

# **Clinical and etiological profile of community acquired Pneumonia in 1 -36 months of age group**



**THESIS**

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**DECLARATION**

I declare that the thesis titled -**Clinical and etiological profile of Community acquired Pneumonia in 1 -36 months of age group**, embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

  
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**CERTIFICATE**

This is to certify that the thesis titled '**Clinical and etiological profile of Community acquired Pneumonia in 1 -36 Months of age group**' is the bonafide work of **Dr Chityala Ashwini** carried out under our guidance and supervision, in the Department of Pediatrics, All India Institute of Medical Sciences, Jodhpur.

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## **LIST OF ABBREVIATIONS**

<b>WHO</b>	World health Organization
<b>CAP</b>	Community Acquired Pneumonia
<b>TLC</b>	Total Leukocyte count
<b>PCV</b>	Pneumococcal Conjugate Vaccine
<b>UNICEF</b>	United Nations children Fund
<b>RSV</b>	Respiratory syncytial virus
<b>H influenza</b>	Haemophilus Influenza
<b>M Pneumonia</b>	Mycoplasma Pneumonia
<b>S Aureus</b>	Staphylococcus Aureus
<b>GERD</b>	Gastro-oesophageal reflux disease
<b>DOB</b>	Difficulty of breathing
<b>CNS disorders</b>	Central Nervous system
<b>LRTI</b>	Lower Respiratory tract Infection
<b>TEF</b>	Tracheoesophageal fistula
<b>HIV</b>	Human Immunodeficiency disease
<b>AIDS</b>	Acquired Immunodeficiency Disease
<b>SCID</b>	Severe Combined Immunodeficiency disease
<b>CGD</b>	Chronic granulomatous disease
<b>PCD</b>	Primary Ciliary dyskinesia
<b>CPAM</b>	Congenital Pulmonary Airway Malformation

<b>LAD</b>	Leukocyte adhesion disease
<b>WBC</b>	Whole blood count
<b>CRP</b>	C reactive protein
<b>PCT</b>	Procalcitonin
<b>PCR</b>	Polymerase Chain reaction
<b>NP swab</b>	Nasopharyngeal swab
<b>IV</b>	Intravenous
<b>MRSA</b>	Methicillin-resistant Staphylococcus aureus
<b>OPD</b>	Outpatient department
<b>CPAP</b>	Continuous positive airway pressure
<b>Hib</b>	Haemophilus influenza type B
<b>COPD</b>	Chronic Obstructive Pulmonary disease
<b>RT PCR</b>	Reverse Transcriptase Polymerase chain reaction
<b>CI</b>	Confident Interval
<b>MEDLINE</b>	Medical Literature Analysis and Retrieval System Online
<b>EMBASE</b>	Excerpta Medica database
<b>ARDS</b>	Acute Respiratory distress syndrome
<b>EBF</b>	Expressed breastfeeding
<b>E. coli</b>	Escherichia Coli
<b>CONS</b>	Coagulase Negative Staphylococcus Aureus
<b>PICU</b>	Paediatric Intensive care unit

<b>IPD</b>	In patient Department
<b>VRDL</b>	Virus research disease laboratory
<b>TB</b>	Tuberculosis
<b>LSCS</b>	Lower segment caesarean section
<b>EBM</b>	Expressed Breast milk
<b>LBW</b>	Low birth weight
<b>CHD</b>	Congenital heart disease
<b>TTNB</b>	Transient Tachypnoea of New-born
<b>MSL</b>	Meconium-Stained liquor
<b>BCG</b>	Bacillus Calmette Guerin
<b>OPV</b>	Oral polio virus
<b>IPV</b>	Inactivated polio Virus
<b>MMR</b>	Measles Mumps Rubella
<b>PHC</b>	Primary health centre
<b>HC</b>	Head circumference
<b>LAMA</b>	Leave against Medical Advice
<b>HFNC</b>	High Flow nasal cannula
<b>CMV</b>	Cytomegalovirus
<b>NVD</b>	Normal Vaginal delivery
<b>URTI</b>	Upper Respiratory tract infection
<b>WOB</b>	Work of breathing

<b>SCR</b>	Sub costal Retractions
<b>ICR</b>	Inter costal Retractions
<b>RR</b>	Respiratory rate
<b>HR</b>	Heart rate
<b>ATT</b>	Antitubercular therapy
<b>BAE</b>	Bilateral air entry

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# INTRODUCTION



## **INTRODUCTION**

Community-acquired pneumonia (CAP) is an acute infection of lung parenchyma by a spectrum of pathogens acquired outside hospital settings or in the community. This subsequently results in inflammation of lung tissue. Clinically, it can be defined as symptoms of fever, cough, tachypnoea (fast breathing), and signs of respiratory distress. In young children, it may present with nonspecific features (1).

Globally, it is a leading cause of death in children under 5-years of age. Pneumonia deaths rates are closely linked to poverty, with the highest mortality rates in poorly developed countries like India.

WHO has categorized CAP under 5-years of age into pneumonia and severe pneumonia. There will be fast breathing with or without chest indrawing in pneumonia, while fast breathing with danger signs as severe pneumonia. Fast breathing is defined as respiratory rates of >60 per minute for infants less than 2months, >50 per minute for infants of 2-12months, >40 per minute for children >12months of age.

The etiological profile of pneumonia is age-based. In Infants and younger children, Viruses and bacterial causes are more common; in adolescents' atypical organisms are more seen. Multiple risk factors predispose to pneumonia-like host factors, environmental factors like poverty, overcrowding, indoor air pollution etc.

The diagnosis of CAP is primarily clinical. WHO clinical criteria help in the classification of severity of pneumonia and management. If clinical findings are inconclusive, chest x rays along with blood investigations may help. Acute phase reactants do not help distinguish bacterial, atypical bacterial, and viral pneumonia but may help decide the antibiotic duration, disease course, determine when therapy can be discontinued.

Lung ultrasound has become a valuable tool in diagnosing disease and complications in recent years. Blood cultures were unnecessary for non-sick-looking children because of the low yield. The polymerase chain reaction of nasopharyngeal aspirates or swabs can be used in a rapid diagnostic tool to identify both bacterial and viral groups of pathogens. Rapid testing should be done in flu season; if positive, antiviral medications can be started. (2)

The management of CAP includes protection by adequate breastfeeding and early start of complementary feeding and prevention of risk factors and treating the child with supportive treatment and adequately with antibiotics. The decision regarding starting antibiotics and

their duration are based on clinical diagnosis and assessment. In severe CAP, the child must be hospitalized and started on IVF fluids if the intake is poor. They may require respiratory support either non-invasive or invasive, based on the clinical parameters of the child.

Prevention is the most critical step in the management of CAP. Vaccination, nutrition, and environmental controls are essential components of the prevention of CAP. The introduction of the pneumococcal vaccine resulted in a reduction in pneumonia hospitalizations among children. After introducing PCV-7 and PCV-13 in the United States, there is a 35 % and 16-27% reduction in hospitalization rate in pneumonia, respectively. (3) The WHO recommends that all routine childhood immunization programs include these vaccines to protect against pneumonia. Vaccinations help reduce childhood pneumonia in two ways. It helps prevent children from developing infections that directly cause pneumonia, such as Hib and *S. pneumoniae*. Second, vaccinations prevent infections that can lead to pneumonia as a complication, such as influenza, measles, and pertussis. This is also called indirect protection.

There is a paucity of data on the etiological profile of CAP in the western part of Rajasthan, especially after the introduction of multiple vaccination programs. There is a poor vaccination rate in western Rajasthan, impacting the CAP and its severity.

Therefore, we planned a cross-sectional study to find out the clinical and etiological profile of CAP from western Rajasthan and to know the impact of vaccination on the severity and outcome of pneumonia in the child.

# **REVIEW OF LITERATURE**

## **REVIEW OF LITERATURE**

### **DEFINITION:**

CAP is defined as an acute infection of lung parenchyma by a spectrum of pathogens acquired outside the hospital setting or community. This subsequently results in inflammation of lung tissue(1).

### **EPIDEMIOLOGY**

#### ***The global prevalence of pneumonia:***

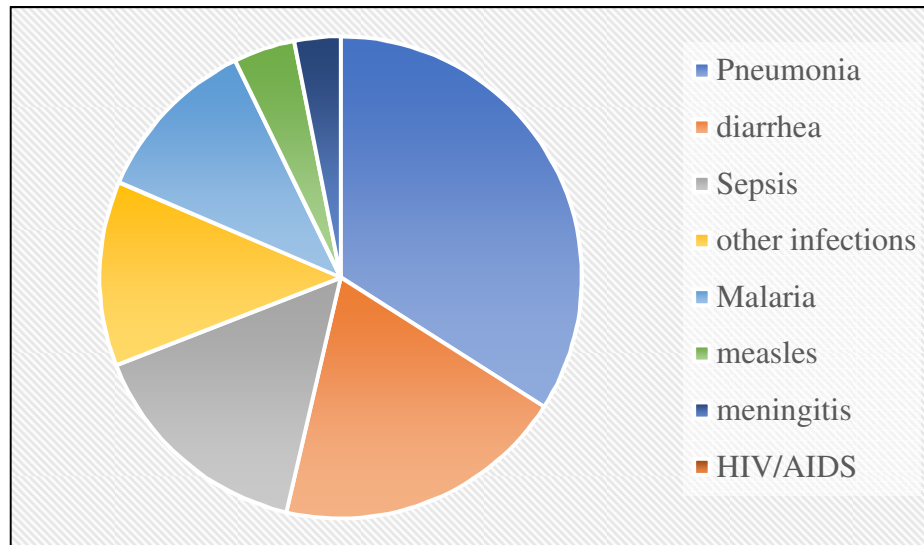
Pneumonia accounts for about 14% of deaths in children under five years of age. It affects the most among the developing countries, with the highest deaths in south Asia and sub-Saharan Africa. The global prevalence of under-five mortalities has been shown in **Fig-1**. Between 2000 to 2015, there was a significant reduction in the incidence of pneumonia from 83.8 million cases to 49.8 million cases which are around a 41 % reduction in pneumonia cases. (4)

David A McAllister conducted a systemic analysis to determine the global, regional, national estimate of pneumonia mortality and morbidity in children younger than five years between 2000 to 2015. It was found that the number of clinical pneumonia cases decreased by 22% (178 million in 2000 to 138 million in 2015). India, Nigeria, China contributed to more than 54% of all global pneumonia cases, with 32% global burden from India. 49% of global death pneumonia occurs in India. All key risk factors for child pneumonia were non-exclusive breastfeeding, crowding, malnutrition, indoor air pollution, HIV, incomplete immunization, and low birth weight(5).

#### ***Indian prevalence of pneumonia:***

The incidence of pneumonia in children under 5years in India was 657 cases per 1000 children in 2000 and 403 cases per 1000 children in 2015. Severe pneumonia accounts for about 8.4 million cases, with 68 cases per 1000 children. The highest affected states include Uttar Pradesh (12.4 million- 565 cases for 1000 children), Bihar (7.3 million), Madhya Pradesh (4.6 million- 563 cases for 1000 children). The most significant reduction was seen in Kerala (82% reduction)

**Figure 1: Global Distribution of Cause-Specific Mortality in Under 5 Children**



## ETIOLOGY

CAP is caused by a wide range of pathological agents. It varies as per the age of children. The age-wise etiology of CAP is summarized in **Table-1**. The common bacterial etiology and their characteristics pattern have been shown in **Table-2**.

The aetiology also differs with underlying host conditions. In chronic respiratory diseases like cystic fibrosis, *Pseudomonas* and *Staphylococcus* are more common. In children with sickle cell, disease *Pneumococcus* is common. Immunocompromised children should be evaluated for opportunistic infections like *Pneumocystis jirovecii*, *cytomegalovirus*, and *funga* species.

**Table-1: Age-wise aetiology of pneumonia**

Age	Aetiological agents
Neonate <3weeks	<i>Group B streptococcus</i> , <i>E. coli</i> , <i>Streptococcus pneumonia</i> , <i>H influenzae</i>
3weeks to 3months	Viruses: <i>RSV</i> , <i>Rhino</i> , <i>influenza</i> , <i>parainfluenza</i> Bacteria: <i>Streptococcus pneumonia</i> , <i>H influenzae</i> , <i>Chlamydia</i>
4month to 4years	Viruses: <i>RSV</i> , <i>Rhino</i> , <i>influenza</i> , <i>parainfluenza</i> Bacteria: <i>Streptococcus pneumonia</i> , <i>H influenzae</i> , <i>Mycoplasma</i>
>5years	<i>Mycoplasma</i> , <i>Chlamydia</i> , <i>streptococcus pneumonia</i> , <i>H influenzae</i>

**Table-2: Common Bacterial Causes of Infectious Pneumonia**

<b>Bacteria</b>	<b>Clinical Characteristics</b>
<i>Streptococcus pneumonia</i>	Consolidation, empyema
<i>Group B streptococci</i>	Seen in Neonates
<i>Group A Streptococcus</i>	Empyema
<i>Staphylococcus aureus</i>	Can cause Pneumatoceles, empyema, nosocomial infection
<i>Mycoplasma</i>	More in adolescents
<i>Chlamydia</i>	More in adolescents
<i>Mixed anaerobes</i>	Aspiration pneumonia

Manon C M *et al.* conducted a prospective study between 2003 to 2005 to find out the causative agents among children hospitalized for CAP. Cases were enrolled as per the WHO clinical criteria, and blood samples and RT PCR swabs were obtained. The detection of streptococcus pneumonia was performed by real-time PCR (20). The results show a high prevalence of viruses and frequent occurrence of co-infection in childhood. The higher proportion of *streptococcal pneumonia* in severe CAP reemphasized the importance of pneumococcal immunization and antibiotics for the treatment of CAP(6)

A systemic review by Rodrigo, DA *et al.* observed *Streptococcus pneumonia*, *Haemophilus influenza*, and *Mycoplasma* were the most common bacterial pathogens. (7)

## Pathology of pneumonia

There are 4-stage in the pathology of pneumonia; these are inflammatory, red hepatization, grey hepatization, and resolution. It has been summarized in **table-3**.

**Table-3: Stages of pneumonia**

<b>Inflammatory phase</b> It occurs within 24 hours and is characterized by alveolar oedema and vascular congestion. Both bacteria and neutrophils are present.	<b>Red hepatization</b> It has the consistency of the liver and is characterized by neutrophils, red blood cells, and desquamated epithelial cells, with Fibrin deposits in the alveoli, which are common.
<b>Grey Hepatization</b> Due to the accumulation of hemosiderin and haemolysis of red cells	<b>Resolution</b> Cellular infiltrates are resorbed, and the pulmonary architecture is restored; if the healing is not ideal, it may lead to parapneumonic effusions and pleural adhesions

## Pathophysiology of Pneumonia

In the lower Respiratory tract, there are many defence mechanisms like mucous ciliary clearance, secretion of immunoglobulin A and macrophages fighting against bacteria, and airway clearance by coughing as a defence mechanism. More recent models postulate that pneumonia results from disruption of a complex lower respiratory ecosystem that is the site of dynamic interactions between potential pneumonia pathogens, resident microbial communities, and host immune defences.

## Pathogenesis of Viral Pneumonia:

Pathogenesis of viral pneumonia occurs in 3 steps-Breach in the epithelial barrier, leading to the inflammation in small calibre vessels resulting in the ventilation and perfusion mismatch which is summarized in the table. Viral pneumonia can also predispose to bacterial pneumonia.

## Pathogenesis of Bacterial Pneumonia (8)

Most often, respiratory tract organisms colonise the trachea and gain access to the lungs, but pneumonia may also result from direct seeding of lung tissue after bacteraemia.

Mechanism of different organisms are summarized below-**table 4**

**Table 4: Pathogenesis of bacterial pneumonia**

Organism	Mechanism of destruction
<i>M. pneumoniae</i>	Attaches to the respiratory epithelium, inhibits ciliary action, cellular destruction and inflammatory response in the submucosa. The infection progresses along the bronchial mucosa and causes obstruction
<i>S. pneumoniae</i>	Produces local oedema that aids in the proliferation of organisms and their spread into adjacent portions of the lung, often resulting in the <i>characteristic focal lobar involvement</i>
<b>Group A <i>Streptococcus</i></b>	More <i>diffuse lung involvement with interstitial pneumonia</i> Pathology includes oedema, exudate, necrosis and local haemorrhage of tracheobronchial mucosa with extension into the interalveolar septa and pleural involvement.
<i>S. aureus</i>	Manifests as confluent bronchopneumonia with complications resulting in <i>pneumatocoles, empyema and bronchopulmonary fistulas</i> .

**In a study conducted by Singh MK *et al* Clinico-bacteriological profile of community-acquired pneumonia in age group 3 to 59months of age children**, which is a cross-sectional study, the most common symptoms in decreasing order of frequency (cough (90.7%, fever 88%, DOB 81%, Refusal to feeds 41% ). The most common organism isolated was *Staphylococcus aureus* in both nasopharyngeal swab (18.7%) and blood cultures (14.7%). other common organisms in NPS shows *streptococcus pneumonia* (6%), *E. coli* (4.7%), *Klebsiella* (4.7 %). In blood culture, the common organism detected after *S aureus* were *E coli* (5.3%), *S pneumoniae* (3.3%), *Klebsiella* (3.3%).



It was observed that staphylococcus aureus was the most common organism in the study, Inclusion of pentavalent vaccine in universal immunization programme may be the cause of change in the etiological profile of pneumonia in under 5 age group(9)

## **RISK FACTORS**

There are several known risk factors for CAP related to the host and environmental factors(7–12).

### **Host factors**

- Low birth weight
- Preterm/term
- Mode of delivery
- Duration of breastfeeding (13,14)
- Type of feeding (Breast milk vs other top feed)(13,15)
- Vaccination status(7,16)
- Malnutrition(17–20)

### **Environmental factors**

- Smoking history
- Overcrowding
- Indoor air pollution

### **Underlying cardiopulmonary and other medical conditions predispose to pneumonia(21)**

- Congenital heart disease
- Bronchopulmonary dysplasia
- Cystic fibrosis
- GERD
- Tracheoesophageal fistula
- Neuromuscular disorders and CNS disorders pseudobulbar palsy
- Congenital and acquired immunodeficiency

A study done by Kasundiya S *et al*, Incidence and Risk Factors for Severe Pneumonia in Children Hospitalized with Pneumonia in Ujjain, India which is the prospective study in

which a total of 270 children were enrolled 64% had severe pneumonia (22). The following are significant risk factors identified for severe pneumonia were Prematurity, History of measles, Incomplete vaccination, A cyanotic heart disease, Home tried treatment, Overcrowding, Poor ventilation and open Defecation. (22)

## **CLINICAL PRESENTATION**

The clinical presentation of CAP is variable. The common clinical presentation of CAP are followings: -

- Fever and cough and coryza
- Fast breathing (Tachypnoea)
- Increased work of breathing (Accessory muscle use cause nasal flaring, intercostal, subcostal and suprasternal retractions)
- General danger Signs
- Decreased feeding, decreased activity, decreased sensorium, seizures, cyanosis
- Associated symptoms: Headache, photophobia and rash in mycoplasma pneumonia(23)

Bacterial pneumonia typically begins suddenly with high fever, cough, and chest pain, drowsiness with intermittent periods of restlessness. Signs of respiratory distress are more specific than fever or cough for pneumonia which includes tachypnoea, hypoxemia (SPO<sub>2</sub> <94% in room air), increased work of breathing, decreased sensorium(24). Grunt is a sign of severe disease and impending failure(20,25)

On clinical examination following findings may be observed: - (26–29)

- Decreased breath sounds
- Bronchial breath sounds
- Adventitious sound: crepitations and/or wheezing
- Bronchophony
- Dullness on percussion

It's often difficult to localize the source of these adventitious sounds in very young children with hyper resonant chests. It is often difficult clinically to distinguish viral pneumonia (especially adenovirus) from disease caused by bacterial pathogens.

Yudhavir *et al.* conducted an observational study in western Rajasthan study of Bacteriological and clinical profile of community-acquired pneumonia in hospitalised children with associated co-morbidity in a tertiary care centre of western Rajasthan(28).

The clinical presentation shows tachypnoea in (89.2%) and retractions (83.8%) were the important findings followed by crepitations (72.3%) wheeze (14.6%) and abnormal breath sounds (15.3%) and the mc organism isolated in blood culture was *Staphylococcus aureus* (10%) followed by *Streptococcus pneumonia* (3.1%) were as in nasopharyngeal aspirate culture was *Streptococcus pneumonia* (18.5%), followed by *Staphylococcus aureus*(30).

## **DIAGNOSIS of CAP**

The diagnosis of CAP is mainly clinical. A routine investigation is not needed in typical CAP. The laboratory test is only needed when the child does not respond to first-line therapy or have an atypical presentation.

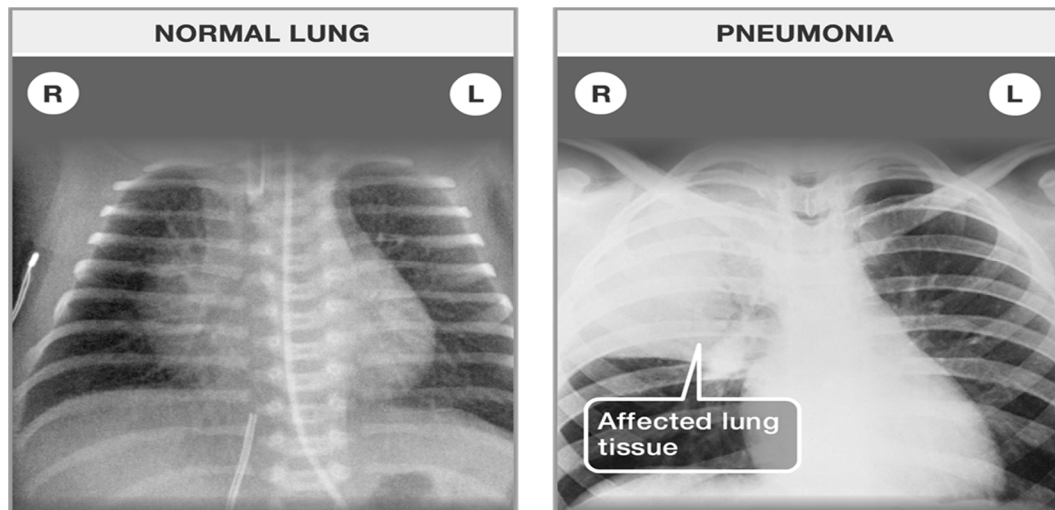
### **Laboratory Evaluation:**

Complete hemogram should be done in children requiring hospital admission or severe pneumonia

- WBC count <15000/microL is suggestive of non-bacterial aetiology, except in neutropenic patients
- WBC >15000/microL is suggestive of pyogenic bacterial disease, however atypical and influenzae pneumonia also has the same. (31)
- Measurements of CRP or PCT do not help distinguish bacterial, atypical bacterial and viral pneumonia but help decide the Antibiotic duration, disease course, determine when therapy can be discontinued(32,33)
- Blood cultures are not required for non-toxic children, but it is required who require hospitalization, IV antibiotics and in severe pneumonia (2,29,34,35)
- PCR testing of respiratory secretions from NP swabs can be used as a rapid diagnostic tool for bacterial like streptococcal and *Mycoplasma pneumonia* and viral gents like RSV and *Hemophilus influenzae*(36). Nasopharyngeal swab for PCR is now the mainstay in the detection of virus, the results are rapid and available within 1 to 6hours. Tests to the viral pathogen are done more in the flu season to increase the yield (2,37,38).
- For pertussis diagnosed by PCR and culture, culture is the gold standard

- Chest x-ray: A infiltrate on chest radiograph supports the diagnosis of pneumonia, viral pneumonia characterised by bilateral interstitial infiltrates with hyperinflation of chest and bacteria pneumonia shows focal consolidation can also identify complications like pleural effusion and empyema. **Figure-2**

**Figure-2 describes the Normal lung and pneumonia**

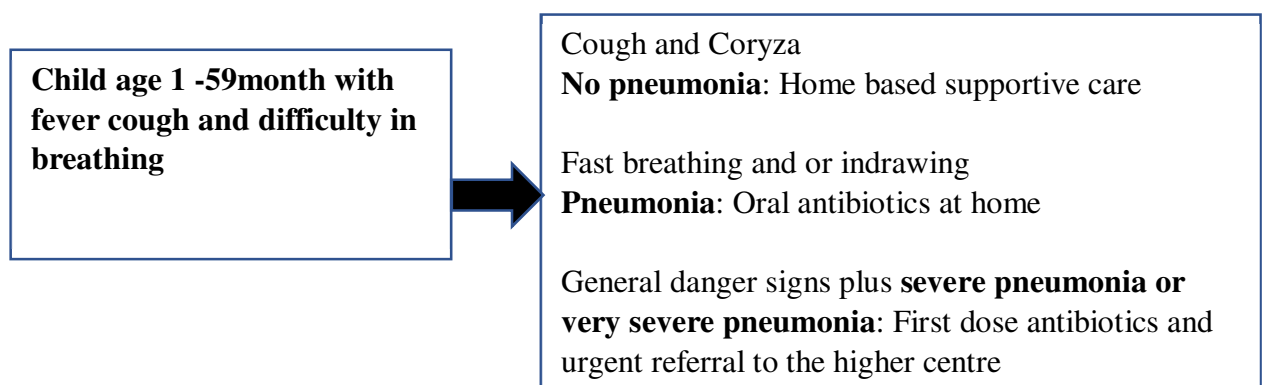


**Normal, B. Right upper lobe consolidation**

- A recent study shows USG is the trending investigation for the CAP. Point-of-care use of portable ultrasonography is highly sensitive and specific in diagnosing pneumonia in children by determining lung consolidations and air Broncho grams or effusions (8,36,37).

### **Management of Pneumonia**

The revised WHO criteria and classification and treatment for childhood pneumonia at health care facilities classify pneumonia in only two categories. (**Table-5**)



## **Outpatient management**

In the child with fast breathing and chest, indrawing without danger signs can be treated with oral amoxicillin for 5 days. In severe pneumonia the child should be treated with IV Penicillin and gentamicin for at least 5 days, IV ceftriaxone was considered a second-line drug(41).

## **Inpatient management;**

The factors suggesting the Need for Hospitalization in CAP in children are the following (40).

- Age < 6 months
- Immunocompromised state
- Toxic appearance
- Moderate to severe respiratory distress
- Hypoxemia (Oxygen saturation < 90% room air)
- Complicated pneumonia (empyema, pleural effusion, pneumothorax.
- Vomiting or inability to tolerate oral fluids or medications
- Severe dehydration
- No response to appropriate oral antibiotic therapy
- Social factors (e.g., the inability of caregivers to administer medications at home

Hospitalized children should receive supportive care like intravenous fluids, respiratory support, including supplemental oxygen, HHHFNC, continuous positive airway pressure (CPAP), mechanical ventilation and vasoactive medications for hypotension.

## **Outcome of CAP**

Most of the children with CAP improve with adequate therapy if the diagnosis is made at the time and instituted the adequate therapy. However, some children with CAP may develop complications. These complications are followings: -(43,44)

In Staphylococcal and streptococcus pneumonia, pneumatocele is pathognomic. Other complications like staphylococcal pneumonia include lung abscess which can erode pericardium can cause purulent pericarditis. Pulmonary infection can also be

pyopneumothorax, disseminated infection to the Joint, bone, liver, brain, mastoid. Empyema and abscess need Intercoastal drainage and abscess should be surgically drained along with good antibiotics coverage.

In Hemophilus pneumonia subacute presentation with bacteraemia, empyema, pericarditis, meningitis, polyarthritis as a complication

### **Mortality in CAP**

According to a study conducted by Davit *et al* which is a systemic review, a study regarding Global child mortality reduced substantially during the Millennium Development Goal period (2000-15). (5) Which shows the incidence of both clinical and severe pneumonia decreased by 30%, case fatality rate decreased by 32% and mortality by 50% for childhood pneumonia. This reduction was due to multiple factors like a decrease in the prevalence of some risk factors of pneumonia (Malnutrition, overcrowding, measles vaccination) increase in socio-economic development and quality care in the hospital sector and the development of Health programme factors. (5). The decrease can be partly attributed to the introduction and scale-up of vaccines against bacterial pneumonia (H influenzae type b and Streptococcus pneumoniae(45).

According to the WHO, Pneumonia killed 14% of all children under five years old but 22% of all deaths in children aged 1 to 5.

### **PREVENTION OF CAP**

CAP can be prevented to large extent. Several preventive factors have been recognised.

**Protect:** Adequate breastfeeding for 6months followed by addition of Complementary solid nutritious foods till 2years

**Prevent:** Regular handwashing with soap, Reducing indoor air pollution and shift to gas stove ventilation, Vaccination as per schedule, Control of overcrowding.

**Vaccination:** Vaccination is not intended to be used for the treatment of active infection. Currently, three vaccines have significantly reduced childhood mortality from and related to pneumonia High rates of vaccination for H. influenzae type b, pertussis, and measles remains important for the prevention of pneumonia.

A study by Rodrigo De Antonio *et al* which is a systemic review evaluated the epidemiology of CAP and implications for vaccination of children living in developing and newly industrialized countries(7) Highest prevalence was in Chinese children < 6months of age. The main bacterial pathogen was streptococcus pneumoniae, Haemophilus influenza and Mycoplasma

The data presented provide the best available evidence on the burden of CAP data up to 2012, before pneumococcal vaccines were widely used in the countries considered, and show critical gaps in the pathophysiology, aetiology and epidemiology of pneumonia in the included countries. Therefore, several preventative and management measures aimed at reducing the burden of CAP in developing and newly industrialised countries are essential (7).

### **Pentavalent Vaccination**

The pentavalent vaccine protects against five diseases: diphtheria, tetanus, pertussis, hepatitis B and Hib. In 2011, the Government of India introduced the Hib-containing pentavalent vaccine in a phased manner.

### **Pneumococcal Vaccine:**

Children must receive all recommended doses in the vaccine schedule for maximum protection. The introduction of PCVs resulted in a reduction in the incidence of pneumonia hospitalizations among children. After the introduction of PCV 7 and PCV 13 in the United States, there is a 35 % and 16-27% respectively reduction in hospitalization rate in pneumonia.

In one study done by Maria Pavia *et al* in 2008, done by Meta-analysis about the efficacy of the pneumococcal vaccine in children younger than 24months. The results showed the efficacy of PCV to prevent clinical pneumonia was 6% (2%–10%) and 7% (95% CI: 2%–11%), whereas for the prevention of radiograph-confirmed pneumonia it was 29% (95% CI: 22%–35%) and 32% (95% CI: 24%–39%), respectively. Pneumococcal vaccine is included in the national immunization program, after adding the burden of pneumonia and decreased mortality among children with pneumonia is observed(16)

## Influenza Vaccination

Influenza vaccine may also prevent pneumonia hospitalizations among children and should be administered to all children >6 months of age. For infants <, 6 months of age, household contacts and other primary caregivers should be immunized.

Influenza virus is the commonest cause of viral pneumonia in high-risk infants, elderly, pregnant women, so the only virus that has an established global vaccination program.

## Measles vaccination:

The measles infection can affect multiple organ systems including the lungs and can suppress the immune response transiently, putting infected children at risk of secondary bacterial pneumonia. The measles vaccine prevents the systemic viral infection caused by measles.

The population should prioritize for influenzae vaccination includes children with comorbidities like Asthma, COPD, Chronic cardiovascular, renal, hepatic, homological disorders and metabolic disorders and children on immunosuppression.

**Table-6: SUMMARY OF RELEVANT STUDIES**

S. n o	Author & Year of publication	Study design and title	Study sample	Outcome measure	Conclusion
1	Pavia M <i>et al</i>	2000 to 2008 Meta-analysis	310 citatio n	To estimate the efficacy of PCV vaccination in children	Pneumococcal vaccine is included in the national immunization program, after adding the burden of pneumonia and decreased mortality among children with pneumonia is observed.
2	Singh MK	Cross-sectional	150	Clinico	Staphylococcal aureus is



	<i>et al</i>	study  Clinic bacteriological profile of CAP in age group 3 to 59months		bacteriological profile of CAP	the most common organism
3	Rodrigo DeAntonio <i>et al</i> 1999- 2011	Systemic Review  Epidemiology of CAP and implications for vaccination of children living in developing and newly industrialized countries		Epidemiology and implication of vaccination of CAP	The main bacterial pathogen was streptococcus pneumoniae, Haemophilus influenza and Mycoplasma
4	Sunil Kumar Kasundriya <i>et al</i> 2020	Prospective study  Incidence and Risk Factors for Severe Pneumonia in Children Hospitalized with Pneumonia in Ujjain, India	270 Patient s	Incidence and Risk Factors for Severe Pneumonia in Children	Awareness of this risk factor reduces the severe pneumonia Prematurity History of measles Incomplete vaccination A cyanotic heart disease Home treatment tried Overcrowding Poor ventilation Open defecation

5	David Macallister <i>et al</i> 2019	Systemic Review  Global, regional and national estimates of pneumonia morbidity and mortality in children <5years		To estimate the burden of pneumonia in the form of incidence, no of clinical pneumonia, risk factors and deaths	Results show there is a significant reduction in incidence and mortality according to the study.
6	Manon Cevey-Macherel <i>et al</i> 2003-2015	Prospective study  To identify the Aetiology of CAP in hospitalized children	99	Causative agents among children hospitalized for community-acquired pneumonia defined by WHO guidelines and to relate and correlate aetiology with clinical severity and surrogate markers	The results show a high prevalence of viruses and a higher proportion of streptococcal pneumoniae in severe CAP reemphasized the importance of pneumococcal immunization and antibiotics for the treatment of CAP. Dehydration and Acute phase reactants are significantly higher in bacterial pneumonia in the study
7	Yudhavir <i>et al</i>	Observational study  Bacteriological and clinical profile of community-acquired		Bacteriological and clinical profile of community-acquired pneumonia	Blood culture was Staphylococcus aureus (10%) followed by Streptococcus pneumonia (3.1%)  Nasopharyngeal aspirate

		pneumonia in hospitalised children with associated co-morbidity in a tertiary care centre of western Rajasthan			culture Streptococcus pneumonia (18.5%), Staphylococcus aureus
8	Jagdish, Prawin Kumar <i>et al</i>	Prospective cohort study Risk factors for the development of pneumonia and severe pneumonia in children	7026	Risk factors for severe pneumonia	Young age and undernutrition in children are independent risk factors for pneumonia

## **Lacunae in the existing knowledge**

1. There are limited data of age-based aetiology of various organisms in CAP in children after the introduction of multiple vaccination programs from India, especially in the western part of Rajasthan.
2. Even after multiple vaccination programs, still there is a lack of adequate vaccination coverage. There are limited studies on the impact of vaccination and the severity of pneumonia in the western part of Rajasthan.

## **RESEARCH QUESTION**

What are the clinical presentation and aetiology of CAP in children 1-36 months of age?

# **AIM & OBJECTIVES**

## **AIM AND OBJECTIVES**

### **AIM:**

The Clinical and Etiological profile of Community-Acquired Pneumonia in children from 1 -36 Months of age group and the impact of vaccination on the severity of pneumonia.

### **PRIMARY OBJECTIVES:**

- To identify age-based aetiology for CAP in children from 1 to 36 months of age.

### **SECONDARY OBJECTIVES:**

- To describe the clinical spectrum and risk factors in community-acquired pneumonia in 1-36 months of age.
- To identify the impact of vaccination on severity and outcome of community-acquired pneumonia.

### **PRIMARY OUTCOME MEASURES:**

- Age-based aetiology of community-acquired pneumonia

### **SECONDARY OUTCOME MEASURES:**

- Hospital admission/length of stay
- Need for respiratory support (O2/CPAP)
- PICU Care
- Requirement of Mechanical ventilation
- Death due to pneumonia

# **MATERIAL & METHODS**

## **RESEARCH DESIGN AND METHODOLOGY**

### **STUDY SETTING:**

Department of Paediatrics (Emergency, OPD, IPD and PICU) with collaboration with the department of microbiology VRDL, AIIMS Jodhpur

### **STUDY DESIGN:**

Cross-sectional Study

### **ELIGIBILITY CRITERIA**

#### **INCLUSION CRITERIA:**

- Children between 1-36 months of age with the clinical diagnosis of pneumonia (as per WHO criteria).
- Parents or guardians give informed written consent for enrolment of a child into the study.

#### **EXCLUSION CRITERIA:**

- Known case of active TB or current treatment for TB.
- Parents and guardians not given consent for enrolment of a child into the study.

### **SAMPLE SIZE:**

As this was a time-bound study, we enrolled the patients with pneumonia who visited the Emergency, OPD, IPD, PICU settings of the department of paediatrics, AIIMS Jodhpur

### **STUDY POPULATION:**

The study included the children of age group 1-36months who came with symptoms of respiratory infection and who fulfilled the WHO criteria for pneumonia

### **ENROLLMENT:**

- All patients who fulfilled the inclusion criteria were enrolled in the study after taking the written consent from the parents/guardians (Appendix 1 and 2)



- Documentation of basic information and sample collection (blood culture and nasopharyngeal culture) were done after written consent

#### **DATA COLLECTION:**

- At admission, demographic data like name, age, date of birth, phone number and patient AIIMS ID were recorded in case record proforma
- Initial evaluation includes a detailed clinical history like symptoms at presentation with a duration of symptoms and danger signs were recorded.
- History of previous hospitalization, previous diagnosis and previous antibiotics usage during the illness were recorded
- In risk factors we took detailed birth history like gestational age, mode of delivery, history of low birth weight and Postnatal factors like EBM on day 1, total duration of breastfeeding, type of feeding (EBM/ Top feed / Animal milk) were recorded.
- In vaccination history focus will be on place (hospital/ Anganwadi) and age at vaccination, have vaccination card or not, bringing vaccination card during hospital visit along with social factors are recorded
- General physical examination includes the vitals at presentation were recorded
- In Anthropometry the weight of the child was recorded by the electronic weighing scale and in children <2years length was recorded by infantometer and >2years height recorded by stadiometer and Z scores calculated by WHO growth charts.
- Basic investigations were sent along with the blood culture is the main investigation we used. Under Aseptic conditions by venepuncture, an adequate amount of blood was withdrawn. The collected sample was inoculated into the BD BACTEC Peds Culture bottles. These bactec bottles were incubated in fluorescent instruments. Each bactec vial contains the CO<sub>2</sub> sensor which can detect the CO<sub>2</sub> produced by the growth of micro-organisms, the sensor is monitored by the instrument with an increase in CO<sub>2</sub> there is an increase in the fluorescent light. The positive result indicates the isolation of organisms.
- Other basic investigations were sent along with chest x-ray
- Nasopharyngeal swab was collected and transported to the Department of Microbiology of AIIMS Jodhpur.
- The collected blood samples and nasopharyngeal swabs were sent to the National Institute of Epidemiology at Chennai.

## **ETHICAL JUSTIFICATION**

1. This study was undertaken only after obtaining the Ethical Clearance and receiving approval from the institute's Ethics committee
2. Children were enrolled after obtaining the proper informed consent from the parents/Guardian

## STATISTICAL ANALYSIS

All the data were entered in the Excel sheet 2010 and statistical analysis was performed using the statistical software SPSS v. 23.0. Qualitative data was represented in the form of Frequency percentage and median values (IQR). Association between Qualitative variables done by Chi-square test. Graphical representation was done in MS excel package; Results were defined by statistical significance with a p-value less than 0.05

**Graphical representation of data:** MS excel package included in Microsoft office 365 was used to obtain various graphs using bar diagrams and pie charts.

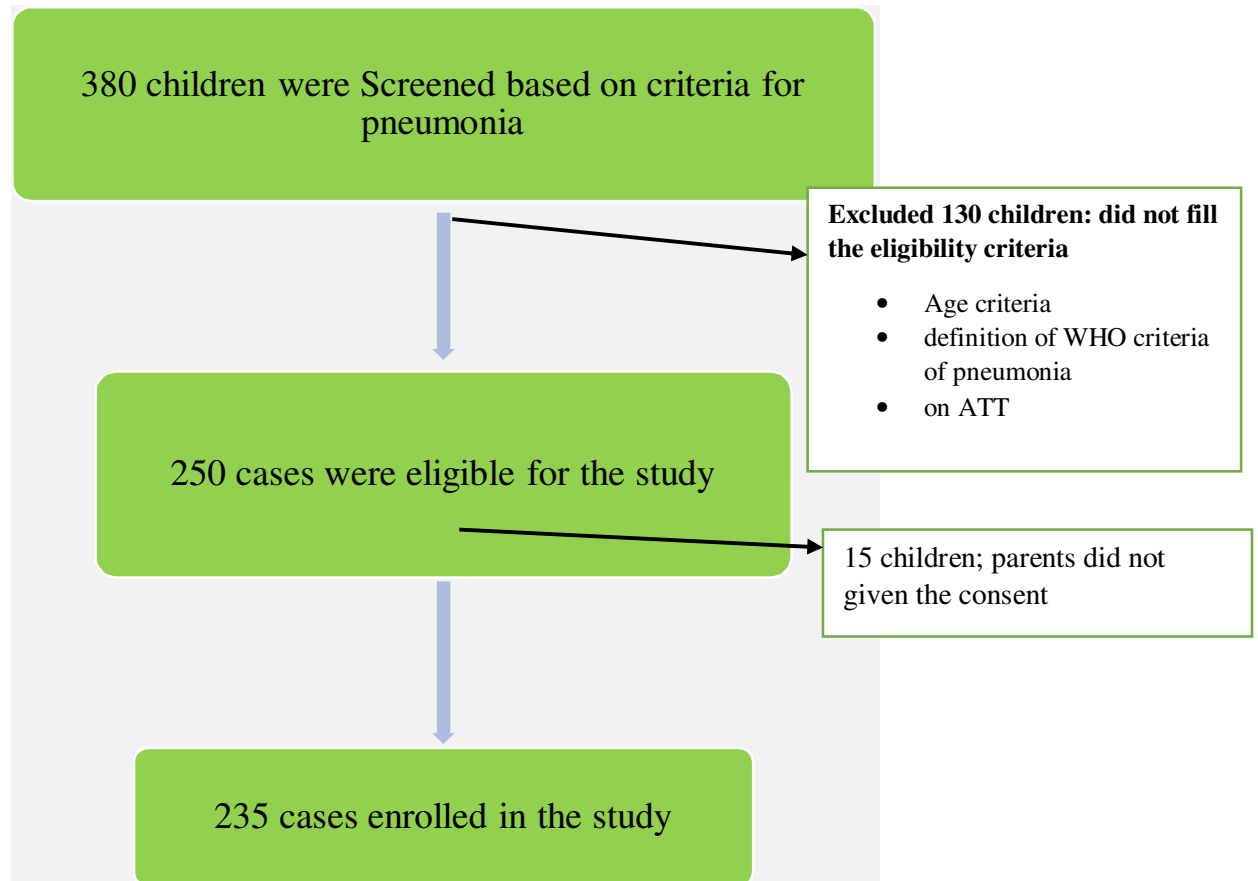
**Statistical software:** MS Excel, SPSS version 23 was used to analyse the data

# **OBSERVATION & RESULTS**

## **OBSERVATION AND RESULTS**

A total of 380 children were screened based on clinical symptoms, out of them, 235 children were enrolled in the study. This has been described in **Fig-3**

**Figure-3: Flow of the study**



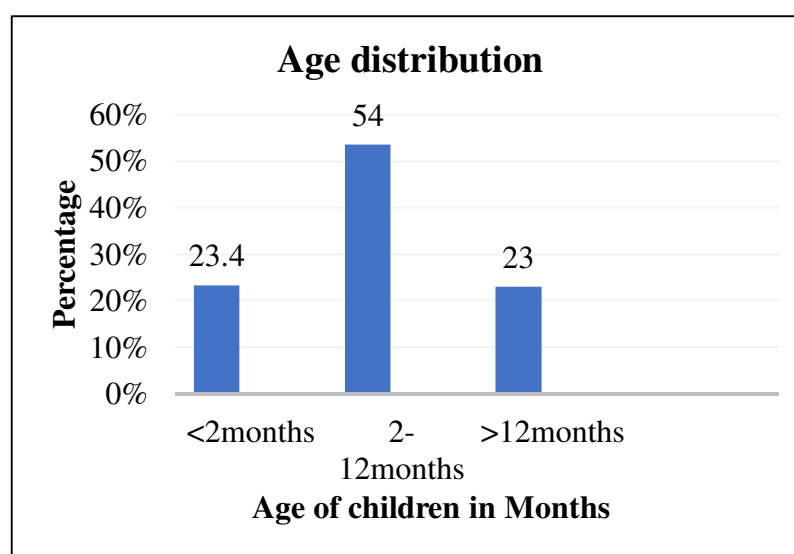
**Baseline characteristics:** The baseline characteristics of enrolled children are summarized in Table 7.

**Table-7: Baseline characteristic of enrolled children (235)**

Baseline characteristics	N (%)
<b>Age (In completed months)</b>	
<2months	55(23.4)
2-12months	126 (53.6)
>12months	54 (22.9)
median age (IQR)	6(2.5,6)
<b>Gender</b>	
Male	147 (62.5)
Female	88 (37.5)
<b>Anthropometry data, Median (IQR)</b>	
Weight (in kg)	5.6 (4.0, 8.0)
Length/Height (in cm)	64 (55,72)
HC (in cm)	40 (38,43)

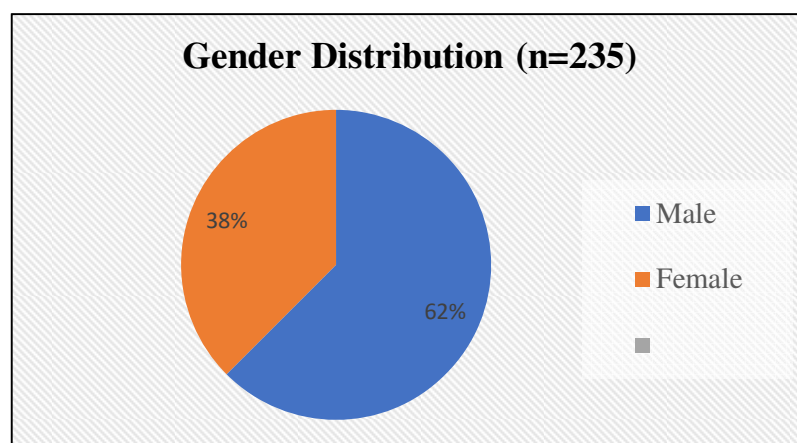
**Age Distribution:** The median (IQR) age of enrolled children was 6 (2.5, 12) months. Out of them, 55(23.4%) were <2 months, 126 (53.6%) children between 2-12months and 54 (22.9%) greater than 12months. It has been shown in **Fig-4**.

**Figure-4: Age distribution of enrolled children (n=235)**



**Gender Distribution:** Among 235 children, the male contributes to 147 (62.5%), females contribute to 88 (37.5%). This has been shown in **Fig-5**.

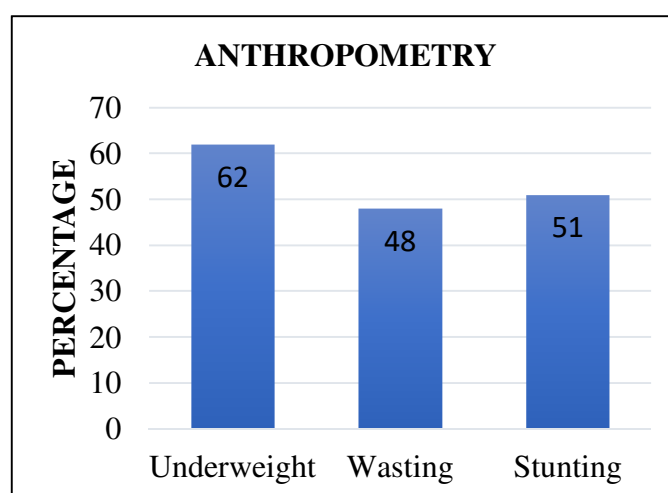
**Figure-5: Gender distribution of study participants (n=235)**



### Anthropometry

Out of the total cases, 235 cases, the median weight of children enrolled in the study was 5.6 (4.0, 8.0) kg and the median length/height was 64 (55, 72) cm. Of 235 participants, 89(37.8%) had normal weight for age, but 146(62%) children were underweight. 115(48.9%) children had normal length/height for age, but 120(51%) were stunted. A total of 121(51.4%) had normal weight for length/height, and 114(48%) had wasted. (**Figure 6**)

**Figure-6: Anthropometry details of enrolled children (n=235)**



## Clinical Manifestations in Study Participants

### Clinical Symptoms:

The most common clinical symptoms were fast breathing (78%) followed by indrawing of the chest (73.9%), fever (72.7%), and cough (71.4%). The median duration of symptoms is described in table-8. Other less common symptoms are vomiting 47(20.9%), lethargy 87 (37.34%), bluish discolouration of lips<sup>10</sup> (4.2%), decreased feeding 80(34.4%). This has been summarized in **Table-8**.

**Table-8: Clinical symptom in the study participants (n=235)**

Clinical Symptom	n (%)	Duration (in days)
		Median IQR
<b>Fever</b>	171 (72.7)	3.0 (2.0, 7.0)
<b>Cough</b>	168 (71.4)	2.0 (2.0, 7.0)
<b>Fast breathing</b>	184 (78)	2 (1.0, 5.0)
<b>Indrawing of chest</b>	173 (73.9)	2 (1.0, 7.0)
<b>Noisy breathing</b>	74 (31.6)	3 (1.0, 15.0)



### Physical examination findings

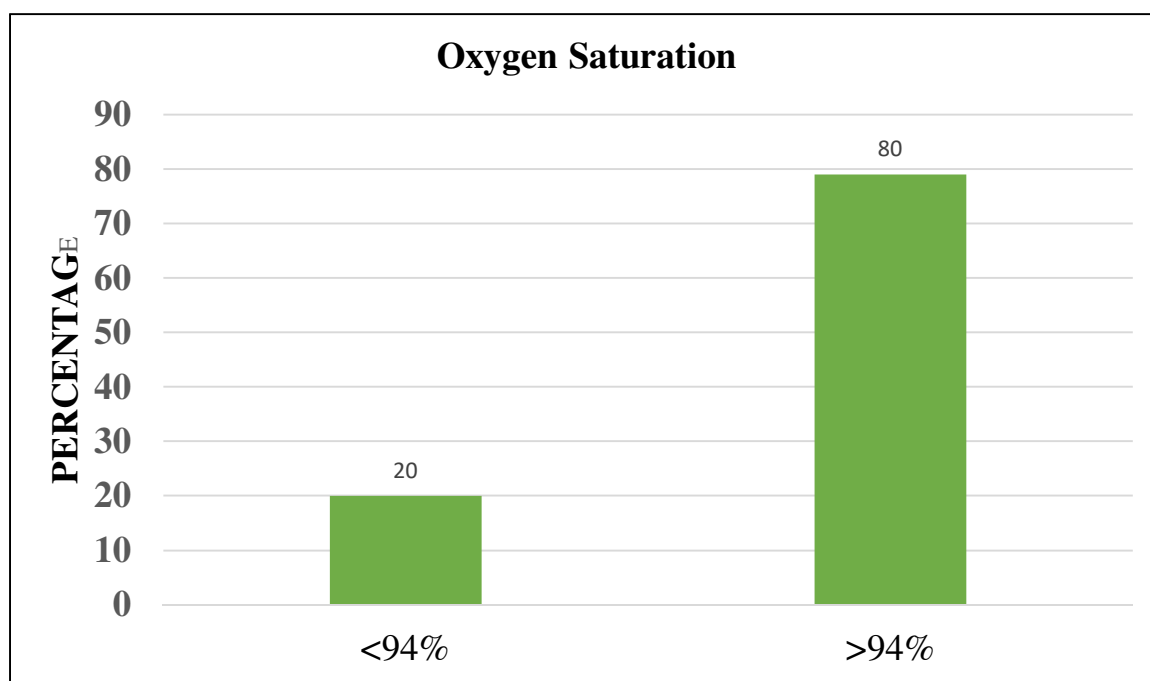
The median respiratory rate was 50 per minute and median SPO2 was 98% on the examination. Among 235 participants SPO2 below <94% came to be 48 (20%) and > 94% to be 187 (79%). On systemic examination, an Indrawing chest was seen in 73.9%, grunt seen in 6.3%, decreased air entry in 21.2%, abnormal breath sounds like crepitation's and wheeze in 57.8%, and conducting sounds in 17.8%. On other systemic examination, cardiac murmur present in 11.4% and Organomegaly in 9.36%. This has been summarized in **Table-9**

**Table-9 General and systemic Examination findings of study participants**

Examination findings	N (%)
Respiratory rate,	<b>50 (42, 60 )</b>
SPO2, Median (IQR)	<b>98 (94, 99 )</b>
Sign of respiratory distress	
Indrawing present	<b>173(73.9)</b>
Grunt	<b>15(6.3)</b>
<b>On Auscultation</b>	
Decreased Air entry	<b>50(21.2)</b>
Added sound	
Crepitations and/or wheeze	<b>136(57.87)</b>
Conducted sound	<b>42(17.8)</b>
CVS- Murmur	<b>27(11.4)</b>
Hepatomegaly/splenomegaly	<b>22(9.36)</b>

**Oxygen saturation (SpO<sub>2</sub>):** Out of total children, the median (IQR) SpO<sub>2</sub> was 98 (94, 99) %, with 48(20%) children had SpO<sub>2</sub> <94% and 187(80%) had SpO<sub>2</sub> >94%, which was shown in figure -7.

**Figure-7: SpO<sub>2</sub> in the enrolled children (n=235)**



### Risk Factors in enrolled children

Out of 235 children, 193 (83.1%) children were delivered at term, while 39 (16.8%) were preterm. Normal vaginal delivery 186 (80%) than LSCS 46 (19.8%). (Figure-10, 11). The median birth weight of children was 2.8kg, and LBW was observed in 50 (23.4%) children (Figure-12) EBM fed babies on day one were 222(95%), top feed babies were 61 (26%), and cow milk-fed babies 47 (20%). 109 (46.38%) children received breastfeeding for < 6 months while 126 (53. 6%) received for > 6 months. Exposure to smoke was present in 5 (2.3%) children. The risk factors have been summarized in **Table-10**.

**Table-10: Prevalence of risk factors in enrolled children (n=235)**

<b>Gestational age</b>	<b>n (%)</b>
Term	193 (83.1)
Preterm	39 (16.8)
<b>Type of delivery</b>	
Normal vaginal delivery	186 (80)
LSCS	46 (19.8)
<b>Birth weight, Median (IQR)</b>	2.8 (2.5, 3.0)
<b>Low birth weight</b>	
Yes	50(23.4)
No	163(76.5)
<b>Expressed breast milk</b>	<b>N (%)</b>
Yes	222(95)
No	11(4.72)
<b>Duration of breastfeeding</b>	
<6months	109 (46.38)
>6months	126 (53. 6)
<b>Top feed</b>	61 (26)
<b>Cow milk</b>	47 (20)
<b>Passive exposure to smoke</b>	5 (2.3)

### Previous Hospitalization History:

Out of the total of 235 children, previous hospitalization history was present in 86(36.9%) of the case (Fig-13). The most common cause of hospitalization was LRTI was present in 58(63%) children, followed by congenital anomalies like TEF and CHD in 12(13%) and neonatal causes were 11(11.9 %) and other causes were 11(11%). A total of 71(78%) children had a history of receiving antibiotics during the previous admission. It has been summarized in **Table-11**.

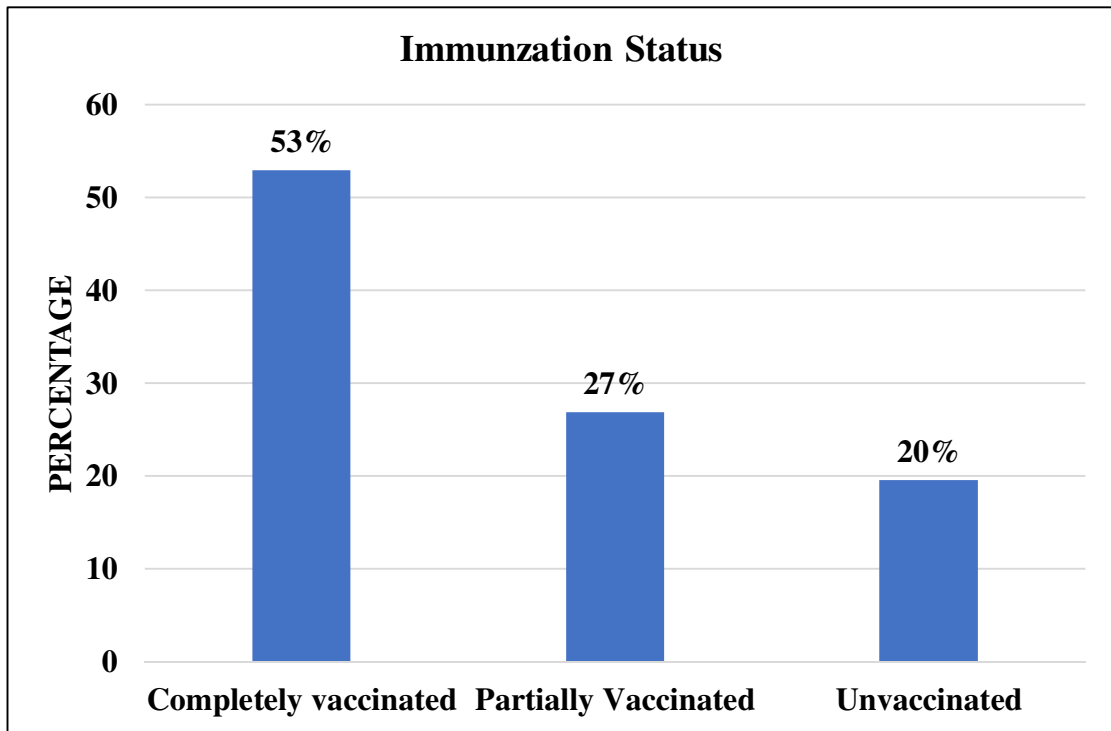
**Table 11: Details of previous details of hospitalization in participants (n=235)**

Particular	n (%)
Previous hospitalization	
Yes	86 (36.9)
No	147 (63)
Previous Diagnosis	
LRTI	58(63)
Neonatal causes	11(11.9)
Congenital Anomalies	12(13)
Others	11(11)
Previous Antibiotics	
Yes	71(78)
No	20(21.9)

### IMMUNIZATION HISTORY:

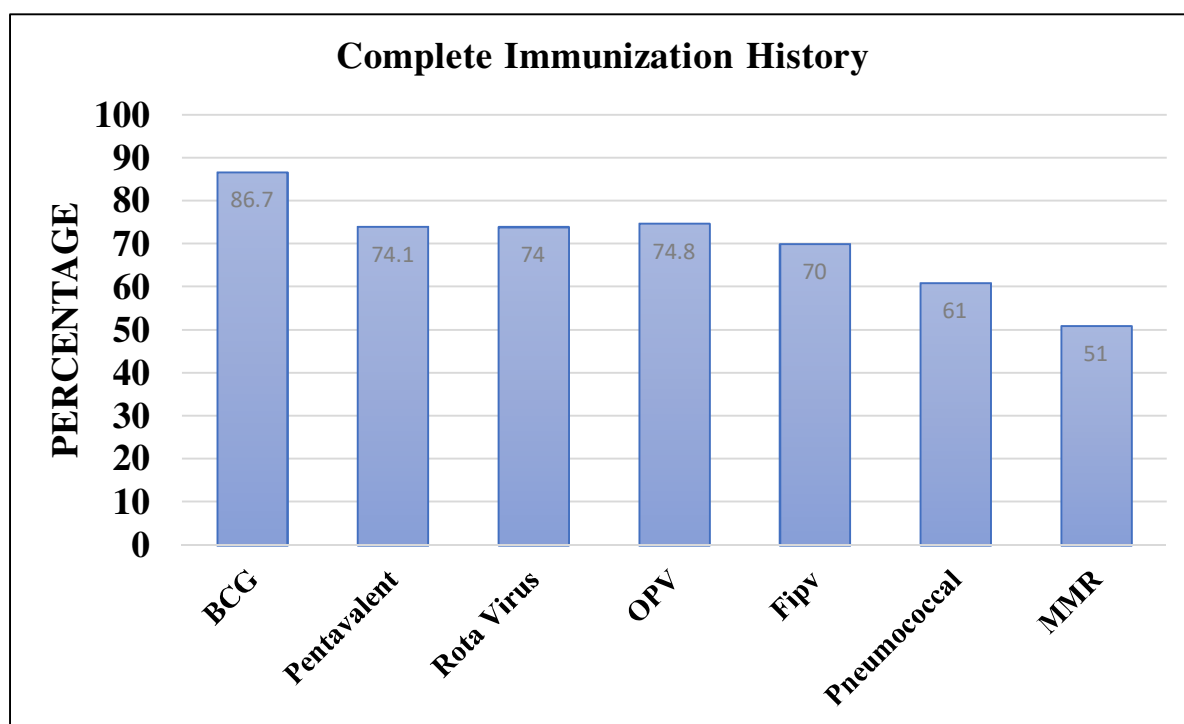
Out of the total 235 children, 125 (53%) were completely immunized, 63 (26.9%) were partially immunized, and 46 (19 %) were unimmunized. It has been shown in -**Figure 8**.

**Figure 8- Details of Vaccination in enrolled children in the study (n=235)**



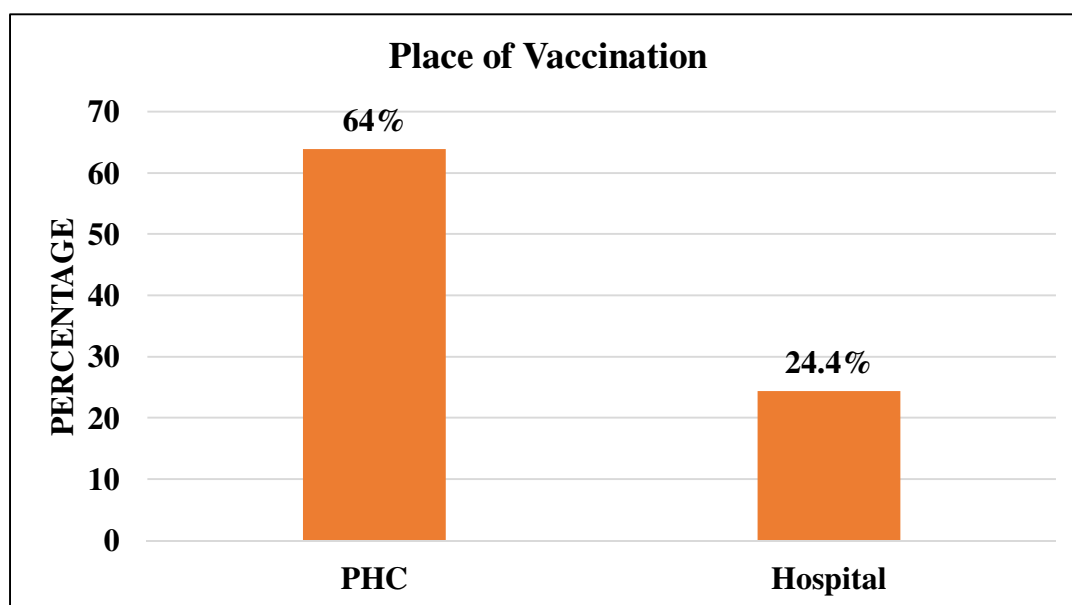
**Type of vaccination:** BCG vaccine was given in 203(86.7%), Pentavalent at least one dose in 158(74.1%), Rotavirus in 158(74%), OPV in 158(74.8%), Fractioned IPV in 158(70%), Pneumococcal at least one d in 141(61%), MMR in 57% (Fig-9).

**Figure-9 Complete Immunization history of the participants**



**Vaccination card:** Out of total vaccination children, 105 (45%) carried the vaccination card during a hospital visit, and 128 (54.9%) did not carry the card. Most of the children get vaccinated at PHC 148 (64%) than hospital 56 (24.44%) (Fig-10).

**Figure-10: Details of place of vaccination in children enrolled (n=204)**



## MANAGEMENT

Out of a total of 235 children, 157 (67%) participants received Intravenous fluids, and 80% among them required antibiotics. The up-gradation of antibiotics was done in 134 (71.6%). Antiviral agents (Oseltamivir) were used in 47 participants. PICU admission was required in 121(51.7%) children. It has been summarized in **Table-12**.

**Table 12: Treatment received among participants**

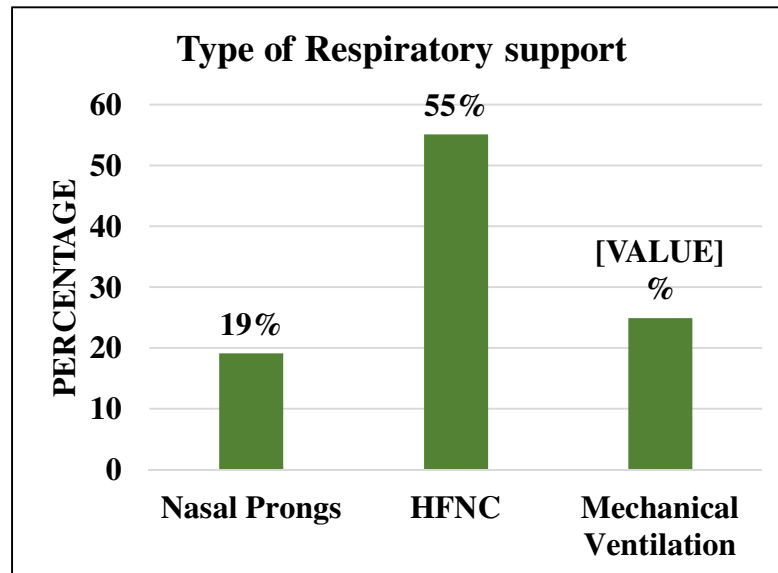
<b>Particular</b>	<b>N (%)</b>
Antibiotics used	187(80)
<b>Antibiotics Upgradation</b>	
Yes	134(71.6)
No	53(28.3)
<b>Antiviral drugs</b>	47(20)
<b>IVF</b>	
Yes	157 (67)
No	77 (32.9)
<b>PICU Admission</b>	
Yes	121(51.71)
No	113(48.26)
<b>Respiratory support</b>	
Yes	161(68)
No	75(31.9)
<b>Type of support</b>	
Nasal prongs	31 (19.2)
HFNC	89 (55.2)
Mechanical Ventilation	41 (25)



## RESPIRATORY SUPPORT:

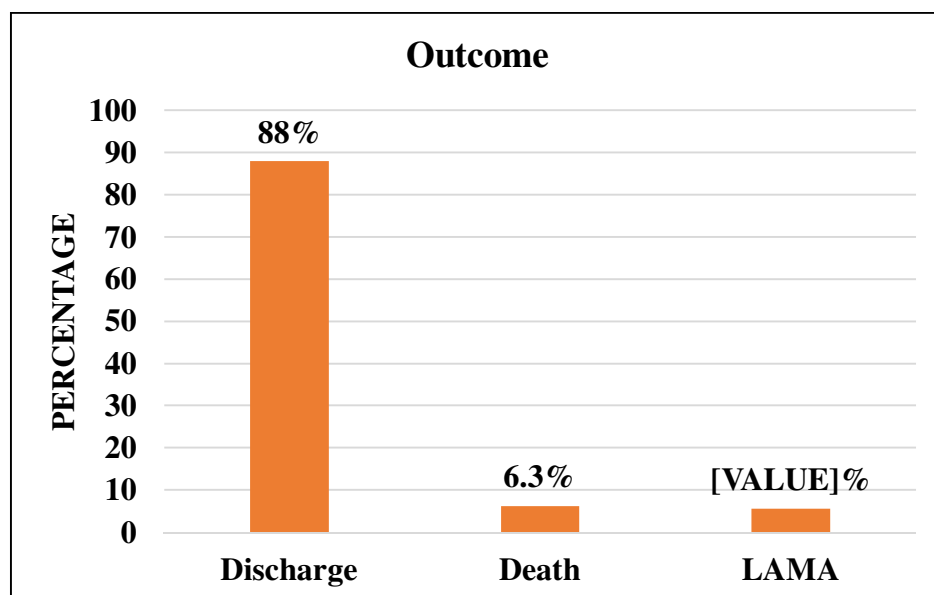
Out of total children 235, 160 (68%) received respiratory support; among them, oxygen received by nasal prongs were 31 (19.2%), HFNC 89 (55.2%), and mechanically ventilated patients were 41 (25%). It has been shown in **figure -11**.

**Figure-11 Different types of Respiratory support in the children (n=161)**



**OUTCOME:** 207 children got discharged (88%); however, 15 (6.3%) children died. 13(5.5%) children took LAMA. It has been shown in **Fig-12**

**Figure-12: outcome in the total children enrolled (n=235)**



## Primary outcome: To identify the age-based Aetiology of CAP

### Etiology of CAP in enrolled Children:

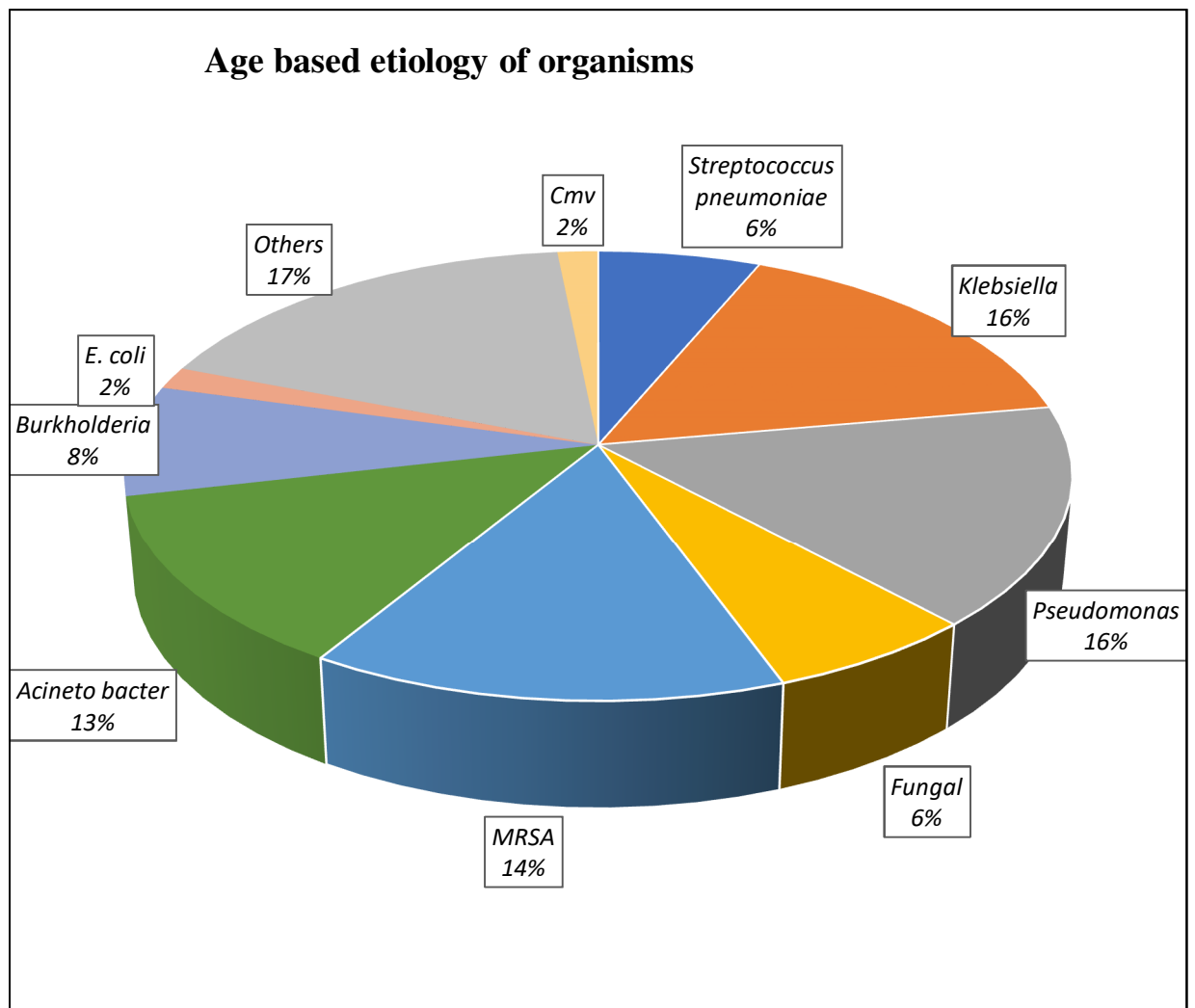
Out of a total of 235 children, in 63(26.8%) etiological agents were identified. The most common organisms identified were *Klebsiella pneumoniae* and *Pseudomonas* in 10(16%) each, followed by *Methicillin-resistant staphylococcus aureus* in 9 (14%) children. It has been shown in **Fig-13**

Age-wise number and type of organism are summarized in **table-13**. There was statistically no significant association was found between the frequency of bacterial organisms detected and the age of the children ( $p= 0.17$ ).

**Table-13: Aetiology of CAP in enrolled children.**

	<b>Total (n%)</b>	<b>&lt;2months (n=55)</b>	<b>2-12months (n=126)</b>	<b>&gt;12 months (n=54)</b>
<i>Streptococcus pneumoniae</i>	4(6.3)	0	3(2.38%)	1(1.85%)
<i>Klebsiella</i>	10(15.8)	4(7.2%)	5(3.9%)	1(1.85%)
<i>Pseudomonas</i>	10(15.8)	1(1.8%)	6(4.76%)	3(5.5%)
<i>Fungal</i>	4(6.3)	2(3.6%)	2(1.58%)	0
<i>MRSA</i>	9(14.2)	0	4(3.1%)	5(9.2%)
<i>Acinetobacter</i>	8(12.6)	4(7.2%)	3(2.38%)	1(1.85%)
<i>Burkholderia</i>	5(7.9)	2(3.6%)	3(2.38%)	0
<i>Escherichia coli</i>	1(1.58)	0	1(0.79%)	0
<i>Others</i>	11(17.4)	4(7.2%)	7(5.5%)	0
<i>Cytomegalovirus</i>	1(1.58)	1(1.8%)	0	0
<b>Total</b>	<b>63 (26.8%)</b>	<b>18(32.7%)</b>	<b>34(26.9%)</b>	<b>11(20.3%)</b>

**Figure-13 Aetiology of organisms in enrolled children (n=235)**

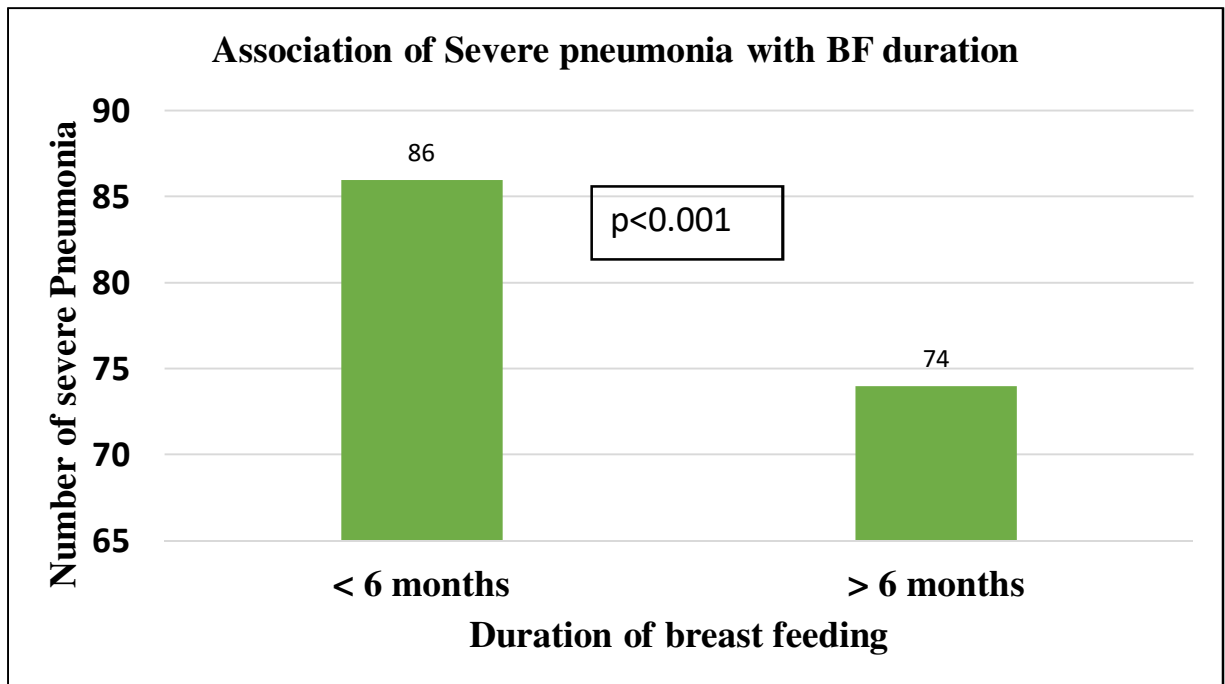


## SECONDARY OBJECTIVE: Association of Severity of Pneumonia with Risk Factors

### *Association of the severity of pneumonia with the duration of breastfeeding*

Children with < 6-months of breastfeeding had statistically more severe pneumonia than who received BF for > 6 months [86 (78.9) vs 74 (58.73%);  $p=0.001$ ]. It has been shown in fig-14.

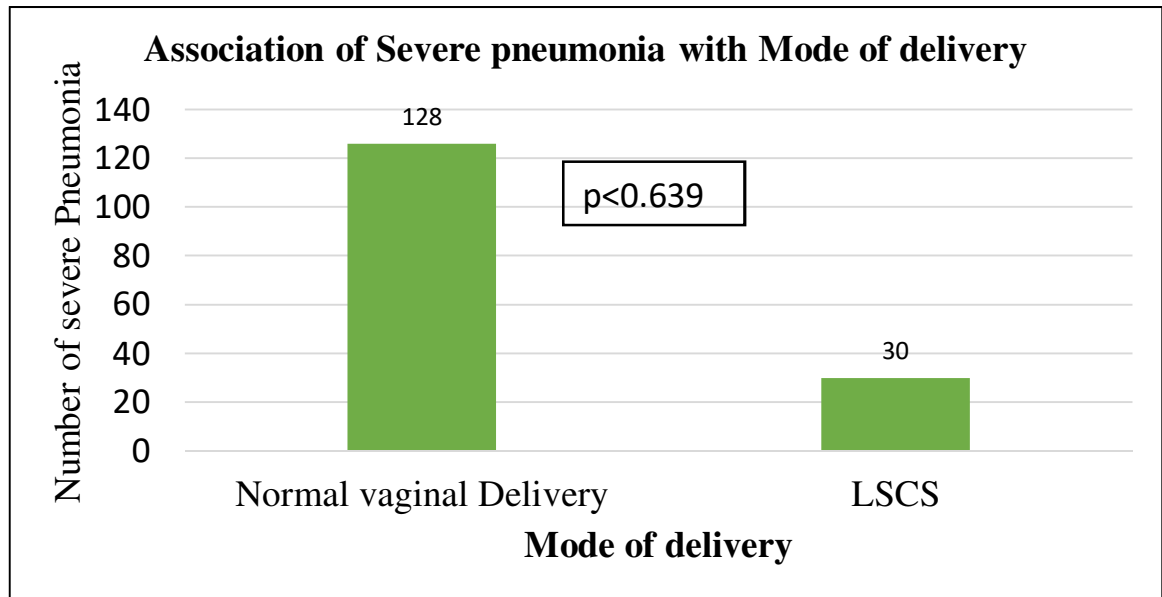
**Figure-14 Association of severe pneumonia with Breastfeeding duration**



### *Association of Severity of pneumonia with the mode of delivery*

There is no significant statistical association found between mode of delivery and severity of pneumonia [128 (81.1%) vs. 30 (18.9%);  $p=0.67$ ]. It has been shown in **figure-15**.

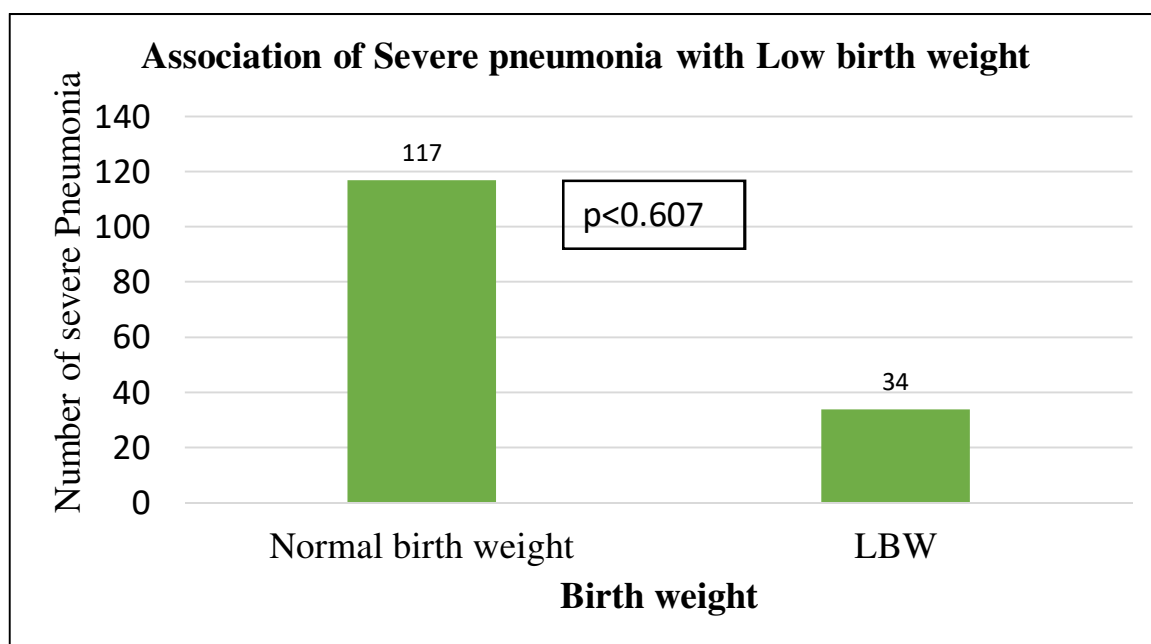
**Figure-15 Association of severe pneumonia with the mode of delivery**



### Association of Severity of pneumonia with low birth weight (LBW)

There is no significant statistical association found between Low birth weight and severity of pneumonia [117(77.4%) vs. 34 (22%);  $p=0.6$ ]. It has been shown in **figure-16**.

**Figure-16 Association of severe pneumonia with Low birth weight**



### Association of Gestational age with the severity of pneumonia

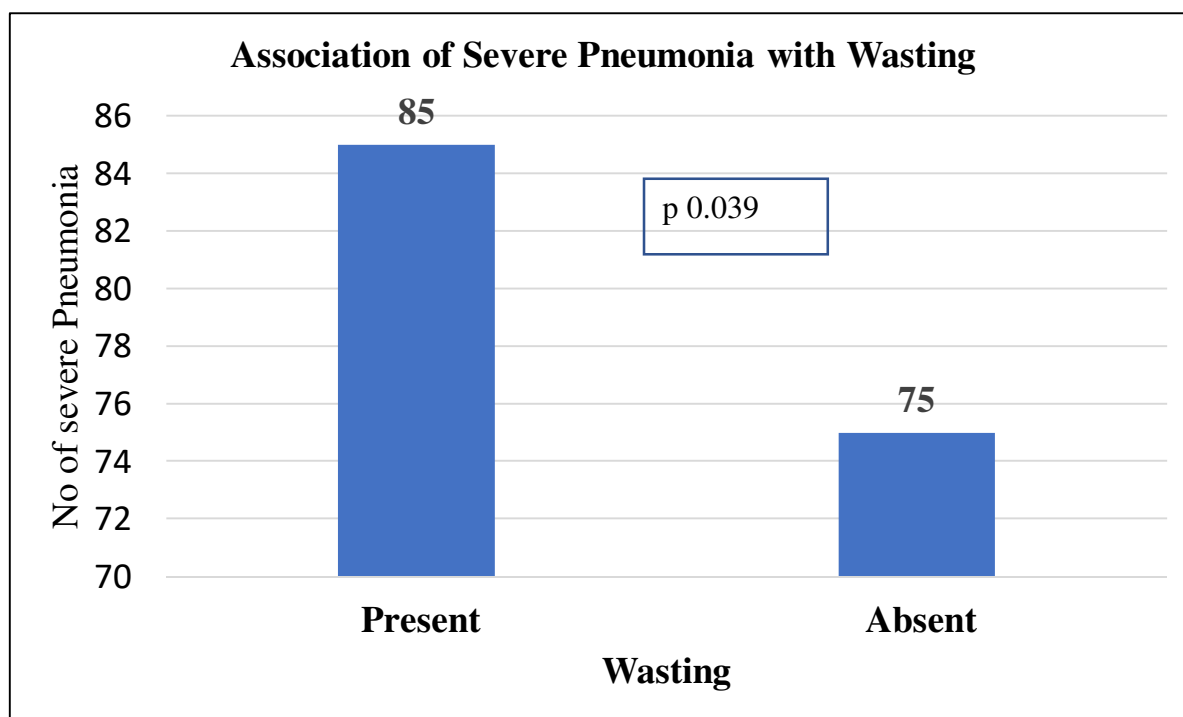
There is no significant statistical association found between gestational age and severity of pneumonia [132(83.5%) vs. 26 (16.4%);  $p=0.8$ ].

## Association of Severity of Pneumonia with Risk Factors

### *Association of the severity of pneumonia with Wasting (Fig-20)*

Children with Wasting had statistically more severe pneumonia than those with normal weight for height. [85 (53.13%) vs 75 (46.88%);  $p=0.039$ ]. It has been shown in **figure-17**.

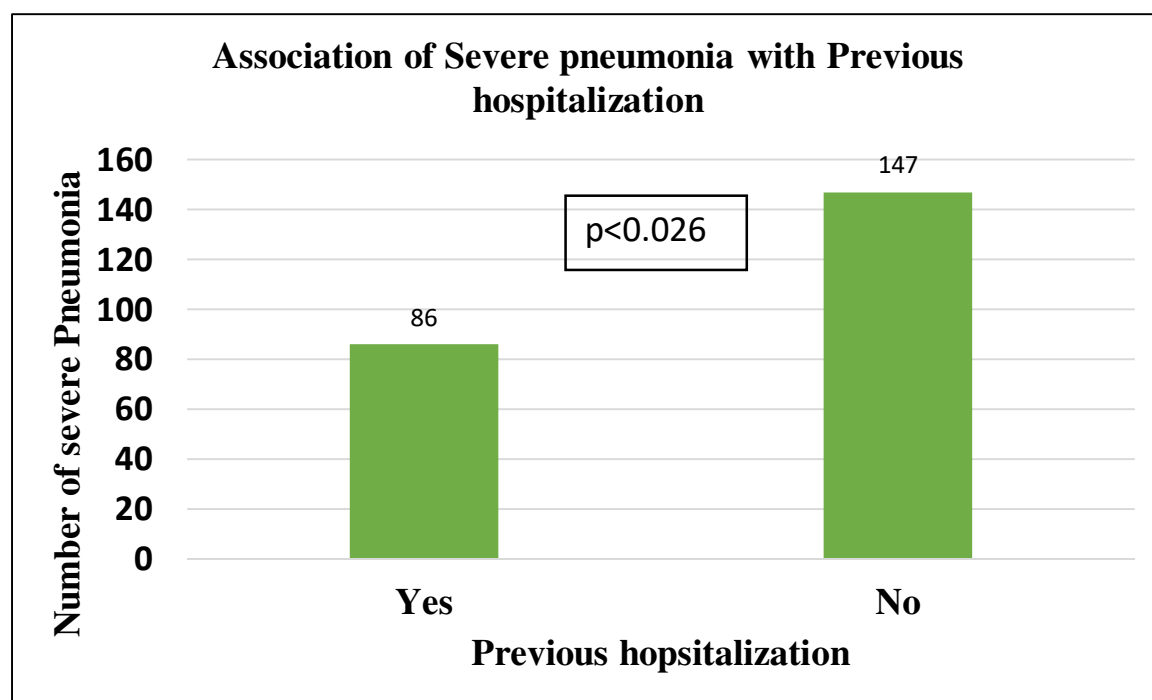
**Figure-17 Association of severe pneumonia with wasting**



### Association of the previous hospitalization with the severity of pneumonia

Children with a history of the previous hospitalization had statistically more severe pneumonia than those who weren't hospitalized [66 (41.7) vs. 92 (58.2%);  $p=0.026$ ] (Fig-18). There is no significant statistical association found between the history of antibiotics in previous hospitalization and severity of pneumonia [55 (79.7%) vs. 14(20%);  $p=0.49$ ].

**Figure-18 Association of severe pneumonia with the previous hospitalization**



### Association of the severity of pneumonia with exposure to smoke

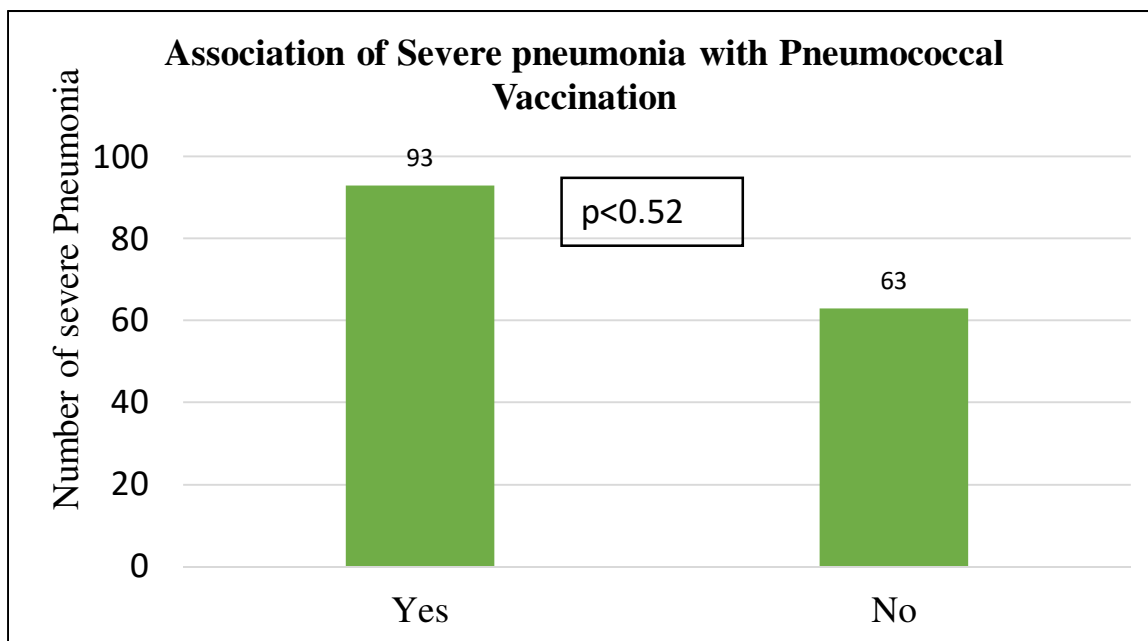
There is no significant statistical association found between Exposure to Parental smoking and severity of pneumonia [4 (2.5%) vs. 156(97.5%);  $p=0.560$ ].



### Association of Severity of pneumonia with pneumococcal vaccination

There is no significant statistical association found between Pneumococcal vaccination and severity of pneumonia [93 (59.6%) vs. 63(40%);  $p=0.52$ ]. It has been shown in figure-19.

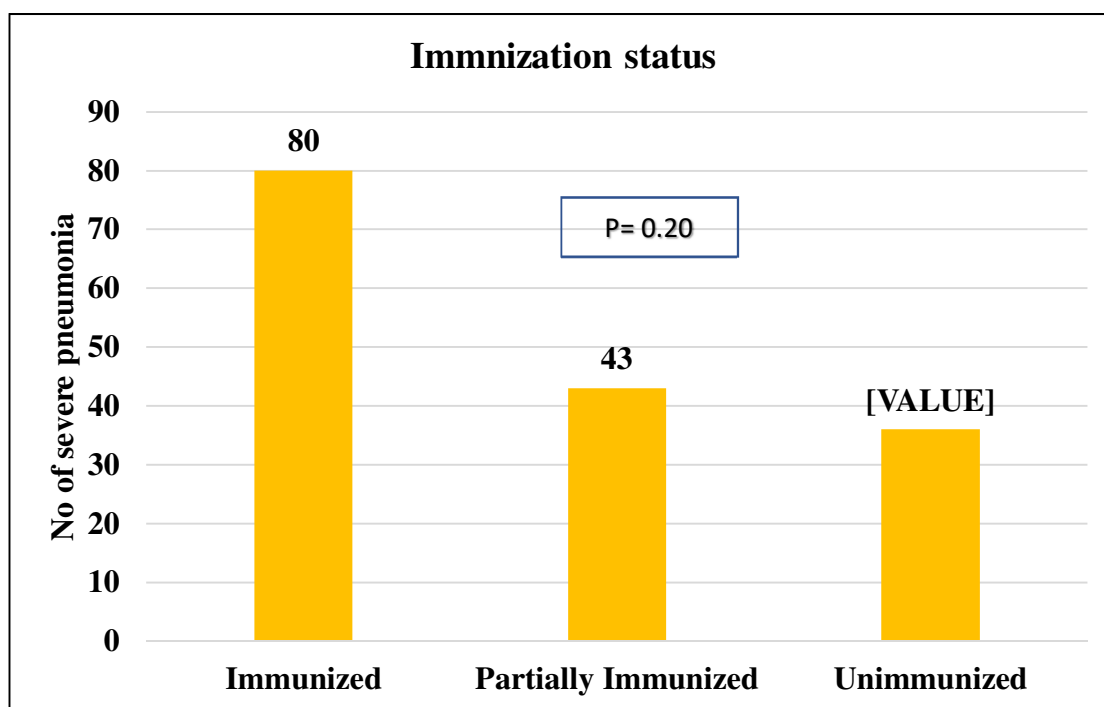
**Figure-19 Association of severe pneumonia with Pneumococcal vaccination**



### Association of the severity of pneumonia with Vaccination status

There is no statistical significance between the severity of pneumonia and immunization status [80 (50%) vs. 43 (27%) vs. 36(22%);  $p=0.20$ ]. It has been shown in figure-20.

**Figure-20 Association of the severity of pneumonia with Vaccination status**



### Association of the severity of pneumonia with the outcome

#### *Association of the severity of pneumonia with Outcome (Fig-24)*

There is statistically more severe pneumonia in children who went LAMA and Death than the discharged children. [135(84%) vs 15(9.38%) vs 10(6.25%);  $p=0.016$ ].

### Association of vaccination status with the outcome of pneumonia

There is a statistically no significant association between discharge and death rate with vaccination status. However, LAMA was significantly more common in unvaccinated children (6 (46.1%) vs. 7(53.85%);  $p=0.004$ ).

# DISCUSSION

## **DISCUSSION**

In this cross-sectional study, we observed the etiology of CAP in 28.6% of the children, which was statistically not significant in different age groups. There was a statistically significant association of duration of breastfeeding, wasting, and previous hospitalization as Risk factors. However, we did not find a statistically significant association of vaccination status, mode of delivery, Gestational age, Low birth weight, Pneumococcal vaccination, and previous antibiotic usage. In this study, the most common detected bacteria were gram-negative bacteria in which *Klebsiella* was the commonest.

Age is one of the important factors for the etiology and predictor for mortality and morbidity. In our study male children predominated over female children which can be explained by gender bias prevalent in this region. However, we did not find a significant association of etiology with the age group. In our study, the maximum number of cases CAP belongs to the age group <12months and the most common organisms observed in the younger age group was gram-negative species like *klebsiella* and *pseudomonas* 10 each followed by MRSA in older children >12months to 36months of age.

We didn't find any statistical significance in the age-based etiology in CAP in children. It could be due to many like geographical region, small sample size, aseptic precautions during collecting samples, receiving of the child from multiple referral centres, vaccination status. In one prospective cross-sectional study conducted by Rajesh KY *et al*, the most common age group identified was <12months with most organisms identified as *streptococcus pneumoniae*, however, which is statistically insignificant coinciding with our study(44).

In a prospective study conducted by Mathew JL *et al*. the most common age group was <12months and identified multiple pathogens in various samples like blood, nasopharyngeal swab and bronchoalveolar lavage cultures with *streptococcus pneumoniae* and *staphylococcus aureus* predominate in NPA and blood cultures respectively and CMV and RSV in NPA and BAL samples and the pattern of organism identified did not correlate with the clinical severity and (47). In another cross-sectional study conducted by Manoj KS *et al* in which the most common age group was <12months and common organism identified in both blood culture and NP swab was *staphylococcus aureus* in all age groups which is partially coinciding with our study in which the older children showing similar organism(9)

In Gender there is a male predominance than the female population in our study however we didn't find any statistical significance which is similar to the study done by Manoj KS. *et al* a cross-sectional study(9). In another study conducted by Srivastava *Et al* which is the prospective case-control study in which there is similar male predominance (48).

The Goal of the clinician in identifying the clinical condition along with its severity and importance is to differentiate pneumonia from other respiratory illnesses with similar presentation. Although no single finding differentiates pneumonia from other respiratory illnesses, Hypoxia and increased work of breathing are important findings that tell us the severity of the disease. In our present study, the most clinical presentation was Fast breathing, Indrawing, Fever, Cough, we also find some nonspecific findings like noisy breathing, decreased feeding, lethargy, bluish discolouration of lips, vomiting which is similar to the prospective study done by kasundriya S *et al* (22).

Identifying the risk factors associated with CAP is useful in guiding the clinical practice and outcome. It is well known to us that breastfeeding babies for more than 6 months improves immunity and prevent the severity of pneumonia. In our study, we found that children with < 6-months of breastfeeding had statistically more severe pneumonia than those who received BF for > 6 months which is similar to another study done by Kasundriya S *et al* which is a prospective study in which lack of exclusive breastfeeding associated with severe pneumonia In another study conducted by Cristiano *et al* in which increase in prevalence rates of breastfeeding and exclusive breastfeeding was associated with decreased number of hospitalizations for pneumonia(49). In one more study conducted by Caroline *et al* which is a cross-sectional study in which increased risk of pneumonia was found in who nonexclusively fed babies(14)

Globally the studies reported that the chance of getting pneumonia is high with a greater risk of hospitalization and mortality in the cases with pneumonia associated with malnutrition due to disturbance in the immunity level. In our study, we found a statistically significant association with wasting and severity of pneumonia which explains undernutrition is an important preventable risk factor for CAP, which is similar to other studies conducted by Jagdish prasad and Prawin Kumar *et al* in western Rajasthan observed that undernutrition is a significant risk factor for severe pneumonia(19) In another study conducted by Dina johar *et al* there is reinfection more in the malnourished patients with pneumonia and there is more

prolonged respiratory support (50). In another study conducted by Nemani T *et al*, a cross-sectional study in which there are increased rates of hypoxia in CAP with malnutrition(17).

The previous hospitalization is considered an important risk factor for severe pneumonia. In our study, the history of the previous hospitalization was significantly associated with severe pneumonia. This can be explained by the previous attack of pneumonia can cause structural changes or residual defects which leads to severe pneumonia from the current episode. A study conducted by the European Respiratory Journal, Teepe *et al*. they found that previous history of URTI or wheezing is independently associated with CAP(6)

We did not find a significant association of severity of pneumonia with the mode of delivery, gestational age, low birth weight, Stunting, previous history of Antibiotics, Exposure to smoke

Immunization of children with vaccines like Hib, Pneumococcal and influenza is considered as a protective factor for severe pneumonia. In a study conducted by DeAntonio R *et al*, there is a significant reduction of pneumonia after the introduction of immunization programs (7). In our study, the completely vaccinated participants were around less in number which was the major drawback. Pneumococcal vaccination was introduced in 9 districts that have high under-5 mortality in Rajasthan, it planned to cover the remaining areas. But due to poor Pneumococcal vaccination noted in our region. There is no statistical significance found between the severity of pneumonia immunization status and pneumococcal vaccination due to small size. In one study conducted by Tukbekova *et al*, published in 2019 to study the impact of vaccination on severity status that they found in unvaccinated the severe pneumonia is more than vaccinated children but didn't find any statistical significance(51).

In management, out of total children  $2/3^{\text{rd}}$  of the children required respiratory support with mechanical ventilation requirement in  $1/4^{\text{th}}$  of the children and PICU requirement half of the individuals.

Out of the total cases, most of the children got discharged, however, 6.3% of children died and 5.5% of children took LAMA. There is statistically more severe pneumonia in children who went LAMA and Death compared to the children who were discharged, and we also found that statistically significant association between LAMA with vaccination status. One study conducted by DeAntonio R *et al*, which is the systemic review states that unvaccinated children had severe pneumonia and there is a reduced incidence of pneumonia after pneumococcal coverage. In another study conducted by Pavia *et al*, a meta-analysis shows

after the addition of pneumococcal vaccination there is decreased mortality among children with pneumonia is observed.

# **STRENGTH & LIMITATION**



## **STRENGTH AND LIMITATIONS OF THE STUDY**

### **Strength of the study**

1. We used standard WHO pneumonia criteria when enrolling the cases.
2. We sent Blood culture for almost all the children who filled the criteria

### **Limitation of the study**

1. Viruses' detection by RTPCR was not done because of Resource Constraints.
2. As this is the Territory care centre most of the patients are referred from other hospitals are sick and required PICU admission and respiratory support
3. As this study was undergone during a covid pandemic

# **SUMMARY & CONCLUSION**

## **SUMMARY**

### **Title of the study: Clinical and etiological profile of Community acquired Pneumonia in 1 -36 Months of age group**

**Background:** Pneumonia is the leading cause of death globally among children less than 5 years and closely linked with poverty with the highest mortality rates seen among developing countries like India. The aetiology of pneumonia is age-based with a wide variety of organisms with the contribution of multiple risk factors like host and environmental factors in evolving the disease. However, there is limited data on the etiological profile of CAP in the western part of Rajasthan. Therefore, this study was carried out to find out the clinical and etiological profile of CAP in different age groups from western Rajasthan and to know the impact of vaccination on the severity and outcome of pneumonia in young children.

#### **Objectives:**

**Primary objectives:** To identify age-based aetiology for Community-Acquired Pneumonia in children from 1 to 36 months of in this hospital setting

**Secondary objectives:** To describe the clinical spectrum, risk factors and to identify the impact of vaccination on severity and outcome of CAP in 1-36 months of age.

**Methodology:** It was a cross-sectional study conducted in the department of paediatrics, AIIMS Jodhpur. The study was approved by the Institutional ethical committee. Children between 1-36 months of age were enrolled after taking the informed consent from the parents. We recorded baseline demographic characteristics, detailed clinical history and examination. Blood was collected for culture and other investigation as required. The data was entered into the MS excel sheet and results were analysed using SPSS version 23 software. The *p-value* <0.05 was considered significant.

**Results:** Out of a total of 380 children screened, 235 children were enrolled. Their median age (IQR) was 6 (2.5, 12) months. There is a male predominance of 142(62.5%). The median (IQR) weight of the enrolled children was 5.6 (4.0, 8.0) kg and the median (IQR) height was 64 (55, 72) cm. Out of 235 children, in 63(26.8%) etiological agents were identified. The most common organisms identified was gram Negative organisms *Klebsiella pneumoniae* and

*Pseudomonas* in 10 (16%) each, followed by *MRSA* in 9 (14%). There was statistically no significant association was found between the frequency of bacterial organisms detected and the age of the children ( $p= 0.17$ ).

The most common clinical presentation observed was fast breathing (78.9%), followed by chest indrawing (73.9%), fever (72.9%), and cough (71.4%). The most common examination findings was tachypnoea seen in 184(78%) children followed by chest retractions in 173(73.9%). SpO<sub>2</sub> < 94% was found in 48(20%) children. Children with < 6-months of breastfeeding had statistically more severe pneumonia than those who received BF for > 6 months ( $p<0.001$ ). The prevalence of underweight, wasting, stunting were 146 (62%), 114(84%), 120(51%), respectively. Wasting was statistically associated with the severity of pneumonia ( $p= 0.039$ ). The previous hospitalization was also statistically associated with the severity of pneumonia ( $p=0.026$ ). In vaccination, 125(53%), 63(26.92%), 46(19.6%) children were completely partially and unvaccinated, respectively. There was no statistical significance between the severity of pneumonia and vaccination status.

Children required PICU transfer in 121(51.7%) and 160 (68%) received respiratory support and mechanical ventilation in 41 (25%) children. 207 children got discharged (88%), however, 15 (6.3%) children died and 13(5.5%) children took LAMA.

## **Conclusion:**

We can identify an etiological agents in about one-fourth of the participant. Gram-negative bacteria were the most common bacteria detected and was not associated with the age of the children. Breastfeeding < 6 months, wasting and the previous hospitalization were the risk factors for severe pneumonia. Vaccination coverage was poor in this study and it was not statistically associated with the severity of pneumonia.

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# APPENDIXES

## APPENDIX - 1

### ETHICAL CLEARNACE CERTIFICATE



अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर  
All India Institute of Medical Sciences, Jodhpur  
संस्थागत नैतिकता समिति  
Institutional Ethics Committee

No. AIIMS/IEC/2020/2046

Date: 01/01/2020

#### ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: AIIMS/IEC/2019-20/974

Project title: "Clinical and etiological profile of community acquired pneumonia in 1-36 months of age group"

Nature of Project: Research Project

Submitted as: M.D. Dissertation

Student Name: Dr. Chityala Ashwini

Guide: Dr. Kuldeep Singh

Co-Guide: Dr. Prawin Kumar, Dr. Varuna Vyas & Dr. Vijaya Lakshmi Nag

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on 23-12-2019 and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Enclose:

1. Annexure 1

Dr. Praveen Sharma  
Member Secretary  
Institutional Ethics Committee  
AIIMS, Jodhpur

Page 1 of 2

Basni Phase-2, Jodhpur, Rajasthan-342005, Website: www.aiimsjodhpur.edu.in, Phone: 0291-2740741 Extn. 3109  
Email: ethicscommittee@aiimsjodhpur.edu.in

## **APPENDIX - 2**

**All India Institute of Medical Sciences**

**Jodhpur, Rajasthan**

### **Informed Consent Form**

Title of Thesis/Dissertation:

**Clinical and etiological profile of Community acquired Pneumonia in 1 -36 Months of age group.**

Name of PG Student : Dr. Ashwini (7286087272)

Patient/Volunteer Identification No. : \_\_\_\_\_

I, \_\_\_\_\_ M/o or F/o \_\_\_\_\_  
R/o \_\_\_\_\_

give my full, free, voluntary consent for my child to be a part of the study, “ **Clinical and etiological profile of Community acquired Pneumonia in 1 -36 Months of age group**” the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions.

I understand that my participation is voluntary and am aware of my right to opt-out of the study at any time without giving any reason.

I understand that the information collected about me and any of my medical records may be looked at by responsible individual from \_\_\_\_\_ (Company Name) or regulatory authorities. I permit these individuals to have access to my records.

Date: \_\_\_\_\_

Place: \_\_\_\_\_ Signature/Left thumb  
impression

This to certify that the above consent has been obtained in my presence.

Date: \_\_\_\_\_

Place: \_\_\_\_\_ Signature of PG Student

1. Witness 1

2. Witness 2

\_\_\_\_\_  
Signature

Name: \_\_\_\_\_

Address: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_  
Signature

Name: \_\_\_\_\_

Address: \_\_\_\_\_

\_\_\_\_\_

### APPENDIX - 3

अखिल भारतीय आयुर्विज्ञान संस्थान

जोधपुर, राजस्थान

सूचित सहमति प्रपत्र

थीसिस / शोध प्रबंध का शीर्षक: आयु समूह के 1 -36 महीने से बच्चों में सामुदायिक और निमोनिया के नैदानिक प्रोफाइल

पीजी छात्र का नाम: अश्विनी

रोगी / स्वयं सेवक पहचान संख्या: \_\_\_\_\_

मैं, \_\_\_\_\_ M / o या F / o \_\_\_\_\_

निवास \_\_\_\_\_ मेरे बच्चे को

अध्ययन का एक हिस्सा बनने के लिए मेरी पूर्ण, स्वतंत्र, स्वैच्छिक सहमति दें। वायरस के कारण 2 वर्ष से कम उम्र के बच्चों में एक्स्ट्राकोलाइटिस हो सकता है, जिसकी प्रक्रिया और प्रकृति मुझे अपनी पूर्ण भाषा में बताई गई है। मैं पुष्टि करता हूं कि मुझे सवाल पूछने का अवसर मिला है।

मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है और बिना किसी कारण के किसी भी समय अध्ययन से बाहर निकलने के मेरे अधिकार से अवगत हूं।

मैं समझता हूं कि मेरे और मेरे किसी भी मेडिकल रिकॉर्ड के बारे में एकत्रित जानकारी को \_\_\_\_\_ (कंपनीकानाम) या नियामक अधिकारियों के जिम्मेदार व्यक्ति द्वारा देखा जा सकता है। मैं इन व्यक्तियों को अपने रिकॉर्ड तक पहुंचने की अनुमति देता हूं।

दिनांक : \_\_\_\_\_

जगह : \_\_\_\_\_ हस्ताक्षर / बाएं अंगूठे का निशान

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त हुई है।



दिनांक: \_\_\_\_\_

\_\_\_\_\_

जगह : \_\_\_\_\_

पीजीछात्रकेहस्ताक्षर

साक्षी 1

साक्षी 2

\_\_\_\_\_

\_\_\_\_\_

हस्ताक्षरहस्ताक्षर

हस्ताक्षरहस्ताक्षर

नाम : \_\_\_\_\_

नाम: \_\_\_\_\_

पता: \_\_\_\_\_

पता: \_\_\_\_\_

## **APPENDIX - 4**

### **PARTICIPANT INFORMATION SHEET (PIS)**

**Title of the Study/Project: Clinical and etiological profile of Community-acquired Pneumonia in 1 -36 Months of age group.**

**Aim and purpose of the research:** Your child is invited to join the study. It is planned to include all such children with pneumonia in this study. The assessment shall include the recording of relevant history and clinical examination findings. Blood culture, nasopharyngeal aspirate will be taken along with other necessary investigations. It will be a one time contact and you can know the findings and their interpretation.

1. Expected duration of the subject participation - One Time
2. The benefits to be expected from the research to the subject or others: knowing about the causative agents of pneumonia will open up new research opportunities so that better ways of prevention and treatment strategies can be formulated for the benefit of the community
3. Any risk to the subject associated with the study: Potentially none. Taking nasopharyngeal aspirate is not expected to inflict any significant complications. Benign complications like vomiting, bleeding can happen. All due precautions will be taken to reduce complications.
4. Maintenance of confidentiality of records: The medical records of the patient shall be kept confidential and accessed only by the treating physician or, if necessary, by the Ethics Committee of the All India Institute of Medical Sciences, Jodhpur.
5. Provision of free treatment, compensation for research-related injury: Not applicable
6. Freedom of the individual to participate and to withdraw from the research at any time without penalty or loss of benefits to which the subject would otherwise be entitled: You are free to participate in and withdraw from this study at any time you so desire. This will in no way affect your ongoing treatment at the Institute.
7. Costs and source of investigation: Investigations mentioned will be done in AIIMS, you are not expected to pay for the cost of this investigation.
8. Telephone number/contact number of Principal Investigator and Co-investigator: In case of any concerns related to your child's treatment, you should contact:
  - a. Dr Kuldeep Singh, Professor and head of department, Department of Pediatrics, All India Institute of Medical Sciences, Jodhpur, Rajasthan, 342005.

b. Dr Ashwini PG student, Department of Pediatrics, All India Institute of Medical Sciences,  
Jodhpur, Rajasthan, 342005.

Phone: 7286087272 Email: ashwini.chityala190@gmail.com

9. It is certified that translation to vernacular is accurate.

## APPENDIX - 5

### आंशिक सूचना शीट

अध्ययन / परियोजना का शीर्षक:

अनुसंधान का उद्देश्य: आयु समूह के 1 -36 महीने से बच्चों में सामुदायिक और निमोनिया के नैदानिक प्रोफाइल

प्रक्रिया: आपके बच्चे को अध्ययन में शामिल होने के लिए आमंत्रित किया जाता है। इस तरह के सभी बच्चों को इस अध्ययन में शामिल किया गया है। मूल्यांकन में उचित इतिहास और परीक्षा निष्कर्षों की रिकॉर्डिंग शामिल होगी। नाक के रास्ते गले के स्राव की जांच (नासॉफिरिन्जियल एस्पिरेट) अन्य आवश्यक जांच के साथ लिया जाएगा। यह एक बार होगा और आप उनके परिणाम को जान सकते हैं।

i) भागीदारी की अपेक्षित सहभागिता - एक बारी

ii) शोध से आपको या दुसरो के लिए अपेक्षित लाभ: तीव्र निमोनिया के बारे में जानने से अनुसंधान के नए अवसर खुलेंगे ताकि समुदाय के लाभ के लिए रोकथाम और उपचार रणनीतियों के बेहतर तरीके तैयार किए जा सकें।

iii) अध्ययन से जुड़े विषय पर कोई जोखिम: संभावित रूप से कोई नहीं। नासॉफिरिन्जियल एस्पिरेट लेने से किसी भी बड़ी जटिलताओं की उम्मीद नहीं है। उल्टी, रक्तस्राव जैसी कुछ जटिलताएं हो सकती हैं। जटिलताओं को कम करने के लिए सभी उचित सावधानी बरती जाएगी।

iv) अभिलेखों की गोपनीयता का रख-रखाव: रोगी के मेडिकल रिकॉर्ड को गोपनीय रखा जाएगा और इलाज चिकित्सक द्वारा या यदि आवश्यक हो, तो अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर की आचार समिति द्वारा किया जाएगा।

v) मुफ्त इलाज का प्रावधान, अनुसंधान से संबंधित चोट के लिए मुआवजा: लागू नहीं

vi) किसी भी समय अनुसंधान से पीछे हटने की स्वतंत्रता, दंड या लाभ के नुकसान के बिना: आप इस इच्छा से किसी भी समय इस अध्ययन से भाग लेने और वापस लेने के लिए स्वतंत्र हैं। यह किसी भी तरह से संस्थान में आपके चल रहे उपचार को प्रभावित नहीं करेगा।

vii) लागत और जांच का स्रोत: उल्लिखित जांच एम्स में की जाएगी, आपको इस जांच की लागत के लिए भुगतान नहीं करना होगा।

viii) प्रधान अन्वेषक और सह अन्वेषक के टेलीफोन नंबर / संपर्क नंबर: आपके बच्चे के उपचार से संबंधित किसी भी चिंता के मामले में, आपको संपर्क करना चाहिए:

डॉ। कुलदीप सिंह, अतिरिक्त प्रोफेसर, बाल रोग विभाग, अखिल भारतीय आयुर्विज्ञान संस्थान,  
जोधपुर, राजस्थान- 342005

पीजी डॉ। अश्विनी छात्र, बाल रोग विभाग, अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर, राजस्थान-  
342005; फोन: 7286087272

ईमेल- Ashwini.chityala190@gmail.com

ix. यह प्रमाणित हो गया है कि अनुवाद में शब्दशः तक सटीक है।

## **APPENDIX - 6**

### **Case Record Form**

<b>Name:</b>	<b>Age/Sex</b>	<b>DOB:</b>
<b>Address:</b>	<b>Contact No:</b>	<b>Reg.No:</b>
<b>DOA:</b>	<b>DOD:</b>	

### **Chief Complaints:**

### **History of Present Illness:**

Onset

Duration

Fever

Cough

Fast breathing: WHO CRITERIA

< 2 months =  $\geq 60$  breaths

2–11 months =  $\geq 50$  breaths

1–5 years =  $\geq 40$  breaths

Noisy breathing

Chest indrawing

Feeding Difficulty

History of the previous hospitalisation

History of IV antibiotics

**Risk factors:**

1. Sex
2. Term/ Preterm
3. Type of delivery (vaginal or LSCS)
4. Birth weight
5. Day of initiation of breastfeeds
6. Type of feeds (EBM/ Top feeds / Animal milk )
7. Duration of breastfeeding
8. History of smoke exposure at home
9. Immunization history ( Last vaccine, Place of vaccine, Vaccination card)
10. Anthropometry
11. Socioeconomic history

**Findings on physical examination:**

1. Temperature
2. Heart rate
3. Respiratory rate
4. Increased WOB (Nasal flaring, SCR, ICR )
5. SPO2
6. Air entry
7. Abnormal sounds
8. Other systemic abnormal findings