CHILDHOOD PNEUMONIA AND HYPOXAEMIA IN AN URBAN DIARRHOEAL HOSPITAL, DHAKA, BANGLADESH

Submitted in total fulfilment of the requirements of the degree of

Master of Medicine (Paediatrics)

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Declaration

To the best of my knowledge and belief, this research work for my thesis does not contain any material which has either been accepted for the award of any other degree in any other university and/or other tertiary institution or been taken material previously published or written by another person, except where due reference has been made in the text.

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Mohammad Jobayer Chisti
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Abbreviations used

ARI - Acute Respiratory Infection
Br-Pn – Broncho-pneumonia
CI - Confidence Intervals
CRF - Case Report Form
CSF - Cerebrospinal Fluid
CXR – Chest X-ray
° C – Degree Celsius
EEG – Electroencephalogram
ERC - Ethical Review Committee
ESP - Essential Service Package
HAZ – Z-score of Height for Age
ICDDR,B – International Centre for Diarrhoeal Disease Research, Bangladesh
IQR – Interquartile Range
LC – Lobar Consolidation
LSW – Longer Stay ward
MDG - Millennium Development Goal
NCHS - National Centre for Health Statistics
NGO - Non-government Organization
O₂ - Oxygen
OR - Odds Ratio
ORS – Oral Rehydration Salt Solution
SCW – Special Care Ward
SD – Standard Deviation
SPSS – Statistical Package for the Social Sciences

SPO$_2$ - Arterial Haemoglobin Oxygen Saturation

SSW – Short Stay Ward

US$ - United States Dollar

WAZ – Z-score of Weight for Age

WHO – World Health Organization

WHZ – Z-score of Weight for Height
Abstract

Childhood pneumonia and hypoxaemia in an urban diarrhoeal hospital, Dhaka, Bangladesh

Background: Pneumonia is the number one killer disease in developing countries, including Bangladesh. There were an estimated two million global deaths from pneumonia annually from 2000 to 2003 in children between 1 and 60 months, and a further one million from pneumonia among neonates. Of these more than 90% occurred in developing countries. Many factors are involved in what has been called the silent global pandemic. Hypoxaemia plays a substantial role in the morbidity and mortality from pneumonia and from other severe illness.

Dhaka Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) admits patients with diarrhoea and other conditions but diarrhoea is the entry point for admission. Children with serious illness such as abnormal mental status, severe pneumonia, malnutrition, cyanosis and hypoxemia, sepsis are admitted to the Special Care Ward (SCW) of the hospital which serves as a critical care medicine ward.

Aim: To explore the clinical characteristics, understanding of pneumonia by the care-givers, and socio-demographic predictors of WHO defined pneumonia, factors associated with deaths in pneumonia, and overall predictors of hypoxaemia in severely ill children under five hospitalized for management of diarrhoea.
Methods: For this prospective cohort study, we enrolled all children under-five of either sex, admitted to the SCW of the Dhaka Hospital of ICDDR,B during September 2007-December 2007. Those with associated WHO-defined pneumonia constituted the study group, and those admitted without pneumonia formed the comparison group. In addition, comparison was made between the survivors and the deaths in pneumonia group. Furthermore, comparison was also made between the WHO defined hypoxaemic (SPO\textsubscript{2} < 90\%) and non-hypoxaemic SCW children.

Results: 198 (77\%) of 258 children had pneumonia. The case fatality was higher in the children with pneumonia, but statistically insignificant. Basic knowledge about clinical features of illness was better for diarrhoea than for pneumonia. Care giver understanding about pneumonia was good in only 17 (7\%) and poor in 131 (51\%). Care giver understanding about diarrhoea was good in 76 (30\%) and poor in 43 (17\%). Among children admitted to SCW at ICDDR,B, children who slept in a bare wooden slat bed with no covering and those whose parents/caregivers had poor knowledge of pneumonia were more likely to have pneumonia than other diagnoses.

The risks for death in pneumonia were: severely underweight, hypoxaemia, severe sepsis on admission (defined at chapter 2 in table 2), and lobar consolidation.

The hypoxaemic children more often had a fatal outcome in contrast to the children who did not have hypoxaemia. The individual predictors of hypoxaemia in children under-five were: lower chest wall indrawing, nasal flaring, and severe sepsis on admission.
Conclusion: Children under-five who sleep in a bare bed and have parents/caregivers with poor knowledge were at risk of pneumonia. Children with diarrhoea complicated by pneumonia who presented with severe underweight, hypoxaemia, severe sepsis, and lobar consolidation were at higher risk of death. Hypoxaemia is associated with higher case-fatality. Clinical predictors of hypoxaemia were lower chest wall indrawing, nasal flaring, and severe sepsis on admission.
Chapter One: Introduction

Pneumonia is the largest single cause of childhood deaths in developing countries [1, 2]. It continuously exerts a huge burden in terms of morbidity, hospitalization, and deaths in children under five years of age in those regions [3-5]. Among the eleven million deaths globally in children under five from 2000 to 2003, an estimated 2 million deaths occurred each year from pneumonia in children between 1 and 60 months, and a further one million from pneumonia among neonates [6]. The large majority of these deaths (90-95%) take place in developing countries [7, 8]. Since 1961, large population based studies that have been carried out on the incidence of clinical pneumonia in children showed that among the 151 million episodes of pneumonia globally, more than 95% occurred in developing countries and 7% to 13% episodes of pneumonia required hospitalization [9, 10].

The aim of Millennium Development Goal (MDG) 4 is to reduce the worldwide childhood mortality by two-thirds, between 1990 and 2015. The success of the MDG 4 will depend on a reduction in this enormous burden of child and neonatal mortality from pneumonia, which is the major disease targeted by the World Health Organization (WHO) programme on acute respiratory infection. A number of priority interventions have been identified to reduce the global burden of deaths from pneumonia. These include improving nutrition and frequency of breast-feeding, lessening indoor air-pollution, reducing congestion of accommodation, getting better access to antibiotics, improving care seeking behaviour and referral practices, and improving the quality of case management [11, 12].
However, the success of the interventions for reducing pneumonia mortality also depends upon sufficient knowledge of pneumonia on the part of care-givers/parents, to appropriate support care seeking for their children [13, 14]. Until now, progress towards MDG 4 has not been satisfactory except for a few countries from Latin America [15, 16] and some countries in Asia [17]. In contrast to these examples, as in many developing countries in Asia, pneumonia still remains as the primary cause of death in children under five in Bangladesh [18, 19], still far away from achieving the MDG 4 before 2015. The conjugate pneumococcal vaccine, primarily targeted against pneumonia for younger children, which may be available in many developing countries, is not sufficiently effective [20] and currently too costly for the Bangladeshi population [21]. Much of the population live in poverty, which potentiates the ongoing burden of pneumonia. A recent study conducted in Dhaka, Bangladesh, reported that 60% of children hospitalized with severe malnutrition and diarrhoea had pneumonia and among this defined population 63% had a fatal outcome [22]. This scenario has been consistently similar for more than a decade in Bangladesh [23, 24], as well as in other developing countries [25, 26].

A number of studies have identified risk factors for pneumonia but these varied from country to country. In the resource-limited settings of developing countries such as Bangladesh, it is important to understand the socio-demographic characteristics of pneumonia, in addition to clinical features, in order to take preventive measures and organise early management. A study finding from Pakistan, a neighbouring country of Bangladesh, showed malnutrition, young age, and lower immunization status to be individual risk factors for pneumonia [27]. Studies conducted in another neighbouring country, India, showed too early or too delayed complementary
feeding, living in crowded area, parental smoking, and poor house hygiene to be risk factors for pneumonia [28-30]. Studies conducted in other developing countries reported malnutrition, large family size, low birth weight, vitamin A deficiency, lack of exclusive breast feeding, poor socio-economic status, both maternal and paternal illiteracy and indoor air pollution as the risks of pneumonia [2, 31-36]. Several studies carried out in Bangladesh over the last few decades identified most of these factors as the risks of pneumonia [23, 24]. Two studies, the most recent one having been conducted in an urban diarrhoeal hospital in Dhaka, observed strong association of severe malnutrition with pneumonia [22, 37]. Interestingly, no effective pneumonia control programme has been launched in Bangladesh even though there has been previous experience of successful reduction of morbidity and mortality from diarrhoea through the popular implementation of oral rehydration therapy, strongly supported by mass media education [38]. We sought to understand if there was sufficient awareness among caregivers about simple clinical signs of pneumonia. The success of treatment for pneumonia depends upon the level of knowledge of pneumonia by care-givers/parents [13, 14]. If there is poor knowledge, caregivers may delay bringing their child to the health care facility in time. However, compared to data on caregiver knowledge of diarrhoea in Bangladesh, there are no published data on caregiver knowledge about pneumonia. A better understanding of the characteristics of children presenting with pneumonia would help parents seek care and health workers provide the appropriate measures for each patient, and assist in public health campaigns against pneumonia.

Risk factors for death from pneumonia differ to some extent in developing countries compared to developed countries. An important difference is in the wide vaccination
coverage and better treatment facilities in the developed countries [36]. The case-fatality rate in pneumonia also varies [32, 39-42]. Partly it depends on presence or absence of other associated co-morbidities; thus the case fatality is often much higher when pneumonia presents with diarrhoea [26, 43] and/or malnutrition [44-46]. Mortality is also much higher when it is associated with measles [23]. Studies in South America and in Africa have identified severe malnutrition as one of the risk factors for deaths from pneumonia [16, 47]. Studies conducted in India reported that being unable to drink, and suffering from diarrhoea and malnutrition are predictors of deaths from pneumonia [26, 48]. Several recent reviews have also revealed that a significant higher percentage of under-five childhood deaths from pneumonia occurred with under-nutrition as an underlying cause [6, 46, 49]. Studies from Peru, the Gambia, and India identified a number of other risk factors for deaths from pneumonia, including early infancy, lack of exclusive breast feeding, inadequate immunization, and poor parental literacy [16, 26, 47]. Severe malnutrition has also been observed as a prominent risk factor for death from pneumonia in Bangladesh [23, 24, 50].

A most recent review revealed that to reduce the mortality from pneumonia effective management is a major issue [51]. For the initiation of effective case management, the health care professionals at facilities where children initially present (often at the community or district health clinics) should have sufficient knowledge to identify the risk factors for deaths from pneumonia. This is important to ensure appropriate, early management and referral of the sickest children to higher level facilities where it is safe to do so. This process could reduce morbidity and mortality, and better skills in recognition and management in primary care facilities would also reduce
hospitalization and costs. Ultimately this in turn would help to achieve the MDG by 2015.

Hypoxaemia is a common and serious complication in severely ill children [52]. Most severely ill children with hypoxaemia present with pneumonia [53], but hypoxaemia can also occur with a number of other illnesses, particularly during the neonatal period [54, 55]. Much work has been done looking at clinical signs of hypoxaemia in patients with pneumonia. Little is known about the clinical signs of hypoxaemia in non-pneumonia under-five sick children. Data are limited where incidence and clinical signs of hypoxaemia among the neonates and under-five children were addressed properly [54, 56].

Hypoxaemia is one of the major risks of death from pneumonia [53, 55, 57, 58]. Many pneumonia related deaths occur before the child enters the health care system [59]. Timely oxygen supplementation improves the outcome of the hypoxaemic children [60-62]. In developing countries, patients are initially brought to smaller health facilities providing initial essential support [in the case of Bangladesh this support is termed as essential service package (ESP)]. At this level of facility, many health care providers are not adequately confident in the use of oxygen supplementation for severely ill children [63]. Pulse oximetry is the most reliable, non-invasive, accurate method of measuring arterial haemoglobin oxygen saturation (SpO₂) in pneumonia [58] and also in other illnesses in children [64, 65] and particularly useful where oxygen is in short supply or where health workers lack confidence in assessing clinical parameters [63]. Nevertheless, many health facilities in developing countries, where the case fatality of sick children, including those with
pneumonia, is high, experience limited availability and supply of oxygen [52, 57, 66, 67] and rarely have oximetry. Such is generally the situation in ESP clinics in Bangladesh. Additionally, it is almost impossible for the under-privileged care givers of the patients to meet the cost of oxygen, which even in very small amounts is very expensive. Pulse oximetry, which facilitates detection of hypoxaemia and rational use of oxygen, is almost always unavailable [52, 68]. This is why clinicians in those regions frequently have to depend on clinical indicators to determine who should be given the limited oxygen supply, or who will be referred to a facility where oxygen is accessible [69].

Although clinical signs are the most widely used method in most of the health facilities in developing countries, these signs are not overly sensitive or specific. No single clinical sign has been found to be reliable as a predictor of hypoxemia. Fast breathing was found to be useful for the indication of oxygen supplementation in some settings but a number of studies showed conflicting results [70]. Moreover, children with diarrhoea and dehydration may present with fast breathing due to metabolic acidosis even in the absence of hypoxaemia [71]. As additional confounding, children with severe malnutrition might not have fast breathing due to sub-optimal inflammatory responses, reduced power of the respiratory muscles, and depletion of potassium and magnesium [72]. As in other hospitals in Bangladesh and in other developing countries, Dhaka hospital of ICDDR,B also experiences a very high disease burden and fatality due to hypoxaemia in severely ill children under five. Children with hypoxaemia often present there with dehydrating diarrhoea, with pneumonia and/or malnutrition. However, there are no published data on the clinical predictors and outcome of hypoxaemia among the diarrhoeal children who present
with pneumonia and other associated problems such as malnutrition. So it is very important to have a clear understanding of the diagnostic criteria of hypoxaemia for the appropriate supplementation of oxygen in order to reduce the morbidity and mortality from hypoxaemia in a resource-poor setting like Bangladesh.

The three objectives of this study were:

- To describe the socio-demographic characteristics and clinical features of children under five years of age with WHO-defined pneumonia, admitted to an urban diarrhoeal hospital in Bangladesh. Our further aim was to evaluate the knowledge of caregivers about pneumonia in comparison with their knowledge of diarrhoea (chapter 3, result 1 and chapter 4, description 1).

- To identify factors associated with death among children under five with pneumonia admitted in the SCW of the Dhaka hospital (chapter 3, result 2 and chapter 4, description 2).

- To identify the clinical predictors as well as outcome of hypoxaemia in severely ill, hospitalized children under-five having diarrhoea with concomitant pneumonia in the Dhaka Hospital of ICDDR,B (chapter 3, result 3 and chapter 4, description 3).
Chapter Two: General Methods

**Study design:** This was a prospective cohort study in which we enrolled all the children under five admitted to the Special Care Ward (SCW) of the Dhaka Hospital of ICDDR,B between September 1 and December 31, 2007. The study was approved by the Ethical Review Committee (ERC) of the centre and an informed oral consent was obtained from respective parents/guardians of all participating children.

**Setting:** This study was conducted at the Dhaka Hospital of ICDDR,B, Dhaka, Bangladesh, which provides care and treatment to around 110,000 diarrheal patients, with or without associated complications and with or without other health problems, each year. The recently conducted randomized study among 1.5 million urban and rural Bangladeshi population showed that the annual prevalence of diarrhoea ranged from 15% to 25% [73]. The vast majority of the patients come from poor socio-economic backgrounds from urban and peri-urban Dhaka, the capital city of Bangladesh.

Children who present to the hospital are first assessed by an experienced nurse in the triage area. Based on this assessment, the patient may be admitted to the short stay ward (SSW) if presenting with dehydrating diarrhoea but no other complication. Alternatively the nurse may refer the patient to be assessed by the physician for admission to either the longer stay ward (LSW) or the SCW. Patients presenting with complication of diarrhoea and/or other associated illness, are admitted to the LSW while those who present with severe acute illness, not only associated with severe dehydration, are admitted to the SCW. Such severe acute illness may include patients experiencing respiratory difficulty, cyanosis, apnoea, hypothermia or hyperthermia,

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clinical sepsis, marked lethargy, impaired mental status including convulsion, poor peripheral perfusion not attributable to dehydration, or coma. The triage nurse also refers children without diarrhoea to other city hospitals and patients with diarrhoea but no sign of dehydration to a primary health care clinic located within the hospital premises, and operated by a local health non-government organization (NGO). Patients admitted to the LSW and SCW often need laboratory investigations and administration of appropriate antibiotic and other supportive management, such as closer observation and frequent assessment. Soon after admission into the SCW the attending physician assesses the patient by taking an explicit medical history, performing a thorough clinical examination and initiating appropriate therapy after collection of blood and/or cerebrospinal fluid (CSF), and performing a chest X-ray. Oxygen saturation by pulse-oximeter and blood glucose level by bedside Glucocheck machine is performed on almost all of the patients of the SCW.

**Participants:** Diarrhoea was an entry point for the study and that it was graded some or severe dehydration. During the study period (September1, 2007 to December 31, 2007) all the eligible children were enrolled from among those admitted to the Special Care Ward (SCW) of the hospital. In total, 258 children under five were admitted to the study unit during the study period. A clinical diagnosis of pneumonia was made according to the WHO algorithm of acute respiratory infection (ARI) (Table 1). Children diagnosed with tuberculosis and those whose caregivers did not give consent were not included in the study.

Children with any form of WHO-defined pneumonia with severe clinical malnutrition were also considered to have very severe pneumonia. Children who had
severe stunting [<-3 Z score of height for age (HAZ) of the median of the National Centre for Health Statistics (NCHS)], or severe underweight (<-3 Z score of weight for age (WAZ) of the median of the NCHS), or severe wasting (<-3 Z score of weight for height (WHZ) of the median of the NCHS) or had nutritional oedema were considered as severely malnourished [74, 75]. Diarrhoea was defined as the passage of abnormally loose stool three or more times per day. Hypoxaemia was defined if the SpO2 was < 90% [76].
### Table 1: WHO algorithm for the diagnosis of pneumonia (children presenting with cough and/or respiratory difficulty)

<table>
<thead>
<tr>
<th>Age</th>
<th>Clinical parameter</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 months of age</td>
<td>• Respiratory rate ≥ 60/min and/or</td>
<td>Severe pneumonia</td>
</tr>
<tr>
<td></td>
<td>• Lower chest wall indrawing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• (but no signs of very severe pneumonia)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any of the below:</td>
<td>Very severe pneumonia</td>
</tr>
<tr>
<td></td>
<td>• Central Cyanosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Not able to drink</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Head nodding</td>
<td></td>
</tr>
<tr>
<td>2 months - 60 months of age</td>
<td>• Respiratory rate ≥ 50/min (for 2 months - 11 months of age)</td>
<td>Pneumonia</td>
</tr>
<tr>
<td></td>
<td>• Respiratory rate ≥ 40/min (for 12 months - 60 months of age)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• (But no signs of severe or very severe pneumonia).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lower chest wall indrawing</td>
<td>Severe pneumonia</td>
</tr>
<tr>
<td></td>
<td>• (but no signs of very severe pneumonia).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any one of the following:</td>
<td>Very severe pneumonia</td>
</tr>
<tr>
<td></td>
<td>• Central cyanosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Unable to drink</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Head nodding</td>
<td></td>
</tr>
</tbody>
</table>

In our study there are three comparison groups. 1) Children fulfilling the clinical criteria for WHO-defined pneumonia constituted the study group, and those admitted without pneumonia formed the comparison group. 2) The characteristics of the pneumonia children who died were compared with those who survived. 3) The characteristics and outcome of the hypoxaemic children under five were compared.
with those who were not hypoxaemic. The results and discussions of these three comparison groups are presented in chapters 3 and 4 respectively.

Clinical management of the children attending the hospital was done following the standard management guidelines of the hospital [22, 77]. These include management of dehydration using oral (for those with some dehydration) or intravenous fluids [for those with severe dehydration, and also those who were unable to drink due to any reason]; oxygen supplementation in hypoxaemia, appropriate antimicrobial therapy; appropriate feeding, micronutrients, vitamins and minerals as and when required. Antibiotics were used in children who presented with severe cholera, invasive diarrhoea, malnutrition, pneumonia, sepsis, and other infections. Oral antibiotics were used in children with severe cholera, invasive diarrhoea, and non-severe pneumonia whereas injectable antibiotics were used in those with severe malnutrition, severe and very severe pneumonia, sepsis, and other severe infections. Children with WHO-pneumonia did not receive any fluid in addition to feeding except those who required correction of dehydration or maintenance of hydration. Oral correction was done by oral rehydration salt solution and intravenous correction was done by either cholera saline or normal saline. Overall clinical management of the pneumonia was done according to WHO algorithm [78] and overall management of severe protein-energy malnutrition followed the hospital’s protocolized guidelines [22, 78]. Oxygen supplementation was given after confirmation of hypoxaemia by using pulse oxymetre which had been practised as a standard policy of the hospital.

**Procedures:** Case report forms (CRF) were developed, pretested, and finalized for data acquisition. All relevant clinical, laboratory and socio-demographic
characteristics were included and defined accordingly. For each patient age, sex, admission dehydration, nutritional status, mental status, rectal temperature (°Celsius), peripheral perfusion, sepsis, and severe sepsis and outcome were recorded. Other measurements taken were those of arterial haemoglobin O₂ saturation, blood glucose, complete blood count, serum electrolytes, blood culture and the presence of radiographic changes on chest x-ray. During the data collection the hospital did not have any qualified radiologist, so radiological pneumonia was diagnosed when at least two SCW clinicians came into same consensus after examining the individual X-ray film. Clinical and socio-demographic characteristics were evaluated and compared between children with and without pneumonia. The clinical characteristics were history of taking vitamin A capsule within last six months, history of measles within last six months, measles vaccination, breast feeding, dehydrating diarrhoea, convulsion on or after admission, hypoglycaemia on or after admission, hypoxaemia, severe stunting, severe underweight, severe wasting and death. The socio-demographic characteristics included: understanding of pneumonia by the care-givers; type of bed the child slept in; education status of parents; employment status of the mother; socio-economic status of the family; presence of a window or exhaust fan in the kitchen, and a separate living room in the house; and having smoker in the house who smokes inside the bed room.

Further comparison was made between understanding of pneumonia and knowledge of diarrhoea by the care-givers. For a second analysis: between children who died and those who survived pneumonia) other additional variables - living outside Dhaka district, sepsis, severe sepsis, lobar consolidation were assessed. For a third comparison between children with hypoxaemia and without hypoxaemia, assessment
also took in any history of convulsion prior to admission into the hospital, cyanosis, dehydration status, abnormal mental status (irritable / lethargic / convulsing / comatose) on admission, lower chest wall indrawing, nasal flaring, head nodding, grunting respiration, and inability to drink. Definitions of important variables are shown in Table 2.
### Table 2: Definition of important clinical and socio-demographic study parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental status</td>
<td>normal / irritable / lethargic / convulsing / comatose</td>
</tr>
<tr>
<td>Dehydrating diarrhoea</td>
<td>diarrhoeal children presenting with some or severe dehydration</td>
</tr>
<tr>
<td>Some/severe dehydration</td>
<td>defined by “Dhaka methods” of assessment of dehydration which is almost similar to WHO method and approved by WHO [77]</td>
</tr>
<tr>
<td>Hypoxaemia, if SPO₂ without O₂ is &lt; 90%</td>
<td>≤3 z score of height for age of the median value of the NCHS</td>
</tr>
<tr>
<td>Severe underweight, ≤-3 z score of weight for age of the median value of the NCHS</td>
<td></td>
</tr>
<tr>
<td>Severe wasting, ≤-3 z score of weight for height of median value of the the NCHS</td>
<td></td>
</tr>
<tr>
<td>Lower chest wall indrawing</td>
<td>inward movement of the bony structures of the lower chest wall with inspiration</td>
</tr>
<tr>
<td>Grunting respiration</td>
<td>it is an expiratory sound occurs due to partial closure of glottis as an effort to maintain intra-alveolar pressure for the prevention of alveolar collapse</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>blood glucose &lt; 3.0 mmol/L</td>
</tr>
<tr>
<td>Sepsis</td>
<td>presence of any two of the following: tachynoea, tachycardia, thermo-instability (hypo or hyperthermia), and abnormal WBC count (&gt;11000/cc or, &lt;4000/cc or, band and neutrophil ration ≥ 0.1) plus hypotension [79] in the absence of clinical dehydration or after correction of dehydration</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>sepsis plus signs of poor peripheral perfusion (absent peripheral pulses) [79]</td>
</tr>
<tr>
<td>Understanding of feature of pneumonia by the care givers</td>
<td>Clinical feature of pneumonia: (a) cough and / or respiratory difficulty, (b) faster respiration than normal, (c) lower chest wall indrawing, (d) unable to drink, (e) cyanosis;</td>
</tr>
<tr>
<td>Good:</td>
<td>must talk about more than one criteria including “a”</td>
</tr>
<tr>
<td>Average:</td>
<td>could only talk about “a”</td>
</tr>
<tr>
<td>Poor:</td>
<td>could say nothing about the clinical features of pneumonia</td>
</tr>
<tr>
<td>knowledge of diarrhoea by the care givers</td>
<td>Definition of diarrhoea: passage of abnormally loose or watery stool three or more times per day</td>
</tr>
<tr>
<td>Good:</td>
<td>could give definition properly</td>
</tr>
<tr>
<td>Average:</td>
<td>could talk about very frequent passage of loose/watery stool with many frequency but could not mention the exact number</td>
</tr>
<tr>
<td>Poor:</td>
<td>could talk about loose/watery stool one time per day but not more or could not say anything about loose/watery stool</td>
</tr>
<tr>
<td>Bare bed</td>
<td>Sleep on wooden or bamboo bed with no mattress or blanket cover</td>
</tr>
<tr>
<td>Socio-economic status</td>
<td>Wealthy: monthly income more than 10,000 taka (US$ 150)</td>
</tr>
<tr>
<td>Middle class</td>
<td>monthly income 5,000 - 10,000 taka (US$ 75 -150)</td>
</tr>
<tr>
<td>Poor</td>
<td>monthly income less than 5,000 taka (US$ 75)</td>
</tr>
</tbody>
</table>
Analysis: All data were entered onto personal computer and edited before analysis using SPSS for Windows (version 15.0; SPSS Inc, Chicago) and Epi Info (version 6.0, USD, Stone Mountain, GA). Differences in proportions were compared by the Chi-square test, differences of means were compared by Student’s t-test and differences of median were compared by Mann-Whitney test, as appropriate. A probability of less than 0.05 was considered statistically significant. Strength of association was determined by calculating odds ratio (OR) and 95% confidence intervals (CI). Initially variables were analysed in a univariate model and finally, after adjusting for the co-variates, logistic regression analysis was performed to identify variables that were significantly associated with pneumonia (chapter 3), to identify variables that were significantly associated with deaths among the pneumonia children (chapter 3), and to identify the variables that were significantly associated with hypoxaemia among all the SCW study children (chapter 3). We also calculated the sensitivity and specificity of the individual predictors of hypoxaemia explored by the logistic regression.
Chapter Three: RESULTS

1. Socio-demographic and clinical characteristics associated with pneumonia in children with diarrhoea in an urban hospital in Dhaka, Bangladesh

(1) Clinical features of pneumonia: In total, 263 children under five were admitted to the study unit during the study period. Two were diagnosed with pulmonary tuberculosis and three patients left against medical advice soon after admission. These 5 patients were not included in the study. The study population therefore included 258 children. Among them 198 children had pneumonia and 60 children did not have pneumonia but had other serious medical problems. Among the 198 pneumonia children 24 died in the study period (case fatality percentage 12%). Among the 258 children in the study population, 119 (46%) were hypoxaemic on admission. The parents/care-givers of the 258 study children consented to be enrolled into the study.

Of the children with pneumonia, 55% (109/198) were male and 45% (89/198) female. Corresponding figures for children without pneumonia were 63% (38/60) and 37% (22/60) respectively. The median age of children with pneumonia was 6 months and 10.5 months for children without pneumonia. Mean body weight was 5.3 kg and 6.2 kg respectively. 31% (60/198) pneumonic cases were non-breast-fed compared to 45% (27/60) among the non-pneumonic children.

Compared to children with diagnoses other than pneumonia, children with pneumonia more often had a history of longer (median, IQR) duration of fever on admission [72.0 hours (24.0, 120.0) vs. 37.0 hours (13.0, 90.0): p = 0.008] (Table 5);
they more often presented with higher (mean ± SD) rectal temperature (37.8 ± 1.3 vs. 37.4 ± 1.3: p = 0.042), hypoxaemia (55% vs. 11%; p < 0.001) (Table 3) which often remained in longer duration (median, IQR) during their stay at the hospital [5.0 hours (0.0, 12.0) vs. 0.0 hours (0.0, 0.0): p < 0.001] (Table 5), and were less likely to have had convulsions on or after admission (8% vs. 20%; p = 0.012) (Table 3). Children with pneumonia had a lower prevalence of hypoglycaemia (7% vs. 22%; p = 0.002) and hyponatraemia (21% vs. 35%; p = 0.021); and more frequently presented with higher (median, IQR) WBC count [14000.0/cc^3 (10000.0, 20000.0) vs. 11850.0/cc^3 (8525.0, 15800.0): p = 0.035] (Table 5).

The case fatality among children with pneumonia was higher (12% vs. 8%; p = 0.56), but the difference was not statistically significant (Table 3). Children who did not receive a vitamin-A capsule within the last 6 months, did not receive vaccine against measles, had a history of measles within the last 6 months, had severe wasting, severe stunting, and severe underweight, sepsis, severe sepsis, meningitis, hypernatraemia, and hypokalaemia were similarly distributed among the groups (Table 3).

(2) Socio-demographic risk factors: Among the entire sample, 17 (7%) and 76 (30%) care givers had a good understanding of pneumonia and diarrhoea respectively whereas 131 (51%) and 43 (17%) had a poor understanding (Table 6). In logistic regression analysis, after adjusting for potential confounders such as illiterate mother, illiterate father, employed mother, history of smoking who smokes inside the bed room, poor socio-economic status, not having window or exhaust fan in the kitchen room, separate living room; children with pneumonia were more likely
to sleep in a bare wooden slatted or bamboo bed (OR 2.7, 95% CI 1.40 - 5.21, \( p = 0.003 \)), and they were also more likely to have parents/caregivers with poor knowledge of pneumonia (OR 1.94, 95% CI 1.02 - 3.70, \( p = 0.043 \)) (Table 4). There were no other significant differences between pneumonia and non-pneumonia patients in terms of the socio-demographic factors measured (illiterate mother, illiterate father, employed mother, poor socio-economic status, H/O active smoker in the family, and not having separate living room, not having window or exhaust fan in the kitchen room) (Table 4)

**Consort diagram of the study population**

Children under five were admitted to the study unit during the study period

= 263

Children were excluded from the study = 5 (2 due to pulmonary tuberculosis and 3 had left the hospital against medical advice)

Total study population = 258

Hypoxaemia = 119
Non-hypoxaemic = 139

Pneumonia = 198

Children with serious medical problems other than pneumonia = 60

Died = 24
Survivors = 174

Died = 5
Survivors = 55

Mohammad Jobayer Chisti, MMed thesis
Table 3: Characteristics of pneumonia and non-pneumonia patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pneumonia (n = 198) n (%)</th>
<th>Non-pneumonia (n = 60) n (%)</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not received Vitamin-A capsule (within last 6 months)</td>
<td>99 / 197 (50)</td>
<td>32 / 60 (53)</td>
<td>0.88 (0.48 - 1.64)</td>
<td>0.780</td>
</tr>
<tr>
<td>History of measles (within last 6 months)</td>
<td>32 / 194 (17)</td>
<td>8 / 59 (14)</td>
<td>1.27 (0.52 - 3.20)</td>
<td>0.724</td>
</tr>
<tr>
<td>No Measles vaccination (after 9 months of age)</td>
<td>17 / 63 (27)</td>
<td>5 / 31 (16)</td>
<td>1.92 (0.57 - 6.78)</td>
<td>0.363</td>
</tr>
<tr>
<td>Non breast-fed</td>
<td>60 / 197 (31)</td>
<td>27 / 60 (45)</td>
<td>0.54 (0.28 - 1.01)</td>
<td>0.054</td>
</tr>
<tr>
<td>Convulsion on/after admission</td>
<td>15 / 198 (8)</td>
<td>12 / 60 (20)</td>
<td>0.33 (0.13 - 0.81)</td>
<td>0.012</td>
</tr>
<tr>
<td>Hypoglycaemia on/after adm</td>
<td>14 / 197 (7)</td>
<td>13 / 59 (22)</td>
<td>0.27 (0.11 - 0.66)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypoxaemia</td>
<td>108 / 198 (55)</td>
<td>11 / 60 (18)</td>
<td>5.35 (2.51 - 11.63)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HAZ (&lt;=-3 z score) Severe stunting</td>
<td>57 / 197 (29)</td>
<td>17 / 60 (28)</td>
<td>1.03 (0.52 - 2.06)</td>
<td>0.942</td>
</tr>
<tr>
<td>WAZ (&lt;=-3 z score) Severe underweight</td>
<td>80 / 195 (41)</td>
<td>26 / 60 (43)</td>
<td>0.91 (0.49 - 1.70)</td>
<td>0.867</td>
</tr>
<tr>
<td>WHZ (&lt;=-3 z score) Severe wasting</td>
<td>45 / 195 (23)</td>
<td>16 / 60 (27)</td>
<td>0.82 (0.41 - 1.69)</td>
<td>0.691</td>
</tr>
<tr>
<td>Sepsis</td>
<td>104 (53)</td>
<td>39 (65)</td>
<td>0.60 (0.31 – 1.13)</td>
<td>0.119</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>21 (11)</td>
<td>8 (13)</td>
<td>0.77 (0.30 – 2.02)</td>
<td>0.724</td>
</tr>
<tr>
<td>Meningitis (isolation of bacteria from CSF)</td>
<td>5 (3)</td>
<td>2 (3)</td>
<td>0.75 (0.12 – 5.75)</td>
<td>0.666</td>
</tr>
<tr>
<td>Hyponatraemia (&lt; 130 mmol/L)</td>
<td>36 (21)</td>
<td>20 (35)</td>
<td>0.44 (0.22 -0.89)</td>
<td>0.021</td>
</tr>
<tr>
<td>Hypernatraemia (&gt; 150 mmol/L)</td>
<td>25 (15)</td>
<td>3 (5)</td>
<td>2.75 (0.75 – 11.88)</td>
<td>0.153</td>
</tr>
<tr>
<td>Hypokalaemia (&lt; 3.5 mmol/L)</td>
<td>56 (33)</td>
<td>21 (37)</td>
<td>0.73 (0.38 – 1.42)</td>
<td>0.403</td>
</tr>
<tr>
<td>Death</td>
<td>24 / 198 (12)</td>
<td>5 / 60 (8)</td>
<td>1.52 (0.52 - 4.78)</td>
<td>0.56</td>
</tr>
</tbody>
</table>
### Table 4: Association of socio-demographic factors with pneumonia

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pneumonia (n = 198)</th>
<th>Non-pneumonia (n = 60)</th>
<th>Non-adjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>OR (95% CI)</td>
<td>p value</td>
</tr>
<tr>
<td>Illiterate mother</td>
<td>82 / 193 (42)</td>
<td>27 / 59 (46)</td>
<td>0.88 (0.47 - 1.64)</td>
<td>0.768</td>
</tr>
<tr>
<td>Illiterate father</td>
<td>74 / 193 (38)</td>
<td>22 / 59 (37)</td>
<td>1.05 (0.55 - 2.0)</td>
<td>0.99</td>
</tr>
<tr>
<td>Employed mother</td>
<td>36 / 195 (18)</td>
<td>14 / 60 (27)</td>
<td>0.74 (0.35 - 1.59)</td>
<td>0.518</td>
</tr>
<tr>
<td>H/O smoking who smokes inside the bed room</td>
<td>123 / 194 (63)</td>
<td>32 / 59 (54)</td>
<td>1.46 (0.78 - 2.75)</td>
<td>0.265</td>
</tr>
<tr>
<td>Poor socio-economic status (monthly income &lt;5000 taka)</td>
<td>125 / 195 (64)</td>
<td>34 / 60 (57)</td>
<td>1.37 (0.73 - 2.56)</td>
<td>0.374</td>
</tr>
<tr>
<td>Poor understanding of pneumonia by caregivers</td>
<td>106 / 195 (54)</td>
<td>25 / 59 (42)</td>
<td>1.62 (0.86 - 3.04)</td>
<td>0.142</td>
</tr>
<tr>
<td>Not having window or exhaust fan in the kitchen room</td>
<td>76 / 193 (39)</td>
<td>22 / 57 (37)</td>
<td>1.09 (0.57 - 2.08)</td>
<td>0.892</td>
</tr>
<tr>
<td>Sleeping on uncovered wooden or bamboo bed (bare bed)</td>
<td>138 / 194 (71)</td>
<td>32 / 59 (54)</td>
<td>2.08 (1.09 - 3.95)</td>
<td>0.023</td>
</tr>
<tr>
<td>Separate living room</td>
<td>86 / 187 (46)</td>
<td>20 / 56 (36)</td>
<td>0.65 (0.34 - 1.26)</td>
<td>0.227</td>
</tr>
</tbody>
</table>
Table 5: Compare between means of pneumonia and non-pneumonia cases

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pneumonia (n = 198) [Median (IQR)] / (Mean ± SD)</th>
<th>Non-pneumonia (n = 60) [Median (IQR)] / (Mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>6.0 (3.0, 12.0)</td>
<td>10.5 (2.4, 24.0)</td>
<td>0.078</td>
</tr>
<tr>
<td>Duration of fever (temp ≥ 38° Celsius) prior to admission (hours)</td>
<td>72.0 (24.0, 120.0)</td>
<td>37.0 (13.0, 90.0)</td>
<td>0.008</td>
</tr>
<tr>
<td>Rectal temperature (° C)</td>
<td>37.8 ± 1.3</td>
<td>37.4 ± 1.3</td>
<td>0.042</td>
</tr>
<tr>
<td>Total duration in hours of child remain hypoxaemic (SPO2 &lt; 90%)</td>
<td>5.0 (0.0, 12.0)</td>
<td>0.0 (0.0, 0.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total WBC count (/cc)</td>
<td>14000 (10,000, 20,000)</td>
<td>11850 (8525, 15800)</td>
<td>0.035</td>
</tr>
</tbody>
</table>

IQR = inter quartile range, SD = standard deviation

Table 6: Overall understanding of care givers about pneumonia and diarrhoea

<table>
<thead>
<tr>
<th>Variable</th>
<th>Understanding of pneumonia (n = 254) n (%)</th>
<th>Understanding of diarrhoea (n = 254) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good understanding</td>
<td>17 (7)</td>
<td>76 (30)</td>
</tr>
<tr>
<td>Average understanding</td>
<td>106 (42)</td>
<td>135 (53)</td>
</tr>
<tr>
<td>Poor understanding</td>
<td>131 (51)</td>
<td>43 (17)</td>
</tr>
</tbody>
</table>
2. Factors associated with death among the children under-five with pneumonia admitted in the SCW in an urban diarrhoea treatment centre, Dhaka, Bangladesh

In total, 198 children under-five with WHO-defined pneumonia were admitted to the study unit during the study period. Among them 24 children died (study group) and 174 children survived (comparison group) during this time. In univariate analysis the risk factors for death in children with pneumonia were oedematous malnutrition (25% vs. 10%; p = 0.04), clinical sepsis (79% vs. 49%; p = 0.010), poor peripheral perfusion as indicated by uncountable/absent radial pulse (29% vs. 7%; p = 0.003) (Table 7), low systolic blood pressure (mmHg) (62.0 ± 41.0 vs. 98.4 ± 28.4: p = 0.001) and diastolic blood pressure (mmHg) (27.5 ± 21.9 vs. 56.7 ± 19.4: p < 0.001), low SpO₂ (%) on admission (80.0 ± 12.0 vs. 89.1 ± 10.0: p = 0.001), hypernatraemia (30% vs. 12%; p = 0.017) and renal failure [measured by serum creatinine level (micromole/L)] [156.5 (119.3, 264.3) vs. 75.0 (67.1, 116.3): p = 0.026] (Table 8). No other variables (age, patient brought from outside the Dhaka district, illiterate mother, poor socio-economic status, poor understanding of pneumonia by caregivers, use of bare bed for sleeping, non-breast-fed, non-vaccinated, dehydrating diarrhoea, hypoglycaemia, total WBC count, hyponatraemia, hypokalaemia) were found to be significantly associated with death for pneumonia in univariate analysis (Table 7 and 8). In logistic regression analysis after adjusting with co-variates pneumonic children with fatal outcome were more likely to be severely underweight (OR 5.17, 95% CI 1.21 - 22.02, p = 0.026), hypoxaemic (OR 17.52, 95% CI 1.92 - 159.97, p = 0.011), more often had severe sepsis (OR 8.68, 95% CI 1.81 - 41.52, p = 0.007), lobar consolidation (OR 11.90, 95% CI 2.30 - 61.58, p = 0.003), and were
less likely to have metabolic acidosis (OR 0.85, 95% CI 0.75 - 0.97, p = 0.012) (Table 9).

**Table 7: Comparison among the survivors and deaths in children under-five with pneumonia in SCW**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Deaths n (%)</th>
<th>Survivors n (%)</th>
<th>OR (95% CI) (Unadjusted)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Came from outside Dhaka district</td>
<td>5 / 24 (21)</td>
<td>19 / 174 (11)</td>
<td>2.15 (0.62 - 7.07)</td>
<td>0.181</td>
</tr>
<tr>
<td>Illiterate mother</td>
<td>12 / 20 (60)</td>
<td>99 / 173 (57)</td>
<td>0.89 (0.31 - 2.49)</td>
<td>0.999</td>
</tr>
<tr>
<td>Poor socio-economic status (monthly income &lt;5000 taka)</td>
<td>16 / 22 (73)</td>
<td>109 / 173 (63)</td>
<td>1.57 (0.54 - 4.74)</td>
<td>0.509</td>
</tr>
<tr>
<td>Bare bed</td>
<td>16 / 20 (80)</td>
<td>122 / 174 (70)</td>
<td>1.70 (0.50 - 6.36)</td>
<td>0.507</td>
</tr>
<tr>
<td>Dehydrating diarrhea (some/severe dehydration)</td>
<td>15 / 24 (62)</td>
<td>76 / 174 (44)</td>
<td>2.15 (0.83 - 5.66)</td>
<td>0.130</td>
</tr>
<tr>
<td>Non breast-fed</td>
<td>10 / 24 (42)</td>
<td>50 / 173 (29)</td>
<td>1.76 (0.67 - 4.56)</td>
<td>0.300</td>
</tr>
<tr>
<td>No vaccination</td>
<td>4 / 24 (17)</td>
<td>16 / 171 (9)</td>
<td>1.81 (0.46 - 6.61)</td>
<td>0.301</td>
</tr>
<tr>
<td>Uncountable/absent radial pulse</td>
<td>7 / 24 (29)</td>
<td>12 / 173 (7)</td>
<td>5.46 (1.70 - 17.97)</td>
<td>0.003</td>
</tr>
<tr>
<td>Oedematous malnutrition</td>
<td>6 / 24 (25)</td>
<td>17 / 174 (10)</td>
<td>3.08 (1.00 - 9.74)</td>
<td>0.040</td>
</tr>
<tr>
<td>Clinical sepsis</td>
<td>19 / 24 (79)</td>
<td>85 / 174 (49)</td>
<td>3.98 (1.32 - 12.80)</td>
<td>0.010</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>11 / 24 (46)</td>
<td>10 / 173 (6)</td>
<td>13.79 (4.43 - 43.84)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypoglycaemia on/after admission</td>
<td>3 / 24 (13)</td>
<td>11 / 173 (6)</td>
<td>2.10 (0.43 - 9.14)</td>
<td>0.386</td>
</tr>
<tr>
<td>Lobar consolidation</td>
<td>11 / 21 (52)</td>
<td>16 / 150 (6)</td>
<td>9.21 (3.05 - 28.30)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypoxaemia</td>
<td>22 / 24 (92)</td>
<td>86 / 174 (49)</td>
<td>11.26 (2.45 - 71.52)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>WAZ (&lt;-3 z score) Severe underweight</td>
<td>18 (75)</td>
<td>62 / 171 (36)</td>
<td>5.27 (1.85 - 15.78)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Table 8: Comparison of mean / median among the survivors and deaths in children under five with pneumonia in SCW

<table>
<thead>
<tr>
<th>Variables</th>
<th>Deaths (n = 24) Median (IQR) / (Mean ± SD); (%)</th>
<th>Survivors (n = 174) Median (IQR) / (Mean ± SD); (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>8.3 (5.5, 11.5)</td>
<td>5.0 (2.9, 12.0)</td>
<td>0.233</td>
</tr>
<tr>
<td>Systolic blood pressure (mm of Hg)</td>
<td>62.0 ± 41.0</td>
<td>98.4 ± 28.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm of Hg)</td>
<td>27.5 ± 21.9</td>
<td>56.7 ± 19.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SPO2 without oxygen on admission (%)</td>
<td>80.0 ± 12.0</td>
<td>89.1 ± 10.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Total WBC count (/cc)</td>
<td>15,050 (10,250, 31,125)</td>
<td>14,000 (9,975, 19,150)</td>
<td>0.185</td>
</tr>
<tr>
<td>Serum Sodium (mmol/L)</td>
<td>144.7 ± 21.8</td>
<td>136.9 ± 11.6</td>
<td>0.107</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>3.5 ± 1.5</td>
<td>4.0 ± 1.2</td>
<td>0.148</td>
</tr>
<tr>
<td>TCO2 (mmol/L)</td>
<td>11.7 ± 6.4</td>
<td>15.4 ± 6.9</td>
<td>0.018</td>
</tr>
<tr>
<td>Serum creatinine (micromole/L)</td>
<td>156.5 (119.3, 264.3)</td>
<td>75.0 (67.1, 116.3)</td>
<td>0.026</td>
</tr>
<tr>
<td>Hyponatraemia (&lt; 130 mmol/L)</td>
<td>3 (13)</td>
<td>33 (22)</td>
<td>0.61 (0.14 – 2.34)*; 0.579</td>
</tr>
<tr>
<td>Hyponatraemia (&gt; 150 mmol/L)</td>
<td>7 (30)</td>
<td>18 (12)</td>
<td>3.57 (1.16 - 10.78)*; 0.017</td>
</tr>
<tr>
<td>Hypokalaemia (&lt; 3.5 mmol/L)</td>
<td>11 (48)</td>
<td>45 (30)</td>
<td>2.43 (0.93 – 6.29)*; 0.073</td>
</tr>
</tbody>
</table>

*Odds ratio (Confidence Interval)
### Table 9: Results of logistic regression to explore the risk factors for deaths among pneumonia patients in SCW

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adjusted</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lobar consolidation</td>
<td>11.90 (2.30 - 61.58)</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypoxaemia</td>
<td>17.52 (1.92 - 159.97)</td>
<td>0.011</td>
</tr>
<tr>
<td>WAZ (z score)</td>
<td>5.17 (1.21 - 22.02)</td>
<td>0.026</td>
</tr>
<tr>
<td>WAZ (≤ -3 z score)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic acidosis</td>
<td>0.85 (0.75 - 0.97)</td>
<td>0.012</td>
</tr>
<tr>
<td>Severe underweight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>8.68 (1.81 - 41.52)</td>
<td>0.007</td>
</tr>
<tr>
<td>Oedematous malnutrition</td>
<td>2.18 (0.38 - 12.61)</td>
<td>0.386</td>
</tr>
</tbody>
</table>

3. Clinical predictors and outcome of hypoxaemia among the sick children under five with concomitant pneumonia admitted in the SCW in an urban diarrhoeal treatment centre, Dhaka, Bangladesh

Among 258 children admitted 119 (46%) had hypoxaemia (study group) and 138 children did not have hypoxaemia (comparison group) during the study period. Among the hypoxaemic children 62 (52%) were male and their median (IQR) age was 5 (2.5, 10.0) months. Among the 198 pneumonic children in the study sample, 108 (55%) were hypoxaemic. Twenty-seven percent of patients with non-severe pneumonia were hypoxaemic compared to 56% and 62% among those with severe and very severe pneumonia, respectively (Table 10). This distribution of hypoxaemia among the radiologically proven pneumonia patients was 103/192 (54%) and it was highest among the patients with lobar consolidation [23/27 (85%)] (Table 10). The hypoxaemic children more often had a fatal outcome (21% vs 4%; p < 0.001), and more often presented with history of convulsion (unadjusted) (88% vs. 71%; p = 0.003) in contrast to the children who did not have hypoxaemia (Table 11). In logistic regression analysis, after adjusting with co-variate, the individual predictors of hypoxaemia in children under five were lower chest wall indrawing (OR 6.91, 95% CI 3.66-13.08, p < 0.001), nasal flaring (OR 3.22, 95% CI 1.45-7.17, p =
0.004), and severe sepsis (OR 4.48, 95% CI 1.62-12.42, p = 0.004) (Table 12). The sensitivity of history of convulsion, lower chest wall indrawing, nasal flaring, and severe sepsis to predict hypoxaemia are 87%, 84%, 31%, and 18% respectively and their specificity are 28%, 59%, 92%, and 94%, respectively (Table 13). The sensitivity and specificity and the positive predictive value and negative predictive value of combination of these variables were inconsistent (Table 13). All other parameters (head nodding, grunting respiration, abnormal mental status, dehydrating diarrhoea, cyanosis, and unable to drink) did not show any significant association with hypoxaemia (Table 11).

Thus, from our current data we can make an algorithm that predicts the need for oxygen (where pulse oxymetre is not available) in children under five (Table 13):

- All children presenting with history of convulsion prior to admission and/or lower chest wall indrawing should receive oxygen supplementation
- Nasal flaring and/or severe sepsis are highly specific for the indication of oxygen supplementation
### Table 10: Distribution of hypoxaemia among the study children

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pn by CXR Hypoxaemic 5 / 18 (radiology not done in 2 patients)</td>
<td>No Pn by CXR Hypoxaemic 1 / 6 (17)</td>
<td>Pn by CXR Hypoxaemic 47 / 83 (CXR was not done in 2 patients)</td>
<td>No Pn by CXR Hypoxaemic 1 / 3 (33)</td>
<td>No Pn by CXR Hypoxaemic 3 / 7 (43)</td>
</tr>
<tr>
<td>LC nil</td>
<td>Br-Pn Hypoxaemic 5 / 18 (28)</td>
<td>LC Hypoxaemic 9 / 10 (90)</td>
<td>Br-Pn Hypoxaemic 38 / 73 (52)</td>
<td>LC Hypoxaemic 14 / 17 (82)</td>
</tr>
<tr>
<td>No Pn by CXR Hypoxaemic 3 / 7 (43)</td>
<td>Pn by CXR Hypoxaemic 5 / 36 (14)</td>
<td>Pn by CXR Hypoxaemic 3 / 12 (25)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pn = pneumonia, CXR = chest X ray, LC = lobar consolidation, Br-Pn = broncho-pneumonia
Table 11: Characteristics of the hypoxaemic children under five admitted in the SCW of the Dhaka Hospital of ICDDR,B

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hypoxaemic (119) n (%)</th>
<th>Non-hypoxaemic (138) n (%)</th>
<th>OR (95% CI) (unadjusted)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>62 (52)</td>
<td>84 (60)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age (months) (median, IQR)</td>
<td>5.0 (2.5, 10.0)</td>
<td>8.0 (3.0, 21.0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>History of convulsion</td>
<td>104 (88)</td>
<td>99 (71)</td>
<td>2.98 (1.39 - 6.48)</td>
<td>0.003</td>
</tr>
<tr>
<td>Lower chest wall indrawing</td>
<td>100 (84)</td>
<td>57 (41)</td>
<td>7.48 (3.97 - 14.22)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nasal flaring</td>
<td>37 (31)</td>
<td>11 (8)</td>
<td>5.21 (2.40 - 11.55)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Head nodding</td>
<td>5 (4)</td>
<td>3 (2)</td>
<td>1.99 (0.40 - 10.75)</td>
<td>0.480</td>
</tr>
<tr>
<td>Grunting respiration</td>
<td>7 (6)</td>
<td>3 (2)</td>
<td>2.83 (0.64 - 14.18)</td>
<td>0.190</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>11 (9)</td>
<td>10 (7)</td>
<td>1.31 (0.50 - 3.49)</td>
<td>0.710</td>
</tr>
<tr>
<td>Dehydrating diarrhoea (some/severe)</td>
<td>53 (45)</td>
<td>72 (52)</td>
<td>0.75 (0.44 - 1.26)</td>
<td>0.30</td>
</tr>
<tr>
<td>Abnormal mental status (irritable / lethargic / convulsing / comatose)</td>
<td>96 (81)</td>
<td>98 (71)</td>
<td>1.78 (0.95 - 3.36)</td>
<td>0.070</td>
</tr>
<tr>
<td>Unable to drink</td>
<td>53 (45)</td>
<td>45 (33)</td>
<td>1.64 (0.96 - 2.82)</td>
<td>0.070</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>21 (18)</td>
<td>8 (6)</td>
<td>3.43 (1.37 - 8.84)</td>
<td>0.005</td>
</tr>
<tr>
<td>Outcome (Died)</td>
<td>25 (21)</td>
<td>4 (3)</td>
<td>8.98 (2.84 - 31.54)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Table 12 Results of logistic regression to explore the predictors of hypoxaemia among the admitted children under five in SCW of the Dhaka Hospital of ICDDR,B

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted OR</th>
<th>Adjusted 95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of convulsion</td>
<td>1.35</td>
<td>0.58 - 3.15</td>
<td>0.481</td>
</tr>
<tr>
<td>Lower chest wall indrawing</td>
<td>6.91</td>
<td>3.66 - 13.08</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nasal flaring</td>
<td>3.22</td>
<td>1.45 - 7.17</td>
<td>0.004</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>4.48</td>
<td>1.62 - 12.42</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Table 13: Sensitivity, specificity, positive and negative predictive value of predictors of hypoxaemia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypoxaemic (119) n (%)</th>
<th>Non-hypoxaemic (138) n (%)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of convulsion</td>
<td>104 (88)</td>
<td>99 (71)</td>
<td>88</td>
<td>28</td>
<td>51</td>
<td>72</td>
</tr>
<tr>
<td>Lower chest wall indrawing</td>
<td>100 (84)</td>
<td>57 (41)</td>
<td>84</td>
<td>59</td>
<td>64</td>
<td>81</td>
</tr>
<tr>
<td>Nasal flaring</td>
<td>37 (31)</td>
<td>11 (8)</td>
<td>31</td>
<td>92</td>
<td>77</td>
<td>61</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>21 (18)</td>
<td>8 (6)</td>
<td>18</td>
<td>94</td>
<td>72</td>
<td>57</td>
</tr>
<tr>
<td>In combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower chest wall indrawing and nasal flaring</td>
<td>34 (29)</td>
<td>7 (5)</td>
<td>29</td>
<td>75</td>
<td>83</td>
<td>61</td>
</tr>
<tr>
<td>Lower chest wall indrawing plus history of convulsion</td>
<td>80 (67)</td>
<td>49 (36)</td>
<td>73</td>
<td>64</td>
<td>62</td>
<td>75</td>
</tr>
<tr>
<td>Lower chest wall indrawing plus severe sepsis</td>
<td>20 (17)</td>
<td>6 (4)</td>
<td>17</td>
<td>96</td>
<td>77</td>
<td>57</td>
</tr>
<tr>
<td>Nasal flaring plus history of convulsion</td>
<td>30 (25)</td>
<td>10 (7)</td>
<td>20</td>
<td>93</td>
<td>75</td>
<td>54</td>
</tr>
<tr>
<td>Nasal flaring plus severe sepsis</td>
<td>5 (4)</td>
<td>1 (1)</td>
<td>4</td>
<td>99</td>
<td>83</td>
<td>55</td>
</tr>
</tbody>
</table>
Chapter Four: DISCUSSION

1. Socio-demographic and clinical characteristics associated with pneumonia in children with diarrhoea in an urban hospital in Dhaka, Bangladesh

Discussion: Care-givers were observed to have a poorer understanding of pneumonia in contrast to understanding of diarrhoea in our patient population. The prevalence as well as mortality from diarrhoea has been substantially reduced by more than 90% in the population of Bangladesh over the last few decades [80]. There has been mass media coverage to educate the people about diarrhoea. Moreover, the introduction of oral rehydration solution (ORS) for the management of ongoing loss of diarrhoea has become widely acceptable. The recent introduction of zinc for the routine management of diarrhoea and associated mass media (both audio and visual) coverage has also contributed significantly to better knowledge of diarrhoea among this population [73]. On the other hand, mass media coverage of pneumonia is much less and most education on pneumonia is on television, which is out of reach of poor population in Bangladesh. Visual media might be more effective for the proper education of the clinical signs of pneumonia as fast breathing and lower chest wall indrawing, the key signs of pneumonia, need visual display to capture the careful attention of care-givers. As most of the admitted children came from the poor socio-economic status, care-givers had minimum access to such information through the media.

Sleeping in a bare bed (Figure 1 and figure 2) and children having parents or care-givers with poor knowledge of pneumonia were observed to be significantly associated with pneumonia. This relationship persisted when potential confounders
had been controlled for (Table 4). Lower middle class and poor people, the majority of the study population, typically sleep on a wood or bamboo bed. Pieces of wood or bamboo are usually put together with a regular gap of two to three centimetres from each other and fit 40 to 60 centimetres above the soil (Figure 1). Often the gaps between the pieces of wood or bamboo become plugged by dirt (Figure 2) and most of the care-givers are not aware of cleaning the dirt. This dirt might become the reservoir of sources of infection. While sleeping in a bare bed children might inhale dirt, which might contain bacteria that lead to infection in the respiratory tract. If bed cover was used over the wooden slates, the dirt in between wooden slates might be well covered which would protect the children from the potential source of infection. On the other hand, education of care-givers about the cleaning of the dirt might help their children from acquiring infection. However this is speculative, and further research would be necessary to evaluate the validity of the finding, and whether plugged dirt is the source of infection. Poor knowledge of pneumonia by the parents or care-givers, another factor significantly associated with pneumonia, might not alert the care-givers to seek care for their children when there are early signs of pneumonia.
Figure 1: Picture of a bare bed showing the regular gaps in between the pieces of wood.

Figure 2: Picture of a bare bed pointing out the plugged dirt in between gaps in the wood.
Children with pneumonia often presented with hypoxaemia and remained hypoxaemic for longer compared to those without pneumonia. Children with pneumonia present with inflammation in the lung parenchyma and often experience increased oxygen demand and inadequate oxygen supply due to the reduction of diffusion of oxygen at the level of the blood gas barrier at alveolar region of respiratory zone of lung leading to hypoxaemia. Unlike other studies, children without pneumonia in the comparison group of our study population were also severely ill. Thus, our finding underscores the global importance of oxygen supplementation among all sick children with pneumonia where pulse oxymetry is not available.

Convulsion, hypoglycaemia, and hyponatraemia were observed less frequently among the children with pneumonia, however convulsions among children with pneumonia were associated with hypoxaemia. The observed higher incidence of convulsion among the children without pneumonia might be explained by the presence of a higher proportion (35% vs. 21%) of hyponatraemia (serum sodium < 130 mmol / L) among the children with diagnoses other than pneumonia. Moreover, higher observation of hypoglycaemia and hyponatraemia among the children without pneumonia might also be responsible for the higher incidence of convulsion among them [81]. Other likely relates such as hypernatraemia, meningitis, and fever (≥ 38° Celsius) were equally distributed among the children with or without pneumonia. Isolation of bacteria from diarrhoeal stool was higher among the children without pneumonia (37% vs. 17%). Bacterial diarrhoea usually caused anorexia and prolonged anorexia might have an impact on the observed higher incidence of hypoglycaemia among the children without pneumonia which has been reported.
earlier [82, 83]. Children without pneumonia more often had dehydration (56% vs. 46%) compared to children with pneumonia. Dehydrating diarrhoea is more often associated with cholera and loss of sodium is high in cholera stool which potentially explains our observation.

Pneumonia was more common in younger infants. Younger infants are very vulnerable to infection, especially to respiratory infection probably due to depressed cell mediated immunity. This speculation about depressed immunity and age distribution has been reported earlier [84, 85]. The relatively lower mean weight observed among the children with pneumonia has also been reported earlier [28, 30] but in the current study the birth weight was not recorded, largely because parents/care-givers did not know the birth weight of their children. The distribution of severe underweight (defined in general methods and also in the Table 3) was similar among the groups.

Children with pneumonia often presented with higher rectal temperature and fever. The medical literature reports a high core temperature to be a common finding in bacterial pneumonia [23, 35, 86]. The observation of leucocytosis in pneumonic children is also common [87, 88].

A higher but statistically insignificant case-fatality among the children with pneumonia was observed. A number of previous studies and reviews have shown the significant higher case-fatality in pneumonia [16, 26, 80, 89, 90]. As the site for the current study was SCW and all admitted children were seriously ill, it is understandable that the comparison group had also serious illness other than
pneumonia. The comparison group of our study children had illness such as sepsis, severe sepsis (defined in Table 2), hypoxaemia, severe undernutrition, meningitis, hyponatraemia, hypernatraemia, and hypokalaemia (Table 14). These severe illnesses in the comparison group might have an impact on the result.

<table>
<thead>
<tr>
<th>Illnesses</th>
<th>Children without pneumonia (60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>39 (65)</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>8 (13)</td>
</tr>
<tr>
<td>Severe undernutrition</td>
<td>26 (43)</td>
</tr>
<tr>
<td>Meningitis (isolation of bacteria from CSF)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Hypoxaemia</td>
<td>11 (18)</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>13 (22)</td>
</tr>
<tr>
<td>Hyponatraemia (&lt; 130 mmol/L)</td>
<td>20 (35)</td>
</tr>
<tr>
<td>Hypernatraemia (&gt; 150 mmol/L)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Hypokalaemia (&lt; 3.5 mmol/L)</td>
<td>21 (37)</td>
</tr>
</tbody>
</table>

N = number, % = percentage, CSF = cerebrospinal fluid

Although it was not significant, we also observed that a higher proportion of children with pneumonia compared to those without pneumonia did not receive measles vaccination. However, obtaining their history over the last six months prior to admission we also did not observe any significant difference related to illness with measles among the children with or without pneumonia. This explains our initial observation of measles vaccinations among the groups.

Though it was not significant, a lower proportion of non-breast-fed children among the pneumonic children compared to non-pneumonic children was observed in our study. Previous studies have reported this factor to be significantly associated with
pneumonia; but a reduced sample size in our study population might also have played a role in failing to find any significant difference. However, unlike the current study the control groups in those studies did not include seriously ill patients without pneumonia [2, 35]. But a recent study from the Dhaka Hospital of ICDDR,B supports the findings of this study [37].

There was no significant benefit for children who received vitamin-A capsule within the last 6 months or for those who had a history of measles within the last 6 months among the groups. National polio vaccination coverage is very popular in Bangladesh. It usually takes place four times a year and also covers slum areas. During the polio vaccination all children usually receive Vitamin A capsule. The good nationwide coverage of Vitamin A capsule administration might have an impact on our study finding.

A slight male predominance was observed in our study population. This might reflect the fact that parents are more likely to bring boys to hospital in this society, as also reflected in the sex distribution of the general patient population of our hospital (males vs. females 5:4). However, male predominance in pneumonia has been reported earlier [29, 35].

There was no significant statistical difference between children who had severe wasting, severe stunting, and severe underweight among the children with and without pneumonia. We further failed to observe a significant difference for illiterate mother, illiterate father, employed mother, poor socio-economic status, smoking in the family, and not having separate living room, not having window or exhaust fan in
the kitchen room among the groups. Most of these clinical and socio-demographic parameters have been reported to be significantly associated with pneumonia in a number of previous studies [27, 31, 33, 36]; however, as mentioned earlier, the control groups in those studies did not include seriously ill patients without pneumonia. Thus, the even distribution of these factors might reflect the severity of illness of both the groups of children in the current study.

The major limitation of the current study is the probable lack of study power due to the small numbers with pneumonia which might have limited the ability to identify more subtle differences between the groups and to identify further relevant associations with pneumonia. A large number of comparisons between the groups are also a significant limitation of this study.

In conclusion, knowledge about pneumonia among caregivers was very poor. Policy makers should consider educating caregivers through the mass media in a way similar to the successful mass media programme of oral rehydration therapy in diarrhoea management. The finding that patients with pneumonia were significantly more likely to sleep in a bare bed may indicate a potential risk factor for pneumonia.

Further studies should investigate whether this is a potential reservoir for infectious agents.
2. Factors associated with death among the children under five with pneumonia admitted in the SCW in an urban diarrhoeal treatment centre, Dhaka, Bangladesh

Discussion: Severe underweight, hypoxaemia, severe sepsis, and lobar consolidation were observed as the individual associated factors for deaths in pneumonia after adjusting with co-variates. The finding that severe undernutrition is a risk factor for death is supported by a number of earlier studies [46, 91, 92]. Severely underweight children have depressed cell mediated and humoral immune responses and often become susceptible to infection with fatal outcome [72, 93].

We know that pneumonic children often experience hypoxaemia [52, 54, 58, 63]. In our study the pneumonic children with fatal outcome often had more severe hypoxaemia on admission, which more often persisted even 36 hours after admission. This was in contrast to survivors. Severe hypoxaemia has previously been reported as a risk of death in pneumonia [94, 95].

The compromised and ineffective peripheral circulation in severe sepsis might have contributed to further deterioration of the pneumonic children. We know that children with severe sepsis always have higher case-fatality [96] and the observation of severe sepsis as a risk factor for death in pneumonia has previously been described [97].

Lobar consolidation is a high proxy of bacterial pneumonia [98]. Additionally, bacterial pneumonia is highly associated with death [40]. This probably explains our
observation of higher deaths in lobar consolidation, though the isolation of bacteria was low in our study. This has also been found in other studies [45]. Lobar consolidation more often presented with hypoxaemia in our study population, in contrast to other types of pneumonia in radiology. This may also explain our observation that pneumonic children with lobar consolidation were more likely to die. Lobar consolidation as a risk of death was also reported in a number of earlier studies [45, 48, 97].

Metabolic acidosis was more often observed among the pneumonic children who survived. Pneumonia children who survived more often presented with severe cholera (defined as the presence of dehydration on admission and whose stool culture revealed *Vibrio cholerae*) (8% vs. 0%) in contrast to pneumonic children with fatal outcome. Metabolic acidosis is a common picture of severe cholera [99] which explains our observation.

In univariate analysis, oedematous malnutrition, clinical sepsis, poor peripheral perfusion, and hypernatraemia were observed more often among the deaths. Children with oedematous malnutrition are highly susceptible to infection [72]. Higher case-fatality among these patients has previously been reported [22]. No significant association between kwashiorkor and mortality in the multivariate model was observed. Clinical sepsis and poor peripheral perfusion are the progression and components of severe sepsis, so their higher observation among the deaths in pneumonia is understandable. Higher association of death in children with pneumonia and hypernatraemia has also been reported previously [100].
The pneumonia patients who died were more often observed to present with renal failure. A higher proportion of our pneumonic children with fatal outcome had ineffective perfusion, which might explain the higher observation of renal failure among them.

We observed that age, district of residence, socio-economic status, breast-feeding, vaccination status, and dehydrating diarrhoea were not significantly associated with death. Thus, these factors might reflect common features in severely ill young children. These findings are consistent with an earlier study [47]. We also observed a similar distribution of hypoglycaemia, WBC count, hyponatraemia, and hypokalaemia among the deaths and survivors, probably for the same reasons.

Poor understanding of pneumonia by care-givers and sleeping in a bare bed were not significantly associated with pneumonia mortality. We know that these two factors were revealed as the independent socio-demographic associated factors for the presence of pneumonia among SCW inpatients (chapter 3) but did not have any influence to the deaths among the pneumonia children.

Here we have analysed only hospital deaths, but most pneumonia deaths take place in the community. Many of these children never could reach the hospital facility and much of this is likely to be due to poor recognition of signs. Thus it is likely that poor understanding of pneumonia is strongly associated with death. However, a community-based study is needed to explore this.
In conclusion, the associated factors for death in SCW patients under five with pneumonia were severe malnutrition, hypoxia, severe sepsis, and lobar consolidation. Identification of these factors is essential to initiate prompt and appropriate management to reduce deaths from pneumonia in children.

3. Clinical predictors and outcome of hypoxaemia among the sick children under-five with concomitant pneumonia admitted in the SCW in an urban diarrhoeal treatment centre, Dhaka, Bangladesh

Discussion: We observed that hypoxaemia is significantly related to deaths. We have already mentioned that more than three-quarters of our study population had pneumonia and that they often remained hypoxaemic for a longer period (chapter 3, Table 5) in contrast to non-pneumonia children. Moreover, even after providing continued oxygen supplementation for 36 hours, children having pneumonia with fatal outcome remained hypoxaemic (chapter 4, Table 8), which reflects the extent and severity of lung infection. These probably explain the reason for the higher deaths among the children under-five age with hypoxaemia. Association of deaths with hypoxaemia has been reported in a number of earlier studies [57, 62, 101].

We observed lower chest wall indrawing, nasal flaring and severe sepsis as the individual predictors of hypoxaemia among the SCW children under five. The sensitivity of lower chest wall indrawing is quite impressive with reasonable specificity unlike previous studies. However, unlike other studies all of our study children had diarrhoea and more than three-quarters of them had pneumonia. That means all diarrhoeal children who come to heath facilities with this single sign irrespective of having severe pneumonia or not should always receive oxygen
supplementation. A number of previous studies among the non-diarrhoeal children also reported a chest wall indrawing as the predictor of hypoxaemia [53, 68, 102].

In severe sepsis, the presence of hypoxaemia due to inadequate tissue perfusion is understandable. The sensitivity of severe sepsis is quite low though the specificity is quite impressive as it is in nasal flaring. This means that children who come with any of the parameters of severe sepsis and/or nasal flaring must get oxygen supplementation, though we might fail to supplement oxygen to a number of hypoxaemic children due to their poor sensitivity. We did not find any published data where severe sepsis had been shown as a predictor of hypoxaemia. This is the new finding of our study and the different nature of our study population might be responsible for this notable finding. But nasal flaring as the predictor of hypoxaemia among the non-diarrhoeal children has been reported earlier [52, 68].

We also observed that hypoxaemic children more often presented with history of convulsion within 24 hours prior to admission. Neurological examination had been performed for all of those children. We could not perform EEG but performed bedside blood glucose, serum electrolytes and lumber puncture, as and when required. CSF examination did not reveal any significant different abnormalities among the groups. The distribution of hypoglycaemia (9% vs. 12%, \( p = 0.67 \)), hyponatraemia (serum sodium < 130 mmol/L) (22% vs. 42%, \( p = 0.06 \)) and hypernatraemia (serum sodium > 150 mmol/L) (22% vs. 11%, \( p = 0.15 \)) was not significantly different among the hypoxaemic and non-hypoxaemic children. The temperature (°C) was also evenly distributed among the groups (37.6 ±1.4 vs. 37.8 ±1.2). Thus we did not find any reason for the higher proportion of hypoxaemic patients experiencing
convulsions, apart from the ready explanation of hypoxaemia itself which might be responsible for the convulsion of those children. Consequently, this represents another novel finding for our particular study population.

We observed that more than half of the pneumonic children (both diagnosed by WHO and radiologically) were hypoxaemic. This was also observed among almost half of the total study population (pneumonia and non-pneumonia); hypoxaemia was higher among severe and very severe pneumonia cases and highest in those with lobar consolidation.

The prevalence of hypoxaemia may varies from region to region [53-55, 62]. But high prevalence of hypoxaemia among the pneumonic and non-pneumonic children in our study population might be due to the fact that most of our study children were seriously ill and had a severe form of pneumonia, severe malnutrition and sepsis. Higher prevalence of hypoxaemia in this type of sick children has also been reported earlier [103]. The air entry into the consolidated area of lung is usually poor causing the reduced oxygen supply to the lung and simultaneously requirement of oxygen gradually increases and leading to hypoxaemia. The higher prevalence of hypoxaemia among children with lobar consolidation has also been reported previously [97].

We also observed slight male predominance among the hypoxaemic children and those were often young infants. This finding might be contributed by the presence of a higher proportion of male children in our overall study population. The higher prevalence of hypoxaemia among children has been reported earlier [62].
We observed head nodding, grunting respiration, abnormal mental status, dehydrating diarrhoea, cyanosis, and inability to drink were not revealed as predictors of hypoxaemia. The distribution of *Vibrio cholerae* among the hypoxaemic children was significantly lower (2% vs. 8%, \(p = 0.017\)) and cholera is responsible for the severe form of diarrhoea which often presents with dehydration. Thus, dehydrating diarrhoea (some/severe) was, understandably, not associated with hypoxaemia in our study population. The other clinical parameters mentioned above have been revealed as predictors of hypoxaemia in a number of previous studies [52, 54, 60, 68, 104]. In our study the percentage of distribution of these clinical parameters was much higher among the hypoxaemic children; but due to the lack of a sufficient number of observations we might have failed to reveal these parameters as predictors of hypoxaemia in our study.

In conclusion, hypoxaemia is associated with high case fatality. Children under five with diarrhoea presenting with lower chest wall indrawing, nasal flaring, and severe sepsis are more likely to be hypoxaemic although their individual cohesion of sensitivity and specificity are not so impressive. Among the all clinical signs evaluated here, chest wall indrawing is the best predictor of hypoxaemia. Among diarrhoeal children who required hospital admission, a history of convulsion is also an important predictor of hypoxaemia in univariate analysis with high sensitivity. In order to initiate early \(O_2\) supplementation in combination with other appropriate management to reduce morbidity and deaths, the identification of these simple clinical predictors of hypoxaemia is critical. It has great value where pulse oximetry is not available.
Chapter Five: Summary and key points:

- The awareness of pneumonia by the parents/care-givers of the children under-five admitted to the SCW of the Dhaka hospital of ICDDR,B was much poorer than that of diarrhoea.

- Among our sample of SCW patients those with pneumonia were more likely to sleep in a bare bed and to have a caregiver with poor knowledge of pneumonia than those patients without pneumonia.

- Children with pneumonia more often had hypoxaemia which often remained in longer duration compared to children without pneumonia.

- Severe under nutrition is a strong risk factors for death in pneumonia.

- Hypoxaemia is also a strong risk factor for death in pneumonia.

- Other risk factors for death in children with pneumonia were severe sepsis and lobar consolidation.

- Hypoxaemia is most evidenced among the patients with lobar consolidation (85%).

- Hypoxaemia is associated with high case fatality among the children with or without pneumonia.
Chapter 5 – **Summary and key points:**

- Chest wall indrawing is the best predictor of hypoxaemia in our study

- History of convulsion before admission has also high sensitivity but low specificity as predictor of hypoxaemia

- Nasal flaring and severe sepsis are the other two predictors of hypoxaemia
Chapter Six: Recommendations and future directions

- Future community level research about risks, knowledge and modifiability of poor bed hygiene and pneumonia would further evaluate our observation. This would guide policy makers to take effective measures to improve knowledge and awareness of bed hygiene and to improve the level of knowledge of pneumonia by the caregivers. This in turn may reduce the incidence, morbidity, and mortality of pneumonia as effectively as it has been done in diarrhoea by promoting ORS and zinc.

- Improvement of public awareness about the clinical features of pneumonia through a variety of mass media campaign involving different levels of health professionals and the community is a sine quanon.

- The prevention and management of malnutrition is central to the global effort to reduce deaths from pneumonia. Therefore, further research is necessary to improve the prevention, detection, management and outcome of pneumonia in severe malnutrition in resource poor settings especially in Bangladesh.

- Policy makers should make pulse oximetry available to local health complexes and district hospitals.

- Health workers should receive training about the clinical predictors of hypoxaemia where pulse oximetry is not available or out of order, especially in a resource poor setting like Bangladesh. They would learn to decide who
should get the oxygen first from the limited supply and how to deliver proper oxygen supplementation to those children.

- Policy makers should also think about the supplementation of O₂ to children who present with history of convulsion and add this policy to the national guidelines.

- Furthermore, research is needed to understand how to improve the quality of pneumonia case management, including the effective provision of oxygen, especially in limited facilities.
Appendices

Appendix - I - Data sheet

Childhood pneumonia and hypoxaemia in an urban diarrhoeal hospital, Dhaka, Bangladesh

Socio-demographic History:

1. Child’s name: ........................................................................................................

2. Age (months) 

3. Sex 
   1 = male, 2 = female

4. Date of admission

5. Study ID number

6. Hospital Registration No:

7. Place of normal residence
   1= within Dhaka city, 2=within Dhaka district, 3= outside Dhaka district

8. Distance of residence from Dhaka Hospital (Km)

9. Education status of mother
   1 = none (illiterate), 2 = literate (can read and write)

10. Education status of father
    1 = none (illiterate), 2 = literate (can read and write)
11. Mother’s occupation
1 = Unemployed (house wife), 2 = Day labourer, 3 = Hawker, 4 = Garments worker, 5 = permanent private job, 6 = government job, 7 = others

12. History of smoking by family member who smokes inside bed room
1 = None smokes, 2 = Father smokes, 3 = Mother smokes, 4 = Both parents smoke
5 = others smokers (e.g.: grand father, uncle)

13. What is the amount of income of the mothers per months

14. What is the amount of income of the others per months

15. What is the total family income per months

16. Socioeconomic status (family):
1 = rich (>10000 taka / month); 2 = middle class (5000-10000 taka / month);
3 = poor (income <5000taka / month)

17. Intake of capsule Vitamin-A within last 6 months
1 = yes, 2 = no

18. History of measles in the past
1 = never, 2 = within last 3 months, 3 = within 3-6 months

19. Do you have a separate living room
1 = yes, 2 = no

20. Is there any window / exhaust fan in the cooking room?
1 = yes, 2 = no
21. What kind of bed is used during sleeping?
1 = on madur (local bed cover) over earth floor, 2 = on madur over bed, 3 = on foam over bed, 4 = sleeping on bare bed, 5 = others

22. Understanding of feature of pneumonia by the care givers
[Clinical feature of pneumonia: (a) cough and / or respiratory difficulty, (b) faster respiration than normal, (c) lower chest wall indrawing, (d) unable to drink, (e) cyanosis]
1 = Good (must talk about more than one criteria including “a”), 2 = Average (could only talk about “a”), 3 = Poor (could say nothing about the clinical features of pneumonia)

23. knowledge of diarrhoea by the care givers
(Definition of diarrhoea: passage of abnormally loose or watery stool three or more times per day)
1 = Good (could give definition properly), 2 = Average (could talk about very frequent passage of loose/watery stool with many frequency but could not mention the exact number), 3 = Poor (could talk about loose/watery stool one time per day but not more or could not say any thing about loose/watery stool)
History of Present Illness (at admission)

24. Diarrhoea:  
1 = no, 2 = watery, 3 = dysentery [blood in stool], 4 = persistent

25. Duration of diarrhoea prior to admission (hours)

26. Dehydration status  
1 = no sign, 2 = some, 3 = severe

27. Number of stools / day [average]

28. Vomiting:  
1 = yes, 2 = no

29. Duration of vomiting prior to admission (hours) [ If no = 00]

30. Number of vomits/day

31. Fever  
1 = yes, 2 = no

32. Duration of fever in hours

33. Cough  
1 = yes, 2 = no

34. Duration of cough in hours

35. Unable to drink  
1 = yes, 2 = no
36. Duration of unable to drink in hours

37. History of convulsion
   1 = none, 2 = during present illness

38. Feeding history:
   1 = breast fed, 3 = non breast fed

39. What vaccine has the child received?
   BCG: 1 = yes, 2 = no
   Number of doses

   Polio: 1 = yes, 2 = no
   Number of doses

   Hepatitis: 1 = yes, 2 = no
   Number of doses

   DPT: 1 = yes, 2 = no
   Number of doses

   Measles: 1= yes, 2 = no
   Number of doses

   What was the last vaccine child received?
   1 = BCG, 2 = Polio, 3 = Hepatitis B, 4 = DPT, 5 = Measles

40. Other symptoms (specify with duration):

   ________________________________________________________________

   _____________________________________________________________
## Initial Evaluation (at admission)

41. Radial pulse (rate/min)  
   [If imperceptible, coed “000”]

42. Respiratory rate (per minute)

43. Radial pulse volume
   1 = good; 2 = low volume; 3 = uncountable / absent

44. Systolic blood pressure

45. Diastolic blood pressure

46. Rectal temperature (°C)

47. SPO₂ without oxygen on admission

48. SPO₂ with oxygen 12 hour after admission

49. SPO₂ without oxygen (keeping the patient at least 5 minutes without O₂)
   12 hour after admission

50. SPO₂ with oxygen 24 hour after admission

51. SPO₂ without oxygen (keeping the patient at least 5 minutes without O₂)
   24 hour after admission

52. SPO₂ with oxygen 36 hour after admission

53. SPO₂ without oxygen (keeping the patient at least 5 minutes without O₂)
   36 hour after admission
54. SPO$_2$ with oxygen 48 hour after admission

55. SPO$_2$ without oxygen (keeping the patient at least 5 minutes without O2) 48 hour after admission

56. Total duration the child remained hypoxic (SPO2 < 90%)

57. Lower chest wall in drawing
1 = yes, 2 = no

58. Nasal flaring
1 = yes, 2 = no

59. Head nodding
1 = yes, 2 = no

60. Grunting respiration
1 = yes, 2 = no

61. Pedal oedema
1 = yes; 2 = no

62. Cyanosis (central or peripheral or both?)
1 = yes; 2 = no

63. Clubbing
1 = yes; 2 = no
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>64.</td>
<td>Admission weight (Kg)</td>
<td></td>
</tr>
<tr>
<td>65.</td>
<td>Admission length/height (cm)</td>
<td></td>
</tr>
<tr>
<td>66.</td>
<td>Weight / Age (WA) (%)</td>
<td></td>
</tr>
<tr>
<td>67.</td>
<td>WA (z score)</td>
<td></td>
</tr>
<tr>
<td>68.</td>
<td>Weight / Length (WL) (%)</td>
<td></td>
</tr>
<tr>
<td>69.</td>
<td>WL (z score)</td>
<td></td>
</tr>
<tr>
<td>70.</td>
<td>Length / Age (LA) (%)</td>
<td></td>
</tr>
<tr>
<td>71.</td>
<td>LA (z score)</td>
<td></td>
</tr>
<tr>
<td>72.</td>
<td>Mental status</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = normal; 2 = irritable; 3 = lethargic; 4 = convulsing; 5 = comatose</td>
<td></td>
</tr>
<tr>
<td>73.</td>
<td>Problems:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.</td>
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<td>3.</td>
<td></td>
</tr>
</tbody>
</table>
Laboratory Investigation On Admission:

74. Hypoglycaemia on or after admission (< 3 mmol/l)  
1 = yes; 2 = no

75. Total WBC / cu.mm (Not done = 99)

76. Poly% (Not done = 99)

77. Lymphocytes (%) (Not done = 99)

78. Immature poly (%) (Not done = 99)

79. Sodium, mmol/L (Not done = 99)

80. Potassium; mmol/L (Not done = 99)

81. Chloride; mmol/L (Not done = 99)

82. TCO2; mmol/L (Not done = 99)

83. Creatinine; micromol/L (Not done = 99)

84. Stool culture

1 = not done; 2 = no growth; 3 = V. cholerae (any type), 4 = Shigella dysentery type1; 5 = S. flex, 6 = other Shigella, 7 = Salmonella typhi, 8 = other Salmonalae, 9 = polymicrobial, 10 = others

85. CXR findings

1 = suggestive of pneumonia, 2 = not suggestive of pneumonia (Not done = 99)
86. Type of pneumonia
1= Bronchopneumonia, 2= lobar consolidation

Hospital course

87. Severe sepsis after admission
1 = yes, 2 = no

88. Was oxygen available to give on the day of admission?
1 = yes; 2 = no

89. Outcome
1 = usual discharge, 2 = Discharge against medical advice, 3 = absconded, 4 = referred to other hospital, 5 = death
Appendix – II - Protocol

Childhood pneumonia and hypoxaemia in an urban diarrhoeal hospital, Dhaka, Bangladesh

Mohammod Jobayer Chisti, Trevor Duke, Colin F Robertson, Mohammed Abdus Salam, Sophie La Vincente

Background:
Among the eleven million deaths globally in children under five from 2000 to 2003, 3 million deaths occurred from pneumonia. Most of these deaths occur in developing countries. Pneumonia has also been a major killer disease in Bangladesh for the last few decades. There has been no significant reduction of case-fatality from pneumonia over this time, even though a number of studies have identified some consistent factors as the risks of pneumonia. Interestingly, no effective pneumonia control programme has been launched in Bangladesh despite previous experience of successful reduction of morbidity and mortality from diarrhoea through the popular implementation of oral rehydration therapy, strongly supported by mass media education. This may indicate a lack of awareness among caregivers about the assessment of simple clinical signs of pneumonia. Poor understanding of the caregivers of the signs of serious illness and pneumonia may impair health seeking behaviour. However, as compared to caregiver knowledge of diarrhoea in Bangladesh, there is no published data on the level of caregiver knowledge about pneumonia.
Morbidity and mortality are particularly high among the hypoxaemic patients with pneumonia. There is strong evidence that supplementation of oxygen reduces mortality from very severe pneumonia. Detection of hypoxaemia is difficult and best done using pulse oximetry, but the current national guideline for pneumonia in Bangladesh does not reflect these issues properly as simple pulse oximetry is not available in most of the health clinics. Ideally a child with pneumonia should be recognized by caregivers at home if he/she knows the initial symptoms. They should also have sufficient knowledge of the signs of serious illness, so they can bring their child to health care providers/physicians very early. On contact with the primary health clinic, health care providers should recognize the clinical signs of pneumonia and the clinical features of hypoxaemia to facilitate the opportunity for appropriate and timely intervention.

Like other public hospitals in developing countries, Dhaka Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) admits patients with diarrhoea and other health problems. There is a high disease burden due to pneumonia and diarrhoea in children under five. In these circumstances, we particularly aspire to achieve a better understanding of the characteristics of children presenting with pneumonia and/or hypoxaemia which would help us to undertake the appropriate measures for each patient, and assist in public health campaigns against pneumonia. This ultimately can reduce hospitalization, duration of hospital stay of children who are hospitalized, cost of treatment and case fatality.
Objectives: To explore:

1) the clinical characteristics, understanding of pneumonia by the care-givers, and socio-demographic predictors of WHO defined pneumonia;

2) factors associated with deaths in pneumonia; and

3) overall predictors of hypoxaemia in severely ill children under five hospitalized for management of diarrhoea

Methods:

1) Design of the study: This will be a prospective cohort study by a systematic collection of data (a clinical audit).

2) Study site: Special Care Unit (SCU) of the Dhaka Hospital of ICDDR,B

3) Population: Children under five who will be admitted to the study site between September 1 and December 31, 2007. Children with tuberculosis and/or asthma will be excluded from the study

4) Comparisons group: There will be three comparisons, as follows
   - Comparison between children under five fulfilling the clinical criteria for WHO-defined pneumonia and those without pneumonia
   - Comparison between deaths from and survivors of pneumonia in children under five.
   - Comparison between hypoxaemic children under five and those who were not hypoxaemic.

5) Outcomes: The main outcome variable will be death in pneumonia and the explicable variables are knowledge of the care givers about pneumonia,
socio-economic and house hold condition, living condition, malnutrition, hypoxaemia etc.

Data analysis: A pretested case report form (CRF) will be used for data acquisition and data entered onto personal computer and edited before analysis using SPSS for Windows (version 15.0; SPSS Inc, Chicago) and Epi Info (version 6.0, USD, Stone Mountain, GA). Differences in proportions will be compared by the Chi-square test or Fisher exact test as appropriate, differences of means and medians will be compared by Student’s t-test and Mann-Whitney test, as appropriate. A probability of less than 0.05 will be considered statistically significant. Strength of association was determined by calculating odds ratio (OR) and 95% confidence intervals (CI).

Dissemination: The results of this study will be presented in a scientific conference and published in peer reviewed journals. Finding will help guide clinical care of children with pneumonia and help guide the research agenda for improving outcomes for children with pneumonia. The results will be helpful in conducting a community based effectiveness study on health seeking and a hospital based study on the management of severe hypoxaemic pneumonia, the matters which would likely to be incorporated in the national and probably in the WHO / IMCI guidelines for diagnosis and prompt treatment of pneumonia in children under five.
Bibliography


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