MAGNITUDE OF CO-MORBIDITIES AMONG CHILDREN AGED 6 MONTHS TO 12 YEARS REHOSPITALISED WITH PNEUMONIA AT THE KENYATTA NATIONAL HOSPITAL

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ABBREVIATIONS

BMI-   Body Mass Index

CHD-   Congenital heart disease

ECHO-   Echocardiogram

GERD-   Gastroesophageal reflux disease

GINA-   Global initiative for Asthma

HIV-   Human immunodeficiency virus

IMCI-   Integrated Management of Childhood Illnesses

LRTI-   Lower respiratory tract infection

KNH-   Kenyatta National Hospital

MUAC-   Mid Upper Arm Circumference

NASPHAGN-North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

SAM-   Severe acute Malnutrition

SDS-   Standard Deviation Score

PEU-   Pediatric emergency unit

PPE-   Personal protective equipment

UON-   University of Nairobi

UNICEF-   United Nations International Children's Emergency Fund

WHO-   World Health Organization

OPERATIONAL DEFINITIONS

Re-admission-Current pneumonia admission occurring within 1 year of the last documented pneumonia related admission.

Pneumonia- For children aged less than 59 months diagnosis was made based on WHO 2016 pneumonia guidelines which include

- History of either cough or difficulty in breathing and
- Either of the following signs tachycardia or lower chest wall in drawing.

  For children aged more than 5years will be based on 2012 British Thoracic guidelines of persistent fever of >38.5℃, With either tachypnoea or chest retractions and

   Positive CXR findings suggestive of pneumonia

   Asthma-Diagnosis was based on 2020 GINA guidelines

- Symptoms: Presence of wheeze or cough/ difficulty in breathing (worsened early morning or late at night) and
- Signs- positive bronchodilator response.

  GERD-Diagnosis of GERD was based on

- For children less than 2years: Infant GERD questionnaire score of >5 will be considered a possible diagnosis of GERD (Appendix II)
- For children above 2 years: Positive barium swallow findings suggestive of GERD.

  Aspiration Pneumonia-Clinical diagnosis was made based on

- History of Cough and Recurrent Wheeze For >3weeks Or
- Cough/Choking/Apnoea/Cyanosis During Feeds And
- Either one of- Failure to Thrive (weight less than 5th percentile for age on more than one occasion),
- Obvious Neurologic/Developmental Disorders and
- Chest X-ray Findings Suggestive of Aspiration.

  Rickets- Defined as follows;

- History of Delayed Motor Milestones, And
- Any of The Following physical findings-Frontal Bossing, Craniotabes, Open Fontanels, Widened Wrists, Rachitic Rosary, Harrison Sulcus and
- Bone Biochemistry (elevated Alkaline phosphate+/-low calcium or low phosphate)
- +/- Findings Of Any Skeletal /Spine Deformities on Xray.

Congenital Heart Disease-Diagnosis was based on:

- An echocardiogram performed on all children done by a pediatric cardiologist using Phillips EPIQ 7 machine.

Severe Acute Malnutrition -Diagnosis was made based on 2016 WHO guidelines

- For children aged <5years mid upper arm circumference of <11.5 cm, weight for height <-3SD, or signs of severe wasting or edema
- For children aged >5 years-body mass index of <-3 based on the WHO growth chart for age and sex, or signs of severe wasting or edema.

 HIV- Diagnosis was based on 2016 MOH HIV guidelines

- For children <18months a positive DNA/RNA PCR
- For children >18months a positive HIV antibody test

ABSTRACT

Background: Globally pneumonia is the leading cause of death in children under 5 years and it's the leading cause of hospital readmissions. Readmissions are common in children with underlying chronic diseases such as asthma, congenital heart disease, primary immunodeficiency, rickets, HIV and malnutrition. However, there is very limited data in our setting on paediatric readmissions due to pneumonia and the underlying co-morbidities seen. Understanding the common co-morbidities seen in this population is important to inform interventions to reduce avoidable hospital readmissions which are associated with longer duration of stay ultimately leading to high hospital expenditure. The aim of this study is to characterise the common underlying co-morbidities and provide more information on the in-hospital outcomes seen in these patients.

Objectives: The primary objective is to determine the proportion of children aged 6months to 12 years readmitted with pneumonia at KNH who have selected underlying co-morbidities. The secondary objective is to determine the in-hospital clinical outcomes among children readmitted with pneumonia and to compare outcomes between children with and those without co-morbidities.

Methodology: This was a longitudinal study recruited participants aged 6 months to 12 years from KNH paediatrics wards with a previous history of admission due to pneumonia and a current diagnosis of pneumonia. A structured paper-based questionnaire was used to obtain data on relevant medical history, physical examination and nutritional assessment was conducted on all participants and relevant laboratory / radiological investigations done. Presence of underlying co-morbidities was determined based on history, physical examination findings and results of investigations.

Data Analysis: STATA 13 was used. Descriptive statistics was summarized as medians (IQR) or proportions as appropriate. The frequency of comorbidities was summarized as proportions. Outcomes were summarized as means (+SD), medians (IQR) or proportions as appropriate.

Results:97% of children readmitted with pneumonia had an underlying comorbidity and most common comorbidities seen included GERD (61%) aspiration pneumonia (46%), congenital heart disease (41%), rickets (40%), severe acute malnutrition (35%), and HIV (1.3%). The mortality rate among children rehospitalised due to pneumonia was 15% and they had a long duration of stay with a median of 29days.

Conclusion and recommendation: Majority of children rehospitalised due to pneumonia have an underlying comorbidity, and the most common comorbidities are GERD, aspiration pneumonia, congenital heart disease, rickets and severe acute malnutrition. There needs to be a high index of suspicion with early diagnosis and treatment of these underlying conditions. There is need to create a structured system where children with pneumonia readmissions can be identified early and treated to prevent morbidity and mortality.

1.0 CHAPTER ONE: INTRODUCTION

Pneumonia is defined as inflammation of the lung parenchyma and is an acute respiratory infection that affects the lung. According to World health organization ,It is the leading cause of mortality among children under 5 years worldwide, resulting in 808,694 deaths each year and about 2,200 every day .It is estimated that approximately 15% of child deaths in 2017 were caused by pneumonia and more than 90% of these deaths occurred in developing countries (1). Based on studies conducted in high income countries it is the leading cause of readmissions among children accounting for 22.6% (3). According to the Kenyatta national hospital health database there has been a steady increase of paediatric pneumonia readmissions from 2019 to 2020 despite there being adequate measures of diagnosis, management and prevention of pneumonia. Readmissions in children are associated with high financial impact and are also associated with longer duration of hospital stay. Consequently, readmissions increase the psychosocial burdens, financial distress and overall they disrupt the lives of affected children and their families(2).

Readmissions are also associated with longer duration of hospital stay which is estimated to be twice longer compared to first time admissions and they contribute to higher financial burden[2].In developed countries studies have shown that combined cost of initial admission and readmissions among children is approximately 1 billion dollars and readmissions due to pneumonia account for 16% of the total costs which is higher compared to other illnesses(3).In Africa studies on readmissions are limited, yet the problems associated with readmissions are more pronounced in our setting due to limited resources to combat the effects associated with readmissions(4) .

Readmissions are commonly seen in children mostly during infancy and those with underlying chronic co-morbidities. In our setting there are very few studies on paediatric readmissions and knowledge on their burden on the health care system is quite limited. What is known is that 30% of readmissions are preventable especially if the index admission and readmission are causally related(5).Hence it would be important to determine comorbidities commonly seen among this population in our setup. Common conditions seen in children with pneumonia recurrences include asthma, congenital heart diseases, rickets, gastroesophageal reflux, HIV and severe acute malnutrition. In this study readmissions will be defined as current pneumonia admission occurring within 1 year of the last documented pneumonia related admission this is guided by studies carried out on hospital readmissions which indicated that 9 to 48% of

readmissions are preventable and 50% occur within 90days while 80% of them occur within 1 year(6).

The aim of this study will be to identify this special group of patients who are readmitted with pneumonia and to identify the common co-morbidities seen specifically (asthma, gastroesophageal reflux disease, aspiration pneumonia, congenital heart disease, human immunodeficiency virus, severe acute malnutrition and rickets). This study will provide useful information to guide on strategies that can be used to prevent unavoidable readmissions in children especially in our set up. This study will also provide information on hospital stay and mortality among children readmitted with pneumonia in our setting.

2.0 CHAPTER TWO: LITERATURE REVIEW

2.1 Prevalence of pneumonia readmissions in children.

Pneumonia has been identified as a leading cause of hospitalisation and readmissions among children based on studies done in both developed and developing countries. A study done in America by Nakumara et al in 2017 analysing data from 26 states in patients aged less than 18years on prevalence of hospital readmissions found that the rate of readmission due to lower respiratory tract infection was 5.5% (7). The most common diagnosis on readmission was lower respiratory tract infections (bronchiolitis, pneumonia and influenza) which accounted for 48.2% followed by asthma at 10% fluid and electrolyte imbalance at 3.4% and respiratory failure 3.3%. Other factors commonly associated with readmissions included age below 1year, male gender (57% of boys were readmitted compared to 43% of girls) and participants with underlying chronic conditions had the highest risk of readmission perhaps reflecting the higher risk among this group of children for severe or complicated LRTIs. These patients should therefore be the focus for efforts to reduce readmissions. This study recommended optimizing care during initial admission and implementing a treatment algorithm for pneumonia readmissions at tertiary hospitals (7).

Another study conducted in America by Neuman et al in 2014 in 43 children hospitals found that the prevalence of readmission due to pneumonia was 3.3% (3). Factors associated with increased risk of readmissions were age < 1 year, presence of chronic co-morbidities, complicated pneumonia and management in hospitals with reduced pneumonia admissions. Readmissions usually occurred directly after hospital discharge, with more than one-third occurring within 1 week(3). The median cost of a readmission was more than twice that of an index hospitalization and readmissions due to pneumonia accounted for 16% of the total admission cost. Pneumonia was the third major cause of paediatric rehospitalizations after seizures and bronchiolitis and it accounted for 3.2% of all readmissions occurring within a month. The increase in readmission rates within hospitals due to pneumonia provides a valid case for focus on paediatric readmission reduction efforts(3).

A study was conducted in 2017 by Nick brown Et al in Pakistan on recurrence of pneumonia in children and predictors of reoccurrence within a duration of 1 year. They found a prevalence of 3.7% with a male predilection of 55% and they noted that readmissions higher in infants compared to older children. They highlighted that the risk of readmissions increased with increased poverty level(8) .

A study conducted in Tanzania at Kilimanjaro Christian medical centre among 209 children aged 1 to 9years by Peter et al outlined that 31% of patients were readmitted due to pneumonia and the most common underlying conditions were Asthma at 16%, severe acute malnutrition at 14%, HIV and severe acute malnutrition at 5%, neurologic disorders at 2%and congenital heart disease at 1%(9).

Although in our setting it is difficult to accurately identify the cases of recurrent pneumonia due to the lack of resources, Moustafa et al carried out a study among children with recurrent episodes of pneumonia in Upper Egypt Assiut University children's hospital. He found that 1 in every 12 children had recurrences with the commonest underlying disease being congenital heart disease at 25%, primary immunodeficiency at 20%, bronchial asthma at 16%, prematurity at 7%.Children below 3 years had a higher frequency of underlying heart disease, oromotor incoordination, GERD and malnutrition(10).

Mohammed et al conducted a similar study in Iran on recurrent pneumonia and he reported a prevalence of 34% and 89% of children identified to have recurrent pneumonia had an underlying comorbidity. The most common comorbidities include aspiration syndrome at 59%,congenital heart disease at 23%,asthma at 14%,primary immunodeficiency at 9% and pulmonary tuberculosis at 2% (11).

Table 1: Prevalence of readmissions due to pneumonia among children

Author/study title/year	Setting	Study design, study population and sample size	Findings/results
Neuman et al, Readmissions among children previously hospitalised with pneumonia 2014	43 paediatric hospitals in U.S. A	Cohort study Children ages 1-7years N = 82566	Readmission due to pneumonia-22.6%
Peter Forsberg et al Pneumonia among hospitalised children 2012	Kilimanjaro Christian medical college, department of Paediatrics, North Tanzania	Cross-sectional study Children ages 1-9yrs N=209	Readmission due to pneumonia-31%
Nakumara et al paediatric readmission after hospitalisation for lower respiratory infections ,2017	26 states in the U.S. A	Cross-sectional study Children 1-9yrs N=150590	Readmission due to pneumonia-5.5%
Nick brown et al Recurrence of WHO defined fast breathing pneumonia in infants,2017	Primary health centres in Pakistan	Case control study Children ages 2-59months N=4002	Prevalence of readmission due to pneumonia=3.7%
Moustafa et al Recurrent pneumonia in children, magnitude of the problem and risk factors 2019	Assiut University children's hospital, Egypt	Cross-sectional study Children aged 1-16 years N=1226	Prevalence of recurrent pneumonia-12%

Table 2: Common co-morbidities seen in children readmitted with pneumonia

Author/study title /year	Setting	Study design, study population and Sample size	Findings/results
Nakumara et al paediatric readmission after hospitalisation for lower respiratory tract infections,2017	26 states in U.S. A	Cross-sectional study Children 1-9years N=150590	LRTI-48% Asthma-10% Respiratory failure-3.3% URTI-2.7% Fluid and electrolyte imbalance 3.4%
Mohammed et al, underlying causes of recurrent pneumonia in children,2017	Massih Dereshvari hospital, Iran	Cross-sectional study Children 1-18years N=229	Aspiration syndrome-59% CHD-23% Asthma-14% Primary immunodeficiency-9% Pulmonary tuberculosis-2%
El Saeed et al recurrent pneumonia in children, magnitude of the problem and risk factors 2019	Assiut university children's hospital, Egypt	Cross-sectional study children aged 1-16 years N=1226	Congenital heart disease-25% Primary immunodeficiency-20% Bronchial asthma-16% Rickets-7%
Peter Forsberg et al pneumonia among hospitalised children 2012	Kilimanjaro Christian medical college north Tanzania	Cross-sectional study children aged 1-9years N=209	Asthma-16% SAM-14% HIV+SAM-5% Neurological disorders-2% CHD 1st time admission 1%

The above studies show that: readmissions due to pneumonia in paediatrics are common both in developing and developed countries and the common underlying conditions are congenital heart disease, aspiration syndrome, asthma, neurologic disorders, HIV and SAM.

2.2 Underlying Co-morbidities

2.2.1 Aspiration Syndrome

It is defined as all conditions in which foreign substances are inhaled into the lungs which involve oral or gastric contents associated with gastroesophageal reflux, swallowing dysfunction, neurological disease and structural abnormalities.

2.2.2 Gastroesophageal Reflux Disease

Gastroesophageal reflux disease is defined as retrograde movement of gastric contents across the lower oesophageal sphincter that occurs every day physiologically but may also be pathological leading to esophagitis related symptoms or extraoesophageal presentations such as respiratory or nutritional effects(12).According to the NASPGHAN guidelines for 2018 GERD is defined as passage of gastric contents into the oesophagus with or without regurgitation and vomiting leading to troublesome symptoms that affect daily functioning(13).It is one of the common underlying conditions seen among children with recurrent pneumonia especially in infancy. This was reported by Dr Rohit et al in 2019 who conducted a study on prevalence of gastroesophageal reflux disease in children with recurrent /persistent lower respiratory tract infections.120 children aged 6months to 2 years were evaluated for GERD using the infant gastroesophageal reflux questionnaire and those with a score of more than 5 were further evaluated with barium swallow, upper GI studies and oesophageal biopsy. They found that 25% of the children had confirmed GERD and 50% of children with confirmed GERD had an I-Gerd score of more than 5 and they had recurrent pneumonia (14). A similar study was carried out by Kandasamy et al in 2008 to determine the prevalence of GERD in infants using the infant GER questionnaire, they found a prevalence of 30% out of 123 children aged 6months to 2years and 21% had recurrent pneumonia. The author outlined that the I-Gerd score of >5 had a sensitivity of 84% and a specificity of 96% and it was recommended as a valid tool for diagnosis of GERD(15). Other studies on children with recurrent pneumonia include Mohammed et al who conducted a study in Iran among children aged 1 to 18 years reported a prevalence of 77%. Owayed et al carried out a similar study in 2000 and he reported GERD in 5% of children aged 1 to 18years in Canada. Li Lun Chen et al reported a prevalence of 8.9% among children aged 1 to 18years in Taiwan and it was mentioned as one of the major causes of recurrent pneumonia(11)(16)(17).

2.3 Pathological Abnormalities associated with Gerd.

Congenital anomalies	Chromosomal abnormalities	Acquired
Oesophageal anomalies-oesophageal atresia, achalasia, hiatal hernia	Cerebral palsy, convulsive disorder	Food allergy
laryngotracheomalacia	Down syndrome	Obesity
Abdominal wall defects-gastroschisis omphalocele	Neuromuscular disorders	Supine positioning after feeds
Malrotation	Muscular dystrophy	
Gastric outlet obstruction		
Pyloric stenosis		

2.4 Pathophysiology of recurrent pneumonia in GERD

According to Meyer et al the primary cause of gastroesophageal disease is dysfunction of the lower oesophageal sphincter and the antireflux barrier complex (angulation formed by oesophagus, diaphragmatic hiatus and cardia of stomach) which are dysfunctional when there is a hiatal hernia, oesophageal dysmotility or delayed gastric emptying. Aspiration of gastric contents into the lung usually occurs leading to exacerbation of asthma , recurrent pneumonia or vocal cord dysfunction[18].Recurrent pneumonia occurs mainly due to 2 mechanisms 1)reflex neural mechanisms occurring during reflux events that occurs at the lower oesophageal sphincter and 2) due to the direct effect from gastric contents refluxed above the upper oesophageal sphincter which lead to upper airway injury and if aspirated into tracheobronchial tree leads to pulmonary disease[19].This microscopic aspiration of gastric contents into the lungs leads to inflammation which involves the destruction of the local pulmonary innate host defence system hence leading to reduced clearance of microorganisms which favours recurrent bronchopulmonary infections. Also the pepsin and trypsin found in the aspirate causes damage to the lung mucosa and induces neurogenic inflammation via axon reflexes characterised by recruitment and activation of neutrophils and lymphocytes in the respiratory mucosa[20].In vitro studies also suggest that proton pump inhibitors used in treatment of GERD may suppress the neutrophil, CD8+ cells and natural killer cells which may increase susceptibility to pulmonary infection and pneumonia[21].

2.5 Clinical Presentation

Symptoms commonly seen in GERD can be divided into general symptoms which include irritability, arching, choking, gagging and feeding aversion mostly in infants, failure to thrive, refusal to feed and Sandifer syndrome (dystonic neck posturing),gastrointestinal symptoms such as recurrent regurgitation, vomiting, heartburn, chest pain, hematemesis, dysphagia and odynophagia, airway symptoms such as wheezing, stridor, cough, apnoea and hoarseness of voice and clinical signs including dental erosion, apnoeic spells, recurrent pneumonia, asthma and recurrent otitis media(13)

2.5.1 Diagnosis

Kleinman et al highlighted that the I-GERQ was designed and validated as an important tool used to obtain baseline clinical characteristics and can be used for diagnosis of GERD. It was validated for diagnosis of GERD in children aged 1 to14 months by using abnormal pH probe studies and/or abnormal oesophageal biopsies as gold standards(22). The I-Gerd questionnaire for infants was later modified by Orenstein et al in 2006 and a score of >7 has a sensitivity of >74% and specificity of 94% for diagnosing GERD. There are also questionnaires for older children and adolescents which based on a study done by Chiu et al in 2014 a score of >7 was noted to have a sensitivity of 65.5% and a sensitivity of 80%(23). Other tests that can be done include endoscopy and biopsy, oesophageal ph. monitoring, nuclear scintigraphy and barium swallow. Of note there is no gold standard test for diagnosis of GERD.

2.5.2 Aspiration Pneumonia

It is defined as pulmonary sequelae resulting from the abnormal entry of endogenous secretions or exogenous substances into the lower airways. It usually occurs due to breakdown of the usual defences that normally protect the tracheobronchial tree as well as pulmonary complications that result from the aspiration event. Based on studies conducted on recurrent pneumonia, it is one of the commonest causes of recurrent pneumonia globally and in Africa. This has been documented in multiple studies. Mohammed et al reported a prevalence of 51% among children with recurrent pneumonia in Iran and Owayed et al also reported aspiration pneumonia as the commonest comorbidity among children with recurrent pneumonia in Canada at 48%.It was also the leading cause of recurrent pneumonia among children with in Netherlands as outlined by Hoving and brand et al. Khaled et al also reported aspiration pneumonia to be the leading cause of recurrent pneumonia among children in Egypt accounting for 15% of the cases(11)(17)(24)(25).

2.5.3 Predisposing Factors

Anatomical abnormalities	Functional disorders
Nasopharynx-choanal atresia	Delayed maturation-Downs syndrome Werdnig-Hoffman disease Prematurity
Oropharynx-cleft lip/palate Micrognathia Macroglossia (Beckwith Wideman /hypothyroidism) pharyngeal tumours	Static encephalopathy-Cerebral palsy Intrauterine infections Perinatal asphyxia Meningitis
Larynx-Laryngeal cleft/web	Altered consciousness-seizures, cerebrovascular accidents head trauma drug overdose meningitis/ encephalitis general anaesthesia.
Oesophagus-Tracheoesophageal fistula Vascular rings GERD Stricture Achalasia Scleroderma	Neuromuscular disease-muscular atrophy myasthenia gravis
Gastric-incompetent cardiac sphincter Gastric outlet obstruction	Accidental aspiration -drowning ingestion of kerosene, peanuts and betel nut.

2.5.4 Pathophysiology of Aspiration Pneumonia

Normal swallowing is a complex process that requires the coordination of voluntary and involuntary actions. After ingestion and preparation, a food bolus is voluntarily delivered to the pharynx. This activates the involuntary pharyngeal phase in which the soft palate seals the nasopharynx, the larynx is elevated and tilted anteriorly, the true and false vocal folds close and the pharyngeal constrictors sequentially contract to propel the bolus into the oesophagus(26).The upper oesophageal sphincter immediately relaxes and it open up to accept the bolus through laryngeal elevation. Peristalsis then transports the bolus to the stomach. Any intrinsic abnormality in the effectiveness, duration, or timing of any of these components usually leads to aspiration. As highlighted by R.P Boesch et al acid is obviously toxic to the respiratory tract specifically, aspiration of acidic (pH 1–2) contents into the lungs causes desquamation of mucosa, damage to alveolar lining cells and capillaries and acute neutrophilic

inflammation. Also pulmonary aspiration of contents with pH 2.5 has caused pneumonitis in an animal model(26).

Another form is recurrent aspiration of saliva which is the rarest form of aspiration. It is usually diagnosed after the development of significant lung injury. Usually the oral cavity contains potentially pathogenic bacteria and yeast and these organisms once aspirated into the airways they cause recurrent pneumonia or lung abscesses if aspirated in large quantities(27).

2.5.5 Clinical Presentation

Cough during feeds, weak suck, gagging, choking, apnoea and cyanosis during feeds, failure to thrive, sound of wet breathing or rattling, recurrent stridor, recurrent wheeze, hoarseness of voice and recurrent pneumonias.

2.5.6 Diagnosis

Clinical assessment of the child while feeding can be used to give an idea if there is any possibility of aspiration which includes observing the motion of the mouth, tongue and larynx during sucking, bolus formation and swallowing, checking for drooling or excessive accumulation of secretions in the mouth and lastly presence of cough or wet upper airway noises after feeding which suggests laryngeal penetration. Other modes include Video fluoroscopic swallow study also known as modified barium swallow, Fibre optic endoscopic examination of swallowing and flexible bronchoscopy with bronchoalveolar lavage. Chest X-ray can be helpful in identifying lung pathology secondary to aspiration but has low sensitivity in detecting early parenchymal disease, high resolution CT scan is more sensitive than chest radiographs and good at detecting early parenchymal disease.

2.6 Asthma

It is defined as a heterogenous disease usually characterised by chronic airway inflammation defined by the history of respiratory symptoms such as wheeze, shortness of breath ,chest tightness and cough that vary over time and in intensity together with variable expiratory airflow limitation(28).Most studies conducted globally have stated asthma to be one of the major causes of recurrent pneumonia. A comparison study by Patria and Longhi et al in Italy conducted a study on clinical profile of children with recurrent pneumonia. The authors stated that asthma was a significant risk factor for recurrent pneumonia with a P value of 0.0001 which was statistically significant. Another study on recurrent pneumonia among children in Canada by Owayed et al reported that asthma was one of the major causes of recurrent

pneumonia at 19%. However, Hoving and brand et al conducted a similar study in Netherlands and they stated that asthma was not a common cause of recurrent pneumonia and a diagnosis of both asthma and recurrent pneumonia was questionable, but of note is that they excluded children with history of recurrent wheeze(17)(25)(29). Tiago Bittencourt et al in Santo Angelo Brazil in 2017 conducted a study to determine the correlation between asthma with recurrent respiratory infections, 531 children aged 0 to15 years were interviewed and there was a significant relationship between presence of asthma and recurrent chest infections with a prevalence ratio of 2.47.There was also a significant correlation between asthma and lower respiratory tract disease with a prevalence ratio of 7.82(30).

2.6.1 Pathophysiology of recurrent pneumonia in asthma

As mentioned by Moustafa et al Atopic conditions such as asthma are considered an important risk factor for recurrent pneumonia due to defective innate immune response of epithelial cells and interleukin 13 dependent reduced mucociliary functions. Children are susceptible to asthma in which excessive mucus production rather than bronchospasms cause majority of symptoms. Thick mucus in the airways that is high in protein can easily lead to obstruction in the small airways in children. Excessive mucus production in hypersecretory asthma can lead to right middle lobe syndrome atelectasis that lead to secondary infections(10)

2.6.2 Clinical Presentation

Children above 5 years with asthma present with history of the following symptoms shortness of breath ,wheeze ,cough and chest tightness (mostly in older children), the probability of having asthma is increased by the following symptoms that are worse at night or early morning, symptoms that vary over time and intensity and are triggered by viral infection, exercise, allergen exposure, changes in weather, laughter and irritants(28).

In children less than 5years diagnosis is difficult, most common symptoms to look out for include history of wheezing or coughing which occurs with exercise, laughing or in absence of an apparent infection, history of allergies and clinical improvement during 2-3 months of controller treatment and worsening after cessation, additional symptoms include difficult/heavy breathing occurring with exercise, laughing ,crying and reduced activity ,signs include expiratory wheeze(28)

2.7 Diagnosis

Therapeutic trial for 2-3 months with SABA and inhaled corticosteroid with improvement of symptoms especially for children less than 5years.Tests for allergic sensitization used as a

predictor for development of persistent asthma. Lung function tests with bronchial provocation tests used in children more than 5years.Fractional concentration of nitric oxide has not been confirmed to rule in or out the diagnosis of asthma in children. Chest X-ray can be used to rule out other causes of wheeze such as congenital lung emphysema , vascular rings, tuberculosis and foreign body(28)

2.8 HIV Infection

HIV is a blood borne virus which is transmitted via sexual intercourse, shared intravenous paraphernalia and mother to child which can occur during pregnancy, delivery process or during breastfeeding. It is caused by infection with HIV-1 OR HIV-2, which are retroviruses in Retroviridae family, lentivirus genus. Globally there are 36.7 million people living with HIV in 2015 and 1.8 million are children less than 15 years, 87% of all children infected with HIV are less than 15 years, 84% of all new infections and 86% of HIV related deaths are in sub-Saharan Africa. In Kenya 1.5million people are infected with HIV in 2018 and105,613 children aged 0 to14years are living with HIV which accounts for 6% of all infections(31).HIV infection is a major cause of child mortality and studies have shown an increased rate of hospital admissions and readmissions among children with HIV infection more so in developing countries. In a study conducted in South Africa by Manthodi Alina et al in 2003 on causes of readmissions among children with HIV aged less than 10 years with a sample size of 581 admissions, 12% were readmitted and the commonest cause of readmission was bronchopneumonia at 29.7%(32).

2.8.1 Pathophysiology of Recurrent Pneumonia in HIV

Zar et al noted that paediatric patients with HIV are at an increased risk of recurrent lower respiratory tract infections compared to immuno-competent children(33). HIV causes immunological changes such as depletion in CD4 T Cell, cytokine dysregulation and immune dysfunction. The dominant feature is depletion of helper T cells which reverses the normal CD4:CD8 ratio and subsequently leads to immunodeficiency these lead to high risk of recurrent and severe bacterial pneumonia as disease stage progresses(34)

2.8.2 Clinical Presentation and Diagnosis

HIV usually presents with conditions that are frequently found in children who are not HIV infected hence makes diagnosis based on clinical features to be difficult. According to the 2018 HIV testing guidelines for children less than 18months HIV DNA/RNA PCR is confirmatory and for children more than 18 months a positive antibody test is sufficient to confirm HIV

infection. In areas where the above tests are not present there is a diagnostic criterion for presumptive diagnosis in children less than 18months created by WHO in 2010.

2.9 Severe Acute Malnutrition

According to WHO its defined as the cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance and specific functions it can be divide into two related disorders marasmus or kwashiorkor. Its determined based on anthropometric measures mainly height, weight and MUAC with or without presence of bilateral pedal oedema.

A study conducted by Kathryn R Finger et al in 2013 to determine prevalence of all cause readmission following hospital stay in patients with malnutrition, reported an all cause 30 day readmission among children ages 1 to 17yrs of 20% among children with malnutrition compared to 10% among children without malnutrition ,they also reported a higher average cost of readmission at 16200 $ for children with malnutrition compared to 13400$ for children without malnutrition, Pneumonia was ranked among leading cause of readmission among patients with malnutrition(35).

SAM and pneumonia are a leading cause of death and morbidity in under 5 children especially in developing countries. Malnutrition has a direct effect on mortality and been associated with increased   frequency and severity of pneumonia recurrences potentially representing a secondary immune deficiency(36).The severity of malnutrition among children with pneumonia has been shown to directly affect the outcome, this is evidenced by a systematic review by Mohammed Chisti et al whereby they reviewed previous studies on mortality risk among children with pneumonia and malnutrition in low income countries ,they reported a higher risk of mortality among children with severe acute malnutrition compared to children with moderate acute malnutrition(37).West et al reported similar findings on long-term mortality and morbidity among children with LRTI and malnutrition in Gambia in 2015 whereby he stated that mortality risk among children with severe acute malnutrition and pneumonia was 15times higher than for children with pneumonia and moderate malnutrition at 3.2 (36). According to Finger et al severe acute Malnutrition is a major cause of paediatric readmissions and mortality and it is associated with a post hospital syndrome which is an acquired transient period of vulnerability following hospitalisation leading to increased risk for readmission. It is also associated with increased cost for every rehospitalisation and longer hospital stay(35).

2.9.1 Pathophysiology of recurrent Pneumonia in severe acute malnutrition

In severe acute malnutrition the incidence of all types of infection is high in general and pneumonia in particular. This is because malnutrition compromises host defences and increases susceptibility to infectious diseases including pneumonia. Host defence mechanisms are usually recruited on entry of the pathogen into the alveolus, these mechanisms of immune activation often fail since children with severe acute malnutrition are often deficient in immune cells. Another explanation is the low levels of leptin in children with SAM. Leptin is usually produced by adipose tissue during acute phase response as part of antibacterial response ,it usually prevents lymphoid tissue atrophy ,reconstitutes lymphoid cellularity and restores defence activity during malnutrition ,it also modulates activation of CD4 and CD8 T cells from infected malnourished children, leptin levels are usually low in children with severe acute malnutrition and hence they are not able to mount an immune response against bacteria causing pneumonia(37).

2.9.2 Clinical presentation

Common signs and symptoms mostly occur due to malnutrition and also other micronutrient deficiencies as outlined below:

Site	Signs/Symptoms
Face	Moon face(kwashiorkor), simian facies(marasmus)
Eyes	Dry eyes, bitot's spot, periorbital oedema
Mouth	Angular stomatitis, cheilitis, glossitis, spongy bleeding gums and parotid enlargement
Teeth	Enamel mottling, delayed eruption
Skin	Loose, wrinkled/shiny oedematous, dry follicular hyperkeratosis, hypopigmentation
Nails	Koilonychia, thin and soft nail plate
Musculature	Muscle wasting especially buttocks and thighs
Skeletal	Deformities
Abdomen	Distended, hepatomegaly with fatty liver
Cardiovascular	Bradycardia, hypotension, reduced cardiac output
Neurologic	Global developmental delay, loss of knee and ankle reflexes, impaired memory
Hematologic	Pallor, petechiae, bleeding diathesis

Behavioural	Lethargy, apathy, irritable on handling
Growth	Poor weight gain, slow linear growth

Diagnosis

Anthropometric measurements taken specifically weight, height and Mid upper arm circumference +/- oedema

Wasting-severe acute malnutrition is defined as severe wasting and or bilateral oedema with either weight/height less than -3SD of WHO child growth standard or mid upper circumference less than 11.5 cm for children above 6months to 5years. And MUAC definition of malnutrition for various age groups:6-59 months less than125 mm,5- 9 years less than145mm,10-14 years less than170mm.

Stunting-height/age less than -2SD of WHO growth chart for sex and age

Underweight-Weight/age less than -2SD OF WHO growth chart for sex and age.

Classification for stunting, wasting and underweight:

> mild -1 to -2SD
>
> moderate malnutrition -2 to -3 SD
>
> Severe malnutrition less than -3SD

2.10 Congenital heart disease

Congenital heart diseases especially the types that lead to increased pulmonary flow have been identified as predisposing factors for pneumonia readmissions. It's very important to identify these cardiac diseases early in children with recurrent readmissions due to pneumonia because co-existence of cardiac disease and pneumonia leads to a higher mortality rate. A study carried out by Dr Pankaj Kumar et al in 2017 to identify the incidence of congenital heart disease in children with recurrent lower respiratory tract infections among children aged 1-10yrs in India found that out of 100 children 43% had an underlying congenital heart disease with a male predominance of 53% and the most common type of congenital heart disease was acyanotic at 90%.The common acyanotic heart diseases noted were ventricular septal defects at 43%,atrial septal defect at 28%patent ductus arteriosus at 17.9% while the most common cyanotic heart diseases were tetralogy of Fallot at 66% and single ventricle at 33% .Most children with a recurrent lower respiratory tract infection and underlying heart disease were between ages 1-5 years at 45%(38).

2.10.1 Pathophysiology of recurrent Pneumonia in congenital heart disease

In acyanotic heart diseases which are most commonly seen in children with pneumonia there is usually a left to right shunts which leads to increased blood flow to the lung hence causing pulmonary oedema which is a nidus for infection resulting in presentation with recurrent episodes of pneumonia(39).Children with underlying congenital heart disease have dilated blood vessels or heart chambers which may compress the bronchi causing impaired drainage of pulmonary segments that leads to atelectasis with secondary infection(10).Children with CHD are also at increased risk of aspiration of feeds due to tachypnoea which results in frequent lower respiratory infections. Of note most children with underlying CHD are malnourished resulting from severity of the underlying conditions ,anorexia, decreased intake leading to inability to mount an immune response during an infectious process(40).

2.10.2 Clinical Presentation

Symptoms include poor feeding (lethargy and tiring with early stopping of feeds), failure to thrive, fast breathing, easy fatigability and diaphoresis. Common signs include tachycardia, poor perfusion, heart murmur, tachypnoea, grunting, chest retractions, wheezing, hepatomegaly, oedema.

2.10.3 Diagnosis

Chest radiograph is important in distinguishing between pulmonary and cardiac disease, electrocardiogram can be helpful in evaluation of suspected cardiac disease however not recommended in asymptomatic children. Another modality is echocardiography which is the gold standard for diagnosing underlying congenital heart diseases in children.

2.11 Rickets

It is defined as a disease of growing bone that is caused by unmineralized matrix at the growth plate and occurs in children before fusion of epiphyses. It mainly occurs due to vitamin D deficiency amongst other causes(12).Different studies carried out on rickets in children have shown a correlation with repeated lower respiratory tract infections and burden of disease especially in developing countries(41). Najada et al in 2004 carried out a study on frequency of rickets among hospitalised infants and its correlation to respiratory disease in West Asia and he found that 85% of patients with rickets were admitted due to pneumonia and having rickets was associated with a longer duration of stay of(9.5 vs 7.5)(42).In Kenya a study carried out by Prof Irimu et al on prevalence of rickets in children among 3 different regions in Kenya

among children less than 5years found that rickets was most prevalent in Nairobi at 4.01% compared to central region at 0.92% it was associated with pneumonia infection and longer hospital stay(43).A few studies on recurrent pneumonia also determined the prevalence of rickets among children with recurrent pneumonia ,Moustafa et al of Egypt reported that 7% of the children had rickets(44) while Mohammed Reza et al of Iran reported a prevalence of 0.8%(11).

2.11.1 Pathophysiology of recurrent Pneumonia in rickets

There is a high prevalence of respiratory tract infections seen in children with vitamin D deficiency. It is mostly found among paediatric population with recurrent pneumonia and this may be attributed to many factors such as patients with rickets have generalised hypotonia leading to physical changes in the chest that reduce chest and lung volumes and compromise lung compliance leading to inability to clear secretions(10). Vitamin D also has an important role on host's immune system modulating both innate and adaptive immunity and it usually regulates the inflammatory cascade. Most immune cells usually express vitamin D receptor, which is activated when cells are stimulated. Vitamin D usually regulates inflammation and immunity by controlling macrophage and dendritic cell activity and various toll like receptor mediated events in neutrophils. It also diminishes the function of human dendritic cells by decreasing maturation, antigen presentation and production of cytokines IL 12 and IL23.

Lastly it also induces expression of 2 antimicrobial peptides cathelicidin and B defensin which play a key role in innate immunity owing to their chemotactic action and toxin neutralization hence children with rickets have altered immunity due to low vitamin D levels which predisposes them to recurrent pneumonia(45).

2.11.2 Clinical Presentation

Symptoms include history of delayed milestones, failure to thrive, listlessness, protruding abdomen, muscle weakness. Signs such as frontal or parietal bossing of the skull, craniotabes, delayed fontanelle closure, delayed dentition, carries, widened wrists, bow legs, knock knees, Harrison sulcus, rachitic rosary, spine deformities (kyphosis, scoliosis, lordosis), valgus or Varus deformity, windswept deformity, anterior bowing of tibia and femur and coxa vara

2.11.3 Diagnosis

Based on the 2019 WHO review on nutritional rickets, there are no internationally recognised diagnostic criteria for rickets, However, a consensus group, representing 11 international scientific organizations participated in a conference in May 2014 to create a global evidence-

based diagnostic criteria for rickets and osteomalacia. Normally, rickets has been screened and diagnosed based on a combination of parameters including history, physical examination findings, biochemical testing and radiographs. Recommended laboratory investigations include serum vitamin D levels, parathyroid hormone levels and bone biochemistry (calcium levels, phosphate levels and alkaline phosphatase).A study conducted on specificity and sensitivity of elevated serum alkaline phosphatase levels in comparison to radiographs as a test for rickets among breastfed infants and young children aged 6–15 months, found that levels of ALP above 552 U/L had a positive predictive value of 40% and a specificity of 97%.Lastly radiographs, have traditionally been used to confirm the diagnosis of rickets and are often considered the gold standard for this purpose. Abnormal radiographic findings are first evident long after biochemical and histological abnormalities are present. Radiographs are, therefore, not a suitable tool for screening and prevention of the condition. The Japanese Society for Bone and Mineral Research and the Japan Endocrine Society recommended the following indicators to diagnose nutritional rickets : Definite rickets Rachitic changes on radiographs (cupping and fraying of metaphysis, widening of epiphyseal plate) High blood alkaline phosphatase , Hypophosphatemia or hypocalcaemia Clinical signs: bone deformities such as genu varum and valgus, abnormal spinal curvature, craniotabes, open fontanelles, rachitic rosary, joint swelling (46)

2.12 Inpatient clinical outcomes among children rehospitalised with pneumonia

Very few studies have looked at short clinical outcomes especially in children readmitted due to pneumonia. One study done by Li Lun Chen et al in 2021 on clinical characteristics and outcomes among children ages 1 to 18years with recurrent pneumonia in Taiwan noted that children with recurrent pneumonia had a longer hospital stay (4 vs 7 days), longer ICU stay (2 vs 6 days) and higher case fatality of (0% vs 5.1%) among those with vs without recurrent pneumonia(16). Paulo Sergio et al, in 2016 among children with repeated readmissions within a duration of 1 year in paediatric intensive care unit in Brazil, found that out of 758 children aged 0 to 10 years,75 (9.8%) was readmitted and of note most of the readmissions were common in children with underlying chronic co-morbidities at an odds ratio of 1.07 and those with cognitive disability at an odds ratio of 1.08.

The common co-morbidities seen included neuromuscular disorders at 34%, cardiovascular at 24%, respiratory at 4% and renal at 1%, they also reported that patients who were re-hospitalised had longer hospital stay of 20days compared to first time admissions who had an

average hospital stay of 9days. Patients who were readmitted also had a higher mortality rate of 21% compared to first time admissions at 5.1%(47)Another study done by Jeffery et al among 87 paediatric intensive care units in the United states in 2011, to assess frequency ,risk factors and outcomes of early unplanned readmissions with a sample size of 96189 patients aged between 1-18yrs , reported rate of readmission was 12.3 % and most common reason for readmissions were respiratory causes at 56%,infectious   at 35%, neurological at 28% and cardiovascular at 20%.This study noted that readmissions had a prolonged length of stay of 3.1days compared to index admissions who had a mean duration of stay of 2 days .The patients who were readmitted also had a higher mortality of 4% compared to index admissions at 2.5%(48).A conclusion was made that the most common conditions leading to readmissions were respiratory, infectious and neurological accounting for 25% of all causes.

2.13 In hospital outcomes among children with pneumonia and various underlying co-morbidities

Children admitted due to pneumonia with comorbid conditions have been shown to have poorer prognostic outcomes such as death and increased hospital stay than those without comorbid conditions leyenaaar et al found that children with chronic conditions including immunologic, metabolic, cardiovascular ,chronic respiratory disorders and gastrointestinal conditions have a longer length of hospital stay after pneumonia admissions compared to children without co-morbidities(49)

2.13.1 HIV

Studies done in Malawi found that severe pneumonia was an independent predictor of death in children with HIV infection and exposure(50),Macpherson et al documented that HIV was highly associated with increased mortality among children aged 5-14years admitted due to pneumonia in Kenya(51).HIV infected children with pneumonia in public hospitals in South Africa had a longer duration of hospitalisation 1.8 days longer in the ward and 5.7 days longer in PICU than HIV uninfected children(52).

2.13.2 Rickets

In Yemen, Banerjee al reported that rickets was a major cause of mortality among children with pneumonia however a mismatched case control study in children hospital in Ethiopia researchers did not find an increase in mortality in children with pneumonia and rickets compared to children only with pneumonia(49)(53).Najada et al found significantly longer hospital stay among rachitic infants compared to non-rachitic infants(9.5 days vs

7.2days)(53).Similarly Nepalese children with severe pneumonia who had vitamin D levels <50nmol/l had longer duration illness compared with patient levels >75nmol/l(54).

2.13.3 Severe Acute Malnutrition

In developing countries, both severe and moderate degrees of malnutrition have been found to substantially increase the risk of death and readmissions among children with pneumonia, in comparison to those without malnutrition(55) However, Caggiano et al. found that children who had community acquired pneumonia with co morbid malnutrition did not show significant differences from other patients in terms of deaths or length of stay(56) A 'la et al found that under five paediatric patients in Indonesia with pneumonia and malnutrition had a higher average length of hospital stay (8 days) than that expected for children without co morbidities (5.5 days)(57).

2.13.4 Congenital heart disease

A study carried out by Sadoh et al. in 2013 showed that children with congenital heart disease had a significantly longer duration of admission (11.50 days) than patients without congenital heart disease (7.38 days). However, none of the children that had congenital heart disease died, while 8.7% of the children without CHD died(58) A 'la et al. also found that in under five children hospitalized with pneumonia, those that had congenital heart diseases had a higher average length of hospital stay(9.43 days), which was higher than that set as standard for children without co morbidities in Indonesia (5.5days)(57)

2.13.5 Asthma

A major risk factor for death in children with invasive pneumococcal disease is the presence of underlying co-morbidities(59) .Even after the introduction of pneumococcal vaccine children with asthma are at a higher risk of invasive pneumococcal disease and pneumonia than children without asthma(60).Talbot et al. demonstrated that children and adults with asthma had over a two-fold increased risk of invasive pneumococcal disease compared to those without asthma, putting them at a higher risk of mortality(61).

2.14 Study Justification

Pneumonia is the main cause of death in children especially those under 5 years particularly in developing countries and it is the main cause of readmissions. Studies done in developed countries show that readmissions cost approximately I billion $ annually, hence readmissions are associated with a high economic burden which affects both the patient and the health care system at large. Repeated admissions due to pneumonia also impart medical risks to the patients and have been associated with higher mortality.

However there is limited data in our setting on pneumonia readmissions and common underlying clinical conditions hence this study will aim to provide information on proportion of children readmitted with pneumonia who have selected underlying comorbidities and the common comorbidities seen in this population which will inform clinicians on the common conditions to consider when managing these children in order to ensure early and appropriate treatment which may help prevent complications and reduce associated financial implications. The study shall also seek to identify the inpatient outcomes seen in children who are readmitted due to pneumonia and this will give an insight on the impact of various co-morbidities on hospital stay and on mortality. This information obtained will enable health planners and policy makers in allocation of resources towards early identification of underlying comorbidities as well as mitigation of prolonged hospital stay and high mortality associated with rehospitalisation due to pneumonia. The findings of the study will also provide data that can be used for generation of protocols aimed at identifying comorbid conditions early hence improving clinical outcomes and contributing towards overall child survival.

2.15 Research Question

What proportion of children aged 6months to 12years rehospitalised with pneumonia at KNH have underlying co-morbidities and what are their in-hospital clinical outcomes?

2.16 Study Objectives

2.16.1 Primary Objective

- To determine the proportion of children aged 6 months-12years readmitted with pneumonia at KNH who have selected underlying co-morbidities, specifically (asthma, gastroesophageal reflux disease, rickets, malnutrition, congenital heart disease, human immunodeficiency virus and rickets)

2.16.2 Secondary objectives

- To determine the in-hospital outcomes among children aged 6months-12years re-admitted with pneumonia at KNH.
- To compare in hospital outcomes between readmitted children aged 6months-12years with and without co-morbidities at KNH.

3.0 CHAPTER THREE: METHODOLOGY

3.1 Study Design

This was a hospital based Longitudinal study.

3.2 Study Site

The study was carried out in the general paediatric wards at the Kenyatta national hospital. It is the largest referral hospital in East and central Africa and the second largest in Africa. It also serves as a teaching centre for the university of Nairobi. It has a total bed capacity of 1800 and usually caters for patients referred from all health facilities in the country. It serves as the primary health facility for children who live in Nairobi and its environs. At KNH there are 4 general paediatric wards namely (wards 3A, 3B, 3C and 3D) with a total bed capacity of 120 and a bed occupancy of over 200%. Majority of the patients are admitted with acute childhood illnesses and pneumonia accounts for one third of all admissions (59). The majority are referred from primary care facilities at 65%, direct self-referrals are at 20% and 15% are referred from private hospitals or public facilities (58). Initially children are received at the paediatric emergency unit which is run by paediatric residents, clinical officers and specialised nurses where they are triaged, assessed and stabilised then transferred to either of the wards. At the wards children are usually managed by paediatric consultants, paediatric residents, medical officers, clinical officers, nurses and nutritionists. Each ward has an acute room for the very sick children who need further stabilization with frequent monitoring and a ward setting for the more stable patients. The wards are open for 24 hours daily and new patients are admitted on a daily basis. In this study children readmitted with pneumonia were identified from the 4 paediatric wards within 48hours of admission and followed up until discharge.

3.3 Study period

The study duration was 4 months (May to August 2021)

3.4 Study Population

The study population included paediatric patients aged 6months-12years admitted to the paediatric wards in KNH with a recorded current diagnosis of pneumonia and confirmed to have history of admission due to pneumonia either in KNH or any other health facility within the last 1 year.

3.4.1 Inclusion Criteria

Children aged 6months-12years admitted at KNH with a current diagnosis of pneumonia or lower respiratory tract infection and;

- History of previous admission due to pneumonia in the preceding 1 year
- Documents from a health facility confirming the previous admission due to pneumonia
- Children whose mothers have given consent to participate in the study

3.4.2 Exclusion Criteria
- Children without documentation to confirm history of previous admission.

3.5 Sample Size Calculation

According to the KNH health record system, approximately 100 children are re-admitted with pneumonia annually, hence a representative sample was drawn from this finite population and sample size was determined as follows:

$$n = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where

n' = sample size with finite population correction,

N = size of the target population = 100

Z = Z statistic for 95% level of confidence = 1.96

P = the proportion of readmitted children with either of the selected underlying co-morbidities including asthma, GERD, HIV, SAM, aspiration, rickets and congenital heart disease was estimated to be approximately =50% (based on the fact that none of the previous studies estimated the overall proportion of readmitted children with underlying comorbidities we opted to use p of 50%)

d = margin of error = 5%

$$= \frac{100 \text{ x } 1.96^2 \text{ x } 0.5 \text{ x } 0.5}{0.05^2 (100\text{-}1) + 1.96^2 \text{ x } 0.5 \text{ x } 0.5}$$

n = 80

A total of 80 children were sampled to estimate proportion of children with co-morbidities within 5% level of precision.

3.6 Sampling Method

Consecutive sampling was used whereby all children between ages 6 months and 12years readmitted with pneumonia were identified and those who fit the eligibility criteria and gave consent were recruited until the desired sample size was achieved.

3.7 Case Definitions

Re-admission-Current pneumonia admission occurring within 1 year of the last documented pneumonia related admission.

Pneumonia-For children aged less than 59 months diagnosis was made based on WHO 2016 pneumonia guidelines which include

- History of either cough or difficulty in breathing and
- Either of the following signs tachycardia or lower chest wall in drawing.

For children aged more than 5years diagnosis was based on 2012 British Thoracic guidelines of

- persistent fever of >38.5℃
- With either tachypnoea or chest retractions.

  Positive CXR findings suggestive of pneumonia

Asthma-Diagnosis was based on 2020 GINA guidelines

- Symptoms: Presence of wheeze or cough/ difficulty in breathing (worsened early morning or late at night) and
- Signs- positive bronchodilator response.

GERD-Diagnosis of GERD was based on

- For children less than 2years: Infant GERD questionnaire score of >5 indicated diagnosis of GERD (Appendix II)
- For children above 2 years: Positive barium swallow findings suggestive of GERD.

Aspiration Pneumonia-Clinical diagnosis was made based on

- History of cough and recurrent wheeze for >3weeks or
- Cough/choking/apnoea/cyanosis during feeds and

either one of the following;

- Failure to thrive (weight less than 5th percentile for age on more than one occasion),
- Obvious neurologic/developmental disorders and
- Chest X-ray findings suggestive of aspiration.

Rickets- Defined as follows;

- History of delayed motor milestones and
- Any of the following physical findings-Frontal bossing, craniotabes, open fontanels, widened wrists, rachitic rosary, Harrison sulcus and
- Bone biochemistry (elevated Alkaline phosphate +/-low calcium or low phosphate)

- +/- Findings of any skeletal /spine deformities on Xray (if available)

Congenital Heart Disease-Diagnosis was based on:

- A 2D echocardiogram performed on all children done by a pediatric cardiologist using Phillips EPIQ 7 machine.

Severe Acute Malnutrition -Diagnosis was made based on 2016 WHO guidelines

- For children aged <5years mid upper arm circumference of <11.5 cm, weight for height <-3SD, or signs of severe wasting or edema

- For children aged >5 years-body mass index of <-3 based on the WHO growth chart for age and sex, or signs of severe wasting or edema.

HIV- Diagnosis was based on 2016 MOH HIV guidelines

- For children <18months a positive DNA/RNA PCR

- For children >18months a positive HIV antibody test

3.8 Study Procedure

Data collection was carried out over a duration of 4 months in 2021.It was carried out by the principal investigator and one research assistant (qualified clinical officer) who was recruited and trained on research conduct, ethics and data collection. The principal investigator and research assistant visited the general paediatric wards between 2-6pm and between 6 pm-12 am on a daily basis to recruit children. All children who were admitted due to pneumonia were identified within 48 hours. Once identified those who met the inclusion criteria, the study procedures were explained to the guardian in detail before obtaining informed consent. Consent was provided in English and Kiswahili (Appendix 1A and 1B) based on the guardian's preference. Once signed the research team then went ahead to take a thorough history, physical examination and anthropometric measurements and the data was recorded on a structured questionnaire. The history entailed the presenting complaints and open-ended questions that would guide the clinician in identifying the possible underlying comorbidity.

The physical examination entailed general examination, vital signs (respiratory rate, heart rate, oxygen saturation, temperature) and systemic examination. All findings were recorded in the questionnaire. For anthropometric measurements we used a weighing machine to determine weight, a stadiometer or infantometer to determine height/length respectively. A Shakri tape was used to determine the mid upper arm circumference. The relevant investigations were ordered including a bone biochemistry, HIV test, chest Xray and barium swallow at no added cost to the participant. Echocardiography was performed by a paediatric cardiologist using

Phillips Epic Q 7 machine at the bedside at no added cost. The results were recorded in the questionnaire and a written copy filed in the patients record.

The child was followed up on a daily basis for the first week and then weekly till the end of the study period. Progress was monitored while in the ward and any new findings were recorded. At each visit the guardian was updated on progress of the child. The patients were followed up until discharge to monitor progress and to assess their in-hospital outcomes.

3.9 Quality Assurance

The following measures shall be undertaken to ensure quality assurance:

- All clinical diagnosis were made based on the latest guidelines specific to each condition (Gina guidelines 2020, WHO pneumonia guidelines 2016, Kenya MOH HIV guidelines 2018)

- Up to date WHO recommended Shakri tape was used to assess for MUAC measurements.

- Up to date calibrated weighing scales/height/length measuring equipment were used.

- Research assistants adhered to the study procedure protocols to ensure uniformity in data collection and were trained on data collection.

- All ECHOs were performed by a paediatric cardiologist blinded to patients' condition at no added cost to the patient

- Clinical outcomes were determined on follow up in the wards.

3.10 Data Collection and Study Tools

A structured paper-based questionnaire was used to collect relevant data on history, physical exam findings, laboratory results and radiological results. For asthma, GERD and aspiration a clinical diagnosis was made based on history, physical examination and current guidelines for each diagnosis. Anthropometric measurements (WAZ, WHZ, HAZ and MUAC) were taken to determine nutrition status. A HIV test, bone biochemistry, chest X-ray and ECHO were performed and recorded for all children. Clinical outcomes were determined at discharge and also recorded on questionnaire.

3.11 Ethical Consideration

Ethical approval was sought from KNH/UON research and ethics committee prior to collection and analysis of data. Permission was sought from the KNH administration. A written informed consent was given to the parents /guardians of the study before enrolment. Details, procedures and protocols of the study were explained to the parents or guardians in their preferred language and in case of language barrier a translator was involved, they were also

explained to that in case they decline to participate in the study the child would still get same standard care. Consenting participants were also informed that they could opt out of the study at any given point. All participants were treated with fairness and equality and were not discriminated upon based on tribe, religion or social/economic background. The participants were clearly explained to the investigations prior to collecting data and they were explained to the results and were not be subjected to any unnecessary investigations. The parents and guardians were assured that there may be minimal discomfort during the examination and radiological procedures done and that no added costs were incurred as a result of participating in the study.

Data collected was stored in a password protected computer with access only to the research team and was delinked of all participants identifiers prior to dissemination of study results. Feedback will be provided on the study results to the clinical team at KNH Due to the current COVID 19 pandemic the following measures were undertaken, the primary researcher and the research assistant were trained on safety measures to be taken while collecting data in the general wards, personal protective gear was provided including N95 Masks, eye protection, gowns, gloves and hand sanitizer. He was also trained on how to effectively use the personal protective equipment. All participants had to adhere to safety measures prior to collecting data.

3.12 Data Management and Analysis

Data was entered and managed in Microsoft Excel 2016 data entry sheet. Data cleaning was performed to ensure high quality of data for analysis. The cleaned data was exported into STATA 13 for analysis. The study population was described by summarizing demographic and clinical characteristics into percentages and means (SD) or medians (IQR) for categorical and continuous variables respectively. The primary objective, to determine the proportion of children aged 6months to 12years rehospitalised with pneumonia who had any of the selected underlying comorbidity was determined as a proportion, the numerator was the proportion of re-hospitalized patients with any of the selected co-morbidities while denominator was all children enrolled in the study and the results were presented in bar graphs and charts. In addition, proportion with each of the selected co-morbidities was calculated and presented as proportions with 95% confidence intervals.

The secondary objective to determine in hospital outcomes among children rehospitalised due to pneumonia with underlying comorbidities were determined as medians (IQR) for duration of stay and proportions for mortality and presented as tables and charts as appropriate.

3.13 Data Dissemination plan

The study findings shall be presented to the UoN department of paediatrics and child health as part of requirements for the MMed program in both hard and soft copies. The hard copies will be sent to the university of Nairobi repository for storage. The findings of the study will be shared with the head of paediatrics at KNH hence to help in generating strategies to improve health care. The results will also be submitted for publication in peer reviewed scientific journals

CHAPTER FOUR: STUDY RESULTS

4.1 Participants' screening, enrolment and follow-up.

A total of 90 children were eligible for the study during screening. Ten (10) were excluded from the study. This was due to the fact that five (5) did not have documentation confirming previous admission and five (5) declined to give consent. Eighty (80) respondents consented to the study and were enrolled. A thorough history, physical examination and relevant investigations were carried out to determine the underlying comorbidities as shown in figure 1
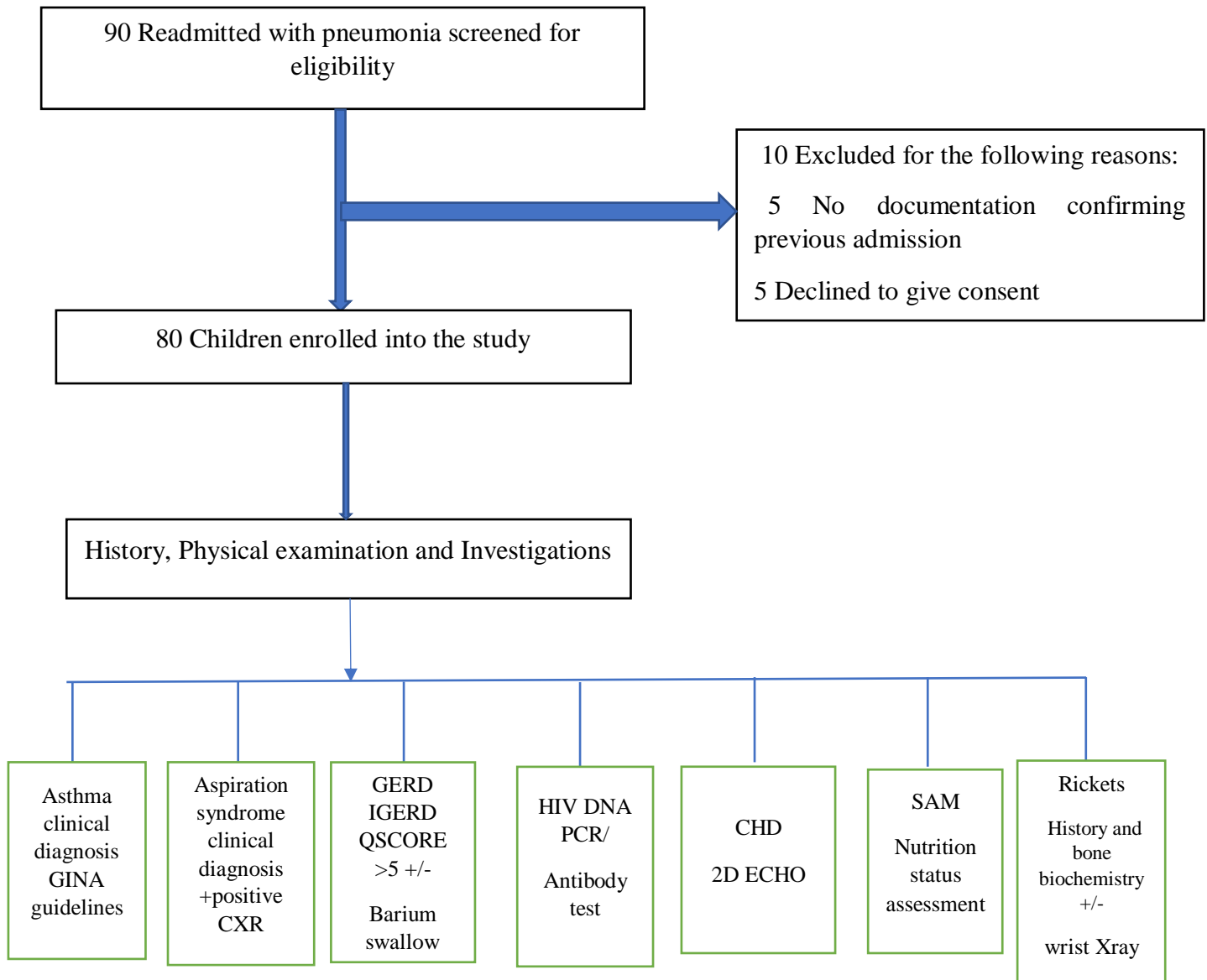
Figure 1: Study participants screening, enrolment and follow up

4.2 Demographic and clinical characteristics of patients readmitted with pneumonia

Among the participants enrolled, 33 (41.3%) were females and 47(58.7%) were males giving a male to female ratio of 1.42:1. Among the participants enrolled, 33 (41.3%) were females and 47(58.7%) were males giving a male to female ratio of 1.42:1.

Majority (93.7%) were aged less than 5 years and the median age of children was 13 months (IQR 9-19).

Nutrition status assessment of children aged less than 5 years weight for height measurement showed that majority were wasted, 25 (31.2%) had moderate wasting while 38 (47.5%) had severe wasting.

weight for age assessment, 25 (31.2%) were moderately underweight and 38 (47.5%) had severe underweight.

Height for age assessment showed that 26 (32.5%) children had moderate stunting and 33 (41.2%) were severely stunted.

On BMI assessment of children aged above 5 years 2 out of 5 children had moderate wasting while 2 out of 5children had severe wasting.

Most of the study participants (96%) were HIV negative.

Table 1: Demographic and clinical characteristics of children

Variable	Characteristic	Freq (%)
Gender	Female	33(41.3)
	Male	47(58.7)
Age	<1 year	37(46.3)
	1-5 years	38(47.5)
	>5 years	5(6.2)
Nutritional status		
WHZ (children < 5 years)	Normal	9(11.3)
	At risk of Wasting	8(10)
	Moderate Wasting	25(31.2)
	Severe Wasting	38(47.5)
WAZ (children < 5 years)	Normal	12(15)
	Moderate Underweight	29(36.3)
	Severe Underweight	39(48.7)
BMI (children > 5 years)	Normal	1(20)
	Moderate Underweight	2 (40)
	Severe Underweight	2(40)
HAZ	Normal	21(26.3)
	Moderate Stunting	26(32.5)
	Severe Stunting	33(41.2)
HIV	Negative	77(96.2)
	Positive	1(1.2)
	Unknown	2(2.6)

4.3 Clinical presentations of children readmitted with pneumonia

The average duration of symptoms was 9±8 days with a minimum duration of 1 day and maximum duration of 40 days. The most common presenting complaints were cough 69 (86.3%) difficulty in breathing 66 (82.5%) and hotness of body 58 (72.5%). These findings are summarized in figure 1 below
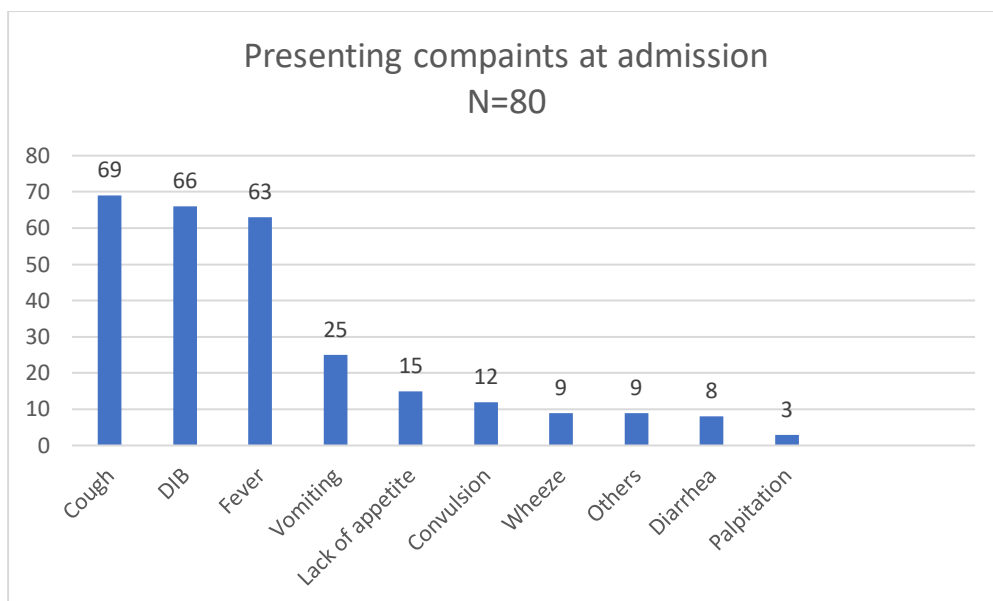
Figure 2: Presenting complaints among children readmitted with pneumonia

The most common presenting symptoms were finger clubbing22 (27.8%) and cyanosis 21 (26.3%) (See Table 2)

Table 2: Presenting symptoms for patients readmitted with pneumonia

Symptoms	Frequency (%)
Pallor	5(6.3)
Cyanosis	21(26.3)
Lymphadenopathy	2(2.5)
Jaundice	2(2.5)
Finger clubbing	22(27.8)
Dehydration	9(11.3)

Approximately half of the patients (54.6%) were tachypnoeic, 54 had hyperthermia and 45 (57.7%) had low oxygen saturation table 3 below summarizes the findings

Table 3: Vital signs among patients readmitted with pneumonia

Vital sign		Freq. (%)
Respiratory rate	Normal	35(45.5)
	Tachypnoea	42(54.6)
Pulse rate	Normal	21(26.9)
	Tachycardia	54(69.2)
	Bradycardia	3(3.9)
Temperature	Normal	20(25.6)
	Hyperthermia	54(69.2)
	Hypothermia	4(5.2)
Oxygen saturation	>90 %	33(42.3)
	≤90 %	45(57.7)

4.4 Primary objective: Proportion of children with underlying comorbidities.

Almost all patients 78 (97.5%, 95%CI:94.1-99.9%)) readmitted with pneumonia had at least one comorbidity. Of these patients, 10 (12.8%,95%CI:5.4-20.2%) had 1comorbidity,25(32.1%, 95% CI:21.7-42.4%) had 2 comorbidities and 43(55.1%, 95% CI:44.1-66.2%) had 3 or more comorbidities as outlined on figure 3.
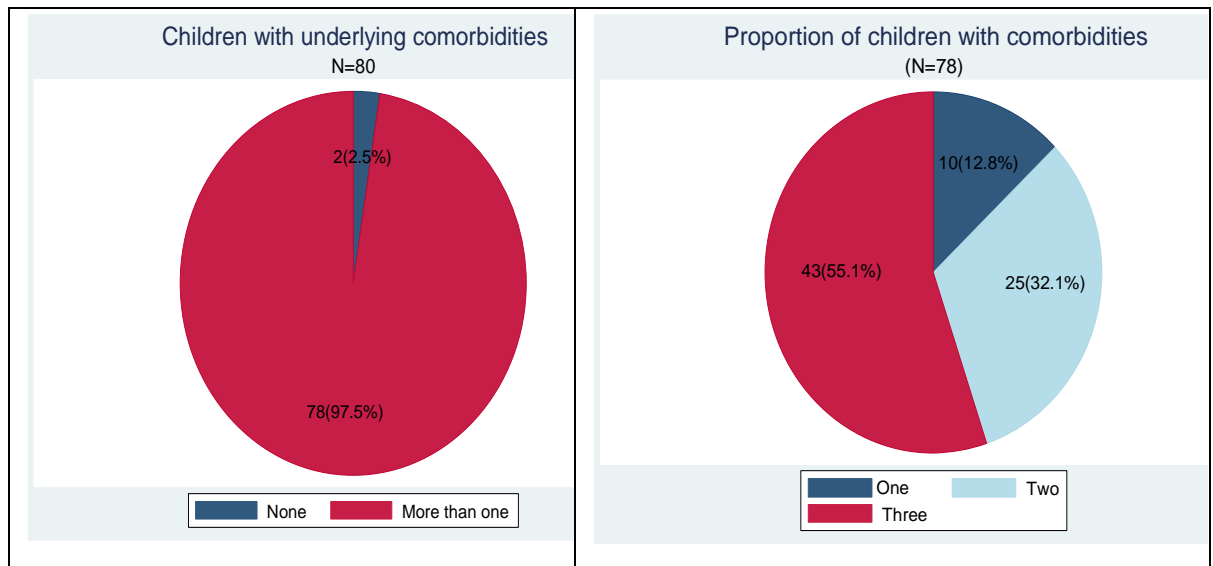
Figure 3: Proportion of children readmitted with pneumonia with underlying comorbidities

4.4.1 Common comorbidities seen among children rehospitalised due to pneumonia

The most common comorbidity identified was GERD in 49 (61.3%) children, aspiration pneumonia in 37 (46.3%), congenital heart disease in 33 (41.3%) Severe acute malnutrition in 28 (35%) and Rickets in 32 (40%). The least common comorbidity found was Asthma (5%) and HIV 1(1.3%). Other comorbidities identified include bronchiolitis (2 children), Pulmonary tuberculosis (4 children) and sickle cell anaemia (1 child) these were categorized under others. Figure 4 below summarizes these findings.
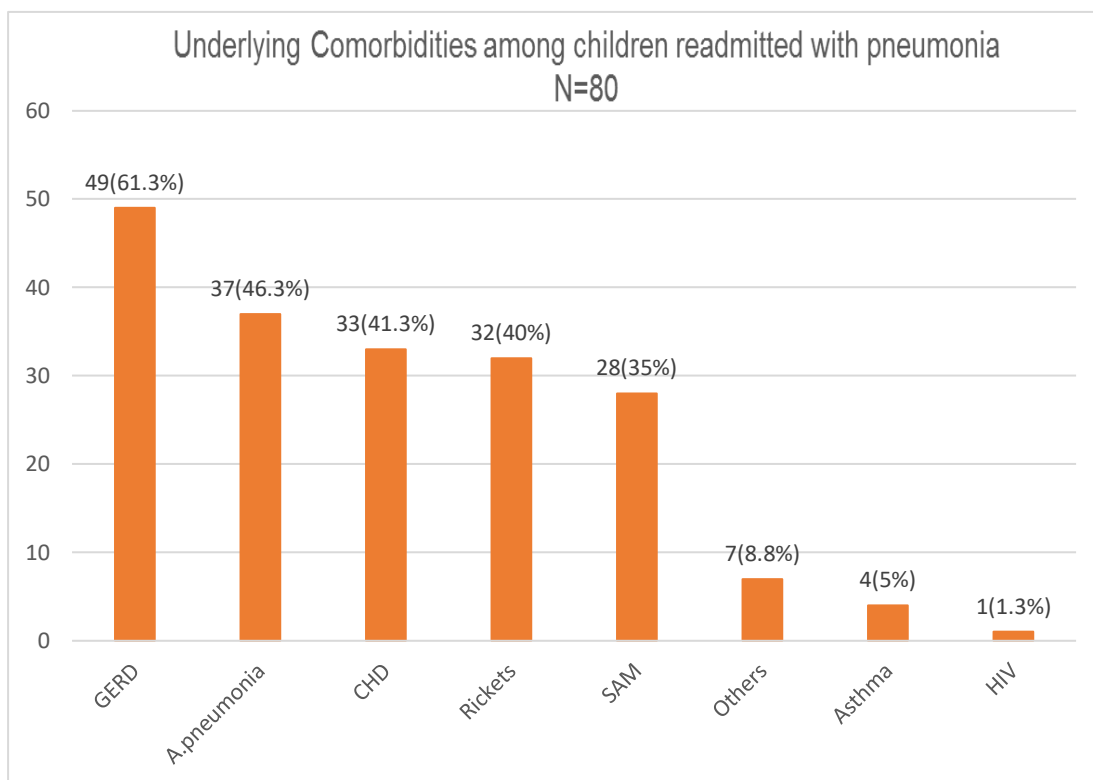
Figure 4: Comorbidities among children readmitted with pneumonia

4.4.2 Distribution of underlying co-morbidities among children readmitted with pneumonia

Out of 35 patients who had congenital heart disease 25(75.8%) had structural disorders, 13(39.4%) had pulmonary arterial hypertension, 7 had dilated cardiomyopathy, 4 had pericardial effusion, 2 had pulmonary artery thrombus and 1 had dextrocardia as shown in Table 4 below.

Table 4: Classification of congenital heart diseases

Type of Congenital heart disease (n=33)			Freq. (%)
Structural			**25(75.8%)**
	Cyanotic	Pulmonary stenosis	1
		Tetralogy of fallot	4
		Double outlet right ventricle	2
		Transposition of great arteries	1
		Truncus arteriosus	1
	Acyanotic	Mild tricuspid regurgitation	1
		Mitral regurgitation	2
		VSD	2
		PDA	4
		AV carnal defect	2
		Coarctation of aorta	1
		Atrial septal defect	2
		Aortic regurgitation	2
Pulmonary arterial hypertension			**13(39.4)**
Others			**15(45.5)**
		Dilated cardiomyopathy	7
		Pericardial effusion	4
		Pulmonary artery thrombus	2
		Dextrocardia	1
		Arrhythmias	1

4.5 Secondary objective: Outcomes of patients readmitted with pneumonia

Out the patients enrolled into the study, 68(85%) were discharged home while 12 (15%) died.
The figure 5 below summarizes the findings.
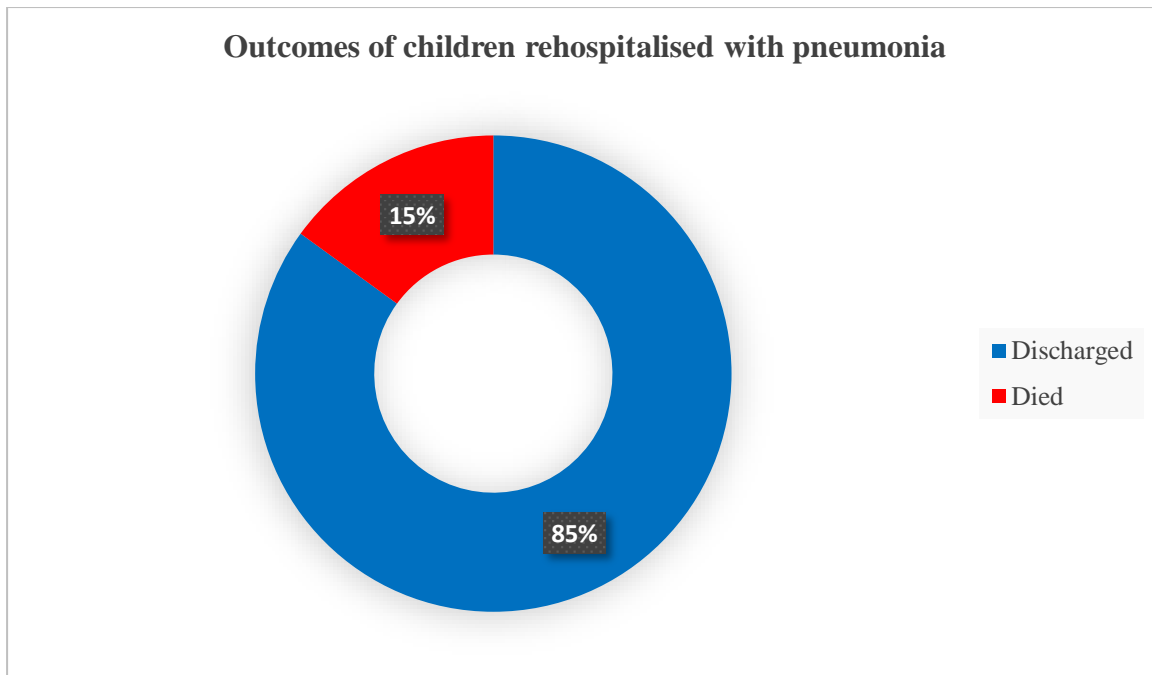
Figure 5: Outcomes of patients readmitted with pneumonia

The median duration of hospital stay was 29 (IQR 13-50) days with the minimum being 5 days and maximum being 119 days. The median duration of stay for children with aspiration pneumonia was 38 days. This was followed by GERD at 37 days and Rickets at 31.5 days. Patients who had asthma had a median of 8.5 days in the hospital. This is summarized in Table 5 below

Table 5: Duration of stay in hospital for readmitted children with various comorbidities

Diagnosis	Median stay days (IQR)	IQR
Aspiration Pneumonia	38	20.5,64.5
GERD	37	21,35
Rickets	31.5	20,30
CHD	30.5	11.5,47.5
SAM	21.5	13.5,41.5
HIV	25	
Asthma	8.5	6.5,12.5

4.5.1 Outcomes among children rehospitalised with pneumonia among children with GERD and Malnutrition

For children above 2years who had upper GI studies we have classified according to severity of GERD, Children with GERD grade III and IV had a longer duration of hospital stay compared to those with grade II at 48 and 61 days respectively. Children with severe acute malnutrition had a shorter median duration of stay of 28days compared to children with moderate malnutrition had 35days.number of deaths were higher among children with severe acute malnutrition and children with GERD grade III as outlined in table 6 and 7.

Table 6: Outcome among children based on level of GERD

Diagnosis	Median duration of stay(days)	IQR	No of deaths out of 26 children
GERD Grade II	49	20,63	1
GERD Grade III	48	32,65	3
GERD Grade IV	61	45,75	1

Table 7: Outcome among children based on level of Malnutrition

Diagnosis	Median duration of stay(days)	IQR	No of deaths
Moderate wasting	35	11,49	3 out of 28
Severe wasting	29	11,48	6 out of 35

CHAPTER FIVE: DISCUSSION

The prevalence of comorbidities among children re-hospitalized due to pneumonia was very high almost 100%. Commonest comorbidities largely comprised of aspiration syndrome, congenital heart disease, rickets and severe acute malnutrition. We found a median duration of stay of 29 days and we had a mortality rate of 15%.

In this present study, we found a male preponderance of 60%. This agrees with a study by Moustafa et al done in Egypt whereby male patients represented 65% while females represented 35% of children with recurrent pneumonia. Similarly, Mohammed et al found a male predilection of 55% among children with recurrent pneumonia in Iran(44).

The majority of children in this study were below 5years and this is similar to a study by Moustafa et al in Egypt whereby 62.7% of children were less than 3years. The findings in this study also agree with Mohammed et al who reported that 1% of the children had onset of symptoms prior to 3 months of age, 6% between 3 and 12 months ,65% between 1 and 5years and 28% after the age of 5years, this is attributed to the fact that children under 5 years have a significantly higher frequency of comorbid conditions such as malnutrition and congenital heart disease (10)(11).

Majority of the children readmitted with pneumonia at KNH had an underlying comorbidity. This is similar to what was reported by Owayed et al in Canada at 92%, Mohammed et al in Iran at 84% and Li Lun Chen et al in Taiwan at 81.7% (52)(11)(16). This high prevalence is likely due to the fact that all studies were conducted in tertiary hospital settings that receive many referral patients that are often times complicated. Moustafa et al stated a lower prevalence of 70% and this could be explained by the fact that the authors in this study excluded all children with neurological disorders(17)(11)(10)(44).

GERD and aspiration pneumonia were the commonest comorbidities among patients readmitted due to pneumonia at 61.3% and 49% respectively. Similarly, Mohammed et al reported aspiration syndrome at 59%. However, this was much higher than what Moustafa et al and Li Lun Chen found (aspiration syndrome at 8.9% and GERD at 7% respectively). This was because Moustafa et al excluded children with neurological disorders while Li Lun Chen excluded patients with aspiration pneumonia(11)(10) (44).

Congenital heart disease was identified in four out of ten children of whom three out of four had structural heart disease and a third had pulmonary arterial hypertension. This was higher than what was noted by Moustafa et al in Egypt at 25%. This disparity could be attributed to the fact that this study was conducted at a national referral hospital that receives patients from the entire country including those with suspected cardiac disease. KNH is among the few facilities in the country with a vigilant paediatric cardiology unit and cardiac surgery. However, there was similarity in distribution of cardiac lesions as most children had acyanotic heart disease with the commonest being VSD. With regard to cyanotic heart lesions the commonest in the other studies was Transposition of great arteries and in our set up it was Tetralogy of Fallot (9).

Prevalence of rickets among children who were rehospitalised with pneumonia was 40%. This is higher compared to Moustafa et al and Khaled et al in Egypt who both reported a prevalence of 7%. Rickets is prevalent in our setup due to inadequate vitamin D and calcium supplementation among pregnant and lactating women. Other factors include; lack of health and nutritional education, overcrowding households and overdressing children leading to limited sun light exposure and inadequate nutrition(10)(24).

Immunodeficiency disorders are among the major causes of recurrent pneumonia and in this study, we identified HIV in 1.3%. This has been similarly stated by Owayed et al in Canada where he reported a prevalence of 2%. Fosberg et al found a higher prevalence of 5% and this could be explained by the fact that there has been a reduction in new HIV infections among children in Kenya from 180,000 children in 2010 to 111,500 in 2020 (UNICEF DATA 2020). There has also been a reduction in mother to child transmission of HIV in our population from 18% in 2013 to 10.8% in 2020 and this is as a result of improved treatment and preventive strategies by the ministry of health (9)(17).

 Asthma was in 5% of children readmitted with pneumonia contrary to Moustafa, Mohammed and li Lun Chen et al at 8%, 19% and 30% respectively. This could be explained by the fact that, our study was conducted in a national referral hospital with a robust paediatric pulmonology clinic whereby patients have better follow-up and are well educated therefore have better asthma control with fewer exacerbations necessitating admission. Hoving and Brand et al found that no child in their study population had asthma but the authors in this study had excluded children with history of wheeze to avoid diagnostic confusion with recurrent (16,17,44)Kenya being a low-income country, malnutrition is still an important public health

issue that is associated with high mortality and morbidity. According to the KDHS 2014 report, 26% of children under 5 years are stunted, 11 % are undernourished and 4 % are wasted. In this study, 35% of children who are readmitted with pneumonia were severely wasted. This percentage is comparable to the study by Moustafa et al where 23% of patients with recurrent pneumonia had malnutrition and the reason could be the similarity in age of the children enrolled in both studies being under 3years (62)(10). Fosberg et al also found malnutrition among children readmitted with pneumonia in Tanzania to be lower at 14%. This is probably due to the fact that some children lacked anthropometric measurements hence the authors were unable to determine their nutritional status(9). Li Lu Chen et al found 1.2% of children with recurrent pneumonia had malnutrition which is lower than what we found and could be due to differences in socioeconomic status of children in our study compared to those in the study in China (16).

In this current study the duration of hospital stay was found to be prolonged at 29days. Since we found very few children who had no comorbidities, we were unable to do a comparison on duration of stay for this group of children. However, li Lun Chen et al reported duration of stay for children with pneumonia and comorbidities to be about 7 days which was longer than for children without comorbidities (16).The difference in median length of stay could be explained by the fact that most of our patients had aspiration ,GERD and congenital heart disease which mostly required surgical intervention.

There is limited data on mortality in children with recurrent pneumonia especially in low-income countries. In this study, mortality among readmitted children with underlying comorbidities is 15%. Paulo et al in Brazil 2016 carried out a study on children readmitted to paediatric ICU with comorbidities and found mortality was at 21% .This disparity can be explained by the difference in the study population(63). Li Lun Chen et al in Taiwan reported a case fatality rate of 5.9% in children with recurrent pneumonia which was significantly higher than for those without comorbidities(16).

5.1 Study Strengths

The study outlined the common presentation, comorbidities and outcomes in children who are rehospitalised with pneumonia and ooutlined the population most at risk of pneumonia readmissions

Study was carried out in the largest National referral hospital hence provides a good representation of children readmitted with pneumonia in this setting.

5.2 Study Limitations

The study looked at only seven conditions found in children readmitted due to pneumonia and did not include all the other causes.

Not all diagnosis was confirmed using laboratory or radiological investigations some were based on clinical diagnosis which may be subjective.

There were few children readmitted with pneumonia who had no comorbidities hence the investigator was unable to compare for associated factors between those with or without comorbidities.

5.3 Conclusions

1. Most of the children who are rehospitalised due to pneumonia at KNH have an underlying comorbidity

2. GERD and aspiration are the commonest comorbidities found among children readmitted with pneumonia.

3. Children readmitted with pneumonia and underlying comorbidities have prolonged median duration of stay (29days) with longer duration in patients with GERD and aspiration

4. Children who are readmitted due to pneumonia with underlying comorbidity have a high mortality of 15%

5.4 Recommendations

To the Ministry of health

To create protocols and guidelines that guide clinicians on common comorbidities to screen out for in children with pneumonia readmissions.

To Kenyatta National hospital

Majority of children hospitalised with pneumonia have an underlying comorbidity, I would highly recommend the need for a well-structured system with a high-risk unit where all

children rehospitalised with pneumonia can be managed and followed up in order to receive more personalised and specialised care.

Create a structured and detailed admission record form highlighting number of previous admissions in order to identify readmissions early.

Sensitize clinicians to have a high index of suspicion in identification of underlying comorbidities among patients readmitted with pneumonia and incorporate a Multidisplinary approach in management so as to provide optimum care.

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STUDY TIMELINE

	Nov 2020	Dec	Jan	Feb	Mar	April	May	Jun	July	Aug	Sept	Oct	Nov 2021
Proposal development	■	■	■	■									
ERC approval				■	■	■							
Data collection							■	■	■				
Data analysis										■	■		
Dissertation Write Up											■	■	
Data presentation													■

STUDY BUDGET

Category	Remarks	Units	Unit cost (Kshs)	Total (Kshs)
Proposal Development	Printing drafts	500 pages	5	2500
	Proposal copies	10	350	3500
Data Collection	Stationery packs (pens, paper and study definitions)	20	100	2000
	Research assistants	3	8000	24000
	Bone biochemistry	80	400	32000
	Chest x-ray	80	1000	80000
	ECHO	80	0	0
Data Analysis	Statistician	1		25,000
Thesis Write Up	Printing drafts	500pages	5	2500
	Printing thesis	10 copies	500	5000
Contingency Funds				10000
Total				**186,500**

Appendix I (a): Consent Form for Participation in the Study (English Version)

Study title: Clinical conditions and in hospital outcomes found in children readmitted due to pneumonia at Kenyatta National hospital

Name of the researcher: Dr Anita Mugambi

Supervisors: Dr Beatrice Mutai, Prof Ezekiel Wafula and Dr Diana Marangu

University of Nairobi department of Paediatrics and Child health, contacts 0204915046

I am a postgraduate student at **University of Nairobi pursuing Master of Medicine degree in Paediatrics and Child health**

I am conducting a study on clinical conditions and In hospital outcomes found in children readmitted due to pneumonia at Kenyatta National Hospital. The purpose of this consent confirmation, is to give you information that you will need to help you decide whether or not your child should participate in the study.

Pneumonia in children is a major cause of readmissions which are very expensive and affect the quality of life of the child affected your participation in this study will help determine the common clinical conditions leading to readmissions in order to come up with strategies that improve care and treatment

If you agree for your child to participate in the study, I shall ask you a few questions concerning his health examine the child and record the findings. I shall also include any X-rays or scans of your child in the study. A scan will be performed to check for any cardiac abnormalities at no added cost. To protect your child's privacy, I shall not include his / her names.

Kindly understand the following: -

Participation is voluntary.

Confidentiality shall be maintained at all times. We shall use a code number to identify your child in a password-protected computer database and will keep all of our paper records in a locked file cabinet.

Refusal of any participation in the study will not attract any penalties. Your child shall continue to receive treatment as required.

Risks: there are minimal risks in participating in this study. All the procedures that shall be done shall not induce any physical pain and there shall be no pricking.

Benefits: Any child found to have been readmitted due to pneumonia in the study shall be managed and closely followed up. There is no monetary compensation for participating in this study.

If you have further questions or concerns about your child participating in this study, please call or send a text message to the study staff on **0729202691**. For more information about your child's rights as a research participant, you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. **2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.**

Your decision to have your child participate in this research is voluntary. You are free to decline or withdraw participation of your child in the study at any time without injustice or loss of benefits (Just inform the study staff and the participation of your child in the study shall be stopped). You do not have to give reasons for withdrawing your child if you do not wish to do so. Withdrawal of your child from the study will not affect the services your child is otherwise entitled to in this health facility or other health facilities.

Consent Form (Statement of Consent)

The person being considered for this study is unable to consent for him/herself because he or she is a minor (a person less than 18 years of age). You are being asked to give your permission to include your child in this study.

Parent/guardian statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered by him or her in a language that I understand. The risks and benefits have been explained to me. I understand that I shall be given a copy of this consent form after signing it. I understand that my participation and that of my child in this study is voluntary and that I may choose to withdraw it any time. I understand that all efforts shall be made to keep information regarding me and my child's personal identity confidential. By signing this consent form, I have not given up my child's legal rights as a participant in this research study.

I voluntarily agree to my child's participation in this research study: Yes   No

I agree to have my child undergo physical measurements for malnutrition: Yes   No

I agree to provide contact information for follow-up: Yes   No

 Parent/Guardian signature /Thumb stamp: _____

Date _____

Parent/Guardian printed name: _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given his/her consent.

Printed Name: _____ Date: _____

Signature: _____

Role in the study: _____

Witness   Printed   Name   _____

Signature:_____ Date; _____

Appendix I (b): Consent Form for Participation in the Study (Swahili Version)

Idhini ya Kushirikishwa Katika Utafiti

KIFANI YA CHEO: HALI YA CLINIKI NA MATOKEO YAKE BAADA YA KULAZWA KUPATIKANA KWA WATOTO AMBAO WAMELAZWA KUTOKANA NA HOMA YA MAPAFU KATIKA HOSPITALI KUU YA KITAIFA KENYATTA.

JINA LA MTAFITI: DR ANITA MUGAMBI

Mimi ni mwanafunzi mmoja wa uzamili katika chuo kikuu cha Nairobi kutafuta bwana ya dawa za shahada katika Paediatrics na afya ya mtoto.

Nafanya utafiti juu ya hali ya kliniki na mambo ya hatari kupatikana kwa watoto imejiunga tena kutokana na homa ya mapafu katika hospitali ya kitaifa ya Kenyatta. Madhumuni ya hii kuthibitisha ridhaa ni kukupa habari kwamba unahitaji kutusaidia kuamua kama mtoto wako anaweza shiriki katika utafiti.

Nimonia kwa watoto ni sababu kubwa ya readmissions ambazo ni ghali sana na kuathiri ubora wa maisha ya mtoto walioathirika ushiriki wako katika utafiti huu utasaidia kujua mambo ya msingi chanzo kikuu kwa readmissions ili kuja na mikakati ya kuboresha huduma za matibabu.

Ukikubali mtoto wako kushiriki katika utafiti, mimi kuuliza maswali machache kuhusu afya yake, kuchunguza mtoto na kurekodi matokeo. Mimi pia ni pamoja na yoyote eksirei au nakala za mtoto wako katika utafiti. Scan utatekelezwa kuangalia kwa upungufu wowote wa moyo bila gharama aliongeza. Kulinda faragha ya mtoto wako, mimi ni pamoja yake / majina yake.

Tafadhali kuelewa yafuatayo: -

Ushiriki ni hiari.

Usiri itakuwa iimarishwe wakati wote. Tutakuwa na idadi code kwa kutambua mtoto wako katika nywila ili kulinda database Kompyuta na kushika yote ya kumbukumbu zetu karatasi katika baraza la mawaziri imefungwa file.

Kukataa ushiriki yoyote katika utafiti si kuvutia adhabu yoyote. Mtoto wako yataendelea kupata matibabu kama inavyotakiwa.

Hatari: kuna hatari ndogo ya kushiriki katika utafiti huu. taratibu zote yatakayotendeka wala kushawishi maumivu yoyote ya mwili na hautakuwa na mchomo.

Faida: Mtoto yeyote kupatikana kuwa imejiunga tena kutokana na homa ya mapafu katika uchunguzi itakuwa imeweza na karibu ikifuatiwa. Hakuna fidia ya fedha kwa ajili ya kushiriki katika utafiti huu. Kama una maswali au wasiwasi juu ya mtoto wako kushiriki katika utafiti huu, tafadhali piga simu au kutuma ujumbe wa maandishi kwa wafanyakazi Utafiti kuhusu **0729202691**. Kwa maelezo zaidi kuhusu haki za mtoto wako kama mshiriki wa utafiti, unaweza kuwasiliana na Katibu / Mwenyekiti, Kenyatta National Hospital-Chuo Kikuu cha

Nairobi Maadili na Kamati ya Utafiti Namba **No. 2726300 Ext. 44102** email **uonknh_erc@uonbi.ac.ke**.

Uamuzi wako wa kuwa na mtoto wako kushiriki katika utafiti huu ni ya hiari. Wewe ni bure kwa kushuka au kuondoa ushiriki wa mtoto wako katika utafiti wakati wowote bila udhalimu au hasara ya faida (Just taarifa wafanyakazi utafiti na ushiriki wa mtoto wako katika utafiti itakuwa kusimamishwa). Si lazima kutoa sababu za kujiondoa mtoto wako kama huna unataka kufanya hivyo. Kuondolewa kwa mtoto wako ya utafiti hakutaathiri huduma mtoto wako vinginevyo haki ya katika kituo hiki cha afya au hospitali nyingine.

Fomu ya Idhini (Maelezo ya Makubaliano):

Mtu kuhesabiwa kwa utafiti huu hawezi kukubali kwa ajili yake / mwenyewe kwa sababu yeye ni ndogo (mtu chini ya miaka 18 ya umri). Wewe ni ya kuulizwa kutoa ruhusa ya pamoja ya mtoto wako katika utafiti huu.

Mzazi / mlezi taarifa:

Nimesoma fomu hii ya idhini au alikuwa habari kusoma na mimi. Mimi alikuwa na nafasi ya kujadili utafiti huu na mshauri utafiti. Mimi kuwa na maswali yangu kujibiwa na kwake katika lugha hiyo mimi kuelewa. hatari na faida kuwa alielezea kwangu. Ninaelewa kwamba watapewa nakala ya fomu hii ya idhini baada ya kusaini yake. Naelewa kwamba ushiriki wangu na ule wa mtoto wangu katika utafiti huu ni wa hiari na nipate kuchagua kujiondoa wakati wowote. Naelewa kwamba juhudi zote zitafanywa ili kuweka maelezo kuhusu mimi na utambulisho binafsi mtoto wangu siri. Kwa kuingia fomu hii ya idhini, hawajakata haki za kisheria mtoto wangu kama mshiriki katika utafiti huu utafiti. hiari kukubali ushiriki mtoto wangu katika utafiti huu: Ndio   La

nakubaliana kuwa na mtoto wangu kupitia vipimo kimwili utapiamlo: Ndio   La

nakubaliana na kutoa taarifa za mawasiliano ya kufuatilia: Ndio   La

Jina la mzazi _____ _____

 sahihi ya mzazi_____

Tarehe

Kauli ya mtafiti

Taarifa Mtafiti, aliyetia, na kikamilifu alielezea maelezo husika ya utafiti huu utafiti kwa mshiriki iliyotajwa hapo juu na kuamini kuwa mshiriki umeelewa na ina kwa kujua kutokana wake / ridhaa yake.

 Jina la mtafiti _____ Tarehe: _____

Sahihi: _____

jina la shahidi_____

Tarehe_____

Sahihi ya shahidi_____

Appendix II: Questionnaire

"Clinical Conditions and Outcomes Found in Children Readmitted Due to Pneumonia at KNH".

RESEARCHER: DR ANITA MUGAMBI

STUDY ID NO.——————————

DATE OF INTERVIEW ————————————

Part 1a: patient details

1. Date of Birth ——————   Age ———————————

2. Gender: a) MALE —————— b) FEMALE ————————

3. Date of previous admission ————————

4. Diagnosis at previous admission ————————

5. Discharge summary of previous admission

   Yes [   ]   No [   ]

6. What are the presenting complains?

Presenting complains   duration (in days)

a)

b)

c)

d)

7. Which of the following general examination findings are present in this patient?

Pallor   [   ]   Jaundice   [   ]

Cyanosis   [   ]   Finger Clubbing   [   ]

Lymphadenopathy [   ]   Dehydration   [   ]

8. Fill in the anthropometric measurements below

   Height/length (cm) ————————

   Weight (kg) ——————————

   Calculated BMI (kg/m^2)——————————

   MUAC (mm) ——————————

9. Nutritional status

WHZ ——————   WAZ ———————   BMI for age Z score ——————————

   HAZ ——————————

10. **VITALS**

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Respiratory rate(breaths/min)   pulse rate(beats/min)   temperature(°C)   Spo2(%)

11. What clinical findings are seen on examination of the patient?

a) Respiratory examination findings

b) Cardiovascular examination findings

a) c)Abdominal examination findings

b) d)Neurologic examination findings

PART 1b: CLINICAL DIAGNOSIS

1) ASTHMA

1) Which of the following symptoms are present in this patient (circle the appropriate answer)

a) Wheeze   YES,   NO   DURATION

b) Cough   YES,   NO   DURATION

c) DIB   YES,   NO   DURATION

2) Is the wheeze worsened by any of the following?

a) Exercise   YES   NO

b) Laughing   YES   NO

c) Crying   YES   NO

d) Early morning/late in the evening   YES   NO

3. Is there any history of allergy in the family (1st degree relatives) YES   NO

4. Does the child have recurrent episodes of running nose   YES   NO

5. Have you noted any rashes on the skin   YES   NO

6. Does the child have dry skin   YES   NO

7. Does the child have itchiness on the skin   YES   NO

8. Has the child ever used an inhaler   YES   NO

If the answer is yes, for how long and what type of inhaler was used

Duration ⎯⎯⎯⎯⎯

Type of inhaler   SABA   ICS   LABA

9. Do the symptoms mentioned in question 1 improve after use of the inhaler?   YES   NO

2) CONGENITAL HEART DISEASE

1) How often does the child feed during the day   _____
2) Have you noted any difficulty during feeds   YES   NO
3) Does the child get tired during feeds   YES   NO
4) Does the child have any obvious anomalies   YES   NO
5) Is there failure to thrive   YES   NO
6) Is there central cyanosis   YES   NO
7) How long does the cyanosis last?   _____

3) GERD   (circle the appropriate score)

1) How often does the baby vomit?   **Score**

   A) 1-3 times   1

   b)3-5 times   2

   c)> 5times   3

2) How much does the baby usually vomit?

a) 1 teaspoon – 1 table spoon   1
b) 1 tablespoon-1 ounce   2
c) > 1 ounce   3

3) Does the baby appear uncomfortable after vomiting?   2

4) Does the baby have refusal to feed?   1

5) Does the baby have poor weight gain   1

6) Does the baby cry a lot during or after feeds?   3

7) Does the baby cry more than usual?   1

8) How many hours does the baby cry or fuss each day

a) 1-3 hours   1
b) > 3hours   2

9) Do you think the baby hiccups more than most babies?   1

10) Does the baby have spells of arching back?   2

11) Has the baby ever stopped breathing while awake and struggling to breathe or turn blue or purple?   6

Total score   _____

4) Aspiration

(Circle the correct option)

1) Does the child have GERD based on the questions above?   YES   NO

2) Is there history of recurrent cough /wheeze for >3weeks?   YES   NO

3) Does the child have difficulty swallowing?   YES   NO

4) Does the child have any of the following signs during feeds?

a) Cough   YES   NO

b) Choking   YES   NO

c) Apnoea   YES   NO

d) Cyanosis   YES   NO

5) Are there any obvious gross anomalies?   YES   NO

   If yes specify _____

6) Does the child have Neuromuscular, neurologic disorders, developmental delay? If yes indicate below   _____

5) PITC

(Circle the correct option)

a) Reactive   b) Non-reactive

6) RICKETS

(Circle the correct option)

a) Is there history of delayed milestones?   YES   NO

b) Is there failure to thrive   YES   NO

c) Are any of the following features present on examination?

1) Craniotabes   YES   NO

2) Frontal/parietal bossing   YES   NO

3) Delayed closure of fontanelles   YES   NO

4) Bow legs   YES   NO

5) Harrison sulcus   YES   NO

6) Rachitic rosary   YES   NO

7) Spine deformity   YES   NO

7) List the possible clinical conditions suspected in this patient

a)

b)

c)

8) OUTCOMES

1) Date of Admission   _____

2) Date of Discharge   _____

3) Date of Death   _____

PART 2: INVESTIGATIONS AND RADIOLOGICAL FINDINGS

(For researcher only)

1) Bone Biochemistry

a) Alkaline phosphatase levels   b) calcium levels   c) phosphate levels

2) HIV

a) Age > 18months- antibody test   Reactive   Non-reactive

b) Age < 18months- HIV PCR   Reactive   Non-reactive

3) Chest x-ray findings

4) Echo findings

a) Structural heart disease   YES   NO

b) Pulmonary pressures(mmhg)

5) Contrast study (if available)

6) Endoscopy (if available)

Appendix III: Height/Length Measurement

Adapted From MOH Kenya IMAM Guidelines (2009)(64)

Children less than age 2 years

1. The measuring board is placed on the ground.

2. The child is placed lying down along the middle of the board.

3. The assistant holds the sides of the child's head and positions the head until it firmly touches the fixed headboard with the hair compressed.

4. The measurer places her hands on the child's legs, gently stretches the child and then keeps one hand on the thighs to prevent flexion.

5. While positioning the child's legs, the sliding foot-plate is pushed firmly against the bottom of the child's feet.

6. To read the height measurement, the foot-plate must be perpendicular to the axis of the board and vertical.

7. The height is read to the nearest 0.1cm

Children ≥2 years

1. The measuring board is fixed upright on level ground.

2. The child stands, upright against the middle of the measuring board.

3. The child's head, shoulders, buttocks, knees, and heels are held against the board by the assistant

4. The measurer positions the head and the cursor.

5. The height is read to the nearest 0.1 cm

6. Measurement is recorded immediately

Appendix IV: Weight Measurement

Adapted from Mutua (2011)

1. A bathroom weighing scale shall be used

2. Calibration to zero shall be done every day and checking against a known 10kg weight

3. A child stands on the scale and the measurement taken.

4. The measurer shall make the reading perpendicular to the pointer to the nearest 0.1 kg

5. For children unable to stand, the guardian shall be weighed holding the child and his/her weight subtracted from the total weight to get the child's weight

6. Two readings shall be made and an average of the two taken

Appendix V: MUAC Measurement

Adapted from Mutua (2011)

1. An arm circumference tape shall be used

2. A child shall sit on a stool or stand upright with the non-dominant arm dropped down and flexed at right angle at the elbow.

3. The shoulder tip (acromion) and elbow tip (radial tuberosity) shall be identified

4. The tape shall be placed from the tip of the shoulder to the elbow and the length noted and the midpoint thereby determined and marked

5. The arm circumference tape shall be applied round the arm at the marked point.

6. The reading is made and recorded in millimetres

Appendix VI: Who Z-Score Charts

BMI-for-age GIRLS
Birth to 5 years (z-scores)

World Health Organization
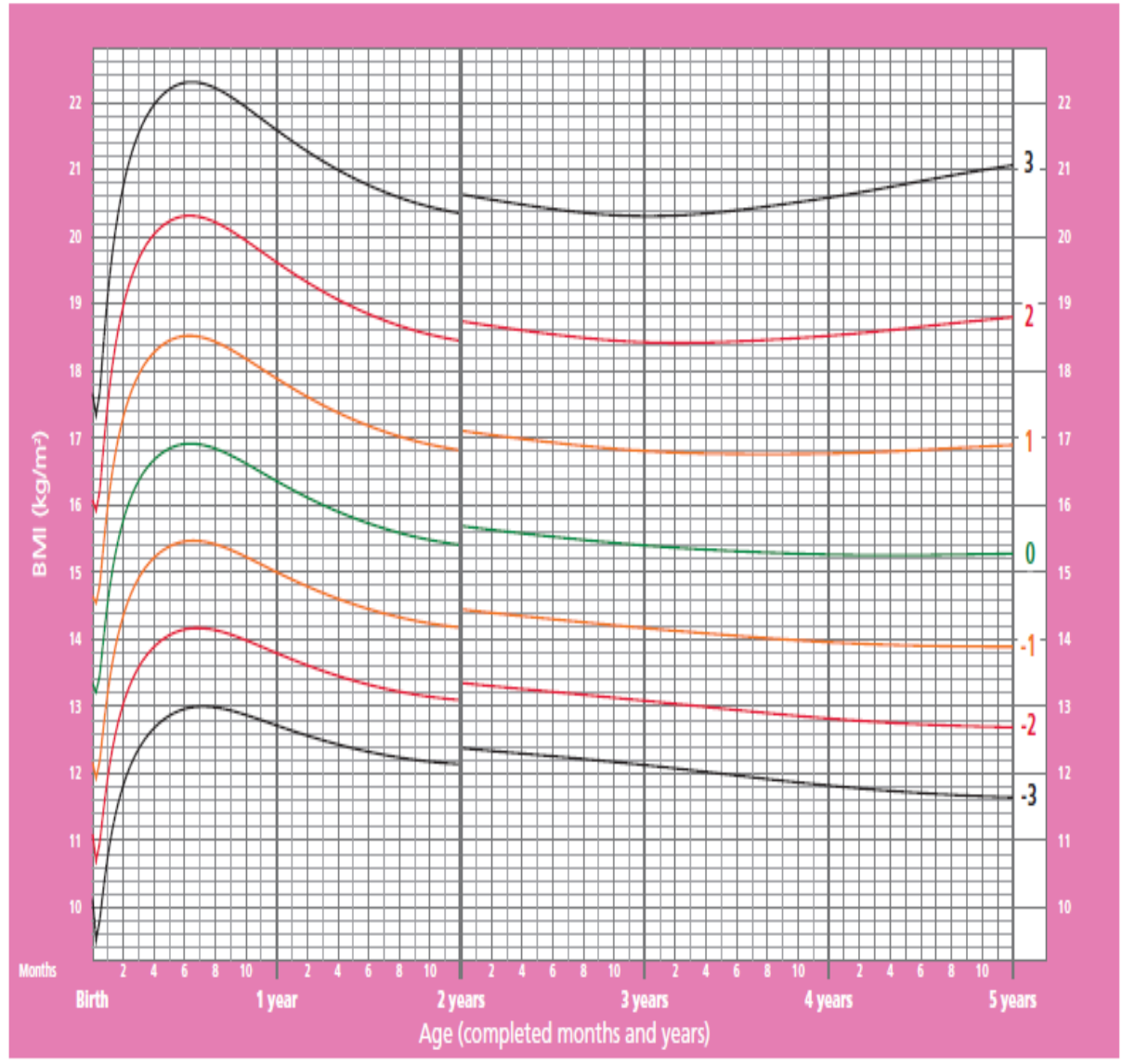
WHO Child Growth Standards

BMI-for-age BOYS

5 to 19 years (z-scores)

World Health Organization

2007 WHO Reference

68

BMI-for-age GIRLS

5 to 19 years (z-scores)

World Health
Organization
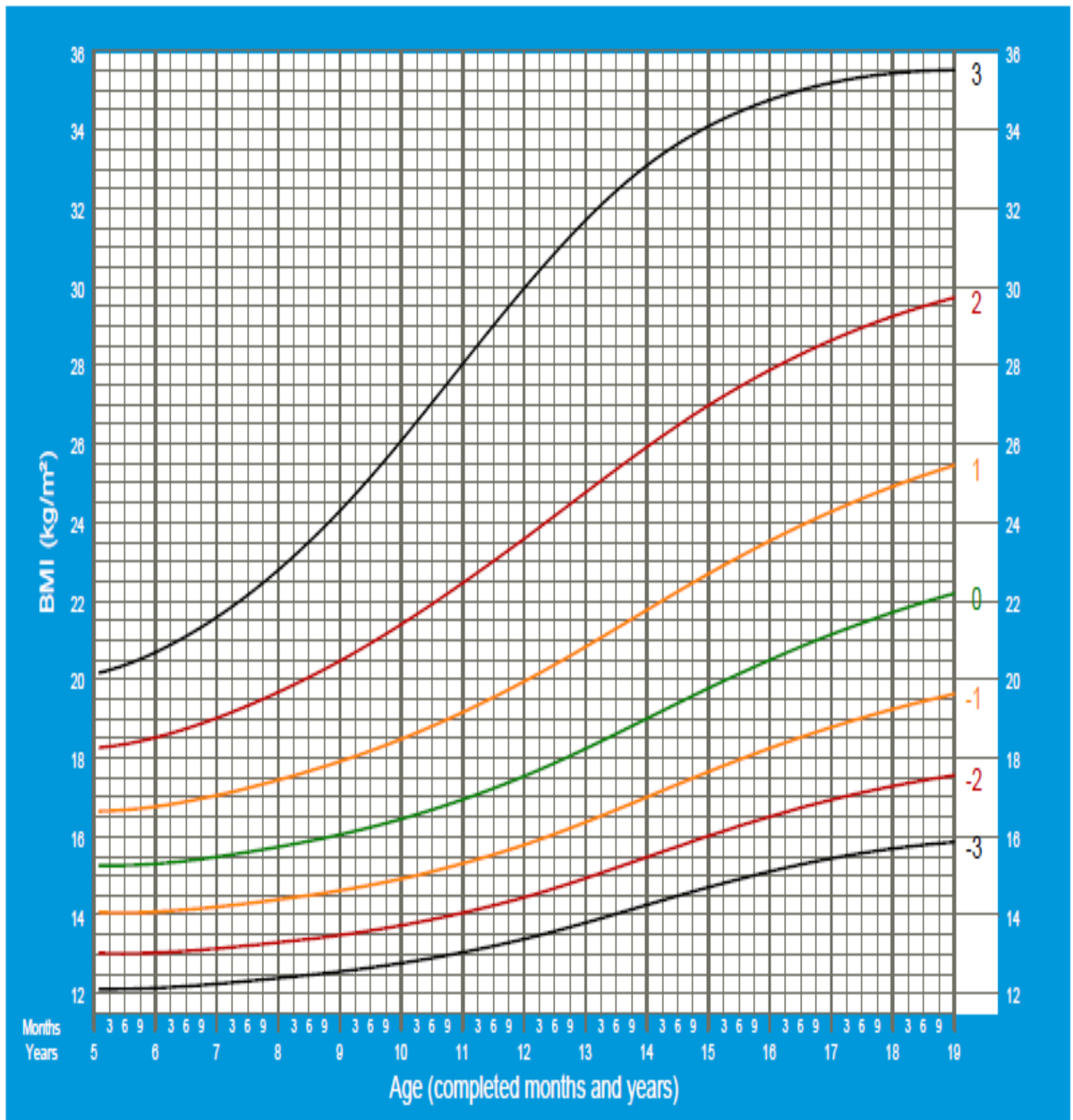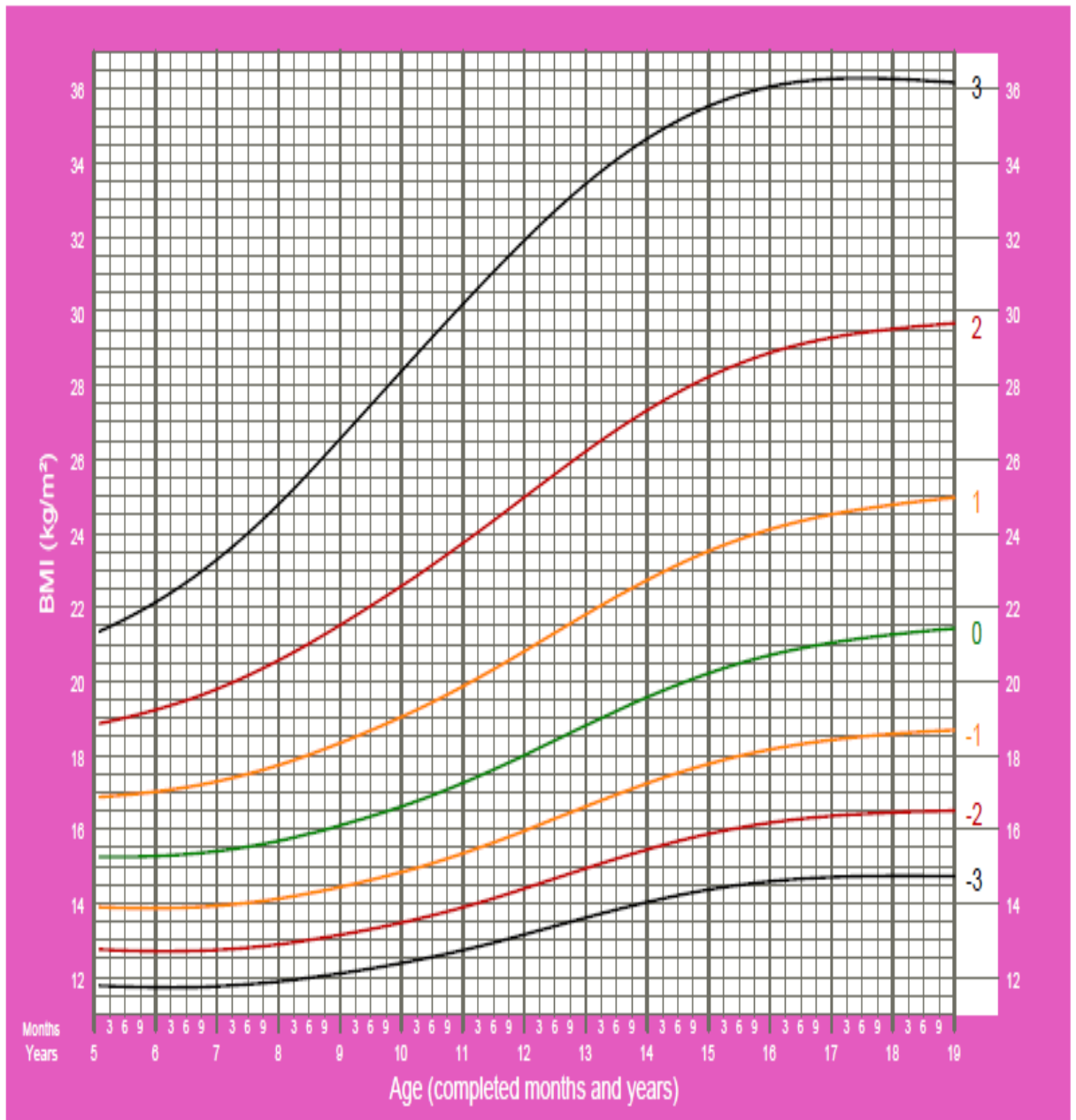
2007 WHO Reference

Length/height-for-age BOYS
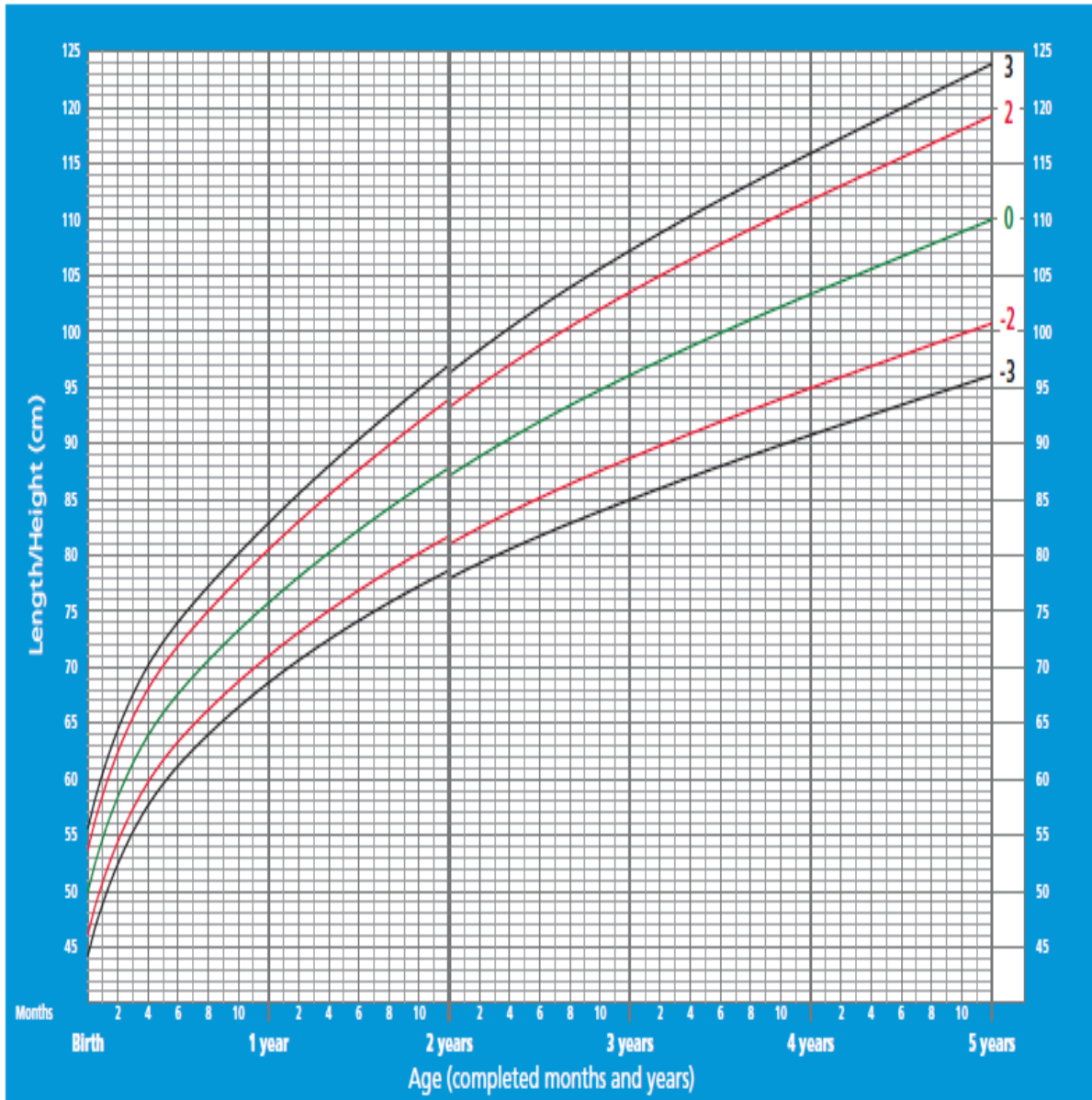
Birth to 5 years (z-scores)

World Health
Organization

WHO Child Growth Standards

70

Length/height-for-age GIRLS

Birth to 5 years (z-scores)

World Health Organization
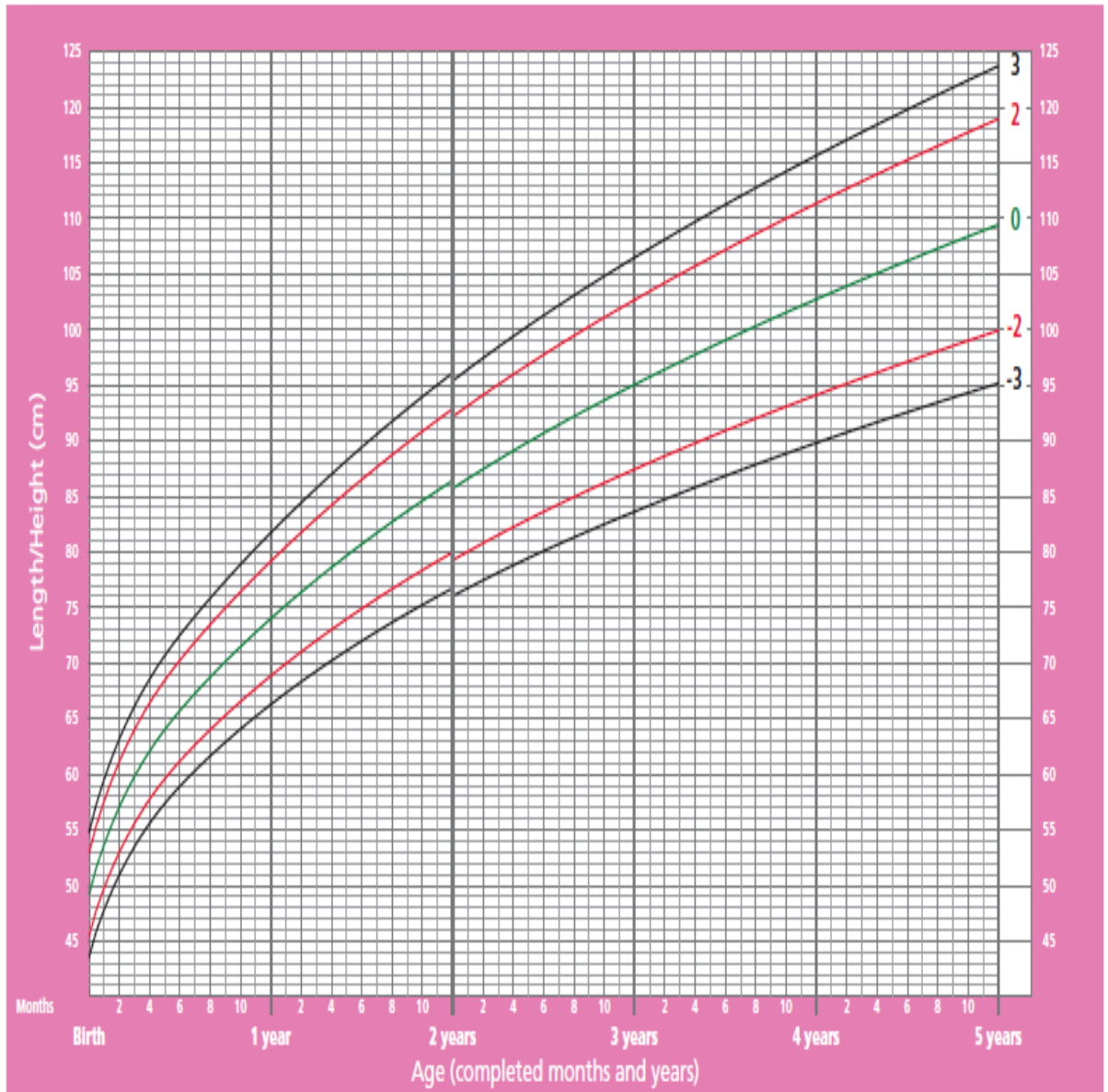
WHO Child Growth Standards

Height-for-age BOYS

5 to 19 years (z-scores)
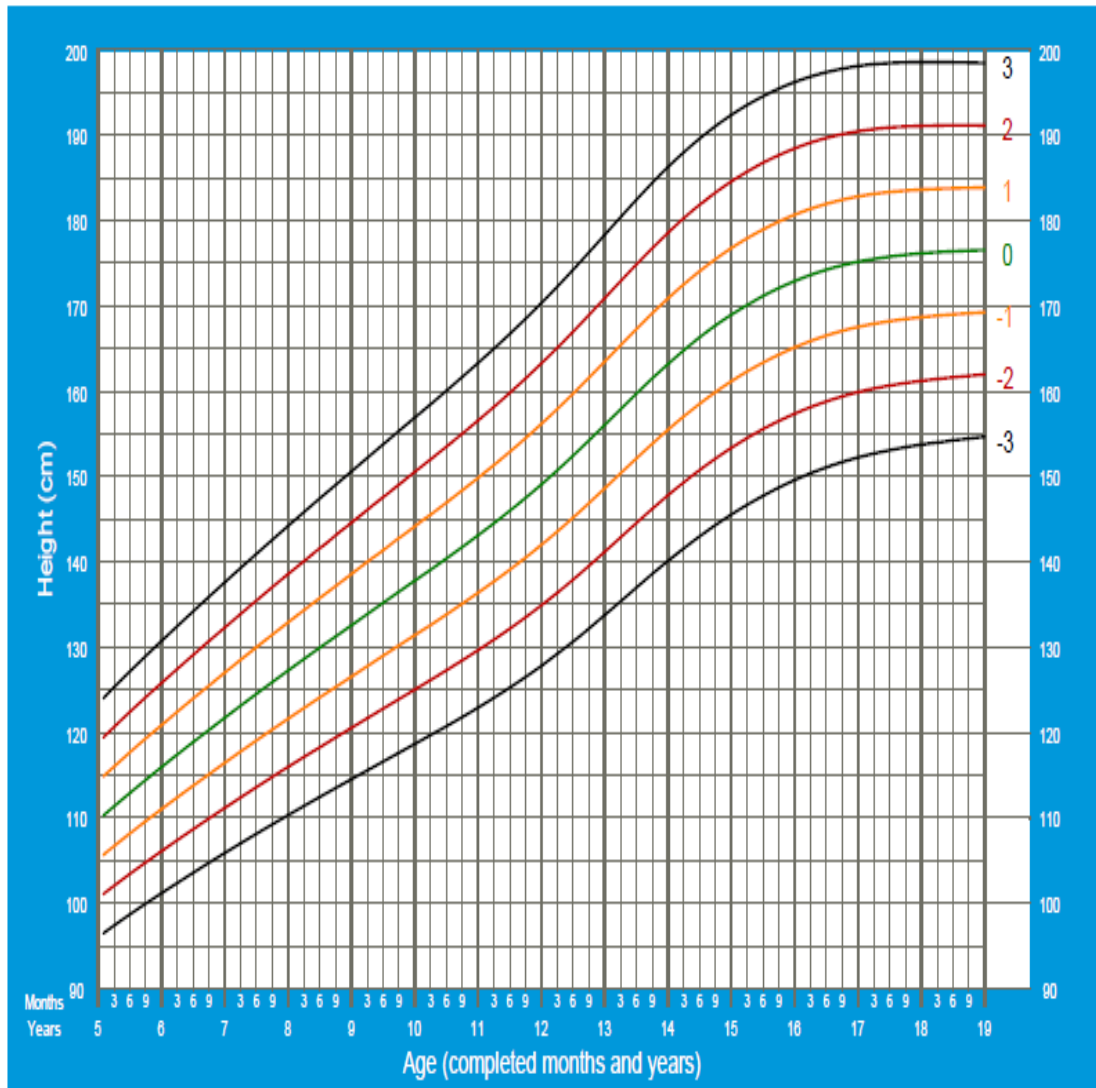
World Health Organization

2007 WHO Reference

72

Height-for-age GIRLS

5 to 19 years (z-scores)

World Health Organization

2007 WHO Reference

73
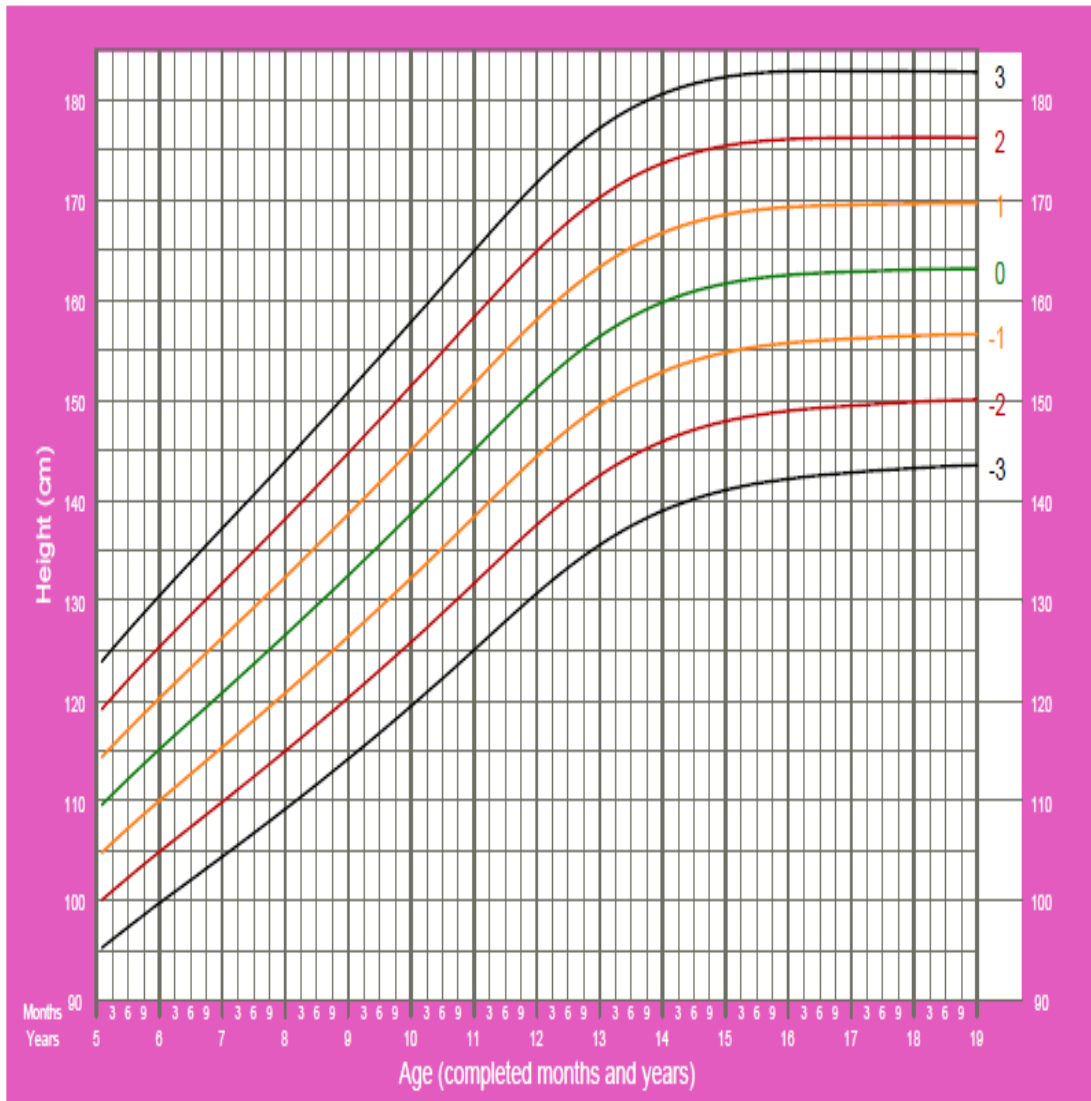
Weight-for-length/height BOYS

Birth to 5 years (z-scores)

World Health
Organization

WHO Child Growth Standards

74
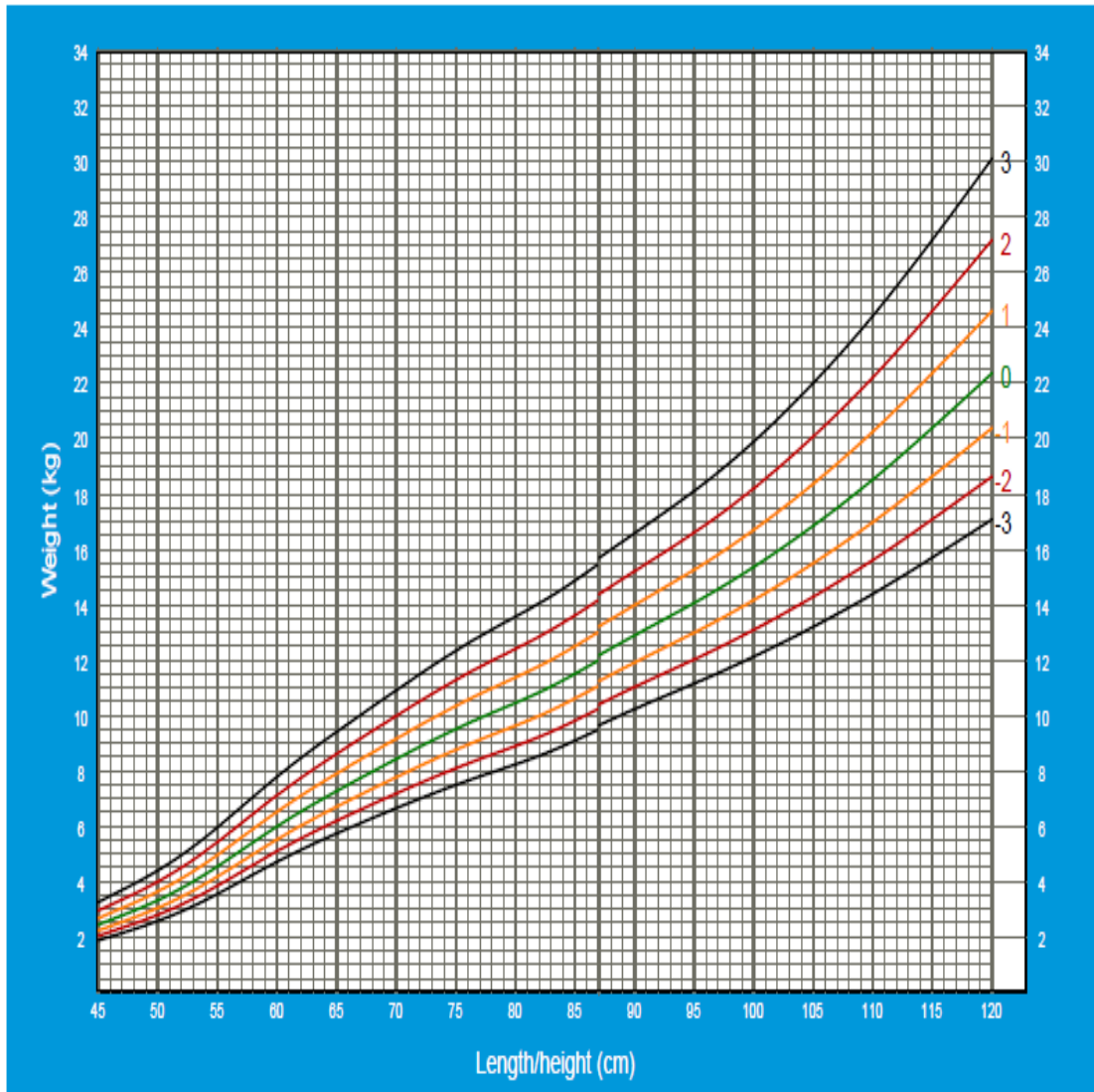
Weight-for-length/height GIRLS

Birth to 5 years (z-scores)

World Health
Organization

WHO Child Growth Standards

Weight-for-age BOYS
Birth to 5 years (z-scores)

World Health Organization
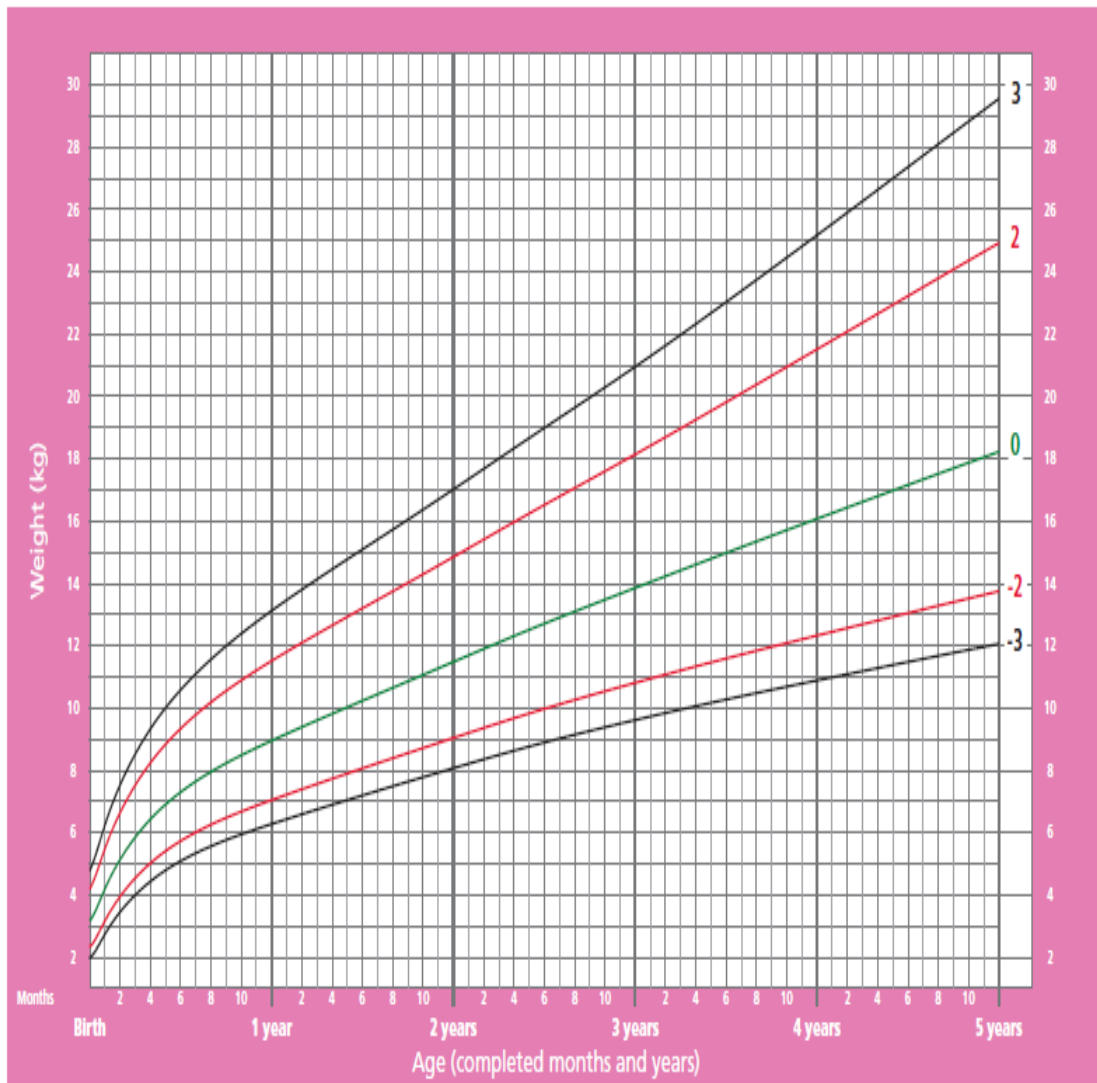

WHO Child Growth Standards

Weight-for-age GIRLS

Birth to 5 years (z-scores)

World Health Organization

WHO Child Growth Standards