2.4)             |         |
|                         | Normal      | 37 (34.9)    | 68 (64.2)    | 106 (50.0)         |         |
| Axial<br>temperature    | Febrile     | 40 (40.4)    | 56 (56.6)    | 99 (46.7)          | .353    |
| veniper utur e          | Hypothermic | 1 (14.3)     | 6 (85.7)     | 7 (3.3)            |         |
|                         | Yes         | 59 (72.8)    | 20 (24.7)    | 81 (38.2)          |         |
| Cyanosis                | No          | 19 (15.4)    | 103 (83.7)   | 123 (58.0)         | .000    |
|                         | Unmeasured  |              | 7 (87.5)     | 8 (3.8)            |         |
| WBC                     | Normal      | 35 (42.7)    | 47 (57.3)    | 82 (38.7)          | .110    |

|                            | Leucopenia<br>Unmeasured | 3 (100)<br>17 (29.3) | 38 (65.5)  | 3 (1.4)<br>58 (27.4) |      |
|----------------------------|--------------------------|----------------------|------------|----------------------|------|
|                            | Normal                   | 47 (39.8)            | 71 (60.2)  | 118 (55.7)           |      |
| Nuetrophil                 | Left shift               | 6 (30)               | 14 (70)    | 20 (9.4)             | .422 |
| Aueri opini                | Decreased                | 2 (50)               | 2 (50)     | 4 (1.9)              | .422 |
|                            | Unreported               | 23 (32.9)            | 43 (61.4)  | 70 (33)              |      |
|                            | Normal                   | 43 (39.4)            | 63 (57.8)  | 109 (51.4)           |      |
| MUAC                       | Below normal             | 33 (39.8)            | 50 (60.2)  | 83 (39.2)            |      |
|                            | Unreported               | 2 (10)               | 17 (85)    | 20 (9.4)             | .023 |
|                            | Normal                   | 97 (67.8)            | 45 (31.5)  | 144 (67.9)           |      |
| WFH                        | Wasted                   | 25 (45.5)            | 28 (50.9)  | 54 (25.5)            | .032 |
|                            | Unreported               | 8 (57.1)             | 5 (35.7)   | 14 (6.6)             |      |
|                            | Normal                   | 19 (46.3)            | 20 (48.8)  | 41 (19.3)            | .043 |
| WFA                        | Below normal             | 52 (36.6)            | 88 (62)    | 142 (66.9)           |      |
|                            | Unreported               | 7 (24.1)             | 22 (75.9)  | 29 (13.7)            |      |
|                            | Normal                   | 16 (37.2)            | 25 (58.1)  | 43 (20.3)            |      |
| HFA                        | Stunted                  | 53 (40.5)            | 76 (58)    | 131 (61.8)           | .096 |
|                            | Unreported               | 9 (23.7)             | 29 (76.3)  | 38 (17.9)            |      |
|                            | Normal                   | 13 (44.8)            | 15 (51.7)  | 29 (13.7)            |      |
| ESR                        | Unreported               | 65 (35.5)            | 115 (62.8) | 183 (86.3)           | .297 |
| Co morbidity               | Yes                      | 73 (38.8)            | 112 (59.6) | 188 (88.7)           | .060 |
|                            | No                       | 5 (20.8)             | 18 (75)    | 24 (11.3)            | .000 |
| <b>Others</b> <sup>y</sup> |                          |                      | 33 (15.6)  |                      |      |

discharge, chest in drawning, whooping cough, wheezing, sore throat, SOB→ shortness of breath,

WBC $\rightarrow$  white blood cells, MUAC $\rightarrow$ mid upper arm circumference, WFA $\rightarrow$  weight for age, HFA $\rightarrow$  height for

age, ESR $\rightarrow$  Erythrocyte sedimentation rate

One hundred eighty eight (88.7%) of the children had at least one more diagnosis in addition to ARI. One can see that, Sever Acute Malnutrition (SAM) was the most common co morbidity (50.9%) followed by Acute Gastroenteritis (AGE) with/without diarrhea (21.2%). Moreover, 68.9% of study participants had two or more co morbidities. The average co morbidity density for each patient was found to be 2 diagnoses with a possible deviation of 1 ( $2\pm 1$ ).

## **5.4 ARI Distributions**

The admission burden of ARIs was 412 (28%) with a URI: LRI ratio of 5:207. Majority, (91.1%) of the participants were pneumonia cases and of which more than half (53.8%) were diagnosed to have severe pneumonia. Pertussis was the second most frequent ARI observed in this study (table-3).

|                    |       |              | Frequency    |            |         |
|--------------------|-------|--------------|--------------|------------|---------|
| Type of ARI        | Value | Poor outcome | Good outcome | $Total^x$  | P-value |
| Severe pneumonia   | Yes   | 47 (43.1)    | 60 (55)      | 109 (51.4) | .050    |
|                    | No    | 31 (30.1)    | 70 (68)      | 103 (48.6) |         |
| Pneumonia          | Yes   | 23 (29.1)    | 55 (69.6)    | 79 (37.3)  | .066    |
|                    | No    | 55 (41.1)    | 75 (56.4)    | 133 (62.7) |         |
| Pertusiss          | Yes   | 6 (35.3)     | 11 (64.7)    | 17 (8.0)   | .845    |
|                    | No    | 72 (36.9)    | 119 (61)     | 195 (92.0) |         |
| AOM                | Yes   | 1 (33.3)     | 2 (66.7)     | 3 (1.4)    | .881    |
|                    | No    | 77 (36.8)    | 128 (61.2)   | 209 (98.6) |         |
| Bronchiolitis      | Yes   | 1 (50)       | 1 (50.0)     | 2          | .717    |
|                    | No    | 77 (36.7)    | 129 (61.4)   | 210 (99.1) |         |
| Tonsilopharyngitis | Yes   | 1 (50)       | 1 (50.0)     | 2          | .717    |
|                    | No    | 77 (36.7)    | 129 (61.4)   | 210 (99.1) |         |

Table-3: ARIs distribution among study participants (N=212), April – September 2019

## 5.5 Antibiotic Use Patterns and Other Interventions

Seventy three (34.4%) children had received an antibiotic by either PO or IV routes of administration within 90 days prior to admission.

Almost all (99.5%) of the cases had been provided with at least one antibiotic while admitted and ceftriaxone plus gentamicine was the most commonly prescribed antibiotic regimen given to 112 (53.1%) (figure-4). Fifty five (25.9%) patients received folic acid while formula milk was given for 23.1% cases.

One should note that, both the type of antibiotic selected and route of administration were poorly adhered to WHO recommendations for pneumonia and severe pneumonia cases provided that other external factors which influence regimen selection were not ruled out. In contrast, the WHO recommendations were highly encouraged in pertussis and AOM treatments in our setting.

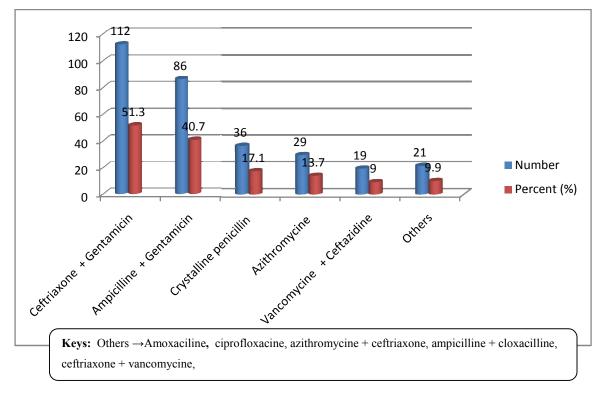
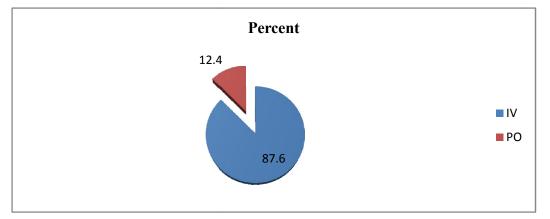


Figure 3: Antibiotic use patterns for ARIs among participants (N=211), April – September 2019.



Around 87.6% of the antibiotics issued for the patients were administered IV (figure-4).

Figure- 4: Routes of administrations for antibiotics give to children with ARIs, (N = 211), April – September 2019.

Seventy eight (37%) of the participants treated with antibiotic(s) had taken their drugs for 5 consecutive days. On the other hand, 7.1% and 55.9% of individuals consumed antibiotics shorter than 5 and longer than 5 days duration respectively. The minimum and maximum duration of antibiotic therapy were 2 and 15 days respectively with a mean value of  $6.42\pm2.108$  days.

Antibiotic regimen change had been made for 35.5% individuals who received these medications and all these changes were typically drug switching. Crystalline penicillin was the most frequently substituted 13 (17.3%) antibiotic and was replaced by ceftriaxone plus gentamicin. In the same fashion, switching gentamicin plus ceftriaxone to amoxicillin was the second major regimen change observed in this study 10 (13.3) (table-4).

| Antibiotic                |                           | Frequ | Percent |
|---------------------------|---------------------------|-------|---------|
| Initial                   | New                       | ency  | (%)     |
| Crystalline penicillin    | Ceftriaxone               | 4     | 5.3     |
| Gentamicine + Ceftriaxone | Amoxicillin               | 10    | 13.3    |
| Gentamicine + Ceftriaxone | Vancomycine + Ceftazidine | 9     | 12.0    |
| Crystalline penicillin    | Ceftriaxone + Gentamicine | 13    | 17.3    |
| Ampicilline + Gentamicine | Ceftriaxone + Gentamicine | 5     | 6.7     |
| Ampicilline + Gentamicine | Vancomycine + Ceftazidine | 10    | 13.3    |
| Othe                      | rs <sup>x</sup>           | 24    | 32.0    |
|                           |                           |       |         |

Table- 4: Antibiotic regimen change pattern for ARI among participants (N=75), April – September 2019.

**Keys**:  $x \rightarrow Crystalline penicillin to amoxicillin, ampicilline + genatamicine to amoxicilline, gentamicine + ceftriaxone to azithromycine, amoxicilline to gentamicine + ceftriaxone, ampicilline + genatamicine to ciprofloxacine, azithromycine added to ceftriaxone, gentamicine + ceftriaxone to ampicilline + cloxacilline, crystalline penicillin to ceftriaxone + vancomycine$ 

## **5.6 Inpatient Treatment Outcomes**

One hundred thirty (61.3%) of the participants admitted for ARIs met the criteria to achieve "good outcome" while 78 (36.8%) had "poor outcome". Pleural effusion/empyema (17), new ARI (8) and sepsis (8) were the most prevalent complications. The outcome was fatal in 3 (1.4%) of the ARI cases, one from pneumonia and two from severe pneumonia. Treatment outcome status was unknown in 4 (1.9%) cases as they left the hospital against medical advice. LOS was

5 days or less in 42.1% of patients while the majority (57.9%) stayed for more than 5 days with a median duration of 8 days.

|              | Out          | comes                      | Frequency | Percent (%) |
|--------------|--------------|----------------------------|-----------|-------------|
| Good outcome | )            |                            | 130       | 61.3        |
|              |              | New ARI                    | 8         | 10.3        |
|              |              | Pleural effusion/empyema   | 17        | 21.7        |
|              | n            | Lung abscess               | 5         | 6.4         |
| Poor         | Complication | Pneumothorax               | 7         | 8.9         |
| outcome      | olic         | Sepsis                     | 8         | 10.3        |
|              | du           | Meningitis                 | 6         | 7.7         |
|              | C            | Pneumonia superimposed HF  | 4         | 5.1         |
|              |              | Others <sup><i>x</i></sup> | 23        | 29.5        |
|              | Dea          | th                         | 3         | 1.4         |
| Unknown      |              |                            | 4         | 1.9         |
| (            |              |                            |           |             |

Table- 5: Frequencies of different in-patient treatment outcomes of participants (N=212), April-September, 2019

**Keys:**  $x \rightarrow$  urinary tract infections, . infective endocarditis ,convulsion, acute gastroenteritis and/or diarrhea, arthritis, pyelonephritis, respiratory acidosis, arrhythmia, osteomylites

HF→ Heart failure

## **5.6.1 Inpatient Complication and Its Frequency Measures**

Seventy eight cases developed in-patient complication in our study which makes the *cumulative incidence risk* for this event to be 368 per 1000 ARI children. Our study is dynamic and the time period at which the individuals are at risk for in-patient complication (risky period) was not same across all participants. Hence, the cumulative risky period (measured in terms of days in this study) was the sum of individual case's risky period. Once the complication is occurred, the risky period at which these individuals are at risk to have it is the time from hospital admission to just onset of complication and was added to be 224 days. For those participants who didn't have the complication, the risky period is the time length from admission to occurrence of cure having in mind that these individuals are unlikely to develop complication once they get cure from ARI and was found to be 774 days. In the same fashion, the risky period for those cases whose status of complication is unknown was assumed the time from admission to self discharge and it was 22 days. The cumulative risky period for the whole participants to experience the first complication was totaled 1020 days. Hence the *incidence rate* of inpatient complication was 0.076 per child-day, i.e. there were 76 new in-patient complication cases from ARI in every 1000

days risky period. More ever, 62 patients had only one complication, 14 patients had two complications and the remaining two cases experienced 3 complications which make the total number of episodes to be 96. The risky period for the patients to acquire repeated complication episodes was 1376 days and hence this gave an *attack rate* of 0.069 per child-day and implies that there are 69 episodes of complications from ARI in every 1000 days of risky period. Note that the number of complication episodes for single case in each 10,000 risky days was 8.8.

#### 5.7 Predictors of Inpatient Poor Outcome

Bivariate logistic regression shown that previous history of ARI [COR = 6.525 (95% CI, 3.296-12.917), P-value = < .001], MUAC less than 11.5 centimeter [COR = .172 (95%CI, .038-.785), P-value = .023], WFA less than -2 standard deviation [COR = .335 (95% CI, .116-.964), P-value = .043], severe pneumonia [COR = 1.769 (95% CI, 1.001-3.127), P-value = .050], initial ceftriaxone plus gentamicine administration [COR = 1.911 (95% CI, 1.077-3.393), P-value = .027], antibiotics 90 days prior to admission [COR = 6.720 (95% CI, 3.575-12.632), P-value = < .001], age [COR = .978 (95% CI, .968-.987), P-value = < .001], presence of co morbidity [COR = 2.782 (1.990-3.889), P-value = < .001], lack of oxygen supplementation [COR = .229 (95% CI, .125-.419), P-value = < .001], wasted body weight [COR = 2.782 (95% CI, 1.267-4.601), P-value = .032], time delayed before admission [COR = 2.782 (95% CI, 1.990-3.889), P-value = < .001] and cyanosis [COR = 15.992 (95% CI, 7.904-32.357), P-value = < .001] were significantly associated with poor outcome in ARIs cases.

However, in multivariate analysis, the first four variables were failed to have significant associations and independent predictors of poor outcome were cyanosis [AOR=11.911(95% CI, 4.354-32.587), P-value = < .001], wasted body weight [AOR = 5.492(95% CI, 1.729-17.445), P-value = .004], initial ceftriaxone plus gentamicine administration [AOR = 3.166 (95% CI, 1.114-8.996), P = .031], antibiotic 90 days prior to admission [AOR = 2.961(95% CI, 1.087-8.069), P-value = .034], co morbidity [AOR = 2.116(95% CI, 1.468-3.654), P-value = < .001] and duration of symptoms [AOR = 1.046(95% CI, 1.001-1.092), P-value = .044] in order of their relative importance. Conversely, older age [AOR = 0.970 (95% CI, 0.955-0.986), P-value = < .001] and oxygen supplementation [AOR = .360 (95% CI, .132-.979), P-value = .045] were protective factors for poor outcome (table-6).

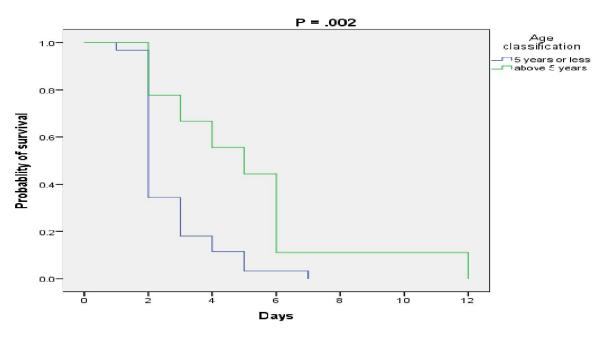
|   |                           |                   | quency (%)                | COR (95% CI for $COR$ ) <sup>w</sup> | P – value <sup>w</sup> | AOR (95% CI for AOR) x | $P - value^{\lambda}$ |
|---|---------------------------|-------------------|---------------------------|--------------------------------------|------------------------|------------------------|-----------------------|
| Variables   | Values                    | Good              | <b>D</b>                  | COR (95% CI 101 COR)                 | I – value              | AOK (95% CI 101 AOK)   | i – value             |
|   | Normal                    | outcome 20 (24.7) | Poor outcome<br>59 (72.8) |                                      |                        |                        |                       |
|   |                           | . ,               | . ,                       |                                      | .000                   |                        |                       |
| Oxygen saturation <sup>z</sup>                      | Below normal <sup>y</sup> | 103 (83.7)        | 19 (15.4)                 | 15.992 (7.904-32.357)                | .000                   | 11.911(4.354-32.587)   | < .001                |
|   | Unreported                | 7 (87.5)          |                           |                                      |                        |                        |                       |
| Oxygen given <sup>z</sup>                           | Yes <sup>y</sup>          | 84 (78.5)         | 23 (21.5)                 |                                      |                        |                        | .045                  |
| Oxygen given  | No                        | 46 (43.8)         | 55 (52.4)                 | .229 (.125419)                       | .000                   | .360 (.132979)         | .043                  |
| History of ARI                                      | Yes <sup>y</sup>          | 17 (30.9)         | 38 (69.1)                 |                                      |                        |                        |                       |
|   | No                        | 108 (72.5)        | 37 (24.8)                 | 6.525 (3.296-12.917)                 | .000                   |                        |                       |
|   | Uncertain                 | 5 (62.5)          | 3 (37.5)                  |                                      |                        |                        |                       |
| Antibiotic 90 days prior to admission <sup>z</sup>  | Yes <sup>y</sup>          | 25 (34.2)         | 48 (65.8)                 |                                      |                        |                        |                       |
|   | No                        | 105 (75.5)        | 30 (21.6)                 | 6.720 (3.575-12.632)                 | .000                   | 2.961 (1.087-8.069)    | .034                  |
|   | 110                       | 105 (75.5)        | 50 (21.0)                 |                                      |                        |                        |                       |
| Age <sup>z</sup>                                    |                           |                   |                           |                                      |                        |                        | < .001                |
|   | Yes <sup>y</sup>          | (1,(54,5))        | 49 (43.8)                 | .978 (.968987)                       | .000                   | 0.970 (0.955-0.986)    |                       |
| Gentamicine + Ceftriaxone <sup><math>z</math></sup> |                           | 61 (54.5)         |                           | 1.911 (1.077-3.393)                  | .027                   | 3.166 (1.114-8.996)    | .031                  |
|   | No                        | 69 (69)           | 29 (29)                   | 1.911 (1.077-5.595)                  | .027                   | 5.100 (1.114-0.570)    |                       |
| Co morbidity <sup>z</sup>                           |                           |                   |                           | 2.782 (1.990-3.889)                  | .000                   | 2.116 (1.468-3.654)    | < .001                |
|   |                           |                   |                           | 2.762 (1.596 5.669)                  | .000                   | 2.110 (1.100 5.05 1)   |                       |
| Duration of symptoms <sup>z</sup>                   |                           |                   |                           | 1.080 (1.032-1.131)                  | .001                   | 1.046 (1.001-1.092)    | .044                  |
| <b>J</b> 1  |                           |                   |                           | 1.000 (1.032-1.131)                  | .001                   | 1.040 (1.001-1.072)    |                       |
|   | Normal                    | 97 (67.8)         | 45 (31.5)                 |                                      | .032                   |                        |                       |
|   | Wasted <sup>y</sup>       | 25 (45.5)         | 28 (50.9)                 | 2.414 (1.267-4.601)                  |                        | 5.492 (1.729-17.445)   | .004                  |
| WFH <sup>z</sup>                                    |                           |                   |                           | 2.111 (1.207 1.001)                  | .052                   | 0.192 (1.12) 11.110)   |                       |
|   | Unreported                | 8 (57.1)          | 5 (35.7)                  |                                      |                        |                        |                       |
|   | Normal                    | 43 (39.4)         | 63 (57.8)                 |                                      |                        |                        |                       |
| MUAC  | Below normal <sup>y</sup> | 33 (39.8)         | 50 (60.2)                 | .172 (.038785)                       | .023                   |                        |                       |
|   | Unreported                | 2 (10)            | 17 (85)                   |                                      |                        |                        |                       |
|   | Normal                    | 19 (46.3)         | 20 (48.8)                 |                                      |                        |                        |                       |
| WFA   | Below normal <sup>y</sup> | 52 (36.6)         | 88 (62)                   | .335 (.116964)                       | .043                   |                        |                       |
|   | Unreported                | 7 (24.1)          | 22 (75.9)                 |                                      |                        |                        |                       |
|   | Yes <sup>y</sup>          | 60 (55)           | 47 (43.1)                 |                                      |                        |                        |                       |
| Severe pneumonia                                    | No                        | 70 (68)           | 31 (30.1)                 | 1.769 (1.001-3.127)                  | .050                   |                        |                       |

## Table-6: Independent predictors for "poor outcome" among participants (N= 212), April-September, 2019

**Keys**:  $W \rightarrow After binary logistic regression, x \rightarrow After multivariate logistic regression y \rightarrow Dummy category, z \rightarrow Independent predictors of poor outcome$ **Note:**The under frequencies (if any) are from 'unknown outcomes' belonged to each category As the age of the child increases by one month, the likelihood to have poor outcome decreases by 3%. Theoretically, this makes the oldest child participated in our study four times less likely to have poor outcome compared with the youngest one. In a similar manner, individuals who had been provided with oxygen supplementation were about 64% less likely to have this poor outcome compared with those who did not have it. Co morbidity was another factor and as the number of co morbidity increases by one, the likelihood to have poor outcome doubles.

#### 5.8 Time to Event for Complications

Log rank test suggested us the probability of younger cases to develop complication during the first 2 days of admission was > 0.8 while it was < 0.2 in the older ones (P= .002). Once again, the probability of the older individuals to survive from complication was < 0.2 just after 6 days of admission. Still one should note that the probability to survive from complication decreases over time for all ARI cases (figure-5). The mean time elapsed for the younger participants to develop in-patient complication was  $2.672\pm0.161$  days (95% CI, 2.356-2.989) while it was  $5.111\pm1.020$  (95% CI, 3.112-7.110) for those older than 5 years. In the same fashion, the median time for the same phenomenon was  $2\pm0.098$  days (95% CI, 1.809-2.191) for the younger and  $5\pm1.491$  days (95% CI, 2.078-7.922).



**Figure -5:** ARI induced in-patient complication survival probabilities compared between five years or younger and older than five years over time

#### 6. Discussion

Four hundred twelve ARI cases had been admitted during the current study period making admission burden of these cases around 28% and is in comparison with Vinod K et al. study where the burden of ARIs was 27.25% (40). But it should be unconcealed that, the URIs: LRIs ratio was 5:207 in our study which was extremely disproportionate compared to the above study which was found to be 8:19. Alexis A. et al. found the hospital burden of ARIs in Bamenda regional hospital to be 54.7%, from which AOM alone accounted 14% on study (52) which was around two fold of the current finding and the possible explanation for the marked differences is that URIs are relatively more clinically benign than LRIs and hence parents in our study area, having plenty of socioeconomic challenges (58), may simply deny to visit health facility. The current burden was lower than those found by Bayisa et al. (29) and Abuka T et al. (42) where pneumonia alone constituted 36% and 33.5% of under-five admissions and this might be due to high enrolment of non-ARI referred cases to Jimma medical center from other health facilities including Nekemte referral hospital and this humiliates the visibility of ARI. The other possible reason is that children older than 5 years are involved in this study where the occurrence of ARIs is relatively rare. Again, the prevalence of pneumonia alone was 13% in this study which was higher than national prevalence (7%) of under-five ARIs (24, 42) and this difference could be simply due to the studies nature, i.e. community versus facility based study. Another study by Mukara KB et al. reported the prevalence of acute middle ear infection was 1.8% (33) which was comparable to our study.

Two hundred eleven (99.5%) patients were given antibiotic therapy in our study which was almost consistent with Peking university people's hospital (95.5%) but higher than Guangdong provincial hospital (82.9%) as both reported by Wen et al (43). This difference might be due to absence of traditional medicine in our setting in contrast to the latter setting where some patients preferred to get these remedies rather than modern medicine.

One hundred eighty five (87.6%) of the antibiotics issued for the patients were administered IV while the remaining were given PO and more IV antibiotics were abused in our study compared to reports from Italian pediatric hospital (48) where 64.6% of antimicrobials were given via IV,

whereas the remains received oral antibiotic therapy. Ceftriaxone plus gentamicine (52.8%) was the most commonly prescribed antibiotic regimen in our observation which was different from Bayisa *et al.* (29) report from Nekemte referral hospital and Italian pediatric hospital (48) where ceftriaxone alone was the most frequently used antibiotic regimen in both settings. It was also unmatched with Brogan et al. (46) where ceftriaxone constitute 56% of antibiotic prescriptions for pediatric pneumonia and all these differences might be either due to difference in local treatment guidelines or physicians need to adhere different treatment protocols which is best for them.

Seventy five (35.5%) cases required change in antibiotic regimen in the current study which was significantly higher than the 28.5%, 18.2% and 24.7% reports from Kumar A *et al.*, Wen *et al.*, and Simbalista R *et al.* respectively (19, 43, 47), and lower than 62.2% reported from China pediatric hospitalizations in Peking university people's hospital (43) and the aforementioned Italian study where this change has been made in 43.4% of cases (48). These differences could be due to either in appropriate initial drug selection, cost preference from parents or difference in local antibacterial resistance for the initial drugs.

The average duration of antibiotic administration (antibiotic period) was  $6.5\pm2.5$  days in our observation and was not much longer than the corresponding value of  $5\pm3$  from Simbalista *et al.* study (43) but almost 2 fold enough longer than Zec *et al.* (49) finding where this period was  $3.56 \pm 1.42$  days. However, it was much shorter than Jining No.1 people's hospital (44) where average length of antibiotic use was  $18.80\pm4.57$  days. These variations might be due to either differences in national/local guidelines for the disease or clinical characteristics of patient population which are sufficient enough to influence treatment decisions.

In our study, seventy three (34.4%) children had received an antibiotic by either the oral or parenteral routes of administration 3 months prior to admission which seems lower than the Naheed A *et al.* report where 56% of children admitted for pneumonia received an antibiotic before hospitalization (59) and this might show that larger proportion of participants in the later study had previous history of infections.

In terms of clinical outcomes, our study revealed that 78 (36.8%) children had poor outcome of whom 75 (36.1%) cases achieved cure after complication compared to 25.7% from Bayisa et al. study and this seems from the higher proportion of patients with co-morbidity in our study. Pleural effusion/empyema was the most frequent complication occurred in 21.7% of cases followed by new ARI and sepsis both in 10% cases; pneumothorax occurred in 8.9%, meningitis in 6.6% and lung abscess in 6.4% of ARI cases. Similarly, the major complications in Bayisa et al. study were pleural effusion in 30%, lung abscess in 14%, septic shock in 10.5%, pneumothorax in 10.5%, pharyngeal abscess in 21% and laryngeal edema in 15.8% of cases and one can note that the first four complications were consistent to our finding while the remains are not (29). The rate of complication, indicated above, in the current study was many times folded higher than Nantanda et al. study report where only 1.9% developed complications: two had empyema and one had pneumothorax (54). This might be in part due to the definitive therapy, delivered there after blood and sputum were obtained for culture. Our finding was again incomparable with Kumar A et al. (19) report where sepsis was the most common complication happened in 6% of subjects, followed by meningitis and pnuemothorax developed in 1% and 0.5% respectively. Complication was detected in 51.7% of the cases studied by Mustapha et al. (52) which was by far higher than our observation. Dehydration and congestive cardiac failure were the most prevalent complications in this study and the reason seems straight forward since children older than 5 years were included in our study who are known to have relatively low total body water, which makes them at relatively low risk of increased fluid loss. Another plausible factor contributing to dehydration differences in the study patients was the weather effect of study areas where our study area is relatively less dry and hot than the latter just for it being located in Sahel regions of the world. Likewise, heart failure was clinically significant complication in our study too and this might be an effect from vicious circle of dehydration or hypoxia which ever exits.

The incidence of poor outcome in our study was higher than a report from Morocco by Jroundi I *et al.* (22) where it was found to be 27.2% among children admitted with severe pneumonia and this might be due to large number of patients with delayed presentation in our study. Our study observed 1.4% mortality rate which was incomparable to death rate reports from Jroundi I *et al.* (22) 4%, Nantanda R *et al.* (54) 15.3%, Dembele *et al.* (51) 4.7%, Kumar *et al.* (45) 3%, Kelly

MS *et al.* (53) 5.8%, Bekele F *et al.*(23) 4.7%, Bayisa *et al* (29) 3.6%, Mustapha *et al.* (52) 8.9%, Han *et al.* (44) 22.8% and Naheed *et al* (59) 4% studies. It was even extremely lower than the case fatality rate reported from Jining hospital, China, by Han et al (44) which was 22.86%. This might be due to the exclusion of already pre- admission complicated cases in our study who are more prone to die. If not, the other possible reason is that only children under 5 years old were participated in most of the above studies. One should note that, 15.3% report from Nantanda R *et al.* study was particularly surprising as definitive therapy was given there and this makes pretty hard to justify even in approximation why this become higher than our report. But, it was slightly larger than 1.2% mortality rate reported by Agweyu A et al (55) and 0.5% noted by Wen et al (43) from Peking university people's hospital yet and this seems due to the prospective nature of our study.

The LOS (days) in our study in terms of mean was  $7.7\pm2.3$  which was almost in agreement with Simbalista R et al. (47) findings where it was  $9.0 \pm 6.0$  and with Wen et al. (43) study from China hospital where this was again  $5.8\pm3.0$  days. It was, however, shorter than Peking university people's hospital, as this mean was  $17.4 \pm 19.9$  days (43) and another study in China hospital by Han et al. (44) which reported average LOS of 26.50±3.21 days and only sever pneumonia cases (and in turn might had complex medical conditions) were involved in these studies which might be the sort of differences for these durations. Conversely, the median LOS of our study was 8 days which was longer than Thomson J et al. (50), Brogan et al. (46) and Kelly MS et al. (53) where this median was 1.3 days, 2 days and 3.8 days respectively. More than half (57.1%) children stayed in hospital for more than 7 days which was by far larger than Nantanda R et al. (54) report where only 14.6% had the same duration and this could be due to high rate of complication or large burden of co-morbidity in our study, as 37.1% and 88.5% of these stay come from these patients respectively, which need more prolonged management. Moreover, empirical therapy, unlike to Nantanda's study setting, was practiced at Jimma medical center and this takes time until this try and error become randomly effective for patient to be discharged.

Our study identified the independent predictors of poor outcome were cyanosis, wasted body weight, initial ceftriaxone plus gentamicine administration, antibiotic 90 days prior to admission,

co morbidity and prolonged duration of symptoms while older age and oxygen supplementation were protective factors for this outcome.

The effect from cyanosis may be due to the fact that airflow resistance increases inversely to the fourth power of the radius, small changes in airway diameter will happen during air way infection due to inflammation which lead to this cyanosis and in turn facilitates system complications like acidosis, respiratory failure and death (60). This seems why patients supplied with oxygen were found to have better outcome in our study.

Initial ceftriaxone plus gentamicine administration was another independent predictor in our study and this might be due to an antibiotic resistance, and if this was the reason, it supports the ongoing and alarming reports a large number of bacteria are becoming resistant to these drugs in Ethiopia (38, 61). Similarly, previous antibiotic use my lead to absolute or cross resistance towards the current medication and contributes to poor outcome.

Wasted body weight was another statistically significant factor for poor outcome and this reflects the fact that both acquired immunity and innate host defense mechanisms are compromised in malnourished patients called 'nutritionally acquired immunodeficiency syndrome' that render them more susceptible to infections and their cascade of events (62).

Presence of co morbidity and prolonged duration of symptoms were other predicting factors for poor outcome and this seems straight forward as patients with these elements are presumed to have complex clinical conditions and in turn negative prognosis (63).

Jroundi I *et al.* (22) ascertained cyanosis had a statistically significant association with poor outcome similar to our study. Unlike the above study; fever, born prematurely, and being exposed to tobacco smoking at home doesn't had statistically significant role in treatment out come in current study. For the fever, the difference might be from the way how the term was operationalized in each study while the variation for the later variables look likes due to the low proportion of cases with them. Importantly, no differences were seen towards the outcome group in relation to mean white blood cells in both studies. However, the occurrence of complications

and outcome of treatment did not significantly differ in the different age groups according to Mustapha MG study (52) which contrasts the current finding and our finding supports the logic immunity boosts with age development which in turn favors better clinical outcomes after infection (64).

Dembele BPP *et al.* (51) declared the risk factors significantly associated with death were age, cyanosis, grunting, fever and this agreed with our finding except the last two contributors. This could be due to scaling difference for the fever i.e. > 38.5°C was used in the former and > 37.5 °C in our study. Similarly, R. Nantanda *et al.* (54), reported that hypoxemia and very severe pneumonia were independent predictors of death from which the later was not in our study. This might be due to the inclusion and perhaps their role towards the poor outcome of other ARIs in our study. Agweyu (55) found that sex was not predictor of death from pneumonia but being aged 2-11 months and having of prolonged duration of symptoms did have which all hold true in this study.

Severe malnutrition was found to be independent determinant of poor outcome in our study which agrees to the studies by Bekele (23), Dembele (51) and R. Nantanda et al. (54) where it was observed that treatment outcomes were heavily influenced by nutritional status of the patients. Bekele again reported that previous history of pneumonia and smoker co residents are significantly associated with treatment outcomes but not in our study and this might be due to lower proportion of these participants in our study.

## 7. Limitation of Study

Even though with its own merits, this study was yet surrounded with plenty of weaknesses. Microbiological and radiological diagnostic modalities were not used, instead most of the cases were assessed only clinically and this may have effect on the accuracy of the diagnoses. We don't have a mechanism to assure weather the post ARI systemic infections were really complications of the ARI itself or simply nosocomial infections. Further, only in- patient clinical outcomes are addressed now and the long term effects of ARIs were not assessed in this study. Another limitation was we used some retrospective, cross sectional and even community based studies to compare our findings. Even though the sample was sufficient to infer within the domain of Jimma medical center, this study was one center study and will not give regional and national generalization on its own.

### 7. Conclusion

Hospital burden of ARIs was enormous in Jimma medical center, pediatric ward even though the fact it is not uniquely high compared to other similar reports. Ceftriaxone plus gentamicine was the most commonly prescribed antibiotic regimen in Jimma medical center, pediatric ward and regimen modification was a common trend of clinical practice. The rate of poor outcome was significantly high in our setting and cyanosis, wasted body weight, initial ceftriaxone plus gentamicine administration, antibiotic 90 days prior to admission, co morbidity and prolonged duration of symptoms were statistically significantly associated factors for this outcome. In contrast older age and oxygen supplementation were protective factors for this poor outcome. The time needed for the children to develop complication after admission was interestingly very short, i.e. no more than couple of days.

### 8. Recommendations

#### **Government and Other Stakeholders**

As mentioned elsewhere in this document, the burden of ARIs was high in our setting with its own clinical implications. This should dictate government and/or other stake holders to design and start implementation of ARI preventive strategies including tackling against the well established risk factors for the disease.

Government and perhaps other concerned bodies should again increase the coverage of health infrastructures to courage the health seeking behavior of citizens. Government could build this behavior via different public health education programs including about the importance of quick visit to health facility after health symptoms. These bodies should do more on poverty reduction programs and should facilitate training for parents about age based balanced diet.

#### Jimma Medical Center

Clinicians should pay due attention and give prioritize to those children who come with the aforementioned predicting factors for the poor outcome. Intensive care should be commenced especially during the first two days after admission and patients should be supplied with oxygen when ever needed.

#### Researchers

As said elsewhere above, there is lack of well designed study on the topic and multiple studies on different areas of the country are needed to be compiled just for us to have conclusive picture about it. Equal importantly, the economic implication of poor outcome for ARIs should be assessed scientifically

Antibiotic use patterns were addressed in our study and researchers should start to evaluate the appropriateness of antibiotic prescription. In addition, ongoing local and regional surveillance is necessary to monitor the antimicrobial susceptibility and prevalence of pathogens associated with the infection.

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# Annex-I

Cure ascertainment criteria for ARIs [Adapted from WHO pediatric pocket book, 2013(5)]

| ARI                | Cure criteria   |
|--------------------|---|
| AOM                | If ear pain and discharge are resolved                  |
| Tonsilopharyngitis | After sore throat and enlarged tonsils subsided         |
| S.pnuemonia        | No respiratory distress and hypoxemia                   |
|                    | They are able to take oral medication                   |
|                    | They are feeding well                                   |
| Pnuemonia          | No difficulty breathing, fast breathing and lower chest |
|                    | wall indrawing  |
| Bronchitis         | When respiratory distress and hypoxaemia have resolved  |
|                    | When there is no apnoea                                 |
|                    | If the child is feeding well                            |
| Pertussis          | Absence of paroxysmal coughing and subsequent           |
|                    | whoop   |

### Annex-II

Questionnaire

Information sheet

Questionnaire No:\_\_\_\_\_

Greeting: Good morning/afternoon

My name is------ I am collecting information about risk factors and treatment outcomes of *Acute Respiratory Infections (ARIs)* which includes Acute otitis media, Pneumonia, Severe pneumonia, Epiglottitis, Pertussis, Bronchiolitis, Bronchitis and Tonsilopharyngitis in children admitted to JUMC. I would like to ask you few questions which take no more than 20 munities so that your genuine response that you are going to give is very important to identify environmental, sociodemographic and economical elements found in Jimma and nearby areas that precipitate these diseases. You are selected to be participant of this study if you give me consent after you have understood the following information sheet:

**Title of the study**: Burden of Pediatric Acute Respiratory Infections, Treatment outcomes and predicting factors for patients admitted to Jimma University Medical Center, Pediatric Ward

**Objective of the study:** To assess burden, treatment outcome (s) and predicting factor (s) of pediatric acute respiratory infections in pediatric patients admitted to Jimma University Medical Center, pediatric ward.

**Risk of the study**: The study has no any risk for the participant and interview will be private to make safe participants from any fear.

**Rights of participants**: Participating and not participation is a full right and participants can stop for participating in the study at any time. They can also skip any question which they want not to respond. They can ask any question which is not clear for them.

#### **Oral informed consent**

Are you interested to participate in the study?

I am willing to participate in this study: \_\_\_\_\_

#### UnkaWaliigaltee

Bakka Jirtanitti nagaan isiniif haata'u:

Ani maqaan koo: \_\_\_\_\_\_ ani kanan isingaafachuuf deemu, wantoota dhukkuba saffisaan ujummoo hargansuu daa'immanii(PediatricAcute Respiratory Infections(ARIs) qabsiisuu danda'anii fi bu'aalee yaalii fayyaan boodaa walqabatudha. Dhukkubootni kanneenis afaan Ingiliffaatiin "Acute otitis media, Pneumonia, Severe pneumonia, Epiglottitis, Pertussis, Bronchiolitis, Bronchitis and Tonsilopharyngitis" kan jedhamanidha.Kanaafuu gaaffileen muraasa kan,daqiiqaa digdama caalaa isin hin fudhatne isin gaafadha. Deebii isinnaaf deebistan barbaachisummaan isaa wantoota dhukkuba kana qabsiisuu danda'an addaa baasuuf ta'a. Kanaafuu qorannoo kana irratti hirmaachuu fi deebii nuuf laachuu keef dursa fedha keetiin eeyyamaa ta'uun keeni barbaachisa. Kanaaf unka armaan gadii kana erga dubbistee booda mallattoo keetiin mirkaneessuu qabda.

**Mata duree qorannoo**: Miidhaa, dhukkuba hargansuu daa'immanii, wantoota dhukkubicha fiduu danda'an akkasumas, bu'aalee yaalaan booda dhufan adda baasuudha.

**Kaayyoo qorannoo**:Miidhaa, wantoota dhukkubicha fiduu danda'anii fi bu'aalee yaalaan boodaa dhufan adda baasuu ta'a.

**Miidhaa qorannoo**:Sababa hirmaattanii fi hirmaachuu dhiiftaniif wanti rakkoo yaalaa isinirra gahu hin jiraatu. Yaadni isin nuuflaattanii fi fudhatnu hundi nama biraatti dabarsamee hin kennamu yookaan hinhimamu.

**Mirga dhukkubsaan/gaafatamaanqabu**: qorannicha irratti yaada kennuu fi dhiisuun mirga guutuudha. Gaaffii deebisuuf fedhii hin qabneyoo jiraates irra darbuun ni danda'ama. Akkasumas, gaaffiin isaaniif hin galle yoo jiraate gaafachuuf mirga qabu.

#### Unkawaliigalteeafaanii:

Qorannicha irratti yaada kennuuf/hirmachuuf fedhii qabdaa? Yoo fedhii qabaattee mallattoodhaan mirkaneessi: መጠይቅ

የመረጃ ወረቀት

መጠይቅ ቁጥር : \_\_\_\_\_

ስም -----እባላለሀሱ፡ በጅማ ዩኒቨርሲቲ የሕክምና ማሪከል የሕጻናት ማቆያ ክፍል ስለ *አጣዳል* የመተንፈሻ እንፌክሽን ሕክምና ውጤት እና ወሳኝ ሁኔታዎች መረጃዎችን በመሰብሰብ ላይ ነኝ። ለምትሰጡት ትክክለኛ ምላሽ በጅማ እና በአቅራቢያ በሚገኙ አካባቢያዊ ፤ ማህበራዊ እና ኢኮኖሚያዊ ክፍሎችን ለመለየት በጣም አስፈላጊ ነው . የሚከተሉትን የመረጃ ወረቀት ከተረዱ በኋላ በዚህ ጥናት ተሳታፊ እንድሆኑ ተመርጠዋል ።

**የጥናቱ ዓላማ -** በጅማ የሕክምና ማዕከል የሕጻናት ማቆያ ክፍል ውስጥ የተኙ የሕፃናት ሕመምተኞች **አጣዳፊ የመተንፈሻ እንፈከሽን ሕክምና** ውጤት እና ወሳኝ ሁኔታዎች ለማጥናት

**የጥናቱ አዴጋ** - ጥናቱ ለተሳታፊ ምንም አዴጋ የለውም እናም ቃለ-መጠይቅ የግል ይሆናል

**የተሳታፊዎቹ መብቶች** : መሳተፍ እና አለመሳተፍ ሙሉ መብት እና ተሳታፊዎች በማንኛውም ጊዜ ከዋናቱ መውጣት ይችላሉ **።** በተጨማሪም ምላሽ መስጠት የማይፈልጉትን ማንኛውንም ዋያቄ ማለፍ ይችላሉ. ለእነሱ ያልተነገረ ማንኛውም ዋያቄ መጠየቅ ይችላሉ.

#### የቃል አተንባበር ስምምነት

በጥናቱ ለመሳተፍ ፍላንት አለዎት?

በዚህ ጥናት ለመሳተፍ እፈልጋለሁ : \_\_\_\_\_

| Card№:            | Bed №:               | Sex: Male       | Female            |
|-------------------|----------------------|-----------------|-------------------|
| Age:              | Address:             | D               | ate of admission: |
| Residency: a)     | rural                | b) urban        |                   |
| Number of chil    | ldren in the family: |                 |                   |
| Educational lev   | vel (mother)         | Educational le  | vel (father)      |
| Grade 1           | -8                   |                 |                   |
| Grade 9-          | 12                   |                 |                   |
| Joined co         | ollege or university |                 |                   |
| Mother occupation | n Fa                 | ther occupation |                   |
| House wife        |                      |                 |                   |
| Government err    | nployee              |                 |                   |
| Private employ    | /ee                  |                 |                   |
| Daily laborer _   |                      |                 |                   |
| Farmer            |                      |                 |                   |
| Student           |                      |                 |                   |
|                   |                      |                 |                   |
| Anthropomet       | ry: MUAC             | WI              | FH                |
| WFA               | HFA                  |                 |                   |
| Chief complia     | nt:                  |                 |                   |

# I. Patient and parent demographics

# IV. Patient vital signs

| S. № | Vital sign                               |        | Value |       |  |
|------|--|--------|-------|-------|--|
|      |  | Actual | Lower | Upper |  |
|      |  | value  | limit | limit |  |
| 1    | Temperature ( in°C)                      |        |       |       |  |
| 2    | Respiratory rate (in breaths per minute) |        |       |       |  |
| 3    | Pulse rate (in beats per minute)         |        |       |       |  |
| 4    | Oxygen saturation (in %)                 |        |       |       |  |

# V. Laboratory investigations

|     |               |                  |        | Values      |             |
|-----|---------------|------------------|--------|-------------|-------------|
| S.№ | Investigation | Analysis         |        |             |             |
|     |               |                  | Actual | Lower limit | Upper limit |
|     |               | WBC              |        |             |             |
| 1   | CBC           | Nue (%)          |        |             |             |
|     |               | Lym (%)          |        |             |             |
|     |               | Mono (%)         |        |             |             |
|     |               | Normal           |        |             |             |
|     |               | Infiltration     |        |             |             |
| 2   | Chest x-ray   | Effusion/empyema |        |             |             |
|     |               | Hyperinflation   |        |             |             |
|     |               | Collapse         |        |             |             |
|     |               | Pneumatocoele    |        |             |             |
| 3   | ESR           |                  |        |             |             |
| 4   | G-stain       | Microorganism    |        |             |             |
| 5   | Culture       | Microorganism    |        |             |             |
| 6   |               |                  |        |             |             |
| 7   | Others        |                  |        |             |             |

## V. Constitutional signs/symptoms

|                       | Mark |                 | Mark |        |
|-----------------------|------|-----------------|------|--------|
| Sign/symptom          | (x)  | Sign/symptom    | (x)  | Others |
| Cough                 |      | Chest           |      |        |
|                       |      | indrawing       |      |        |
| Breath difficulty     |      | Wheezing        |      |        |
| Grunting              |      | Fast breathing  |      |        |
| Nasal discharge       |      | Whooping        |      |        |
|                       |      | cough           |      |        |
| Sputum production     |      | Diminished      |      |        |
|                       |      | breath sounds   |      |        |
| Loss of consciousness |      | Sore throat     |      |        |
| Appetite loss         |      | Enlarged tonsil |      |        |
| Ear discharge         |      | Fever           |      |        |
| Pallor                |      |                 |      |        |

# VI. Diagnosis\_\_\_\_\_

## VII. Co morbidity

| Co morbidity    | Mark (x) | Co morbidity | Mark (x) | Others |
|-----------------|----------|--------------|----------|--------|
| RVI             |          | Tuberculosis |          |        |
| Asthma          |          | Meningitis   |          |        |
| AKI/CKD         |          | UTI          |          |        |
| Heart failure   |          | Anemia       |          |        |
| AGE or Diarrhea |          | SAM          |          |        |

## VIII. Interventions offered

### Pharmacologic

| S.№ |              | Drug and regimen |       |           |          |  |  |  |
|-----|--------------|------------------|-------|-----------|----------|--|--|--|
|     | Drug name    | Dose             | Route | Frequency | Duration |  |  |  |
|     |              |                  |       |           | (days)   |  |  |  |
| 1   | Ampicillin   |                  |       |           |          |  |  |  |
| 2   | Gentamicin   |                  |       |           |          |  |  |  |
| 3   | C.pencilline |                  |       |           |          |  |  |  |
| 4   | Amoxicillin  |                  |       |           |          |  |  |  |
| 5   | Ceftriaxone  |                  |       |           |          |  |  |  |
| 6   |              |                  |       |           |          |  |  |  |
| 7   |              |                  |       |           |          |  |  |  |
| 8   |              |                  |       |           |          |  |  |  |

Is there any regimen change? a) Yes\_\_\_\_\_ b) No\_\_\_\_\_

If yes, use the following table

| S.№ | Regimen change for antibiotics          |  |  |  |        |  |  |  |
|-----|---|--|--|--|--------|--|--|--|
|     | Drug name Dose Route Frequency Duration |  |  |  |        |  |  |  |
|     |   |  |  |  | (days) |  |  |  |
| 1   |   |  |  |  |        |  |  |  |
| 2   |   |  |  |  |        |  |  |  |
| 3   |   |  |  |  |        |  |  |  |
| 4   |   |  |  |  |        |  |  |  |

## Non-pharmacologic

| S.№ | Туре         | Dose | Route | Frequency | Duration |
|-----|--------------|------|-------|-----------|----------|
|     |              |      |       |           | (day)    |
| 1   | Oxygen       |      |       |           |          |
| 2   | Cold         |      |       |           |          |
|     | Compress     |      |       |           |          |
| 3   | Paracentesis |      |       |           |          |
| 4   |              |      |       |           |          |
| 5   |              |      |       |           |          |
| 6   |              |      |       |           |          |

Use po, im, iv, id and in instead of oral, intramuscular, intravenous, intra-dermal and intranasal respectively

| Items         | Event                         |                           | Date |
|---------------|-------------------------------|---------------------------|------|
|               | Same (a                       | fter treatment completed) |      |
|               | Cured                         |                           |      |
| Is there      | ≠ ARI                         |                           |      |
| inhospital    | Pleural effusion or empyema   |                           |      |
| complication? | Lung abscess                  |                           |      |
|               | Pneumo                        | thorax                    |      |
| If yes, which | which Sepsis and septic shock |                           |      |
| and when      | Mening                        | itis                      |      |
|               | Acute r                       | heumatic fever            |      |
|               | Chronic otitis media          |                           |      |
|               | Ø                             |                           |      |
|               | Others                        |                           |      |
|               | 0                             |                           |      |
|               |                               |                           |      |
|               |                               | Self-discharged           |      |
| Discharge     | Alive                         | Discharged                |      |
| status        | Died                          | ·                         |      |

## IX. Post treatment events

# X. Miscellaneous inquiries

| Does anybody smokes in house? a) yes   | b) no               |  |  |  |
|--|---------------------|--|--|--|
| Is there any indoor/outdoor pollution (vehicle pollution, industry pollution, wood |                     |  |  |  |
| pollution)? a) yes b) no   |                     |  |  |  |
| For how long months does the child stay on EBF? a) $< 6$                           | b) ≥6               |  |  |  |
| What is the vaccination status of the child?                                       |                     |  |  |  |
| a) Fully vaccinated b) partially vaccinated  | _ c) not vaccinated |  |  |  |
| Did the child have previous history of ARI? a) yes                                 | _b) noc) uncertain  |  |  |  |
| Antibiotic treatment 90 days prior to admission: a) yes                            | b) no               |  |  |  |
| What was the gestational age of the neonate?                                       |                     |  |  |  |
| What was the birth weight of children (kg)?  |                     |  |  |  |
| For how long the child stay at home while sick?                                    |                     |  |  |  |

| ካርድ ቁጥር፡         | አልጋ ቁ                       | ፕር:         | ፆታ: ወ              | ወንድ         | ሴት |
|------------------|-----------------------------|-------------|--------------------|-------------|----|
| ዕድሜ:             | አድራሻ:                       |             | P                  | መግቢያ ቀን: _  |    |
| ነዋሪነት: ሀ) ነጠር    |                             | ለ) ከተማ _    |                    |             |    |
| በቤተሰብ ውስጥ የ      | ልጆች ብዛት :                   |             |                    |             |    |
| የትምህርት ደረጃዎ      | ምንድነው? እናት                  |             | አባት                |             |    |
| ክፍል 1            | - 8                         |             |                    | _           |    |
| 9-12             | ከፍል 9                       |             |                    |             |    |
| ኮሌጅ              | ወይም ዩኒቨርሲቲ ንብ               | በቷል         |                    |             |    |
| ሥራዎ ምንድን ነው?     | እናት                         | ኣባት         |                    |             |    |
| የቤት ሚስት          |                             |             |                    |             |    |
| የመንግስት ሰሪ        | ሩተኛ                         | _           |                    |             |    |
| የግል ሰራተኛ         | t                           |             |                    |             |    |
| ዕለታዊ ሥራ          | ፈላጊ                         |             |                    |             |    |
| አርሶ አደር          |                             |             |                    |             |    |
| ተማሪ              |                             |             |                    |             |    |
| ሌላ               |                             |             |                    |             |    |
|                  |                             |             |                    |             |    |
| ማንኛውም ሰው (       | ቤት ውስጥ ያጨሳል                 | ? ሀ)አዎ      |                    | ለ) ምንም      |    |
| የውጭ ብክለት አለ      | ? ሀ) አዎ                     | ለ) አይ       |                    |             |    |
| ልጅዎ ለምን ያህል      | ጊዜ በጡት ብቻ ቆይ                | ራተዋል? ሀ) <6 | <u>م</u> (۸) 6 - 1 | 12h)> 1     | 2  |
| የልጁ የክትባት ደረ     | ጃ ምንድን ነው?                  |             |                    |             |    |
| <i>ህ</i> ) ሙሉ በሙ | ሉ ወስደዋል                     | _ ለ) በከፌል ሪ | ወስደዋል              | _ ሐ) ኣልወሰደፃ | u  |
| የርግዜና ጊዜ ስንት ነበ  | C?                          |             |                    |             |    |
| የልጁ የወሊድ ክብያ     | ዴት (ኪ.ግ.) ስንት ነበ            | IC?         |                    |             |    |
| ልጁ ከታመመ በኋላ ሃ    | <sup>ው</sup> ን ያህል ጊዜ በቤት ( | ውስጥ ቆይተዋ    | እ?                 |             |    |

| Iddoo jireenyaa a) baadiyaa b)   |
|--|
| magaalaa   |
| Baay'ina ijoollee maatii keessatti   |
| Sadarkaa barnootaa a) kan haadhaa b) kan bbaa  |
| kutaa 1-8  |
| kutaa 9-12   |
| koollejjii ykn yuuniiversiitii   |
| gahee hojii a) kan haadhaab) kan abbaa   |
| haadhamanaa  |
| hojjataa/ttuu mootumaa   |
| hojii dhuunfaa   |
| hojjataa/ttuuguyyaa  |
| qonnaan bulaa/ttuu   |
| barataa/ttuu   |
| kanbiroo   |
| Mana keessan keessatti namni tamboo xuuxu n ijiraa? a) eyyee b)                            |
| lakkii   |
| Wantootni faalama qilleenssaa fidan(warshaa, konkolaattota fi kkf) naannoo keessan nijiraa |
| a) eyyeeb) lakkii  |
| Daam'imni keessan ji'a meeqaaf harma haadhaa qofa hodhaaturee/ttee? a) < 6b) $\geq$ 6      |
| Sadarkaa talaallii daa'imakeessan maalirra jiraa?  |
| a) guutuub) walakkaac) gonkuma   |

kanaan dura rakkoon infeekshinii qaamaolee harganssuu daa'ima keessan irratt argamee beekaa? a) eyyee\_\_\_\_b) lakkii\_\_\_\_c) hinbeeku\_\_\_\_

Guyyoottaan 90'n darban keesstti daa'imnni keessan dawaa infeekshinii fudhatee/tteea)

eyyee\_\_\_\_\_b)lakkii\_\_\_\_\_

Daa'imni keessaan ji'a meeqaffaatti dhalate/ttee?

Ulfaatinni daa'ima keessanii yeroo dhalatu/ttuumeeqaa(kg)?\_\_\_\_\_

Daamni keessan dhukubsatee/ttee osoo gara mana yaalaa hin dhufin guyyaa meeqafmana

turee/ttee?