CLINICAL PROFILE AND RISK FACTORS FOR SEVERITY AND MORTALITY IN ACUTE BRONCHIOLITIS IN CHILDREN LESS THAN 2 YEARS OF AGE ATTENDING AN URBAN REFERRAL CENTRE

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M.D DEGREE (PEDIATRICS) BRANCH VII

INSTITUTE OF CHILD HEALTH AND HOSPITAL FOR CHILDREN MADRAS MEDICAL COLLEGE

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CERTIFICATE

This is to certify that the dissertation titled, **"Clinical profile and risk factors for severity and mortality in acute bronchiolitis in children less than 2 years of age attending an urban referral centre"** submitted by **Dr.S.Palanivel,** to the Faculty of Pediatrics, The Tamil Nadu Dr.M.G.R Medical University, Chennai, in partial fulfillment of the requirements for the award of M.D. Degree (Pediatrics) is a bonafide research work carried out by him under our direct supervision and guidance, during the academic year 2009-2012.

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DECLARATION

I, **Dr.S.Palanivel**, solemnly declare that the dissertation titled **"Clinical profile and risk factors for severity and mortality in acute bronchiolitis in children less than 2 years of age attending an urban referral centre"** has been prepared by me.

This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Examination in Pediatrics.

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The Institutional Review Board [Ethical committee] of Institute of Child Health and Hospital for Children, Chennai-08, was held on 30.01.2010 at 10.00AM at the Deputy Superintendents chamber.

Members Present: Dr.R.Kulandai Kasthuri
Chair Person.

Members:
1. Dr.K.Gita
2. Dr.P.Jeyachandran
3. Dr.D.Vijaya Sekaran
4. Prof.Girija Shyam Sundar
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Title: "Clinical Profile and Rist Factors for Severity and Mortality inAcute Bronchiolitis in Children Less than 2years of Age Attending An Urban Referral Centre".

The Institutional Review Board was satisfied with the revised format submitted by you. Hence the Institutional Review Board is pleased to approve the study.

To,
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Post Graduate,
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Director and Superintendent.

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CONTENTS

INTRODUCTION

INTRODUCTION

Acute bronchiolitis, an acute infectious disease of the lower respiratory tract, which primarily affects the smaller airways. It is predominantly a viral respiratory disease. It is one of the leading causes of hospitalisation in infants and young children. It occurs usually between one month to 24 months of age with a peak incidence between 3 and 6 months of age. Each year in the United States, approximately two per 100,000 infants die as a result of complications associated with bronchiolitis[1]. In young children, the clinical diagnosis of this disease may overlap with viral wheezing and an acute viral triggered asthma.

Epidemiology

Bronchiolitis occurs most frequently among children less than 12 months of age. Infants less than 6 months are at increased risk of clinically severe disease[2]. Bronchiolitis is a seasonal disease which coincides with outbreaks of viral respiratory pathogens. In temperate climates, the hospital admissions due to bronchiolitis are most common from December to May. In the United States (US), as many as one percent of infants are hospitalized for bronchiolitis and the annual hospital charges associated with bronchiolitis exceed 800 million[3]. The burden of respiratory syncytial virus (RSV) associated bronchiolitis was assessed recently. National data analysis revealed that more than

700,000 infants visit US emergency departments each year because of RSV bronchiolitis and approximately one third of these infants are admitted to the hospital[4]. Environmental and genetic factors may contribute to the severity of disease. Daycare attendance, exposure to passive smoke and household crowding are associated with an increased risk of bronchiolitis related hospitalization[5, 6]. Race and poverty also have been associated with severe bronchiolitis[4]. Other studies have suggested that there might be a genetic predisposition to bronchiolitis. For example, infants with bronchiolitis were more likely to have a family history of asthma or other allergic illness[7].

Over the past 20 years, the rate of hospitalization for bronchiolitis has increased markedly[8]. Recent studies estimated that 2% to 3% of affected children required hospital admission[9]. Some authors have suggested that the widespread use of pulse oximetry monitoring in primary care practices and emergency departments might have contributed to this issue. Other factors, however, such as increased daycare attendance and increase in the number of medically fragile infants, might have led to real increases in the incidence of severe disease[10].

Etiology

Bronchiolitis is usually a consequence of viral respiratory tract infection. RSV is the most common underlying viral agent and has been isolated from 50% to 75% of children younger than two years of age hospitalized with bronchiolitis[11]. Other common respiratory viral pathogens, such as influenza, parainfluenza and adenovirus, have been isolated from children with bronchiolitis[12, 13, 14]. Recent investigations have demonstrated that some children with bronchiolitis may also be infected with rhinovirus[15] or human metapneumovirus[16, 17].

Finally, several studies have reported the recovery of Mycoplasma pneumoniae from infants with bronchiolitis, although this organism is not commonly recognized as a significant cause of disease in young children[12].

Causative agents

i. Respiratory syncytial virus
ii. Parainfluenza viruses - Type 1
Type 2
Type 3
iii. Adenoviruses
iv. Mycoplasma pneumoniae
v. Rhinoviruses

vi. Influenza viruses - Type A

Type B

vii. Enteroviruses

viii. Herpes simplex virus

ix. Mumps virus

Pathogenesis

Bronchiolitis is a result of progressive infection and inflammation of the respiratory mucosa in a young child. The clinical symptoms of obstructive lower respiratory tract infection are a consequence of the partial occlusion of the distal airways. Histological examination of the lungs of affected children often reveals necrosis of the respiratory epithelium, monocytic infiltration with edema of the peribronchial tissues and obstruction of the distal airways with mucus and fibrin plugs. Infants are predisposed to develop wheezing and other symptoms of airway obstruction because of the small luminal calibre of their distal airways and the absence of active immunity to RSV and other respiratory viruses. Viral replication and viral induced production of inflammatory mediators by respiratory epithelial cells contribute to the pathogenesis of disease. After initial infection of respiratory epithelium of the upper airway in an immunologically naive child, viral replication can progress

to the mucosal surfaces of the lower respiratory tract. Desquamation of the respiratory epithelial cells, edema of the mucosal surface and enhanced reactivity of airway smooth muscle lead to the respiratory symptoms that characterize bronchiolitis. Some authors have reported that the clinical spectrum of the disease varies somewhat in association with the underlying viral pathogen[15] and that these differences might reflect differences in the profile and extent of inflammatory mediators such as leukotrienes and cytokines produced by the infected respiratory epithelial cells[18]. The relationship between severe disease and co-infection with multiple respiratory viral agents remains unclear. Environmental factors also play a role in the development of bronchiolitis. It is unclear, however, how exposure to passive smoking might mediate an increased risk of disease or how household over crowding might be associated with an increased severity.

Clinical presentation

An infant with bronchiolitis typically presents with illness during the winter months, although sporadic cases appear throughout the year. More than 50% of affected children are between 2 and 6 months of age[19, 20]. Parents often report that a child attends daycare or has a household contact with cold-like symptoms. Early in the illness, infants usually experience copious rhinorrhea. Typically, infants develop a tight cough associated with poor feeding 4 to 6 days after the initial onset of

symptoms. The proportion of infants with fever seems to vary with underlying pathogen. Overall, infants with respiratory syncytial virus (RSV) associated bronchiolitis are often febrile at the time of presentation for medical care. In patients with adenovirus or influenza associated bronchiolitis, the fever is often higher than 39.8^{o}C. Infants with bronchiolitis often present for medical care with significant tachypnea, mild to moderate hypoxia, and signs of respiratory distress, such as nasal flaring and retractions[19, 20]. Upon examination, the infants typically have audible wheezing, rales or rhonchi, and poor air movement, and the expiratory phase is usually prolonged. Other findings commonly observed in children hospitalized with bronchiolitis include conjunctivitis, rhinitis, and otitis media. Many infants have a distended abdomen caused by hyperinflation of the lungs. Respiratory viral pathogens often can be isolated from infants hospitalized with bronchiolitis. However, the proportion of disease attributable to specific viral pathogen varies by season and year. Viruses can be isolated from nasal wash specimens by enzyme linked immunosorbent assays, indirect fluorescent antibody detection, polymerase chain reaction or viral culture. The results of viral diagnostic testing can be used to limit the inappropriate use of antibacterial therapy. But unfortunately these investigations are not widely available in developing countries like India. Infants with bronchiolitis often have mildly elevated total white blood

cell counts, although the differential cell count is typically normal[19]. Hypoxia is often observed on pulse oximetry or analysis of arterial blood gases. Retention of carbon dioxide can be seen in severe cases. Radiological findings of bronchiolitis include hyperinflation, patchy infiltrates that are typically migratory and attributable to post obstructive atelectasis and peribronchial cuffing[19]. Because bronchiolitis is not a disease of alveolar spaces, a secondary bacterial pneumonia should be suspected if a true alveolar infiltrate is seen on chest radiograph.

Differential diagnosis

The absence of antecedent upper respiratory tract symptoms should suggest to clinicians that an infant with the acute onset of wheezing might not have bronchiolitis. In newborns, congenital anomalies, such as a vascular ring or congenital heart disease should be considered. Gastroesophageal reflux, aspiration pneumonia or foreign body aspiration can mimic the symptoms of bronchiolitis.

Management

General supportive measures are the mainstay of management for bronchiolitis. The management of bronchiolitis consists of cardio respiratory monitoring, proper positioning to facilitate respiratory efforts (upright posture), and administration of humidified oxygen and possibly a trial of bronchodilators. Infants should be made as comfortable as

possible (held in a parent's arms or sitting in the position of comfort). Cardio respiratory monitoring is essential. Oxygen should be administered if the oxygen saturation is less than 94% on room air.

Because of tachypnea, partial nasal obstruction and feeding difficulties, young infants sometimes need intravenous fluids to correct dehydration. The use of bronchodilator therapy in the management of infants with bronchiolitis remains controversial[9, 21-23]. The inclusion of patients with history of recurrent wheezing has introduced bias into some studies and might have resulted in an overestimation of the potential benefit of bronchodilators. A recent meta-analysis found that in eight trials that included 394 children, 54% of patients treated with bronchodilators compared with 25% who received a placebo had an improved clinical score [OR(95%CI) = 0.29(0.19–0.45)]. Bronchodilator therapy was not associated with reduced need for or duration of hospitalization[24]. Similarly, a recent randomized, double-blinded, placebo controlled trial demonstrated that nebulized epinephrine did not shorten the duration of hospitalization[25]. A meta-analysis conducted by Hartling, et al[26] also found insufficient evidence to support the use of nebulized epinephrine in hospitalized children. The role of steroids in the treatment of infants with bronchiolitis also has been controversial[27]. A meta-analysis of six placebo controlled trials demonstrated that

corticosteroid therapy was associated with a significant reduction in the duration of hospitalization stay [OR (95%CI) = 0.43(0.05–0.81)]. However, if the studies that included patients with a history of recurrent wheezing were omitted from the analysis, this difference was no longer significant[28]. Dexamethasone also had no beneficial effect in children with respiratory failure caused by RSV bronchiolitis[29]. But, some studies have demonstrated that the use of steroids may be of benefit to infants with bronchiolitis if given before hospitalization[30, 31]. In a randomized, placebo controlled trial, Csonka, et al demonstrated that infants treated with oral prednisolone upon initial evaluation and during the first 3 hospital days had a one day reduction in the duration of symptoms and length of hospital stay. Some clinicians have concluded that early treatment with steroids might shorten the duration of illness.

RSV is the most common cause of bronchiolitis; however, specific antiviral therapy of symptomatic infants has been of limited value. Aerosolized ribavirin treatment of mild to moderately ill infants with laboratory confirmed RSV bronchiolitis does not prevent the need for mechanical ventilation or reduce the duration of hospital stay. American Academy of Pediatrics (AAP) does not recommend the routine use of ribavirin but suggests that ribavirin might be administered based on specific clinical circumstances and physician experience[31]. Patients who are at risk of persistent viral replication might benefit from

ribavirin therapy. Some experts recommend that ribavirin be considered when caring for severely immunocompromised patients who develop laboratory confirmed RSV associated bronchiolitis, such as children undergoing bone marrow transplantation[32]. Experts debate the role of ribavirin therapy for severely ill infants who require mechanical ventilation. In a single placebo controlled study, investigators found that infants treated with aerosolized ribavirin had a shorter duration of ventilation and of hospital stay[33]. Finally, investigators have yet to demonstrate that other therapies, including interferon, surfactant, vitamin A, mist therapy, or anticholinergics, have any measurable clinical effect. Epidemiologic data for under developed countries like ours are incomplete. Morbidity and mortality may be higher in poorly developed countries because of under nutrition and lack of resources for supportive medical care.

Diagnosing bronchiolitis is important for preventing cross infection in the hospital and for epidemiological purpose. History and physical examination form the primary basis for the diagnosis of bronchiolitis because serological studies are not widely available in resource limited countries like India. In healthy infants and young children acute bronchiolitis is usually a self limited disease. Most of these children begin to improve within one or two weeks. But it can lead to severe disease and mortality in some children.

Figure 1: Assessment and treatment of bronchiolitis[34]

Diagnosis: bronchiolitis

↓↓

Assessment of severity		
Mild	**Moderate**	**Severe**
■ Normal ability to feed ■ Little or no respiratory distress ■ Oxygen saturation 92 per cent or more in room air.	■ May appear short of breath during feeding. ■ Moderate respiratory distress, with some chest wall retractions, nasal flaring. ■ Apnoeic episodes, usually brief, self-limiting. ■ Usually hypoxemic, corrected (to SaO_2 92 per cent or higher) by oxygen.	Symptoms of acute bronchiolitis with one or more of the following conditions, 1.Poor feeding / Need for intravenous hydration 2.Severe respiratory distress with marked retractions, nasal flaring, grunting 3. hypoxemic, not corrected (to SaO_2 92 per cent or higher) by oxygen. 4.Need for mechanical Ventilation

↓↓

Treatment:		
Mild	**Moderate**	**Severe**
1. Treat at home. 2. Inform the parents when to return. 3. Review after 2days.	1. Admit 2. Maintain SpO_2>92% with oxygen supplementation. 3. Careful oral feeds/IV fluids 4. Chest X ray 5. Watch for any deterioration	1. Admit in ICU. 2. Maintain SpO_2 by oxygen supplementation. 3. Mechanical ventilation if needed. 4. NPO 5. IV fluids. 6. Chest x ray/ABG. 7. Cardiorespiratory monitoring.

Complications and outcomes

The case fatality rate for bronchiolitis is highest among infants between 1 and 3 months of age. Premature infants with birth weights less than 1500 g have a bronchiolitis mortality rate of 30 per 100,000 live births[1]. The presence of underlying medical illness, such as congenital heart disease or chronic lung disease, is another important predictor of poor outcome[35]. In these high risk children, the case fatality rate may be as high as 5%. Serious complications, including respiratory failure, apnea and pneumothorax, occur among infants hospitalized with bronchiolitis, more commonly among previous premature infants and infants with congenital anomalies. Overall, serious complications are associated with prolonged hospital stay and increased health care costs. The association between early bronchiolitis and asthma has been debated hotly[36, 37]. Up to 50% of children with a history of previous bronchiolitis develop recurrent wheezing[37, 38]. Some investigators have suggested that a family history of allergic or atopic disease correlates with the subsequent development of asthma. However, this association is incompletely understood[39, 40].

Among healthy former premature infants, hospitalization for RSV bronchiolitis has been associated with an increase in subsequent use of health care resources, particularly those associated with respiratory conditions[41]. Subsequent health care visits for respiratory symptoms

occurred in 64% of infants previously hospitalized, compared with 13% in infants not hospitalization for RSV bronchiolitis. For unclear reasons, secondary bacterial infections of the lower respiratory tract are unusual in infants with bronchiolitis[42]. It is estimated that one half to two thirds of children hospitalized for RSV bronchiolitis are febrile. Investigators in Texas demonstrated that children less than 2 years of age hospitalized for RSV bronchiolitis have a low rate of concurrent serious bacterial infections[43]. Two studies compared febrile RSV positive and RSV negative infants younger than 8 weeks of age. The rates of serious bacterial infections in RSV positive groups ranged from 1.1% to 7%, whereas the rate among RSV negative infants was 12.5% in both the studies. None of the RSV positive children had bacterial meningitis, and the predominant serious bacterial infection in these groups was urinary tract infection[44, 45]. Of note, infants younger than 28 days had rates of serious bacterial infections of 13.3%, regardless of RSV status[45]. Most children older than 1 month with typical signs and symptoms of bronchiolitis, especially children who are RSV positive, may not warrant full evaluation for invasive bacterial infection and may not require empiric antibiotic therapy at the time of hospitalization. The risk of urinary tract infection remains significant. In the first month of life, the risk of serious bacterial infections remains unchanged regardless of whether an infant is RSV positive or negative.

Prevention

A vaccine to prevent RSV infection in young children is needed. Despite several decades of effort, however, vaccine development has been slow[46]. Several obstacles to the successful development of a safe and effective RSV vaccine have been identified.

First, an ideal RSV vaccine would provide immunologic protection to infants less than 2 months of age. This challenge has led some investigators to advocate maternal immunization as a potential strategy. Next, natural infection with RSV does not induce complete and long lasting immunity. An RSV vaccine would be unlikely to induce long lasting immunity, but a reasonable goal might be for an RSV vaccine to protect the most vulnerable children younger than 2 years from serious disease. Finally, the potential for immunoenhancement upon second exposure to RSV antigens has been a serious obstacle to the successful development of an RSV vaccine. Recently, the Centres for Disease Control and Prevention recommended that all healthy children aged 6 to 23 months receive the influenza vaccine[47]. Recent issues with the vaccine supply have limited the early adoption of this recommendation, so the magnitude of its impact remains unknown. Currently, paediatricians rely on passive immunization to prevent serious RSV related infections in high-risk infants. Monthly administration of paluvizumab (a monoclonal antibody directed against a key viral surface

protein) or hyper immune immunoglobulin is associated with a significant reduction in the rate of hospitalization for respiratory illnesses among children younger than 2 years of age with a history of prematurity, chronic lung disease, and hemodynamically significant congenital heart disease[48-50]. RSV prophylaxis should be administered once per month during the RSV season. Because high-risk infants can develop two severe RSV infections within the same season, prophylaxis should be continued throughout the RSV season even in an infant who develops a documented RSV infection while receiving immunoprophylaxis.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

1) **Iqbal SMJ, et al,** [51] from King Edward Medical University/ Mayo Hospital, Lahore conducted an epidemiological and clinical study in acute bronchiolitis during October 2006 to March 2007. They mentioned that overwhelming majority of children suffering from acute bronchiolitis was less than one year of age. There was male predominance. Most of the children were bottle fed. Main presenting features of acute bronchiolitis were respiratory distress, nasal flaring and wheezing.

2) **Thorburn K,** [52] from a tertiary paediatric intensive care unit in a university affiliated children's hospital, UK, had done a cohort study of children with severe RSV infection covering eight consecutive RSV seasons (1999-2007). They concluded that pre existing illness or co-morbidity, in particular multiple pre existing diseases and cardiac abnormality, is associated with a significantly higher risk of mortality from severe RSV infection. Hospital acquired RSV infection is an additional major risk factor for death in children with severe RSV infection.

3) **Holman, et al,** [53] during 1996 through 1998 reported 229 bronchiolitis deaths, resulting in an average annual infant mortality rate of 2.0 per 100 000 live births in United States. The study showed that infants born as VLBW and LBW are at increased risk of dying with bronchiolitis. Although infants weighing less than 2500 g at birth are at increased risk for dying with bronchiolitis, the majority of bronchiolitis deaths occur among infants of normal birth weight.

4) **Shay DK, et al,** [54] done a descriptive analysis of US National Hospital discharge survey data from 1980 to 1996 to describe rates of bronchiolitis associated hospitalizations during 1980-1996. The rates of hospitalization of children with bronchiolitis increased substantially, as did the proportion of total and lower respiratory tract hospitalizations associated with bronchiolitis. Annual bronchiolitis hospitalizations associated with RSV infection among children may be greater than previous estimates for RSV bronchiolitis and pneumonia hospitalizations combined.

5) **Moore HC, et al,** [55] conducted a retrospective population based cohort study of 212068 singleton births of 37 to 42 weeks gestation to examine the associations between the number of hospital admissions for bronchiolitis and pneumonia and elective caesarean

delivery. This study concluded that delivery by elective caesarean was independently associated with infant hospitalizations for bronchiolitis but not pneumonia. Elective caesarean delivery without labour may result in impaired immunity in the newborn leading to high risk of early viral lower respiratory infections.

6) **El-Radhi, et al**, [56] from Queen Mary's Hospital, Sidcup, UK, studied the relationship between fever and the clinical course of 90 infants (59 boys, 31 girls) hospitalised during between November 1997 and February 1998 with bronchiolitis prospectively. The findings of this study suggest that most infants with bronchiolitis are afebrile and that fever is associated with more severe bronchiolitis.

7) **Koehoorn, et al,** [57] analysed the outpatient and inpatient health records of 93058 infants born in the Georgia Air Basin between 1999 and 2002 to investigate the epidemiological features of bronchiolitis. It is a population based cohort study. Adjusted Cox proportional-hazard analyses indicated an increased risk of bronchiolitis in the first year of life (follow-up period: 2 to 12 months) for boys, infants of First Nations status, infants with older siblings and infants living in neighbourhoods with smaller proportions of maternal post secondary education. The risk also was

high for infants born to young mothers less than 20 years of age or mothers who did not initiate breastfeeding in the hospital. Infants with LBW or VLBW and those with underlying congenital anomalies also had increased risk. Maternal smoking during pregnancy increased the risk of hospitalized bronchiolitis.

8) **Semple MG, et al,** [58] conducted a prospective cohort study in Alder Hey Children's Hospital, UK with 378 infants admitted to hospital with a diagnosis of bronchiolitis over 3 consecutive endemic winter seasons (2002 - 2005) to examine demographic, environmental and clinical factors associated with severe bronchiolitis in infants admitted to hospital and quantify the independent effects of these factors. Of the 378 infants, 299 (79%) were antigen positive to respiratory syncytial virus (RSV). They found male sex ($p = 0.035$) and exposure to passive smoking ($p = 0.001$) were associated with severe disease. Premature birth, low birth weight, low admission weight and low corrected age on admission were also associated with need for mechanical ventilation ($p = 0.002$).

9) **Fjaerli HO, et al,** [59] from Akershus University Hospital, Norway performed a population based retrospective survey for the period 1993 to 2000 in children younger than two years of age hospitalised for RSV bronchiolitis. They concluded that the length of

hospitalisation and morbidity was high in preterm infants, children with a congenital heart disease and in children with trisomy 21, the last group being at particular high risk for severe disease.

10) **Al-Muhsen SZ, et al, [60]** investigated the risk factors associated with RSV infection in Saudi children admitted in pediatric intensive care unit (PICU) of a tertiary hospital during January 2003 to January 2009. They have found that prematurity is associated with increased severity of RSV bronchiolitis. 37% of the infants admitted in the PICU were found to be of premature birth. Moreover, children with underlying pulmonary pathology and cardiac abnormalities were also more prone to RSV infection.

11) **Horn SD, et al, [61]** from Salt Lake City, USA, analysed the data from 304 infants (</=1 year) with RSV bronchiolitis or RSV pneumonia admitted to nine children's hospitals from April 1995 to September 1996 retrospectively to determine the outcomes of infants hospitalized for respiratory syncytial virus (RSV) associated respiratory illnesses. They compared two 215 term infants (GA > or =37 weeks) and 89 infants with GA <37 weeks, divided according to GA into 3 subgroups (< or =32, 33 to 35, and 36 weeks). They found significant differences for the rate of intubation (P=.002) and ICU and hospital length of stay (P=.021 and P<.0001, respectively), with the highest resource use in 33 to 35 weeks GA

infants, which remained significant in multiple regression analyses. The study concludes that, prematurity < or =35 weeks GA significantly increases the risk for severe outcomes among infants hospitalized for RSV. Infants 36 weeks GA had outcomes similar to term infants.

12) **Shaw KN, et al,** [62] from the Division of General Pediatrics, Children's Hospital of Philadelphia, conducted a study with two hundred thirteen infants younger than 13 months with bronchiolitis. They were prospectively followed up to identify the historical, physical, and laboratory clues at initial emergency department evaluation that would help to predict disease severity. Based on their total course of illness, the patients were classified as having mild (139 patients) or severe (74 patients) disease, and the initial emergency department evaluation findings of these two groups were compared. They concluded that six independent clinical and laboratory findings were strongly associated with more severe illness: (1) "ill" or "toxic" general appearance; (2) oxygen saturation less than 95%, as determined by pulse oximetry; (3) gestational age, younger than 34 weeks; (4) respiratory rate, 70/min or greater; (5) atelectasis on a chest roentgenogram; and (6) age, younger than 3 months. The infant's oxygen saturation as determined by pulse oximetry was the single best objective predictor of more severe disease.

STUDY JUSTIFICATION

STUDY JUSTIFICATION

- In healthy infants and young children acute bronchiolitis is usually a self limited disease. Treatment in most of these cases is only supportive measures. Most of these children begin to improve within one or two weeks. But it can lead to severe disease and mortality in some children.
- If we know the factors which predispose to severe bronchiolitis and mortality in acute bronchiolitis, plan of management can be targeted effectively.
- Keeping this in mind, this study was designed to study the clinical profile of acute bronchiolitis in our hospital and risk factors for severe disease and mortality in children less than 2 years of age.

AIM OF THIS STUDY

AIM OF THIS STUDY

- To describe the clinical profile and
- To study the risk factors for severity and mortality in infants and young children less than 2 years of age presenting with acute bronchiolitis at an urban referral hospital.

SUBJECTS AND METHODS

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1. Methodology

Study design

Descriptive study / Nested case control study.

Study place

General medical wards and PICU, Institute of Child Health and Hospital for Children, Egmore, Chennai.

Study period

January 2010 to October 2011

Study population

Cases admitted with signs and symptoms of acute bronchiolitis in general medical wards and PICU of ICH and HC, Egmore, Chennai.

Case definition[63]

Acute bronchiolitis is defined as the first episode of breathlessness in a child between 31 days to 24 months of age associated with the following signs and symptoms,

1. Upper respiratory illnessess like cough, rhinorrhea
2. With or without fever
3. Respiratory distress
    - tachypnea (RR> or =60 / min in infants < 2 months

> or =50/ min in 2 months to 1 year

> or =40 / min in children > 1 year)

- Chest retractions, nasal flaring, grunting.

4. Wheeze and crepitations
5. With or without cyanosis
6. Normal or hyperinflation in chest X ray
7. No family h/o atopy, asthma.

Mild bronchiolitis

- Normal ability to feed
- Little or no respiratory distress
- No requirement for oxygen therapy –i.e. oxygen saturation 92 percent or more in room air.
- Will recover fully in one to two weeks.

Moderate bronchiolitis

- May appear short of breath during feeding.
- Moderate respiratory distress, with some chest wall retractions, nasal flaring.
- May have apnoeic episodes, usually brief, self limiting.
- Usually hypoxemic, corrected (to SpO_2=92 per cent or higher) by oxygen supplementation.

Severe bronchiolitis

Severe acute bronchiolitis is defined as signs and symptoms of acute bronchiolitis with one or more of the following conditions,

1. Poor feeding / Need for intravenous hydration
2. Severe respiratory distress with marked retractions, nasal flaring, grunting
3. Hypoxemia(SpO_2 <92%) not correctable with oxygen supplementation.
4. Need for mechanical ventilation.

Inclusion criteria

Children between the age group of 31 days to 24 months who meet the case definition for acute bronchiolitis

Exclusion criteria

1. Children with abnormal chest X ray findings like consolidation, patch and cyst will be excluded.
2. Children in whom structural malformations are identified such as CLE will be excluded.
3. Children who have known immunodeficiency will be excluded.

Cases

All cases of acute bronchiolitis, fulfilling the criteria for severe disease and those who have died.

Controls

All cases of mild and moderate acute bronchiolitis.

Case : Control Ratio; 1: 2

Sample size: 215

2. **Manoeuvre**

- Study population was recruited based on inclusion and exclusion criteria after obtaining parent consent.
- Then they are subjected to clinical examination and graded into mild, moderate and severe cases and they were divided into severe (case) and non severe (control) groups.
- Using prestructured proforma, information is gathered regarding patients age, sex, other demographic details and risk factors considered for this study from all patients.
- The following demographic and clinical variables were compared between severe and non severe groups to asses their value as risk factors for severe disease.

1. Age (less than 3 months)
2. Male sex
3. Poor socioeconomic status
4. Family history of atopy

5. Upper respiratory illness in the family
6. Indoor air pollution
7. Exposure to passive smoking
8. Caesarean delivery
9. Preterm birth (less than 34 weeks)
10. Low birth weight (less than 2.0 kg)
11. History of neonatal admission
12. History of neonatal mechanical ventilation
13. Lack of breast feeding (those breastfed less than 3 months duration)
14. Fever
15. Underlying congenital cardiac lesions
16. Underlying congenital airway anomalies
17. Over weight (weight for length >2 z score)
18. Clinical pallor

3. **Statistical analysis**

- Statistical analysis was done using SPSS software with 17.0 version.

- Descriptive statistics like number, proportion, percentage, range and inferential statistics like p value was arrived at using Chi square test.

- Univariate analysis with severity as the outcome variable was done. This provided an Odds Ratio with 95% confidence interval [OR(95%CI)] for each factor.

- All the significant variables from univariate analysis were applied into the binary logistic regression model. Multivariate binary logistic regression models were constructed to identify associations between the environmental, demographic and clinical covariates and outcome measures (disease severity).

4. Ethics

Patient consent and IRB approval obtained

OBSERVATIONS

OBSERVATIONS

Total cases studied : 215

Number of severe cases : 48

Number of non severe cases : 167

Totally 215 children, diagnosed as bronchiolitis from January 2009 to October 2011, were included in this study. Out of whom 137(63.7%) children were males, 78(36.3%) children were females with male to female ratio of 1.7:1.

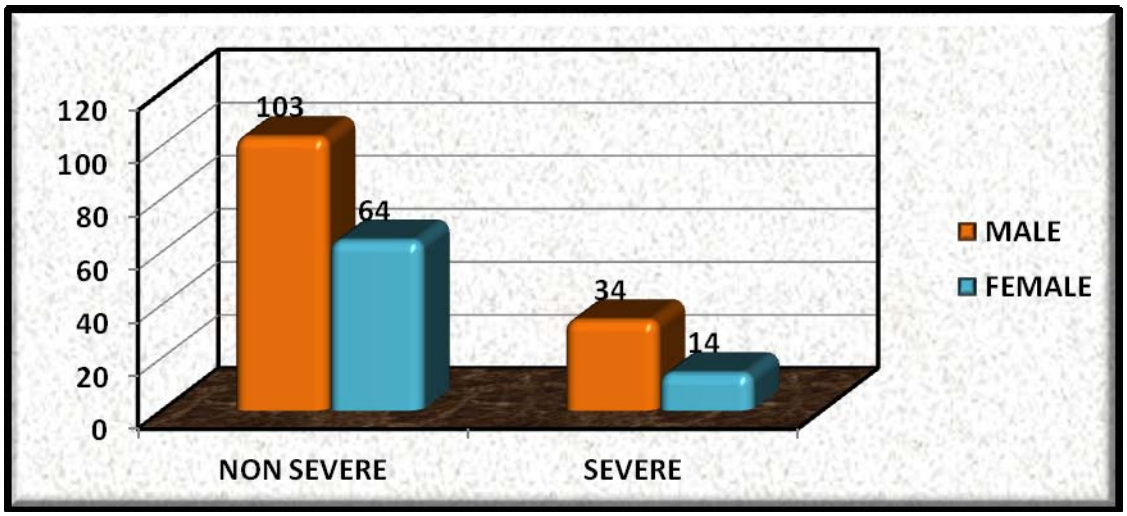

Figure 2: Comparison of sex distribution of acute bronchiolitis among severe and non severe groups.

Among these 215 children, 33 (15.3%) belong to less than 3 months of age group, 92 (42.8%) children were between 3 and 6 months of age, 83(38.6%) children were between 6 and 12 months of age group,

7(3.3%) were belong to more than one year of age group. Lowest age reported was 35 days. The mean age reported in this study is 4.6 months.

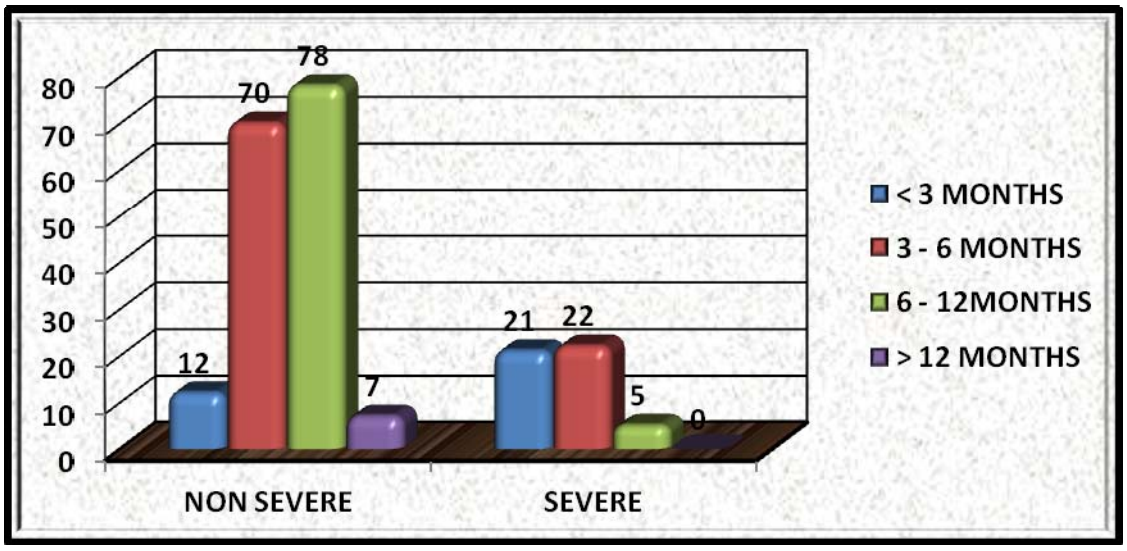

Figure 3: Comparison of age distribution of acute bronchiolitis among severe and non severe groups.

Most of these cases (83.3%) were reported between the months of October and January. Rest of the cases were spread throughout the year.

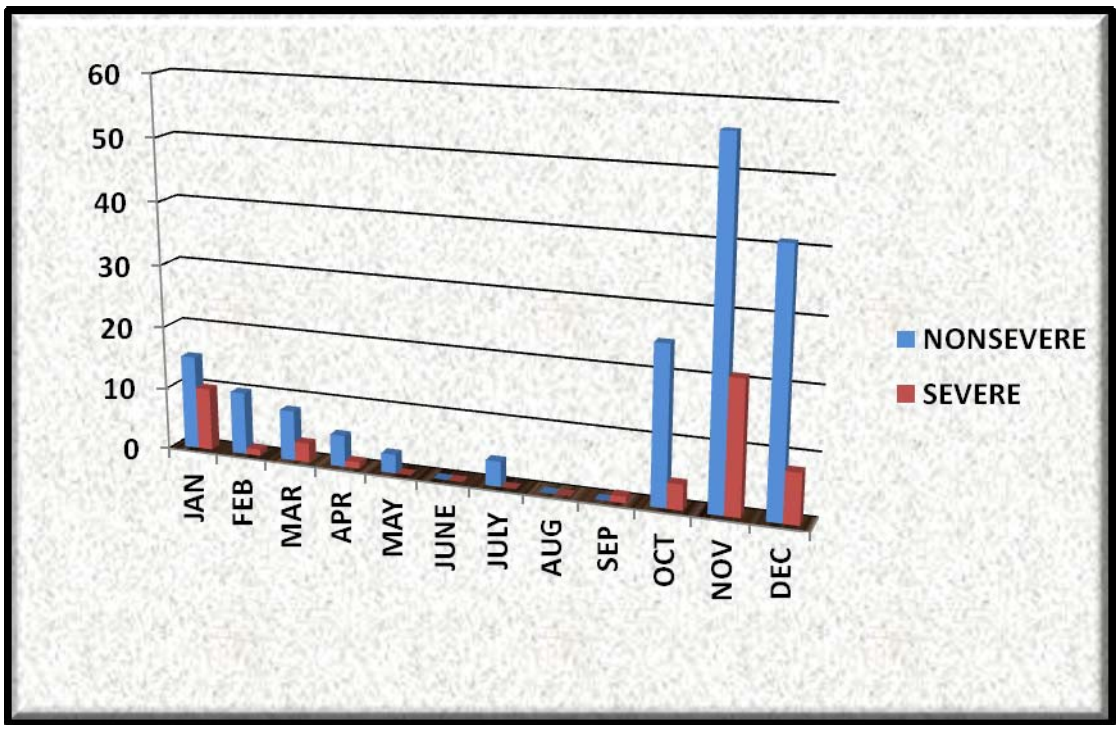

Figure 4: Comparison of seasonal pattern of acute bronchiolitis among severe and non severe groups.

79(36.7%) of these children required less than two days of hospitalisation, 88(40.9%) children stayed in the hospital for 2 to 5 days while 44(20.5%) children stayed for 5 to 10 days and only 4(1.9%) children required more than 10 days of hospitalisation. The mean duration of hospital stay is 3.52 days.

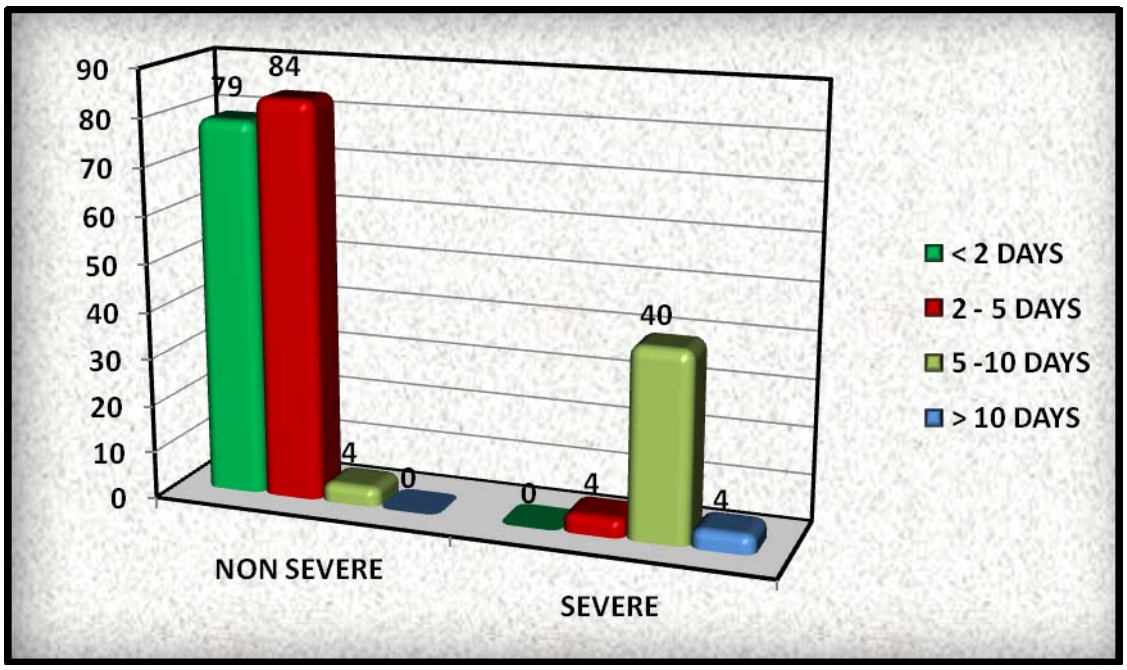

Figure 5: Comparison of duration of hospital stays of among severe and non severe groups.

While looking into the socioeconomic status, 172 (80%) children in this study belong to middle (both upper middle and lower middle) socioeconomic status according to modified kuppusamy's scale, whereas 28(13%) of children belong to lower (both upper lower and lower) socioeconomic status and only 15(7.0%) of them belong to upper socioeconomic status.

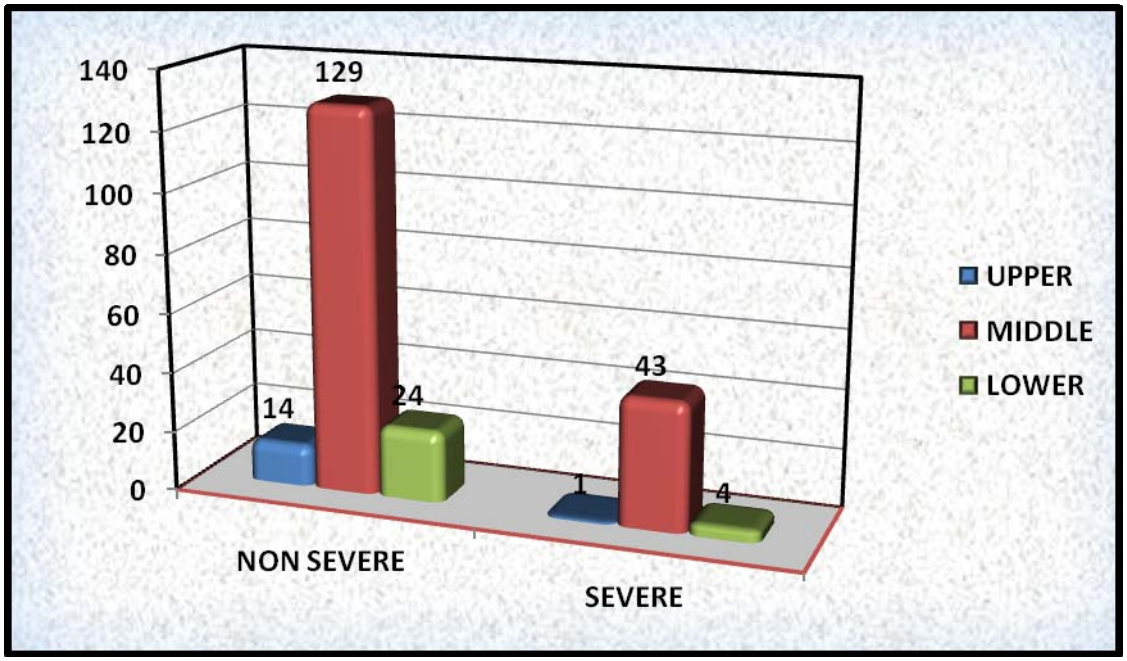

Figure 6: Comparison of socioeconomic profile among severe and non severe groups.

All children in our study had upper respiratory illness in the form of cough, running nose or sneezing, of whom 185 (86.0%) children had upper respiratory symptoms for less than two days duration prior to hospitalisation, whereas 29 (13.5%) children had these symptoms between 2 to 5 days duration and only one child (0.5%) had symptoms for more than five days duration.

Among these 215 children, fever was documented in 150(69.8%) children. Among those 150 febrile children 131(87.3%) of them had low grade fever (temperature recorded less than 101 degree F) and 19(12.7%) children had fever of high grade (more than or equal to 101 degree F) in nature. But none of these children had history of chills or rigors. In 117(78.0%) children, the fever was present for less than 2 days duration,

while in 31(20.7%) children, the fever was present between 2 to 5 days duration and only 2(1.3%) children had fever for more than 5 days duration.

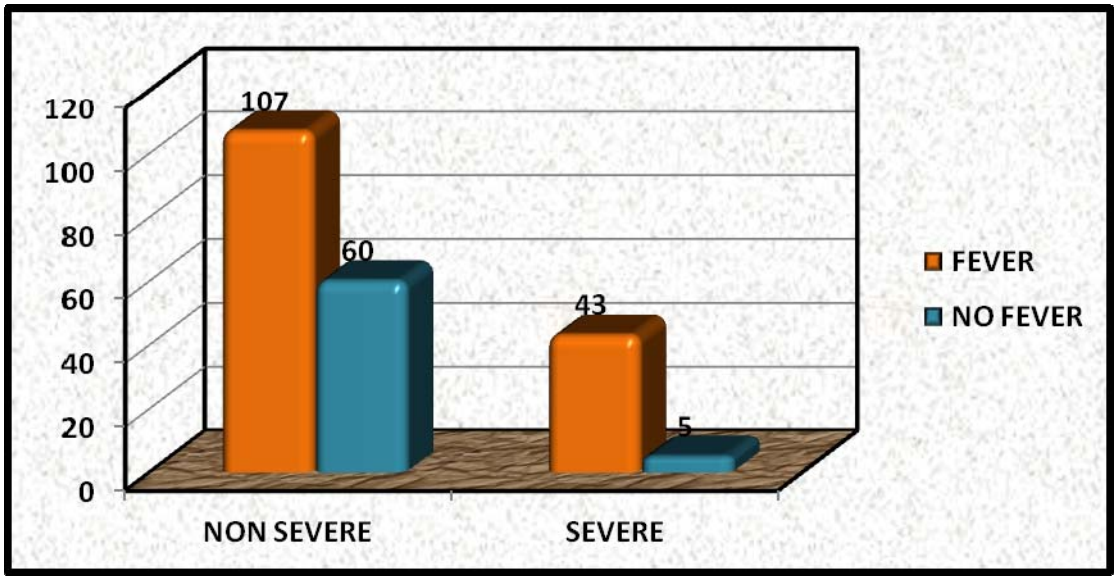

Figure 7: Comparison of presence of fever among severe and non severe groups.

All 215(100%) children had history of difficulty in breathing. Out of them, 184(85.6%) of children had these symptoms for less than two days duration and 31(14.4%) children were symptomatic for 2 to 5 days duration. But none of these children had these symptoms for more than 5 days duration.

Among these 215 children, 10(4.7%) children had various forms of congenital cardiac lesions. 4 children were already diagnosed prior to this hospital admission but in other 6 children, the diagnosis was established during this present hospitalisation. Among these 10 children, 6 children

had ventricular septal defect, two children had atrial septal defect and another two of them had patent ductus arteriosus.

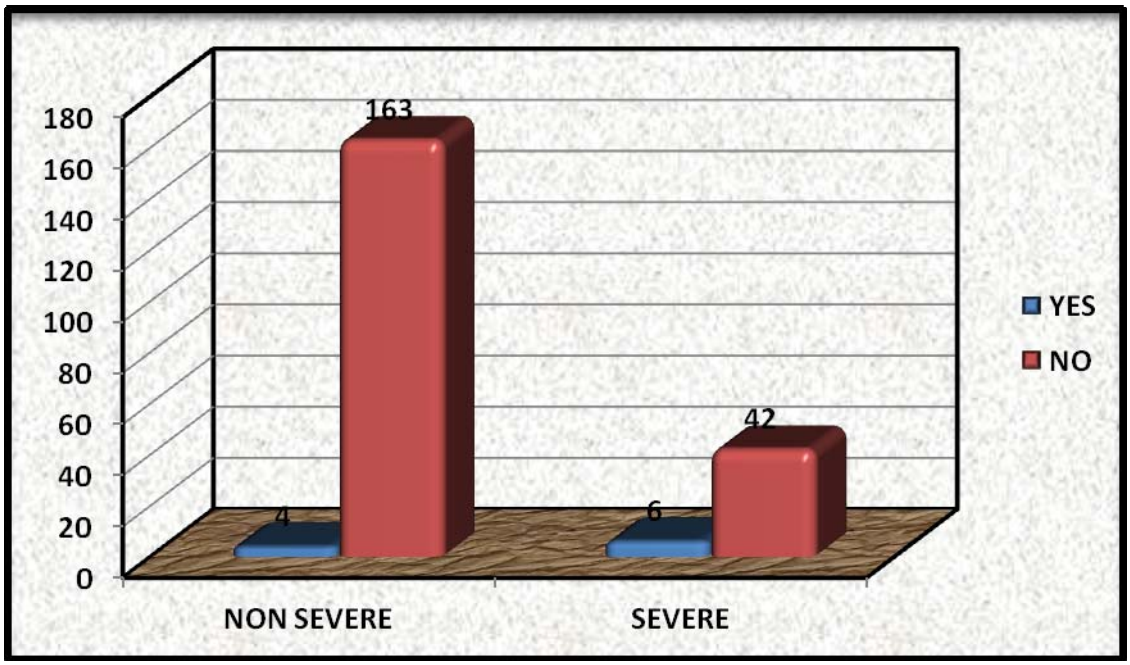

Figure 8: Comparison of congenital cardiac illness among severe and non severe groups.

Congenital airway anomalies were present in 10(4.7%) children. Among these, eight children had laryngomalacia (5- already diagnosed, 3- diagnosed at this time) and two children had tracheomalacia (both of them were diagnosed at this time). Among those with congenital cardiac lesions and congenital airway anomalies, the clinical course was longer and severe ($p < 0.05$).

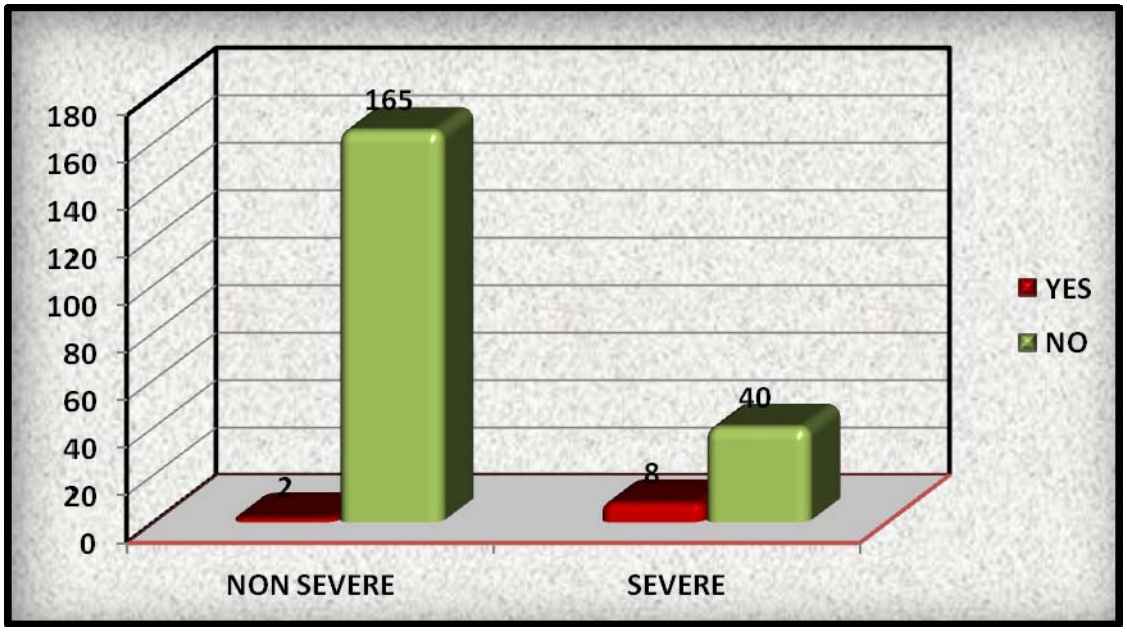

Figure 9: Comparison of airway anomalies among severe and non severe groups.

While analysing the family history of these 215 children, family history of upper respiratory illness in the form of cough, cold, sneezing or running nose in any member of the family (father, mother, grant parents or siblings) was present in 26(12.1%) cases. This is most commonly seen among those children, who had severe clinical course (p <.0.05)

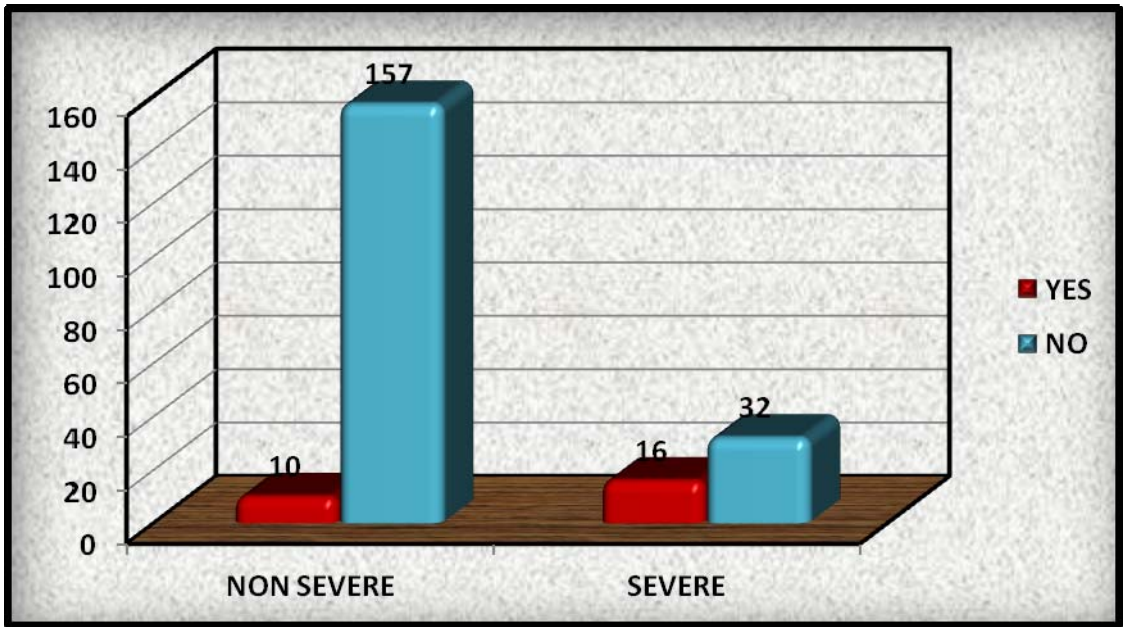

Figure 10: Comparison of URI in the family among severe and non severe groups.

Family history of smoking (in anyone of the family member) was present in 23(10.7%) cases.

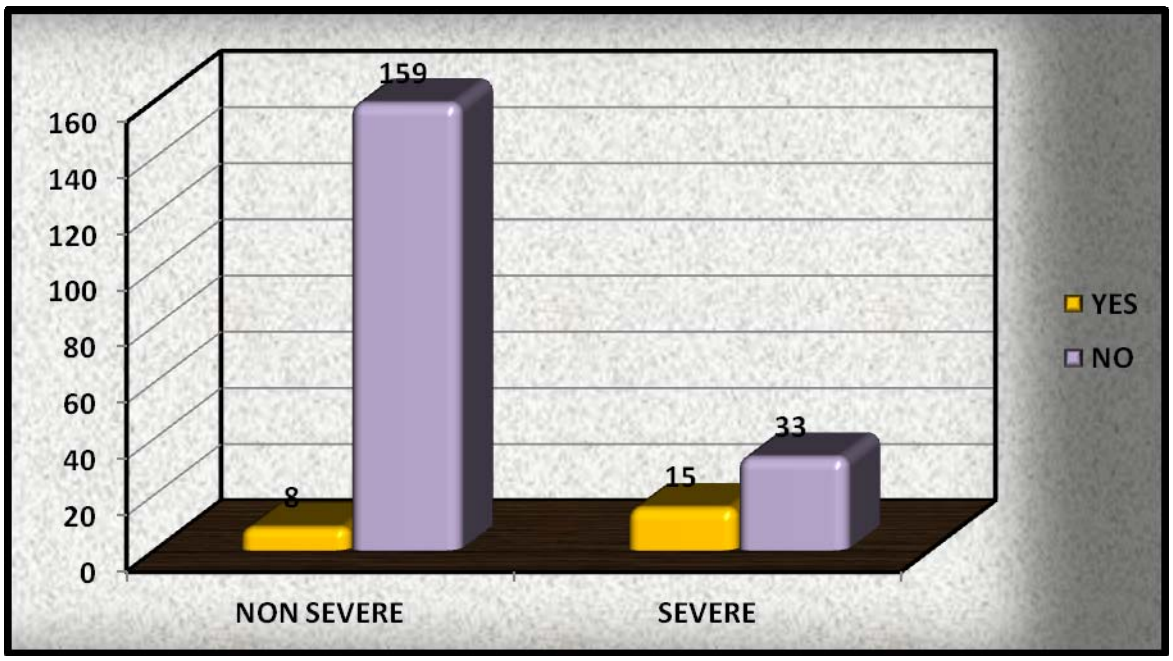

Figure 11: Comparison of exposure to passive smoking among severe and non severe groups.

Family history of allergy or atopy was present in 20(9.3%) cases. But this history was most commonly seen in those who had milder clinical course. Indoor air pollution was present in 21(9.8%) cases.

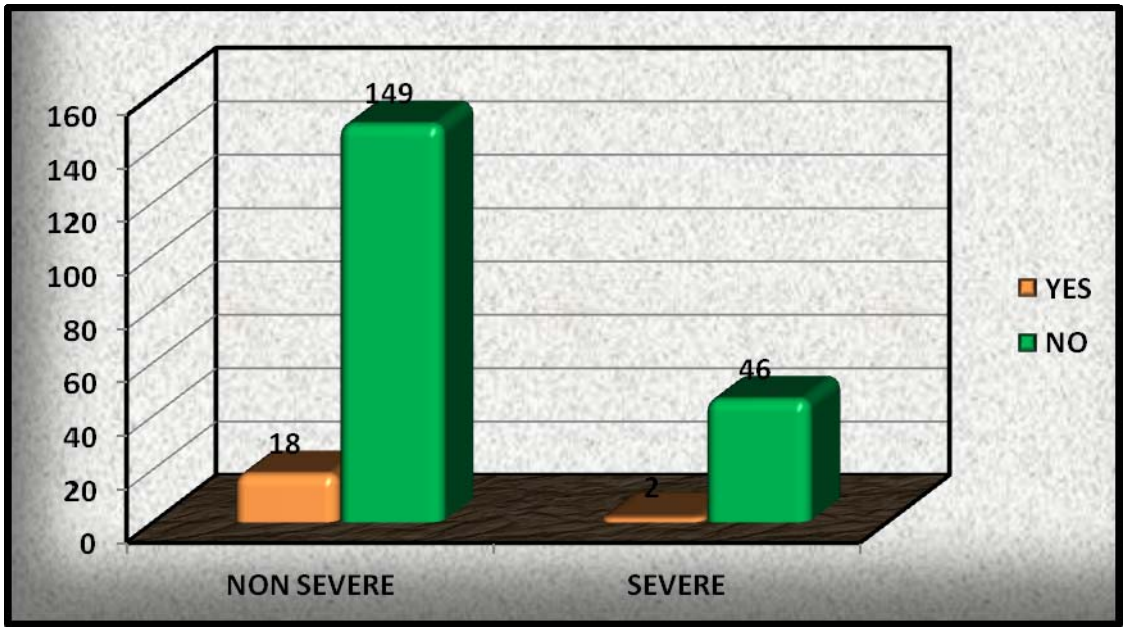

Figure 12: Comparison of family history of atopy among severe and non severe groups.

While probing into the birth and neonatal history, 137(63.70%) children were delivered by caesarean section and 78(36.30%) of children were delivered by normal vaginal delivery.

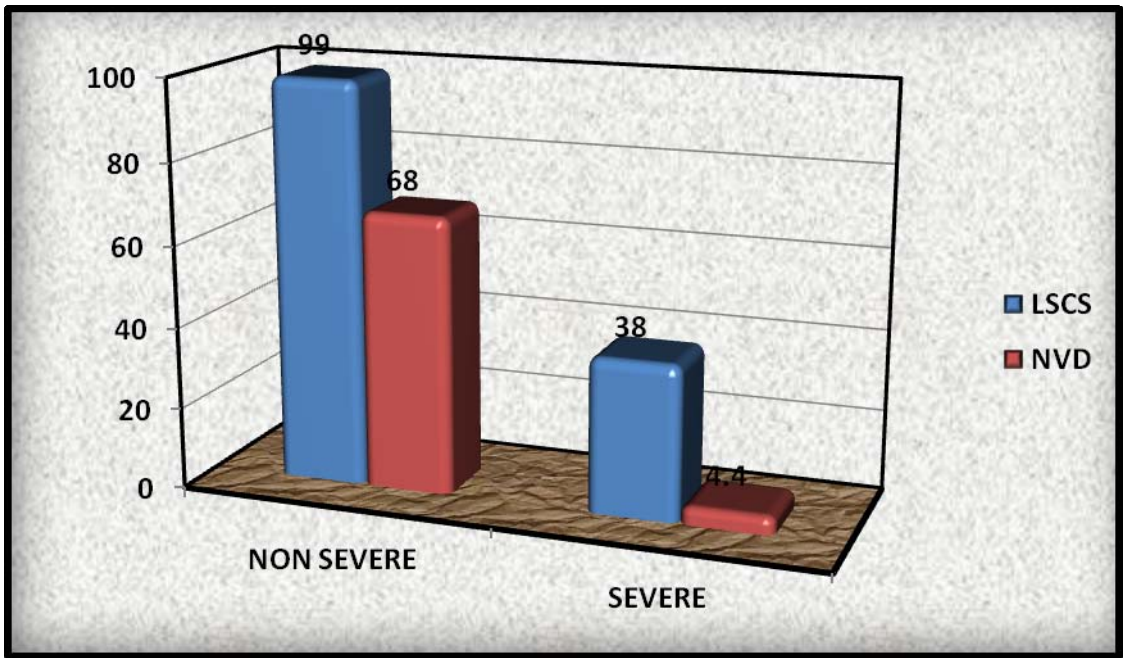

Figure 13: Comparison of type of delivery among severe and non severe groups.

Among them 189(87.90%) of children were delivered after 34 completed weeks and 26(12.10%) of them were delivered before 34 completed weeks.

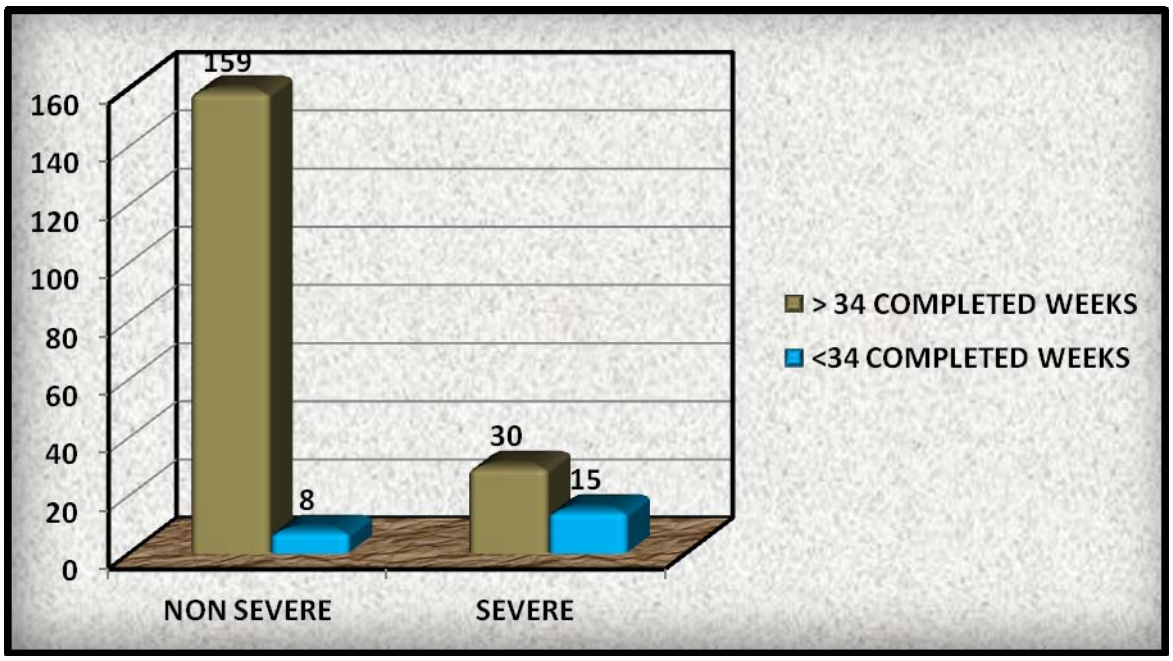

Figure 14: Comparison of gestational age among severe and non severe groups.

While looking into the birth weight of these children, 180(83.70%) of children had birth weight of 2.0 to 4.0 kgs. 33(15.40%) children had birth weight of less than 2.0 kgs and 2(0.9%) children had birth weight of more than 4.0 kgs.

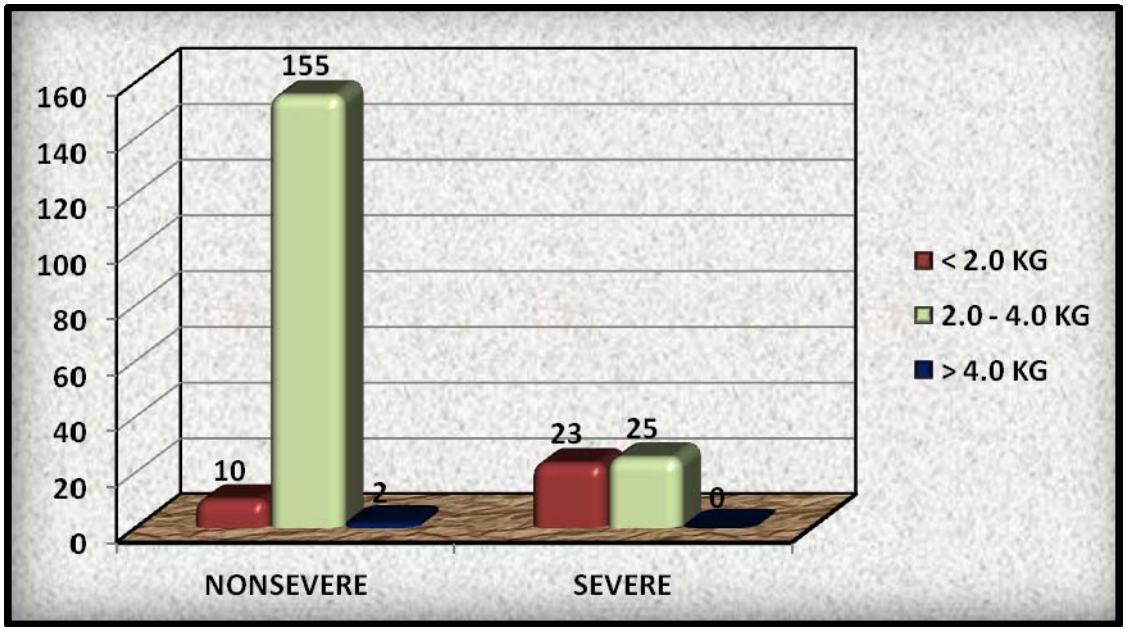

Figure 15: Comparison of birth weight among severe and non severe groups.

Out of these 215 children, 21(9.8%) had history of admission in the neonatal nursery. These babies were admitted in the neonatal nursery for various reasons like low birth weight, respiratory distress, preterm care, sepsis and etc. Among these 21 children, 9(4.2%) were ventilated in the newborn period.

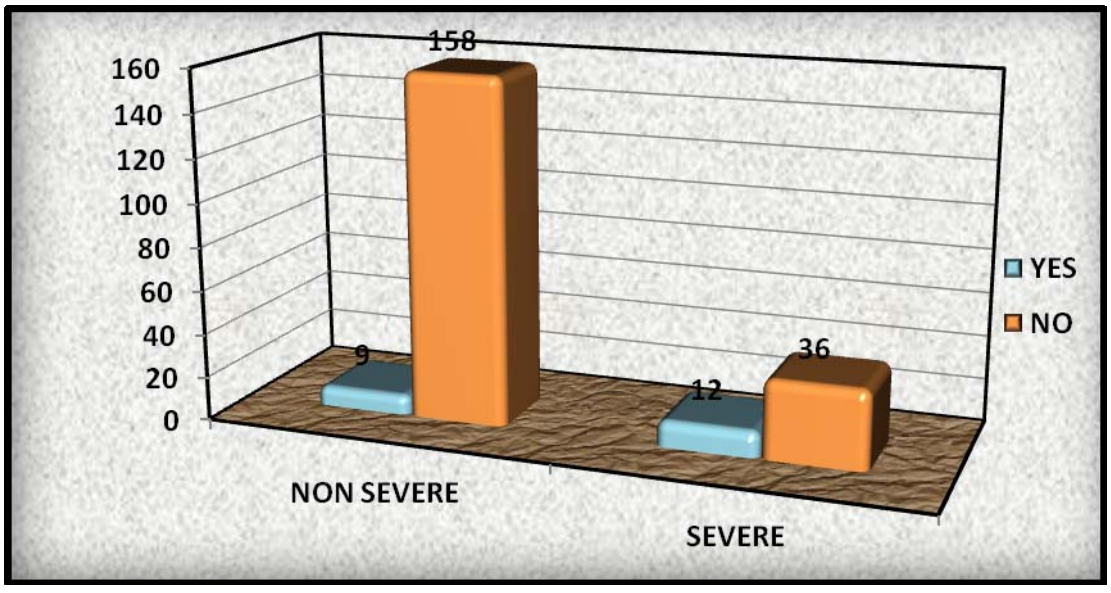

Figure 16: Comparison of history of neonatal admission among severe and non severe groups.

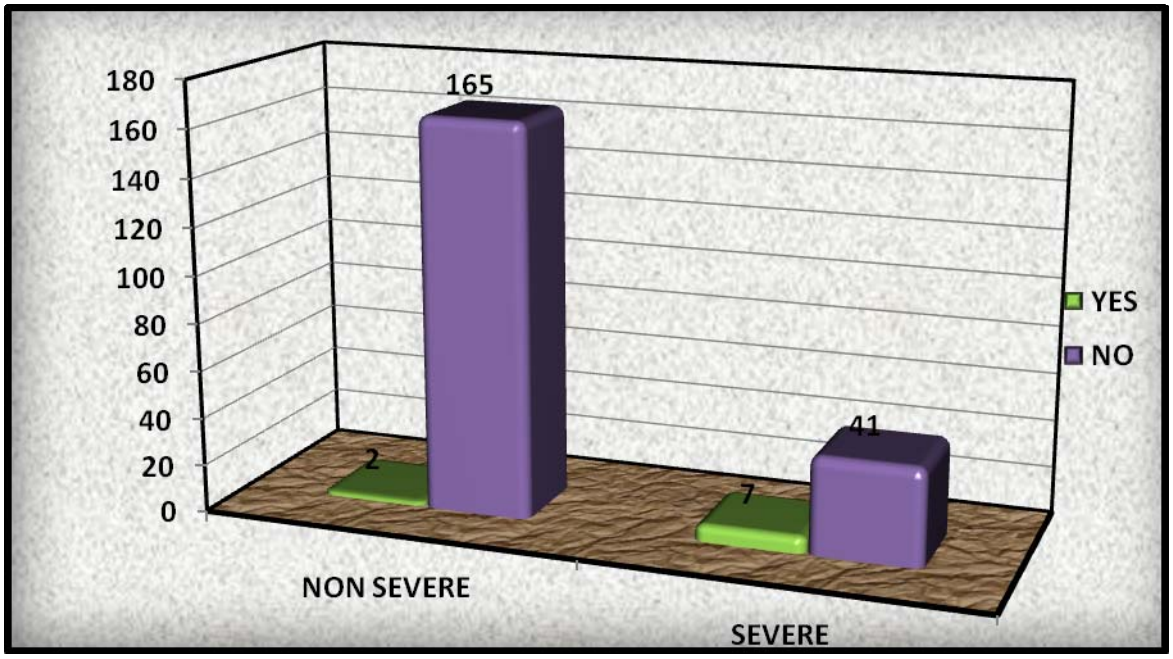

Figure 17: Comparison of history of neonatal mechanical ventilation among severe and non severe groups.

Among these 215 children, 148(68.80%) children were fed exclusively with breast feeds for more than 3 months, but 67(31.20%) children were given breast feeds for less than 3 months period and given other type of feeds like cow's milk, artificial feeds during the first six months period.

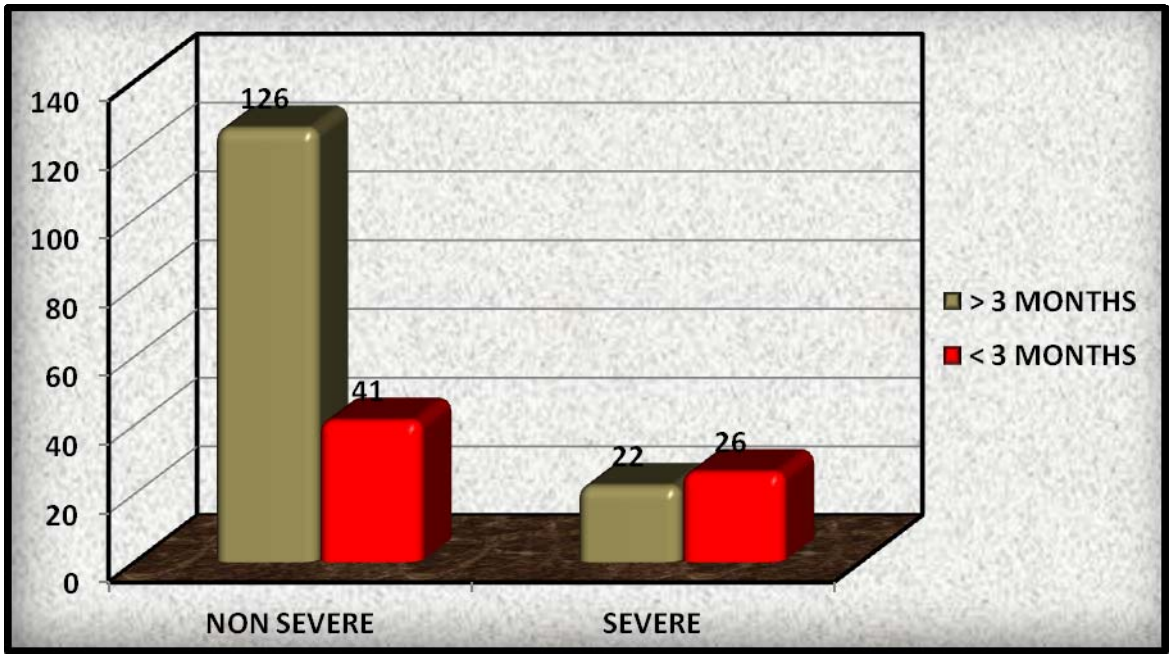

Figure 18: Comparison of duration of exclusive breast feeding of acute bronchiolitis among severe and non severe groups.

On examination, 167(77.67%) children had normal mental status (alert) according to AVPU scale, 25(11.62%) children were found to be in verbal state, 18(8.37%) children were found in pain responsive state and 5(2.32%) children were found to be in unresponsive status. All these children (100%) had respiratory rate of more than normal for the corresponding age according to FIMNCI guidelines. Among these 215 children, 205(95.30%) had chest in drawing. Nasal flaring was present in 51(23.70%) children. 40(18.6%) children had grunting and cyanosis was present in 10(4.70%) children.

While analysing the anthropometric measurements of these 215 children, 192(89.30%) children had age appropriate (between -2 z score to +2 z score) weight for length according to WHO growth standards, whereas 15(7.0%) children had their weight for length between +2 z score to +3 z score and 8(3.7%) children had their weight for length less than -2 z score. While analysing the length for age, 212(98.6%) children had normal values (between -2 z score to +2 z score), whereas in 3(1.4%) children the length falls below -2 z score. Clinical pallor was noticed in 20(9.3%) children.

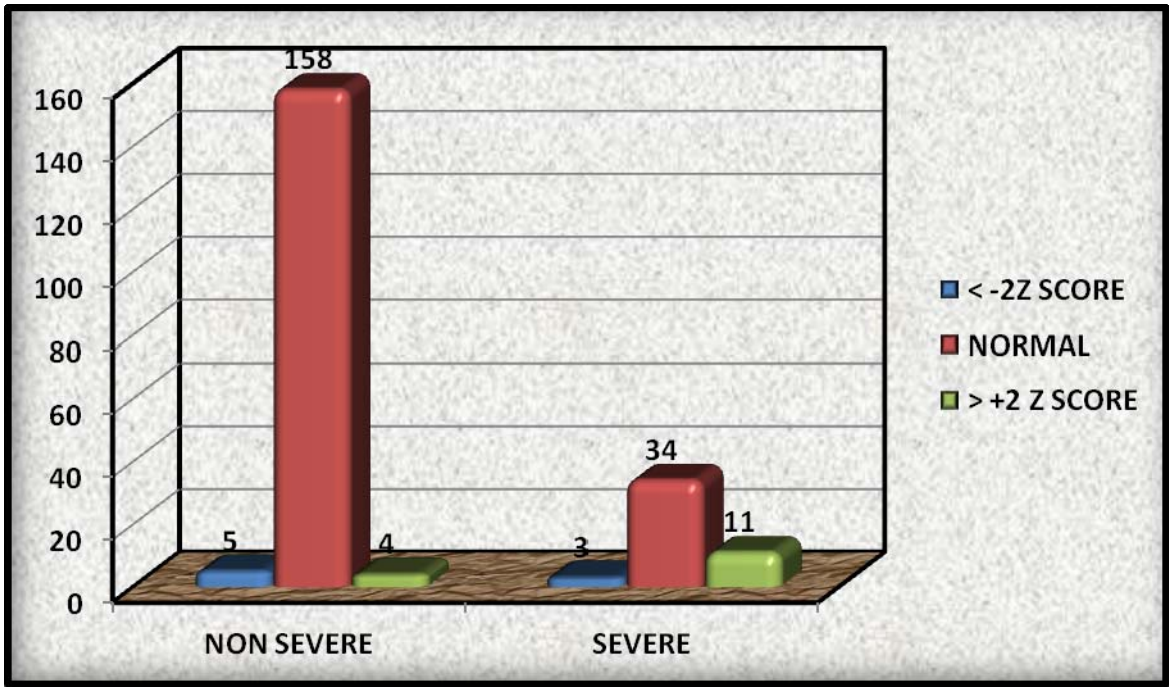

Figure 19: Comparison of weight for length among severe and non severe groups.

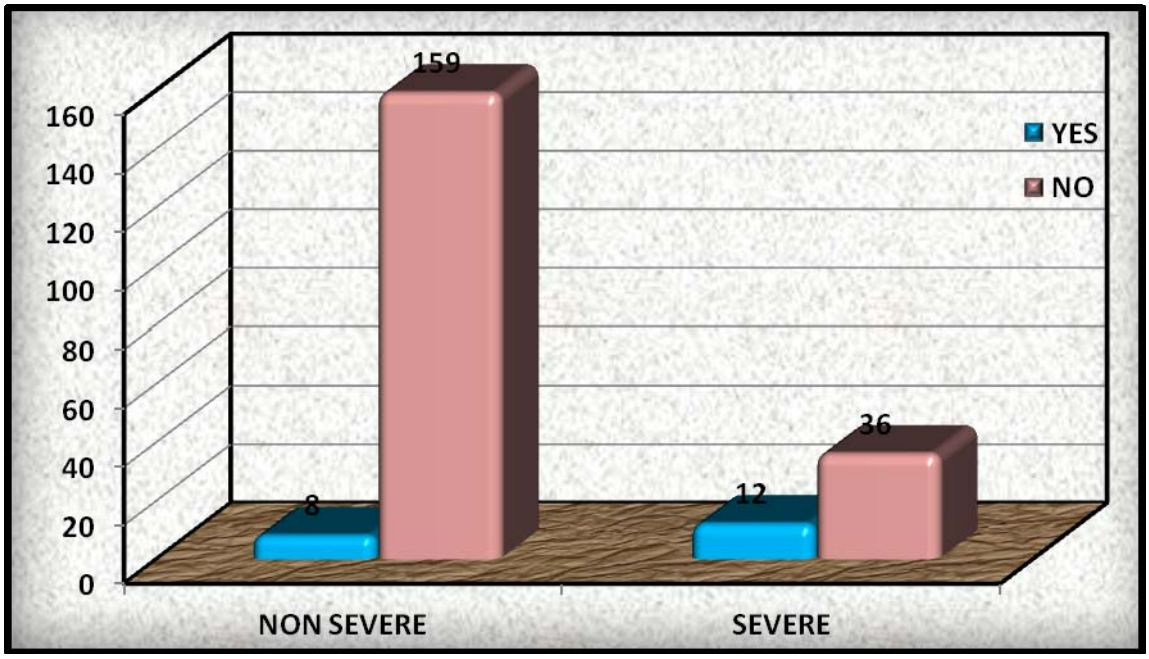

Figure 20: Comparison of pallor among severe and non severe groups.

In our study, only 3(1.40%) children had recurrent apnoea which required intubation and mechanical ventilation. Refusal of feeds and vomiting were seen in 48(22.30%) and 33(15.30%) children respectively.

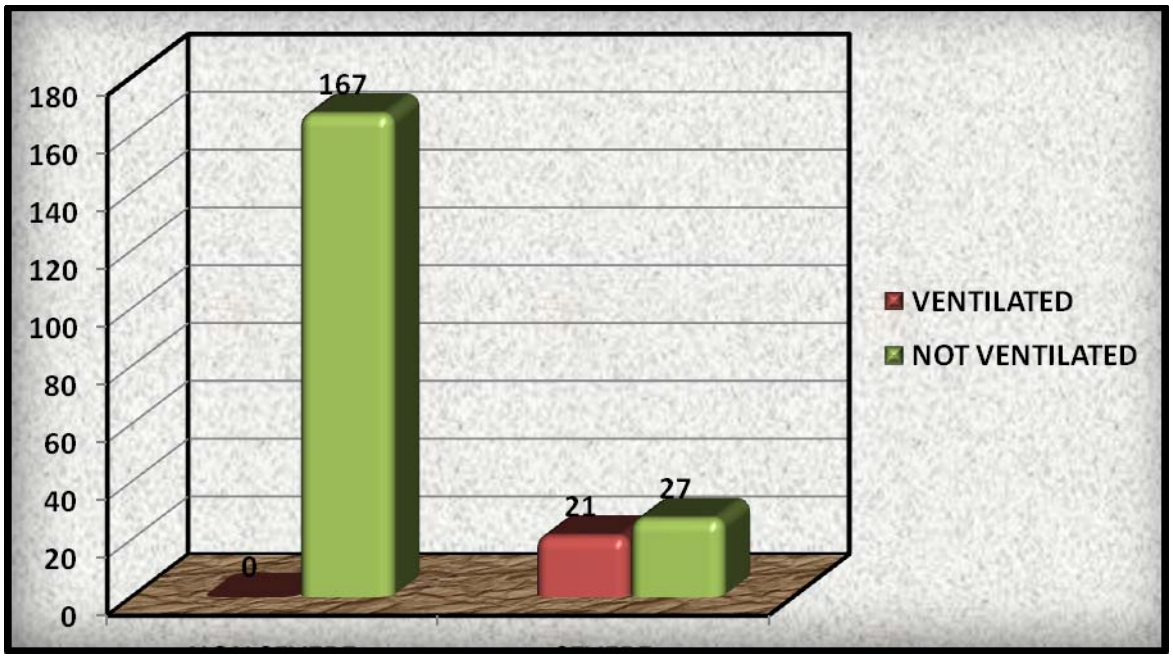

Figure 21: Comparison of need for ventilation among severe and non severe groups.

54(25.10%) children had tachycardia (heart rate more than normal range for age according to PALS guidelines). The blood pressure measurement of these children showed normal BP according to PALS guidelines in 202(94%) children but 10(4.70%) children had high systolic pressure with wide BP and 3(1.4%) children had hypotension. Among these 215 children, 39(18.1%) children presented in shock (25- fluid responsive shock, 8- dopamine responsive shock, 3- catecholamine responsive shock and 3- refractory shock) which required fluids and inotropic support. Out of them, 3 children presented with refractory shock and despite effective management and ventilatory support, they expired.

Oxygen saturation was maintained more than 92% without oxygen in 136(63.3%) children, whereas 40(18.6%) children required oxygen up to 10 litres/min to maintain saturation more than 92% and 39(18.10%) children failed to maintain the saturation even with oxygen supplementation.

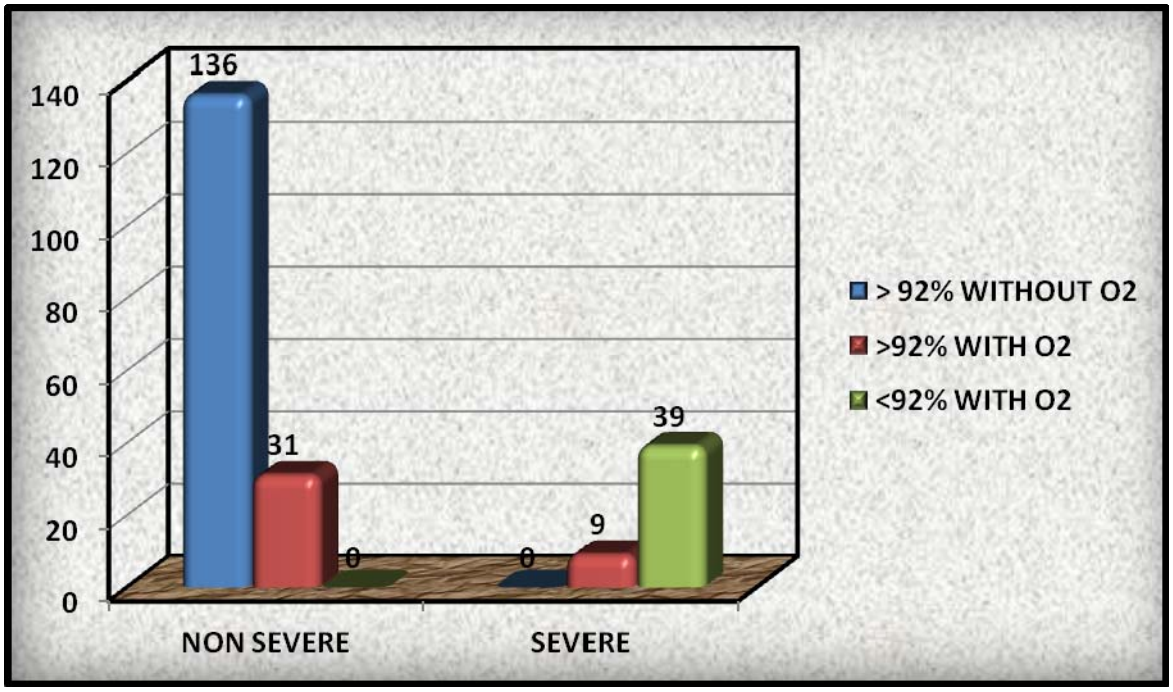

Figure 22: Comparison of oxygen saturation among severe and non severe groups.

Wheeze and crepitations were present in 207 (96.3%) and 196 (91.2%) children respectively. Hepatomegaly and splenomegaly were noted in 37(17.2%) and 7(3.3%) children respectively. Chest x ray showed bilateral hyperinflation in 182(84.65%) children and it was normal in 33(15.35%) children.

97(45.10%) children in our study population, required intravenous hydration. Treatment with adrenaline aerosol therapy was given in 123 children(57.20%), followed by salbutamol and hypertonic saline aerosol therapy in 84(39.10%) and 8(3.70%) children respectively.

The mean hospital stay in children treated with adrenaline, hypertonic saline and salbutamol nebulisation were 3.2 days, 3.55 days and 4.02 days respectively. Out of these 215 children, 21(9.8%) children needed assisted ventilation and 4 of them expired with a mortality rate of 1.86%.

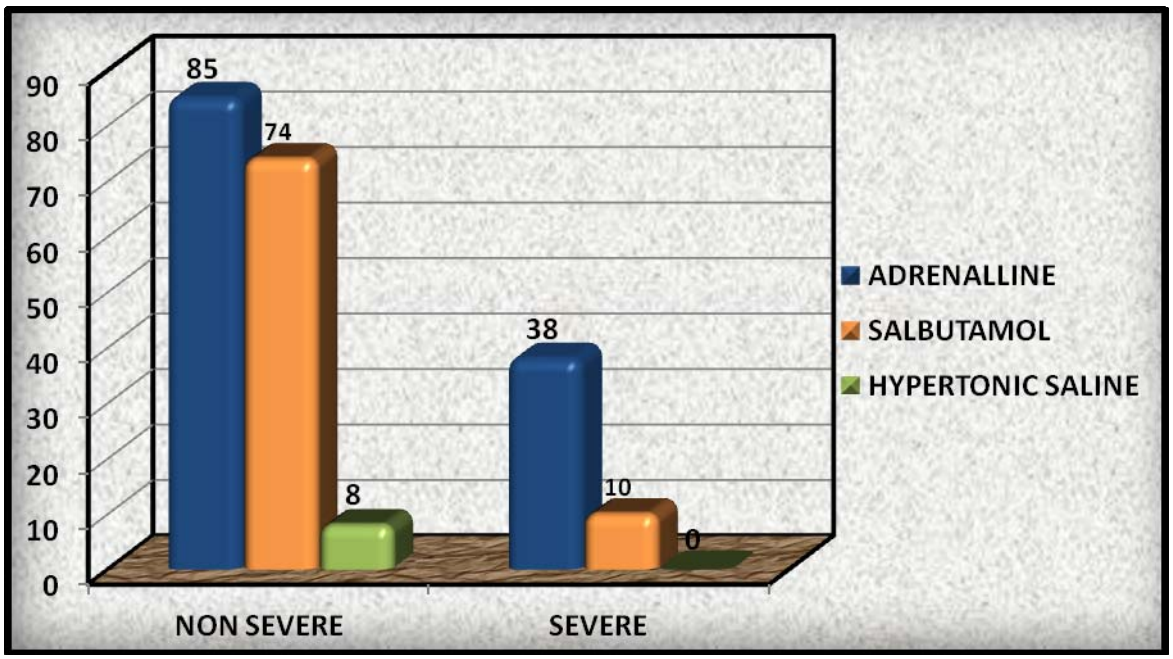

Figure 23: Comparison of various types of nebulisation used among severe and non severe groups.

Risk factor analysis - Univariate analysis:

Demographic, environmental and clinical characteristics of the participants were analysed for associations among disease severity groups. The result of this analysis is given in the table (1, 2, 3 and 4). Several factors are associated with severity and mortality of acute bronchiolitis.

- Age group less than 3 months was found 10.04 times more commonly among severe bronchiolitis group when compared to the non severe group [OR(95%CI) = 10.04(4.43 – 22.77)]
- Male sex was seen in 34(15.8%) and 103(47.9%) children among case and control groups respectively. But it is not statistically significant.
- Fever was found (4.82 times) more commonly among severe bronchiolitis group when compared to the non severe group [OR(95%CI) = 4.82(1.81 – 12.83)]
- Caesarean delivery was observed (2.61 times) more commonly among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 2.61(1.21 – 5.59)].
- Preterm less than 34 completed weeks was more commonly observed (11.92 times) among severe bronchiolitis group when

compared to non severe group [OR(95%CI) = 11.92(4.75 – 29.91)].

- Birth weight of less than 2.0 kilograms was more commonly observed (14.44 times) among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 14.44(6.14 – 33.92)].
- History of admission in NICU in the neonatal period for various reasons was more commonly observed (5.85 times) among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 5.85(2.29 – 14.93)].
- History of mechanical ventilation in the neonatal period for various reasons was more commonly observed (14.08 times) among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 14.08 (2.82 – 70.34)].
- Breastfeeding for less than 3 months duration was (3.63 times) more among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 3.63(1.86 – 7.08)].
- History of upper respiratory illness in the family is was more commonly seen 7.85 times among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 7.85(3.26 – 18.86)].

- Exposure to passive smoking was (9.03 times) more among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 9.03(3.54 – 23.04)].
- Underlying congenital cardiac lesions were more commonly observed (5.82 times) among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 5.82(1.57 – 21.57)].
- Underlying congenital airway anomalies were more commonly observed (16.5 times) among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 16.5(3.37 – 80.71)].
- Over weight and obesity (weight for length > +2 z score) were more commonly observed (12.11 times) among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 12.11(3.63 – 40.17)].
- Pallor was more commonly observed (6.62 times) among severe bronchiolitis group when compared to non severe group [OR(95%CI) = 6.62(2.52 – 17.38)].

Table 1: Comparison of demographic factors among severe and non severe bronchiolitis groups – Univariate analysis.

S.No	Variable		Severe disease n (%)	Non severe disease n (%)	OR (95% CI)	P value
1.	**Age**	**< 3 months**	**21(43.75)**	**12(7.19)**	**10.04(4.43 – 22.77)**	**0.000**
		3 – 6 months	22(45.83)	70(41.91)	1.17(0.61 – 2.23)	
		6 – 12 months	5(10.42)	78(46.71)	0.13(0.05 – 0.35)	
		> 12 months	0(0.0)	7(4.19)	-	
2.	Sex	Male	34(70.80)	103(61.70)	1.59(0.75 – 3.02)	0.245
		Female	14(29.20)	64(38.30)	0.66(033 – 1.32)	

Table 2: Comparison of environmental factors among severe and non severe bronchiolitis groups – Univariate analysis.

S.No	Variable	Severe disease n(%)	Non severe disease n(%)	OR (95% CI)	P value
1.	SE status Upper	1(2.1)	14(8.40)	0.23(0.029 – 1.81)	
	Upper middle	32(66.70)	68(40.70)	2.91(0.82 – 5.71)	
	Lower middle	11(22.90)	61(36.50)	0.51(0.24 – 1.08)	0.130
	Upper lower	4(8.30)	22(13.20)	0.59(0.19 – 1.83)	
	Lower	0	2(1.20)	-	
2.	F/H Atopy	2(4.16)	18(10.77)	0.35(0.08 – 1.60)	0.165
3.	Indoor air pollution	8(16.70)	13(7.8)	2.36(0.91 – 6.10)	0.068
4.	**URI in the family**	**16(33.30)**	**10(6.0)**	**7.85(3.26 – 18.86)**	**0.000**
5.	**Passive smoking**	**15(31.30)**	**8(4.8)**	**9.03(3.54 – 23.04)**	**0.000**

Table 3: Comparison of perinatal factors among severe and non severe bronchiolitis groups – Univariate analysis.

S. No	Variable	Severe disease n (%)	Non severe disease n (%)	OR (95% CI)	P value
1	**Delivery LSCS** NVD	**38(79.17)** 10(20.83)	**99(59.28)** 68(40.72)	**2.61(1.21 – 5.59)** 0.38(0.17 – 0.82)	**0.012**
2	**Gestational age <34 wks** >34 wks	**18(37.5)** 30(62.5)	**8(4.8)** 159(95.2)	**11.92(4.75 – 29.91)** 0.08(0.03 – 0.21)	**0.000**
3	**Birth weight <2 kg** 2-4 kg > 4 kg	**23(47.9)** 25(52.1) 0	**10(6.0)** 155(92.8) 2(1.2)	**14.44(6.14 – 33.92)** 0.08(0.03 – 0.19) -	**0.000**
4	**H/O Neonatal admission**	**12(25.0)**	**9(5.4)**	**5.85(2.29 – 14.93)**	**0.000**
5	**Neonatal mechanical ventilation**	**7(14.6)**	**2(1.2)**	**14.08(2.82 – 70.34)**	**0.000**
6	**Breast feeding < 3 month** >3 month	**26(54.2)** 22(45.8)	**41(24.6)** 126(75.4)	**3.63(1.86 – 7.08)** 0.27(0.14 – 0.53)	**0.000**

Table 4: Comparison of clinical factors among severe and non severe bronchiolitis groups – Univariate analysis.

S. No	Variable	Severe disease n (%)	Non severe disease n (%)	OR (95% CI)	P value
1.	URI Duration < 2 days 2 – 5 days > 5 days	44(91.7) 4(8.3) 0	141(84.4) 25(15.0) 1(0.6)	2.02(0.67 – 6.12) 0.51(0.17 – 1.56) -	0.42
2.	**Fever**	**43(89.6)**	**107(64.1)**	**4.82(1.81 – 12.83)**	**0.001**
3.	Fever duration < 2 days 2 – 5 days > 5 days	39(90.7) 4(9.3) 0	78(72.9) 27(25.2) 2(1.9)	3.62(0.79 – 11.04) 0.30(0.29 – 1.62) -	0.55
4.	Dyspnea duration < 2 days 2 – 5 days > 5 days	45(93.75) 3(6.25) 0	139(83.23) 28(16.76) 0	3.02(0.87 – 10.41) 0.33(0.09 – 1.14) -	0.068
5.	**Underlying congenital cardiac lesions**	**6(12.5)**	**4(2.39)**	**5.82(1.57 – 21.57)**	**0.003**
6.	**Underlying airway anomalies**	**8(16.67)**	**2(1.9)**	**16.5(3.37 – 80.71)**	**0.000**
7.	Weight for < -2 z score Length -2 to +2z score **> +2 z score**	3(6.25) 34(70.83) **11(22.92)**	5(2.99) 158(94.61) **4(2.40)**	2.16(0.49 – 9.38) 0.13(0.05 – 0.34) **12.11(3.63 – 40.17)**	0.000
8.	**Pallor**	**12(25.0)**	**8(4.8)**	**6.62(2.52 – 17.38)**	**0.000**

Multivariate analysis:

Multivariate binary logistic regression analysis after adjustment for confounding factors shows that, infants with fever, caesarean delivery, mechanical ventilation in the newborn period and upper respiratory illness in the family were independently associated with increased risk of developing severe disease. The results are given in table 5.

Table 5: Comparison of risk factors among severe and non severe bronchiolitis groups – Multivariate analysis.

S.No	Variable	OR(95%CI)	Significance
1.	Fever	4.52 (1.05 – 19.32)	Significant
2.	Caesarean delivery	16.61(3.30 – 83.67)	Significant
3.	Neonatal mechanical ventilation	18.24(1.14 – 52.52)	Significant
4.	Upper respiratory illness in the family	15.26 (2.99 – 77.88)	Significant

DISCUSSION

DISCUSSION

Bronchiolitis is an acute, infectious disease of the upper and lower respiratory tract resulting in obstruction of the smaller airways. Although it may occur in all age groups, as the larger airways of older children and adults better tolerate mucosal edema and severe symptoms are usually only evident in young infants. It usually occurs in children less than two years of age and presents with coughing, wheezing, and shortness of breath often caused by respiratory syncytial virus.

In our study, we have included 215 children who were diagnosed as bronchiolitis. Out of them, 167(77.67%) children had mild and moderate disease, whereas 48(22.33%) children had severe disease similar to El Radhi A, et al study[56]. Among those 48 children presented as severe disease, 4 of them died with a mortality rate of 1.86% similar to Thorburn K[52] study, with a mortality rate of 1.7% and other studies showing mortality rate ranging from 0.5 to 7%. This wide range in mortality could be due to varying prevalence of pathogenic organisms in different regions of the world.

In our study, 125(58.10%) children were belong to less than 6 months of age which is comparable with Shay DK, et al study in which 57% of cases were less than 6 months of age group[54]. The mean age

group in our study is 4.6 months which is comparable to El-Radhi A, et al study[56]. Out of 215 children in our study, 63.7% children were males and 36.3% children were females similar to Al-Muhsen SZ, et al study[60]. Most of these cases (83.3%) were reported between the months of October to January. This seasonal pattern is comparable to Al-Muhsen SZ, et al study[60]. All children in our study presented with a short duration of upper respiratory illness in the form of cough, cold, sneezing or running nose along with breathing difficulty which similar to other studies[51-60]. Among the 215 children, fever was documented in 150(69.8%) children in our study, of which 87.3% children had low grade fever, which is comparable to El-Radhi A, et al study[56]. The duration of hospital stay was ranging from 1- 15 days with a mean hospital stay of 3.52 days, which is similar to El-Radhi A, et al study[56], in which the mean duration of hospital stay was 3.3 days, whereas Fjaerli HO, et al study[59] showed 4.0 days, as the mean duration of hospital stay.

In our study, congenital cardiac lesions and congenital airway anomalies were present in 10(4.7%) each. This is comparable with Fjaerli HO, et al study[59]. Family history of respiratory illness, exposure to passive smoking, indoor air pollution and family history of atopy were present in 26(12.10%), 23(10.70%), 21(9.80%) and 20(9.3%) cases respectively which is comparable with Al-Muhsen SZ, et al study[60].

While analysing the perinatal history, preterm less than 34 completed weeks was present in 26(12.10%) children whereas Fjaerli HO, et al[59], reported preterm births in 7.0% cases only.

Demographic, environmental and clinical characteristics of the study population were analysed for association with severity of illness using Pearson Chi-square test. While analysing the risk factors, age less than 3 months, presence of fever, caesarean delivery, preterm less than 34 weeks, birth weight less than 2.0 kg, history of neonatal admission, history of neonatal mechanical ventilation, breast feeding for < 3 months duration, presence of respiratory illness in the family, exposure to passive smoking, underlying congenital cardiac lesions, underlying congenital airway anomalies, weight for height >+2 z score, presence of pallor were more commonly observed among severe disease group when compared to non severe group. While applying all these significant univariate variables into the binary logistic regression model, fever, caesarean delivery, neonatal mechanical ventilation and upper respiratory illness in the family became more significant ($p < 0.05$). So, these four factors such as fever, caesarean delivery, neonatal mechanical ventilation and upper respiratory illness in the family independently predict the severity of bronchiolitis.

Fever

In our study fever in infants with bronchiolitis was most commonly observed among severe bronchiolitis groups when compared to non severe group as similar to El-Radhi, et al study[56]. Fever is independently associated with increased severity of bronchiolitis. The findings of our study suggest that most infants with bronchiolitis are afebrile and that fever is associated with more severe bronchiolitis. Infants with RSV-associated bronchiolitis are often febrile at the time of presentation for medical care; in patients with adenovirus or influenza-associated bronchiolitis, however, fever is often higher than 39.8^{o}C. A rise in body temperature by 1°C results in 10% increase in energy expenditure. These changes are accompanied by an increase in oxygen consumption of 10–12% for every 1°C rise in temperature[25]. The necessity for oxygen supplementation was one of the main factors contributing to prolonged hospitalisation. It is possible that a reduction of body temperature by frequent use of antipyretic agents could reduce the oxygen requirement and possibly the degree of hypoxia[56].

Age less than 3 months

In our study, age less than 3 months was most commonly observed among severe bronchiolitis groups when compared to non severe group. This is because of the less tolerability of the smaller airway to respiratory

distress in very young infants when compared to older infants. Other studies have shown the same result[64-69].

Preterm less than 34 weeks

In our study, preterm birth less than 34 completed weeks was most commonly observed among severe bronchiolitis groups when compared to non severe group. Other investigators like Shay DK, et al, Semple MG, et al, Flaerli HO, et al and Bradly JP, et al[54,58,59,64] had given the same result. The probable reason could be the immaturity of the lungs with some degree of bronchopulmonary dysplasia and immaturity of the immune system[35,70,71]. But this needs further investigations for validation.

Cigarette smoking

In our study, exposure to smoking in the post natal period was most commonly observed among severe bronchiolitis groups when compared to non severe group. Semple MG, et al, Bradly JP, et al and Lanari, et al studies also revealed postnatal exposure to smoking worsens the severity of RSV bronchiolitis infection in infants[58, 64, 72]. Moreover, a study done by Gurkan, et al[73], in which nicotine levels were measured at index of hospital admission, showed that infants hospitalized for severe bronchiolitis were exposed more recently to cigarette smoke. According to 1997 economic analysis of the medical effects of smoking on children, 22000 hospitalizations and 1100 deaths from RSV occur

every year due to parental second hand smoke[74]. Smoking exposure has been shown to reduce pulmonary function and increases the airway hyper reactivity in children. Thus infants exposed to second passive smoke seem to have a predisposition to developing severe bronchiolitis after infection with RSV.

Family history of upper respiratory illness

In our study, family history of upper respiratory illness was most commonly observed among severe bronchiolitis groups when compared to non severe group. Family history of upper respiratory illness is independently associated with increased severity of bronchiolitis. Bronchiolitis is transmitted through droplets that contain viral particles. These are exhaled into the air by breathing, coughing, or sneezing. These droplets can be carried on the hands, where they survive and can spread infection for several hours. Marguet C, et al, [65] study states those viral co-infections in bronchiolitis raised cumulative pathogenic effect and consequently a more severe illness, although other hypotheses as successive infections or healthy carriage might be also supported[75]. So when there is an upper respiratory illness in the family, it will predispose to co-infection or successive infection and consequently severe disease.

Pallor

In our study, pallor was most commonly observed among severe bronchiolitis group when compared to non severe group. Pallor was independently associated with increased severity of bronchiolitis. In anaemia there will be some degree of hypoxia which increases oxygen demand. In such situation, a child developes any respiratory pathology, which increases the oxygen demand, will lead to rapid deterioration in the clinical course. However, many studies not addressed this issue and hence there is a need for further studies to look into this aspect.

Family history of atopy

Our study shows that there is no significant association between family history of atopy and severity of bronchiolitis. Our results were based on overall family history of atopy/ allergy. A study done by La Via W et al[76], mentions that overall family history of atopy does not significantly affects the length of stay or any other complications due to bronchiolitis. But in various other studies, family history of atopy is mentioned as a protective factor against severe disease[64]. However, their results were based on maternal atopy in the form of asthma and allergies.

Caesarean delivery

In our study, caesarean delivery was most commonly seen among severe bronchiolitis groups when compared to non severe group. Caesarean delivery was independently associated with increased severity of bronchiolitis and is similar to studies done by Moore HC, et al, Hitt E, et al[55,77]. Act of normal labour promotes the production of various cytokines and stimulates the immune system in both the mother and the baby. Therefore the cytokine levels differs in a newborn baby delivered by elective caesarean delivery, as shown by the lower levels of interleukin (IL) 6 and IL-10 in their cord blood sample than in those who had a normal vaginal delivery[55]. This explains the reason for increased risk of severity in babies born of elective caesarean section.

Associated CHD and airway anomalies

In our study, underlying congenital cardiac lesions and congenital airway anomalies were more commonly observed among severe bronchiolitis group when compared to non severe group and is similar to observations of Shay DK, et al, Semple MG, et al, Flaerli HO, et al and Perales AB, et al[54,58,59,78].

Neonatal mechanical ventilation

History of neonatal mechanical ventilation was most commonly observed among severe bronchiolitis group when compared to non severe group. History of neonatal mechanical ventilation is independently associated with severity of bronchiolitis. This is similar to observation of Perales AB, et al[78]. Neonatal mechanical ventilation and oxygen therapy causes injury to airway of newborn babies and the airway undergoes some degree of bronchopulmonary dysplasia. This predisposes these babies to develop severe disease[35].

Low birth weight

Birth weight of less than 2.0 kilograms was most commonly observed among severe bronchiolitis group when compared to non severe group. This is probably related to their airway morbidity due to low birth weight in the newborn period. This is similar to Perales AB, et al study[78].

Over weight and obesity

Over weight and obesity were more commonly observed among severe bronchiolitis group when compared to non severe group. Obesity can profoundly alter respiratory mechanics, respiratory muscle function, lung volumes, control of breathing, and gas exchange[79]. The pulmonary function test in obese children will show restrictive pattern. There is a

reduction in functional residual capacity (FRC) and diffusion capacity in obese children[80]. So, the tolerability of these children to significant degree of respiratory distress is low when compared with normal children. This predisposes obese children to severity and mortality in acute bronchiolitis. However, many studies not addressed this issue and hence there is a need for further studies to look into this aspect.

CONCLUSION

CONCLUSION

- Clinical profile of acute bronchiolitis in our study correlates with other literature.
- In our study, the following factors are the independent predictors of severity and mortality of acute bronchiolitis.
    1. Fever
    2. Caesarean delivery
    3. Neonatal mechanical ventilation
    4. Upper respiratory illness in the family.
- If a child with acute bronchiolitis has the above mentioned risk factors, severity should be anticipated and the child should be monitored closely for signs of clinical deterioration.
- Proper antenatal and neonatal care to reduce the neonatal morbidity may have a positive impact on outcome of bronchiolitis.
- Creating awareness to the public regarding the separation of family members having upper respiratory illness from young infants will reduce severity of bronchiolitis.

LIMITATION

LIMITATION

Our study had few limitations as the case definition for bronchiolitis was based mainly on the clinical criteria without any laboratory confirmation of acute bronchiolitis due to non-availability of diagnostic facilities.

BIBLIOGRAPHY

BIBLIOGRAPHY

1) Holman RC, Shay DK, Curns AT, et al. Risk factors for bronchiolitis-associated deaths among infants in the United States. Pediatr Infect Dis J 2003; 22: 483– 490.
2) Henderson FW, Clyde WA, Collier AM, et al. The etiologic and epidemiologic spectrum of bronchiolitis in pediatric practice. J Pediatr 1979; 95: 183– 190.
3) Kim HW, Arrobio JO, Brandt DC, et al. Epidemiology or respiratory syncytial virus infection in Washington, DC. Am J Epidemiol 1973; 98: 216– 225.
4) Leader S, Kohlhase K. Recent trends in severe respiratory syncytial virus (RSV) among US infants, 1997 to 2000. J Pediatr 2003; 143(5 Suppl): S127–S132.
5) Reese AC, James IR, Landau LI, et al. Relationship between urinary nicotinine level and diagnosis in children admitted to hospital. Am Rev Respir Dis 1992; 146:66– 70.
6) Panitch HB, Callahan CW, Schidlow DV. Bronchiolitis in children. Clin Chest Med 1993; 14 :715– 731.
7) Camilli AE, Holberg CJ, Wright AL, et al. Parental childhood respiratory illness and respiratory illness in their infants. Pediatr Pulmonol 1993; 16:275–280.

8) Anderson LJ, Parker RA, Strikas RA, et al. Daycare center attendance and hospitalization for lower respiratory tract illness. Pediatrics 1988; 82:300–308.

9) Perlstein PH, Kotagal UR, Boling C, et al. Evaluation of an evidence-based guideline for bronchiolitis. Pediatrics 1999; 104:1334– 1341.

10) Deshpande SA, Northern V. The clinical and health economic burden of respiratory syncytial virus disease among children under 2 years of age in a defined geographical area. Arch Dis Child 2003; 88:1065–1069.

11) Glezen WP, Taber LH, Frank AL, et al. Risk of primary infection and reinfection with respiratory syncytial virus. Am J Dis Child 1986; 140:543– 546.

12) Loda FA, Clyde WAJ, Glezen WP, et al. Studies on the role of viruses, bacteria, and M. pneumoniae as causes of lower respiratory tract infections in children. J Pediatr 1968; 72:161–176.

13) Foy HM, Cooney MK, Maletzky AJ, et al. Incidence and etiology of pneumonia, croup and bronchiolitis in preschool children belonging to a prepaid medical care group over a four-year period. Am J Epidemiol 1973; 97:80–92.

14) Glezen WP, Loda FA, Clyde WA, et al. Epidemiologic patterns of acute lower respiratory disease of children in a pediatric group practice. J Pediatr 1971; 78:397–406.

15) Korppi M, Kotaniemi-Syrjanen A, Waris M, et al. Rhinovirus-associated wheezing in infancy: comparison with respiratory syncytial virus bronchiolitis. Pediatr Infect Dis J 2004; 23:995-999.

16) Freymouth F, Vabret A, Legrand L, et al. Presence of the new human metapneumovirus in French children with bronchiolitis. Pediatr Infect Dis J 2003; 22:92–94.

17) Williams JV, Harris PA, Tollefson SJ, et al. Human metapneumovirus and lower respiratory tract disease in otherwise healthy infants and children. N Engl J Med 2004; 350:443– 450.

18) Sznajer Y,Westcott JY,Wenzel SE, et al. Airway eicosanoids in acute severe respiratory syncytial virus bronchiolitis. J Pediatr 2004; 145:115– 118.

19) Ackerman BD. Acute bronchiolitis: a study of 207 cases. Clin Pediatr 1962; 1:61–81.

20) Wohl MEB, Chernick V. Treatment of acute bronchiolitis. N Engl J Med 2003; 349:82– 83.

21) Shay DK, Holman RC, Newman RD, et al. Bronchiolitis-associated hospitalizations among US children, 1980–1996. JAMA 1999; 282:1440 –1446.

22) Mallory MD, Shay DK, Garrett J, et al. Bronchiolitis management preferences and the influence of pulse oximetry and respiratory rate on the decision to admit. Pediatrics 2003; 111:E45– 51.

23) Patel H, Platt RW, Pekeles GS, et al. A randomized, controlled trial of the effectiveness of nebulized therapy with epinephrine compared with albuterol and saline in infants hospitalized for acute viral bronchiolitis. J Pediatr 2002; 141:818– 824.

24) Kellner JD, Ohlsson A, Gadomski AM, et al. Bronchodilators for bronchiolitis. Cochrane Database Syst Rev 2000; (2):CD001266. bronchiolitis: in-patient focus 1055

25) Wainwright C, Altamirano L, Cheney M, et al. A multicenter, randomized, double-blind, controlled trial of nebulized epinephrine in infants with acute bronchiolitis. N Engl J Med 2003; 349:27–35.

26) Hartling L, Wiebe N, Russell K, et al. A meta-analysis of randomized controlled trials evaluating the efficacy of epinephrine for the treatment of acute viral bronchiolitis. Arch Pediatr Adolesc Med 2003; 157:957–964.

27) Springer C, Bar-Yishay E, Uwayyed K, et al. Corticosteroids do not affect the clinical or physiological status of infants with bronchiolitis. Pediatr Pulmonol 1990; 9:181 –185.

28) Garrison MM, Christakis DA, Harvey E, et al. Systemic corticosteroids in infant bronchiolitis: a meta-analysis. Pediatrics 2000; 105:E44.

29) Van Woensel JB, van Aalderen WM, de Weerd W, et al. Dexamethasone for treatment of patients mechanically ventilated for lower respiratory tract infection caused by respiratory syncytial virus. Thorax 2003; 58:383– 387.

30) Weinberger M. Corticosteroids for first-time young wheezers: current status of the controversy. J Pediatr 2003; 143:700–702.

31) American Academy of Pediatrics Committee on Infectious Diseases. Reassessment of the indications for ribavirin therapy in respiratory syncytial virus infections. Pediatrics 1996; 97:137–140.

32) Moscona A. Management of respiratory syncytial virus infections in the immunocompromised child. Pediatr Infect Dis J 2000; 19:253–254.

33) Smith DW, Frankel LR, Mathers LH, et al. A controlled trial of aerosolized ribavirin in infants receiving mechanical ventilation for severe respiratory syncytial virus infection. N Engl J Med1991; 325:24–29.

34) Fitzgerald DA, Kilham HA, Bronchiolitis: assessment and evidence-based management, Clinical Update. mja.com.au | The Medical Journal of Australia, MJA 2004; 180 (8): 399-404.

35) Grimaldi M, Gouyon B, Michaut F, et al. Severe respiratory syncytial virus bronchiolitis: epidemiologic variations associated with the initiation of palivizumab in severely premature infants with bronchopulmonary dysplasia. Pediatr Infect Dis J 2004; 23:1081–1085.

36) Korppi M, Piippo-Savolainen E, Korhonen K, et al. Respiratory morbidity 20 years after RSV infection in infancy. Pediatr Pulmonol 2004; 38:155–160.

37) Hegele RG, Ahmad HY, Becker AB, et al. The association between respiratory viruses and symptoms in 2-week-old infants at high risk for asthma and allergy. J Pediatr 2001; 138:831– 837.

38) Bont L, Steijn M, van Aalderen WM, et al. Impact of wheezing after respiratory syncytial virus infection on health-related quality of life. Pediatr Infect Dis J 2004; 23:414– 417.

39) Lemanske RF. Viruses and asthma: inception, exacerbation, and possible prevention. J Pediatr 2003; 142:S3– 8.

40) Gern JE. Mechanisms of virus-induced asthma. J Pediatr 2003; 142:S9–14.

41) Sampalis JS. Morbidity and mortality after RSV-associated hospitalizations among premature Canadian infants. J Pediatr 2003; 143(5 Suppl):S150 – 156.

42) Melendez E, Harper MB. Utility of sepsis evaluation in infants 90 days of age or younger with fever and clinical bronchiolitis. Pediatr Infect Dis J 2003; 22:1053– 1056.

43) Purcell K, Fergie J. Concurrent serious bacterial infection in 2396 infants and children hospitalized with respiratory syncytial virus lower respiratory tract infection. Arch Pediatr Adolesc Med 2002; 156:322– 324.

44) Titus MO, Wright SW. Prevalence of serious bacterial infection in febrile infants with respiratory syncytial virus infection. Pediatrics 2003; 112:282– 284.

45) Levine DA, Platt SL, Dayan PS, et al. Risk of serious bacterial infection in young febrile infants with respiratory syncytial virus infections. Pediatrics 2004; 113:1728– 1734.

46) Coffin SE, Offit PA. New vaccines against mucosal pathogens: rotavirus and respiratory syncytial virus. Adv Pediatr Infect Dis 1997; 13:333– 348.

47) Harper SA, Fukuda K, Uyeki TM, et al, Centers for Disease Control and Prevention (CDC) Advisory Committee on

48) Navas L, Wang E, deCarvalho V, et al. Improved outcome of respiratory syncytial virus infection in a high-risk hospitalized population of Canadian children. Pediatric Investigators Collaborative Network on Infections in Canada. J Pediatr 1993; 121:348– 354.

49) Meissner HC, Long SS, American Academy of Pediatrics Committee on Infectious Diseases and Committee on Fetus and Newborn. Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus infections. Pediatrics 2003; 112:1447–1452.

50) Willson DF, Landrigan CP, Horn SD, et al. Complications in infants hospitalized for bronchiolitis or respiratory syncytial virus pneumonia. J Pediatr 2003; 143:S142– 149.

51) Iqbal SMJ, Afzal MF, Sultan M. Acute Bronchiolitis: Epidemiological and Clinical Study, ANNALS VOL 15. NO. 4 OCT. - DEC. 2009.

52) Thorburn K. Pre-existing disease is associated with a significantly higher risk of death in severe respiratory syncytial virus infection. Arch Dis Child. 2009; 94(2):99-103 (ISSN: 1468-2044).

53) HOLMAN, et al. The Pediatric Infectious Disease Journal:June 2003 - Volume 22 - Issue 6 - pp 483-489.

54) Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980-1996. JAMA. 1999 Oct 20; 282(15):1440-1446.

55) Moore HC, Klerk N, Holt P, Richmond PC, Lehmann D. Hospitalisation for bronchiolitis in infants is more common after elective caesarean delivery, Arch Dis Child doi:10.1136/ archdischild-2011-300607.

56) El-Radhi A, Barry W, Patel S. Association of fever and severe clinical course in bronchiolitis, Arch Dis Child. 1999 September; 81(3): 231–234.

57) Koehoorn M, Karr CJ, Demers PA, Lencar C, Tamburic L, Brauer M. Descriptive Epidemiological Features of Bronchiolitis in a Population-Based Cohort, PEDIATRICS Vol. 122 No. 6 Dec 1, 2008 pp. 1196 -1203 (doi: 10.1542/peds.2007-2231).

58) Semple MG, Taylor-Robinson DC, Lane S, Smyth RL. Household Tobacco Smoke and Admission Weight Predict Severe Bronchiolitis in Infants Independent of Deprivation: Prospective

Cohort Study, PLoS ONE | www.plosone.org, July 2011 | Volume 6 | Issue 7 | e22425.

59) Fjaerli HO, Farstad T, Bratlid D. Hospitalisations for respiratory syncytial virus bronchiolitis in Akershus, Norway, 1993–2000: a population-based retrospective study, BMC Pediatrics 2004, 4:25, http://www.biomedcentral.com/1471-2431/4/25.

60) Al-Muhsen SZ. Clinical profile of Respiratory Syncytial Virus (RSV) bronchiolitis in the intensive care unit at a Tertiary Care Hospital, Curr Pediatr Res 2010; 14 (2): 75-80.

61) Horn SD, Smout RJ. Effect of prematurity on respiratory syncytial virus hospital resource use and outcomes. J Pediatr. 2003; 143(5 Suppl):S133-141 (ISSN: 0022-3476).

62) Shaw KN, Bell LM, Sherman NH. Outpatient assessment of infants with bronchiolitis. Am J Dis Child. 1991; 145(2):151-155 (ISSN: 0002-922X).

63) Clinical practice guidelines, NSW health, assessment & management of acute bronchiolitis.

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64) Bradley JP, Bacharier LB, Bonfiglio J, Schechtman KB, Strunk R, Storch G, Castro M. Severity of respiratory syncytial virus bronchiolitis is affected by cigarette smoke exposure and atopy. Department of Internal Medicine, Washington University School of Medicine, St Louis, Missouri 63110-1093, USA. Pediatrics. 2005 Jan;115(1):e7-14.

65) Marguet C, Lubrano M, Gueudin M, Le Roux P, Deschildre A. (2009) In Very Young Infants Severity of Acute Bronchiolitis Depends On Carried Viruses. PLoS ONE 4(2): e4596. doi:10.1371/journal.pone.0004596.

66) Marlais M, Evans J, Abrahamson E. Clinical predictors of admission in infants with acute bronchiolitis, Paediatric infectious diseases Thorax 2010;65:A15 doi:10.1136/thx.2010.150912.28.

67) Lebel MH, Gauthier M, Lacroix J. Respiratory failure and mechanical ventilation in severe bronchiolitis. Arch Dis Child 1989; 64:1431–1437.

68) O'Dempsey TJD, Laurence BE, McArdle TF, et al. The effect of temperature reduction on respiratory rate in febrile illnesses. Arch Dis Child 1993; 68:492–495.

69) Outwater KM, Crone RK. Management of respiratory failure in infants with acute viral bronchiolitis. Am J Dis Child 1984; 138:1071–1075.

70) Zaw W, McDonald J. Respiratory syncytial virus bronchiolitis in ex-preterm infants in the Scottish highlands: review of hospital admissions and an analysis of hospital cost. Scottish Medical Journal (2003) Volume: 48, Issue: 4, Pages: 108-110.

71) Siezen CL, et al. Genetic susceptibility to respiratory syncytial virus bronchiolitis in preterm children is associated with airway remodeling genes and innate immune genes. Laboratory for Health Protection Research, National Institute for Public Health and the Environment, Bilthoven, The Netherlands. Pediatr Infect Dis J. 2009 Apr; 28(4):333-335.

72) Lanari M, Giovannini M, Giuffre L, et al. Prevalence of respiratory syncytial virus infection in Italian infants hospitalized for acute lower respiratory tract infections, and association between respiratory syncytial virus infection risk factors and disease severity. Pediatr Pulmonol. 2002; 33:458 – 46.

73) Gurkan F, Kiral A, Dagli E, Karakoc F. The effect of passive smoking on the development of respiratory syncytial virus bronchiolitis. Eur J Epidemiol. 2000; 16:465– 468.

74) Aligne C, Stoddard J. Tobacco and children. An economic evaluation of the medical effects of parental smoking. Arch Pediatr Adolesc Med. 1997; 151:648 – 653.

75) Kusel MMH, de Klerk NH, Holt PG, Kebadze T, Johnston SL, et al. (2006) Role of respiratory viruses in acute upper and lower respiratory tract illness in the first year of life. A birth cohort study. Pediatr Infect Dis J 25: 680–686.

76) La Via W, Grant S, Stutman H, Marks M. Clinical profile of pediatric patients hospitalized with respiratory syncytial virus infection. Clin Pediatr (Phila). 1993; 32:450 – 454.

77) Hitt E. Cesarean Delivery\ Linked to Infant Bronchiolitis, Arch Dis Child. Published online October 28, 2011

78) Perales AB. Perinatal history and hospitalization for bronchiolitis. A comparison with the impact-RSV Study Group. An Esp Pediatr. 2000 Dec; 53(6):527-532.

79) Koenig SM. Pulmonary complications of obesity. Am J Med Sci. 2001 Apr; 321(4):249-279.

80) Li A, Chan D, Wong E, Yin J, Nelson E, and Fok T. The effects of obesity on pulmonary function. Arch Dis Child. 2003 April; 88(4): 361–363.

ANNEXURE

I. PROFORMA

1.	Patient name	
2.	Age / Sex	
3.	IP. No	
4.	Ward no	
5.	Address	
6.	Date / Time of admission	
7.	Income	
8.	Socioeconomic status	
CLINICAL HISTORY		
9.	H/O Upper respiratory illness	a) yes b) no
	If yes, duration	
	Type	
10.	H/O Fever	a) yes b) no
	If yes, duration	
	Grade	a) low b) high
	Chills& rigors	a) present b) absent
11.	Breathing difficulty	a) yes b) no
	If yes, duration	
12.	Any known cardiac disease	a) yes b) no
	If yes, type of disease	
	Any treatment taken	
13.	Any known lung disease	a)yes b) no
	If yes, duration	
	Any treatment taken	
BIRTH HISTORY		
14.	Type of delivery	a) preterm b) term c) post term
	If preterm, gestational age	
15	Nature of delivery	a)LSCS b)NVD
16.	Birth weight	
17.	Neonatal complications	
18.	Neonatal mechanical ventilation	a) yes b) no
FEEDING HISTORY		
19.	Type of feed giving	
20.	How long exclusively breastfed	
21.	When was weaning started	

FAMILY HISTORY		
22.	Any H/O respiratory illness in the family	a)yes b) no
	If yes, type of illness	
23.	H/O Smoking in the family	a)yes b) no
24.	Indoor air pollution	a)yes b) no
25.	Family H/O Atopy, asthma	
CLINICAL EXAMINATION		
26.	Level of consciousness	
27.	Hydration status	
28.	Weight for height	
29.	Height for age	
30.	Edema	a) yes b) no
31.	Shock	a) yes b) no
32.	Pallor	a) yes b) no
33.	Respiratory distress	a) yes b) no
	If yes, severity	
34.	Patients own respiration	a) adequate b)inadequate
35.	whether intubated	a) yes b) no
36.	Chest retractions	a) yes b) no
	If yes, severity	
37.	Nasal flaring	a) yes b) no
	If yes severity	
38.	Grunting	a) yes b) no
	If yes, severity	
39.	Cyanosis	a) yes b) no
	If yes, type	
40.	Apnea	a) yes b) no
	If yes, no of episodes	
	Duration of each episode	
41.	Poor feeding	a) yes b) no
42.	Pulse Rate	
	Rhythm	
	Type	
	Grade	
43.	Respiratory rate	
44.	Temperature	
45.	Blood pressure	
46.	Nutritional status	
47.	SPO2	

48.	Respiratory system Examination	
49.	X ray finding	
TREATMENT		
50.	O2 given	a) yes b) no
	Rate	
51.	Diet	a) oral feeds b) IV fluids
52.	If IV fluids, type of fluid	
	Rate	
53.	Nebulisation given	a) yes b) no
54.	Adrenalline / salbutamol /hypertonic saline	
55.	Antibiotics prescribed	a) yes b) no
56.	Specify drug and dose	
DISCHARGE FORM		
1.	Patient name	
2.	IP no	
3.	Date of discharge	
4.	Final diagnosis	
5.	Clinical status at discharge	
6.	Prescribed drugs at discharge	
7.	Any underlying illness	

II. ABBREVIATIONS

RSV	-	Respiratory Syncytial Virus
LBW	-	Very Low Birth Weight
LBW	-	Low Birth Weight
PICU	-	Pediatric Intensive Care Unit
ICU	-	Intensive Care Unit
GA	-	Gestational Age
ICH & HC	-	Institute of Child Health and Hospital for Children
CLE	-	Congenital Lobar Emphysema
OR (95%CI)	-	Odds Ratio(95%Confidence Interval)
AVPU Scale	-	Alert, Verbal, Pain responsive, Unresponsive scale
FIMNCI	-	Facility Based Integrated Management of Neonatal and Childhood Illness
WHO	-	World Health Organization
PALS	-	Pediatric Advanced Life Support
BP	-	Blood Pressure
NICU	-	Neonatal Intensive Care Unit
SE Status	-	Socio Economic Status
URI	-	Upper Respiratory Illness
LSCS	-	Lower Segment Caesarean Section
NVD	-	Normal Vaginal Delivery

INFORMATION SHEET

The clinical profile of Acute bronchiolitis in our hospital and risk factors for severe disease and mortality in children 31 days to 24 months of age.

Investigator name : Dr. S. Palanivel

Guides : Prof. M. Raghunadan, MD, DCH.
Dr. K. Nedunchelian, MD, DCH.
Dr. S. Geetha, MD, DCH.
Dr.P.Umakanthan, MD, DCH.

(To be read to caretakers in the presence of witness)

Yours child is suspected to have acute bronchiolitis infection. Acute bronchiolitis is predominantly a viral disease. It is one of the leading causes of hospitalisation in infants and young children. It occurs usually between 1 month to 24 months of age with a peak incidence between 3 to 6 months of age.

In healthy infants and young children acute bronchiolitis is usually a self limited disease. Treatment in most of these cases consists only supportive measures. Most of these children begin to improve within one or two weeks. But it can lead to severe disease and mortality in some children.

If we know the factors which predisposing to severe bronchiolitis and mortality due to acute bronchiolitis, plan of management can be targeted effectively.

This study will describe the clinical profile of acute bronchiolitis in our hospital and risk factors for severe disease and mortality in children 31 days to 24 months of age.

How is the study being done?

If your child is suspected to have acute bronchiolitis, he/she will be subjected into thorough clinical examination and according to the findings he/she will be graded into mild or moderate or severe case.

Using patient data entry form, information is gathered regarding patients age, sex, other demographic details and risk factors considered for this study

If he/she has mild or moderate disease, he/she will be included in the control group. If he/she has severe disease he/she will be included in the case group.

The risk factors are compared between cases and controls and adjusted OR with 95% CI will be arrived by multivariate analysis for each risk factor.

Can I refuse to join the study?

You may refuse to participate or withdraw from the study at any time. In both cases your child will be treated in the usual manner in this hospital.

Is there benefit or harm to be in this study?

By this study we can identify the clinical profile of acute bronchiolitis and risk factors for severe disease and mortality in our settings.

If we know the factors which predisposing to severe bronchiolitis and mortality due to acute bronchiolitis, plan of management can be targeted effectively.

There is no harms to the patients in this study.

Confidentiality:

The data collected from the study will be used for the purpose of the study only. The results of the study are to be published. Personal information of the children participating in the study will be kept confidential. There will not be any disclosure about yours childs information without your permission.

Subject rights:

I understood that if I wish further information regarding my childs rights as a research subject, I may contact the hospital where the study is taking place.

INFORMED CONSENT FORM

I have been fully informed about the study and the benefits of this study and the possible harm that can happen. I understand that the doctor will ask questions and examine my child to make sure it is safe for him/her to enter the study.

This authorization is valid for this study. “I have understood and received a copy of this consent form”. I agree for my child’s participation in this research study.

Signature / Thumb print of parent or guardian:

Signature of investigator:

Witness signature:

Date:

Principal investigator:

Address:

Phone number:

தகவல் அளிக்கப்பட்ட ஒப்புதல் படிவம்

எனது குழந்தைக்கு பிராங்கியோலைட்டிஸ் வியாதி இருக்கலாமென்று மருத்துவர் மூலம் தெரிவிக்கப்பட்டது.

இந்த ஆய்வு பற்றி எனக்கு விளக்கமாக எனது தாய்மொழியில் தெரிவிக்கப்பட்டது. இந்த ஆய்வில் பங்கெடுத்துக் கொள்வதால் குழந்தைக்கு ஏற்படக்கூடிய அபாயங்கள் மற்றும் நன்மைகள் பற்றி எனக்கு விவரமாக தெரிவிக்கப்பட்டது. இந்த ஆய்வில் எனது குழந்தை பங்கெடுத்துக் கொள்ள முழு மனதுடன் சம்மதிக்கிறேன். கேள்விகள் கேட்பதற்கு எனக்கு வாய்ப்பளிக்கப்பட்டது.

இந்த ஆய்விலிருந்து கிடைக்கும் முடிவுகளை பயன்படுத்துபவரை கட்டுப்படுத்தாமலிருக்க நான் சம்மதிக்கிறேன்.

குழந்தையின் பெயர் -

குழந்தையின் பெற்றோர் / கண்காணிப்பாளர் பெயர் -

குழந்தையின் பெற்றோர் / கண்காணிப்பாளர் கையெழுத்து -

தேதி -

எழுதப்படிக்கத் தெரியாத பெற்றோர் / கண்காணிப்பாளர் கைவிரல் ரேகை -

சாட்சியின் பெயர் -

சாட்சியின் கையெழுத்து -

தேதி -

ஆய்வாளர் / ஆய்வு மருத்துவர் பெயர்

-

ஆய்வாளர் / ஆய்வு மருத்துவர் கையெழுத்து -

தேதி -