INFLUENCE OF COMORBIDITIES ON OUTCOME OF SEVERE PNEUMONIA AMONG CHILDREN AGED 2-59 MONTHS ADMITTED IN BONDO SUB COUNTY HOSPITAL PAEDIATRIC WARD

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DECLARATION

I declare that this thesis is my original work and it has not been presented for examination in any other University.

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Supervisor's Declaration

We confirm that the work presented on this thesis was conducted by the student under our supervision as University supervisors

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DEDICATION

I dedicate this work to my wife and daughters to honour them for the misery they went through during my studies, without complains.

ACKNOWLEDGEMENT

I would like to take this opportunity to sincerely acknowledge all who contributed in making this thesis a success. First of all, I would like to thank the almighty God for the gift of life and good health throughout the period of my study. My special thanks go to my supervisors Professor George Ayodo and Dr. Shehu Shangari (PhD) for their guidance, advice, encouragement and tireless support during the whole process. Much thanks go to the medical superintendent Bondo sub county hospital Dr. Michael Oduor and the health records manager Mrs. Millicent for the support during data collection process. Finally, I would like to appreciate the clinical medicine students of KMTC bondo campus March 2019 class who participated in data collection as research assistants. May God bless all abundantly.

ABBREVIATION/ACRONYMS

AIDS	-	Acquired immunodeficiency syndrome
ARI	-	Acute respiratory infection
CAP	-	Community acquired pneumonia
COPD	-	Chronic Obstructive Pulmonary Disease
HAART	-	Highly Active Antiretroviral Therapy
HAP	-	Hospital Acquired Pneumonia
HEU	-	HIV Exposed Uninfected
HIV	-	Human immunodeficiency virus
I.M	-	Intramuscular
I.V	-	Intravascular
IMCI	-	Integrated management of childhood illnesses
IPD	-	Invasive Pneumococcal Disease
JOOUST	-	Jaramogi Oginga Odinga University Of science and technology
KDHS	-	Kenya Demographic Health Survey
KEMRI	-	Kenya Medical Research Institute
LMIC	-	Low and Middle Income Countries
MUAC	-	mid upper arm circumference
PEM	-	Protein Energy malnutrition
RTI	-	respiratory tract infection
SAM	-	Severe acute malnutrition
SCD	-	Sickle Cell Disease
VAP	-	Ventilation Acquired Pneumonia
WHO	-	World health organization

OPERATIONAL DEFINITION OF TERMS

Comorbidity: The conditions that co-occur or happen concurrently with pneumonia condition

HIV Exposure: Children aged zero to eighteen months, born to HIV positive mothers who have a negative HIV PCR test.

HIV Infected: children aged eighteen months and above with a positive HIV antibody test.

Malaria: Children admitted to the ward with a positive blood slide test for malaria Parasites.

Outcome: The final event following admission with severe pneumonia. In this context can be either discharge alive or dead.

Severe Pneumonia: A child admitted with a history of cough or difficulty in breathing and any danger sign e.g oxygen saturation <90%, Cyanosis, Inability to drink or breast feed, grunting and altered level of consciousness (AVPU<A).

ABSTRACT

Severe pneumonia is defined by a history of cough or difficulty in breathing and any danger sign like; oxygen saturation <90%, Cyanosis, Inability to drink or breast feed, grunting and altered level of consciousness (World Health Organization, 2019). Pneumonia is the leading infectious cause of death among children worldwide. 740,180 children under the age of five died from severe pneumonia in the year 2019, accounting for 14% of all pediatric fatalities among this age group and 22% of all deaths among children aged 1 to 5 years. More than 95% of all new cases of pneumonia in children less than 5 years occur in developing countries due to the increased prevalence of undernutrition. Studies have shown that severe acute malnutrition is an independent predictor of mortality in patients of severe pneumonia, this can be used to identify cases at increased risk of mortality among this group and measures taken to reduce the cases of severe acute malnutrition will further decrease the mortality. Clinical and epidemiological studies reported evidence that maternal HIV infection can deeply affect the maternal/fetal unit, interfering with the immunomodulatory factors which shape immune maturation in fetuses. This puts HIV exposed uninfected children at risk of severe infections like severe pneumonia. Other comorbidities such as sickle cell disease also puts a child at risk of developing severe infections caused by encapsulated organisms like pneumococcal organism due to auto-splenectomy. The role of HIV infection as a comorbidity leading to immunodeficiency cannot be underestimated in children with severe pneumonia. The specific objectives of this study were to determine the prevalence of comorbidities related to severe pneumonia among children aged 2-59 months admitted in Bondo sub county hospital, to determine the outcome of severe pneumonia with specific comorbidities among children aged 2-59 months admitted in Bondo sub county hospital and to determine the influence of nutritional status on outcome of severe pneumonia with specific comorbidities among children aged 2-59 months admitted in Bondo sub county hospital. 141 children of either gender from 2– 59 months of age with the clinical diagnosis of severe pneumonia, made according to integrated management of childhood illnesses (IMCI) guidelines were recruited into the study. The study employed a retrospective cross-sectional study design where secondary data was extracted from the inpatient files of those admitted as from July 2017 to June 2019. The study employed a systematic sampling technique. The samples size was 141 and data was collected using a structured observation checklist from within a period of two months after obtaining ethical approval for the study. Data was analyzed using descriptive and inferential statistics in the statistical package for the social sciences V24 (SPSS V24). The findings showed that 44.7% (63/141) of the children had severe pneumonia and at least one comorbidity. It was further noted that a child admitted to the hospital with severe pneumonia and comorbidity had six times increased risk of death compared to a child with severe pneumonia only [OR 6.06 (1.32-27.78) P value 0.02]. Specifically, there is four times increased risk of death among HIV-exposed uninfected children [OR 3.92 95% CI (1.18-13.04) P = 0.026] and the risk of death increased six times when the child was both HIV-exposed uninfected and malnourished [OR 6.02 95% CI (1.61-22.58) P = 0.008]. Therefore, the study concludes that there is a significant influence of nutritional status on the outcome of severe pneumonia and rejects the null hypothesis. The findings of this study would inform policy makers on the need to review pneumococcal pneumonia immunization schedule among children with severe acute malnutrition and their HIV exposed uninfected counterparts. It therefore recommends that health care providers should intensively examine children with malnutrition and HIV exposed uninfected (HEU) so as to rule out pneumonia or detect it early enough before it gets severe. Lastly, community health volunteers should be empowered with knowledge on nutritional counseling of the community members to reduce the burden of malnutrition among these children at the household level.

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CHAPTER ONE
INTRODUCTION

1.1 Background of the Study

Severe pneumonia is defined by a history of cough or difficulty in breathing and any danger sign like; oxygen saturation <90%, Cyanosis, Inability to drink or breast feed, grunting and altered level of consciousness (World Health Organization, 2019). According to the World Health Organization (WHO) (2022), pneumonia is the leading infectious killer of children globally. 740,180 children under the age of 5 died from pneumonia in 2019, accounting for 14% of all pediatric fatalities among this age group and 22% of all deaths among children aged 1 to 5 years. The report further stated that pneumonia affects children and families everywhere, but the number of deaths is highest in southern Asia and sub-Saharan Africa. As observed by Zhang *et al.*, (2016) pneumonia can be prevented with simple interventions and treated with affordable, low-tech medication and care. Pneumonia with comorbidities is common, and many factors determine whether contact with an etiologic agent will result in a severe episode of pneumonia and whether the episode will be fatal (Tuti *et al*., 2017). These factors can be related to the child (eg. age, sex, and underlying diseases), disease (eg. type of infection), environment, family and its socioeconomic status, or health system and type of care (Sonego *et al.*, 2015). A study by Goyal *et al.*, (2021) reported that on univariate analysis, younger age, male gender and low weight for height, were significant risk factors for pneumonia. On multivariate analysis, one-unit increase in age in months (OR = 0.97; 95% CI: 0.97–0.98) and weight for height z-score (OR = 0.76; 95% CI: 0.72–0.79) had a protective effect.

In the era prior to widespread pneumococcal vaccination, Babl and colleagues reported that children with asplenia, immunosuppression, human immunodeficiency virus (HIV) infection, nephrotic syndrome, and advanced liver disease had incidence rates of invasive pneumococcal disease (IPD) that were up to 100-fold greater than rates among children without these and other risk conditions in the same age group, likely reflecting a lack of effective host defenses (Pelton *et al.*, 2014). A study by Ladhani *et al.*, (2013) reported that children with malignancy, primary immunodeficiency, or HIV infection, and those receiving immunosuppressive treatment continue to be at high risk for IPD despite high rates of 7- valent pneumococcal conjugate vaccine (PCV7) uptake.

In low-income and middle-income countries (LMICs), childhood malnutrition is prevalent and increases the incidence and severity of illnesses like pneumonia (Kirolos *et al.*, 2021). Wiens *et al.,* (2013) posited that in addition to having an adverse effect on mortality, undernutrition makes pneumonia episodes more often and severe, potentially due to a secondary immunological disorder that has not been well characterized. According to Christi *et al.,* (2009) undernutrition in a child with severe pneumonia who needs to be hospitalized can also be linked to a reduced metabolic capacity to overcome the amplified physical and physiological demands of the illness, such as increased temperature, cardiac output, and work of breathing. They went on to argue that, as a consequence, the presence of severe acute malnutrition can raise pneumonia mortality by 15-fold, and that in a score of mortality risk among infants with pneumonia, extremely low weight-for-age and unwillingness to feed contributed as much as hypoxia. Williams *et al*., (2016) posited that severe acute malnutrition is an independent predictor of mortality in patients of severe pneumonia. This can be used to identify cases at increased risk of mortality and measures taken to reduce the cases of severe acute malnutrition would therefore further decrease the mortality. According to Ofulla *et al.,* (2016) various factors contribute to the high level of mortality rate among children suffering from pneumonia. The environmental factors, including the dry climatic condition affecting the ability of the patients to get a balanced diet and improve on their nutritional value. For children with HIV, pneumonia becomes one of the opportunistic conditions that affect their body.

There is an increasing level of identification of the children who are exposed to other pathogens, including the pneumonia pathogens among HIV infected children (Lanaspa *et al.*, 2015). In the developing nations, Bliss *et al.,* (2008) noted that the socio-economic conditions in the countries also contribute to the increased risk of people with HIV getting other diseases. They further argued that in cases where the comorbidity happens to be HIV, studies have shown that such children are 40 times more likely to get pneumonia than their HIV free counterparts are. Specifically, they are prone to infection by atypical organisms and antibiotic resistant strains.

Evans *et al.*, (2016) observed that previous clinical and epidemiological studies reported evidence that maternal HIV infection can deeply affect the maternal/fetal unit, interfering with the immunomodulatory factors which shape immune maturation in fetuses. This puts

HIV exposed uninfected children at risk of severe infections like severe pneumonia. Other comorbidities such as sickle cell disease also puts a child at risk of developing severe infections caused by encapsulated organisms like pneumococcal organism due to auto-splenectomy. The role of HIV infection as a comorbidity in children with severe pneumonia on the outcome cannot be underestimated (Goyal *et al.*, 2021).

1.2 Statement of the Problem

Despite being the leading cause of death in children under five years in the developing world, most countries are still lacking proper surveillance system for severe pneumonia (World Health Organization, 2019). There are efforts focused on the prevention and treatment of severe pneumonia and indeed, Kenya was among the first African countries to introduce and use Pneumococcal Conjugate Vaccine (PCV) in 2011 (KEMRI, 2020). However, other studies have shown that comorbidities are important risk factor for pneumonia episodes and, increasing the risk of pneumonia mortality significantly (Black, *et al.*, 2013). Little however has been done to understand and relate how the comorbidities influence the outcome of severe pneumonia among children aged less than five years. According to Dean *et al.*, (2016) the comorbidities and severe pneumonia-related cases were to blame for the increasing rates of admissions in the hospitals. They further identified pneumonic condition was as a leading cause of admissions to the hospitals with more than 18% of the total admissions attached to pneumonia and related diseases. Notably, the comorbidities and the associated conditions cause increased rates of hospitalizations and mortality rates in different countries.

Kabue *et al.*, (2016) observed that bondo region does not have enough trained personnel that assist in taking care of the patients with a full understanding of the role of comorbidities on the outcome of the disease. The area has high prevalence of sickle cell disease, malnutrition as well as adult HIV infection. This points towards a high number of HIV exposed uninfected children from HIV positive parents. Bondo sub county hospital being the referral hospital in bondo sub-county, records high numbers of children admitted with severe pneumonia. Indeed severe pneumonia is the second most common cause of hospital admission in the pediatric ward. There is limited data on the influence of these comorbidities on the outcome of severe pneumonia among children aged 2-59 months in bondo sub county hospital as well as the prevalence of each comorbidities. It is

against the backdrop of these challenges that the researcher aimed to study the influence of comorbidities on outcome of severe pneumonia among the children aged 2-59 months admitted in Bondo sub-county hospital.

1.3 Objectives

This study was defined by the following broad and specific objectives

1.3.1 Main Objective

To assess the influence of comorbidities on outcome of severe pneumonia among children aged 2-59 months admitted in Bondo sub-county hospital.

1.3.2 Specific Objectives

1. To determine the prevalence of comorbidities among children aged 2-59months admitted with severe pneumonia in Bondo sub-county hospital.
2. To determine the outcome of severe pneumonia among children aged 2-59 months with specific comorbidities admitted in Bondo sub county hospital.
3. To determine the influence of nutritional status on outcome of severe pneumonia among children aged 2-59 months with specific comorbidities admitted in Bondo sub county hospital.

1.4 Research Questions

1. What were the prevalence of comorbidities among children aged 2-59months admitted with severe pneumonia in Bondo sub-county hospital?
2. What were the outcome of severe pneumonia among children aged 2-59 months with specific comorbidities admitted in Bondo sub county hospital?
3. What were the influence of nutritional status on the outcome of severe pneumonia among children aged 2-59 months with specific comorbidities admitted in Bondo sub county hospital?

1.5 Justification

Bondo sub county hospital is located in Siaya County that has high prevalence of HIV infection and consequently a high prevalence of HIV exposed uninfected children. The

area is malaria endemic zone and therefore presents numerous cases of sickle cell disease. Finally the area experience little rainfall throughout the year and therefore the climatic condition doesn't support farming of diversified farm produce which eventually expose the families to malnutrition (KDHS, 2014). The study was informed by the need to classify the specific comorbidities related to severe pneumonia in children aged 2-59 months admitted in Bondo sub county hospital as well as to unearth the factors that contribute to severe pneumonia in these groups of children. Since there is limited information on prevalence of each comorbidity related to severe pneumonia in this group of children in bondo sub county hospital, the researcher intended to make it clear and also reveal the outcome of severe pneumonia among children with specific comorbidities. Lastly, limited studies have been conducted on the relationship between HIV exposed uninfected children and the outcome of severe pneumonia, therefore the study intended to add to the body of knowledge in relation to this topic.

1.6 Significance

The study findings provide a viable platform for informed and useful policy and operational decisions to improve and strengthen existing guidelines related to the management and prevention of severe pneumonia among children aged 2-59 months. The policy developers would use the study findings to review the pneumococcal immunization schedule for HIV exposed uninfected as well as malnourished children since they are at increased risk of developing severe pneumonia than their normal counterparts. The study also identified need for further research on antibiotics with better outcome on severe pneumonia with specific comorbidities among children aged 2-59months.

1.7 Limitations

Since the study employed retrospective cross sectional study using secondary data, the study was limited by the poor health record keeping in the context of the study area, this led to longer time taken to locate the in-patient files and retrieve them from the archives. To overcome this challenge the researcher prolonged the duration of data collection until when the desired sample size was achieved. Some of the inpatient files were missing important information on the outcome of severe pneumonia and therefore the researcher

traced the patients through phone call either to the caretaker or the area administrator before such participants were included into the study.

CHAPTER TWO
LITERATURE REVIEW

2.1 Introduction

This chapter presents literature review on current information on severe pneumonia related comorbidities, outcome of comorbidity related severe pneumonia and the influence of nutritional status on the outcome of severe pneumonia.

2.2. Comorbidities Related to Severe Pneumonia

There are several disease conditions (comorbidities) related to severe pneumonia. They either alter the ability of the body to fight the pneumonia causing organisms or put the body of an individual at increased risk of being infected by these organisms. Some of the comorbidities identified by Devine *et al.,* (2015) include but not limited to poor nutrition, poor oral hygiene, sedation, sickle cell disease, HIV infection/ exposure among others. The comorbidities related to pneumonia include the conditions that co-occur or happen concurrently with the pneumonia condition. A cohort study by Ngari *et al.,* (2017) among 4,184 Kenyan children <5 years admitted with severe pneumonia reported that 25% had severe acute malnutrition. As observed by Walson and Berkley (2018) it has become clear that whilst malnutrition results in increased incidence, severity and case fatality of common infections, risks continue beyond acute episodes resulting in significant postdischarge mortality .they further posited that a well established concept of a 'vicious-cycle' between nutrition and infection has now evolved to encompass dysbiosis and pathogen colonization as precursors to infection; enteric dysfunction constituting malabsorption, dysregulation of nutrients and metabolism, inflammation and bacterial translocation. All of these interact with a child's diet and environment.

In Ethiopia, nasopharyngeal carriage of *Streptococcus pneumonia* was assessed in 361 children at an outpatient clinic (Gebre *et al.*, 2017). Overall, 44% were colonized by *S. pneumoniae* (not serotyped, 18% multidrug resistant) and colonization was associated with the number of siblings in the household and presence of malnutrition defined by weight-for-age, capturing aspects of both wasting and stunting: adjusted odds ratio 2.1 [95% confidence interval (CI) 1.2–3.4]. In Venezuela, amongst 1064 children living in rural areas of the Orinoco Delta, S. *pneumoniae* colonization was (nonsignificantly on multivariable analysis) more common among stunted children (Verhagen *et al.*, 2017).

Previous studies have demonstrated a significantly lower concentration of IgG2 in HEU infants (22% lower levels compared to HIV unexposed uninfected (HUU) infants) and their lower representation out of the total IgG. In a study by Baroncelli *et al*., (2022) it was evident that although mothers had received Highly active antiretroviral therapy (HAART) for a median of 19 months, the level of IgG2 was comparable to the one observed in HEU infants born to mothers treated with short-term HAART. These findings suggest that the immunological functional defects due to HIV infection persist in women under continuous HAART and interfere with the delicate balance of the maternal–fetal unit. The lack of correlation between total IgG and IgG2 in the HEU population (but not in HUU) is suggestive of a selective impairment of IgG2 passage through the placenta in mothers living with HIV. The deficit of IgG2 has been associated with increased vulnerability to bacterial diseases especially those caused by encapsulated organisms like streptococcus pneumoniae which is the commonest cause of pneumonia. Contrasting results have been obtained in different studies on HEU infants: some reported reduction in transfer of specific antibodies against *H. influenzae*, diphtheria, pertussis, pneumococcus, measles, tetanus, and *Plasmodium falciparum* (*B*abakhanyan *et al.*, 2016). The study has also revealed a moderately high prevalence of pneumonia among children with sickle cell disease. This can be attributed to the fact that children with sickle cell disease undergo autospleenectomy which make them to be at high risk of developing infections caused by encapsulated organisms like streptococcus pneumoniae.

2.2.1 Pneumonia among HIV infected children

For children with HIV, pneumonia becomes one of the opportunistic conditions that affect their body. There is a rising level of identification of the children who are predisposed to other pathogens, including the pneumonia pathogens. In the developing nations, the socio-economic conditions in the countries also make portion of the reasons the people with HIV are more at risk of getting other diseases as observed by Lanaspa *et al.*, (2015). Other researchers have documented the vulnerability to which people with HIV can get respiratory pathogens. Having HIV is a risk factor for getting the pneumonia condition (Rabie & Goussard, 2016).

According to Iroh *et al*., (2018), whereas HIV infection is a well-known risk factor for mortality and morbidity in pneumonia, the role of HIV exposure, particularly its association with malnutrition, has been less explicated. Preidis *et al.*, (2011) observed that severe acute malnutrition predicted mortality in HIV-exposed Malawian children with

pneumonia (OR 5.1) more so than HIV-infected children (OR 2.2). HIV exposure was the strongest independent risk factor for severe pneumonia (incidence rate ratio 4.04) in a South African child health study in which no children were HIV-infected, and both HIV exposure and malnutrition were associated with an increased incidence of pneumonia (Le *et al.,* 2015).

A research looked into the relationship between HIV exposed-uninfected (HEU) status, malnutrition, and the risk of death in Ugandan children hospitalized with pneumonia. On univariate analysis, both HIV exposure and infection were associated with lower anthropometric indices, and in a multivariable model, mid-upper arm circumference was significantly associated with overall mortality (odds ratio (OR), 0.96). Overall mortality was associated with HIV infection (OR 5.0), but not with HEU status. Iroh *et al.,* (2018) opined that malnutrition may have a part in poor pneumonia outcomes in HIV-infected and HEU children who require hospitalization.

2.2.3 Pneumonia among HIV Exposed uninfected children

The prevalence of HIV infection is high in women of childbearing age in sub-Saharan Africa but, due to efficient health policies that expanded lifelong access to antiretroviral treatment in the past decade, the number of cases of pediatric HIV is constantly decreasing (UNAIDS, 2021). The UNAIDS report further indicated that as a consequence, the number of infants born from women living with HIV who do not acquire the infection (HIV-exposed uninfected, HEU) has increased by more than half a million between 2018 and 2020 in the region. HEU children are at an increased risk of morbidity, especially due to infectious causes, and have a 2–threefold higher mortality rate compared to their counterparts not exposed to HIV (Patel *et al.,* 2020). As posited by Zicari *et al.,* (2019) this increased vulnerability is probably correlated to maternal HIV infection since, despite optimal antiretroviral therapy (ART), the functional immunological defects caused by HIV cannot be completely reversed. The maternal IgG transplacental transfer can have a crucial role in modulating the immune system of the infants and in protecting them from infections during the first 3–6 months of life, when infants have to rely only on maternal-derived immunoglobulins because of the inability to synthesize their own. Hyper-gammaglobulinemia, which is common in African mothers living with HIV (Jallow *et al*., 2019) has a significant impact on IgG transfer from the

mother to the fetus (Zicari *et al.,* 2019). As observed by Babakhanyan, *et al.,* (2016) although the underlying mechanisms are not fully elucidated, it has been suggested that IgG levels over 15 g/l can cause the saturation of FcRN receptors, which mediate the IgG transplacental passage and indeed, in clinical studies, maternal IgG levels over 15 g/l have been associated with abnormal IgG concentrations in HEU infants. Impairments of IgG transfer in HEU infants have been observed by some authors (Dangor, 2015), but others reported similar IgG levels in HIV-exposed and –unexposed infants (Ray *et al*., (2019), or described a differential IgG passage depending on the characteristics of pathogen-specific antibodies (Alonso *et al.,* 2021).

2.2.4 Pneumonia among the children with sickle cell disease

Sickle cell disease (SCD) is a term for a number of genetic disorders in which haemoglobin is structurally abnormal, causing in the episodic formation of sickle-shaped red blood cells and a wide range of clinical manifestations (Booth *et al.,* 2009). It is the most prevalent genetic disorder worldwide, with about 300,000 affected infants delivered each year (Carter *et al.,* 2014). Miller *et al.,* (2007) observed that sickle cell disease patients are prone to developing invasive pneumococcal disease due to the inability of their defective immune system to effectively handle encapsulated bacteria.

It was observed that patients with SCD were at risk of fatal sepsis with encapsulated bacteria, such as *Streptococcus pneumoniae,* because of the inherent autosplenectomy that occurs in SCD. This risk is thwarted with oral penicillin prophylaxis during the first 5 years of life, and with stringent vaccination against *Streptococcus pneumoniae* alongside routine childhood immunization. But compared with the general African American pediatric population, Navalkele *et al*., (2017) reported that the rate of invasive pneumococcal disease (IPD) in patients with SCD still remains high, resulting in hospitalization and fatalities.

The treatment approach among the people of pneumonic conditions would need similar antibiotics as the sickle cell disease. Furthermore, the effect and the general side effects of the treatment approaches for the sickle cell, and pneumonia is also identical. Sickle cell affects the spleen, which makes it easy for people to get pneumonia (Bundy *et al*., 2017). He further postulated that, the destruction of the spleen makes it a challenge for the people already with pneumonia to cope and adapt to the treatment measures.

In handling the issues of pneumonia among children, there is a need to discuss the effects of the sickle T cell equally. Conterno and Martí-Carvajal (2016) reported that those with the Sickle Cell diseases are also most affected with acute chest syndrome. Therefore, concurrent development of the two conditions would mean there is an increasing level of chest pain, breathing challenges, and fever among the patients. They further noted that the two conditions do not cause each other, but rather, they can only trigger each other in the body of the patient. Acute sickle cell disease is likely to trigger the conditions of acute chest syndrome, otherwise known as pneumonia.

When the patient is affected by the Sickle Cell Disease, the red blood cells are shifting into a crescent shape. The changing of the red blood cell condition is an indication that more of the red blood cells would die within the body (Flores *et al.,* 2019). They also observed that the shape of the blood cells can ensure the blood flow is blocked, making the patient unhealthier and less immune to other infections. Therefore, those with the SCD condition are likely to get pneumonia.

Scholars have documented the factors that would increase the possibility of getting infected by pneumonia bacteria. The elements in the body that keep pneumonia-causing agents are identified as predictors of the disease. These include, poor oral care, tube feeding, and smoking are leading predictors of pneumonia in the body (Quan *et al.,* 2016). Pneumonia is caused by a mixture of the different factors and not just a single cause. Combined efforts create necessary conditions that will assist the pathogens in growing and developing the pneumonic conditions (But *et al.,* 2017).

2.3 Influence of Nutritional status on the Outcome of Severe Pneumonia

Walson and Berkley (2018) reported that worldwide, 5.6 million children die before their fifth birthday each year, with 80% of these deaths befalling sub-Saharan Africa and Asia. Almost half of these deaths occur in children with malnutrition (Victora *et al.,* 2021). Robust epidemiological evidence suggests this is because of an elevated vulnerability to life threatening infections amongst malnourished children (Walson & Berkley 2018). There are many children with dietary deficiencies around the globe with pneumonia cases. The developing nations have had swelling instances of severe pneumonia as a result of nutritional deficiency in the corresponding countries as observed by Elsayh *et*

al., (2013). They continued to postulate that the public health institutions considering preventing the cases of severe pneumonia should work through the process of solving the nutrition problems as well as excellently balance nutrition among the children.

Pneumonia and malnutrition are interactive and different studies have shown the interaction between the cases of starvation and the severe cases of pneumonia (Torres *et al.,* 2015). As observed by Walson and Berkley (2018) there is a high mortality rate among malnourished children with pneumonia. It was also noted by Christi *et al.,* (2015) that families with children with malnutrition are likely to seek medication relatively late. They further stated that the families tend to treat other conditions as opposed to the pneumonia and nutritional requirements. The combination of these different factors effectively assists in explaining the interaction between pneumonic diseases and malnutrition.

Schlaudecker *et al.,* (2011) postulated further that malnutrition causes a lower level of immunity in the body leading to infections such as pneumonia among children. Undernutrition, defined by wasting, stunting, and specific nutritional deficiencies, is associated with approximately half of all deaths in such children with severe pneumonia (Requejo & Bhutta, 2015). As observed by Li *et al*., (2018) there is a direct link in the cases of the countries with nutritional challenges to the circumstances of death from pneumonia. They observed that studies from the developing countries places pneumonia and malnutrition as the leading causes of death among the children. Further, the symptoms of the children dying through the two conditions are identified to have similar clinical features. They as well postulated that issues like cough, fever, rapid breathing, and lung challenges form the leading clinical characteristics of the children with pneumonia and 56% of the death cases of children with pneumonic conditions had significant nutritional deficiency.

It is estimated that children with severe acute malnutrition (SAM) have 15 times a higher chance of contracting pneumonia (Bamford *et al.,* 2018). In summary, there is a direct relation in the statistics of the children having cases of pneumonia and the malnutrition condition in the developing nations.

As reported by Fitzpatrick *et al.*, (2019) the relationship between pneumonia condition and malnutrition can be explained using the malnutrition-infection complex which has different stages. The first stage is for the body to fight the disease. The second stage of infection is having an existing deficiency that causes the disease. They also observed that when the child is malnourished, the body assists the pathogen in the process of promulgation and invasion.

In addition to having a direct influence on mortality, malnutrition increases the frequency and severity of pneumonia episodes, presumably indicating a secondary immunological deficiency that has not yet been well characterized (Rytter *et al*., 2014). Undernutrition in a child with severe pneumonia that necessitates hospitalization can also be associated with a decreased metabolic capacity to cope with the illness's increased physical and physiological demands, such as increased temperature, cardiac output, and labor of breathing. As a consequence, severe acute malnutrition can increase pneumonia mortality by 15-fold, and in a score of mortality risk among infants with pneumonia, extremely low weight-for-age and refusal to feed contributed as much to mortality risk as hypoxia (Reed *et al.*, 2012).

In another study by Moschovis *et al.,* (2015) involving 2,660 individuals from 16 LMIC locations, the results showed that stunting was associated with a longer course of recovery from illness in a childhood pneumonia. Ngari *et al*., 2017 conducted a cohort study of 4,184 Kenyan children <5 years admitted with severe pneumonia and found out that 25% had severe acute malnutrition, and this was strongly associated with one year post-discharge mortality. The study suggested the need to research more on the influence of severity of malnutrition on the outcome of severe pneumonia among children.

In addition to being a major factor in the risk of infection, nutritional status affects the health trajectory and outcomes after hospital discharge. Undernutrition was the main predictor of mortality risk in Kenya, where children who were discharged from the hospital alive had an eight-fold increased chance of dying the following year compared to their peers from the community (Moisi *et al.,* 2011). The modifiable factors connected to these post-care deaths were not clearly defined in the above study, but the researchers further suggested probable targets that included enhancing the nutritional content of therapeutic and supplementary feeds, suboptimal infant feeding practices, food insecurity,

an unhealthy gut microbiome, recurrent infections due to persistent susceptibility and exposure to pathogens, and limited access to care. Kirolos *et al.*, (2021) revealed the following conclusions in a meta-analysis of 33544 underweight children from 23 studies: the estimated OR of mortality from pneumonia was 2.0 (95% CI 1.6 to 2.6) and 4.6 (95% CI 3.7 to 5.9) for children moderately and severely underweight, respectively. It also revealed that the OR of mortality from pneumonia for children who were extremely underweight was 5.3 (95% CI 3.9 to 7.4) before the year 2000 and 4.1 (95% CI 3.0 to 6.0) after the year 2000. The prevalence of underweight children admitted to hospital for pneumonia varied (median 40.2%, range 19.6- 66.3) but was significant in several LMIC settings (Kirolos *et al.*, 2021).

According to the Kenya Demographic Health Survey (KDHS) 2014 West Pokot and Kitui counties had the highest proportions of stunted children (46 percent each). Kilifi (39 percent), Mandera (36 percent), and Bomet (36 percent) are among the other counties with significant rates of stunting children. The counties of Nyeri, Garissa, and Kiambu had the lowest proportion of stunted children, each with 16 percent or less. More than 11 percent of children in Garissa, Wajir, Mandera, Marsabit, Turkana, West Pokot, and Samburu are wasted, with Turkana having the highest incidence at 23 percent. According to the same report, the counties with the lowest proportion of wasted children are Siaya and Kisumu (each 1 percent or less). In five counties, one-quarter or more of the children were underweight, they include; Mandera, Marsabit, Turkana, West Pokot, and Samburu. According to the KDHS (2014) data, 4% or less of children in Nyeri and Nairobi were underweight.

KDHS (2014) report comparing KDHS data over time revealed an overall improvement in Kenyan children's nutritional status. Since 1998, stunting has decreased from 38% to 26%, wasting has decreased from 7% to 4%, and the proportion of underweight children has decreased from 18% to 11%. Kenya has achieved the 2015 Millennium Development Goal (MDG) objective of lowering the proportion of underweight children under the age of five to 11%. (Ministry of Devolution and Planning, 2013).

2.4 The Outcome of Severe Pneumonia with specific Comorbidities Related

The presence of severe cases of pneumonia and the other instances of pneumonia have impacts on patients. Pneumonia along with the comorbidity, are principal causes of death among the patients in different parts of the world (Williams *et al.,* 2016). According to Kolditz *et al.,* (2016) the development of the comorbidities related to pneumonia is also responsible for the increasing admissions of the patients to the Intensive Care Unit. They further reported that there are different indicators on the increased mortality as an outcome of severe pneumonia and the comorbidities.

The mortality rate of the children with community-acquired pneumonia (CAP) range between 5.16 and 6.11 cases for every 1000 patients each year (Luna *et al.,* 2016). They further reported that a study of the impact of the CAP in the developed nations revealed the condition to be one of the leading causes with a total of 28% of the mortality rates in the countries of study. According to Dean *et al.,* (2016) the comorbidities and severe pneumonia-related cases are to blame for the increasing rates of admissions in the hospitals. They further identified pneumonic condition was as a leading cause of admissions to the hospitals with more than 18% of the total admissions attached to pneumonia and related diseases. Notably, the comorbidities and the associated conditions cause increased rates of hospitalizations and mortality rates in different countries.

As a result of respiratory failure, many severe pneumonia patients have had cardiac failure and fluid overload within their systems. The conditions are worse for the case of the children. The upgrade of hypoxemia would mean the children are the most at risk of getting respiratory distress syndrome in a way to further explain the impact of comorbidities related to severe pneumonia. A study by Quansey *et al.,* (2015) described the impact acute respiratory distress syndrome has on the mortality rate of the children as severe sepsis. They further noted that patients with sepsis have a higher risk of death. The development of respiratory distress syndrome is a significant outcome. Walson and Berkley (2018) observed that there is a high mortality rate among malnourished children with pneumonia. It was also noted by Christi *et al.,* (2015) that families with children with malnutrition are likely to seek medication relatively late.

2.5 Conceptual Framework

The independent variables in the study included comorbidities related to severe pneumonia which were: malnutrition, HIV infection, HIV exposure, sickle cell disease and malaria. The study therefore sought to ascertain the effects of these comorbidities on the outcome of severe pneumonia in this group of children. The intervening variables considered in the study included Age and Gender of the children with severe pneumonia. The Study sought to find out how age and gender would modify the outcome of severe pneumonia in a child who had the comorbidities stated above. Finally the outcome variable was considered as either discharge from the hospital alive which was a good outcome or having died from the disease which was a worst outcome.

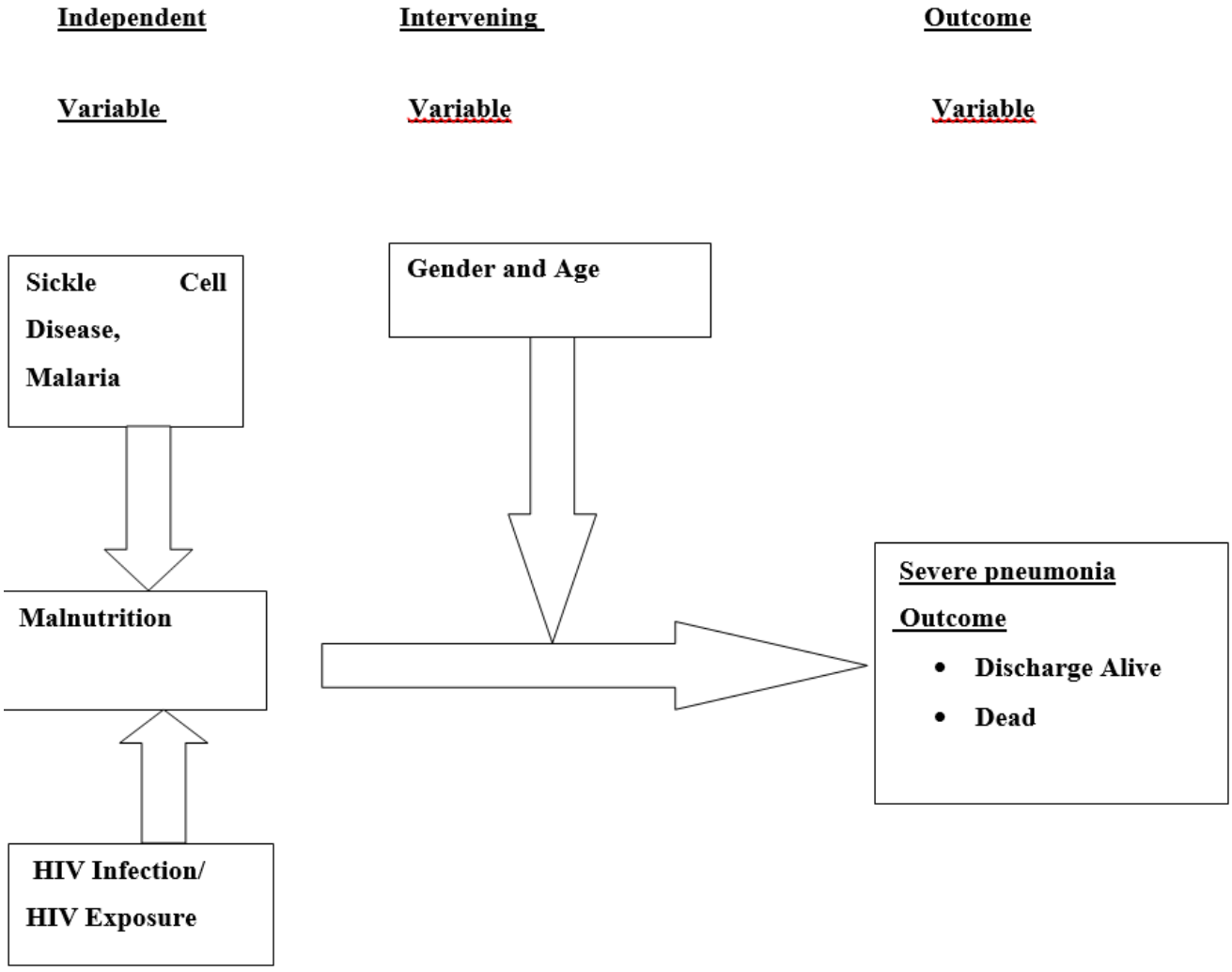

Figure 1 : Conceptual Framework

CHAPTER THREE
RESEARCH DESIGN AND METHODOLOGY

3.1. Introduction

This chapter entails an explanation of the study design, description of the various variables, characteristics of the study population, sampling and sample size determination as well as both the data collection related information and ethical aspects of this study.

3.2 The Study Site

The hospital-based study was conducted in Bondo Sub County hospital located in Nyanza region, Siaya County, Bondo Sub County, Bondo Constituency in Bondo Township. It has a catchment area of 197,883 (KNBS 2019) and majorly comprise of Luo ethnic group, the economic activity in the area is majorly fishing, mining and trading. The hospital is located adjacent to Bondo Town, next to Kenya Medical Training College - Bondo campus situated along Kisumu – Usenge Road approximately 63km from Kisumu and 30km from Usenge. It has a population of approximately 238,780 (KDHS, 2014).

Bondo lies in an altitude of 1140 meters and 1400 meters above sea level and from longitude $33^0 58^0$East and 34^0 35^0West. It boarders Alego Usonga sub county to the north, Gem to the east, Rarieda to the south and Mbita sub county across the Winam Gulf to the South East. To the west is Uganda. It covers a total of $1972km^2$ out of which $972km^2$ is land mass while the rest, $1000km^2$ is water surface. The area has warm, dry and humid climate with mean rainfall ranging between 800mm – 1600mm and bimodal rainfall pattern of long rains occurring between March and May and short rains occurs between October and November (Balaton-Chrimes, 2021).

Bondo sub county hospital is the referral hospital in Bondo and Rarieda Sub County. The site will be ideal for the study because being the referral facility in the two sub counties, most of the cases of severe pneumonia are referred to and managed in this higher level of healthcare provision.

3.3 Research Design

The study employed a hospital based retrospective cross sectional study design with quantitative approach. This entailed the use of secondary data obtained from the hospital records.

3.4 Target Population

The target population were children aged 2-59 months admitted with severe pneumonia in Bondo sub county hospital for a period of two years under review (July 2017- June 2019). According to the hospital records, it was evident that for the period of two years within June 2017 and July 2019, 330 children were admitted with severe pneumonia in the paediatric ward at Bondo sub county hospital. There was no significant difference in the distribution of the disease according to gender.

3.5 Study population

The study population was 218 in patient files of children admitted with severe pneumonia during the period of two years (June 2017 and July 2019) which were retrievable from the hospital archives. From these the sample size was calculated.

3.6 Inclusion and exclusion criteria

3.6.1 Inclusion criteria

The study included data collected from in patient files which had the following mandatory information

- Age of the child
- Weight of the child
- HIV status
- Diagnosis of severe pneumonia
- Mid upper arm circumference
- Final outcome of the disease (dead or discharged alive)

3.6.2 Exclusion criteria

Data was not collected from the following in patient files

- In patient files that were missing any of the mandatory information mentioned in the inclusion criteria above.

3.7 Sample Size Determination

The study employed scientifically proven sample size estimation method by

Yamane (1967:886). This was the best method since in this study, prevalence wasn't of great importance.

$$n=N/1+ \{N (e)^2\}$$

Where; e = the precision, set at 5% which is 0.05

n=sample size

N= population size

Therefore

$$n= 218/1+ \{218 (0.0025)\}$$

$$=141$$

3.8 Sampling Technique

A systematic sampling method was used where all the children who had been admitted in the ward having met a prescribed inclusion criteria above, were recruited to participate in the study. The in- patient numbers were enumerated in a piece of paper and the researcher then picked the enumerated inpatient numbers using simple randomization method. The files were then retrieved from the hospital archives and screened for completeness of mandatory data until the desired sample size was achieved. The required information was then extracted from the files using a pretested structured observation checklist. Those files which were not retrievable and those with inadequate information were not included in the study.

3.9 Research Instruments

The data was collected in the following forms. Secondary data was extracted from the in-patients' files using a structured observation checklist. The observation checklist was organized in a manner to collect information relevant to the objectives of the study from the individual patient's file. During the data collection exercise, the researcher and the five research assistants observed Covid 19 prevention strategies by wearing of face masks at all times, keeping social distance as well as regularly washing their hands before and after handling the patient's files.

3.10 Pre-testing/Piloting Study

A pilot study was conducted at Madiany sub county hospital in Rarieda Sub County which has many similarities with the study area, Bondo sub county hospital, where 18

files were retrieved and information extracted as per the data collection tool. This helped in identifying unforeseen challenges with the data collection tool as well as the study design thereby helped the researcher to modify the tools appropriately.

3.11 Validity & Reliability

3.11.1 Validity

The extent to which the research data collection tool measures what it is intended to measure and hence meets the study objectives is known as validity. To ensure validity of the data collection tool, the researcher shared and discussed the data collection tool with an experienced supervisor who made necessary corrections and additions to the tool before it was finally used for data collection.

3.11.2 Reliability

Reliability is the degree to which the same or comparable results may be attained under different conditions, at different times, and by different respondents or interviewers. To ensure reliability of the data collection tool, the researcher conducted a pilot study at Madiany sub county hospital. After the pilot study, the variables in the data collection tool which couldn't be retrieved from the in- patient files were modified or removed so as to ensure completeness of data collection tool. These changes were factored and used to improve the quality of the final data collection tool.

3.12 Data Analysis Procedures

Table 3.1: Data Analysis Procedures

S/NO	Objective	Statistical test
1	To identify comorbidities related to severe pneumonia among children aged 2-59 months in Bondo sub county hospital.	inferential statistics (mean/ proportion)
2	To determine the outcome of severe pneumonia with specific comorbidities among children aged 2-59 months in Bondo sub county hospital	Fisher's exact test & Binary logistic regression
3	To determine the effects of nutritional status on outcome of severe pneumonia with specific comorbidities among children aged 2-59 months in Bondo sub county hospital	Binary logistic regression

3.13 Data Management and Ethical Considerations

Once the research proposal was approved by the school of health sciences, an introductory letter was presented to the researcher to seek ethical approval. The research protocol was then reviewed by Jaramogi Oginga Odinga teaching and referral hospital institutional ethics & review committee (IERC) approval number IERC/JOOTRH/384/21. On getting the approval of the committee, the authority to carry out the research was obtained from Siaya county medical research coordinator who then gave permission to conduct research in the county. An authority letter from the county was then presented to bondo sub county hospital medical superintendent to allow the researcher conduct the study in the hospital. The medical superintendent then instructed the hospital medical records officer to allow the researcher access to the medical records. The in-patient files of the participants from which secondary data was extracted, were coded with unique codes and the identity of the participant remained anonymous.

3.14 Data storage/archiving and destruction

The data collected was cleaned, entered in Microsoft excel and stored in a computer well-protected with a complex password in-order to reduce accessibility by unauthorized persons. The raw data collected using the observation checklist was stored in a lockable

drawer until six months after publishing the study findings after-which, the raw data would be destroyed by shredding the data collection tool.

3.15: Data Dissemination

The results of the study were disseminated to the various stakeholders in order to inform policy and decision making. These included Siaya county research coordinator, bondo sub county hospital medical superintendent, Jaramogi Oginga Odinga University of science and technology school of health sciences as well as Jaramogi Oginga Odinga teaching and referral hospital ethical review committee.

CHAPTER FOUR

RESULTS

4.0 Introduction

This chapter presents the results regarding demographic characteristics of the children and mothers/caregivers, specific comorbidities related to severe pneumonia among children aged 2-59 months in Bondo sub county hospital, the outcome of severe pneumonia with specific comorbidities among children aged 2-59 months in Bondo sub county hospital as well as on the comorbidities associated with malnutrition in children under five years admitted to in Bondo sub county hospital as well as nutritional factors associated with outcome of severe pneumonia.

4.1 Demographic characteristics of the children and Caregiver

The mean age of the children was 16.4±13.8 months and majority, 49.6% (n=70) of them were aged < 12 months. As regards to the gender of the children, 54.6% (n=77) were male while 45.4% (n=64) accounted for female children.

In relation to caregiver's characteristics, majority of the respondents, 95.0% (n=134) were parents of the sampled children while the remaining 5.0% (n=7) were guardians of the children. In terms of marital status of the caregivers, majority 84.4% (n=119) were married, 14.2 % (n=20) were single, 0.7% (n=1) were divorcees and widowed each as shown in table 4.1 below.

Table 4.1: Demographic characteristics of children and caregivers

Variable	Attribute	Frequency	Percentage %
Age in months	Mean ±SD= 16.4±13.8		
	<12 months	70	49.6
	12-23 months	33	23.4
	24 -36 months	20	14.2
	36- 59 months	18	12.8
Gender	Male	77	54.6
	Female	64	45.4
Informant	Parent	134	95.0
	Guardian	7	5.0
Marital Status	Married	119	84.4
	Single	20	14.2
	Divorced	1	0.7
	Widowed	1	0.7

4.2: Outcome of severe pneumonia with specific comorbidity

The overall mortality rate from severe pneumonia among the study population was 11.4% (n=16). The mortality rate for children below 12 months was 18.6% (n=13) and for the children between 12 months to 23 months was 9.1% (n=3) With respect to gender, the mortality rate for female participants was higher than that for male {14.1% (n=9) vs 9.1% (n=7)}, as shown in **table 4.2** bellow.

Table 4.2: Outcome of severe pneumonia with specific comorbidity

	Patients	Deaths	Mortality rate
	N	N	%
Overall	141	16	11.4
Age in months			
<12	70	13	18.6
12-23	33	3	9.1
24 -36	20	0	0.0
36- 59	18	0	0.0
Gender			
Male	77	7	9.1
Female	64	9	14.1

4.3: Prevalence of various comorbidities among children with severe Pneumonia

The results in **Figure 2** bellow show the proportion of comorbidities among children with severe pneumonia. There were 63 out of 141 children with different comorbidities in which 7.9% (n=5) were HIV infected, 28.6% (n=18) were HIV exposed, 25.4% (n=16) had sickle cell disease, 36.5% (n=23) had malnutrition and 1.6% (n=1) had other disease infections. Fisher's test of association was used to determine the association between specific comorbidities and outcome of severe pneumonia.

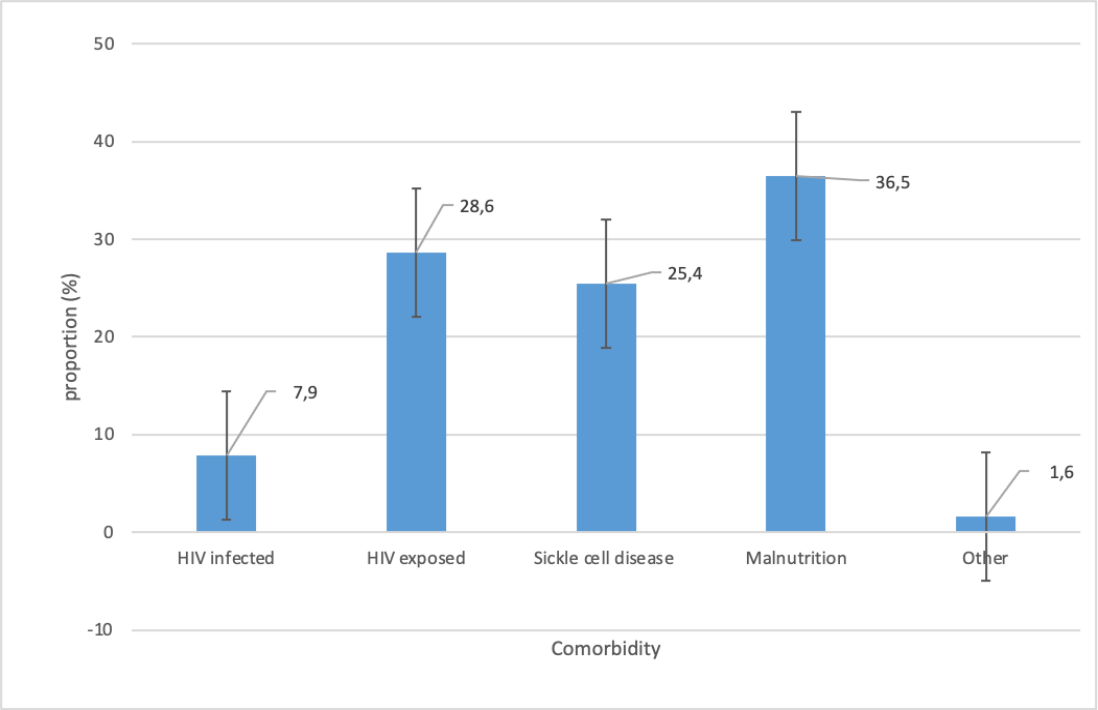

Figure 2: Proportion of Specific comorbidities related to severe pneumonia

4.4 Association between Specific comorbidities and outcome of severe pneumonia

When fishers exact test was used to test association between severe pneumonia and death in the group of children with different specific comorbidities, it only revealed that there was a statistically significant association between HIV exposure as a comorbidities and death in children with severe pneumonia (P-value=0.009). As shown in **Table 4.3 .**The results further showed that majority, 80.0% (n=5) of those who were HIV infected were discharged alive while 20.0% (n=1) of them died. Similarly, about 87.5% (n=14) of those with sickle cell anaemia were discharged alive and 78.3% (n=18) of those who were diagnosed with malnutrition were discharged alive.

Table 4.3: Association between Specific comorbidities and outcome of severe pneumonia

		Outcome		
	n(%)	**n(%)**	**N**	Fishers' exact
Specific Comorbidity	Dead	Discharge alive	Total	
HIV Infected	1(20.0)	4(80.0)	5	
HIV exposed	5(27.8)	13(72.2)	18	p-value =0.009
Sickle cell disease	2(12.5)	14(87.5)	16	
Malnutrition	5(21.7)	18(78.3)	23	
Other comorbidity	0(0.0)	1(100.0)	1	
TOTAL	13(20.6)	50(79.3)	63	

4.5: Association between Medication used and Number of days spent in Ward

To find out what type of medication would last patient shorter days in the ward, Kruskal-Wallis test of difference was used to determine if there was a significant difference in average number of days spent in ward (**Table 4.4**). The results revealed that there was no significant difference in average number of days spent in the ward and the types of medicine used (P-value=0.2235, chi-squared=4.377). However, the average number of days spent in the ward by those who used Crystalline penicillin only was 4.1 days (n=14), 7.1 days (n=89) for those who used Crystalline penicillin & Gentamycin, 4.7 days (n=37) for those who used Ceftriaxone and average of 4.0 days (n=1) for those who used other medications.

Table 4.4: Kruskal- Wallis test of difference between average numbers of days spent in hospital by type of medication

	N	Average number of days spent in the ward	Rank Sum	chi-squared	P-value
Medication Used				4.377	0.2235
Crystalline penicillin only	14	4.1	801.0		
Crystalline penicillin & Gentamycin	89	7.1	6794.5		
Ceftriaxone	37	4.7	2353.5		
Other medication	1	4.0	62.0		

4.6 Association between Medication used and Outcome of Severe Pneumonia

In **Table 4.5** bellow, Fisher's exact test of association was used to test the association between medication used and outcome of severe pneumonia among under 5 years sampled children in Bondo Sub-County hospital. However, the results showed that there was no significant association between medications used and outcome of pneumonia (P-value=1.00).

Specifically, the results revealed that 12.4% (n=11) of those who used Crystalline penicillin plus gentamycin died of severe pneumonia while 87.6% (n=78) of them were discharged alive.

Table 4.5: Association between medication used and outcome of severe Pneumonia

	Outcome			
	Dead	Discharge	P-value	**Total**
Medication used			1.000	
Crystalline penicillin	1(7.1)	13(92.9)		14
Crystalline penicillin plus gentamycin	11(12.4)	78(87.6)		89
Ceftriaxone	4(10.8)	33(89.2)		37
any other	0(0.0)	1(100.0)		1
Total	16(11.3)	125(88.7)		

4.7: Effects of nutritional status on the outcome of severe pneumonia

4.7.1 Anthropometric measurement of children with severe pneumonia.

The results in **Table 4.6** shows that of the total children sampled, 6.4% (n=9) severe acute malnutrition (MUAC of less than 11.5cm), 9.9% (n=14) had moderate acute malnutrition (MUAC of 11.5 cm to 12.4cm) while 64.5% (n=91) were normal (MUAC of 13.5 cm and above).

In terms of weight for height Z score, majority 73.8% (n=104) of the children were normal (WHZ score between >-2 to ≤-1SD), 19.1% (n=27) had moderate acute malnutrition (WHZ score between >-3 to ≤-2 SD). The remaining 7.1% (n=10) had severe acute malnutrition (WHZ score of ≤ -3 SD).

Table 4.6: Anthropometric measurement of children with severe pneumonia

		Frequency (n)	Percent (%)
MUAC of the child(cm)	**Classification**		
< 11.5cm	Severe Acute Malnutrition	9	6.4
11.5 – 12.4cm	Moderate Acute Malnutrition	14	9.9
12.5 – 13.4cm	At risk of Malnutrition	27	19.2
13.5 cm and above	Normal	91	64.5
WHZ – score			
≤ -3	Severe acute malnutrition	10	7.1
>-3 to ≤-2	Moderate acute malnutrition	27	19.1
>-2 to ≤-1	At risk	104	73.8

4.7.2: Association between Specific Comorbidity and Anthropometric measures

Fisher's exact test at 5% significance level was used to test whether there was a significant association between comorbidity and body anthropometric measurement

(MUAC and WHZ score). The results in **Table 4.7** revealed that both MUAC of the child and WHZ score were significantly associated with Comorbidities (P-value=0.001).

It was further observed that 40% (n=2) of the participant who were HIV infected were severely malnourished (MUAC less than 11.5 cm), while 20% (n=1) of them ware at risk of malnutrition (MUAC between 12.5cm and 13.4cm). Among participants who had sickle cell disease, 25% (n=4) were at risk of malnutrition (MUAC between 12.5 cm and 13.5 cm) and the remaining 75% (n=12) were normal (MUAC of 13.5 cm and above).

The proportion of comorbidities with respect to WHZ score as presented in **Table 4.7** revealed that majority, 60.0% (n=3) of the participants who were HIV infected were moderately malnourished (WHZ between >-2 to ≤-1), while 66.7% (n=12) of those who were HIV exposed were moderately malnourished (WHZ between >-2 to ≤-1) and finally 81.2% (n=13) of those who had sickle cell disease were moderately malnourished (WHZ between >-2 to ≤-1).

Table 4.7: Association between Specific comorbidity and Anthropometric measurers

	Comorbidities					
	HIV Infected n(%)	HIV exposed n(%)	Sickle cell disease n(%)	Malnutrition n(%)	Other n(%)	Fisher's exact p-value
MUAC of child						
< 11.5cm	2(40.0)	1(5.5)	0(0.0)	5(21.7)	0(0.0)	0.001
11.5 – 12.4cm	0(0.0)	2(11.1)	0(0.0)	11(47.8)	0(0.0)	
12.5 – 13.4cm	1(20.0)	5(27.8)	4(25.0)	6(26.1)	0(0.0)	
13.5 cm and above	2(40.0)	10(55.6)	12(75.0)	1(4.4)	1(100.0)	
WHZ – score						0.001
>-2 to ≤-1	3(60.0)	12(66.7)	13(81.2)	1(4.4)	1(100.0)	
>-3 to ≤-2	1(20.0)	5(27.8)	3(18.8)	15(65.2)	0(0.0)	
≤ -3	1(20.0)	1(5.5)	0(0.0)	7(30.4)	0(0.0)	

4.7.3 Influence of MUAC and WHZ score on the outcome of severe pneumonia

Bivariate analysis for the effect of body MUAC and WHZ score was done under binary logistic regression with 5% level of significance. According to the results in **Table 4.8**, MUAC and WHZ score were statistically significant factors influencing outcome of severe pneumonia. Participants with MUAC of less than 11.5 cm were 9.6 times more likely to die of severe pneumonia as compared to those with MUAC of 13.5 cm and above (OR=9.60, 95%CI=2.1 – 44.1, P-value=0.004). With regards to weight for height Z-score, participants with WHZ score of <-3SD were 7.04 times more likely to die of severe pneumonia as compared to those who had WHZ score between >-2 to ≤-1 SD (OR=7.04, 95%CI=1.67 - 29.64, P-value=0.008).

Table 4.8: The effect of MUAC and WHZ score on the outcome severe pneumonia

	Outcome of severe pneumonia				
	Dead n(%)	Discharged alive n(%)	OR	P-value	95% CI
MUAC of the child(cm)					
< 11.5cm	3(60.0)	2(40.0)	9.60	0.004	2.1 – 44.1
11.5 – 12.4cm	2(11.11)	16(88.89)	0.92	0.943	0.1-8.1
12.5 – 13.4cm	4(14.81)	23(85.19)	2.09	0.272	0.6- 7.8
13.5 cm and above	7(7.69)	84(92.31)	Ref	-	-
WHZ SCORE					
>-2 to ≤-1	9(8.65)	95(91.35)	Ref	-	-
>-3 to ≤-2	3(11.11)	24(88.89)	1.32	0.694	0.33 - 5.25
<-3	4(40.00)	6(60.00)	7.04	0.008	1.67 - 29.64

4.8: Overall effect of comorbidity on outcome of severe pneumonia.

In order to establish the overall influence of comorbidity on the outcome of severe pneumonia among children aged 2-59 months in bondo sub county hospital, a bivariate

logistic regression revealed that there was a significant influence of comorbidity on the outcome of severe pneumonia. The patients with comorbidity were 6.06 times more likely to die from severe pneumonia as compared to those with no comorbidity (OR=6.06, 95%CI=1.32, 27.78, P-value=0.02) as shown in **Table 4.9.** The results further showed that 80.0% (n=4) of those who were HIV infected were discharged alive while 20.0% (n=1) of them died. Similarly, about 88.0% (n=14) of those with sickle cell anaemia were discharged alive and 78.3% (n=18) of those who were diagnosed with malnutrition were discharged alive.

For the specific comorbidity, bivariate logistic regression as shown in **Table 4.10** revealed that patients with severe pneumonia and were HIV exposed were 3.92 times more likely to die as compared to those who were not exposed (OR=3.92, 95%CI=1.18, 13.04, P-value=0.026).

Table 4.9: Effect of comorbidity on the outcome of severe pneumonia

	OUTCOME				
	Discharged n(%)	Dead n(%)	OR	95%CI	P-value
Comorbidity					
No	58(96.67)	2(3.33)	Ref		
Yes	67(82.72)	14(17.28)	6.06	1.32,27.78	0.020

The results of table 4.13 shows that there is six times increased risk of death in children who are malnourished and have severe pneumonia [OR 6.06 (1.32-27.78) P value 0.02].

Table 4.10: Association between Specific comorbidities and outcome of severe pneumonia

	Outcome				
	Discharged n(%)	Dead n(%)	OR	95%CI	P-value
HIV Infected					
No	121(88.97)	15(11.03)	Ref		
Yes	4(80.00)	1(20.00)	2.01	0.21 , 19.25	0.542
HIV exposed					
No	112(91.06)	11(8.94)	Ref		
Yes	13(72.22)	5(27.78)	3.92	1.18 , 13.04	0.026
Sickle cell anaemia					
No	111(88.80)	14(11.20)	Ref		
Yes	14(87.50)	2(12.50)	1.13	0.23 , 5.51	0.877
Malnutrition					
No	107(90.68)	11(9.32)	Ref		
Yes	18(78.26)	5(21.74)	2.70	0.84 , 8.70	0.096

CHAPTER FIVE

DISCUSSION

5.1 Prevalence of comorbidities related to severe pneumonia

The primary objective of this study was to determine the influence of comorbidities on the outcome of severe pneumonia among children aged 2-59 months. The results suggest that there is a statistically significant association between comobidities and outcome of severe pneumonia among the children in this age group.

The comobidity with highest prevalence among children in this age group is malnutrition followed by HIV exposed uninfected (HEU). The study findings are commensurate with the findings of a cohort study of , by Ngari *et al.,* (2017) among 4,184 Kenyan children <5 years admitted with severe pneumonia which reported that 25% had severe acute malnutrition, and this was strongly associated with 1 year post-discharge mortality. This study has further demonstrated that there is an association of malnutrition with death among children in this age group suffering from severe pneumonia. It has become clear that whilst malnutrition results in increased incidence, severity and case fatality of common infections, risks continue beyond acute episodes resulting in significant postdischarge mortality (Walson & Berkley, 2018). A well established concept of a 'vicious-cycle' between nutrition and infection has now evolved to encompass dysbiosis and pathogen colonization as precursors to infection; enteric dysfunction constituting malabsorption, dysregulation of nutrients and metabolism, inflammation and bacterial translocation. All of these interact with a child's diet and environment.

In Ethiopia, nasopharyngeal carriage of *Streptococcus pneumonia* was assessed in 361 children at an outpatient clinic (Gebre *et al.,* 2017). Overall, 44% were colonized by *S. pneumoniae* (not serotyped, 18% multidrug resistant) and colonization was associated with the number of siblings in the household and presence of malnutrition defined by weight-for-age, capturing aspects of both wasting and stunting: adjusted odds ratio 2.1 [95% confidence interval (CI) 1.2–3.4]. In Venezuela, amongst 1064 children living in rural areas of the Orinoco Delta, S. *pneumoniae* colonization was (nonsignificantly on multivariable analysis) more common among stunted children (Verhagen *et al.,* 2017).
Previous studies have demostrated a significantly lower concentration of IgG2 in HEU infants (22% lower levels compared to HIV unexposed uninfected (HUU) infants) and

their lower representation out of the total IgG. In a study by Baroncelli *et al*., (2022) it was evident that although mothers had received HAART for a median of 19 months, the level of IgG2 was comparable to the one observed in HEU infants born to mothers treated with short-term HAART . These findings suggest that the immunological functional defects due to HIV infection persist in women under continuous HAART and interfere with the delicate balance of the maternal–fetal unit. The lack of correlation between total IgG and IgG2 in the HEU population (but not in HUU) is suggestive of a selective impairment of IgG2 passage through the placenta in mothers living with HIV. The deficit of IgG2 has been associated with increased vulnerability to bacterial diseases especially those caused by encapsulated organisms like streptococus pneumoniae which is the commonest cause of pneumonia. Contrasting results have been obtained in different studies on HEU infants: some reported reduction in transfer of specific antibodies against *H. influenzae*, diphtheria, pertussis, pneumococcus, measles, tetanus, and p*lasmodium falciparum (*Babakhanyan *et al*., 2016). The study has also revealed a moderately high prevalence of pneumonia among children with sickle cell disease. This can be attributed to the fact that children with secklecell disease undergo autospleenectomy which make them to be at high risk of developing infections caused by encapsulated organisms like streptococus pneumoniae.

5.2 The outcome of severe pneumonia with specific comorbidities

The overall mortality rate of severe pneumonia among children with specific comorbidities in this study was 11.4%. The finding of this study is slightly lower than WHO (2022) data that reported that Pneumonia killed 740 180 children under the age of 5 in 2019, accounting for 14% of all deaths of children under 5 years old. However, study by Luna *et al., (*2016) showed that the mortality rate of children with community-acquired pneumonia ranges between 5.16 and 6.11 cases for every 1000 patients annually. In addition, another study showed that severe acute malnutrition independently predicted death in HIV-exposed Malawian children with pneumonia (OR 5.1), more so than HIV-infected children (OR 2.2) (Preidis *et al*., 2011). Similarly, In a South Africa child health study where none of the children were HIV-infected, HIV exposure was the strongest independent risk factor for severe pneumonia (incidence rate ratio 4.04), and both HIV exposure and malnutrition were associated with an increased incidence of pneumonia.

The study also has demonstrated that the mortality rate was higher among children below 12 months as compared to older ones. This could be attributable to the underdeveloped immune system of children younger than 12 months thereby limitting their capacity to handle pneumonia causing micro organisms. Further the mortality rate was observed to be higher in females compared to males.

5.3 Effects of nutritional status on outcome of severe pneumonia

This study reports that children with malnutrition as comorbidities have six fold increased risk of mortality from severe pneumonia,while HIV exposed and uninfected as a comorbidity increase the risk by four folds. The study further, observed that malnutrition increases the risk of death of HIV exposed uninfected children with severe pneumonia. These study findings are in agreement with a meta-analysis conducted among children to ascertain risk of death from diarrhea and pneumonia among HIV uninfected infants that showed that this group of children had 60% chance of dying from pneumonia (Brennan *et al*., 2019). Similarly, malnutrition is not only associated with an increased risk of pneumonia episodes, but increased severity and case fatality. Development of an inpatient paediatric pneumonia mortality risk score (RISC) in Malawi (n=16475) by Hooli *et al.*, (2018) identified severe malnutrition as having similar predictive value to hypoxaemia and coma (Kotloff, *et al.,* 2013). In Kenya, among 4187 children admitted to hospital with severe pneumonia, 25% were severely malnourished, again a strong risk factor for inpatient death alongside signs of disease severity (Ngari *et al.,*2017). A subset of children was followed after discharge from hospital; 37% of deaths occurred after discharge.

The study has further demonstrated an association of malnutrition with death among children suffering from severe pneumonia and indeed, malnutrition has previously been demonstrated as a predisposing factor for severe pneumonia. According to Kirlos *et al.*, (2021), the OR of death from pneumonia for those severely underweight was 5.3 (95% CI 3.9 to 7.4) in pre-2000 and remained high post-2000 at 4.1.This was further supported by a study from Malawi analyzing over 100,000 episodes of pneumonia over an 11-year period which found that those with severe undernutrition and with severe acute malnutrition had a 12% and 35% increase, respectively, in the odds of pneumonia mortality (Le Roux *et al.*, 2015). Nutritional status was the major driver of post-

discharge mortality. According to Myatt et al., (2016) MUAC was an efficient single marker of mortality risk, performing better than weight-for-height Z-score, the traditional marker of acute malnutrition, including after adjustment for age and gender which are known confounders of MUAC. It could be argued that because MUAC changes with age, it predominantly captures the youngest children, rather than nutritional status. However, mortality was far higher amongst all children with MUAC <11.5 cm than amongst those who were simply aged under 6 months and the relationship between MUAC and mortality appeared to be less confounded by age than other nutritional indices.

Using a routine data from a health facility in western Kenya, we have replicated the previous research findings that comorbidities increase the risk of death among children with severe pneumonia. This demonstrates that routine data is useful not only for monitoring the quality of care (Harries *et al.,* 2013), but also if well utilized can be useful for highlighting areas of concern for action and strategies (Omore *et al.,* 2016). In this regard, this study shows that comorbidities increase risk of death, and further action should be taken to address the concerns. Of significance in our findings is the need to exploit the routine data to support continuity of clinical care or assess the standards or quality of data.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

Having analyzed the data collected from the sampled population, the researcher can conclude that Comorbidity with highest prevalence among children with severe pneumonia is malnutrition followed by HIV exposure .The mortality rate of severe pneumonia among children aged 2-59 months in bondo sub county hospital is 11.4% and the longer a patient spent in the ward the more likely it was for the patient to die. Finally, there is a significant association between nutritional status and outcome of severe pneumonia among children aged 2-59 months.

6.2. Recommendations

6.2.1 Recommendation for action

The study finding shows that HIV exposed uninfected and malnourished children aged under five years with severe pneumonia are at high risk of death, consequently, there is a need to come up with measures to reduce death among these groups. Indeed, Clinicians should explore aggressive management with the correct dosing of the recommended first line antibiotics and closely monitor this group for antibiotic treatment failure so as to adjust the treatment to second line without any unnecessary delays.

The community health volunteers should be empowered with knowledge on nutritional counselling of the community members so as to reduce the burden of malnutrition among these children at the household level. The caregivers should be encouraged to report to the hospital immediately they realize a sign of sickness in their children. This is in order to prevent the severe conditions.

6.2.2 Recommendation for future research

Finally, the study shows that comorbidities increase the risk of death among children with severe pneumonia, in particular, HIV exposed uninfected and malnourished. Consequently, there is a need for improved clinical practice and intervention for severe pneumonia among these children but specifically, HIV exposed uninfected children. The study recommends a rigorous cohort study with a bigger sample size to identify more

comorbidities associated with the outcome of severe pneumonia. More importantly, it is Prudent to determine if exposure to HIV and /or HAART in utero or during infancy have direct immunological consequences that increase the vulnerability of this population.

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APPENDICES

Appendix I: Observation Checklist

SHEET NUMBER: ……

PART A: DEMOGRAPHIC CHARACTERISTICS

1. Gender of the child

   Male ☐ female ☐

2. Age of the child in months

   …….

3. Marital status of the parent

   ☐ Married ☐ not married ☐ divorced ☐ widowed

4. Who takes care of the child (informant at the time of admission)

   ☐ Parent ☐ guardian

B. OUTCOME OF SEVERE PNEUMONIA

5. How many days has the child been sick before coming to the hospital

   ……..

6. What were the presenting complains at the time of admission?

   ……

   ……

   ……

7. How was the diagnosis of severe pneumonia arrived at

   IMCI criteria (clinical)

   Radiological (CXR)

   Both radiological and IMCI

8. What were the findings on abdominal examination

   Spleenomegaly

   Hepatomegaly

   No organomegaly

9. Was abdominal ultrasound done

   Yes No

10. If yes what were the findings

Spleenomegally

Asplenia

Other findings: specify: ……..

11. What were the findings on respiratory examination

Use of accessory muscles for respiration

Radiological consolidations and opacifications

Others : specify…….

12. What was the medication used to treat severe pneumonia

Crystalline penicillin alone crystalline penicillin plus gentamycin

Ceftriaxone any other (specify)……

13. How many days was the child managed in the ward before the outcome

……..

14. What was the outcome

Dead discharged alive

C. COMORBIDITIES

15. Was there any comorbidity

Yes No

16. Specify the comorbidity

HIV INFECTED

HIV EXPOSED

SICKLE CELL

MALNUTRITION

OTHERS: ……..

17. Was the child on follow up for the above listed comorbidity before admission

Yes No

18. If yes specify the care

……

19. How long ago was the comorbidity diagnosed

<3months 3-6months 6-12 months

>12months

D. NUTRITIONAL STATUS

20. What is the actual weight for age

…….

21. What is the expected weight for age of the child

……

22. What is the Percentage weight for age

……..

23. What is the Mid upper arm circumference

……

24. What is the weight for height/length Z score (WHZ score)

< -1 < -2 < -3

Appendix II: Ethical Approval



COUNTY GOVERNMENT OF KISUMU
DEPARTMENT OF HEALTH

Telephone: 057-2020801/2020803/2020321
Fax: 057-2024337
E-mail: ercjoorth@gmail.com

When replying please quote

JARAMOGI OGINGA ODINGA TEACHING & REFERRAL HOSPITAL
P.O. BOX 849
KISUMU

Ref: IERC/JOOTRH/384/21

Date: 5th March, 2021

To: Timon Kwach Akoo

Dear Timon,

Supervisors: George AyodoAndShehuShagari

RE: STUDY TITLE:-
EFFECTS OF NUTRITIONAL STATUS ON THE OUTCOME OF SEVERE PNEUMONIA WITH SPECIFIC COMORBIDITIES AMONG CHILDREN AGED 2-59 MONTHS IN BONDO SUBCOUNTY HOSPITAL

This is to inform you that ***JOOTRH IERC*** has reviewed and approved your above research proposal. Your application approval number is ***IERC/JOOTRH/363/20.*** The approval period is ***5th March, 2021 – 5th March, 2022.***

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by ***JOOTRH - IERC***.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to ***JOOTRH - IERC*** within 72 hours of notification
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to ***JOOTRH - IERC*** within 72 hours
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to JOOTRH - ***IERC***.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

In case the study site is JOOTRH, kindly report to Chief Executive Officer before commencement of data collection.

Yours sincerely,

SECRETARY, IERC