# A Case Study of Respiratory Tract Infections in Gambella:

Influence of Climatic Factors on Acute Lower Respiratory Infection in Children Under-5 years in Gambella Region, Ethiopia.

## Valentine Ntaghe Odu Nigeria

57<sup>th</sup> Master of public health/International Course in Health Development

KIT (Royal Tropical Institute)
Vrije Universiteit Amsterdam (VU)

### A Case Study of Respiratory Tract Infections in

**Gambella:** Influence of Climatic Factors on Acute Lower respiratory infection in Children Under-5 years in Gambella Region, Ethiopia

A thesis submitted in partial fulfillment of the requirement for the degree of Master of Science in Public Health

Ву

Valentine Ntaghe Odu

Nigeria

#### Declaration:

Where other people's work has been used (from either a printed or virtual source or any other source), this has been carefully acknowledged and referenced in accordance with academic requirements.



#### Signature:

57<sup>th</sup> Master of Public Health/International Course in Health Development (MPH/ICHD) 14 September 2020 -3 September 2021 KIT (Royal Tropical Institute) Vrije Universiteit Amsterdam Amsterdam, The Netherlands

September 2021

Organized by:

KIT (Royal Tropical Institute) Amsterdam, The Netherlands

In co-operation with:

Vrije Universiteit Amsterdam (VU) Amsterdam, The Netherlands

### Table of Contents

LISTS OF FIGURES	5
LIST OF TABLES	ε
LIST OF ABBREVIATIONS	7
GLOSSARY	ε
ACKNOWLEDGEMENTS	S
ABSTRACT	10
INTRODUCTION	11
CHAPTER 1: BACKGROUND	12
1.1 Acute Lower Respiratory Infection and Respiratory syncytial virus	12
1.2 Study Area	13
1.3 Socio-demographic context	13
1.4 Humanitarian situation.	14
1.5 Weather Conditions.	14
1.6 Living condition and source of energy	14
1.7 Health system setup.	15
1.8 Food and Nutrition	16
CHAPTER 2: PROBLEM STATEMENT, JUSTIFICATION, OBJECTIVES AND METHODOLOGY	18
2.1 Problem statement	18
2.2 Justification	19
2.2.1 Research Question:	20
2.3 Study Objective	20
2.3.1 General Objective:	20
2.3.2 Specific Objectives:	20
2.4 Methodology	20
2.4.1 Study method:	20
2.4.2 Search strategy for Chapter 1 and Objective 3	21
2.4.2 Data collection:	22
2.4.3 Data processing and analysis	22
2.4.4 Analytical framework	23
CHAPTER 3: STUDY FINDINGS /RESULTS	26
3.1 Description of the seasonal pattern of ALRI admission cases.	26
3.2 correlation analysis of admission cases with climatic variables	28

3.3 factors other than meteorologic factors from literature that explains the seasonal occurrence of ALRI in Kule Camp, Gambella	31
CHAPTER 4: DISCUSSION	36
4.1 Seasonal patterns of acute Lower respiratory infections in under-5 caused by RSV in Gambella	36
4.2. Relationship between meteorological parameters and seasonal incidence of ALRI in children under-5 caused in Gambella.	37
4.3. Relationship between most important non-meteorological factors that influence seasonal occurrence of ALRI in children under-5 caused in Gambella.	39
4.4 Reflections on the conceptual framework	43
4.5 Strengths and limitations of the study	43
4.5.1 Study Strengths	43
4.5.2 Study limitations	43
CHAPTER 5: CONCLUSION AND RECOMMENDATION	45
CONCLUSION	45
RECOMMENDATIONS	45
Ministry of Health Ethiopia4	45
Health Officers attending to refugees in the camp	46
Cross-cutting for NGOs, multilateral organizations like UNHCR, researchers and policymakers	46
REFERENCES	48
ANNEX	59
Annex I: Table showing Literature search strategy with keywords	59
Annex II: Table shows the number of acute lower respiratory infection (ALRI) cases in children under in Kule camp, Gambella, Ethiopia and meteorological parameters according to each period of the months with corresponding year	
Annex III: Table showing standard deviations of variables before and after Logarithmic transformation6	54
Annex IV: Graph showing the distribution of logarithmic transformed data (ALRI cases) for children under-5 in Gambella.	54
Annex V: Chart for Interpretation of correlation matrix (44)6	55
LISTS OF FIGURES Figure 1	3
Figure 21	.5
Figure 3	16

Figure 4	24
Figure 5	39
Figure 6	66
Figure 7	29
LIST OF TABLES Table 1	21
Table 2	6
Table 3	
Table 4	30

#### LIST OF ABBREVIATIONS

**ALRI** Acute Lower Respiratory Infection

**GAM** Global Acute Malnutrition

GBD Global burden of disease

International Classification of disease and related health problems 10

**IPD** In-patient Department

**LIC** Low- Income Country

**LRTI** Lower Respiratory Tract Infection

**LMIC** Low and middle- Income country

**FDRE** Federal Demographic Republic of Ethiopia

MIC Middle-income Country

MSF Médecins Sans Frontières

NMA National Meteorological Agency of Ethiopia

**OPD** Out-patient Department

**RSV** Respiratory Syncytial Virus

**SNNPRS** Southern Nations Nationalities and Peoples Regional State

**UNHCR** United Nations High Commissioner for Refugees

**VDD** Vitamin D Deficiency

WHO World Health Organization

#### **GLOSSARY**

**Refugee**: An individual who has been forcefully made to flee out of his country either due to war, violence or ill-treatment. Often times they are afraid to return to their country (1).

Acute Lower Respiratory Infection: According to World Health Organization (WHO) International Classification of disease and related health problems 10 (ICD-10), 'Those infections that affects airways below the epiglottis and include acute manifestation of laryngitis, tracheitis, bronchitis, bronchiolitis, lung infections like pneumonia or any combination among them or with upper respiratory infections, including influenza' (2).

**Temperature**: This is the degree to which a body is hot or cold (3).

Climate: "describes the average weather conditions for a particular location and over a long period of time" (4).

**Drought**: A prolonged period of dryness that occurs naturally within the climate cycle that can happen anywhere in the world. When it happens, it causes a reduction in food and water, leading to illness and death (5).

**Humidity**: The amount of water vapor in the atmosphere usually expressed as relative humidity. That is 'the ratio of the vapor pressure to the saturated vapor pressure with respect to water. Expressed as a percentage (6).

**Malnutrition**: "Refers to deficiencies or excess in nutrient intake, imbalance of essential nutrients or impaired nutrient utilization". It represents a spectrum of illnesses that is under nutrition and the other over nutrition—undernutrition manifests as being underweight, stunting, wasting and micronutrient deficiencies (7).

**Immunization**: A process of acquiring protection against an infectious organism by way of vaccination (8).

**Immunity**: 'protection from an infectious disease'. A person with immunity against a particular infectious organism cannot become infected when exposed to the same agent (8).

**Pollution**: This is the process of introducing harmful materials called pollutants into the environment. There are different forms where pollution can occur: air, land and water (9).

#### **ACKNOWLEDGEMENTS**

Completing this work would not have been possible without the participation and encouragement from many people whose names may not be completely enumerated. Your heart-warming contributions are greatly appreciated and acknowledged. First, however, I will like to express my deep appreciation and indebtedness to the following: The Netherland Government for their financial support, my course tutors at KIT for their immerse guidance and teaching throughout my study. I say thank you.

To my family, friends, colleagues and others who, in one way or the other, supported me emotionally, spiritually and financially, thank You.

Above all, to the almighty God, the giver of wisdom, knowledge, understanding and good health.

#### **ABSTRACT**

**Introduction:** Globally, acute lower respiratory infection (ALRI) is responsible for frequent hospitalization of children under -5 years caused by RSV. There is a documented evidence of climatic and non-climatic factors contributing to the risk of ALRI. However, in the Kule refugee camp in Gambella, West Ethiopia, we do not know which factors influence the infection's seasonal pattern. I am reporting findings on these factors and provide recommendations for preventive strategies.

**Methodology:** Secondary data analysis and literature review were done. Secondary data were retrieved from MSF already collected admission data for acute lower respiratory infection (3,628 cases) of under-5 from Kule camp clinic for July 2014-December 2020. This was plotted on a graph and describe for a seasonal pattern.

Meteorological data (temperature, rainfall, relative humidity, wind speed and hours of sunlight) was obtained from the 'world weather online' website, then analyzed using a time series approach. Finally, the association between monthly climatic factors and ALRI cases were analyzed using correlations (Spearman's rank and Partial correlation) by doing a four months lag.

The literature reviewed (2010 - 2021) using search engines and databases to explore non-climatic factors that could explain the seasonal occurrence of ALRI.

This study period is 21 June-11 August 2021 (3 months study).

**Result:** The Infection showed a seasonal pattern. Major peaks in rainy season (July through December), and smaller peaks in February. All meteorological factors were statistically significant. Rainfall, sunlight and relative humidity (low positive correlation), Temperature, sunlight and wind speed (low negative correlation). All non-climatic factors had significant associations with seasonal variation in ALRI. Household factors (overcrowding, indoor cooking, and cooking fuel type) and Child factors (immunization, lack of vitamin D, age, and nutrition).

**Discussion:** All factors do not act independently; instead, they combine. This result would help in anticipating future outbreaks of infection. Thereby, prevention and control strategies can be initiated in a timely way. In addition, cost-effective preventive strategies like health education, environmental control, and better cooking fuel, among others, are necessary to reduce infection incidence during the periods of peak cases(wet season).

**Keywords:** Acute lower respiratory infection, Under-five children, Gambella, refugee, meteorological factors.

**Word Count: 12,601** 

#### INTRODUCTION

My name is Valentine Odu, a trained medical doctor from Nigeria. After my undergraduate training as a medical doctor, I had two years of clinical experience and 7years of public health experience. My working experience started at an infectious disease hospital (Dr Lawrence Henshaw Hospital, Calabar). I worked as a medical officer attending to infectious disease cases like Tuberculosis, HIV/AIDS, and respiratory tract infections. Being a medical officer at the disease hospital made me understand the magnitude and burden those infectious diseases contribute to the community. Therefore, my curiosity was awakened to how I can reduce this burden. In one instance, when called to attend to a patient with severe difficulty in breathing and a history of recently treated chest infection which was not appropriately managed. Unfortunately, the patient died. This further proved to me that we could do much more to prevent deaths from infectious diseases. It was also observed that most children, mainly under-5 years, presented at the Outpatient department were diagnosed with Acute lower respiratory infection.

I got interested in this study,' Influence of Climatic Factors on Acute Lower respiratory infection in Children Under-5 years in Gambella region, Ethiopia ', when MSF proposed it due to the 2020 outbreak of Acute lower respiratory disease most likely caused by Respiratory syncytial virus in Ethiopia among children from Kule refugee Camp, Gambella region. It was suspected that climatological factors and other socio-demographic factors were related to the seasonal outbreak of the infection.

The research was not without difficulties as I struggled to get meteorological data from Ethiopia, which took quite some time to materialize. Also, getting data from MSF was successful, though not without some organizational bureaucracy focused on medical data protection. Another challenge was to carry out the data analysis, of which I was not experienced in using the STATA software.

Finally, I succeeded through all the obstacles with the unflinching help of my thesis supervisor Dr Karsten Jaap, and my statistician friend from Nigeria, Erinfolami Paft-tope. This thesis can help MSF, the Ethiopian government and other relevant stakeholders to prepare for seasonal outbreaks of the infection by making sure that preventive strategies are put in place like vaccination before RSV season (if this becomes available as in westerns settings where the most vulnerable population is passively protected against RSV infection in the RSV-season), washing of hands at baby daycare units, optimizing care of symptomatic patients by providing oxygen and provision of personal protective equipment like face masks before and during RSV season.

#### **CHAPTER 1: BACKGROUND**

#### 1.1 Acute Lower Respiratory Infection and Respiratory syncytial virus

Acute lower respiratory (ALRI) in under-5 children is a frequent cause of hospitalization in this age. Respiratory syncytial virus (RSV) has been identified as the main infectious pathogen at this stage (10). ALRI symptoms include rapid breathing, cyanosis, chest wall indrawing and inability to drink in a child with respiratory symptoms (2). Pneumonia is the most common form of ALRI that causes mortality worldwide in childhood; however, there are other forms of ALRI: Bronchitis, bronchiolitis, tracheitis, and laryngitis (10).

The transmission mode is through inhaling infected aerosols of close contacts or by direct inoculation into the eyes or mouth (11). In addition, some genetically predisposed respiratory pathology like asthma in early childhood has a strong association with ALRI though this association has not been fully understood yet. Still, it can be linked to the fact that atopic conditions increase the susceptibility to respiratory infections. This can also be reversal causation because microbial infections can also predispose to Atopy (12).

Although the infection may start like the common cold with a runny nose, it can quickly progress to bronchitis. Bronchitis is characterized by fever, cough with or without nasal discharge, difficulty breathing, etc. Thus, the reason why children deteriorate faster. It may be devastating in children with underlying health conditions like chronic lung disease, congenital heart diseases, premature births and down syndrome (11).

On the other hand, there are protective factors in under-5 children that reduces their risk for ALRI. For example, children from 24-59 months of age are at lower risk than children from 0-11 months. over time, the children's immunity improves; also, after recovery from the infection, children buildup immunity for that specific virus, hence their ability to fight infections, Like RSV (12).

Furthermore, a study in Rwanda identified several other risk factors influencing ALRI that will be described later. These factors are climatic factors like rainfall, Household -related factors like indoor air pollution and child-related factors such as the age of a child, nutritional status and immunization status (13).

A report from a systematic review in 2017 reveals that about 33million RSV -ALRI cases case and 118 thousand deaths occur yearly in under-5 children, of which 22 million patients and 103 thousand deaths are in lower-income and lower-middle-income countries (10,14). Also, in 2017 according to the global burden of disease (GBD), ALRI was responsible for 704,000 deaths in under-5 years children in Ethiopia (15). An increasing trend was seen in 2018; RSV accounted for 2million cases of ALRI and 800 thousand deaths in children under-5 years. Similarly, in 2019, RSV was the 3<sup>rd</sup> leading cause of death due to respiratory tract infection in children under-5, accounting for 21,733 cases of deaths and 1,938,944 disabilities adjusted life years (DALYs) lost per 100,000 among under-5 children in Ethiopia, more than the DALYs caused by malaria (16).

#### 1.2 Study Area

Gambella is a member state in the Federal Republic of Ethiopia (FDRE) located in the southwestern lowland part of Ethiopia. South Sudan bounds it on the west, Oromia Regional State on the Northeast, and Southern Nations Nationalities and Peoples Regional states (SNNPRS) on the Southeast (see figure 1) (Latitude 8.250°N and 34.583333°E) and an area landmass of 1,104,300Km² (17). Gambella is relatively moist and fertile with sparse settlement and approximately 300,000 people in 25,800 Km² of land. Although most of its highland plateau region is densely populated, and food shortage is one of its major problems, its lowland areas are fertile and less populated (18).

Within the Gambella region is the Kule refugee camp, an isolated, underdeveloped, and far away from urban settlement (19) that is in the North Wello, Amhara of Gambella,314 km from the Ethiopian capital Addis Abba with coordinates 11°42'0" North and 39°41'0"East (20). It accommodates a great majority of the southern Sudanese refugees.

Sudan

Somalia

Somalia

Somalia

Somalia

Somalia

Somalia

Gambella

Region

SNNPR

Region

SNNPR

Region

Figure 1: Map of Ethiopia showing the location of Gambella Region(left), map of Gambella region showing the location of Kule (right) (17,23).

#### 1.3 Socio-demographic context

The population of Gambella is 463,000 (2019 projection based on 2007 census), of which children 0-4 years make up 12% (53,779) (21). Refugees in Gambella account for a large proportion of the general population in Ethiopia. For instance, in October 2017, the refugee count was 399,174,

while the host population was 307,097. This means Gambella refugees alone constituted about 57% of the population (19). Kule camp alone accommodates 43,434 refugees, of which 18% are children 0-4 years and 65% are children below 18years. Females are more than males in the camp in 55% and 45%, respectively (22).

#### 1.4 Humanitarian situation.

Gambella has been facing inter-ethnic and communal conflict with resulting cross border incursions by neighboring southern Sudanese, displacement of individuals and insecurity (food and persons). The number of people displaced between November and December 2019 was 20,943, of which 65% were children (23). According to the UNHCR-operational portal report on 31 December 2019, about 308,978 refugees in the region spread across its refugees' camps (Kule, Nguenyyiel, Tierkidi, Jewi, Pugido 1, Okugo, Pugnido 2 and Aula camps) of which children under five years constituted 17% of the total refugees (21).

In March 2020, refugees in the region reached 312,883, accounting for 41.3% of the Ethiopian refugee population (24). About 31% of households suffered food insecurity because of competing needs for food and shelter, most around the Amhara region where Kule camp is located (19).

#### 1.5 Weather Conditions.

Gambella is characterized by weather conditions with a known adverse effect on health. There is usually high rainfall from May to October and limited rainfall from November to April, leading to droughts (25). In addition, the region is arid, humid and prone to natural hazards such as flooding and droughts. Therefore, it is projected that in the coming years, Gambella will witness extreme weather events and illnesses: extreme temperatures, increased rainfall, prolonged periods of drought, more respiratory disease outbreaks and increase childhood mortality (21).

#### 1.6 Living condition and source of energy

The living condition in the camp is below the minimum standard set by UNHCR (26). As a result, the individuals' vulnerability to ill-health to harsh weather will increase. Only 15% of households live in well-constructed houses that shield them from adverse weather conditions (21). Shelters are built with plastic sheets and Eucalyptus poles, with no partition for separate sleeping and kitchen space (see figure 2) (22,25). Only 60% of the households have shelter (22) because these huts are built for a short stay. Therefore, there is not enough shelter. Families tend to share living spaces leading to overcrowding and the easy spread of respiratory illnesses (27). Generally, the camp has reached its maximum capacity. However, the shortage of shelter remains one of the biggest challenges (22).

Regarding the energy source, refugees in the Kule camp rely majorly on wood fuel (firewood) as a daily energy source for cooking. Access to safe and durable forms remains a significant problem due to the lack of alternative sources. Only 32% of the population have access to solar lanterns, rocket fuel-saving stoves, among others. Hence, 68% of households use traditional three-legged cooking stone fires. Women and children spend long hours in the kitchen, exposing themselves to high levels of smoke, a well-known risk factor for respiratory illnesses (21,22,27).



Figure 2: shows the living condition of refugees in the Kule camp, Gambella (19).

#### 1.7 Health system setup.

Different health levels of healthcare exist in Ethiopia for refugees and host communities (see figure 3) (19,22). As a result, there are two different health bodies that control the various levels of care. Thus, the system operates as "one system, two administrative bodies" whereby the regional bureau at the state levels serves as the primary administrative body managing health facilities at that decentralised level. At the same time, the Administration for Refugees and Returnees Affairs (ARRA) is another administrative body that coordinates and implements primary health services in the camps funded by UNHCR. In addition, some primary health centres and health posts are managed by Non-Governmental Organizations (NGOs) like Médecins Sans Frontières (MSF), among others (19).

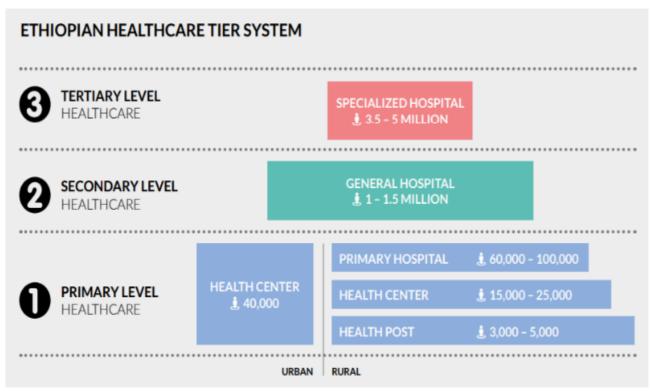


Figure 3: Ethiopia Healthcare system with population cover at each level (19,20).

Immunization is carried out by both UNHCR and ARRA for children and infants. Measles vaccination together with vitamin A prophylaxis is frequently administered to children age 6months to 15 years. In addition, periodic vaccination against pneumonia is given to children 0-5 years. Oral polio vaccine is also administered in the same period as pneumonia. Although children often miss their immunization because of conflict, that displaces them. (19). Currently available medical services include 21 functional clinics, a major hospital, and seven health centres (21).

#### 1.8 Food and Nutrition.

Food availability remains a significant problem in most of Ethiopia. A total of 31% of households suffer from inadequate intake of calories (<2,500kcal per day); 24% of this are in the urban areas, and 33% in the rural area (17,27). Only 86% of the daily food requirements is met (22). In addition, there is a problem of access to food variety. For instance, the share of starchy food consumed is 71.4% (very high). Moreover, the food basket is deficient in proteins and fresh vegetables (22). It is even worse in the rural household that consumes less diverse food when compared to urban households 21.4% and 7%, respectively (17). As a result, in 2016, 10 out of 24 camps had Global Acute Malnutrition (GAM) prevalence above 15% of the emergency threshold (17). In 2019, the GAM among children 6-59 months was 10.4%, anemia prevalence in the same age category was 44.2%, while anemia prevalence in women of childbearing age was 25.6% which is above the WHO standard of <20% for women (27).

The resultant effect of food shortage greatly affects under-5 children and women (pregnant and lactating). Moreover, it increases the risk of severe forms of malnutrition which remains high in camps (27). Also, the risk of dying from respiratory infections is increased in malnutrition (28).

# CHAPTER 2: PROBLEM STATEMENT, JUSTIFICATION, OBJECTIVES AND METHODOLOGY

#### 2.1 Problem statement

The disease's highest burden is in Low-and middle-income countries (LMIC), where the risk of ALRI are more prevalent, timely access to health facilities is not guaranteed, supportive treatment for ALRI may not be present (oxygen) and may be less optimal. In addition, isolation of patients to prevent in-hospital spread may be difficult. Seasonality presenting as an outbreak could prove to be much to handle for the limited number of health facilities with in-patient department capacity for young children. Large scale seasonal prophylaxis by vaccination is impossible. However, if the occurrence of RSV can be predicted, most vulnerable populations like children can be timely vaccinated (29).

Presently, the RSV vaccine (palivizumab), approved by the Food and drug administration (FDC), is available in the United States for prophylaxis against serious attacks of RSV when administered intramuscularly monthly throughout the infective season. This is the only vaccine used in western settings to protect the most vulnerable children (30). However, the cost of 100mg of Palivizumab is between \$904 and \$1868 united states dollars (31) which is very expensive. Therefore, from a financial point of view, this is already a bridge too far, let alone that this could be a logistical nightmare.

However, if other forms of RSV vaccination are available, the camp setting of Kule could be an excellent place to pilot a study on the vaccine. Passive immunization, as in tetanus, could also be a future option in RSV.

Studies that analyzed laboratory-confirmed RSV cases in the middle to low-income countries (LIC) identified a seasonal pattern of RSV incidence, which coincides with seasonal changes like rainfall and temperature (32). Globally, regions with temperate climates like western Europe and the USA show an increase in RSV infection incidence during the winter months and may decrease or be completely absent in summertime. On the other hand, RSV infection shows a sporadic pattern of increased activity during the rainy or cooler months of the year in subtropical regions such as Ethiopia, Rwanda, Nigeria and Bangladesh (30,32).

An observed difference in RVS activities of countries located along the same equatorial latitude and cities in the same region may suggest that the local weather pattern may play a role in causing RSV seasonality (33,34). Furthermore, some countries with tropical temperatures have reported a correlation between RSV infection and peaks in rainfall and warmer temperatures (35-37). Therefore, it has been hypothesized that increased rainfalls and high temperatures were associated with viral stability and survival and enhanced viral transmission in the environment (33). Some studies use environmental data to predict RSV epidemiology (38,39); however, it is not globally applicable because the RSV epidemic season depends on geographic location and altitude (40).

Biological explanations for vulnerability during wet seasons, as described in studies in tropical and temperate regions, hold temperature and humidity accountable for suppressing host immunity, increasing the risk for ALRI. For instance, when cold air is inhaled, it causes vasoconstriction resulting in reduced blood flow in the pulmonary vasculature. This may contribute to an impaired immune response. At the same time, dry weather reduces the mucociliary clearance of the virus from the airway (30). Though, in most tropical climates, RSV infections peak in the wet season (33). This suggests that there is variability in viral behavior with their environment.

Further, social factors could be related to ALRI in under-5 years, which are alternative explanations for seasonality of the infection, such as poor housing conditions and overcrowding during the rainy and winter season. Many households in LMIC face overcrowding because of low income and inadequate living spaces. During the rainy season and in winter, people stay indoors, which increases their exposure to ALRI. Exposure to ALRI is exacerbated by overcrowding and inadequate ventilation linked to poverty and low-income status (12,13,41). Under-5 children in poor socioeconomic conditions are prone to ALRI. This was revealed in a study done in Rwanda where children with ALRI are associated with unimproved household cooking fuel like a stove (13). In Ethiopia, firewood for cooking has been associated with ALRI in households (12).

This research will assess the long-term recurring association between meteorological parameters and ALRI, most likely caused by RSV disease in a population of under-5 children in projects sites in Ethiopia (Gambella) where Médecins Sans Frontieres (MSF) is admitting under -5 children and will discuss other factors that could also determine seasonal outbreaks of ALRI beyond weather alone.

#### 2.2 Justification

A recently published study (41) reported infection with RSV in about a fifth of the infants presenting with severe ALRI, mostly in the rainy season. Generally, about 11% of ALRI cases in infants in Ethiopia are due to pneumonia. Gambella's tropical climate, RSV season typically extends from June to November and would be expected at its highest during rainy seasons (41). It is anticipated that the number of infections will increase during this period. Thus far, there are limited studies that look at the potential association between metrological data and the RSV infection cycle in the Kule region of Gambella.

Outbreaks of RSV over the years could have a similar relationship with meteorological parameters to explain them and possibly lead to better preparedness (bed capacity, isolation measures, oxygen provision, etc.), the ultimate goal of prevention. However, thus far, no studies show the relationship between meteorological parameters and RSV causing cyclical ALRI among children under-5 years in Kule camp.

Despite the availability of some data from different countries and locations with geographic proximity and climatic similarity to Ethiopia, any slight difference in climate, socio-economy, cultural practices, and study timing may influence the research outcome. Hence, research with local data is needed to accurately study the relationship between weather data and the onset of RSV in Gambella.

I choose Gambella because I saw a clear outbreak in 2018 of ALRI and again in 2020. In 2020, additional data showed that 80% of the 55 children admitted by MSF at Kule clinic, the pathogen identified for the outbreak was RSV (MSF unpublished data).

#### 2.2.1 Research Question:

Can seasonal variations in climatological parameters explain acute lower respiratory infection outbreaks in under-5 children caused by RSV in Kule camp, Gambella?

#### 2.3 Study Objective

#### 2.3.1 General Objective:

To explain outbreaks of acute lower respiratory Infections among under-5 children in Gambella, Ethiopia, and make recommendations to the Ministry of Health / MSF on strategic preparedness to optimize in quality and quantity the provided care and possibly prevent outbreaks.

#### 2.3.2 Specific Objectives:

- 1. To describe seasonal patterns in the numbers admitted for Acute Lower respiratory infections in under-5 caused by RSV in Gambella.
- 2. To assess the relationship between meteorological parameters (rainfall, relative humidity, temperature, hours of sunlight and wind speed) that are most important in the seasonal occurrence of acute lower respiratory infection in under-5 caused in Gambella.
- 3. To explore the most important factors from literature other than meteorological factors: child-related factors and household-related factors that could explain the seasonality of acute lower respiratory infection in Gambella.
- 4. To disseminate the research findings and make recommendations to MSF-OCA Holland leading the project in Gambella, the Ministry of Health in Ethiopia and other stakeholders for policymaking and formulation of preventive interventions.

#### 2.4 Methodology

#### 2.4.1 Study method:

This was a secondary data analysis (quantitative) using routinely collected weekly admission data of ALRI for under-5 children in the Kule refugee camp (July 2014 to December 2020). The data source was the MSF's routine data collection system based on DHIS 2.1. This was used to describe the seasonal pattern in ALRI infections.

The case definition that was used for diagnosis of children with the infection (includes bronchitis, bronchiolitis, laryngitis, Tracheitis and Pneumonia) according to the international classification of diseases and related health problems (ICD-10) (2). The diagnosis of cases was aided by using the MSF Clinical guideline -Diagnostic and treatment manual 2017 edition as a guide (42) by clinical officers asking for symptoms of the infection. This was confirmed in an interview with an MSF

clinical officer. Severely affected children were admitted in line with these guidelines to the pediatric ward for further treatment.

Also, historical daily meteorological data (July 2014 to December 2020) of Gambella was obtained online from Weather world Online. These were rainfall, Wind speed, Temperature (maximum and minimum), and relative humidity.

In addition, literature was reviewed to explore other factors apart from climatological related factors that could explain the seasonal occurrence of the infection in the camp.

#### 2.4.2 Search strategy for Chapter 1 and Objective 3

The author reviewed grey and published literature from January 2010 through to March 2021 to identify literature for the background, problem statement and justification of the study (chapter 1 and 2). In addition, the exact length of study and literature search was used to explore other potential risk factors that can explain the seasonal occurrence of ALRI in children under-5 years (objective 2).

Databases and search engines used included: PubMed /Medline, VU library, Embase, Cochrane, Scopus, Google, and Google scholar to identify literature on relevant government websites like WHO, UNICEF to assess grey literature.

A combination of keywords was used to search: Ethiopia, Gambella, Kule, respiratory syncytial virus, respiratory symptoms overcrowding, indoor air pollution, immunization, nutritional status etc. The full table of search terms (see annex I).

Hand search by snowballing the reference list was performed to get relevant articles. Only Articles published in English were considered (see table 1 for a full list of inclusion and exclusion criteria).

Table 1: Criteria for inclusion and exclusion of literatures searched.

#### Inclusion criteria Exclusion criteria When the methods of statistics are not • Studies of hospitalized, institutionalized or refugee-based setting with children. clearly reported. • Risk factors: Household-related factors • Abstract of studies not related to the (over-crowding, in-door air pollution) research question child-related factors (age of child, Publications before 2010 nutritional status, immunization status, Vitamin D receipt). • Publications in languages other than English • Studies in children below ten years Publications with full text not available Studies with multivariate or univariate analysis.

- Study designs: Observational study (casecontrol and cohort), randomized clinical trials, surveys, case series.
- Publications with time series data analysis

#### 2.4.2 Data collection:

**Outcome variables:** This was extracted from the DHIS (District Health Information System). Weekly hospital admission records were already collected by MSF from children under-5 with ALRI at the project site clinic (Kule camp Clinic) from the onset of the project in July 2014 -December 2020.

In Ethiopia, two seasons predominate, one with high rainfall from May to October and one with limited rain, leading to droughts from November to April. To ensure that all extreme meteorological parameters were covered, records from all seasons were considered. These records are usually collected directly into patients' folders by the attending clinical officers. Then, the information in the folders is manually transferred into the EMR (Electronic medical record) by the monitoring and evaluation (M&E) officers. Then, this data from the EMR is uploaded weekly into the DHIS server for each MSF project site (here Kule clinic).

#### Explanatory Variables (meteorological parameters):

These parameters are rainfall(mm), Wind speed(km/h), Temperature (maximum and minimum) (°C), relative humidity (%) and Hours of sunlight(hrs). The meteorological data were extracted online from the World Weather Online (www.worldweatheronline.com) by hovering with the mouse over the historical data graph and copying it into an Excel table (43) (see annex 2).

#### 2.4.3 Data processing and analysis

The author carried out this activity under the guidance of a statistician from Nigeria through the Zoom platform. For this purpose, all variables were first assessed for quality by looking out for missing data and outliers (like a single month with high numbers). Then data sets were aligned together using Microsoft Excel version 2015. After which, the data was transferred to the STATA software version 16(Stata Corp, College Station, TX, USA) for normality testing.

After that, I did a logarithmic transformation of the data set to correct for the wide dispersion of the data evident by the standard deviations (see annex 3). Then a line graph was plotted to prove the normality of the data (see annex 4).

#### Objective 1

A line graph was plotted to determine the seasonal pattern of ALRI admission cases for under-5 children in the Kule camp clinic with data from July 2014 - December 2020. Then it was described to identify any seasonal pattern of infection (see Fig 3).

#### Objective 2:

The time-series approach was used to analyze the association between meteorological parameters and the ALRI cases. Only the Log transformed variables (explanatory and outcome) were used for analysis. Each explanatory variable was plotted on a graph against the outcome variable.

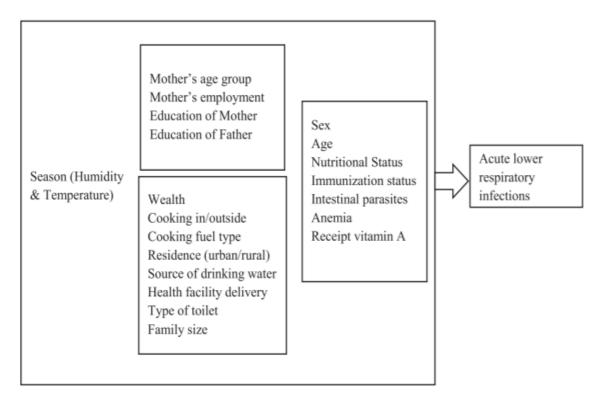
The relationship between variables was done using spearman's rank correlation and Partial correlation. Spearman rank correlations were used for ranking of the variables when they is a high range of numbers. At the same time, Partial correlation was used to measure the strength of a relationship between two variables while controlling for the effect of one or other variables. For instance, when considering the associations between ALRI and rainfall, other variables like hours of sunlight and wind speed are controlled. Therefore, Partial correlation removes collinearity among variables.

The effects of the explanatory variables on the outcome variables (ALRI cases) were evaluated by doing a 1- 4-month linear function Lag (vector autoregressive). For the statistical test, all results were reported with a 95% confidence interval (CI). All variables found significant at a P-value <0.05 were considered most important in the seasonal occurrence of ALRI in children under-5.

#### 2.4.4 Analytical framework

The conceptual framework from the Rwanda demographic health survey (RDHS) 2016 was used to analyze factors associated with ALRI in under-5 in Rwanda communities (see Figure 4) (13).

Figure 4: Conceptual framework of risk factors for acute lower respiratory Infection (13).



The framework gives a more practical understanding of factors influencing ALRI in under-5 in most LMIC and Rwanda. It is composed of 3 blocks: parental, household and child factors.

Within each block, there are different factors: Parents factors (mother age group, mother's employment status, education of mother and father), household and community factors (wealth, cooking fuel type, resident, sources of drinking water, health facility delivery, type of toilet and family size), and child factor (sex, age, nutritional status, immunization status, intestinal parasites, anemia and receipt of vitamin A).

All of which can be more or less affected by the season (humidity and temperature). Furthermore, factors across each block are interrelation. For instance, the mother's educational status can influence breastfeeding practices/choices for the infant, which will impact the child's nutritional status, leading to susceptibility to acute lower respiratory infections. This can be worsened during the cold season due to the suppressant effect of temperature on the child's immune system. A non-breastfed child is more likely to have a severe ALRI than a breastfed child, hence possibly more likely to be admitted during an outbreak.

The framework helps to explain the risk factors for ALRI. Still, it is not a perfect fit for analysis of a refugee setting based on the following: DHS is a population-level assessment that is not specific for a group like refugees. So, the framework contains factors that are not linked to ALRI in a conflict setting. Also, the displaced population has some peculiarities such as their socio-demography, nutritional needs, availability of hygiene, or immunization facilities at varying degrees compared

to the general population. Hence the need to adapt this framework to contain factors that are relevant in a refugee setting that is associated with ALRI.

Seasonal factors (rainfall, temperature, hours of sunlight and wind speed) were analyzed statistically and discussed in relevant sessions. The researcher looked at various seasons (wet and dry) that coincide with peaks or troughs in ALRI admissions.

Included factors were child-related factors: Age of child, nutritional status, immunization status and receipt of Vitamin D. Vitamin A was replaced with vitamin D because it has a relationship with weather and can help explain the possibility of ALRI. In addition, household factors were considered: overcrowding, cooking in/outside, cooking fuel type, and family size.

Excluded factors were: All Parental factors because everyone is relatively equal in income and education during crisis situations, so this factor was less important. In addition, Household factors: wealth, Residence, source of drinking water, health facility delivery, type of toilet and child factor: sex, intestinal parasite, anemia and receipt of vitamin A were all excluded because there were no associations in explaining the seasonal pattern of ALRI in a refugee setting.

#### Limitation in Methodology:

The study is not without limitations. First, the study looks at people in a refugee camp (Kule); hence the demography may not be generalizable, so the seasonal prevalence of ALRI in another setting may differ. Second, co morbidities that can predispose to ALRI, such as HIV in under-5 children and housing-related confounders, are not being assessed. Third, including hygiene factors like hand washing practices are challenging to establish.

Also, most of the literature reviewed could not give specific indicators for Kule camp, such as the number of families per shelter. In addition, the DHIS data is not patient-level data; hence, exploring individual factors such as nutritional status, socio-economic status of households, or other factors using the framework was not feasible due to the limitation of data.

The data of ALRI admissions provided are clinic-based, which may not be a true reflection of medically non-attended cases in the camp or even the entire Ethiopia. As a result, clinic base data may underestimate the true number of cases in the camp. Thereby creates a limitation in generalizing the research findings.

#### Ethical clearance:

The MSF-OCA (Operational Centre Amsterdam) research committee waived the ethical approval because patients were not involved in this research directly, and no clinical samples were required. However, a request for approval was written by the author to gain access to the MSF-OCA DHIS database for the Kule camp, and this was approved by the responsible medical director of MSF-OCA.

#### CHAPTER 3: STUDY FINDINGS / RESULTS

#### 3.1 Description of the seasonal pattern of ALRI admission cases.

The author looked at the seasonal trend in the ALRI admission cases (see figure 5). In the first quarter (January -March), It was observed that at the beginning of the year (January), the cases began to rise for 2015, 2016 and 2018 only and showed a little peak in February. While in 2019 and 2020, the number of cases where relatively constant and then began to drop continuously into the second quarter.

In the second quarter (April-June), the most noticeable rise in cases was in 2018 and 2020, with peaks in May that dropped gradually after that. Meanwhile, there were decreased cases within this period for 2015,2016 and 2017. At the start of June, there was an increase in cases in all the years except 2020. However, the cases increased most in June 2018, above 50.

In the third quarter (July-September), the number of admission cases increased for most of the years except 2015. There was a dramatic increase in the number of cases for 2018, leading to the first highest peak, followed by a slight rise in 2016 for the corresponding period. There was a significant drop in the numbers for both 2018 and 2016 continuously till October. Meanwhile, in the same period in 2015, around August, the number of cases rose and peaked in September, almost reaching 100, then began to drop slowly till October.

In the fourth quarter (October-December), in 2020, there was a steep rise in the number of cases which began early in September (3<sup>rd</sup> quarter) and peaked in November, resulting in the second-highest noticeable peak and continued to rise till the end of the period. There was an increase in cases for other years until November, after which the numbers reduced except in 2015.

In summary, two major peaks in the third quarter in 2018 and fourth quarter in 2020, respectively. Most increases in admission cases were within the third and fourth quarters, while the lowest numbers were recorded between March-May. The cases in the second half of the year (July-December) were more than double (2,494) that of the first half (January -July), which was 1,134 between 2015 and 2020.

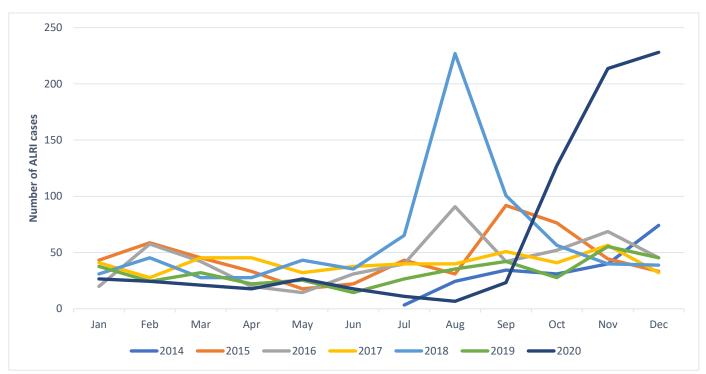


Figure 5: A line graph showing the seasonal pattern of ALRI cases in Kule camp clinic among under-5 children from July 2014 -December 2020.

Table 2: shows data consisting of the numbers of infections with their corresponding months of the year.

Year	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
2014							3	24	34	31	40	74
2015	43	59	45	33	18	22	43	31	92	76		33
2016	20	58		20		31	40	91		52	69	45
2017	41					38	40			41		32
2018	31	45			43	35	65		101	56		39
2019	38	24		22		14	27	35		28		45
2020	27	24	21	18	27	18	11	7	23	127	214	228
Total for each months	200	238	213	166	159	158	229	455	385	411	518	496
Total for 1st and 2nd half of the year	1134						2494					

Data Source: MSF DHIS 1.0

#### 3.2 correlation analysis of admission cases with climatic variables.

The number of admission cases showed periodic spikes and appeared seasonal. Hence, the potential effect of various climatic factors on ALRI was examined. Annual spikes in the number of cases tend to coincide with rainfall and relative humidity (see Fig 4 A/B). An increase in ALRI was preceded by high temperature, rainfall, relative humidity, and wind speed periods. (See Fig 4). In contrast, hours of sunlight did not show any seasonal fluctuation with admission cases.

Associations between ALRI cases with rainfall, relative humidity, wind speed, and temperature showed lags in some months. However, the number of cases increased in some years for rainfall with no lag time (lag 0).

Correlation results using Spearman's rank correlation the following findings were statistically significant (P<0.05) (see table 3): For rainfall and relative humidity it was a low positive correlation for lag months 2-4. This means that with an increase in rainfall and relative humidity, there is a corresponding increase in the number of ALRI. (See table 3)

For average temperature, It was a low negative correlation in lag months 1-4. This means with decreasing temperature, the number of ALRI will increase.

For Wind speed, they was a low negative correlation in lag months 2 and 3. This means that with decreasing wind speed, the number of cases will increase.

Analysis using partial correlation (see table 4). showed that only hours of sunlight appeared significant at lag months 0, 1 and 4. In addition, lag months 0 and 1 showed a low positive correlation. This means that with increasing sunlight, the number of ALRI will also rise. While at lag month 4, the correlation was low negative. For this, an increase in sunlight will be accompanied by a corresponding decrease in admission cases.

Overall, it may seem as though the number of ALRI cases were increasing across the year. However, the number of cases show a downward trend over the years.

A practical guide reference was used for the interpretation of the correlation matrix (44).

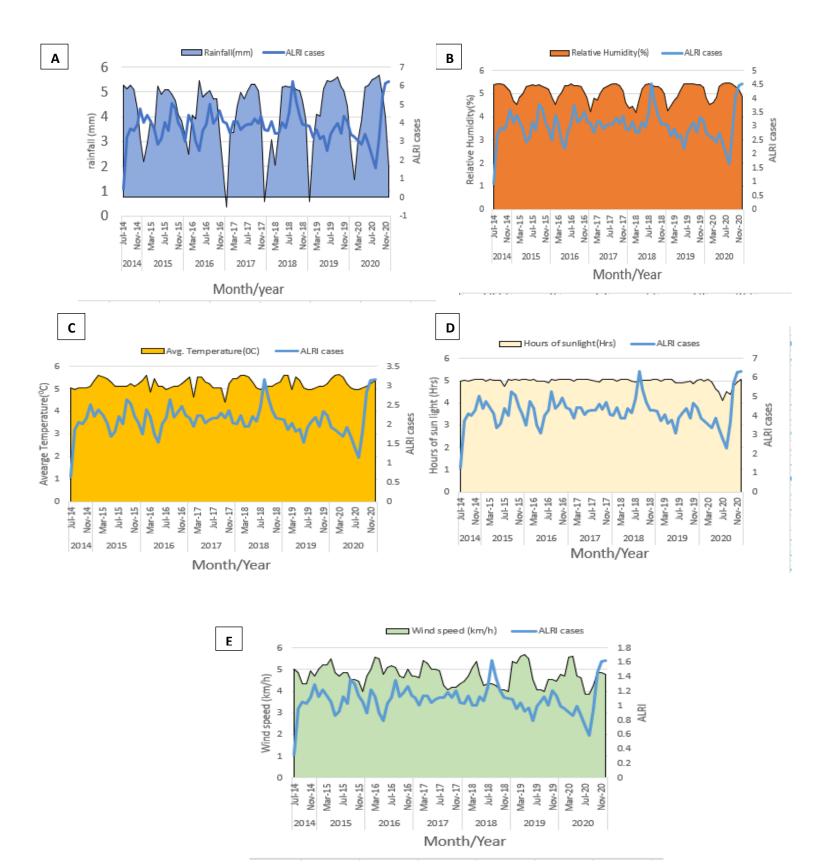


Figure 6: The number of ALRI cases relative to monthly meteorological variables.

Monthly numbers of ALRI cases (blue line, right Y-axis) are shown together with monthly (A) Rainfall (in millimeters, dark blue region), (B) Relative humidity (%, brown region), (C) Temperature (in degrees Celsius, orange), and (D) sunlight (in hours, light yellow), (E) wind speed (in kilometers per hours, green region). Climatic values scales are shown on the left Y-axis.

#### **Spearman correlation matrix**

	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4
Rainfall	-0.1894	0.0572	0.3138***	0.4069***	0.3591***
Relative					
Humidity	-0.0888	0.1887	0.3781***	0.4554***	0.3524***
Average					
temperature	0.0189	-0.2407**	-0.3517***	-0.3917***	-0.3452***
sunlight	0.1647	-0.0429	-0.1115	-0.2084	-0.1399
wind speed	-0.1016	-0.1924	-0.2902**	-0.2672**	0.0039

Table 3: spearman's rank correlation of admitted ALRI and meteorological factors. \*\* < 0.05, and \*\*\* < 0.01. Lag time between the peak of climatic factors and ALRI cases noted in months.

### Partial correlation matrix

Variables	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4
Rainfall	-0.2098	-0.0908	-0.044	0.0105	0.0617
Relative Humidity	0.2038	0.1407	0.1233	0.0834	-0.021
Average					
temperature	0.0107	-0.1127	-0.0341	-0.0154	-0.1372
sunlight	0.2977**	0.2558**	0.0535	-0.1906	-0.3619***
Wind speed	-0.0736	-0.0555	-0.1528	-0.1217	0.0945

Table 4: Partial correlation of admitted ALRI and meteorological factors\*\* < 0.05, and\*\*\* < 0.01. Lag time between the peak of climatic factors and ALRI cases noted in months.

### 3.3 factors other than meteorologic factors from literature that explains the seasonal occurrence of ALRI in Kule Camp, Gambella.

#### Household factors

Over-crowding: A cross-sectional study among Rohingya refugees in India identified household overcrowding as a predictor of ARI in children. Children 13-60 months old were at risk of ARI because of reduced protein-containing meals (< 5 times per week). There was also a significant association between ARI children living in a household with siblings that either had Asthma or allergic conditions. However, this study did not describe the number of persons per household as a baseline risk for infection. The strong link in household overcrowding for this study was that because of the increased number of people in a house, they could be at risk of malnutrition due to competition for food. Malnutrition on its own could further lead to immune compromise for the young child resulting in increased susceptibility for severe infection.

It is explained in this study, though partially, that reduced protein intake (< 5 times per week) is an indication of malnutrition (45). In addition, several other studies have linked ARI in children to overcrowding though not directly only through the pathway of malnutrition (46-48). Another study was carried out in three urban slums in Gulbarga, India, considering socio-economic factors like inadequate housing and its relationship with ALRI incidence. Among 109 diagnosed with Acute respiratory infection in children under-5 years in the study, 8% of them were detected to have ALRI on a background of other social determinants of health that are present among individuals of low social-economic class like poor sanitation, overcrowding, malnutrition, inadequate health facilities among others (49). Overcrowding was identified as a significant risk factor because the extended family system is still practiced in India. This could mean that small houses shelter a large number of people. This was so as 64.75% of the 400 households surveyed were overcrowded.

Adequate housing in the Indian study was defined as follows: the presence of separate kitchen rooms in the house, smoke outlets in kitchen and bathrooms and Pucca style buildings (concrete, stone, clay or metal tiles) while overcrowding was defined in terms of the number of rooms and family members in a house hold (1 room for two people, etc.) and children less than 12 years were calculated as half unit) (49). It was reported as significant that there is an association between ALRI in children whose family member has a history of respiratory illness and became critically ill needing admission. The child's risk of getting sick increases when the children stay in close contact with this family member.

Living with pets such as cats or dogs in a crowded environment has been identified to increase the risk for ALRI in children. Households with pets were reported to have an increased incidence of ALRI (95% CI: 1.07-2.72; OR 1.71). This association was probably due to the allergic reaction some children may have when pets' fur is inhaled (49).

A study in Nigeria showed a strong association between ALRI in children and other socio-economic factors that were still similar to the India study result. It was seen that the effect of smoking is potentiated by poor housing and overcrowding, among others (50). The study also showed that

risk factors for ALRI like lack of immunization, inadequate nutrition, poor breastfeeding practices that have been previously demonstrated (51) are influenced by environmental factors such as overcrowding (50). Age was another risk factor that was associated with overcrowding. The group most at risk for infection was 10-19 months because they are usually weaned off breast milk and introduced to complementary feeding. This leads to a decrease in passive maternal immunity. As a result, when these children are exposed to infections from an overcrowded environment, they easily contract the disease (50).

Furthermore, a Bangladesh study that examined inhouse overcrowding among hospitalized children from the low and high-income household and found an association between overcrowding and ALRI. However, other factors also prevailing like poor economic status, tobacco smoking in households, and inadequate breastfeeding. The risk of Pediatric ALRI increased with household overcrowding. And even worse with the presence of family members that smoked (95% CI 1.00–2.62; OR 1.61). On the other hand, ALRI hospitalization was 3.58 times higher among children from impoverished households than in rich homes (95% CI 2.11–6.08; OR 3.58). Although this association in poor homes was not directly linked to overcrowding, but rather the tradition of exclusive breastfeeding was not practiced (52).

Inadequate housing space was also mentioned in the Indian study (49) that children are often exposed to passive smoking when there leave in such houses. As such their risk for ALRI is increased. This is even worse when wood or coal is frequently used for cooking (52).

#### Cooking in/outside and type of cooking fuel:

Firewood was found to be associated with ALRI when comparing different types of fuel used for cooking. The prevalence of ALRI among children in a household that uses firewood was 41.36% high compared to those that use liquefied petroleum gas (LPG) 9.58%. These children tend to spend much time with their mothers, especially when they cook. This increases the exposure of these children to large amounts of smoke which significantly increases the risk for ALRI (49). We see a similar finding in the study from Nigeria (52), where wood as biofuel indoor was associated with a greater risk for pneumonia and bronchiolitis 2.09 and 1.09, respectively, among under-5 children (50).

Furthermore, a study done in the Rohingya refugee camp among 259 children showed that most families lived in congested spaces with poor ventilation and indoor cooking within a single room space (48). About a quarter of these children have symptoms of ALRI attributed to exposure to indoor pollution within a confined space (48).

A survey In Ethiopia shows that over 90% of the inhabitants use solid biomass fuel for cooking (53). The biomass used in cooking contains different hazardous chemicals like nitrogen dioxide, dioxins, and methylene compounds. The pollutants generated from the kitchen can spread into the rooms, further exposing children to the chemicals (53). This study also showed that the prevalence of ALRI in a household with inside cooking was higher than not cooking inside (53). However, this result was supported by other factors like the educational status of mothers and the age of mothers. For

example, mothers between 44-49 years had a low report of ALRI among their children. It was also reported that the number of ALRI was lower in the highest quintile of wealth because the parents watched television and listened to the news. Watching television increased the awareness about the risk of cooking inside with biomass fuel and stimulated parents to practice healthier habits (53).

The age of the children was also linked to a lower incidence of ALRI. Older children (age >1year) had a relatively lower risk of ALRI because they spend less time indoor and are less exposed to indoor smoke. Meanwhile, mothers of much younger children will prefer to cook inside while taking care of their babies simultaneously (53). These findings were similar in Afghanistan (54).

Under-5 children exposed to unsafe cooking fuel like firewood, biomass among others, were 7.5 times more likely to have ARI than those exposed to safe cooking fuel such as kerosene, natural gas, and LPG. Because unsafe fuel contains harmful substances that interfere with normal lung function leading to infection by RSV causing ALRI (55,56). A histopathological finding suggested that Biomass fuel leads to loss of vital lung capacity, which predisposes to lung disease if exposed for a long time. With continuous exposure, the possibility of having altered lung function increases (53). Pneumonia in children is a frequent outcome of such exposure because children's lungs are immature to get rid of toxic substances like Sulphur oxide, benzene, 1,3-butadiene. This predisposes them to respiratory infections. Studies conducted in Nigeria (57) and Ethiopian urban slums (58) have reported the same associations.

An earlier study in India reported that children living in households that use solid fuels for cooking were associated with a 78% risk of life-threatening respiratory illnesses compared to houses that use cleaner sources of cooking fuels (59,60). A similar result in Ethiopia (58) though the risk of ALRI was three times more among children in households with biomass fuel than their counterparts using clean fuel.

Male children tend to be more at risk of ALRI than their female counterparts of the same age. A study in India revealed that male children spend more time with their mothers in the kitchen. This is because mothers in India culturally prefer to be assisted by boys. Although, this had no direct connection with differences in immunity between the sexes. It only increases the exposure time of the boys to the toxic smoke in the kitchen. Thus, increasing the risk for lungs infections (56).

#### Child-related factors

Age of child: A study among hospitalized children less than 11months of age revealed that they were more likely to suffer from ALRI when compared to their counterparts of age 12-35months (95% CI:0.84-0.98; OR 0.91) and 36-59months (95% CI:0.63-0.74; OR 0.68). This was because appropriate guidelines or protocols in the hospital for infection control practices were not in place, so mothers did not know how to prevent infections in their children. It was also found in another study among refugee children that age 13-60 months happened to be a significant predictor of ARI because these children are young and easily susceptible to infection due to their weak immune

systems. Also, the camp was congested, and this served as a medium for the easy spread of respiratory infection from adults to children (48).

The incidence of ARI was also found to be more among infants (age< 1year), the incidence rate of 38.04% (95% CI:1.18-3.18; OR 1.94) when compared to children 2-3 years incidence rate of 37.84% (95% CI:1.08-3.14; OR 1.84) this was due to high illiteracy rate among caregivers of infants, low utilization of healthcare facilities among others (49). Similarly, in Northwest Ethiopia, among hospitalized children less than one year, there were 3.39 times increased the risk of contracting ALRI due to poor handwashing practices by mothers. And the age of mothers 16 to 27 years was significantly associated with ARI (61). The mother's age was because of their inexperience in providing necessary care for their infants as young mothers.

Furthermore, pneumonia was highly seasonal, mostly occurring during the wet and periods (November to February). It occurs in children under-2 years in the southeast Asian refugee population with an incidence rate for clinical Pneumonia of 0.73 episodes per child year(/CY) (95% CI:0.70-0.73). Radiologically diagnosed pneumonia was 0.22/CY (95% CI:0.20-0.24), of which 61.3% of the cases were due to RSV infection (62).

**Nutritional status:** There is a significant association between the nutritional status and ALRI.A study among under-5 in Ethiopia revealed that good nutrition is necessary for optimum cellular immunity that helps fight against respiratory infections. In this study, ALRI was three times more common in children that were wasted due to poor immune system development (56). Similarly, another Ethiopian study among children under-5 found that the odd of ALRI in severely wasted children was 1.7times higher than in healthy children (61). Another study among 436 children in Enugu, Nigeria, showed that ALRI was more common in malnourished children than in well-nourished children 75.7% (56/74) and 22.6% (82/362), respectively. However, malnutrition in these children existed on a background of inadequate immunization coverage, poor breastfeeding practices like the early commencement of mixed feeding, and in those children that were not breastfed because their mothers were receiving anti-retroviral (HIV medications).

Breast milk contains immunoglobulins which help prevent respiratory infections. Poor feeding affected the optimum function of cellular immunity and innate and humoral immunity (50). The risk of ARI in malnourished children is three times higher than in nourished children (50). A high rate of ALRI was established in children with varying severe degrees of malnutrition (Grade IV and V malnutrition) as defined by the Indian academy of pediatrics classification. The cases of malnutrition were mostly during the winter months (October- January) when food supplies are reduced. During malnutrition, there is depletion of thymolymphatic cells resulting in reduced cell-mediated immunity leading to increased susceptibility to infections (49,63).

#### Immunization status:

Inadequate immunization was found to be a risk factor for developing ARI. About 50% of poorly immunized children were shown to be at risk of ALRI from a study. This was attributed to the non-compliance of mothers to immunization scheduled for their babies (50). ALRI's high prevalence was reported among under-5 with incomplete age required immunization, for instance, lack of measles immunization within the first year of birth. About 81 cases among the 100 children studied had ALRI (61). A similar finding in a systematic review and meta-analysis study showed that incomplete immunization was a risk factor for ALRI because bronchopneumonia is a complication of measles. Hence, Inadequate immunization against measles within the first year of life results in high cases of ARI (64). In addition, a systematic review study on the burden of ARI in crisis-affected populations revealed that seasonal outbreaks of ARI could occur as an outcome of seasonal migrations of refugee populations because when a population is displaced, the proportion of the population that needs to be immune increases to achieve herd immunity. This can lead to secondary pneumonia as a result of the increase in measles epidemics (65).

**Receipt of Vitamin D:** Several studies have a strong association between vitamin D and ALRI. Vitamin D deficiency (VDD) is linked with severe forms of ALRI (66-69). Vitamin D is required for optimal performance of the macrophages, T-cell mediated responses, and activation of antimicrobial properties of monocytes to fight infections (69). In addition, it serves as an immune modulator of the adaptive and innate immune system and regulates the host inflammatory cascade against ALRI (70). Studies have shown that (VDD) is more common in the winter months when there are reduced hours of sunlight when the synthesis of natural Vitamin D is lowest (71).

The skin synthesizes vitamin D from the Ultra-violet (UV) rays of the sun. Though the synthesis depends on a host of factors, for instance, darkly pigmented people have abundant melanin that reduces the natural ability of the skin to produce vitamins. Essentially, it means pale skin people will produce Vitamin D more readily than dark-skinned people. Therefore, subclinical low levels of Vitamin D during the period of the year with less sunlight will increase the risk of ALRI (70).

#### **CHAPTER 4: DISCUSSION**

# 4.1 Seasonal patterns of acute Lower respiratory infections in under-5 caused by RSV in Gambella.

Overall, there are seasonal variations in the number of children admitted for ALRI. For example, more children were admitted in the second half of the year (July-December), which doubled the first half (January -July). Though there were two distinct peaks in the number of cases in 2018 and 2020 beyond the average threshold, this may be due to factors like data entry error. Although, this could not be confirmed because it was secondary data from the DHIS.

In Gambella, ALRI incidence showed a seasonal pattern of occurrence (21), which is in line with literature findings that suggest that admission cases of ALRI are more in the cooler months of the year (30,32). Also, during the rainy season, RSV activity causing ALRI peaked because viral stability and survival are enhanced (33,72).

The weather pattern is significantly associated with increased hospital admissions (33,34), consistent with Spearman's correlation analysis. For example, Gambella has high rainfall from May to October, which coincides with the 3<sup>rd</sup> and 4<sup>th</sup> quarters (second half of the year), then limited rain up to the April of the succeeding year (25). In Kule camp, families share living spaces that become crowded during the rainy season, where people spend more time indoors with limited space leading to overcrowding (26,69,70). This will lead to a spread of respiratory infections (49,50).

Another explanation for the seasonal pattern of infection is biological. For example, studies have shown that immunity is suppressed during cooler periods of the year (13,30,66), and there could be a corresponding reactivation of a dormant RSV virus (72). A study also reported that there is usually an increase in respiratory infections in temperate regions during the spring, autumn and even double during winter (73). Even in Vietnam (74), more children are hospitalized during the summer (May-Oct). Because in Vietnam rainy season runs from October to December, and this coincides with the months of heavy rainfall for Gambella. It is also known that RSV virus activity is said to peak during this period. This supports my result, which suggests that rain within the period precedes changes in the number of admission cases for ALRI (see Fig 6A).

In addition, a review of literature on the burden of RSV among children under -5 years in India revealed the relation between RSV and Rainfall. RSV peaks around the rainy season to early winter (June – October) in India, with some relatively smaller peaks around December to January (75). This was also a similar pattern noticed with ALRI cases in Gambella (see figure 5). In the same study, there were reports of high rainfall preceding an increased RSV activity above the average threshold in 2020 among Lower and middle-income countries other than Ethiopia. However, the reason for this isolated peak is not established.

Production of vitamin D is highest during sunny periods (69,72,76). The production of Vitamin D seems to have a seasonal pattern. Because vitamin D is mainly produced through exposure to the sun, lower levels of Vitamin D are associated with winter while higher levels with summer (76). Naturally, during the rainy season, people spend more time indoors with reduced periods of sunlight.

The partial correlation evaluation for sunlight was significantly at lag months 0,1, and 4. This means that there is a positive correlation between hours of sunlight and ALRI in lag months 0 and 1. Though lag month four correlation was most consistent with the literature (69,72,76) (increase ALRI associated with decrease hours of sunlight) (see table 4). This is a likely explanation; however, there was no data on the serum level of Vitamin D among admitted children with the infection. Also, it was not possible to determine whether refugees were provided with Vitamin D supplements. Therefore, more data are needed to confirm these aspects.

## 4.2. Relationship between meteorological parameters and seasonal incidence of ALRI in children under-5 caused in Gambella.

Temperature and rainfall have been reported in several studies globally to influence RSV activity (30,32,33,72,75). The RSV peak period in Gambella spans from June-November (41); this period is characterized by high rainfall and low temperature. The highest number of admission cases reflected by the two tall peaks in 2018 and 2020 coincides with the peak period of RSV activity. Children under-5 are most vulnerable because of their weak immunity and immature lungs parenchyma, increasing their susceptibility to infections (48,60).

Evaluation using spearman's correlation show statistical significance between the ALRI cases and temperature. However, there was a low negative correlation for ALRI with temperature in lag 2-4 months. This means the incidence of ALRI will increase, and the temperature decrease. The explanation for this result is that decreased temperature reduces the body's protective ability by decreasing secretions from the respiratory mucosa membranes and weakens the immune system by lowering the red blood cells, which eventually results in infections (77).

Low temperatures can reduce the host defense system by affecting the metabolism of Vitamin D (78), thereby cause a decrease in phagocytic activities of the white blood cells (78).

Temperature also affects humans' behaviors. Indoor crowding increases during cooler seasons (77). It also increases the size of infective droplets and improves their deposition on fomites (79). Thus, making it possible to contract infections in a crowded space. RSV has been known to be transmitted by large droplets (80,81). Therefore, Cold temperatures during the rainy seasons in Gambella favors viral survival and transmission.

Experimental studies have shown that RSV inactivation may require some time, especially in lower temperatures (82). Therefore, it is still possible for the infection to continue beyond the present day or weeks. Some studies in Africa and Europe have reported an increase in viral activity in

periods of high rainfall (78,83,84). At the same time, others reported a peak in RSV activities during the cold rainy seasons (85,86).

Relative humidity and temperature affect the respiratory system by two mechanisms: (I) by lowering the body resistance to fight infection (ii) by facilitating the spread of infection in areas that are overcrowded or where ventilation is reduced (87). Some correlation studies between humidity and ALRI were found to be negative (88). A similar finding was reported, which suggested an increase in hospital admissions for ALRI when the relative humidity decreased (87).

Low humidity with reduced air movement increases the risk for respiratory illnesses during cooler seasons (89,90). This is possible because this condition favors water vapor from body cells, particularly the nasal mucosa, leading to micro-injuries that viruses can penetrate, causing infections (87).

In contrast, my study result shows that peaks in the incidence of ALRI were preceded by periods of relatively high humidity (see figure 6 B). Even with Spearman rank correlation. There was a Positive correlation though low, between ALRI admissions and relative humidity.

Although in the tropics, temperature and humidity have different correlations to that observed in temperate countries. Studies in the tropics suggest that stable temperature and higher humidity levels favor large aerosol droplets in the air all around the year (37,91).

Wind speed was significant with Spearman correlation in lag months 2 and 3. However, it was a low negative correlation (see table 3), which means with decreasing wind speed, ALRI cases increases. They were peaks in RSV cases, preceded by a decrease in wind speed (see figure 6E). This finding contrasts the Singapore study (92), which suggested that the number of infections reduced with an increase in wind speed. When it is windy or rainy outside, most people go into their shelter, where they increase proximity to one another. Hence viral condition for viral transmissibility is favored.

However, some studies have argued the opposite. An increase in wind speed leads to an increase in airflow that will cause a cooling effect on the body surface, thereby reducing the body's temperature. This leads to vasoconstriction in the airway preventing viral clearance. These differences are due to the viruses' biological constitution and mode of transmission across humans (77). This will not explain the incident in Gambella because Singapore has different environmental and biological characteristics.

Hours of sunlight is one parameter that is difficult to measure and to relate to the level of exposure to sunlight in babies. However, low amounts have been associated with vitamin D deficiency (VDD). My study results show that hours of sunlight were statistically significant with a positive correlation in lag months 0 and 1.

However, in Lag month 4, the correlation is negative. This is similar to a study that shows that annual hours of sunlight were inversely associated with ALRI cases in children (93). This can be linked to the anti-infective property of vitamin D, which children get when they are exposed to

sunlight (94). Therefore, reduced sunlight can lead to a drop in Vitamin D levels, increasing susceptibility to infection.

The meteorological factors do not work independently of each other. Therefore, outbreaks of ALRI is a combined effect of all factors rather than a single one. Below is an illustration that depicts the interactions between meteorological factors on the ALRI viruses (see fig 5). These interactions is complex and vary between places.

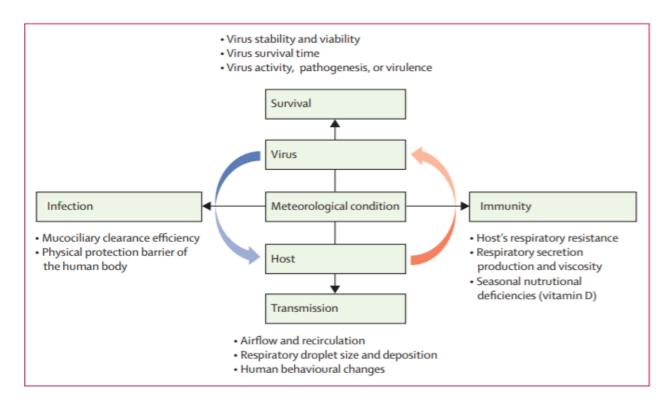


Fig 5: shows the influence of meteorological factors on the ALRI virus (78).

## 4.3. Relationship between most important non-meteorological factors that influence seasonal occurrence of ALRI in children under-5 caused in Gambella.

There is an association of getting ALRI with higher altitudes. Children in higher altitudes have greater odds of getting ALRI than others in lower altitudes (95). In Ethiopia, few houses have access to electricity in the urban areas, and there is limited access to a clean source of cooking fuels in the rural camps. So, refugees frequently use biomass fuels for cooking and keeping their households warm. Especially households that are at high altitudes. Studies have shown that ALRI is a health problem that is more common in areas of high altitude. However, about 10% of the Gambella's region is low land while the remaining 90% is high land (96). But even the low land still has these challenges, which could increase the risk of ALRI.

A study done in Gondar city in Ethiopia revealed that children from households that use animal dung for cooking had a 90% risk of developing ALRI than those who do not (97). In the refugee

camp setting, there are limited available sources of good energy. Individuals survive on firewood for cooking. This can be another explanation for ALRI cases among children. The number of households that uses biomass in the camp is not specified in the literature. However, what is known from reports is that only 33% of household have access to fuel stoves while 65% uses the traditional three-legged cooking stove with biomass (20,21,26). Studies in Pakistan (98), Addis Ababa (58) and Bangladesh (99) have also reported the increased risk of ALRI in children in households that uses biomass fuel like animal dung, firewood among others. Cow dung was identified in a study as an important risk factor for ALRI among under-5 children attending government hospitals in southern Tigray, Ethiopia (55)

Several studies done in Ethiopia, India and other developing countries have shown that the prevalence of ALRI is higher among malnourished children than well-nourished children (46,55,100,101-104). This reflected the fact that children with malnutrition tend to have reduced immunity and, therefore, are predisposed to infections. This is consistent with the prevailing conditions in Gambella refugee camps, where there is a food shortage (<2,500 Kcal per day) (17,27). This is because a large proportion of daily meals do not contain all the needed nutrients. In addition, educational status and parents' income have contributed to poor feeding in children in some low-and middle-income countries (55,104,105). However, this is not the case of Gambella because everyone is a refugee and are exposed to the same socio-economic condition.

A study in India showed that the educational status of the parents, particularly the fathers were associated with the risk of ALRI because the fathers did not ensure that mothers practice healthy nurturing of their babies (49). However, this was because fathers in India are the head of the family, and they stare leadership in the house. So, when they are not educated, they can't make the right decision for the women who will eventually take care of the children. This was consistent with another study in Northwest Ethiopia that showed that poor maternal hygiene was identified as a risk factor for ALRI in infants (61). Because the mother was less educated on proper handwashing, health education for nursing mothers is needed to prevent infections in their babies.

Immunization of children against preventable diseases like pneumonia has been an essential component of pediatric care. Unfortunately, approximately 2,400 children under-5 die from pneumonia daily (106). A retrospective study by UNHCR across 16 refugee camps showed that Pneumonia accounted for 20% of deaths and 17% mortality among children (107).

The prevalence of ALRI was 50% among poorly immunized children from the Nigerian study (50). This was consistent with the previous report in India (108) that indicates the role of immunization in preventing ALRI. This stresses that health education on routine immunization should be targeted at mothers and women of childbearing age in the camp.

In 2014 MSF vaccinated 50,000 children against pneumonia in Gambella (109). This could help build herd immunity and protect those children against ALRI. However, with the frequent influx of refugee children into the camp, over time, this herd immunity would not be adequate to protect the population of newly born children. Regular mass immunization of susceptible children can be

a good intervention to increase coverage for new children arriving at the camp, though no seasonal migration of refugees is documented. This probably may not explain the ALRI cases.

Studies have shown that vaccination of an under -5 group can provide herd immunity for unvaccinated others (110). Therefore, modeling work proposed by Yamin Et AL. can be adopted following this principle of herd immunity for the refugee camps (110).

A study suggests that monoclonal antibody (palivizumab) could be used for immunization to protect individuals from RSV infection if given monthly throughout the season of RSV over five months. Though the setback of this vaccine is that unlike the active immunization for infants, it does not provide herd immunity because there is a chance of acquiring RSV infection in the next season. But this could still protect infants during their most vulnerable age (111). Also, another challenge is that the vaccine is expensive (31). The practice could change if the vaccine becomes more affordable.

Overcrowding is a likely occurrence in Gambella because of the massive influx of southern Sudanese refugees (19,22). Presently, only 50% of Gambella refugees live in transitional houses (22). This will lead to an increased number of families sharing one hut. There was no documented seasonal pattern on refugee migration that could directly explain the seasonality of ALRI. However, overcrowding becomes a secondary effect of refugee influx in camps. This has been linked to an increased risk of ALRI. For example, a family size of more than five was shown to promote the spread of respiratory droplets of infective organisms in a Nigerian study (50). This was also consistent with studies in India (112). Poor living conditions have always been associated with poor health outcomes globally.

In combination with poor hygiene practices like poor hand washing or no cough etiquette, overcrowding can further increase cases. Unfortunately, data on the number of individuals per household was not available. A current survey by UNHCR to get the average number of inhabitants per household can help in this regard.

Vitamin D is essential for strong bones, but it is also needed to prevent respiratory infections. In addition, studies have also shown that the mechanism for this is because Vitamin D produces some metabolites when activated by sunlight that leads to the formation of proteins that have antiviral properties (37). Studies have shown the relation between ALRI with temperature and Vitamin D (66-70). The natural synthesis is UV light-dependent. Hence, during periods of low sunlight in Gambella, Vitamin D supplements will serve an important purpose. Breast milk alone does not provide sufficient Vitamin D for babies; hence a supplement is required (113).

Only vitamin A was prioritized in the UNHCR survey conducted in 2017 (112); so far, Vitamin D supplementation has been less prioritized. A study among Palestinian children in Gaza found that children were 1.96 times more likely to have Vitamin D deficiency than other children who received supplements from the United Nations Relief and Works Agency for Palestine Refugees (UNRWA). The prevalence of Vitamin deficiency was 60.7% and children >1 year were most at risk (114).

Another study that supported this claim was in Indonesia. Indonesia has similar socio-economic challenges like the Gambella camp (indoor pollution, poor nutritional status etc. (115). As a result, nutritional vitamin D deficiency is common in such children (116).

VDD has been linked to the most frequent hospitalizations in children (117-119) and is very common in much younger children with severe pneumonia (119). Also, among newborns, the prevalence of vitamin D deficiency has been documented (120-122). This may be suggestive of the role of maternal nutrition in preventing infections for newborns. Furthermore, studies have shown that Maternal levels of Vitamin D had a positive correlation with plasma concentration of Vitamin D in their babies (123,124). Therefore, maternal levels of Vitamin D above 50nmol/L are needed to prevent deficiencies in newborns (124). Also, women who give birth in the winter are most likely to have lower vitamin D levels than those in the summer (124). This finding further shows the relations between vitamin D and weather. Therefore, the Priority for Vitamin D supplementation should be given to pregnant and nursing mothers during cold and warm seasons.

The high cost of vitamin D can deter low-income earners from buying (125); even worse, when refugees are left to buy, most people in the world will only acquire vitamin D through sunlight (126). The actual challenge would be to determine the quantity of exposure to sunlight that is adequate to prevent ALRI in under-five children. Dairy products are a good source of vitamin D, but also eggs, fish etc. (126,127). These types of foods will be too costly for an average refugee to purchase. Therefore, cost-effective nutritional supplements will mostly be needed.

The Ethiopian government can partner with the UNHCR to provide such support for the refugee population, and MSF can also play a role, for instance, by providing pregnant women with vitamin D supplements during ANC attendance in the winter months (128).

Nutrition has been supported by several studies to be liked with poor immunity and ALRI (117,118,126). In Gambella, acute malnutrition still stands at a high rate among children 6-59months (10.4%). I know that the daily adult food requirement is suboptimal (<2,200 Kcal per day) (22). This will not be different for children. In addition, the food basket in the refugee camps is deficient in protein, fruits and vegetables (22). this leaves parents to feed children with meals less in protein and vegetables. Biologically, proteins are needed for the optimal functioning of the immune system. Therefore, there is a need for nutritional supplementation through fortified foods. As said earlier, However, this does not provide an easy explanation for the seasonality in infection. So far, the World Food programme (WFP) (129) is yet to meet its nutrition target for refugees' due to operational challenges in the distribution of food. These challenges were a result of flooding, droughts, communal clashes and refugee influx. As a result, the school feeding programme was interrupted, conditional cash transfers using mobile networks were disconnected, and access to refugee camps was difficult. Therefore, there is a need for the government to support nutritional programmes.

The age of a child is an important risk factor for ALRI. (48,49,60). This is because of their immature immune cells and delicate skin. Therefore, they are frequently prone to any slight change in

weather conditions. Also, because babies cannot verbally express themselves, they may often die from illnesses without their caregivers knowing. Therefore, parents should be educated to recognize harmful conditions and try to avoid exposing children to known risk factors for ALRI (artificial feeding instead of breastfeeding).

#### 4.4 Reflections on the conceptual framework

The Analytical framework I adapted from the RDHS provided me with a more in-depth analysis of the most important factors that can explain the seasonal occurrence of ALRI. For example, I was able to review MSF immunization coverage for Gambella. It was also a nice tool because the interrelations between different factors were now better understood. For instance, the relation between hours of sunlight with vitamin D and poor nutrition could be discussed without ambiguities. Therefore, this will be a preferable model for a refugee setting.

#### 4.5 Strengths and limitations of the study.

#### 4.5.1 Study Strengths

- 1. This research is useful because it will contribute to an effective policy formulation addressing respiratory infections among under -5 children living in refugee camps, especially in a region like Gambella where majority of household still rely on firewood as a source of cooking fuel.
- 2. Discussing and analyzing factors (climatic and non-climatic) that influence the seasonal outbreak of ALRI is potentially useful in understanding and possibly predicting future outbreaks of ALRI In refugee settings.
- 3. My study can be helpful in planning and implementing health programs that involve mobilization of specific resources or services like training of health care staff, especially when surveillance is not possible or routinely done by prompt anticipation of periods of highest admissions following the more or less predictable seasonal changes.
- 4. This research is useful to health authorities in determining when to prioritize commencement of vaccination programs and what population to focus such as pregnant women attending antenatal (128).
- 5. My study shows the prevailing conditions in a refugee camp that are impactful on the rate of ALRI among children, such as the high residential density of refugees in the camp. Therefore, it shed light on a central problem of refugee healthcare.

#### 4.5.2 Study limitations

1. The research may not be conclusive enough because several other factors possibly play a role that could not be explored in detail in this research, like social dynamics (number of families in a household, frequency of indoor or outdoor cooking), environmental factors (drought) like what is seen in Gambella, and immunization coverage among children. In addition, human behaviors are also was not accounted for, like the number of times women cook with their children in the kitchen could not be obtained. This can be an area for further studies.

- 2. The data of ALRI admissions provided are clinic-based, which may not be a true reflection of medically non-attended cases in the camp or even the entire Ethiopia. Data based on clinical admission may easily underestimate the true number of cases in the camp.
- 3. Information on health-related factors like co-morbidities among the children admitted for ALRI was not accessed, such as presence or absence of malnutrition among the admitted cases. These factors could be confounding factors in this study.

#### CHAPTER 5: CONCLUSION AND RECOMMENDATION

#### **CONCLUSION**

This research aimed to identify most important factors in the seasonal outbreak of acute lower respiratory infection in Kule camp, Gambella, among children under-5. Based on the quantitative data analysis with climatic variables and Literature review on the most relevant factors that influence the seasonal pattern of ALRI.

It can be concluded that admission cases of ALRI show a seasonal pattern of occurrence. Climatic factors (rainfall, temperature, relative humidity, wind speed, hours of sunlight) were found to be significant for seasonal variations in ALRI cases.

Other non-climatic factors that were most important in seasonal outbreaks were household factors (overcrowding, indoor cooking and type of cooking fuel) and Child-related factors (age, nutritional status, vitamin D receipt, and immunization). The result indicates that all factors are considered important and responsible for outbreaks. None of these factors work independently of each other.

This study has demonstrated that most factors identified that could explain the seasonality of ALRI are modifiable; this includes: Malnutrition, inadequate immunization, poor nutritional supplementation, overcrowding, indoor air pollution, poor housing). Furthermore, these factors can be addressed by simple strategies such as education of parents, adequate nutrition, Nutritional supplementation, avoidance of pollution by reducing the use of biomass, immunization, provision of good housing.

Finally, many cofounders' factors influence the associations between ALRI with meteorological parameters and other factors as refugees prefer to indoors during the rainy season. Indoor climate may be a factor to consider. Therefore, future research could look at the role of indoor and outdoor climate on ALRI.

#### RECOMMENDATIONS

#### Ministry of Health Ethiopia

#### Long term:

- 1.For further research, reliable epidemiological studies with larger data sets (studies in multinational sites in Ethiopia with similar climatological and geographical features) that captures more frequently hourly or daily instead of monthly environmental data may sufficiently help explain seasonal occurrences ALRI.
- 2. Should adapt RSV preventive policy specific to the seasonal pattern of ALRI in Gambella; This should be part of the Ethiopian's national health plan. This will protect the most vulnerable children (under-5). This is important if a vaccine or causative treatment becomes available that is affordable as well.

### Health Officers attending to refugees in the camp

#### long term:

3. Should continue routine surveillance of ALRI among children in the refugee camps. It would serve as an important tool for detecting outbreaks before they occur. Since, globally, there is no licensed vaccine or antiviral drugs by the WHO. Also, because ALRI episodes in refugee settings are dynamic. This can improve the ability of health workers to anticipate a seasonal increase in cases to prepare or intervene timely.

#### Short term:

- 4. There should be sensitization and enlighten refugees in the camp by spreading the message to not cook inside, keep children out of the huts when cooking, and not smoke inside; this may impact the peaks.
- 5. Mothers should be educated on practices that can promote health, such as clearing the child nostrils, nutrition advice, emphasis on immunization, providing warm clothes for children in cold season, and improving room moisture by handing damp cloths in the room. This will improve breathing for children during the cold season. Through this means, emphasis on environmental management to prevent infection can be communicated.
- 6. Children in households situated in higher altitudes should be given priority in risk prevention than their counterparts in lower altitudes because the temperature drops at higher altitudes. Therefore, the risk of infection is higher in such children.
- 7. Should prepare and implement community-based plans targeted towards improving food, vitamin D supplementation for breastfeeding children in the form of drop. And for women during antenatal. However, care should be taken in the administration of vitamin D because overdose is toxic.

# Cross-cutting for NGOs, multilateral organizations like UNHCR, researchers and policymakers

- 8. Should scale up the delivery of food to the vulnerable group in the camps. This can be done through ensuring conditional cash transfers, commencement of school feed programme, working with the community to provide local support for delivery of food in conflict periods. This will improve daily food needs (vitamins and proteins) and the nutritional status of children in the camp (128).
- 9. The Ethiopian government, through the Administration for Refugees and Returnees Affairs (ARRA) and other stakeholders like MSF, should provide access to clean energy sources for cooking. Such as the distribution of modern stoves, which will reduce the use of unclean cooking fuel and improve living conditions by providing weatherproof materials for huts.

#### **REFERENCES**

- 1. United Nations High Commissioner for Refugees (UNHCR). What is a Refugee? Definition and meaning | USA for UNHCR [Internet]. Unrefugees.org. 2021 [cited 29 July 2021]. Available from: <a href="https://www.unrefugees.org/refugee-facts/what-is-a-refugee/">https://www.unrefugees.org/refugee-facts/what-is-a-refugee/</a>
- 2. World Health Organization (WHO). International Statistical Classification of Diseases and Related Health Problems. 10th ed. Geneva: World Health Organization; 2010. [cited 29 July 2021].
- 3. Melissa C. Medical Definition of Temperature [Internet]. Medicinenet.com. 2021 [cited 29 July 2021]. Available from: https://www.medicinenet.com/temperature/definition.htm
- 4. World Meteorological Organization (WMO). Climate [Internet]. World Meteorological Organization. 2021 [cited 29 July 2021]. Available from: <a href="https://public.wmo.int/en/our-mandate/climate">https://public.wmo.int/en/our-mandate/climate</a>
- 5. World Meteorological Organization (WMO). Drought [Internet]. World Meteorological Organization. 2021 [cited 29 July 2021]. Available from: https://public.wmo.int/en/ourmandate/water/drought
- 6. American Meteorological Society (AMETSOC). Relative humidity Glossary of Meteorology [Internet]. Glossary.ametsoc.org. 2012 [cited 29 July 2021]. Available from: <a href="https://glossary.ametsoc.org/wiki/Relative humidity">https://glossary.ametsoc.org/wiki/Relative humidity</a>
- 7. World Health Organization (WHO). Malnutrition [Internet]. Who.int. 2021 [cited 29 July 2021]. Available from: <a href="https://www.who.int/health-topics/malnutrition#tab=tab">https://www.who.int/health-topics/malnutrition#tab=tab</a> 1
- 8. Centers for Disease Control and Prevention (CDC). Immunization Basics | CDC [Internet]. Cdc.gov. 2018 [cited 29 July 2021]. Available from: <a href="https://www.cdc.gov/vaccines/vac-gen/imz-basics.htm">https://www.cdc.gov/vaccines/vac-gen/imz-basics.htm</a>
- 9. National Geographic Society. pollution [Internet]. National Geographic Society. 2021 [cited 29 July 2021]. Available from: https://www.nationalgeographic.org/encyclopedia/pollution/
- 10. Li X, Willem L, Antillon M, Bilcke J, Jit M, Beutels P. Health and Economic Burden of Respiratory Syncytial Virus (RSV) Disease and the Cost-Effectiveness of Potential Interventions Against RSV Among Children Under 5 Years in 72 Gavi-eligible Countries. BMC Medicine [Internet]. 2020 [cited 15 March 2021];18.
- 11. Yassine H, Sohail M, Younes N, Nasrallah G. Systematic Review of the Respiratory Syncytial Virus (RSV) Prevalence, Genotype Distribution, and Seasonality in Children from the Middle East and North Africa (MENA) Region. Microorganisms. 2020;8(5):713.
- 12. Ramette A, Spycher B, Wang J, Goutaki M, Beardsmore C, Kuehni C. Longitudinal Associations Between Respiratory Infections and Asthma in Young Children. American Journal of Epidemiology [Internet]. 2018 [cited 15 June 2021];187(8):1714-1720.

- 13. Harerimana J, Nyirazinyoye L, Thomson D, Ntaganira J. Social, Economic and Environmental Risk Factors for Acute Lower Respiratory Infections Among Children Under Five Years of Age in Rwanda [Internet]. researchgate.net. 2021
- 14. American Academy of Pediatrics Committee on Infectious D, American Academy of Pediatrics Bronchiolitis Guidelines C. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalisation for Respiratory Syncytial Virus Infection. Pediatrics. 2014;134(2):415–20
- 15. Anteneh Z, Hassen H. Determinants of Acute Respiratory Infection Among Children in Ethiopia: A Multilevel Analysis from Ethiopian Demographic and Health Survey. International Journal of General Medicine. 2020; Volume 13(1):17-26.
- 16. GBD Compare | IHME Viz Hub [Internet]. Vizhub.healthdata.org. 2021 [cited 17 March 2021]. Available from: <a href="https://vizhub.healthdata.org/gbd-compare/">https://vizhub.healthdata.org/gbd-compare/</a>
- 17. Ethiopia Central Statistical Agency (ECSA). Comprehensive Food security and Vulnerability Analysis (CFSVA). Addis Abba: World Food Programme (WFP); 2019 p. 1-3.
- 18. Geocurrent. Gambella: Ethiopia's Troubled Western Lowlands [Internet]. Ethiopia: Geocurrent; 2010 p. 1. Available from: <a href="https://www.geocurrents.info/geopolitics/gambella-ethiopia's-troubled-western-lowlands">https://www.geocurrents.info/geopolitics/gambella-ethiopia's-troubled-western-lowlands</a>
- 19. United Nations High Commissioner for Refugees (UNHCR). Working Towards Inclusion: Refugees within the National Systems of Ethiopia [Internet]. Addis Ababa: United Nations High Commissioner for Refugees; 2017 [cited 28 July 2021]. Available from: <a href="https://www.unhcr.org/5a55ed8c4.pdf">https://www.unhcr.org/5a55ed8c4.pdf</a>
- 20. Maplandia. Kule Map | Ethiopia Google Satellite Maps [Internet]. Maplandia.com. 2021 [cited 28 July 2021]. Available from: <a href="http://www.maplandia.com/ethiopia/amhara/north-wello/kule/">http://www.maplandia.com/ethiopia/amhara/north-wello/kule/</a>.
- 21. United Nations International Children's Fund (UNICEF). Situation Analysis of Children and Women: Gambella Region [Internet]. 1st ed. Addis Abba, Ethiopia: UNICEF; 2018 [cited 15 March 2021]. Available from: https:// unicef.org
- 22. United Nations High commissioner for Refugees (UNHCR). Kule Camp Profile [Internet]. 1st ed. Addis Ababa: UNHCR; 2019 [cited 28 July 2021]. Available from: https://reliefweb.int/sites/reliefweb.int/files/resources/72233.pdf
- 23. International Organization for Migration, Displacement Tracking Matrix, Gambella Region. Round 14 [Internet]. 14th ed. Gambella, Ethiopia: IOM; 2018 [cited 15 March 2021]. Available from: https://iom.int
- 24. Varalakshmi V, Aditya S, Andrea W. What are the Social Dynamics Between Refugees and their Ethiopian Hosts? [Internet]. World Bank Blogs. 2020 [cited 15 March 2021]. Available from:

## https://blogs.worldbank.org/dev4peace/what-are-social-dynamics-between-refugees-and-their-ethiopian-hosts

- 25. World Bank (WB). Economics of Adaptation to Climate Change, Ethiopia, 2010: UNICEF, Generation El Niño: Long-term Impacts on Children's Well-being. Final Report, 2018
- 26. United Nations High Commissioner for Refugees (UNHCR). A Handy Guide to UNHCR Emergency Standards and Indicators, 2000. [accessed 29 July 2021]. Available from: <a href="https://www.refworld.org/docid/3dee456c4.html">https://www.refworld.org/docid/3dee456c4.html</a>
- 27. United Nations High Commissioner for Refugees (UNHCR). Ethiopia Country Refugee Response Plan 2020-2021 [Internet]. Geneva: UNHCR; 2020 [cited 29 July 2021]. Available from: <a href="https://reporting.unhcr.org/sites/default/files/Ethiopia%20CRP%202020-2021.pdf">https://reporting.unhcr.org/sites/default/files/Ethiopia%20CRP%202020-2021.pdf</a>
- 28. Walson J, Berkley J. The impact of malnutrition on childhood infections. Current Opinion in Infectious Diseases. 2018;31(3):231-236.
- 29. Haynes A, Manangan A, Iwane M, Sturm-Ramirez K, Homaira N, Brooks W et al. Respiratory Syncytial Virus Circulation in Seven Countries with Global Disease Detection Regional Centers. Journal of Infectious Diseases [Internet]. 2013 [cited 18 March 2021];208(suppl 3): S246-S254.
- 30. American Academy of Pediatrics Committee on Infectious D, American Academy of Pediatrics Bronchiolitis Guidelines C. Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. Pediatrics. 2014;134(2):415–20
- 31. Mac S, Sumner A, Duchesne-Belanger S, Stirling R, Tunis M, Sander B. Cost-effectiveness of Palivizumab for Respiratory Syncytial Virus: A Systematic Review. Pediatrics. 2019;143(5): e20184064.
- 32. Bloom-Feshbach K, Alonso W, Charu V, Tamerius J, Simonsen L, Miller M et al. Latitudinal Variations in Seasonal Activity of Influenza and Respiratory Syncytial Virus (RSV): A Global Comparative Review. PLoS ONE [Internet]. 2013 [cited 18 March 2021];8(2): e54445.
- 33. Thongpan I, Vongpunsawad S, Poovorawan Y. Respiratory Syncytial Virus Infection Trend is Associated with Meteorological Factors. Scientific Reports [Internet]. 2020 [cited 18 March 2021];10(1). Available from: <a href="https://doi.org/10.1038/s41598-020-67969-5">https://doi.org/10.1038/s41598-020-67969-5</a>
- 34. Chadha M, Hirve S, Bancej C, Barr I, Baumeister E, Caetano B et al. Human Respiratory Syncytial Virus and Influenza Seasonality Patterns—Early Findings from the WHO Global Respiratory Syncytial Virus Surveillance. Influenza and Other Respiratory Viruses [Internet]. 2020 [cited 18 March 2021];14(6):638-646.
- 35. Pica N, Bouvier N. Environmental Factors Affecting the Transmission of Respiratory Viruses. Current Opinion in Virology [Internet]. 2012 [cited 18 March 2021];2(1):90-95.

- 36. Fall A, Dia N, Cisse E, Kiori D, Sarr F, Sy S et al. Epidemiology and Molecular Characterization of Human Respiratory Syncytial Virus in Senegal after Four Consecutive Years of Surveillance, 2012–2015. PLOS ONE [Internet]. 2016 [cited 18 March 2021];11(6): e0157163.
- 37. Rodriguez-Martinez C, Sossa-Briceno M, Acuna-Cordero R. Relationship Between Meteorological Conditions and Respiratory Syncytial Virus in a Tropical Country. Epidemiology and Infection [Internet]. 2015 [cited 18 March 2021];143(12):2679-2686. Available from: <a href="https://sci-hub.se/10.1017/S0950268814003793">https://sci-hub.se/10.1017/S0950268814003793</a>
- 38. Li, Y. et al. Global Patterns in Monthly Activity of Influenza Virus, Respiratory Syncytial Virus, Parainfluenza Virus, and Metapneumovirus: A Systematic Analysis. Lancet Global Health. [Internet]. 2019 [cited 18 March 2021]; 7, e1031—e1045.
- 39. Chen Z, Zhu Y, Wang Y, Zhou W, Yan Y, Zhu C et al. Association of Meteorological Factors with Childhood Viral Acute Respiratory Infections in Subtropical China: An Analysis over 11 years. Archives of Virology [Internet]. 2013 [cited 18 March 2021];159(4):631-639. Available from: https://sci-hub.se/10.1007/s00705-013-1863-8
- 40. Welliver R. The Relationship of Meteorological Conditions to the Epidemic Activity of Respiratory Syncytial Virus. Pediatric Respiratory Reviews [Internet]. 2010 [cited 18 March 2021]; 10:6-8.
- 41. Frank R, Abate W. Epidemiology of Severe Respiratory Syncytial Virus Infection in Ethiopian Infants: A Prospective Study. European Respiratory Journal [Internet]. 2020 [cited 18 March 2021];56(64):3501. Available from: <a href="http://www.ers-education.org/">http://www.ers-education.org/</a>
- 42. Médecins Sans Frontières (MSF). Clinical Guidelines-Diagnosis and Treatment Manual. 1st ed. Paris: MSF; 2017.p.44-78.
- World Weather Online. Gambella Monthly Climate Averages [Internet]. WorldWeatherOnline.com. 2021 [cited 1 August 2021]. Available from: https://www.worldweatheronline.com/gambela-weather-averages/et.aspx.
- 44. Mutaka M. Statistics Corner: A Guide to Appropriate Use of Correlation Coefficient in Medical Research. Malawi Medical Journal. 2012;24(3):69-71.
- 45. Oishi S, Alam N. Risk Factors Associated with Acute Respiratory Infection (ARI) Among Children Under 10-years in Rohingya Refugee Camp. Recent Research in Science and Technology. 2020;12(1):32-35.
- 46. Asghar S, Srivastava M, Srivastava J, Gupta P, Zaidi Z. Prevalence of Acute Respiratory Infections among Children Under Five years of age Attending Rural Health Training Centre of Era's Lucknow Medical College and Hospital. International Journal of Community Medicine and Public Health. 2017;4(10):3752.

- 47. Cox M, Rose L, Kalua K, de Wildt G, Bailey R, Hart J. The Prevalence and Risk Factors for Acute Respiratory Infections in Children aged 0-59 months in rural Malawi: A Cross-sectional Study. Influenza and Other Respiratory Viruses. 2017;11(6):489-496.
- 48. Chalabi D. Acute respiratory infection and malnutrition among children below 5 years of age in Erbil governorate, Iraq. Eastern Mediterranean Health Journal. 2013;19(01):66-70.
- 49. Ramani V. Acute Respiratory Infections Among Under- Five Age Group Children at Urban Slums of Gulbarga City: A Longitudinal Study. Journal of Clinical and Diagnostic Research. 2016;10(5):9-12.
- 50. Ujunwa F, Ezeonu C. Risk Factors for Acute Respiratory Tract Infections in Under-Five Children in Enugu Southeast Nigeria. Annals of Medical and Health Sciences Research. 2014;4(1):95.
- 51. Prasad DP, Chandreashekhar HG, Madhavi VR. Study of Risk Factors of Acute Respiratory Infections in Under-fives in Solapur. Nat J Comm Med. 2010; 1:64–67.
- 52. Islam M, Sultana Z, Iqbal A, Ali M, Hossain A. Effect of in-house Crowding on Childhood Hospital Admissions for Acute Respiratory Infection: A Matched Case—Control Study in Bangladesh. International Journal of Infectious Diseases. 2021; 105:639-645.
- 53. Geremew A, Gebremedhin S, Mulugeta Y, Yadeta T. Place of Food Cooking is Associated with Acute Respiratory Infection among Under-Five Children in Ethiopia: Multilevel Analysis of 2005–2016 Ethiopian Demographic Health Survey data. Tropical Medicine and Health. 2020;48(1).
- 54. Rana J, Uddin J, Peltier R, Oulhote YJEE. Associations Between Indoor air Pollution and Acute Respiratory Infections among Under-Five Children in Afghanistan: Do Socio-economic Status and Sex Matter? Int J Environ Res Public Health. 2019; 3:323–4.
- 55. Alemayehu S, Kidanu K, Kahsay T, Kassa M. Risk Factors of Acute Respiratory Infections among Under Five Children Attending Public Hospitals in Southern Tigray, Ethiopia, 2016/2017. BMC Pediatrics. 2019;19(1).
- 56. Mondal D, Paul P. Effects of Indoor Pollution on Acute Respiratory Infections among Under-Five Children in India: Evidence from a Nationally Representative Population-Based Study. PLOS ONE. 2020;15(8): e0237611.
- 57. Ana GR, Fakunle GA, Ogunjobi AA. Indoor Airborne Microbial Burden and Risk of Acute Respiratory Infections among Children Under Five in Ibadan, Nigeria. Indoor and Built Environment. 2015 May;24(3):308–14.
- 58. Sanbata H, Asfaw A, Kumie A. Association of biomass fuel use with acute respiratory infections among under-five children in a slum urban of Addis Ababa, Ethiopia. BMC public health. 2014 Dec;14(1):1122.

- 59. Upadhyay AK, Singh A, Kumar K, Singh A. Impact of Indoor air Pollution from the Use of Solid Fuels on the Incidence of Life-threatening Respiratory illnesses in Children in India. BMC public health. 2015 Dec;15(1):300.
- 60. Abha P, Deepti P. Risk Factors of Acute Lower Respiratory Tract Infection: A Study in Hospitalized Central Indian Children Under 5 Year Age. MOJ Current Research & Reviews. 2018;1(3):129-133.
- 61. Dagne H, Andualem Z, Dagnew B, Taddese A. Acute Respiratory Infection and its Associated Factors among Children Under-Five Years Attending Pediatrics Ward at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia: institution-based cross-sectional study. BMC Pediatrics. 2020;20(1).
- 62. Turner C, Turner P, Carrara V, Burgoine K, Tha Ler Htoo S, Watthanaworawit W et al. High Rates of Pneumonia in Children Under Two Years of Age in a South East Asian Refugee Population. PLoS ONE. 2013;8(1): e54026.
- 63. Tekle A, Worku A, Berhane Y. Factors Associated with Acute Respiratory Infection in Children Under the age of 5 years: Evidence from the 2011 Ethiopia Demographic and Health Survey. Pediatric Health, Medicine and Therapeutics. 2015; Volume 2015(6):9-13.
- 64. Jackson S, Mathews K, Pulanić D, Falconer R, Rudan I, Campbell H et al. Risk Factors for Severe Acute Lower Respiratory Infections in Children A Systematic Review and Meta-Analysis. Croatian Medical Journal. 2013;54(2):110-121.
- 65. Bellos A, Mulholland K, O'Brien K, Qazi S, Gayer M, Checchi F. The Burden of Acute Respiratory Infections in Crisis-Affected Populations: A Systematic Review. Conflict and Health. 2010;4(1):3.
- 66. Audi A, Allbrahim M, Kaddoura M, Hijazi G, Yassine H, Zaraket H. Seasonality of Respiratory Viral Infections: Will COVID-19 Follow Suit? Frontiers in Public Health. 2020;8(567184).
- 67. Larkin A, Lassetter J. Vitamin D Deficiency and Acute Lower Respiratory Infections in Children Younger Than 5 Years: Identification and Treatment. Journal of Pediatric Health Care. 2014;28(6):572-582.
- 68. Garg D, Sharma V, Karnawat B. Association of Serum Vitamin D with Acute Lower Respiratory Infection in Indian Children Under 5 Years: A Case Control Study. International Journal of Contemporary Pediatrics. 2016;28(2):1164-1169.
- 69. Dinlen N, Zenciroglu A, Beken S, Dursun A, Dilli D, Okumus N. Association of vitamin D Deficiency with Acute Lower Respiratory Tract Infections in Newborns. The Journal of Maternal-Fetal & Neonatal Medicine. 2015;29(6):928-932.
- 70. Esposito S, Lelii M. Vitamin D and Respiratory Tract Infections in Childhood. BMC Infectious Diseases. 2015;15(1):485.

- 71. Ali S, McDevitt H. Question 1: Does vitamin D Supplementation Prevent Acute Lower Respiratory Tract Infections in Children? Archives of Disease in Childhood. 2015;100(9):892.1-895.
- 72. Fisman D. Seasonality of Viral Infections: Mechanisms and Unknowns. Clinical Microbiology and Infection. 2012;18(10):946-954.
- 73. Price R, Graham C, Ramalingam S. Association between Viral Seasonality and Meteorological Factors. Scientific Reports. 2019;9(1).
- 74. Althouse B, Flasche S, Minh L, Thiem V, Hashizume M, Ariyoshi K et al. Seasonality of Respiratory Viruses Causing Hospitalizations for Acute Respiratory Infections in Children in Nha Trang, Vietnam. International Journal of Infectious Diseases. 2018; 75:18-25.
- 75. Ghia C, Rambhad G. Disease Burden Due to Respiratory Syncytial Virus in Indian Pediatric Population: A Literature Review. Clinical Medicine Insights: Pediatrics. 2021; 15:117955652110292.
- 76. Shoben A, Kestenbaum B, Levin G, Hoofnagle A, Psaty B, Siscovick D et al. Seasonal Variation in 25-Hydroxyvitamin D Concentrations in the Cardiovascular Health Study. American Journal of Epidemiology. 2011;174(12):1363-1372.
- 77. Wang J, Li X, Christakos G, Liao Y, Zhang T, Gu X et al. Geographical Detectors-Based Health Risk Assessment and its Application in the Neural Tube Defects Study of the Heshun Region, China. International Journal of Geographical Information Science. 2010;24(1):107-127.
- 78. Xu B, Wang J, Li Z, Xu C, Liao Y, Hu M et al. Seasonal Association between Viral Causes of Hospitalized Acute Lower Respiratory Infections and Meteorological Factors in China: A Retrospective Study. The Lancet Planetary Health. 2021;5(3): e154-e163.
- 79. Morley C, Grimwood K, Maloney S, Ware R. Meteorological Factors and Respiratory Syncytial Virus Seasonality in Subtropical Australia. Epidemiology and Infection. 2018;146(6):757-762.
- 80. Pica N, Bouvier N. Environmental Factors Affecting the Transmission of Respiratory Viruses. Current Opinion in Virology. 2012;2(1):90-95.
- 81. Kutter J, Spronken M, Fraaij P, Fouchier R, Herfst S. Transmission Routes of Respiratory Viruses among Humans. Current Opinion in Virology. 2018; 28:142-151.
- 82. Hervás D, Reina J, Hervás J. Meteorologic Conditions and Respiratory Syncytial Virus Activity. Pediatric Infectious Disease Journal. 2012;31(10): e176-e181.
- 83. Chen Z, Zhu Y, Wang Y, Zhou W, Yan Y, Zhu C et al. Association of Meteorological Factors with Childhood Viral Acute Respiratory Infections in Subtropical China: An Analysis over 11 years. Archives of Virology. 2013;159(4):631-639.
- 84. Morand S, Owers K, Waret-Szkuta A, McIntyre K, Baylis M. Climate Variability and Outbreaks of Infectious Diseases in Europe. Scientific Reports. 2013;3(1):1774.

- 85. Murray E, Klein M, Brondi L, McGowan J, Van Mels C, Brooks W et al. Rainfall, Household Crowding, and Acute Respiratory Infections in the Tropics. Epidemiology and Infection. 2011;140(1):78-86.
- 86. Dowell S. Seasonality Still Confusing. Epidemiology and Infection. 2011;140(1):87-90.
- 87. Liu Y, Liu J, Chen F, Shamsi B, Wang Q, Jiao F et al. Impact of Meteorological Factors on Lower Respiratory Tract Infections in Children. Journal of International Medical Research. 2015;44(1):30-41.
- 88. Loh T, Lai F, Tan E, Thoon K, Tee N, Cutter J et al. Correlations Between Clinical illness, Respiratory Virus Infections and Climate Factors in a Tropical Pediatric Population. Epidemiology and Infection. 2011;139(12):1884-1894.
- 89. Altuğ H, Gaga E, Döğeroğlu T, Brunekreef B, Hoek G, Van Doorn W. Effects of Ambient air Pollution on Respiratory Tract Complaints and Airway Inflammation in Primary School Children. Science of The Total Environment. 2014;479-480:201-209.
- 90. Shaman J, Kohn M. Absolute Humidity Modulates Influenza Survival, Transmission, and Seasonality. Proceedings of the National Academy of Sciences. 2010;106(9):3243-3248.
- 91. Janet S, Broad J, Snape M. Respiratory Syncytial Virus Seasonality and its Implications on Prevention Strategies. Human Vaccines & Immunotherapeutic. 2017;14(1):234-244.
- 92. Ali S, Tam C, Cowling B, Yeo K, Yung C. Meteorological drivers of respiratory syncytial virus infections in Singapore. Scientific Reports. 2020;10(1):20469.
- 93. Walker J, Gilchrist F, Carroll W. Less sun, more cough: Annual hours of Sunshine are inversely Associated with Hospital Admissions for Children with Lower Respiratory Tract Infection. European Respiratory Journal. 2019;54(63):1.
- 94. Tang J, Loh T. Correlations between Climate Factors and Incidence-A Contributor to RSV Seasonality. Reviews in Medical Virology. 2013;24(1):15-34.
- 95. Horner A, Soriano J, Puhan M, Studnicka M, Kaiser B, Vanfleteren L et al. Altitude and COPD Prevalence: Analysis of the Prepocol-Plantino-Bold-Epi-Scan Study. Respiratory Research. 2017;18(1):162.
- 96. Degife A, Zabel F, Mauser W. Land Use Scenarios and Their Effect on Potential Crop Production: The Case of Gambella Region, Ethiopia. Agriculture. 2019;9(5):105.
- 97. Mekuriaw Alemayehu KA, Hardeep R, et al. Household Fuel use and Acute Respiratory Infections in Children under five years of age in Gondar city of Ethiopia. J Environ Earth Sci. 2014;4(7):77–85.
- 98. Janjua N, Mahmood B, Dharma V, Sathiakumar N, Khan M. Use of Biomass Fuel and Acute Respiratory Infections in Rural Pakistan. Public Health. 2012;126(10):855-862.

- 99. Khan M, B. Nurs C, Mofizul Islam M, Islam M, Rahman M. Household air Pollution from Cooking and Risk of Adverse Health and Birth Outcomes in Bangladesh: A Nationwide Population-based Study. Environmental Health. 2017;16(1):57.
- 100. Sharma D, Kuppusamy K, Bhoorasamy A. Prevalence of Acute Respiratory Infections (ARI) and their Determinants in under five Children in Urban and Rural Areas of Kancheepuram District, South India. Ann Trop Med Public Health. 2013; 6:513–518.
- 101. Fekadu GA, Terefe MW, Alemie GA. Prevalence of Pneumonia among Under-five Children in Este Town and the Surrounding Rural Kebeles, Northwest Ethiopia: A Community Based Cross Sectional Study. Science Journal of Public Health. 2014; 2:150–155.
- 102. Cardoso AM, Coimbra CE Jr, Werneck GL. Risk Factors for Hospital Admission due to Acute Lower Respiratory Tract Infection in Guarani Indigenous Children in Southern Brazil: A Population-based Case-Control Study. TropMed Int Health. 2013; 18:596–607.
- 103. Stewart J, Kyle M, Harish N. Risk Factors for Severe Acute Lower Respiratory Infections in Children A Systematic Review and Meta-analysis. Croat Med J. 2013; 54:110–121.
- 104. Bipin P, Nitiben Talsania Sonaliya KN. A Study on Prevalence of Acute Respiratory Tract Infections (ARI) in Under five Children in Urban and Rural Communities of Ahmedabad district, Gujarat. Natl J Community Med. 2011; 2:255–259.
- 105. Tekle A, Worku A, Berhane Y. Factors Associated with Acute Respiratory Infection in Children Under the age of 5 years: Evidence from the 2011 Ethiopia Demographic and Health Survey. Pediatric Health, Medicine and Therapeutics. 2015; Volume 2015(6):9-13.
- 106. United Nations Children's fund (UNICEF). Pneumonia 2018. Available from: <a href="https://data.unicef.org/topic/child-health/pneumonia/">https://data.unicef.org/topic/child-health/pneumonia/</a>. [cited 2020 February, 2021]
- 107. Hershey C, Doocy S, Anderson J, Haskew C, Spiegel P, Moss W. Incidence and Risk Factors for Malaria, Pneumonia and Diarrhea in Children Under 5 in UNHCR Refugee camps: A Retrospective Study. Conflict and Health. 2011;5(1):24.
- 108. Prajapati B, Talsania N, Lala M, Sonalia K. Epidemiological Profile of Acute Respiratory Infections (ARI) in Under Five Age group of Children in Urban and Rural communities of Ahmedabad district, Gujarat. International Journal of Medical Science and Public Health. 2012;1(2):52.
- 109. Médecins Sans Frontieres (MSF). MSF vaccinate 50,000 children against pneumonia in Gambella, Ethiopia [Internet]. 2015 [cited 7 August 2021]. Available from: https://msfaccess.org/msf-vaccinate-50000-children-against-pneumonia-gambella-ethiopia
- 110. Yamin D, Jones F, DeVincenzo J, Gertler S, Kobiler O, Townsend J et al. Vaccination Strategies against Respiratory Syncytial Virus. Proceedings of the National Academy of Sciences. 2016;113(46):13239-13244.

- 111. Janet S, Broad J, Snape M. Respiratory Syncytial Virus Seasonality and its Implications on Prevention Strategies. Human Vaccines & Immunotherapeutic. 2017;14(1):234-244.
- 112. Savitha A, Gopalakrishnan S, Umadevi R. Acute respiratory infections among under five children in a rural area of Kancheepuram district, Tamil Nadu, India: A Cross-Sectional Study. International Journal of Community Medicine and Public Health. 2018;5(8):3445.
- 113. United Nations High Commissioner for Refugees (UNHCR). Standardised Expanded Nutrition Survey (SENS) Refugee Camps Gambella Final Report, 2017 [Internet]. Ethiopia: UNHCR; 2017 p. 36-179. Available from: <a href="https://data2.unhcr.org/en/documents/download/62744">https://data2.unhcr.org/en/documents/download/62744</a>
- 114. við Streym S, Kristine Moller U, Rejnmark L, Heickendorff L, Mosekilde L, Vestergaard P. Maternal and Infant Vitamin D status during the first 9 months of Infant Life—A Cohort Study. European Journal of Clinical Nutrition. 2013;67(10):1022-1028.
- 115. Chaudhry A, Hajat S, Rizkallah N, Abu-Rub A. Risk Factors for Vitamin A and D Deficiencies among Children Under-five in the state of Palestine. Conflict and Health. 2018;12(1):13.
- 116. McAllister D, Liu L, Shi T, Chu Y, Reed C, Burrows J et al. Global, Regional, and National Estimates of Pneumonia Morbidity and Mortality in Children Younger than 5 years between 2000 and 2015: A Systematic Analysis. The Lancet Global Health. 2019;7(1): e47-e57.
- 117. Schlaudecker E, Steinhoff M, Moore S. Interactions of Diarrhea, Pneumonia, and Malnutrition in Childhood. Current Opinion in Infectious Diseases. 2011;24(5):496-502.
- 118. Haugen J, Basnet S, Hardang I, Sharma A, Mathisen M, Shrestha P et al. Vitamin D Status is Associated with Treatment Failure and Duration of Illness in Nepalese Children with Severe Pneumonia. Pediatric Research. 2017;82(6):986-993.
- 119. Mohamed W, Al-Shehri M. Cord Blood 25-Hydroxyvitamin D Levels and the Risk of Acute Lower Respiratory Tract Infection in Early Childhood. Journal of Tropical Pediatrics. 2012;59(1):29-35.
- 120. Piloya T, Odongkara B, Were E, Ameda F, Mworozi E, Laigong P. Nutritional Rickets Among Children Admitted with Severe Pneumonia at Mulago Hospital, Uganda: A Cross-Sectional Study. BMC Pediatrics. 2018;18(1).
- 121. Poh B, Rojroongwasinkul N, Nguyen B, Ruzita A, Sandjaja, Yamborisut U. 25-hydroxy-vitamin D Demography and the Risk of Vitamin D Insufficiency in the South East Asian Nutrition Surveys (SEANUTS). Asia Pac J Clin Nutr. 2016;25(3):538–48.
- 122. Ariyawatkul K, Lersbuasin P. Prevalence of Vitamin D Deficiency in Cord Blood of Newborns and the Association with Maternal Vitamin D Status. European Journal of Pediatrics. 2018;177(10):1541-1545.

- 123. Oktaria V, Graham S, Triasih R, Soenarto Y, Bines J, Ponsonby A et al. The Prevalence and Determinants of Vitamin D Deficiency in Indonesian Infants at Birth and Six Months of Age. PLOS ONE. 2020;15(10): e0239603.
- 124. Hollis B, Johnson D, Hulsey T, Ebeling M, Wagner C. Vitamin D Supplementation During Pregnancy: Double-blind, Randomized Clinical Trial of Safety and Effectiveness. Journal of Bone and Mineral Research. 2011;26(10):2341-2357.
- 125. Agarwal N, Faridi M, Aggarwal A, Singh O. Vitamin D Status of Term Exclusively Breastfed Infants and their Mothers from India. Acta Paediatrica. 2010;99(11):1671-1674.
- 126. Blue Cross Blue Shield. Most People Don't Need Vitamin D Testing [Internet]. Bcbs.com. 2015 [cited 7 August 2021]. Available from: <a href="https://www.bcbs.com/news/press-releases/most-people-dont-need-vitamin-d-testing">https://www.bcbs.com/news/press-releases/most-people-dont-need-vitamin-d-testing</a>.
- 127. Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academy Press, 2010.
- 128. Bokharee N, Khan Y, Wasim T, Mallhi T, Alotaibi N, Iqbal M et al. Daily Versus Stat Vitamin D Supplementation During Pregnancy; A Prospective Cohort Study. PLOS ONE. 2020;15(4): e0231590.
- 129. Word Food Programme (WFP). Ethiopia Country Strategic Plan (2020-2025) | World Food Programme [Internet]. Wfp.org. 2020 [cited 10 August 2021]. Available from: https://www.wfp.org/operations/et02-ethiopia-country-strategic-plan-2020-2025.

ANNEX
Annex I: Table showing Literature search strategy with keywords.

Type of document	Source	Keywords used
Published peer- reviewed paper	PubMed/Medline VU library Google Google Scholar Cochrane Library Scopus JSTOR ScienceDirect	Factors, determinants, Acute Lower respiratory infection, pneumonia, children, under-5 years, Gambella, admissions, refugee, Ethiopia. low-income countries, respiratory syncytial virus, prophylaxis, Palivizumib, overcrowding, socio-economic condition, immunization status, Nutritional status, rainfall, temperature, relative humidity,
Grey Literature	WHO American Academy of Pediatrics, Ethiopian Demographic and Health survey, Ethiopian public health Institute (EPHI), UNICEF	Number, children under-5 years, Acute Lower respiratory infection, Indoor air pollution, health facility.

Reports	WHO, Ethiopian	Ethiopia, Gambella, Kule, south Sudanese, refugees, displaced
	Demographic and	people, young children, nutrition, weather, temperature, wind
	Health survey	speed, rainfall, burden, mortality, morbidity, health facility.
	(EDHS), World	
	bank, UNHCR,	
	Ethiopian central	
	statistical agency,	
	UNICEF,	
	International	
	organizations for	
	migration (IOM),	
	EPHI, World	
	weather online.	

Annex II: Table shows the number of acute lower respiratory infection (ALRI) cases in children under-5 in Kule camp, Gambella, Ethiopia and meteorological parameters according to each period of the months with corresponding year.

Year	Months	serial number	ARI Cases	Average Rainfall	Relative Humidity	Max. Temperature(°C)	Min. Temperature(°C)	Avg. Temperature(°C)	Hours of sunlight(hr)	Wind speed(km/h)
		Humber	Cases	(mm)		remperature( c)	Temperature( C)	Temperature( C)	Surmgrit(iii)	speed(kiii/ii)
				(111111)	(%)					
2014	Jul-14	1	3	407.92	90	22	12	19	338	4.5
	Aug-14	2	24	337.94	91	22	11	18	346	4.3
	Sep-14	3	34	417.23	91	23	12	19	333	3.7
	Oct-14	4	31	320.7	89	24	11	19	348	3.7
	Nov-14	5	40	112.44	81	25	11	19	359	4.4
	Dec-14	6	74	24.49	72	26	12	20	372	4.1
2015	Jan-15	7	43	6.7	50	30	14	23	372	4.5
	Feb-15	8	59	17.7	44	33	16	26	336	4.8
	Mar-15	9	45	64.29	57	31	16	25	360	4.8
	Apr-15	10	33	36.81	65	30	15	24	353	5.2
	May-15	11	18	399.52	83	26	14	22	350	4.3
	Jun-15	12	22	258.08	86	25	13	20	350	4.1
	Jul-15	13	43	321.32	89	24	12	20	252	4.3
	Aug-15	14	31	331.93	87	24	13	20	366	4.3
	Sep-15	15	92	259.67	88	24	13	20	344	3.9
	Oct-15	16	76	177.53	84	26	13	21	364	3.9
	Nov-15	17	44	86.41	82	25	13	20	356	3.8
	Dec-15	18	33	62.78	75	26	13	21	364	3.3
2016	Jan-16	19	20	26.71	57	29	14	23	371	4.1
	Feb-16	20	58	10.01	44	33	17	26	348	4.5
	Mar-16	21	42	82.2	57	32	26	17	372	5.3

	Apr-16	22	20	66.59	66	29	15	24	337	5.2
	May-16	23	14	521.11	87	24	14	20	330	4.2
	Jun-16	24	31	225.25	86	24	13	20	339	4.6
	Jul-16	25	40	269.01	91	21	12	18	305	4.7
	Aug-16	26	91	303.3	87	23	12	19	362	4.6
	Sep-16	27	42	204.62	86	25	12	20	349	4.1
	Oct-16	28	52	204.59	85	25	12	20	371	4
	Nov-16	29	69	34.34	67	27	13	21	360	4.5
	Dec-16	30	45	4.7	54	29	13	23	372	4.1
2017	Jan-17	31	41	0.6	34	33	14	25	372	4.1
	Feb-17	32	28	33.1	54	30	24	15	334	4
	Mar-17	33	45	32.1	52	31	16	25	372	5.1
	Apr-17	34	45	132.1	64	30	15	25	358	4.9
	May-17	35	32	280.6	79	27	14	22	370	4.5
	Jun-17	36	38	198.5	83	26	13	21	360	4.5
	Jul-17	37	40	306.7	88	23	12	19	353	4.4
	Aug-17	38	40	429.8	91	22	13	19	336	3.6
	Sep-17	39	51	448	91	23	13	19	326	3.4
	Oct-17	40	41	306.1	86	25	20	13	358	3.5
	Nov-17	41	56	92.5	72	26	13	21	359	3.5
	Dec-17	42	32	0.8	46	31	14	24	372	3.7
2018	Jan-18	43	31	4.9	39	31	15	24	372	3.8
	Feb-18	44	45	22.5	41	32	17	26	335	4.1
	Mar-18	45	28	5.45	33	33	16	26	372	4.6
	Apr-18	46	28	29.53	48	31	15	25	360	5
	May-18	47	43	375.3	75	27	15	22	358	4.2
	Jun-18	48	35	395.57	90	22	13	19	334	3.6
	Jul-18	49	65	379.4	91	22	13	18	323	3.7
	Aug-18	50	227	397	90	22	13	19	337	3.7
	Sep-18	51	101	319.77	85	25	13	20	344	3.6

	Oct-18	52	56	305.42	85	25	13	20	357	3.4
	Nov-18	53	40	184.9	77	26	14	21	357	3.4
	Dec-18	54	39	62.4	64	29	15	22	372	3.3
2019	Jan-19	55	38	0.8	35	33	17	26	372	5
	Feb-19	56	24	16.7	42	33	18	26	336	4.9
	Mar-19	57	32	88.8	51	33	25	18	372	5.4
	Apr-19	58	22	77.9	57	31	16	25	358	5.5
	May-19	59	25	340.4	74	28	15	23	369	5.2
	Jun-19	60	14	524.5	93	22	14	19	301	3.9
	Jul-19	61	27	508.9	93	22	13	18	311	3.4
	Aug-19	62	35	557.2	93	22	13	18	310	3.4
	Sep-19	63	42	634.9	93	23	13	19	321	3.3
	Oct-19	64	28	373.4	89	25	13	20	333	3.9
	Nov-19	65	55	310.6	88	24	13	20	296	3.9
	Dec-19	66	45	136.5	80	26	14	21	356	3.8
2020	Jan-20	67	27	13.8	54	30	15	24	360	4.2
	Feb-20	68	24	2.5	44	32	17	26	338	4.1
	Mar-20	69	21	20.5	47	33	16	27	372	5.3
	Apr-20	70	18	60.8	57	30	16	25	321	5.4
	May-20	71	27	381.4	85	25	14	21	221	4.1
	Jun-20	72	18	422.8	92	23	14	19	190	4
	Jul-20	73	11	564.3	95	21	14	18	120	3.2
	Aug-20	74	7	622	94	22	14	18	191	3.2
	Sep-20	75	23	710.7	93	23	14	19	169	3.6
	Oct-20	76	127	244.4	84	25	13	20	258	4.3
	Nov-20	77	214	79.9	77	26	13	21	316	4.3
	Dec-20	78	228	5.1	58	28	15	23	358	4.2

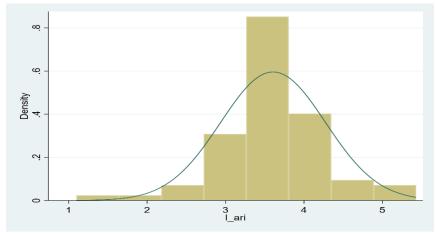
Data source: Weather data from World weather online (<u>www.worldweatheronline.com</u>)

Annex III: Table showing standard deviations of variables before and after Logarithmic transformation.

Before logarithmic transformation							
Variable Observations Mean Std. Dev. Min Max							
ALRI cases	78	46.51282	41.19537	3	228		
Rainfall(mm)	78	218.4324	189.9892	0.6	710.7		
Relative humidity	78	73.03846	18.62371	33	95		
Average temperature( <sup>0</sup> C)	78	21.16667	2.902827	13	27		
Hours of sunlight(Hrs)	78	336.141	48.87294	120	372		
wind speed(km/hr)	78	4.191026	0.598957	3.2	5.5		

After logarithmic transformation							
Variable	Observations	Mean	Std. Dev.	Min	Max		
ALRI cases	78	3.605685	0.669544	1.098612	5.429346		
Rainfall(mm)	78	4.573471	1.732173	-0.51083	6.56625		
Relative humidity	78	4.252333	0.293779	3.496508	4.553877		
Average temperature( <sup>0</sup> C)	78	3.043007	0.139021	2.564949	3.295837		
Hours of sunlight(Hrs)	78	5.80259	0.191645	4.787492	5.918894		
wind speed(km/hr)	78	1.422996	0.141671	1.163151	1.704748		

Annex IV: Graph showing the distribution of logarithmic transformed data (ALRI cases) for children under-5 in Gambella.



Source: MSF DHIS 2.0

Annex V: Chart for Interpretation of correlation matrix (44)

Size of Correlation	Interpretation
.90 to 1.00 (90 to -1.00)	Very high positive (negative) correlation
.70 to .90 (70 to90)	High positive (negative) correlation
.50 to .70 (50 to70)	Moderate positive (negative) correlation
.30 to .50 (30 to50)	Low positive (negative) correlation
.00 to .30 (.00 to30)	negligible correlation