University of Ghana http://ugspace.ug.edu.gh

UNIVERSITY OF GHANA

COLLEGE OF HEALTH SCIENCES

BACTERIAL AETIOLOGY AND RISK FACTORS ASSOCIATED WITH CHILDHOOD OTITIS MEDIA IN ACCRA, GHANA

BY

VIDA BANNAH

(10701647)

THIS THESIS IS SUBMITTED TO THE UNIVERSITY OF GHANA, LEGON, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF AN MPHIL MEDICAL MICROBIOLOGY DEGREE

SEPTEMBER, 2021

University of Ghana http://ugspace.ug.edu.gh

DECLARATION

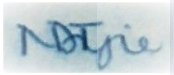
I, Vida Bannah, declare that the work presented in this thesis is the result of my research work carried out in the Department of Medical Microbiology Research Laboratory, University of Ghana Medical School (UGMS), Korle-bu, under the supervision of Dr. Nicholas T.K.D. Dayie and Prof. Eric Sampane-Donkor, and all references cited in this work have been duly acknowledged.

Sign… …….

Date: 30th September 2021

Vida Bannah

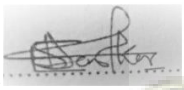
(Student)

Sign……  ……..

Date: 30th September 2021

Dr.Nicholas T.K.D. Dayie

(Main Supervisor)

Sign…  ……..

Date: 30th September 2021

Prof. Eric Sampane-Donkor

(Co-Supervisor)

University of Ghana http://ugspace.ug.edu.gh

DEDICATION

I dedicate this work to the Almighty God, my dear husband, (Mr Daniel Ebo Bannah), my lovely children (Alexis Ewuradjoa Nhyira Bannah and Ethan Kofi Adom Bannah), and finally my ever-supportive aunty, (Gifty Arthur).

University of Ghana http://ugspace.ug.edu.gh

ACKNOWLEDGEMENT

I would like to acknowledge my supervisor, Dr. Nicholas T.K.D. Dayie and Prof. Eric Sampane-Donkor, both of the Department of Medical Microbiology, University Of Ghana Medical School (UGMS), Korle-bu. Miss Ruth Amo of the Ear, Nose and Throat (ENT) unit of Princess Marie Louise Hospital (PMLH), Naomi Boateng and Joyce Antwi of the ENT unit of Mamprobi Hospital, Captain Oteng and the entire staff of the ENT and paediatric units of the 37 Military Hospital.

I would also like to appreciate the efforts of Dr. Appiah-Korang Labi, Miss Mary-Magdalene Osei, Mr. Fleischer C.N. Kotey, Mr. Joseph Anamsi, Mr. Amos Akumwena, and the entire staff and interns of the Department of Medical Microbiology, UGMS.

Finally, I acknowledge the great help I received from Mr. Shittu Bunkumi Dhikrullahi, my colleagues, family, and friends. Thank you for the diverse help to make this work a great success!

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

TABLE OF CONTENTS

DECLARATION i
DEDICATION ii
ACKNOWLEDGEMENT iii
TABLE OF CONTENTS iv
LIST OF TABLES vi
LIST OF ABBREVIATIONS viii
ABSTRACT x
CHAPTER ONE 1
1.0 INTRODUCTION 1
1.1 Background 1
1.2 Problem Statement 3
1.3 Rationale 4
1.4 Aim 5
1.5 Specific Objectives 5
CHAPTER TWO 6
2.0 LITERATURE REVIEW 6
2.1 The Anatomy of the human ear 6
2.2 Overview of Otitis Media 7
2.2.1 Types of Otitis Media 8
2.2.2 Aetiology of Otitis Media in Children 9
2.2.3 Pathogenesis of The Different Types of OM 11
2.3 Diagnosis of Otitis Media 13
2.4 Management of Otitis Media in Children 14
2.5 Risk Factors associated with Otitis Media 16
2.6 Epidemiology of Otitis Media 17
2.6.1 Global Epidemiology 17
2.6.2 Epidemiology in Africa 19
2.7 Otitis Media in Ghana 19
2.8 Antimicrobial Resistance 21
2.9 Prevention of Otitis Media 22
CHAPTER THREE 24

University of Ghana http://ugspace.ug.edu.gh

3.0 MATERIALS AND METHOD 24
3.1 Study Site 24
3.2 Study Design and Sampling 24
3.3 Specimen and Data Collection 25
3.4 Specimen Processing 26
3.4.1 Bacterial Identification 26
3.5 Antimicrobial Susceptibility Testing 28
3.6 Data Processing 29
3.7 Ethical Considerations 29
CHAPTER FOUR 30
4.0 RESULTS 30
4.1 Socio-Demographic and Clinical Information of the Study Participants 30
4.2 Bacterial Isolates Distribution 32
4.3 Antimicrobial Susceptibility Profile 35
4.4 Risk Factors for Otitis Media among the Study Participants 38
CHAPTER FIVE 33
5.0 DISCUSSION 33
CHAPTER SIX 40
6.0 CONCLUSIONS, RECOMMENDATIONS, AND LIMITATIONS 40
6.1 Conclusions 40
6.2 Recommendations 40
6.3 Limitations 41
REFERENCES 42
APPENDIX I: CONSENT FORM 53
APPENDIX II: STUDY QUESTIONNAIRE 58

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

LIST OF TABLES

Table 1: Demographic characteristics and clinical information of study participants..... 31

Table 2: Distribution of isolated bacterial pathogens in otitis media 33

Table 3: Antimicrobial susceptibility pattern of bacterial pathogens of otitis media 37

Table 4: The potential risk factors associated with ASOM and CSOM in children with otitis media 39

University of Ghana http://ugspace.ug.edu.gh

LIST OF FIGURES

Figure 1: Anatomy of the human ear 6

Figure 2: Total percentage of isolated bacterial pathogens from children with ASOM and CSOM 34

University of Ghana http://ugspace.ug.edu.gh

LIST OF ABBREVIATIONS

OM…….....Otitis media

AOM…….....Acute otitis media

ASOM…….....Acute suppurative otitis media

API…….....Analytical Profile Index

OME…….....Otitis media with effusion

CSOM…….....Chronic suppurative otitis media

ET…….....Eustachian Tube

ENT…….....Ear, Nose and Throat

KBTH…….....Korle-Bu Teaching Hospital

PML…….....Princess Marie Louise Children's Hospital

MEF…….....Middle Ear Fluid

SPSS…….....Statistical package for social sciences

USA…….....United States of America

USD…….....United States Dollars

URTI…….....Upper Respiratory Tract Infection

URI…….....Upper Respiratory Infection

CAD…….....Canadian Dollars

AUD…….....Australian Dollars

University of Ghana http://ugspace.ug.edu.gh

WHO…….....World Health Organisation

NACL……..... Sodium chloride

CLSI…….....Clinical Laboratory

TM…….....Tympanic membrane

OE…….....Otitis externa

AAP…….....American Academy of Pediatrics

37MH…….....37 Military Hospital

MH…….....Mamprobi Hospital

E. coli……..… *Escherichia coli*

ESBL……Extended Spectrum Beta-lactamases

AMPC……..……... Ampicillinase C

P. aeruginosa…… *Pseudomonas aeruginosa*

spp.…….…….... Species

GNB……..Gram-negative bacteria

GPB……...Gram-positive bacteria

CoNS……Coagulase Negative Staphylococcus

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

ABSTRACT

Background: Otitis media (OM), also known as middle ear infection, has a high prevalence among young children. Young children have horizontally aligned Eustachian tubes (ET), smaller and shorter middle ear anatomical features and more frequent upper respiratory tract infections than adults. These make them more vulnerable to OM. The complications of OM include hearing loss, delayed speech development, impaired intellectual development, and societal challenges in later life. Nonetheless, there is a paucity of data regarding the bacterial aetiologies responsible for the condition and their associated antimicrobial susceptibility patterns, and little is known about the risk factors associated with OM.

Aim: This study aimed to investigate the bacterial aetiologies and risk factors associated with otitis media among children in Accra, Ghana

Materials and method: The research was a cross-sectional study in which children below 13 years old attending the ear, nose and throat clinics (ENT) of the Princess Marie Louise Children's Hospital (PMLH), 37 Military Hospital and Mamprobi Hospital with suppurative otitis media were recruited during the study period. Following standard bacteriological methods, sterile ear swabs were used to take middle ear discharge from study participants for culture and antimicrobial susceptibility testing. A standard questionnaire was also used to collect data on socio-demographic characteristics, potential risk factors and clinical information.

Results: Out of the 100 swabs from the 100 study subjects, 97 swabs gave positive yields, out of which 87.3% were pathogens. The most commonly-isolated pathogen was *Pseudomonas aeruginosa* (38.5%), followed by *Klebsiella pneumoniae* (19.8%) and *Proteus mirabilis* (11.5%). A high level of resistance was recorded for ampicillin, piperacillin-tazobactam, cefuroxime, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole, tetracycline and ceftriaxone. Of the

University of Ghana http://ugspace.ug.edu.gh

potential risk factors of ASOM and CSOM evaluated, only child history of ASOM showed a statistically significant association with the development of CSOM.

Conclusion: *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, and *Proteus mirabilis* were the common bacteria aetiologic agents of childhood OM. Poor responses to first-line antibiotics such as ampicillin and amoxicillin-clavulanate were reported, hence ciprofloxacin and gentamicin are recommended to be used in the management of OM in children. A history of ASOM was the risk factor identified to be associated with developing CSOM.

University of Ghana http://ugspace.ug.edu.gh

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Otitis media (OM), also known as middle ear inflammation, is a range of diseases of the middle ear, commonly affecting young children (Schilder *et al*., 2016; Bowatte *et al*., 2018; Tesfa *et al*., 2020). The infection comprises acute otitis media (AOM), otitis media with effusion (OME) and chronic suppurative otitis media (CSOM) (DeAntonio *et al*., 2016; Schilder *et al*., 2016; Bowatte *et al*., 2018). OM can either present as suppurative or non-suppurative (Afolabi *et al*., 2012).

It easily occurs in young children due to the anatomy of their Eustachian tube (ET). Their Eustachian tube is more flexible, horizontal, and shorter, allowing for easier entry of pathogens of nasopharyngeal origin into the middle ear (Qureishi *et al*., 2014; Sakulchit *et al*., 2017; Tadesse *et al*., 2019). The ET protects the middle ear cavity through ventilation, by clearing middle ear fluid (MEF) and stops nasopharyngeal bacteria pathogens from entering the middle ear by being a natural barrier (Coticchia *et al*., 2013; Qureishi *et al*., 2014; Schilder *et al*., 2016; Bowatte *et al*., 2018).

Otitis media causes children to frequently visit the paediatrician, and it brings about medical costs on parents through its treatment (Ladomenou *et al*., 2010; Cai *et al*., 2017). The economic burden of the disease is enormous-in 1992, in the USA, an estimated 4.1 billion USD was spent on direct treatment of otitis media, and Canada spent 470 million CAD in 1994 (Cai *et al*., 2017). In 2008 in Australia, an amount ranging from 100 to 400 million AUD was spent on otitis media either directly or indirectly (Cai *et al*., 2017). Even though in developed countries, CSOM is no longer common (Awuah *et al*., 2012), chronic OM remains the predominant ear disease and the main cause of ill health in poorer countries. Learning and behavioural problems are encountered due to

University of Ghana http://ugspace.ug.edu.gh

hearing loss from recurrent OM (Awuah *et al*., 2012). An annual mortality of around 20,000 has been attributed to complications with OM, with the highest death toll recorded in children less than five years old (Monasta *et al*., 2012; DeAntonio *et al*., 2016) and developing countries being the most affected by the burden of the infection (Appiah-Korang *et al*., 2014).

Acute otitis media commonly affects children and families worldwide (Ladomenou *et al*., 2010). It may occur as a single or recurrent infection and it is the leading primary cause of antimicrobial agent prescription and incorrect use (Ladomenou *et al*., 2010). The contribution to antibiotics resistance is increased due to the wrong diagnosis, leading to avoidable treatment (Harmes *et al*., 2013; Bowatte *et al*., 2018).

Otitis media with effusion has to do with the collection of fluid in the middle ear space due to Eustachian tube dysfunction and ear infection occurs without signs and symptoms (Kucur *et al*., 2015; Cai *et al*., 2017). OME is detected by the presence of an effusion, glue-like fluid behind an intact ear drum (Qureishi *et al*., 2014; Schilder *et al*., 2016). Loss of hearing occurs and is noticed through the conduct of children, as well as their speech development and performance at school (Kucur *et al*., 2015; Schilder *et al*., 2016).

The problem caused by one type of otitis media, which is CSOM, worldwide consists of 65 to 330 million individuals with discharging ears with 60% of that number having hearing loss, and as such, is the main cause of hearing loss in children in the developing countries (WHO, 2004; Schilder *et al*., 2016). CSOM occurrence broadly differs from one country to another, however, it has a peak rise in developing countries (Schilder *et al*., 2016; Mukara *et al*., 2017). CSOM is usually associated with death as compared to the other types of OM, hence it can be said that OM is associated with death aside from morbidity (Qureishi *et al*., 2014).

University of Ghana http://ugspace.ug.edu.gh

1.2 Problem Statement

Otitis media is one of the commonest paediatric infections (Harmes *et al*., 2013; Cai *et al*., 2017; Mukara *et al*., 2017; Bowatte *et al*., 2018). AOM and OME are the predominant middle ear inflammatory ailments affecting children (Cai *et al*., 2017). Young children have horizontally aligned Eustachian tubes, smaller and shorter middle ears, as well as more frequent upper respiratory tract infections than adults, and these make them the most vulnerable to OM (Mukara *et al*., 2017; Bowatte *et al*., 2018). OM is widespread globally, and in emerging economies, it is the main cause of hearing loss (WHO, 2004; Monasta *et al*., 2012; Santoshi Kumari *et al*., 2016; Mukara *et al*., 2017; Filipe *et al*., 2020). Apart from hearing loss, CSOM is known to cause complications such as intracranial and extracranial problems and death (Qureishi *et al*., 2014; Orji *et al*., 2015; Filipe *et al*., 2020). In addition, Orji *et al.* (2015) identified one humiliating problem caused by CSOM to be continuous ear discharge, and this is normally seen to occur in individuals in emerging economies for years. A study conducted in Ghana revealed that hearing loss occurred in children who had suffered from AOM (Awuah *et al*., 2012). Hearing loss may lead to a delay in language, speech, and intellectual skills development, and this results in societal challenges later in life (Schilder *et al*., 2016; Mukara *et al*., 2017; Bowatte *et al*., 2018). OM is also known to be the cause of surgery requests in children (WHO, 2004; Qureishi *et al*., 2014; Kucur *et al*., 2015; Schilder *et al*., 2016; Walker *et al*., 2017), and this is a major health concern. One precipitating factor of OME occurrence is that its early diagnosis is a challenge in young children, owing to its deceptive nature (Kucur *et al*., 2015). This is because signs and symptoms are not easily noticeable in children (Qureishi *et al*., 2014; Schilder *et al*., 2016). According to Filipe *et al.* (2020) and Mukara *et al.* (2017), people have scanty knowledge about OM and its associated complications, hence the need for health education bordering around OM (Mukara *et al*., 2017; Filipe *et al*., 2020).

University of Ghana http://ugspace.ug.edu.gh

In addition, the primary cause of antibiotic use and reduced quality of life in children is due to OM (Schilder *et al*., 2016; Walker *et al*., 2017; Bowatte *et al*., 2018;). Hence, treatment of OM could potentially select for the emergence of multidrug-resistant organisms. The development of multi-drug-resistant bacteria increases the risk of using new and more expensive drugs. Conclusively, OM results in a major social and economic burden on families and the health care system (Afolabi *et al*., 2012; Bowatte *et al*., 2018;) and this burden is highly seen in developing countries (Tadesse *et al*., 2019).

1.3 Rationale

OM presents a significant public health challenge globally, causing children, who are disproportionately burdened with the disease, to frequently visit the paediatrician. It is the leading cause of inappropriate antimicrobial prescription and drug use among children. In addition, diagnosing OM on time is not always likely, since it is seen in young ones who are not able to voice out pains (Kucur *et al*., 2015; Mukara *et al*., 2017). In a study carried out by Mukara *et al.* (2017), children affected by OM had their parents unaware until they were examined, thus leading to delayed diagnosis. Prevention of OME and appropriate management schedule for children with OME can occur when the risk factors and prevalence are properly laid down (Kucur *et al*., 2015). This same principle of establishing the risk factors can also be applied to prevent the occurrence of AOM and CSOM. Currently in Ghana, there is no active surveillance with regard to investigating OM, resulting in the paucity of data regarding the bacterial aetiologies responsible for the condition and their associated antimicrobial resistance patterns. Management of OM is normally empirical, and hence the need to continuously monitor causative organisms and their antimicrobial resistance patterns, thereby enhancing treatment options available to clinicians.

University of Ghana http://ugspace.ug.edu.gh

Additionally, very little is known about the risk factors associated with the disease and as such, currently there is no existing data in Ghana for risk factors associated with otitis media. Such information is relevant to the formulation and implementation of effective preventive strategies against acquisition of the infections, as well as guiding treatment plans to combat the infections (Kucur *et al*., 2015; Ladomenou *et al*., 2010). Therefore, this study was very important and aimed at determining the bacterial etiologies, antimicrobial susceptibility patterns and risk factors associated with otitis media among children in Accra.

1.4 Aim

The study aimed to determine the bacterial aetiologies and risk factors associated with otitis media among children in Accra, Ghana.

1.5 Specific Objectives

The specific objectives of this study were:

- To determine the bacterial aetiologies of otitis media among children visiting the Ear, Nose, and Throat Clinic of Princess Marie Louise Children's Hospital, 37 Military Hospital and Mamprobi Hospital.
- To determine the antimicrobial susceptibility patterns of the aetiologic agents.
- To determine risk factors for ASOM and CSOM associated with childhood otitis media at the selected hospitals.

University of Ghana http://ugspace.ug.edu.gh

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 The Anatomy of the human ear

The human ear can be divided into three parts: the outer, middle and inner ear (Schilder *et al*., 2016). The outer ear is made up of the pinna and the ear canal (Schilder *et al*., 2016). The eardrum, a thin cone-shaped membrane, separates the outer ear from the middle ear (Schilder *et al*., 2016). The middle ear comprises the middle ear cavity and the ossicles (the malleus, incus and stapes), which are attached to the eardrum and the middle ear cavity is connected to the nasopharynx by the Eustachian tube (Schilder *et al*., 2016). Figure 1 shows the anatomy of the human ear.

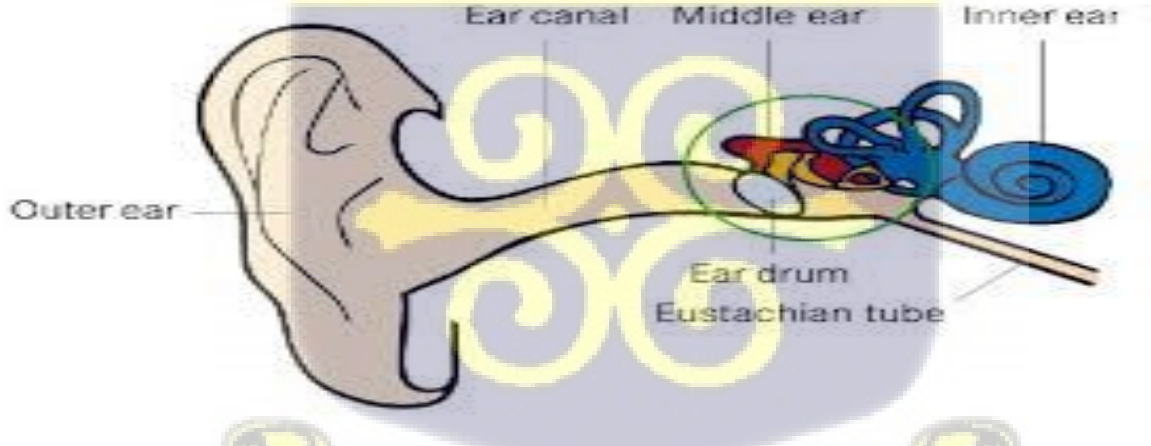


Figure 1: The Anatomy of the human ear (https://www.bloggang.com/mainblog).

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

2.2 Overview of Otitis Media

Otitis media (OM), which is the main cause of visits to the paediatrician, is an inflammatory process that affects the middle ear (Schilder *et al*., 2016; Cai *et al*., 2017; Chandarakesan *et al*., 2018). It is made up of different subtypes which present differently, this includes acute otitis media (AOM), otitis media with effusion (OME) and chronic suppurative otitis media (CSOM) (DeAntonio *et al*., 2016; Schilder *et al*., 2016; Bowatte *et al*., 2018; Chandarakesan *et al*., 2018). Young children are prone to OM due to the anatomy of their Eustachian tube (ET), their Eustachian tube is more flexible, horizontal, and shorter, allowing for easier entry of pathogens of nasopharyngeal origin into the middle ear (Qureishi *et al*., 2014; Sakulchit *et al*., 2017; Tadesse *et al*., 2019). The ET protects the middle ear cavity through ventilation, by clearing middle ear fluid (MEF) and acts as a natural barrier by preventing nasopharyngeal bacteria pathogens from entering the middle ear (Coticchia *et al*., 2013; Qureishi *et al*., 2014; Schilder *et al*., 2016; Bowatte *et al*., 2018).

Due to the frequent visit of children to the paediatrician, there is a burden of medical costs to the parents through treatment (Ladomenou *et al*., 2010; Cai *et al*., 2017). OM is also known to be the primary cause of antibiotic use and reduced quality of life in children (Schilder *et al*., 2016; Walker *et al*., 2017; Bowatte *et al*., 2018). Recurrent or chronic forms of OM can lead to complications such as hearing loss which eventually leads to language delay and learning problems (DeAntonio *et al*., 2016; Tesfa *et al*., 2020). It is placed as the second cause of hearing loss and the fifth global burden of disease with incidences mostly occurring in low and middle-income countries like South Asia and Sub-Saharan Africa (Tesfa *et al*., 2020). An annual mortality of around 20,000 has been attributed to complications with OM, with the highest death toll recorded in children less than five years old (Monasta *et al*., 2012; DeAntonio *et al*., 2016).

University of Ghana http://ugspace.ug.edu.gh

2.2.1 Types of Otitis Media

The different forms of OM present in diverse modes (Qureishi *et al*., 2014). AOM refers to the rapid onset of signs and symptoms of active infection of the middle ear (Schilder *et al*., 2016; Cai *et al*., 2017). It can occur in the suppurative form as acute suppurative otitis media (ASOM) described by an acute eardrum perforation with discharge (Qureishi *et al*., 2014; Santoshi Kumari *et al*., 2016; Filipe *et al*., 2020). It is estimated that at least, one episode of acute otitis media will occur in nearly 80% of children (Harmes *et al*., 2013; Monasta *et al*., 2012; Coticchia *et al*., 2013), commonly affecting children under two years of age (Coticchia *et al*., 2013; Qureishi *et al*., 2014; Hounkpatin *et al*., 2016) with the highest occurring between six and fifteen months (Coticchia *et al*., 2013; Qureishi *et al*., 2014). Recurring and extended episodes of AOM can lead to hearing loss and delayed language development, negatively impacting the performance of the affected children (Uhari *et al*., 2009). The nasopharynx is known to be a reservoir of upper respiratory tract pathogens, and these pathogens have been demonstrated to cause AOM by entering the middle ear through the Eustachian tube (Marom *et al*., 2012; Gisselsson-Solén *et al*., 2014;). The presence of these pathogens in the middle ear brings about inflammation and the collection of pus, leading to AOM (Qureishi *et al*., 2014). Colonization and adhesion to cells by bacteria in the middle ear are believed to be promoted by viral infections in the nasopharynx which provide an enabling environment (Marom *et al*., 2012; Gisselsson-Solén *et al*., 2014; Qureishi *et al*., 2014). AOM presents with signs and symptoms such as tugging, holding or rubbing the ear, otalgia, irritability, fever, and symptoms of upper respiratory tract infections like runny nose or cough (Schilder *et al*., 2016; Sakulchit *et al*., 2017).

Otitis media with effusion is defined as the collection of fluid in the middle ear without signs or symptoms of ear infection (Harmes *et al*., 2013; Qureishi *et al*., 2014; Kucur *et al*., 2015; Buzatto *et al*., 2017; Cai *et al*., 2017). It is also known as serous or secretory otitis media or glue ear (Kucur

University of Ghana http://ugspace.ug.edu.gh

et al., 2015). The frequently reported symptom due to fluid collection in the middle ear is hearing loss; this can lead to language delay or learning problems (Qureishi *et al*., 2014). A factor considered to be responsible for the development of OME is the immature immunity of young children, irrespective of the function or dysfunction of the Eustachian tube (Kucur *et al*., 2015), and may also serve as a risk factor for AOM (Marom *et al*., 2012; Qureishi *et al*., 2014).

CSOM is described as a persistent discharge from the middle ear through the tympanic membrane (TM) or eardrum perforation lasting two weeks or more (WHO, 2004). In developing countries, CSOM is a significant cause of preventable hearing loss in children (WHO, 2004). A sound understanding of the risk factors for CSOM helps in proper treatment and prevention (Wang *et al*., 2016).

2.2.2 Aetiology of Otitis Media in Children

The aetiological agents of otitis media can be bacteria, viruses, fungi (Argaw-Denboba *et al*., 2016; Ejiofor *et al*., 2016; Tesfa *et al*., 2020), *Mycoplasma pneumoniae*, and *Chlamydia trachomatis* (Ejiofor *et al*., 2016) with bacteria usually being a major cause (Argaw-Denboba *et al*., 2016; Ejiofor *et al*., 2016; Tesfa *et al*., 2020). Fungi as stated are an etiological agent of OM. Focus has been placed on bacteria as the causes of chronic suppurative otitis media with less attention placed on other mycological agents (Juyal *et al*., 2014). Ear discharge being chronic plays a key role in fungal infection of the middle ear (Ghosh *et al*., 2015), therefore, patients with prolonged ear discharge and without response to antibiotic management, should be quarried for fungal infection of the middle ear by an ENT specialist (Juyal *et al*., 2014). Chronic ear discharge creates humidity and alkaline pH in the middle ear and due to this there is prolonged use of topical steroids and antibiotics leading to fungal infection of the middle ear (Ghosh *et al*., 2015). Prolonged use of topical steroids or antibiotics can lead to the elimination of bacterial flora and eventually fungal

University of Ghana http://ugspace.ug.edu.gh

elements occurrence (Juyal *et al*., 2014). Aside from prolonged usage of antibiotics and steroids, be it topical or systemic, certain conditions such as Human immunodeficiency virus (HIV) infection, chemotherapy, diabetes, and malignancy makes one prone to fungal infections of the middle ear (Juyal *et al*., 2014). Fungal isolates normally obtained from various studies include *Aspergillus* species (spp), *Candida* spp, and saprophytic fungi ((Juyal *et al*., 2014; Ghosh *et al*., 2015). A study done in India, by Ghosh *et al*. (2015) isolated fungal elements in order of predominance to be: *Aspergillus* spp, *Candida* spp and other saprophytic fungal elements (Ghosh *et al*., 2015). According to another study by Juyal *et al*. (2014), the predominant fungal isolates obtained were *Aspergillus* spp, *Candida* species and *Penicillium* spp (Juyal *et al*., 2014). Viral URTI initiates AOM by causing nasopharyngeal inflammation (Marom *et al*., 2012; Schilder *et al*., 2016). Common and important respiratory viruses that have been studied in detail in relation to AOM pathogenesis include Influenza A virus (IAV), respiratory syncytial virus (RSV), human rhinovirus (HRV), and adenovirus (Marom *et al*., 2012). The virus that is mainly linked to being associated with AOM is RSV (Pettigrew *et al*., 2011). Even with or without positive bacterial cultures, 2 to 22% of RSV have been detected in the middle ear fluid of AOM patients (Marom *et al*., 2012). Also, in young hospitalized children with respiratory distress, it has been established that RSV has a key influence on the occurrence of AOM (Marom *et al*., 2012).

Streptococcus pneumoniae, *Haemophilus influenzae*, and *Moraxella catarrhalis* are bacterial etiological agents that generally cause AOM (Pettigrew *et al*., 2011; Marom *et al*., 2012; Gisselsson-Solén *et al*., 2014; Qureishi *et al*., 2014; DeAntonio *et al*., 2016; Ngo *et al*., 2016). AOM can also be caused by *Staphylococcus aureus* (WHO, 2004; Aduda *et al*., 2013; Qureishi *et al*., 2014). *Streptococcus agalactiae*, Gram-negative enteric bacteria, and *Chlamydia trachomatis* are pathogens found in the middle ear of neonates below two weeks of age (Harmes *et al*., 2013).

University of Ghana http://ugspace.ug.edu.gh

These bacteria commonly isolated from the effusions in AOM are often involved in upper respiratory tract infection (WHO, 2004; Pettigrew *et al*., 2011; Marom *et al*., 2012; Qureishi *et al*., 2014; Suzuki *et al*., 2014). The bacteria implicated in OME are normally similar to those seen in recurrent AOM (Qureishi *et al*., 2014). Bacteria can be isolated from middle ear fluid cultures in 50 to 90% of cases of AOM and OME (Harmes *et al*., 2013). Additionally, Osazuwa *et al*. (2011), also indicated that bacteria cause over 50% of OM infections (Osazuwa *et al*., 2011). The frequently isolated bacteria from CSOM can be aerobic – for example, *Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus pyogenes, Proteus mirabilis, and Klebsiella* species – or anaerobic, for example, *Bacteroides* species, *Peptostreptococcus* and *Proprionibacterium* (WHO, 2004; Afolabi *et al*., 2012; Aduda *et al*., 2013). In a study done in Kenya in looking out for the bacteriology of CSOM in children, commonly isolated *Proteus* species, *Staphylococcus aureus, Enterococcus* species, *Pseudomonas* species, *Escherichia coli* and *Klebsiella species* (Aduda *et al*., 2013). Another study also conducted in Nigeria had *Pseudomonas aeruginosa, Klebsiella* species, *Streptococcus* species, and *Escherichia coli* isolated from the middle ear discharge of patients with CSOM (Afolabi *et al*., 2012).

2.2.3 Pathogenesis of The Different Types of OM

Bacteria are generally known to be the causative agents of AOM (Pettigrew *et al*., 2011). However, AOM pathogenesis involves both viral and bacterial interactions during an upper respiratory tract infection (Pettigrew *et al*., 2011; Marom *et al*., 2012; Schilder *et al*., 2016). Studies have shown that from one month after the start of viral upper respiratory tract infection (URTI) in children, one-third of these children get AOM (Marom *et al*., 2012). Commonly isolated AOM pathogens, namely *Streptococcus pneumoniae, Haemophilus influenzae*, and *Moraxella catarrhalis*, which are also known to frequently cause URTI, are normal flora of the nasopharynx that colonize it from

University of Ghana http://ugspace.ug.edu.gh

early stages of human life (Pettigrew *et al*., 2011; Marom *et al*., 2012; Suzuki *et al*., 2014). These pathogens, in colonizing the nasopharynx, do not cause any disease until the nasopharyngeal makeup is altered (Marom *et al*., 2012; Schilder *et al*., 2016). Viral upper respiratory infection promotes an inflammatory process in the nasopharynx and ET, which leads to increased bacterial adherence and colonization, hence making it easier for bacteria to enter the middle ear cavity (Pettigrew *et al*., 2011; Marom *et al*., 2012). The ET dysfunction occurs, leading to negative middle ear pressure, and as a result of negative middle ear pressure, pathogenic bacteria and viruses tend to easily find their way into the middle ear, leading to OM (Marom *et al*., 2012; Schilder *et al*., 2016).

OME can occur as a result of AOM or after an URTI, -leading to ET dysfunction (Lieberthal *et al*., 2013; Kucur *et al*., 2015; Schilder *et al*., 2016). In stating AOM as a cause of OME, it could be due to AOM taking an extended period to resolve (Qureishi *et al*., 2014). In terms of ET dysfunction playing a role in the pathogenesis of OME, it does that through negative middle ear pressure, which leads to middle ear fluid accumulation (Qureishi *et al*., 2014).

Chronic suppurative otitis media occurs due to an earlier episode of AOM which did not resolve entirely due to insufficient treatment or no treatment leaving a persistent eardrum perforation (WHO, 2004; Afolabi *et al*., 2012; Qureishi *et al*., 2014; Filipe *et al*., 2020). This complication of AOM with perforation is what is frequently seen in developing countries to cause CSOM (Qureishi *et al*., 2014). Ventilation tube insertion also leaves the ear drum perforated, leading to CSOM (Qureishi *et al*., 2014; Schilder *et al*., 2016), and this is frequently seen in children in developed countries (Qureishi *et al*., 2014).

Chronic suppurative otitis media initiates through bacteria from the external canal moving to the middle ear through a permanent perforation in the eardrum (WHO, 2004; Aduda *et al*., 2013). It

University of Ghana http://ugspace.ug.edu.gh

is important to take note that the external canal rarely harbours these bacteria implicated in CSOM, but the bacteria may multiply during certain conditions, such as high humidity and inflammation (WHO, 2004; Aduda *et al*., 2013).

2.3 Diagnosis of Otitis Media

The different forms of OM are distinguished from each other based on the history and examination outcomes (Qureishi *et al*., 2014). In AOM, common symptoms such as otalgia, fever, otorrhea, irritability, loss of appetite, lack of energy and vomiting are not enough for diagnosis (Qureishi *et al*., 2014; Schilder *et al*., 2016), hence diagnosing using an otoscope as well, is what is recommended (Harmes *et al*., 2013; Schilder *et al*., 2016;). AOM is diagnosed in a child based on moderate to severe bulging of the tympanic membrane (TM), new onset of otorrhea not initiated by otitis externa (OE), mild bulging of the TM with recent onset of ear pain which is less than 48 hours or extreme erythema of the TM (Lieberthal *et al*., 2013). Based on oto- instrumental examination, children who do not have middle ear effusion are not diagnosed of AOM (Lieberthal *et al*., 2013).

OME can occur as a result of AOM or after an upper respiratory tract infection -leading to ET dysfunction (Lieberthal *et al*., 2013; Schilder *et al*., 2016). It is characterized by hearing loss, less attention, awkwardness, poor balance, interactive complications and late speech development (Qureishi *et al*., 2014; Schilder *et al*., 2016). Otoscopy, which has sensitivity and specificity of 90% and 80%, is useful in diagnosis, whilst pneumatic otoscope gives an enhanced diagnosis (Qureishi *et al*., 2014; Schilder *et al*., 2016).

Diagnosis of CSOM is based on a TM perforation with discharge, of which the discharge must have been in existence for 2 weeks or more (WHO, 2004; Qureishi *et al*., 2014). This diagnosis

University of Ghana http://ugspace.ug.edu.gh

can be achieved by using otoscopy or otomicroscopy (Schilder *et al*., 2016). In differentiating CSOM from AOM and OE, the history is vital in the process (WHO, 2004; Qureishi *et al*., 2014). During diagnosis of CSOM, a history of ear pain is not a usual feature but may suggest AOM or OE. An ear discharge persisting for a long time is a vital feature of CSOM, thus the duration of ear discharge without pain helps to differentiate between CSOM and AOM (WHO, 2004; Qureishi *et al*., 2014).

2.4 Management of Otitis Media in Children

The management of AOM involves administering antipyretics, analgesics and antibiotics (Qureishi *et al*., 2014; Sakulchit *et al*., 2017). Analgesics and antipyretics are administered for the relief of pain and fever, with ibuprofen and paracetamol as common ones normally mentioned (Harmes *et al*., 2013; Lieberthal *et al*., 2013; Schilder *et al*., 2016). It is important to take note that pain and fever are the main focus in managing AOM (Lieberthal *et al*., 2013; Schilder *et al*., 2016). However antibiotic treatment is not always required and it is prescribed for some classes of patients who are expected to benefit from it (Harmes *et al*., 2013; Qureishi *et al*., 2014; Schilder *et al*., 2016; Sakulchit *et al*., 2017). To prevent antibiotic resistance through frequent antibiotic use, an initial observation can be optionally done among selected children with mild symptoms or signs within three days (Harmes *et al*., 2013; Lieberthal *et al*., 2013). These selected children include firstly those who are six to twenty-three months of age with unilateral AOM and presenting mild signs or symptoms. Secondly twenty-four months or older with unilateral or bilateral AOM and presenting mild signs or symptoms (Harmes *et al*., 2013; Lieberthal *et al*., 2013). According to Lieberthal *et al*. (2013) and Harmes *et al*. (2013), the first line of antibiotic therapy for AOM is amoxicillin or amoxicillin-clavulanate. The alternative for penicillin-allergic patients is oral

University of Ghana http://ugspace.ug.edu.gh

cephalosporins (Harmes *et al*., 2013; Lieberthal *et al*., 2013; Schilder *et al*., 2016; Sakulchit *et al*., 2017) and clarithromycin (Schilder *et al*., 2016). In an event of failure of initial antibiotic therapy, intravenous or intramuscular ceftriaxone can be administered (Harmes *et al*., 2013; Lieberthal *et al*., 2013). The efficiency of macrolides is less in treating *Streptococcus pneumoniae* and *Haemophilus influenzae* implicated in AOM (Lieberthal *et al*., 2013; Sakulchit *et al*., 2017), however, increased dosage of azithromycin seems to be efficient (Harmes *et al*., 2013). Clindamycin is effective against penicillin-resistant *Streptococcus pneumonia,* but not efficient for the treatment of *Haemophilus influenzae* infections, and therefore has limited use (Lieberthal *et al*., 2013; Sakulchit *et al*., 2017). *Streptococcus pneumoniae* resistance has been recorded by using trimethoprim/sulfamethoxazole for treatment, hence currently not recommended (Harmes *et al*., 2013; Lieberthal *et al*., 2013).

Management of OME is focused on one regaining hearing ability as the disease is notably characterised by hearing difficulties (Qureishi *et al*., 2014; Schilder *et al*., 2016). OME can resolve naturally in many children without treatment (Qureishi *et al*., 2014; Schilder *et al*., 2016; Cai *et al*., 2017). According to current guidelines, three months of observation is suggested for children with OME who are not likely to have interferences in their speech and intellectual development (Qureishi *et al*., 2014; Schilder *et al*., 2016). Children who are subjected to ventilation tubes (a form of surgery) are those who still record hearing difficulties after three months (Harmes *et al*., 2013; Qureishi *et al*., 2014; Schilder *et al*., 2016). Hearing aids can also be used in the management process (Qureishi *et al*., 2014; Schilder *et al*., 2016). Medications such as decongestants, antihistamines, antibiotics, and steroids are not effective regimens, and hence not appropriate to be used (Harmes *et al*., 2013; Qureishi *et al*., 2014).

University of Ghana http://ugspace.ug.edu.gh

CSOM management is focused on eliminating infection and fixing eardrum perforation (WHO, 2004; Qureishi *et al*., 2014). As part of management, aural toilet is regularly done (WHO, 2004; Qureishi *et al*., 2014). Aural toilet, according to WHO, is defined as decreasing infected material from the middle ear by cleaning ear discharge (WHO, 2004). Management of CSOM can be successful if aural toilet is jointly done with antibiotics or antiseptics (WHO, 2004; Qureishi *et al*., 2014). Findings of various studies have revealed that topical quinolone, especially ciprofloxacin, is efficient in treating CSOM thus resolving otorrhoea (WHO, 2004; Qureishi *et al*., 2014; Schilder *et al*., 2016). With the perforation of the eardrum, it is occasionally observed for sealing of perforation, and in instances where perforation fails to seal without discharge, a surgical procedure known as tympanoplasty is done (WHO, 2004).

2.5 Risk Factors associated with Otitis Media

Avoidance of risk factors is the first step in preventing OM (Mukara *et al*., 2017). Host risk factors for OM include age which is children less than five years old, gender (male sex), race, low birth weight less than 2.5 kg, premature birth which is less than 37 weeks gestation, and pacifier use (Qureishi *et al.*, 2014; Biagio *et al.*, 2014). Schilder *et al*. (2016) identified immunodeficiency as a host risk factor as well. Environmental factors including season, absence of breastfeeding, infection of the upper respiratory tract, attending a daycare facility, number of siblings, low socioeconomic status, individual and family history of OM, and passive exposure to cigarette smoke are also related risk factors (Biagio *et al*., 2014; Qureishi *et al*., 2014; Santoshi Kumari *et al*., 2016). In emerging economies where OM is very predominant, studies have identified risk factors to include low socio-economic class, household smoke exposure, decreased breastfeeding duration, recurrent upper respiratory infection, snoring, low parental education, malnourishment

University of Ghana http://ugspace.ug.edu.gh

and overcrowded households (Sophia *et al*., 2010). Poor sanitation has also been identified as a risk factor as well for OM in emerging economies (Afolabi *et al*., 2012; Schilder *et al*., 2016; Vaghela *et al*., 2016). Sub-Saharan Africa is known to have the highest effect of CSOM, and this is due to risk factors such as low immunity, poverty, insufficient health facilities, and contact with a high amount of bacteria pathogens (Filipe *et al*., 2020). A study carried out among South Indian children, reported risk factors for OM to be seasonal rhinitis, frequent runny nose, passive smoking and snoring (Sophia *et al*., 2010). According to Hounkpatin *et al*. (2016), the risk factors identified in a study in Parakou, Benin, for children with AOM aged a few days to five years were prolonged cases of rhinitis, wood and charcoal smoke exposure, low socio-economic status, history of AOM of the individual or siblings, and poor nutritional status of children. Socio-cultural variations in a study population influence the different risk factors identified (Sophia *et al*., 2010).

2.6 Epidemiology of Otitis Media

2.6.1 Global Epidemiology

Acute otitis media (AOM) and otitis media with effusion (OME) have a peak prevalence in children with respect to the variety of inflammatory ailments that affect the middle ear (Cai *et al*., 2017). Almost 90% of children younger than the age of 3 years worldwide are affected by OM (Santoshi Kumari *et al*., 2016; Mukara *et al*., 2017; Bowatte *et al*., 2018). AOM global incidence (new episodes per hundred people per year) is valued as 709 million cases per year, with half of the cases occurring in children below the age of five (Monasta *et al*., 2012; Qureishi *et al*., 2014; Ngo *et al*., 2016; Schilder *et al*., 2016; Sakulchit *et al*., 2017). The global AOM incidence rate for Central Europe is 3.64 with 40% of cases occurring in children under five years, for West Sub-

University of Ghana http://ugspace.ug.edu.gh

Saharan Africa is 43.36 with 56% occurring in children under five years and Central Sub-Saharan Africa is 43.37 with 58% occurring in children under five years (Monasta *et al*., 2012). Areas with AOM incidence lower than 5 are Asia Pacific High Income (3.75), Asia East (3.93), Europe Eastern (3.96) and Latin America Southern (4.25) (Monasta *et al*., 2012). A global systematic review revealed that the annual number of new cases of CSOM is 31million, with 22% representing children under five years (Monasta *et al*., 2012; Qureishi *et al*., 2014; Schilder *et al*., 2016). The lowest incidence of CSOM occurs in the following countries: Latin America Andean with 1.70 per thousand, followed by Asia Pacific High Income (3.02) and North America High Income (3.06). Oceania has the highest incidence with 9.37, followed by Central Sub-Saharan Africa (7.56) and West Sub-Saharan Africa (7.22) (Monasta *et al*., 2012). Worldwide, CSOM incidence rate is highest in the first year of life (15.40 per thousand) and reaches its lowest value after 65 years of age (2.51) (Monasta *et al*., 2012). The global addition of AOM annual new cases to CSOM annual new cases can be valued at 740 million, with its complications leading to more than 20,000 deaths (Monasta *et al*., 2012; Schilder *et al*., 2016; Bowatte *et al*., 2018). The recorded death rate is known to occur in children less than five years (Monasta *et al*., 2012; DeAntonio *et al*., 2016; Tesfa *et al*., 2020). Frequent cases of OME occurs in children below four years of age and by age 10, about 80% of children would have encountered one or more incidents of OME (Kucur *et al*., 2015; Schilder *et al*., 2016). In a study conducted in the Netherlands, 80% of children suffered at least, one episode of OME before the age of four (Cai *et al*., 2017). In a study from China, 6.3% OME prevalence was obtained from 1431 children between the ages of two to six years (DeAntonio *et al*., 2016). According to a study by Sophia *et al*. (2010), in a cross-sectional study of 800 children, the prevalence of OM was found to be 8.6% with OME being the highest diagnosed with a 6% prevalence (Sophia *et al*., 2010). In a study from Russia, a report was made

University of Ghana http://ugspace.ug.edu.gh

for an overall estimated prevalence for the different OM subtypes between age zero to seven years, in which in the year 1991, a prevalence of 5% was reported and increased to 7.8% in 1996 (DeAntonio *et al*., 2016). Between 1991 and 1996 for ages zero to seven years, the estimated incidence increased from 13.6 per 1000 children to 34.5 per 1000 children with a huge increment observed in children less than one year (DeAntonio *et al*., 2016).

2.6.2 Epidemiology in Africa

A study conducted in Nigeria measured the community prevalence of OM in a sample of 600 children aged less than twelve years, and OM prevalence from the study was found to be 14.7%, with the highest in children between the ages of one and four years (9.2%) (DeAntonio *et al*., 2016). Therefore, the prevalence of AOM, OME and CSOM in this same study for children less than twelve years were 11.8%, 0.4% and 2.5% respectively (DeAntonio *et al*., 2016). In Egypt, infections from across five regions among children less than four years had an OM prevalence being about 10% (DeAntonio *et al*., 2016). Prevalence ranges for children less than two months, two to eleven months and one to four years were 8.2%, 10.6% and 10.8% respectively (DeAntonio *et al*., 2016). In a study conducted in the Gasabo District of Kigali City, Rwanda, among 810 children, the prevalence of OM was reported to be 5.8% (Mukara *et al*., 2017).

2.7 Otitis Media in Ghana

Studies done on otitis media in Ghana are very few. Two studies have been done in Ghana so far, the first one dates as far back as 1987 by Brobby and Zadik (1987) and the second work, which was a retrospective study was done in 2014 by Appiah-Korang *et al*. (2014).

Highlighting the studies of Brobby and Zadik (1987), they focused on identifying bacteria etiological agents and the most economically available antibiotic treatment for otitis media. Thirty patients (16 females and 14 males) with acute otitis media visiting the Ear, Nose and Throat unit

University of Ghana http://ugspace.ug.edu.gh

of Komfo Anokye Teaching Hospital from 1st March to 29th June 1984 were understudied (Brobby and Zadik, 1987). They identified *Streptococcus pyogenes* (Lancefield group A) (25.5%), *Pseudomonas aeruginosa* (18.5%), *Staphylococcus aureus* (14%), *Corynebacterium* spp (12%), Coliforms (11%), *Proteus* spp (7%), *Staphylococcus epidermidis* (7%), *Streptococcus* species (not Lancefield group A) (5%) (Brobby and Zadik, 1987). *Haemophilus influenzae* and *Streptococcus pneumoniae* which were known to be identified with developed countries were not isolated in this study (Brobby and Zadik, 1987). Penicillin was the drug of choice unless Gram-negative rods like *Pseudomonas* spp were cultured. Due to the difficulty in buying expensive antibiotics in developing countries, a method of a double-blind study of antibiotics active against Gram-negative rods was adopted by Brobby and Zadik (1987), with a 6 months follow up.

With work done by Appiah-Korang *et al*. (2014), the focus of the study was to establish the aetiological agents of ear discharge where most of their participants were diagnosed with otitis media (Appiah-Korang *et al*., 2014). It was a retrospective study, where a review of laboratory records of submitted ear swabs for culture for over two years in the Korle Bu Teaching Hospital Accra, Ghana was done (Appiah-Korang *et al*., 2014). Over the two years, three hundred and fifty-one (351) swabs were received for processing by the laboratory, out of which 277 (78.9%) swabs showed positive growth on culture plates (Appiah-Korang *et al*., 2014). Children under five years had their swabs giving a higher number of positive growth of 127 (47%) (Appiah-Korang *et al*., 2014). *Pseudomonas* spp. was the predominant bacterial isolate (46%) followed by *Staphylococcus aureus* (12.5%) and *Proteus* spp. (12.2%) (Appiah-Korang *et al*., 2014). *Candida* species (spp) was the commonest isolated fungal element (69.2%) (Appiah-Korang *et al*., 2014). *Pseudomonas* spp. was susceptible to commonly used antibiotics such as ciprofloxacin and gentamicin (Appiah-Korang *et al*., 2014).

University of Ghana http://ugspace.ug.edu.gh

In conclusion, they indicated that discharging ear was mostly found in children under five years old (Appiah-Korang *et al*., 2014). *Pseudomonas* spp. was identified as the common bacteria cause of discharging ear followed by *Staphylococcus aureus* and the predominant fungal agent was *Candida* spp (Appiah-Korang *et al*., 2014). In the empirical treatment of discharging ear with otitis media inclusive, the drug of choice was ciprofloxacin and gentamicin (Appiah-Korang *et al*., 2014).

2.8 Antimicrobial Resistance

One major task confronting the public health sector is the resistance of bacteria to antibiotics (Harmes *et al*., 2013). Treatment of bacterial infections has become difficult as these antibiotic-resistant bacteria limit the efficiency of antibiotics used. Prolonged antibiotic exposure leads to the proliferation of antibiotic-resistant bacteria (Schilder *et al*., 2016). The primary cause of antibiotic use and reduced quality of life in children is OM (Schilder *et al*., 2016; Walker *et al*., 2017; Bowatte *et al*., 2018). It is important that a correct diagnosis of middle ear infection is made in children, as the wrong diagnosis could lead to unnecessary treatment with antibiotics, and contribute to increased antibiotic resistance (Harmes *et al*., 2013; Bowatte *et al*., 2018). Aside from that, in emerging economies, policies governing antibiotic prescription is limited, and hence there is an inappropriate use of antibiotics due to OM leading to multidrug-resistant organisms (Orji *et al*., 2015). Azithromycin in high doses seems to be more efficient in the treatment of AOM, but too much usage comes with high resistance (Harmes *et al*., 2013). *Streptococcus pneumoniae* resistance to trimethoprim/sulfamethoxazole has been recorded, hence it is no more suitable for AOM management (Harmes *et al*., 2013). A study emanating from Nigeria reported high resistance levels for all 35 isolates obtained, and this included *Streptococcus pneumoniae,*

University of Ghana http://ugspace.ug.edu.gh

Haemophilus influenzae, and *Staphylococcus aureus*, which were resistant to one or more antibiotics (74.2% were resistant to penicillin, 62.8% to streptomycin, 57.0% to gentamicin, 68.0% to chloramphenicol, and 77.7% to nalidixic acid) (DeAntonio *et al*., 2016). Another research study showed that the majority of the isolated pathogenic bacteria from a ten-year retrospective analysis in an area in Northeastern Ethiopia have become resistant to antibiotics that are easily accessible with the highest antibiotic resistance rates being recorded for ampicillin, ceftriaxone, amoxicillin and tetracycline (Argaw-Denboba *et al*., 2016).

2.9 Prevention of Otitis Media

OM is a multifactorial disease, hence its prevention can be achieved using different approaches, where the approaches look at the reduction of modifiable risk factors (Schilder *et al*., 2016). Firstly, one such approach is to decrease or eliminate pathogenic bacterial colonization in the nasopharynx achieved through the use of vaccines (Marom *et al*., 2012; Schilder *et al*., 2016). In 2000, the 7-valent pneumococcal conjugate vaccine (PCV7), which was directed against seven serotypes of *S. pneumoniae*, became available (Marom *et al*., 2012; Schilder *et al*., 2016). The vaccine was part of the early-stage vaccination programme for children at two, four and six months, in which a booster dose was given at twelve to fifteen months (Schilder *et al*., 2016). PCV7 has caused a 29% reduction in AOM caused by pneumococcal serotypes (Kingery *et al*., 2016; Schilder *et al*., 2016) and a 20% reduction in the use of ventilation tubes for chronic recurrent OM (Schilder *et al*., 2016). Currently, the 13-valent pneumococcal conjugate vaccines (PCV13) which are available for use, have been associated with further reduction in the prevalence of AOM (Marom *et al*., 2012; Schilder *et al*., 2016) and its associated complications (Schilder *et al*., 2016).

University of Ghana http://ugspace.ug.edu.gh

Thus, vaccination can be seen as preventing pneumococcal-associated OM which eventually could have led to chronic OM (Schilder *et al*., 2016).

Additionally, another way to prevent OM is the prevention of viral URI by the use of Vaccines targeting respiratory viruses (Marom *et al*., 2012; Schilder *et al*., 2016). Since viral URTI initiate AOM, the prevention of viral URTI would help in the reduction of AOM (Marom *et al*., 2012; Schilder *et al*., 2016). Currently, influenza Virus vaccines, are the only available vaccines against viral respiratory infection, known to reduce AOM in relation to influenza (Marom *et al*., 2012; Schilder *et al*., 2016).

Another approach is the administration of antivirals (non-vaccine viral approach) in the early management of viral URI (Marom *et al*., 2012; Schilder *et al*., 2016). According to studies, there is a reduction in the development of AOM by 43 to 85% in young children treated with oseltamivir between 12 to 48 hours of influenza symptom onset (Schilder *et al*., 2016).

Furthermore, environmental risk factors, such as daycare attendance, exposure to tobacco smoke and pacifier use should be avoided, particularly for children from six to twenty-four months (Kingery *et al*., 2016; Schilder *et al*., 2016). Another main way of preventing OM is breastfeeding, which protects against OM, with protection being higher for those breastfed exclusively (Kingery *et al*., 2016; Schilder *et al*., 2016).

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

CHAPTER THREE

3.0 MATERIALS AND METHOD

3.1 Study Site

The study was conducted at the Ear, Nose and Throat (ENT) departments of Princess Marie Louise Children's Hospital, 37 Military Hospital (37 MH) and Mamprobi Hospital (MH). PMLH, also known as children's hospital is one of the few specialist children's hospitals in Western Africa. It is a government hospital located at Derby Avenue Accra. It has a 74-hospital-bed capacity and is the second-largest paediatric facility in Ghana. It has an ENT clinic that attends to about 25 cases of otitis media on each clinic day. 37 Military Hospital is a specialist hospital located in Accra, on the main road between Kotoka International Airport and Central Accra. It is the largest military hospital in Ghana with an ENT clinic. Mamprobi Hospital is also a government hospital located in the Mamprobi Township in the Greater Accra Region. It has an ENT unit that attends to about 10 children with otitis media daily.

3.2 Study Design and Sampling

This was a cross-sectional study involving children below 13 years of age with otitis media at the ENT unit of PMLH, 37 MH and MH from September 2020 to March 2021. Written Consent was obtained from parents or guardians of younger children and older children. Diagnosis of OM was based on medical examinations done by ENT specialists who were nurses. Medical examinations were achieved through interviews (with parents, guardians and older children) to obtain a history of middle ear infection and using an otoscope. 100 children with suppurative otitis media visiting the ENT clinic of PMLH, 37MH and MH were recruited in the study. The inclusion criteria for the selection of otitis media participants were children below the age of 13 years who had been

University of Ghana http://ugspace.ug.edu.gh

diagnosed with otitis media. The exclusion criteria were children with craniofacial abnormalities, such as cleft lip, and palate and Down syndrome, and those on antimicrobial therapy.

The minimum number of study participants was determined based on the prevalence of 5.8% (Mukara *et al*., 2017) using the formula:

$n= (Z^2 P (1-P))/E^2$

Z= z-score value for 95% percentile (1.96)

p= proportion of the study (5.8%)

E= allowable error for the study (0.05)

A minimum of 84 participants was calculated to be recruited for the study. However, the sample size was increased to 100.

3.3 Specimen and Data Collection

In specimen collection, 70% alcohol was used to clean the external canal, and afterwards, sterile swab sticks were used by the ENT specialists to collect the middle ear discharge from the study participants. Each swab specimen obtained was kept in 1 ml of skim milk-tryptone-glucose-glycerin (STGG) medium and labelled with a unique bar code. These samples were transported on ice packs within three hours to the research laboratory of the Department of Medical Microbiology. On arrival at the laboratory, each sample was vortexed for one minute and stored at a -80 °C freezer for future analysis. Socio-demographic characteristics, potential risk factors and clinical information for each child were collected using a standard questionnaire (Appendix II) answered by parents or guardians. The following 10 potential risk factors were studied: preschool attendance,

University of Ghana http://ugspace.ug.edu.gh

parental education, presence of recurrent URTI, child history of OM, family history of OM, household income, breastfeeding duration, the average size of the family, passive exposure to parental smoke and parental employment. The study instrument used were a standard questionnaire, medical examination and laboratory investigation.

3.4 Specimen Processing

The stored swab specimens at -80 ^{o}C were thawed and vortexed briefly. These vortexed specimens were inoculated in about 5 ml of tryptic soy broth for enrichment. After overnight incubation at 37 ^{o}C, the samples were cultured on chocolate, blood, and MacConkey agar plates, using a sterile wire loop. The blood and chocolate agar plates were incubated at 37^{o}C for 24–48 hours in 5%-10% CO_2 achievable by a candle jar to isolate potential organisms such as *Streptococcus pneumoniae*, *Haemophilus influenza*, and *Moraxella catahallis*. The MacConkey agar plates were incubated at 37 ^{o}C for 24 hours in an aerobic condition to identify Gram-negative rods which were implicated in OM (Afolabi *et al*., 2012; Carroll, *et al*., 2016; Hailegiyorgis *et al*., 2018).

3.4.1 Bacterial Identification

Isolates were identified to the species level based on colonial morphology on culture plates, Gram staining and other standard bacteriological procedures (Afolabi *et al*., 2012; Hailegiyorgis *et al*., 2018).

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

3.4.1.1 Gram Staining

Gram staining was done on the isolates from the various agar plates to identify their various Gram reaction (Gram-positive and Gram-negative) and their morphologies (Afolabi *et al*., 2012; Hailegiyorgis *et al*., 2018). This aided in the possible standard bacteriological tests to do to arrive at the specific bacterial species (Carroll, *et al*., 2016).

A loopful of each colony was emulsified in normal saline to make a thin preparation on a slide. After the smears were dried, they were stained with crystal violet stain. The stain was washed off after one minute with clean water. Afterwards, the smears were covered with Gram's iodine for a minute and then washed off with clean water. Decolourization was done immediately with acetone–alcohol, washed off with clean water, and counterstained with safranin for 2 minutes. The stain was then washed off the slides and allowed to air dry. The smears were observed microscopically using the oil immersion objective (Carroll, *et al*., 2016).

3.4.1.2 Standard Bacteriological Identification Methods

Biochemical tests such as catalase and coagulase were done for Gram-positive cocci. Mannitol agar plates also aided in the identification of *Staphylococcus aureus* from coagulase-negative *Staphylococcus* and bile solubility test for *Streptococcus pneumonia*e. Indole, oxidase, triple sugar iron, citrate, motility and urease tests were also done to identify the Gram-negative rods. Analytical profile index (API) 20E was further used to speciate Gram-negative rods for which the conventional methods could not provide identification (Carroll, *et al*., 2016).

Disc testing for bacterial identification was done using an optochin disc to differentiate between *Streptococcus pneumoniae and Streptococcus viridans.* Aesculin bile agar, 6.5% sodium chloride

University of Ghana http://ugspace.ug.edu.gh

(6.5% NaCl) broth, and pyruvate were done to identify *Enterococcus species* and to differentiate between *Enterococcus feacalis* and *Enterococcus feacium* (Carroll, *et al*., 2016).

3.5 Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was performed by the Kirby Bauer disc diffusion technique (Afolabi *et al*., 2012; Hailegiyorgis *et al*., 2018). This was carried out by emulsifying pure colonies of isolates in sterile normal saline using a sterile inoculating loop and the bacterial suspension was adjusted to 0.5 MacFarland standard. A sterile cotton swab was dipped into the suspension and pressed against the side of the tube, and then used to inoculate a Mueller Hinton agar plate before the application of single antibiotic discs, which were placed not less than 24 mm apart. The application of the antibiotic discs was done using sterile forceps. Incubation of the agar plates was done aerobically at 37ºC for 16-18 hours. Mueller Hinton agar with 5% sheep blood was used for *Streptococcus pneumoniae* sensitivity with incubation done in 5% carbon dioxide at 37ºC for 20 - 24 hours (Carroll, *et al*., 2016). Antibiotic selection was based on the 2021 Clinical and Laboratory Standards Institute (CLSI) guidelines with the following antibiotic classes: aminoglycosides, β-lactams, carbapenems, lincosamide, fluoroquinolones, macrolides, sulphonamides, glycopeptides and tetracyclines. The individual antibiotics tested were ampicillin (10 µg), cefuroxime (30 µg), amoxicillin-clavulanic (30 µg), ceftriaxone (30 µg), Penicillin (10 µg), amikacin (30 µg), ciprofloxacin (5 µg), gentamicin (10 µg), ceftazidime (30 µg), cefepime (30 µg), piperacillin-tazobactam (110 µg), trimethoprim-sulfamethoxazole (25 µg), meropenem (10 µg), tetracycline (30 µg), clindamycin (2 µg), erythromycin (15 µg) and vancomycin (30 µg).

The zones of inhibition around each of the antibiotic discs were interpreted according to the 2021 Clinical and Laboratory Standards Institute (CLSI) guidelines.

University of Ghana http://ugspace.ug.edu.gh

3.6 Data Processing

Data obtained were entered into Microsoft Excel 2019 and analysis was done with Statistical Package for Social Sciences (SPSS) version 23. Descriptive analyses such as counts, frequencies, and percentages were computed on the data obtained. Results were presented in the form of graphs and tables. Additionally, logistic regression was used to determine risk factors for ASOM and CSOM associated with childhood otitis media. P value less than 0.05 was interpreted as significant, and results were presented in the form of a table.

3.7 Ethical Considerations

Ethical clearance was obtained from the Ethical and Protocol Review Committee of the College of Health Sciences, the University of Ghana with Protocol Identification number: **CHS-Et/M.7 - 5.3/2020-2021** and the 37 Military Hospital Institutional Review Board with protocol identification: **37MH-IRB IPN/MAS/434/2020**. Formal permission was also sought from the administration of the ENT clinics of PMLH and MP to recruit the children that fall within the inclusion criteria. Additionally, the objectives of the study were explained to participants, and informed consent (Appendix I) was obtained from them before soliciting information. It was communicated to the guardians of the children that participation in the study was not obligatory, and they could freely withdraw from the study at any time without any penalty. Codes were used to identify each participant, and the data collected was stored on a password-protected computer to ensure confidentiality.

University of Ghana http://ugspace.ug.edu.gh

CHAPTER FOUR

4.0 RESULTS

4.1 Socio-Demographic and Clinical Information of the Study Participants

A total of 100 children with otitis media were recruited for the study. The age distribution of the participants ranged from three weeks to twelve years old. The majority (74%) of the children were below five years of age, and a greater proportion of the participants were males (59%). ASOM was the most commonly diagnosed infection (68%) and CSOM was recorded among 32% of the study participants. Otorrhea was a major symptom, with a frequency of 100%. Over 80% had otalgia and a lower frequency of children (3%) had other medical conditions.

The summary of the demographic data and clinical information of the study participants is found in Table 1.

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

Table 1: Demographic characteristics and clinical information of study participants

VARIABLES	FREQUENCY	PERCENT
Gender		
Male	59	59
Female	41	41
Age (Years)		
< I	15	15
1-4	59	59
5-10	23	23
11-12	3	3
Diagnosis		
ASOM	68	68
CSOM	32	32
Otorrhea		
ASOM	50	50
CSOM	50	50
Otalgia		
ASOM	66	66
CSOM	18	18

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

4.2 Bacterial Isolates Distribution

From the study, out of the 100 samples, 97 (97%) gave positive cultures whiles 3 (3%) of samples recorded no growth on culture. Out of the 97% positive cultures, 12.4% gave more than one organism whilst 87.6% gave only one type of organism. One hundred and twelve (112) isolates were obtained from the positive cultures, 98% were bacteria and the rest were fungal agents (*Candida* species). Additionally, out of the 98% bacteria isolated, Gram-negative bacteria (75.5%) were the predominant as compared to Gram-positives (24.5%), with *Pseudomonas aeruginosa* (33.6%) being the predominant Gram-negative bacteria and coagulase-negative *Staphylococcus* (10%) representing the highest isolated Gram-positive bacteria (Table 2). Furthermore, 87.3% were pathogenic bacteria with the frequently isolated pathogenic bacteria being *Pseudomonas aeruginosa* (38.5%) followed by *Klebsiella pneumoniae* (19.8%), *Proteus mirabilis* (11.5%), *Staphylococcus aureus* (10.4%), *Escherichia coli* (7.3%), *Citrobacter species* (4.2%), *Pseudomonas* species (3.1%), *Enterococcus faecalis* (2.1%) with *Morganella morganii*, *Serratia marcescens* and *Streptococcus pneumoniae* recording 1% each. Coagulase-negative *Staphylococcus*, *Streptococcus viridans* and *Bacillus* species were treated as probable contaminants.

Pseudomonas aeruginosa, *Pseudomonas* species, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Escherichia coli*, *Citrobacter* species, *Morganella morganii*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus pneumoniae* were the commonly isolated pathogenic bacteria from ASOM whiles *Pseudomonas aeruginosa*, *Pseudomonas* species, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Escherichia coli*, *Citrobacter* species, *Serratia marcescens* and *Staphylococcus aureus* were the most common pathogenic bacteria recorded from CSOM in this

University of Ghana http://ugspace.ug.edu.gh

study. Table 2 shows the frequency of isolated bacterial pathogens in ASOM and CSOM. Figure 2 shows the total percentage of isolated bacterial pathogens from children with ASOM and CSOM.

Table 2: Distribution of isolated bacterial pathogens in otitis media

Bacterial pathogens	**OTITIS MEDIA *n = 96***	**PERCENT**
Pseudomonas aeruginosa	37	38.5
Klebsiella pneumoniae	19	19.8
Proteus mirabilis	11	11.5
Staphylococcus aureus	10	10.4
Escherichia coli	7	7.3
Citrobacter species	4	4.2
Pseudomonas species	3	3.1
Enterococcus feacalis	2	2.1
Morganella morganii	1	1
Serratia marcescens	1	1
Streptococcus pneumoniae	1	1

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

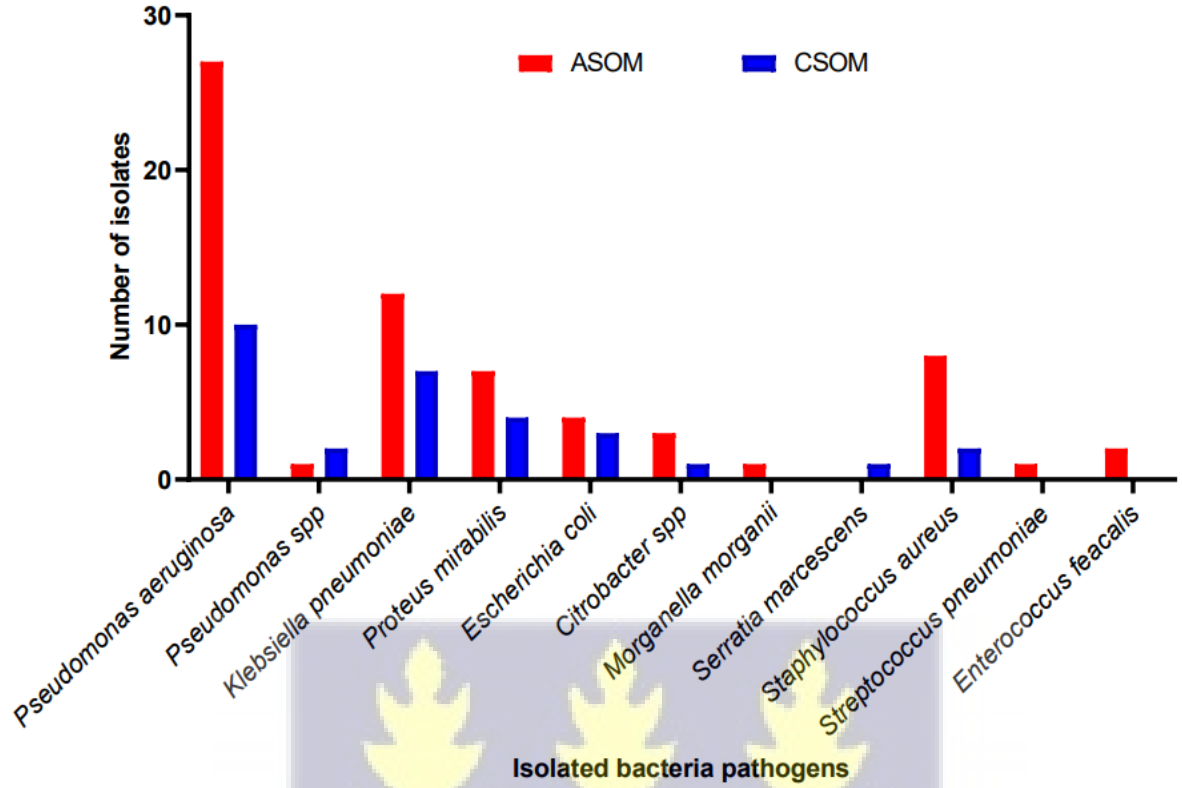


Figure 2: Total percentage of isolated bacterial pathogens from children with ASOM and CSOM

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

4.3 Antimicrobial Susceptibility Profile

Antimicrobial susceptibility testing was carried out for all the pathogenic bacterial isolates recovered. The sensitivity patterns of *Pseudomonas aeruginosa* obtained are as follows: 100% sensitivity to amikacin, ceftazidime, cefepime, ciprofloxacin, piperacillin-tazobactam, and meropenem, and 86.49% sensitivity to gentamicin. *Pseudomonas* species likewise recorded 100% sensitivity to ceftazidime, cefepime, ciprofloxacin, piperacillin-tazobactam, and meropenem, and 66.67% each to amikacin and gentamicin. *Staphylococcus aureus* showed 100% sensitivity to ciprofloxacin, ampicillin, penicillin, cefuroxime, augmentin, clindamycin, linezolid and > 70% susceptibility to trimethoprim-sulfamethoxazole, tetracycline, and erythromycin. *Streptococcus pneumoniae* showed sensitivity to all antibiotics tested against it, except trimethoprim-sulfamethoxazole and tetracycline. *Enterococcus faecalis* was susceptible to all the antibiotics tested against it. *Proteus mirabilis* showed > 80% level of susceptibility to antibiotics tested against it, except ampicillin, for which the susceptibility was 45.6%. *Morganella morganii* and *Serratia marcescens* both recorded 100% sensitivity to amikacin, cefepime, gentamicin, ciprofloxacin, meropenem, trimethoprim-sulfamethoxazole, and tetracycline. Most of the bacterial isolates showed high to moderate susceptibility to amikacin, cefepime, gentamicin, ciprofloxacin and meropenem, except *E. coli*, which showed 42.86% susceptibility to cefepime and 28.57% to ciprofloxacin.

For resistance rates, *Klebsiella pneumoniae*, *Escherichia coli*, *Morganella morganii*, *Serratia marcescens* and *Citrobacter* species were observed to be highly resistant to most of the antibiotics tested against them. From this study, eight (8) extended-spectrum *beta-lactamase* (ESBL) producers were isolated, and these were distributed equally between *Klebsiella pneumoniae* (50%) and *Escherichia coli* (50%). Furthermore, six (6) ampicillinase C (Amp C)-producing organisms,

University of Ghana http://ugspace.ug.edu.gh

which included *Citrobacter* species, *Morganella morganii* and *Serratia marcescens*, were also identified, and they showed high antibiotic resistance. It was observed that all the Gram-negatives (Enterobacteriaceae) against ampicillin tested were highly resistant. Additionally, observation showed high to moderate resistance of bacterial isolates to piperacillin-tazobactam, cefuroxime, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole, tetracycline, and ceftriaxone. The antimicrobial resistance pattern of the isolated bacterial pathogens is shown in Table 3.

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

Table 3: Antimicrobial susceptibility pattern of bacterial pathogens of otitis media (%)

Antibiotics	**The antibiotic-resistant pattern of bacterial isolates**																
	AMK	CAZ	CEF	GEN	CIP	PTZ	MEM	AMP	PEN	CXM	AMC	SXT	TET	CC	ERY	CRO	VAN
Pseudomonas aeruginosa	0	0	0	13.5	0	0	0	-	-	-	-	-	-	-	-	-	-
Pseudomonas spp	33.3	0	0	33.3	0	0	0	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	-	-	-	0	0	-	-	0	0	0	0	30	20	0	20	-	-
Klebsiella pneumoniae	5.3	-	21.1	10.5	5.3	26.3	0	100	-	36.8	26.3	21.1	42.1	-	-	21.1	-
Proteus mirabilis	0	-	0	0	0	0	0	54.4	-	0	0	18.2	0	-	-	0	-
Morganella morganii	0	-	0	0	0	100	0	100	-	100	100	0	0	-	-	100	-
Serratia marcescens	0	-	0	0	0	100	0	100	-	100	100	0	0	-	-	100	-
Escherichia coli	28.6	-	57.1	0	71.4	57.1	0	100	-	100	100	85.7	85.7	-	-	57.1	-
Citrobacter species	0	-	0	0	25	100	0	100	-	100	100	75	50	-	-	100	-
Streptococcus pneumonia	-	-	0	-	-	-	0	0	-	0	0	100	100	0	0	0	0
Enterococcus feacalis	-	-	-	-	-	-	-	0	0	-	-	-	-	-	-	-	0

Amikacin-AMK, Ceftazidime-CAZ, Cefepime-CEF, Gentamicin-GEN, Ciprofloxacin-CIP, Piperacillin-tazobactam- PTZ, Meropenem-MEM, Ampicillin-AMP, Penicillin-PEN, Cefuroxime-CXM, Amoxicillin-clavulanate-AMC, Trimethoprim-sulfamethoxazole-SXT, Tetracycline-TET, Clindamycin-CC, Erythromycin-ERY, Ceftriaxone-CRO, Vancomycin-VAN, "-" – antibiotics not tested, 0 – percentage resistance.

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

4.4 Risk Factors for Otitis Media among the Study Participants

On logistic regression analysis, most of the potential risk factors did not show any association with developing ASOM and CSOM in the children. However, children were more likely to develop CSOM if they had a history of ASOM (*OR*= 6.699, 95% CI= 2.13 - 21.09). Therefore, child's history of ASOM showed a statistically significant association with the development of CSOM. Details can be found in Table 4.

University of Ghana http://ugspace.ug.edu.gh

Table 4: The potential risk factors associated with ASOM and CSOM in children with otitis media

Risk factor	Odds ratio	95% CI	*p*-value
Passive exposure to parental smoke	15.580	(0.88 - 275.29)	0.063
Presence of recurrent URTI	2.715	(0.73 - 10.04)	0.135
Breastfeeding duration	2.470	(0.63 - 9.70)	0.195
Parental education	1.179	(0.35 - 3.92)	0.789
Parental employment	0.528	(0.08 - 3.32)	0.496
Child history of OM	6.699*	(2.13 - 21.09)	0.001
Family history of OM	1.090	(0.30 - 3.91)	0.895
Average size of the family	1.613	(0.50 - 5.18)	0.422
Pre-school attendance	1.264	(0.59 - 2.71)	0.547
Household income	0.498	(0.21 - 1.73)	0.111

*Significant at 0.05 alpha level

INTEGRI PROCEDAMUS

University of Ghana http://ugspace.ug.edu.gh

CHAPTER FIVE

5.0 DISCUSSION

This study evaluated the bacterial aetiologies of OM, the antibiotic susceptibility patterns, and associated risk factors for developing the infection among children in Accra, Ghana.

A high prevalence of OM was observed in children under 5 years (74%), an observation that is similar to findings from studies that also reported a higher prevalence of 80.11% in Addis Ababa, Ethiopia (Hailegiyorgis *et al*., 2018), 84.2% in Southern Ethiopia (Tadesse *et al*., 2019), and 71.7% in Zamfara, Nigeria (Bilkisu *et al.*, 2017). In contrast, a lower prevalence (51.5%) has also been reported by Appiah-Korang *et al*. (2014) from Ghana. This could be because children of this category have immature immunity, which makes them prone to frequent upper respiratory tract infections, and they also have a more flexible, horizontal and short Eustachian tube (ET), allowing easier entry of pathogens from the nasopharynx into the middle ear (Osazuwa *et al*., 2011; Qureishi *et al*., 2014).

Data from this study indicate that more males suffer from OM than females and this is comparable to other studies which reported similar proportions of 51.3% in Southern Ethiopia (Tadesse *et al*., 2019), 62.3% in Zamfara, Nigeria (Bilkisu *et al.*, 2017), 53% in Ibadan, Nigeria (Okesola *et al*., 2011), and 60% in Abakaliki, Nigeria (Nnebe-Agumadu *et al*., 2011). This, however, is in contrast to what was reported by Hailegiyorgis *et al*. (2018) from Addis Ababa, Ethiopia and Al-Marzoqi *et al*. (2013) in Iraq, in whose studies females were in the majority, with 51.5% and 52% proportions, respectively.

Acute suppurative otitis media (ASOM) was the most common diagnosis (68%) as compared to chronic suppurative otitis media (CSOM) (32%). This is corroborated with a study made by Cai *et al*. (2017) which reported that AOM occurs more often in children than CSOM. Studies have

University of Ghana http://ugspace.ug.edu.gh

reported the yearly global diagnosis for acute otitis media (AOM) to be valued at 709 million as compared to CSOM, which is 31 million, with half of the cases occurring in children under five years (Monasta *et al*., 2012; Qureishi *et al*., 2014; Schilder *et al*., 2016). Also, the findings of this study were in line with a study performed in Nigeria (Nnebe-Agumadu *et al*., 2011), in which 67% of cases were recorded for ASOM. Otorrhea was a major symptom among the study participants, with a frequency of 100%, and this is indicative of discharging middle ears of the study participants. Eighty-four per cent (84%) of the children had otalgia, and this conforms to the high prevalence of ASOM (68%) obtained. Although otalgia is a major symptom that is highly associated with ASOM, some of the participants with CSOM in this study also experienced otalgia. This observation of fewer study participants recording otalgia in CSOM confirms what is known in available literature that otalgia is normally not a primary symptom in CSOM (Qureishi *et al*., 2014).

Most of the samples from the study participants gave positive cultures (97%) and is comparable to other works done in Iraq and Northern Ethiopia, in which 96.4% (Al-marzoqi *et al*., 2013) and 98.2% (Wasihun *et al*., 2015) were obtained respectively. It was observed to be higher than 75.6% in Southern Ethiopia (Tadesse *et al*., 2019), 84.9% in Zamfara, Nigeria (Bilkisu *et al*., 2017), 75% in Awka, Nigeria (Ejiofor *et al*., 2016) and 87.7% in Abakaliki, Nigeria (Nnebe-Agumadu *et al*., 2011). The difference in results could be due to the study population on antibiotics during enrolment, category of the study population, sample size and varied methodology. Although the main aim of this study was focused on bacterial etiologies, *Candida* species (2%) were recovered. The proportion of Gram-negative bacteria (GNB) and Gram-positive bacteria (GPB) isolates indicated that GNB (75.5%) were the most dominant, a finding comparable to previous research conducted by Nnebe-Agumadu *et al*. (2011) (88.53%) and Afolabi *et al*. (20I2) (75%) from

University of Ghana http://ugspace.ug.edu.gh

Nigeria. Another study in Nigeria by Okesola *et al*. (2011) recorded a higher GNB dominance (98.6%), but contradictory to other reports from Nigeria (Bilkisu *et al*., 2017) and Morocco (Es-Said *et al*., 2014) in which Gram-positive bacteria were predominant with values of 68.9% and 64% respectively. The difference in results could be that OM can be caused by different bacteria at different geographical locations.

From this study, it was observed that *Pseudomonas aeruginosa* (38.5%) was the frequently isolated bacteria followed by *Klebsiella pneumoniae* for ASOM and CSOM. *P. aeruginosa* being predominant in this study is similar to a retrospective study done in Ghana by Appiah-Korang *et al*. (2014) where *Pseudomonas aeruginosa* was the frequently-isolated pathogen, with children below the age of 13 years making up a greater percentage of the study participants and OM being the prevalent diagnosis. Our findings, where *P. aeruginosa* was the commonly isolated bacteria, were similar to other studies that were done in Nigeria by Nnebe-Agumadu *et al*. (2011), Okesola *et al*. (2011), and Osazuwa *et al*. (2011) which reported 57.4%, 44.3% and 28.3% of *P. aeruginosa* respectively. Additionally, Okesola *et al*. (2011) reported *Klebsiella pneumoniae* as the second most predominant isolate, similar to the findings of the current study. This, however, differs from studies done in Ethiopia (Tadesse *et al*., 2019), Nigeria (Bilkisu *et al*., 2017), and Iraq (Al-Marzoqi *et al*., 2013), where *Staphylococcus aureus* was the most predominant bacterium isolated. This could be explained by climatic conditions in the different geographical locations, which impact the distribution of microorganisms. It was also observed from this study that some of the aetiological agents of ASOM, such as *Pseudomonas aeruginosa*, *Pseudomonas* species, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Escherichia coli*, *Citrobacter* species, *Morganella morganii*, and *Enterococcus faecalis* were in contrast to existing literatures in which *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catahallis*, are known as the common cause of AOM (

University of Ghana http://ugspace.ug.edu.gh

Pettigrew *et al*., 2011; Marom *et al*., 2012; Aduda *et al*., 2013; Gisselsson-Solén *et al*., 2014; DeAntonio *et al*., 2016; Ngo *et al*., 2016) and especially commonly reported in developed countries (Osazuwa *et al*., 2011; Ejiofor *et al*., 2016). However, this study identified 1% of *Streptococcus pneumoniae* from ASOM samples. Irrespective of these contrasting outcomes, the results of the current study were in accordance with other studies conducted in Ghana (Appiah-Korang *et al*., 2014) and Nigeria (Nnebe-Agumadu *et al*., 2011; Ejiofor *et al*., 2016), where similar isolates were obtained from ASOM samples. Variations in climate and geographical location could be the reason for the difference in the distribution of bacteria. Furthermore, bacterial isolates such as *Pseudomonas aeruginosa*, *Pseudomonas* species, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Escherichia coli* obtained for CSOM were in line with other study outcomes (Afolabi *et al*., 2012; Aduda *et al*., 2013; Tiedt *et al*., 2013; Appiah-Korang *et al*., 2014).

Single colonies from culture were observed from 85 (87.6%) samples, which were in agreement with studies that demonstrated 94.6%, 93%, and 72.6% by Hailegiyorgis *et al*. (2018) in Addis Ababa, Ethiopia, Tadesse *et al*. (2019) in Southern Ethiopia and Osazuwa *et al*. (2011) in Benin City, Nigeria respectively. However, in contrast to our study, another finding by Al-Marzoqi *et al*. (2013) in Iraq had mixed growth from cultures being of a higher frequency. This may suggest more CSOM cases were recorded than ASOM, with available literature highlighting that > 90% of chronic discharging ears yield two or more bacterial isolates (Qureishi *et al*., 2014).

In this study, *Pseudomonas aeruginosa* and *Pseudomonas* species reported a high level of susceptibility (> 60%) to all the antibiotics tested against them; antibiotics inclusive of amikacin, ceftazidime, cefepime, ciprofloxacin, piperacillin-tazobactam, meropenem and gentamicin. The observed susceptibility rate of *Pseudomonas aeruginosa* is similar to an earlier study carried out by Bilkisu *et al*. (2017) in Nigeria, with susceptibility profiles for ceftazidime, gentamicin,

University of Ghana http://ugspace.ug.edu.gh

ciprofloxacin and piperacillin-tazobactam similar to findings reported by Ahmad, (2013) in Saudi Arabia. The finding of this study, was, however, contrary to a study by Wasihun *et al.* (2015) from Northern Ethiopia, in which *Pseudomonas aeruginosa* was the most resistant isolate in the study. *Staphylococcus aureus* showed > 70% level of susceptibility to antibiotics tested against it, comparable to the findings of Wasihun *et al.* (2015) in Northern Ethiopia, in which gentamicin, ciprofloxacin, and erythromycin were relatively susceptible. A high level of *Streptococcus pneumoniae* resistance to trimethoprim-sulfamethoxazole, and tetracycline and high susceptibility to amoxicillin-clavulanate agrees with the pool analysis study done by Van Dyke *et al*. (2017). Lesser resistance of *Proteus mirabilis* to antibiotics tested against it is comparable to studies conducted by Wasihun *et al.* (2015) in Northern Ethiopia and Aduda *et al.* (2013) in Kenya, with its high resistance to ampicillin supported by Es-Said *et al*. (2014) in Morocco. Resistance of *Klebsiella pneumoniae* to many antibiotics has been reported in studies by Tadesse *et al*. (2019) in Southern Ethiopia and Wasihun *et al.* (2015) in Northern Ethiopia. Additionally, the resistance of *Klebsiella pneumoniae* and *Escherichia coli* to ampicillin, cefuroxime, amoxicillin-clavulanate and ceftriaxone has been reported in an earlier study by Es-Said *et al*. (2014) in Morocco. The high level of resistance recorded by *Klebsiella pneumoniae* and *Escherichia coli* could be because some of the isolates were phenotypically positive for extended-spectrum beta-lactamases (ESBL) production. In this study, low percentages (1%, 4.2% and 1%) were recorded for *Morganella morganii*, *Citrobacter* species and *Serratia marcescens*, respectively, but they showed a high level of resistance to cephalosporins, penicillin and penicillin inhibitor combinations due to the reason that they are ampicillinase C (Amp C) organisms.

Findings from the antimicrobial susceptibility profile in this study reveal that the aetiological agents were mostly susceptible to amikacin, cefepime, gentamicin, ciprofloxacin and meropenem.

University of Ghana http://ugspace.ug.edu.gh

Sensitivity to ciprofloxacin and gentamicin has been reported in other studies (Nnebe-Agumadu *et al*., 2011; Appiah-Korang *et al*., 2014; Wasihun *et al.*, 2015; Tadesse *et al*., 2019; Tesfa *et al*., 2020). A high level of resistance was recorded for ampicillin, piperacillin-tazobactam, cefuroxime, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole, tetracycline and ceftriaxone. Resistance to ampicillin, amoxicillin-clavulanate, tetracycline and trimethoprim-sulfamethoxazole has been reported in a previous study by Appiah-Korang *et al*. (2014) in Ghana. Resistance to ampicillin, ceftriaxone and tetracycline has also been reported in Eygpt (Argaw-Denboba *et al*., 2016) with ampicillin and trimethoprim-sulfamethoxazole resistance reported in Southern Ethiopia (Tadesse *et al*., 2019). Recorded resistance to commonly prescribed antibiotics for OM management such as ampicillin, amoxicillin-clavulanate and cefuroxime could be due to their frequent usage. This is quite alarming and not encouraged to be used as first-line drugs for OM treatment. Ciprofloxacin and gentamicin, which are commonly known ototopic drugs, are recommended to be used in the management of OM in children.

This study is the first to investigate factors that predispose children to otitis media (OM) in Accra, Ghana. The onset of OM as reported by many studies is influenced by several variables such as gender, upper respiratory tract infections (URTI), age and absence of breastfeeding. Knowledge and avoidance of these risk factors are the first steps in preventing OM. Risk factors for ASOM and CSOM associated with childhood OM were analyzed but there was no statistically significant relationship between ASOM and CSOM and most of the potential risk factors. However, child history of ASOM showed a statistically significant relationship, with an odds ratio of 6.699 indicating that children with a history of ASOM are six times more likely to develop CSOM. This finding is in line with results from a previous study in Parakou, Benin (Hounkpatin *et al*., 2016). A child history of ASOM which was identified as a risk factor associated with CSOM could mean

University of Ghana http://ugspace.ug.edu.gh

that a child with an episode of ASOM stands a chance of getting CSOM. Child's history of ASOM is an important risk factor for other episodes of ASOM to occur, which eventually could lead to CSOM. This is because an individual could be exposed to the same environmental risk factors (Hounkpatin *et al*., 2016).

University of Ghana http://ugspace.ug.edu.gh

CHAPTER SIX

6.0 CONCLUSIONS, RECOMMENDATIONS, AND LIMITATIONS

6.1 Conclusions

The commonest bacterial aetiological agents of childhood OM were *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Proteus mirabilis*. Most aetiological agents showed a high level of resistance to ampicillin, piperacillin-tazobactam, cefuroxime, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole, tetracycline, and ceftriaxone while with commonly used antibiotics, such as ciprofloxacin and gentamicin, showed a higher level of susceptibility, hence recommended for management of OM in children. Child's history of ASOM was the risk factor identified to be associated with developing CSOM. Knowledge of these risk factors will aid to formulate effective preventive strategies to curb childhood OM occurrence in Accra, Ghana.

6.2 Recommendations

Firstly, as the aetiological agents demonstrated high resistance towards ampicillin, cefuroxime, and amoxicillin-clavulanate, it is recommended that their use in treating otitis media among children in the country be discontinued, and ciprofloxacin and gentamicin used instead.

Furthermore, a follow-up study to investigate the genetic basis for the phenotypic resistances observed in commonly used antimicrobials and the search for virulence factors of the resistant organisms should be carried out.

It is also recommended that further research work should be done on children with otitis media in other parts of the country, to provide additional insight into the causative agents and risk factors.

University of Ghana http://ugspace.ug.edu.gh

6.3 Limitations

The limitation identified in this study was that anaerobic incubation could not be done, hence anaerobes which are normally implicated in chronic suppurative otitis media were not isolated.

University of Ghana http://ugspace.ug.edu.gh

REFERENCES

Abraham, Z. S., Ntunaguzi, D., Kahinga, A. A., Mapondella, K. B., Massawe, E. R., Nkuwi, E. J., & Nkya, A. (2019). Prevalence and etiological agents for chronic suppurative otitis media in a tertiary hospital in Tanzania. *BMC Research Notes*, *12*(1), 1–6. https://doi.org/10.1186/s13104-019-4483-x

Aduda, D. S. O., Macharia, I. M., Mugwe, P., Oburra, H., Farragher, B., Brabin, B., & Mackenzie, I. (2013). Bacteriology of chronic suppurative otitis media (CSOM) in children in Garissa district, Kenya: A point prevalence study. *International Journal of Pediatric Otorhinolaryngology*, *77*(7), 1107–1111. https://doi.org/10.1016/j.ijporl.2013.04.011

Ahmad, S. (2013). *Antibiotics in chronic suppurative otitis media : A bacteriologic study*. 191–194. https://doi.org/10.1016/j.ejenta.2013.06.001

Al-marzoqi, A. H., Hussein, H. J., Mohammad, Z., Taee, A., & Yheea, S. K. (2013). *Otitis Media ; Etiology and Antibiotics Susceptibility among Children under Ten Years Old in Hillah city, Iraq*. *3*(3), 1–8.

Amusa, Y. B., Ijadunola, I. K., & Onayade, O. O. (2005). Epidemiology of otitis media in a local tropical African population. *West African Journal of Medicine*, *24*(3), 227–230. https://doi.org/10.4314/wajm.v24i3.28202

Appiah-Korang, L., Asare-Gyasi, S., Yawson, A., & Searyoh, K. (2014). Aetiological Agents of Ear Discharge: A Two-year Review in a Teaching Hospital in Ghana. *Ghana Medical Journal*, *48*(2), 91. https://doi.org/10.4314/gmj.v48i2.6

Argaw-Denboba, A., Abejew, A. A., & Mekonnen, A. G. (2016). Antibiotic-Resistant Bacteria Are Major Threats of Otitis Media in Wollo Area, Northeastern Ethiopia: A Ten-Year

University of Ghana http://ugspace.ug.edu.gh

Retrospective Analysis. *International Journal of Microbiology*, *2016*, 1–9. https://doi.org/10.1155/2016/8724671

Awuah, P., Duah, I., & Amedofu, G. (2012). Prevalence of Hearing Loss in Patients with Acute Otitis Media. *Journal of Science and Technology (Ghana)*, *32*(1), 11–17. https://doi.org/10.4314/just.v32i1.2

Biagio, L., Swanepoel, D. W., Laurent, C., & Lundberg, T. (2014). Paediatric otitis media at a primary healthcare clinic in South Africa. *South African Medical Journal*, *104*(6), 431–435. https://doi.org/10.7196/SAMJ.7534

Bilkisu, I. G., Bello, A. M., Fatima, M., Murtala, R., Usman, M. S., Khadija, O. I., & Usman, M. W. (2017). Antibiotic susceptibility pattern of bacterial isolates in children with otitis media in Zamfara, North-Western Nigeria. *African Journal of Microbiology Research*, *11*(43), 1558–1563. https://doi.org/10.5897/ajmr2017.8712

Bowatte, G., Tham, R., Perret, J. L., Bloom, M. S., Dong, G., Waidyatillake, N., Bui, D., Morgan, G. G., Jalaludin, B., Lodge, C. J., & Dharmage, S. C. (2018). Air pollution and otitis media in children: A systematic review of literature. *International Journal of Environmental Research and Public Health*, *15*(2). https://doi.org/10.3390/ijerph15020257

Brobby, G W; Zadik, P. (1987). Bacteriology of otitis media in Ghana. *Tropical Doctor*, *17*, 91–92. https://doi.org/10.1177/004947558701700217

Buzatto, G. P., Tamashiro, E., Proenca-Modena, J. L., Saturno, T. H., Prates, M. C., Gagliardi, T. B., Carenzi, L. R., Massuda, E. T., Hyppolito, M. A., Valera, F. C. P., Arruda, E., & Anselmo-Lima, W. T. (2017). The pathogens profile in children with otitis media with effusion and adenoid hypertrophy. *PLoS ONE*, *12*(2), 1–12. https://doi.org/10.1371/journal.pone.0171049

University of Ghana http://ugspace.ug.edu.gh

Cai, T., & McPherson, B. (2017). Hearing loss in children with otitis media with effusion: a systematic review. *International Journal of Audiology*, *56*(2), 65–76. https://doi.org/10.1080/14992027.2016.1250960

Chandarakesan, A., Muruhan, S., & Sayanam, R. R. A. (2018). Morin Inhibiting Photocarcinogenesis by Targeting Ultraviolet-B-Induced Oxidative Stress and Inflammatory

Carroll, C. Karen; Hobden, A. Jeffery; Miller, Steve; Morse, Stephen; Mietzner, Timothy; Detrick, Barbara; Mitchell, Thomas; McKerrow, James; Sakanari, J. (2016). Jawetz, Melnick, & Adelberg's Medical Microbiology. In *Mc Graw Hill Education* (27th ed., pp. 38–271). McGraw-Hill Education.

Cytokines Expression in Swiss Albino Mice. *International Journal of Nutrition, Pharmacology, Neurological Diseases* |, *8*, 41–46. https://doi.org/10.4103/ijnpnd.ijnpnd

Chochua, S., D'Acremont, V., Hanke, C., Alfa, D., Shak, J., Kilowoko, M., Kyungu, E., Kaiser, L., Genton, B., Klugman, K. P., & Vidal, J. E. (2016). Increased nasopharyngeal density and concurrent carriage of streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis are associated with pneumonia in febrile children. *PLoS ONE*, *11*(12), 1–13. https://doi.org/10.1371/journal.pone.0167725

CLSI. (2018). A Consumer Complaint Framework with Resulting Strategies. In *Journal of Services Marketing* (Vol. 8, Issue 3). https://doi.org/10.1108/08876049410065598

Coticchia, J. M., Chen, M., Sachdeva, L., & Mutchnick, S. (2013). New paradigms in the pathogenesis of otitis media in children. *Frontiers in Pediatrics*, *1*(DEC), 1–7. https://doi.org/10.3389/fped.2013.00052

University of Ghana http://ugspace.ug.edu.gh

Dayie, N. T. K. D., Tetteh-Ocloo, G., Labi, A. K., Olayemi, E., Slotved, H. C., Lartey, M., & Donkor, E. S. (2018). Pneumococcal carriage among sickle cell disease patients in Accra, Ghana: Risk factors, serotypes and antibiotic resistance. *PLoS ONE*, *13*(11), 1–14. https://doi.org/10.1371/journal.pone.0206728

DeAntonio, R., Yarzabal, J. P., Cruz, J. P., Schmidt, J. E., & Kleijnen, J. (2016). Epidemiology of otitis media in children from developing countries: A systematic review. *International Journal of Pediatric Otorhinolaryngology*, *85*, 65–74. https://doi.org/10.1016/j.ijporl.2016.03.032

Ejiofor, S. O., Edeh, A. D., Ezeudu, C. E., Gugu, T. H., & Oli, A. N. (2016). Multi-Drug Resistant Acute Otitis Media amongst Children Attending Out-Patient Clinic in Chukwuemeka Odumegwu Ojukwu University Teaching Hospital, Awka, South-East Nigeria. *Advances in Microbiology*, *06*(07), 495–501. https://doi.org/10.4236/aim.2016.67049

Es-Said, I., Mahdoufi, R., Yagoubi, M., & Zouhdi, M. (2014). Isolation and antibiotic susceptibility of bacteria from otitis media infections in children in Rabat Morocco. *Journal of Biology, Agriculture and Healthcare*, *4*(28), 153–159. http://www.iiste.org/Journals/index.php/JBAH/article/view/18845/19209

Filipe, M., Karppinen, M., Kuatoko, P., Reimer, Å., Riesbeck, K., & Pelkonen, T. (2020). Suppurative otitis media in Angola: clinical and demographic features. *Tropical Medicine and International Health*, *25*(10), 1283–1290. https://doi.org/10.1111/tmi.13466

Ghosh, A., Rana, A., & Prasad, S. (2015). Prevalence of Fungal Infection in Chronic Suppurative Otitis Media-A Study at Tertiary Care Hospital in Western Uttar Pradesh. *Indian Journal of Microbiology Research*, *2*(3), 159. https://doi.org/10.5958/2394-5478.2015.00006.0

University of Ghana http://ugspace.ug.edu.gh

Gisselsson-Solén, M., Henriksson, G., Hermansson, A., & Melhus, Å. (2014). Risk factors for carriage of AOM pathogens during the first 3 years of life in children with early onset of acute otitis media. *Acta Oto-Laryngologica*, *134*(7), 684–690. https://doi.org/10.3109/00016489.2014.890291

Hailegiyorgis, T. T., Sarhie, W. D., & Workie, H. M. (2018). Isolation and antimicrobial drug susceptibility pattern of bacterial pathogens from pediatric patients with otitis media in selected health institutions, Addis Ababa, Ethiopia: A prospective cross-sectional study. *BMC Ear, Nose and Throat Disorders*, *18*(1), 1–7. https://doi.org/10.1186/s12901-018-0056-1

Harmes, Kathryn; Blackwood, Alexander; Burrows, Heather; Cooke, James; Harrison, Van; Passamani, P. (2013). Otitis Media: Diagnosis and Treatment. *American Family Physician*, *88*(7).

Hounkpatin, S. H. R., Adedemy, J. D., Flatin, M. C., E. Awassi, S. F., Afouda, S. L., Avakoudjo, F., Adjbabi, W., & Vodouhè, S. J. (2016). Risk Factors for Acute Otitis Media in Children Aged 0 to 5 Years in Parakou. *International Journal of Otolaryngology and Head & Neck Surgery*, *05*(02), 73–78. https://doi.org/10.4236/ijohns.2016.52012

Juyal, D., Negi, V., Sharma, M., Adekhandi, S., Prakash, R., & Sharma, N. (2014). Significance of fungal flora in chronic suppurative otitis media. *Annals of Tropical Medicine and Public Health*, *7*(2), 120–123. https://doi.org/10.4103/1755-6783.146400

Kingery, Joe; Taylor, Wanda; Braun, D. (2016). Acute otitis media. *Osteopathic Family Physician*, *8*(6), 22–25. https://doi.org/10.1136/pgmj.14.153.197

Kucur, Cuneyt; Şimşek, Eda; Kuduban, Ozan; Özbay, I. (2015). Prevalence of and risk factors for otitis media with effusion in primary school children: Case-control study in Erzurum, Turkey.

University of Ghana http://ugspace.ug.edu.gh

Turkish Journal of Pediatrics, *57*(3), 230–235. http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L607409424

Ladomenou, F., Kafatos, A., Tselentis, Y., & Galanakis, E. (2010). Predisposing factors for acute otitis media in infancy. *Journal of Infection*, *61*(1), 49–53. https://doi.org/10.1016/j.jinf.2010.03.034

Lieberthal, A. S., Carroll, A. E., Chonmaitree, T., Ganiats, T. G., Hoberman, A., Jackson, M. A., Joffe, M. D., Miller, D. T., Rosenfeld, R. M., Sevilla, X. D., Schwartz, R. H., Thomas, P. A., & Tunkel, D. E. (2013). The diagnosis and management of acute otitis media. *Paediatrics*, *131*(3). https://doi.org/10.1542/peds.2012-3488

Marom, T., Nokso-Koivisto, J., & Chonmaitree, T. (2012). Viral-bacterial interactions in acute otitis media. *Current Allergy and Asthma Reports*, *12*(6), 551–558. https://doi.org/10.1007/s11882-012-0303-2

Momtazmanesh, S., Ochs, H. D., Uddin, L. Q., Perc, M., Routes, J. M., Vieira, D. N., Al-Herz, W., Baris, S., Prando, C., Rosivall, L., Abdul Latiff, A. H., Ulrichs, T., Roudenok, V., Aldave Becerra, J. C., Salunke, D. B., Goudouris, E., Condino-Neto, A., Stashchak, A., Kryvenko, O., … Rezaei, N. (2020). All together to fight COVID-19. *American Journal of Tropical Medicine and Hygiene*, *102*(6), 1181–1183. https://doi.org/10.4269/ajtmh.20-0281

Monasta, L., Ronfani, L., Marchetti, F., Montico, M., Brumatti, L., Bavcar, A., Grasso, D., Barbiero, C., & Tamburlini, G. (2012). Burden of disease caused by otitis media: Systematic review and global estimates. *PLoS ONE*, *7*(4). https://doi.org/10.1371/journal.pone.0036226

Mukara, K. B., Lilford, R. J., Tucci, D. L., & Waiswa, P. (2017). Prevalence of Middle Ear

University of Ghana http://ugspace.ug.edu.gh

Infections and Associated Risk Factors in Children under 5 Years in Gasabo District of Kigali City, Rwanda. *International Journal of Pediatrics*, *2017*, 1–8. https://doi.org/10.1155/2017/4280583

Ngo, C. C., Massa, H. M., Thornton, R. B., & Cripps, A. W. (2016). Predominant bacteria detected from the middle ear fluid of children experiencing otitis media: A systematic review. *PLoS ONE*, *11*(3), 1–27. https://doi.org/10.1371/journal.pone.0150949

Nitsche, M. P., & Carreño, M. (2015). Antibiotics for acute otitis media in children. *Medwave*, *15*, e6295. https://doi.org/10.5867/medwave.2015.6295

Nnebe-Agumadu, U., Okike, O., Orji, I., & Ibekwe, R. C. (2011). Childhood suppurative otitis media in Abakaliki: Isolated microbes and in vitro antibiotic sensitivity pattern. *Nigerian Journal of Clinical Practice*, *14*(2), 159–162. https://doi.org/10.4103/1119-3077.84006

Okesola, A., & Fasina, O. (2011). Trends in the Resistance Pattern of Bacterial Pathogens of Otitis Media in Ibadan, Nigeria. *African Journal of Clinical and Experimental Microbiology*, *13*(1), 46–50. https://doi.org/10.4314/ajcem.v13i1.5

Orji, F. T., Dike, B. O., & Oji, O. (2015). Determinants of non-healing ear discharge in chronic suppurative otitis media in a developing country. *European Archives of Oto-Rhino-Laryngology*, *272*(10), 2713–2718. https://doi.org/10.1007/s00405-014-3255-4

Osazuwa, F., Osazuwa, E., Osime, C., Igharo, E. A., Imade, P. E., Lofor, P., Momoh, M., Omoregie, R., & Dirisu, J. (2011). Etiologic agents of otitis media in Benin City, Nigeria. *North American Journal of Medical Sciences*, *3*(2), 95–98. https://doi.org/10.4297/najms.2011.395

University of Ghana http://ugspace.ug.edu.gh

Pettigrew, M. M., Gent, J. F., Pyles, R. B., Miller, A. L., Nokso-Koivisto, J., & Chonmaitree, T. (2011). Viral-bacterial interactions and risk of acute otitis media complicating upper respiratory tract infection. *Journal of Clinical Microbiology*, *49*(11), 3750–3755. https://doi.org/10.1128/JCM.01186-11

Qureishi, A., Lee, Y., Belfield, K., Birchall, P.J., Daniel, M. (2014). Update on otitis media prevention and treatment. Infection and Drug Resistance, 7, 15-24. https://doi.org/10.2147/IDR.S39637

Sakulchit, T., & Goldman, R. D. (2017). Sakulchit, T., & Goldman, R. D. (2017). Antibiotic therapy for children with acute otitis media. Canadian Family Physician Medecin de Famille Canadien, 63(9), 685–687. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/28904032%0Ahttp://www.pubmedcentral.n. *Canadian Family Physician Medecin de Famille Canadien*, *63*(9), 685–687. http://www.ncbi.nlm.nih.gov/pubmed/28904032%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC5597011

Schilder, A. G. M., Chonmaitree, T., Cripps, A. W., Rosenfeld, R. M., Casselbrant, M. L., Haggard, M. P., & Venekamp, R. P. (2016). Otitis media. *Nature Reviews Disease Primers*, *2*, 1–19. https://doi.org/10.1038/nrdp.2016.63

Shak, J. R., Vidal, J. E., & Klugman, K. P. (2013). Influence of bacterial interactions on pneumococcal colonization of the nasopharynx. *Trends in Microbiology*, *21*(3), 129–135. https://doi.org/10.1016/j.tim.2012.11.005

Shrestha, B., Amatya, R., Shrestha, I., & Ghosh, I. (2012). Microbiological Profile of Chronic Suppurative Otitis Media. *Nepalese Journal of ENT Head and Neck Surgery*, *2*(2), 6–7.

University of Ghana http://ugspace.ug.edu.gh

https://doi.org/10.3126/njenthns.v2i2.6793

Sophia, A., Isaac, R., Rebekah, G., Brahmadathan, K., & Rupa, V. (2010). Risk factors for otitis media among preschool, rural Indian children. *International Journal of Pediatric Otorhinolaryngology*, *74*(6), 677–683. https://doi.org/10.1016/j.ijporl.2010.03.023

Suzuki, M., Dhoubhadel, B. G., Yoshida, L. M., & Ariyoshi, K. (2014). Nasopharyngeal bacterial interactions in children. *Emerging Infectious Diseases*, *20*(2), 324. https://doi.org/10.3201/eid2002.121724

Tadesse, B., Shimelis, T., & Worku, M. (2019). Bacterial profile and antibacterial susceptibility of otitis media among pediatric patients in Hawassa, Southern Ethiopia: Cross-sectional study. *BMC Pediatrics*, *19*(1), 1–8. https://doi.org/10.1186/s12887-019-1781-3

Tesfa, T., Mitiku, H., Sisay, M., Weldegebreal, F., Ataro, Z., Motbaynor, B., Marami, D., & Teklemariam, Z. (2020). Bacterial otitis media in sub-Saharan Africa: A systematic review and meta-analysis. *BMC Infectious Diseases*, *20*(1), 1–12. https://doi.org/10.1186/s12879-020-4950-y

Tiedt, N. J., Butler, I. R. T., Hallbauer, U. M., Atkins, M. D., Elliott, E., Pieters, M., Joubert, G., & Seedat, R. Y. (2013). Paediatric chronic suppurative otitis media in the Free State Province: Clinical and audiological features. *South African Medical Journal*, *103*(7), 467–470. https://doi.org/10.7196/SAMJ.6636

Uhari, M., & Mantysaari, K. (2009). REVIEW ARTICLE A Meta-Analytic Review of the Risk Factors for Acute Otitis Media. *Paediatrics*, *22*(6), 1079–1083.

Vaghela, M., Doshi, H., & Rajput, S. (2016). An analysis of ear discharge and antimicrobial

University of Ghana http://ugspace.ug.edu.gh

sensitivity to the bacteria used in its treatment. *International Journal of Research in Medical Sciences*, *4*(7), 3498–3503. https://doi.org/10.18203/2320-6012.ijrms20162319

Van Dyke, M. K., Pirçon, J. Y., Cohen, R., Madhi, S. A., Rosenblüt, A., Parra, M. M., Al-Mazrou, K., Grevers, G., Lopez, P., Naranjo, L., Pumarola, F., Sonsuwan, N., & Hausdorff, W. P. (2017). Aetiology of acute otitis media in children less than 5 years of age: A pooled analysis of 10 similarly designed observational studies. *Pediatric Infectious Disease Journal*, *36*(3), 274–281. https://doi.org/10.1097/INF.0000000000001420

Walker, R. E., Bartley, J., Flint, D., Thompson, J. M. D., & Mitchell, E. A. (2017). Determinants of chronic otitis media with effusion in preschool children: A case-control study. *BMC Pediatrics*, *17*(1), 1–10. https://doi.org/10.1186/s12887-016-0767-7

Wang, J., Chen, B., Xu, M., Wu, J., Wang, T., Zhao, J., Zhang, Q., & Zhang, Y. (2016). Etiological factors associated with chronic suppurative otitis media in a population of Han adults in China. *Acta Oto-Laryngologica*, *136*(10), 1024–1028. https://doi.org/10.1080/00016489.2016.1183818

Wasihun, A. G., & Zemene, Y. (2015). Bacterial profile and antimicrobial susceptibility patterns of otitis media in Ayder Teaching and Referral Hospital, Mekelle University, Northern Ethiopia. *SpringerPlus*, *4*(1), 1–9. https://doi.org/10.1186/s40064-015-1471-z

WHO. (2004). Chronic suppurative otitis media - Burden of Illness and Management Options. *WHO Library Cataloguing-in-Publication Data*, 84. https://doi.org/10.1016/j.amjoto.2007.09.002

Zhang, Y., Xu, M., Zhang, J., Zeng, L., Wang, Y., & Zheng, Q. Y. (2014). Risk factors for chronic and recurrent otitis media-A meta-analysis. *PLoS ONE*, *9*(1).

University of Ghana http://ugspace.ug.edu.gh

https://doi.org/10.1371/journal.pone.0086397

Zielnik-Jurkiewicz, B., & Bielicka, A. (2015). Antibiotic resistance of Streptococcus pneumoniae in children with acute otitis media treatment failure. *International Journal of Pediatric Otorhinolaryngology*, *79*(12), 2129–2133. https://doi.org/10.1016/j.ijporl.2015.09.030

University of Ghana http://ugspace.ug.edu.gh

APPENDIX I: CONSENT FORM

Research title: Bacterial aetiology and risk factors associated with childhood otitis media in Accra, Ghana

Principal investigator: Vida Bannah

Address: Department of Medical Microbiology, University of Ghana Medical School, P.O Box 4236, Korle-Bu.

Introduction: This research is being conducted to find out the different bacteria that cause otitis media in children and the factors that predispose children in Ghana to the disease. Please read this consent form carefully. You will also be provided with explanations of the content for clarity. Kindly append your signature to this document only after you have understood the purpose of this study. A photocopy of the original document will be given to you for your record.

Why the study?

Otitis media (OM), also known as middle ear infection, has a high prevalence among young children. The complications of OM include hearing loss, delayed speech development, impaired intellectual development and societal challenges in later life. OM is widespread globally and in developing countries, it is the main cause of hearing loss. It causes major economic and social burdens on families and healthcare systems. To prevent OM from occurring and have an appropriate treatment plan for children affected, it is necessary to establish the risk factors of OM and causal agents for OM. Identifying these factors leads to intervention and effective prevention. To lessen the severe complication of otitis media and guide medical practitioners in their antibiotic prescription, emphasis needs to be placed on bacterial etiologies and their antibiotic susceptibility patterns.

University of Ghana http://ugspace.ug.edu.gh

There is currently limited data on the bacterial aetiology and risk factors of OM in children in Ghana, and the purpose of this study is to fill that gap.

General information and your part in the study

Children up to the age of 12 years diagnosed with otitis media with the consent of parents or guardians qualify for this study. Patients must not be on antibiotics. Ear, nose and throat specialists will take ear swabs from the middle ear of patients. You will be contacted through your phone number for any required information.

Possible risks and discomforts

This research will cause minimal physical pain or damage during the swabbing of the middle ear.

Possible benefits of the research study

Money exchange will not be involved in this research, both on the part of the researcher and the participant. This research will aid physicians in the treatment and management of patients with OM and curb the occurrence of associated complications, such as hearing loss, delayed speech development, and impaired intellectual development in Ghana.

Confidentiality

Every information obtained from this study will be concealed (hidden) during and after the study. Numbers and codes will be used for the identification of participants. Your clinical conditions and all documents with your name will be handled only by members of the research team.

Voluntary participation and right to leave the research

Participation in this research is a personal decision, and you can freely choose to allow your ward to participate in the study or not without any consequences. Should you choose to allow your ward

University of Ghana http://ugspace.ug.edu.gh

to participate, you could freely rescind your decision at any time within the conduction of the study, without incurring any penalty.

Contacts for additional information

For questions about the research project, you may contact the researcher, Vida Bannah on the phone number 0243258176, or Dr. Nicholas T. K. D. Dayie on 0208449415. You could also seek these individuals out at the Department of Medical Microbiology, University of Ghana Medical School.

University of Ghana http://ugspace.ug.edu.gh

CONSENT FOR ENROLLMENT OF WARD

The above document describing the procedures, purpose, benefits, and risks for the research with the title **"Bacterial aetiology and risk factors associated with childhood otitis media in Accra, Ghana"** has been read and explained to me. I have been allowed to have any questions about the research answered to my satisfaction. I agree to enrol my ward in this study.

_____ _____

Date Signature/ Thumbprint of volunteer

For parents/guardians who cannot read, or cannot write on the form themselves, a witness must sign here on their behalf:

I was present while the procedures, purpose, benefits, and risks of the research were read to the parent/guardian. All questions were answered, and the parent/guardian agreed to enrol his ward in this study.

_____ _____

Date Name and signature of parent/guardian

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

_____ _____

Date Name and signature of parent/guardian

University of Ghana http://ugspace.ug.edu.gh

ASSENT FORM FOR OLDER CHILDREN

The above document describing the procedures, purpose, benefits, and risks for the research with the title "Bacterial aetiology and risk factors associated with childhood otitis media in Accra, Ghana" has been read and explained to me. I have been allowed to have any questions about the research answered to my satisfaction. I agree to enrol in this study.

_____ _____

Date Signature/ Thumbprint of volunteer

University of Ghana http://ugspace.ug.edu.gh

APPENDIX II: STUDY QUESTIONNAIRE

DIRECTIONS: Please answer each question as accurately as possible by circling the correct answer or filling in the space provided.

Participant's ID…….

Date……..Folder Number…….....

Contact Tel. Numbers……

E-mail Address……

Postal Address……

SOCIO-DEMOGRAPHIC CHARACTERISTICS

Age ……

Sex: Male/ Female

Residence: Urban/ Rural

Education: Not yet/Crèche/Nursery/Kindergarten/Primary

Average size of the family ……

Household income …..……..

POTENTIAL RISK FACTORS

Breastfeeding duration: (Never/<6 months/6-12 months/> 12 months)

Parental employment: ……...

Parental education: Not educated/ Primary/ JHS/ SHS/ Tertiary

Child history of otitis media: Yes/ No

Family history of otitis media: Yes/No

Passive exposure to parental smoke: Yes/No

University of Ghana http://ugspace.ug.edu.gh

Presence of recurrent upper respiratory tract infections: Yes/No

CLINICAL INFORMATION

Diagnosis: ASOM/OME/CSOM

Fever: Yes/ No

Runny nose: Yes/No

Cough: Yes/ No

Otalgia (ear pain): Yes/ No

Tugging (pulling of the ear): Yes/ No

Holding of the ear: Yes/No

Rubbing of the ear: Yes/No

Otorrhea (ear discharge): Yes/No

Have you reported to the doctor: Yes/ No

Are you on antibiotics: Yes/ No

If yes, what type of antibiotics: ……..

How often do you visit the clinic: Weekly/ Monthly/ 3-6months?

Do you have other medical conditions: Yes/ No

If yes, please specify ……

THANK YOU.