DISSERTATION

Microbiological Isolates of Chronic Suppurative Otitis Media at the University Teaching Hospital and Beit Cure Hospital in Lusaka, Zambia

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DECLARATION

I hereby declare that this study is my original work and has not been presented for dissertation at any other university.

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DEDICATION

This dissertation is dedicated to my family for their constant support during its compilation. Many thanks to my wife Max'thyala .E.M. Phiri and my children, Ivanna and Sibongile for their encouragement, support and prayers throughout the study. Special thanks to my parents, Mr. and Mrs. L.Z Phiri for their encouragement and support throughout the study.

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Contents

LIST OF FIGURES AND TABLES

FIGURES

TABLES

Acronyms and Abbreviations

AOM	Acute otitis media
CI	Confidence Interval
BCH	Beit Cure Hospital
CSOM	Chronic suppurative otitis media
CLSI	Clinical Laboratory Standards Institute
CT	Computerized tomography
ERES	Excellence in Research and Science
ET	Eustachian Tube
EAC	External Auditory Canal
E. coli	Escherichia coli
FB	Foreign body
GERD	Gastro-oesophageal reflux Disease
HIV	Human Immunodeficiency Virus
KNH	Kenyatta National Hospital
MRI	Magnetic resonance imaging
MRSA	Methicillin-Resistant Staphylococcus Aureus
OME	Otitis media with effusion
RCT	Randomised controlled trial
SPP	species
TM	Tympanic membrane
UON	University of Nairobi
UTH	University Teaching Hospital
WHO	World Health Oganisation

ABSTRACT

Background: Chronic Suppurative Otitis Media (CSOM) is a common cause of hearing loss and many complications such as meningitis. Many approaches to treatment of CSOM have been unsatisfactory because CSOM microbiological isolates as well as their sensitivity patterns vary from place to place.

Objectives: To determine the pattern of microbiological isolates of CSOM and the demographic characteristics of patients with CSOM at the University Teaching Hospital, (UTH) and Beit Cure Hospital (BCH) in Lusaka, Zambia.

Study design: The study was a hospital based Cross sectional descriptive study

Study Setting: The study was conducted at the ENT outpatient clinics of UTH and BCH in Lusaka, Zambia.

Methodology: 100 CSOM patients were included in the study. Quantitative data on the participants' demographic details and clinical features were obtained using structured questionnaires. The middle ear discharge was aseptically collected using a sterile cotton swab. In the laboratory, samples were inoculated on agar media to isolate microorganisms and antibiotic susceptibility testing was done using Kirby Bauer method as per CLSI guidelines.

Results: Out of the 100 CSOM patients studied, 33(33%) were children below 18yrs and 67(67%) were adults. 59(59%) of the patients had unilateral CSOM while 41 had bilateral CSOM which gave a total of 141 ears that were analyzed. 119(84.4%) had pure cultures, 20(14.2%) had mixed cultures and 2(1.4%) had no growth. Of the 169 microbiological isolates, the most frequent isolates were *Proteus mirabilis* 49(29.0%), *Pseudomonas aeruginosa*, 32(18.9%), coagulase negative S*taphylococcus* 18(10.7%) and *klebsiella pneumonie* 17(10.1%). High sensitivity rates were revealed to Gentamycin (64-100%), meropenem (68-100%), ceftazidime (85-100%), ceftriaxone (64-80%), and ciprofloxacin (66-88%). High resistance rates were recorded to Amoxicillin-clavulanate (as high as 100%), ampicillin (as high as 100%), tetracycline (as high as 91.2%) and cotrimoxazole (as high as 100%) and penicillin (as high as 100%).

Conclusion: *Proteus mirabilis* was the most dominant microbiological isolate followed by *Pseudomonas aureginosa*. The isolated microorganisms had high susceptibility rates to gentamycin, meropenem, ceftazidime, ceftriaxone and ciprofloxacin. There were high resistance rates to amoxicillin-clavulanate, ampicillin, tetracycline, cotrimoxazole and penicillin.

CHAPTER ONE

1.0 INTRODUCTION

Chronic Suppurative Otitis Media (CSOM) is chronic inflammation of the middle ear cleft (Eustachian tube, middle ear, and mastoid cavity) which presents with recurrent ear discharge or otorrhoea through a tympanic perforation [1]. The World Health Organization (WHO) definition for CSOM requires only two weeks of Otorrhoea [1**].**

The infection commonly occurs during the first 6 years of a child's life, with a peak around 2 years [2].The common causative organism of CSOM includes aerobic bacteria such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Haemophilus influenza*, *Staphylococcus aureus* and *Klebsiella* species [3,4]. Anaerobic bacteria identified as CSOM causative organisms include *Bacteroides* and *Fusobacterium* species [5]. *Aspergillus* and *Candida* species are common fungal isolates of CSOM [1, 19]. However, CSOM causative organisms and there sensitivity pattern vary generally from place to place due to differences in climatic conditions and manner of antibiotic use [6,].

Apart from being a cause of complications such as facial palsy, mastoiditis, brain abscess and labyrinthitis, CSOM is a major cause of acquired hearing impairment especially in developing countries [1]. Educational, vocational and social problems are but some of the problems that stem from hearing impairment. These include impaired speech and language development, poor academic performance and poor social interaction [1].

It is therefore important to obtain data on Local patterns of microbiology of CSOM for objective planning and successful implementation of methods for adequate treatment of CSOM.

1.1 Epidemiology

According to the World Health Organisation (WHO), about 330million individuals, globally, suffer from CSOM [1]. 60% of these suffer from significant hearing impairment [1]. CSOM accounts for 28 000 deaths and a Disease burden of over 2 million Disability adjusted Life Years (DALYs) [1].

Countries (developing countries) in the South-east Asia and Western Pacific regions, Africa, and several ethnic minorities in the Pacific Rim bear Over 90% of the burden [1].

The WHO estimates that, in Africa, over 2.4 million people have CSOM, accounting for almost 4% of the global CSOM burden [1]. Using higher prevalence rates, it has been estimated that up to 25 million people in Africa have CSOM, 50% of whom may have hearing impairment [1].

CSOM most often occurs in the first 5 years of life [7].It is common in children with craniofacial anomalies. CSOM generally has equal distribution between males and females. Socio-economic factors such as poor living conditions and overcrowding, poor hygiene and nutrition have been suggested as a basis for the widespread prevalence of chronic suppurative otitis media in the developing countries [1, 7].

1.2 Background

1.2.1 Anatomy and Physiology of middle ear cleft

The middle ear cleft is made up of the middle ear, Eustachian tube (ET), mastoid air cells and antrum [8, 9].The middle ear cavity is an irregular air filled space that contains ossicles (malleus, incus, and stapes) which are important in sound transformation transmission, and amplification [10]. Middle ear, while offering a conductive pathway for sound transmission, functions as an impedance-matching device by coupling the low impedance of air to the high impedance of the fluid-filled cochlea [10].

The Eustachian tube is a narrow air pressure equalizing tube connecting the middle ear laterally to the nasopharynx [9]. Its functions includes pressure regulation (ventilation) that equilibrates middle ear air pressure with atmospheric air pressure [9], protection of the middle ear from nasopharyngeal sound pressure and secretions, and clearance of secretions produced within middle ear into the nasopharynx which is provided by the mucociliary system of the ET [8]. The mastoid bone contains Air cells, antrum and additus[8]. The middle ear cleft is related to the temporal lobe of the brain superiorly, the sigmoid sinus posteromedially, the inner ear medially, the external ear laterally, and the internal jugular vein inferiorly [8].

1.2.2 Pathogenesis and Risk factors for CSOM

The pathogenesis of CSOM is multifactorial with factors such as Eustachian tube dysfunction, genetic predisposition, and environmental factors playing a role [12].

A dysfunctional and structurally immature Eustachian tube (ET) is the most important factor in the pathogenesis of otitis media **[**13]. Negative middle-ear pressure, resulting from ET dysfunction, causes an influx of bacteria and viruses from the nasopharynx when the ET

opens [13]. Infants and young children are especially at risk for reflux (containing bacteria and viruses) into the middle ear from nasopharynx via the ET because their ET is short, horizontal, and 'floppy' [11].The bacteria and viruses in the middle ear elicit an inflammatory response causing an acute infection [13]. CSOM is initiated by an episode of acute infection of the middle ear that fails to resolve and result in a permanent TM perforation [13]. Children with a cleft palate or deformity of the mid-face, skull base, nose or paranasal sinuses have a statistically higher incidence of OM at all ages, especially during the first 2 years of life which is attributed to the associated ET dysfunction [14]. Bacteria can also reach the middle ear from the external ear canal through a non-intact tympanic membrane [14]. Other risk factors for CSOM include low socioeconomic status, poor housing conditions (such as congested houses with more than 10 people, Indoor-cooking) infant day care attendance, supine bottle feeding, and passive smoking. The clinical risk factors include upper respiratory tract infections, allergy, and Adenoid hypertrophy [1, 15].

1.2.3 Microbiology

CSOM is commonly caused by bacteria [1]. This can either be aerobic or anaerobic, gram negative or gram positive bacteria [16, 17, 18]. The aerobic microorganisms most frequently isolated in CSOM are *Pseudomonas aeruginosa* and *Staphylococcus aureus* [1]. Commonly isolated Gram-negative organisms include organisms such as *Proteus spp, Klebsiellaspp, Escherichia spp* and *Haemophilus influenza* [1, 17]. The most frequently isolated anaerobic organisms are *Bacteroides spp* [18, 19,]. Fungal organisms that include *Aspergillus species* and *Candida species* are also isolated in CSOM [19].The Etiological organisms for otitis media vary with time and geographical area as well as continent to continent [6, 19]. This variation can be attributed to differences in climatic conditions, emergency of antibacterial resistance (which could be due to indiscriminate use of antibiotics), differences in cultural practices, nutrition and social economic factors among many others [19].

1.2.4 Pathophysiology and Complications of CSOM

Chronic inflammation in CSOM leads to proliferation of mucosal lamina propria, granulation tissue formation, enzymatic mucosal ulceration and bone destruction. Ossicular chain destruction and/ or ankylosis together with the tympanic membrane perforation contribute to hearing loss [20]. It is often conductive, but with involvement of the cochlear and cranial nerve VIII, it can be sensorineural hearing Loss.

Complications of chronic otitis media are divided into extra-cranial (extra temporal and intra temporal) intracranial complications [21]. The extra-temporal complications include abscess

formation such as the Lucs (temporalis region), Citelli (sub-periosteal), and the Bezold‟s (sternocleidomastoid) abscesses. The intratemporal components of the extra-cranial complications include: mastoiditis, petrositis, facial paralysis and labyrinthitis. The intracranial complications include meningitis, brain abscess,subdural abscess, sigmoid sinus thrombophrebitis, and otitichydrocephalus [21].

1.2.5 Types of CSOM

Clinically CSOM is divided intoTubotympanic type (safe type) and Atticoantral type (unsafe type) [22]. The Tubotympanic disease involves the anteroinferior part of the middle ear cleft and is associated with a central perforation, with no risk of serious complications. The Atticoantral type of CSOM involves the posterosuperior part of the middle ear cleft. It is associated with an attic or a marginal perforation, cholesteatoma, granulation tissue or osteitis. Risk of complications is high in this variety and is considered unsafe [22].

CSOM is also divided into active (with otorrhea) and inactive (with no otorrhea) types. Each of these are subdivided into squamosal (associated cholesteatoma) and mucosal (not associated with cholesteatoma) types [22].

1.2.6 Diagnosis of CSOM

CSOM diagnosis is based on history and clinical examination (otoscopy) [1, 12].

CSOM patients present with a history of prolonged or recurrent ear discharge which typically is not associated with pain, discomfort or fever [1, 22]. The discharge varies from fetid, purulent, and cheese like to clear and serous. It can be bilateral or unilateral. Otorrhoeain CSOM without cholesteatoma is usually copious, mucopurulent and non foul smelling, whereas scanty foul smelling and sometimes sanguineous otorrhoea is seen in CSOM with cholesteatoma [22]. A common presenting symptom that is often associated with otorrhea is hearing loss in the affected ear. [12].

On Otoscopic examination the external auditory canal may or may not be oedematous and is not typically tender. It may contain discharge from the Middle ear. The examination also shows evidence of TM perforation. TM perforations are of varying features with regard to location, size, shape, dryness or wetness [22]. TM perforations can be central or marginal, total or subtotal. The middle ear may show additional features of chronic inflammation such as an aural polyp, granulation tissues, atrophic areas and ossicular destruction 1, 23]. A 512-Hz tuning fork examination is a critical part of the evaluation to establish if hearing loss is present and whether it is conductive or sensorineural [23].

1.2.7 Investigations of CSOM

CSOM investigations Include appropriate ear discharge swab that are taken for microscopy, culture and sensitivity tests [1]. This is reserved for cases that fail standard topical antibiotic therapy. This is a useful guide to the identification of causative agents and appropriate choice of antibiotics [1]. In the event that there is no response to medical treatment in the presence of granulation tissue, then biopsies of the granulation tissue should be taken to rule out a neoplastic or granulomatuos process [24].

Audiometry (Pure Tone Audiometry and Speech Audiometry) should be done in all patients with CSOM to establish the type and degree of hearing loss and thus determine the mode of rehabilitation and management of choice.

High resolution Temporal bone CT scan is done in the event that extracranial or intracranial complications are suspected or when surgery is being planned. It allows for assessment of the bony architecture of the middle ear and mastoid, the status of the middle ear ossicles, and the integrity of the cochlea and semicircular canals [23].

1.2.8 Management

The aims of management of CSOM are eradication of disease, closure of the tympanic membrane perforation and restoration of function to as near normal as possible [1]. Treatment could be medical, surgical or both, including rehabilitation through use of Hearing aids. Medical treatment consists of aural toilet, use of topical steroids, topical antiseptics and topical or systemic antibiotics [1]. Aural toilet must be combined with antibiotics or antiseptics to be effective [1]. Topical antibiotics are the first line of treatment of uncomplicated otorrhea [25]. Some of the topical drugs used in management of CSOM include ciprofloxacin, tobramycin, gentamicin and chloramphenicol. Topical antibiotics have been found to be more effective in treating otorrhea than antiseptics or systemic antibiotics [26, 27]. Systemic antibiotics are considered in patients at risk for complicated or invasive ear infections [27].Surgical intervention is treatment of choice to effect closure of TM perforation as spontaneous closure of TM perforation is uncommon in CSOM even after adequate medical therapy. Surgery done for TM perforation closure includes myringoplasty and tympanoplasty. Tympanomastoidectomy has been advocated as the surgical treatment of choice in CSOM with mastoiditis [1, 23].Surgery is also indicated for diseases such as cholesteatoma, polypoid disease and infected bone in order to create a dry and safe ear that is free of infection. Reconstruction of the sound transmission mechanism is vital through ossicular chain reconstruction and use of ossicular prosthesis to replace damaged ossicles.

CHAPTER TWO

2.0 LITERATURE REVIEW

Bacterial isolates from a CSOM patient can be pure or mixed, Anaerobic and/or aerobic, gram negative and/or gram positives. They may occur in association with other organisms such as fungi. *Pseudomonas aeruginosa,* and *Staphyloccocus aureus* are the most common organisms isolated in many middle ear infections in many parts of the world [1, 3, 16,17]. Other common microorganisms isolated include *Proteus, klebsiella, E.coli,* and *bacteroides* species. By and large, Microbiological isolates of CSOM and their antimicrobial sensitivity patterns, in many studies conducted, vary depending on different factors that include climatic conditions, prior use of antibiotics, patient population, specimen collection and processing techniques [1, 28, 29]. This is illustrated in Table1 below. In different geographical areas, even within the same country, microbiological isolates from CSOM may vary as would sensitivity patterns. Differences in geographical conditions and local antimicrobial prescribing practices account for different antimicrobial resistance profiles of bacteria among different populations [29]. This is demonstrated by studies done by Hatcher et al, Aduba et al, and Mwaniki in Kenya.

Hatcher J Et al conducted a study on the prevalence of ear problems in school children in Kiambu district, Kenya [30]. A total of 5368 children from 57 randomly chosen primary schools in Kiambu district were examined. Among other findings in the study, it was found that the most common etiological organisms for CSOM were *Pseudomonas spp*(34%), *Proteus spp*(34%) *and Eschericia coli* (19%). These results were comparable with other studies in Africa and indicate a considerable burden of ear disease in Kiambu district, Kenya.

A prevalence study by Aduba et al on CSOM bacterial flora conducted In 2010 In Garissa district, Kenya, among a cohort of school children (in public and private primary schools and Islamic religious schools) showed different findings from that of Hatcher J Et a l in Kenya[16]. Of the 261 ear swab samples processed, 336 isolates - either in mixed or pure flora - were identified, being almost exclusively aerobes. *Proteus spp, Enterococcus, Staphylococcus aureus* and *Pseudomonas spp*. were isolated in 32.7%, 28.6%, 12.8% and 11.3% respectively. Proteus was susceptible to majority of the antibiotics tested for, while *Enterococcus* was poorly susceptible. This portends an important consideration for clinical management and therapeutic decision-making.

In a prospective study conducted by Mwaniki in 2009 at Kenyatta National Hospital, Nairobi, Kenya, a total of 100 ears were examined and microbiological studies done [31]. Pure cultures were obtained in 82% of samples while 17% were mixed and in 1% no organisms were isolated. Of the isolates, *Staphylococcus aureus* accounted for 39%, P. *aeruginosa*(36%), *Proteus* (6%)and *E. coli* (6%). Anaerobes accounted for 4%, fungal isolates (2%) i.e. *Aspergillus* and *Candida albicans*. The results were different from the ones obtained by Hatcher e al and Aduba et al in similar studies (above) in the same country.

Some studies conducted in Nigeria had findings similar to other studies in Africa where *Pseudomonas spp* were found to be the most common bacterial isolates of CSOM.
Ofolabi et al in 2012, at the University of Ilorin Teaching Hospital, Nigeria, conducted a prospective study on the pattern of bacterial isolates in middle ear discharge in CSOM patients [3]. A total of 134 outpatients aged 5-64yrs participated in the study. These were patients that were attending the ENT outpatient clinic. The patients were interviewed using a structured questionnaire and microbiological analysis of their ear discharge was done. The mean age of the study participants was 17.0 (S.D. =15.1±1.30). About 55.2% of the respondents were under 10yrs. 53.7% of the respondents were males with Male:Female ratio of 1.2:1. It was established in the study on gram stain that the common causative organisms were predominantly gram negative (71.6%) with *Pseudomonas aeruginosa* having been the commonest middle ear pathogenic organism identified. The sensitivity pattern highly favoured ciprofloxacin as the antiobiotic of choice for CSOM treatment. The study concluded that *Pseudomonas aeruginosa* is the commonest causative organism and Ciprofloxacin is the most sensitive antibiotic for CSOM treatment.

In another study conducted by Ibekwe et al in Enugu, Nigeria, on Pathogenic organisms in chronic suppurative otitis media involving 62 patients, It was found that *Pseudomonas aeruginosa* was responsible for CSOM in 46%, *Staphylococcus aureus* in 29%, *Proteus mirabilis* in 13%, *Streptococcus pyogenes* in 6%, *Aspergillus niger* in 5% and *Mucor* sp. in 2% [32].

Similar to findings by Aduba et al Garissa, Kenya, in 2010, studies conducted in Ethiopia and Malawi showed that *proteus* species were the commonest CSOM organisms isolated [33]. These studies, like other studies had both single and mixed microbial isolates. Anaerobes and fungi were the least common organisms isolated. However, unlike the organisms isolated by Aduba et al in Kenya which were found to be sensitive to common antibacterial agents,

similar organisms isolated by Muluye et al in Ethiopia in 2013 had multiple antibiotic resistant patterns. This illustrates variation in sensitivity patterns in similar microbial isolates in different geographical areas.

Chirwa in 2014 (Dissertation, University of Nairobi), conducted a study on the Microbiology of Chronic Otitis Media at Queen Elizabeth Central Hospital, Blantyre Malawi [34].The study involved 104 outpatients who had clinical evidence of CSOM. It was found that COM was most prevalent in children and young adults than in the older age group. 64 (61.5%) were aged 18 years and below, While 40 (38.5%) were aged 18 years and above. The mean and median ages were 17.79 years and 14 years respectively. Analysis of the total 118 specimens collected revealed that pure and mixed culture growth were obtained in equal numbers of 58(49%) each while in 2(2%) specimens there was no growth. Gram negative rods accounted for 84(72.4%) and gram positive cocci 32(27.6%). most common bacterial isolate causing CSOM were aerobic bacteria- *Proteus mirabilis* 44(28.6%), *Pseudomonas aeruginosa* 32(20.8%) and *Staphylococcus aureus* 31(20.1%). Anaerobes were isolated in 39(33.6%) of total sampled specimens and most common were *Bacteroides* species 18(15.5%) followed *by Peptostreptococcus* species 12(10.3 %) and *Clostridium* species 7(6.0 %).The most commonly isolated fungi were *Candida* and *Aspergillus* species.

In South Africa, Meyer et al [35] conducted a prospective study on the Spectrum of microorganisms and antibiotic sensitivity in a South African cohort at the Groote Schuur Hospital (GSH) in Cape Town from 2005 to 2009. Seventy-nine patients were included in the study with a mean age of 39 years (range 13 - 83 years). *Proteus mirabilis* (36%; 18/50) was the most common isolate in otitis media followed by *staphylococcus aureus* and *pseudomonas aeruginosa*. These results parallel the microbiology pattern reported by Loock[36] at a tertiary hospital in Cape Town in chronic otitis media patients with *Proteus spp*(29%) being the commonest isolate, followed by *P. aeruginosa* (24%) and *S. aureus (14%).*

Table 1: Summary of some studies on bacterial isolates of CSOM

Investigator	Type of study	Sample size	Year of Study	Country	Common organisms isolated.	Sensitivity
Muhammad [37]	Descriptive, cross sectional study	220	2011	Pakistan	*Pseudomonas aeruginosa*	tazocin (piperacillin/tazobactum) (100%), gentamicin (50%)
Dawit et al [19]	Descriptive cross –sectional study	112	2000	Ethiopia (Addis Ababa)	*Proteus species (31%), Staphylococcus aureus (18%), Escherichia coli (16%), Klebssiela(12%)*	kanamycin (72%), augmentin (84%) and gentamicin (88%).
Osazuwa et al [38]	Descriptive cross sectional study	569	2009-2010	Nigeria, (Bernin)	*Pseudomonas aeruginosa Proteus sp*	Generally high level resistance. Ofloxacin, gentamycin
Kumara et al [39]	Descriptive cross sectional study	100	2012	India	*Pseudomonas spp (43.2%) Staphylococcus aureus(31%*	Amikacin, ciprofloxacin
Prakashet al[40]	Descriptive cross-sectional study	204	2012	India	*Staphylococcus Aureus 48.7%, pseudomonas aeruginosa 19.9%*	Amikacin, cetriaxone, Gentamycin.
Aduba et al[16]	Descriptive Cross-sectional study	261ear samples	2010	Kenya	*Proteus spp 32.8%, Enterococcus 28.6%, S. aureus 12.8% Pseudomonas 11%*	Most isolates susceptible to commonly used antibiotics
Shamweel [41]	Descriptive Cross sectional	164	2013	Saudi Arabia.	*MSSA] (45.1%)* P. aeruginosa *(19.5%).*	Ciprofloxacin, Cotrimoxozole,

2.1. STATEMENT OF THE PROBLEM AND STUDY JUSTIFICATION.

Despite that there are many approaches to the treatment of CSOM, most have been unsatisfactory owing to variations in microbiological isolates of CSOM in different places of the world. This is dependent on different factors that include climatic conditions, prior use of antibiotics, and patient population [19]. Antibiotics in many cases of CSOM are prescribed indiscriminately which result in different antimicrobial resistance profile of bacteria and thus inadequate treatment of CSOM. This ultimately results in many serious complications such as brain abscesses, meningitis, mastoiditis and labyrinthitis to mention but a few.

In Zambia, no study has been conducted on the microbiological profile of CSOM. There is therefore no knowledge on the pattern of microbiological isolates of CSOM that would guide treatment regimens.

It is therefore important to conduct a study on the pattern of microbiological isolates of CSOM in Lusaka, Zambia, as it will provide knowledge that will guide the formulation of rational treatment protocols (especially empirical treatment) for CSOM and thus prevent the problems that stem from it.

2.2 RESEARCH QUESTION

What is the microbiological profile of CSOM at UTH and BCH in Lusaka, Zambia?

2.3 SUDY OBJECTIVES

2.3.1 General objective

To determine the pattern of microbiological isolates and the associated demographic factors of CSOM in patients attending the ENT outpatient clinics at UTH and BCH in Lusaka, Zambia

2.3.2 Specific objectives

To determine the associated demographic factors of CSOM among patients with CSOM attending the ENT outpatient clinics at UTH and BCH in Lusaka, Zambia.

To determine the pattern of microbiological isolates of CSOM among patients with CSOM attending the ENT outpatient clinics at UTH and BCH in Lusaka, Zambia

CHAPTER THREE

RESEARCH DESIGN AND METHODOLOGY

3.0 STUDY DESIGN

The study was a hospital based cross-sectional descriptive study.

3.1 STUDY AREA

This study was conducted in the ENT outpatient clinics at UTH and BCH situated in Lusaka District in Zambia.

3.2 SAMPLE SIZE DETERMINATION

The sample size was determined by the Yamane (1967:886) formula to yield a representative sample for proportions. (Yamane, T, 1967) [42, 43].

$$n_0 = \frac{N}{1 + Ne^2}$$

Where

n_0 Is the sample size

e Is the desired level of precision?

N Is the targeted population size. For the purpose of this study, it is equal to 120. It was arrived at upon consideration of a study period of 6 weeks and because a monthly average of 50 and 30 CSOM patients attend BCH and UTH Outpatient ENT Clinics respectively.

Required sample

$$n_0 = \frac{120}{1+(120*0.05^2} = 92.3 \approx 93$$

To cater for attrition (10%), the desired sample size (calculated) was 103 CSOM.

3.3 STUDY POPULATION

The study population comprised of CSOM patients attending ENT outpatient clinic at UTH and BCH in Lusaka District during the study period.

3.4 SAMPLING PROCEDURE

The sampling frame including CSOM patients attending ENT outpatient clinic was stratified into BCH and UTH. Proportionate samples of 64 and 39 patients from BCH and UTH were selected using a systematic sampling method. This method allowed for recruitment of every first 5 patients upon showing up in the clinic and omission of the 6th patient from the study (Target population/ Sample required= 1.165 hence exclusion criteria is based in 1/0.165) with strict application of the inclusion and exclusion criteria. This sampling method enabled the principle investigator to achieve targeted random and representative sample within the study period of 6 weeks. 3 of the 103 patients did not have their specimens processed in the laboratory and so were not included in the analysis.

3.5 INCLUSION AND EXCLUSION CRITERIA

3.5.1 Inclusion criteria

1. Patients of all age groups with actively draining CSOM (using WHO CSOM definition)

2. CSOM Patients attending the outpatient ENT clinics at UTH or BCH.

3. CSOM patients who consented or for whom a legal guardian had consented to participate in the study.

3.5.2 Exclusion criteria

1. Patients not consenting to participate in the study

2. Patients with less than 2 weeks duration of ear discharge

3. Patients already on antibacterial and anti-fungal treatment (ear drops/systemic) within the previous 2 weeks.

4. All known HIV or immunosuppression patients

3.6 RECRUITMENT, CONSENTING AND DATA COLLECTION PROCEDURE

The study team comprised of:

1. Principle investigator

2. 2 Nurses

3. 1 Laboratory technician

4. A microbiologist

The principle investigator and a nurse were available in the ENT outpatient clinics at both BCH and UTH for the recruitment of sample patients during each clinic day until the desired sample size was achieved. On the first day of contact and within the ENT clinic, the principle investigator did the following for each identified study participant:

1) Explain the study to the patient/ legal guardian and obtain consent.
2) Take demographic and medical history and conduct a physical examination.
3) Collect ear pus sample and deliver it to the laboratory.

The Information obtained in the patient's history and physical examination was entered in the patient's Data form.

3.6.1 Bacterial isolation

Using an aseptic technique (outlined below) pus discharge from the participants charging ears was collected by the principle investigator within the ENT clinic on the first day of contact before any topical or systemic antibiotics or anti-fungal medication was started. Using sterile gloves (after washing of hands with soap) under direct visualisation with good lighting, and under microscopy for the majority of the patients, a sterile swab was passed through a sterile aural speculum placed in the EAC (to avoid contamination from the skin of the auditory canal) and then advanced to the middle ear or the inner two-thirds of the EAC to collect pus specimen. The sample obtained was put in a swab transport tube that contained a transport media and then labelled with a unique patient identifier. The ear was cleaned of the pus by ear wicking or suctioning. Using a laboratory carrier, the sample was taken to the microbiological laboratory for culture, microscopy and sensitivity. Laboratory analysis of the specimen collected was done at UTH microbiology laboratory as it is conveniently located, equipped and adequately staffed. In the laboratory, by the laboratory technician, the specimens collected were inoculated on sheep Blood Agar, MacConkey's media, and chocolate agar media to culture aerobic bacteria. Anaerobic blood agar incubated in an anaerobic jar was used to culture anaerobic bacteria. Fungi were cultured on Sabouraud´s dextrose agar. The culture plates were incubated at 37°C for 24-48 hours. Owing to the fact that anaerobes grow slowly compared to aerobes, anaerobic culture plates were incubated for up to 7 days to allow for anaerobic bacterial growth. Isolates from the culture plates were identified Using gram staining, colony morphology, catalase, coagulase, oxidase and biochemical strips. Lactophenol cotton blue was used for final identification of fungal growth. Antimicrobial susceptibility tests were done on Mueller-Hinton agar using disk

diffusion method as described by Kirby Bauer. The antimicrobial agents tested were: tetracycline (30µg), chloramphenicol (30µg), gentamicin (10µg), ciprofloxacin (5µg), cotrimoxazole (25µg), ceftriaxone (30µg) and amoxicillin-clavulanate (10µg), meropenem, oxacillin, ceftazidime, cefoxitin, cefotaxime, ampicillin and penicillin. Susceptibility data were interpreted according to Clinical and Laboratory Standards Institute (CLSI, 2015) by the microbiologist.

3.6.2 Data collection instrument

Data was collected using interviewer administered structured questionnaires (Appendix II). Section A consisted of preliminary data on patients' characteristics. Section B consisted of the patients' medical history. Section C consisted of physical examination findings. Section D consisted of laboratory data obtained from the specimens. Thus, using a questionnaire both demographic data and medical history were obtained. Sterile swabs and sterile specimen bottles were used to obtain specimens for microscopy and culture. The laboratory data obtained was entered in the patient's proforma.

3.7. Quality assurance procedures

Quality control was a continuous process throughout the study to maximize validity and reliability of the findings of the study. To achieve this, a number of measures were put in place. These included the use of trained health professionals to obtain data. The principal investigator was responsible for history taking, physical examination and Specimen collection. Aseptic techniques were strictly adhered to in collecting specimen from patients. In the laboratory, an internal quality assessment of the procedures for the study was conducted to ensure that reliable results are obtained. The materials to be used as culture media were checked for identity, expiry dates, PH (acidic but not less than 5.5), homogeneity, colour and gel strength. Tests were conducted to verify freedom from contamination and to demonstrate correct performance of media. Tests for contamination included sampling, incubation (at suitable temperatures, 30+/-2^{o}C, for minimum 48hours) and inspection from each batch. Using standard laboratory protocols, the culture media was tested for nutritive capacity and inhibitory capacity. The results were interpreted using reference media.

Only one microbiology laboratory technician was used to process the specimens. Reporting of the results for gram staining and growths was done by a microbiologist. The principle investigator ensured that the data collected was entered in the patient's proforma

3.8 Limitations

Owing to the reason that the study was a hospital based study, the study will not be reflective of the microbiological pattern in the community of Lusaka.

Identification of HIV positive patients was difficult to achieve as not all patients disclosed their HIV status. Due to the fact that their immune systems are compromised, HIV infected persons are prone to atypical microbiological patterns that could have affected the outcome of this study.

3.9 Data management

The filled in questionnaire was cross checked for completeness at the end of each interview. Any missing entries were entered.

The laboratory request forms were checked for completeness and the desired test indicated.

3.10 Data retrieval and storage

All data collected in the study was sorted, coded and entered in a computer using SPSS program (version 21). Data was crossed checked against the data files for any inconsistencies and obvious data entry errors. The data entry and editing was done throughout the study process.

3.11 Data Analysis

Data was analysed using SPSS (Statistical Package for the Social Sciences) version 18. Chi-square tests were done to establish bivariate relationships and logistic linear regression to test causal association between the microbiological profile and other independent variables. Findings are presented in form of texts, tables, graphs and charts. Conclusions and recommendations have been made based on the results.

3.12 Ethical Consideration

Ethical approval was obtained from the KNH-UON Ethics Research Committee in Nairobi, Kenya, as well as ERES (Excellence in Research and Science) Converge Ethical and Research Committee in Zambia. Approval to allow the study to be conducted in BCH and UTH institutions was obtained from the respective institutions. The respondents were made to consent to participate in the study upon recruitment. Participants below the age of 18 were allowed to give Assent and have their parents or legal guardians give consent for them to participate in the study. They were informed that participation is voluntary and that they have the right to accept or withdraw or refuse to participate in the study. The researcher gave full

information about what the research entails and ensured respondents are competent enough to give consent. Full consent and explanation form is in Appendix I and the assent form in appendix III. The questionnaires were administered only after obtaining consent from the participants. Participants' privacy was highly maintained by ensuring that they were not exposed when filling questionnaires. The researcher ensured the anonymity of respondents by concealing their identity and keeping research data confidential for research purposes only. All concerns causing any sort of discomfort to respondents were resolved immediately and mitigation strategies put in place. The patients had not incurred any extra cost by participating in the study and were not coerced to take part in the study. Participants who had CSOM or other ear disease were managed accordingly and for those who required referral to other medical specialists, referrals were made accordingly The findings of the study will be shared with other medical practitioners in different forum through publication, scientific conferences to mention but two.

CHAPTER FOUR: STUDY FINDINGS

Data collection for this study was carried out from January to February 2016 at the ENT out-patient clinics of UTH and BCH in Lusaka, Zambia. A 100 CSOM patients were studied

4.0 Demographic characteristics

The age range of the study patients was 6 months to 68 years (Figure 1). Of the patients studied, 33(33%) were children below the age of 18, while 67(67%) were adults. 19(19%) were children aged below the age of 5.The mean age was 24.5 years with a standard deviation of 18.0 years. Male patients were 57(57%), while 43(43%) were females, giving a male to female ratio of 1.33:1. Of the adult patients, 44 (65.7%) had not attained tertiary level of education, and 3% were illiterate. 29 (43.3%) of the adult patients were employed while 38 (56.7%) were not. 21(63.6%) of the legal guardians/parents of the children were employed. 55(55%) of the study patients were from households that had less than 5 members, while only 5(5%) had come from households that had more than 10 members. Only 17(17%) patients had come from households where a member smoked. 81 (81%) of the patients stayed in peri-urban areas of Lusaka while 19(19%) stayed in urban areas of Lusaka. Charcoal was the commonest fuel that was used for cooking, accounting for 63% of the patients. 35% of the patients used electricity and 2% used firewood. The demographic characteristics of the study patients are summarized in table 2 below.

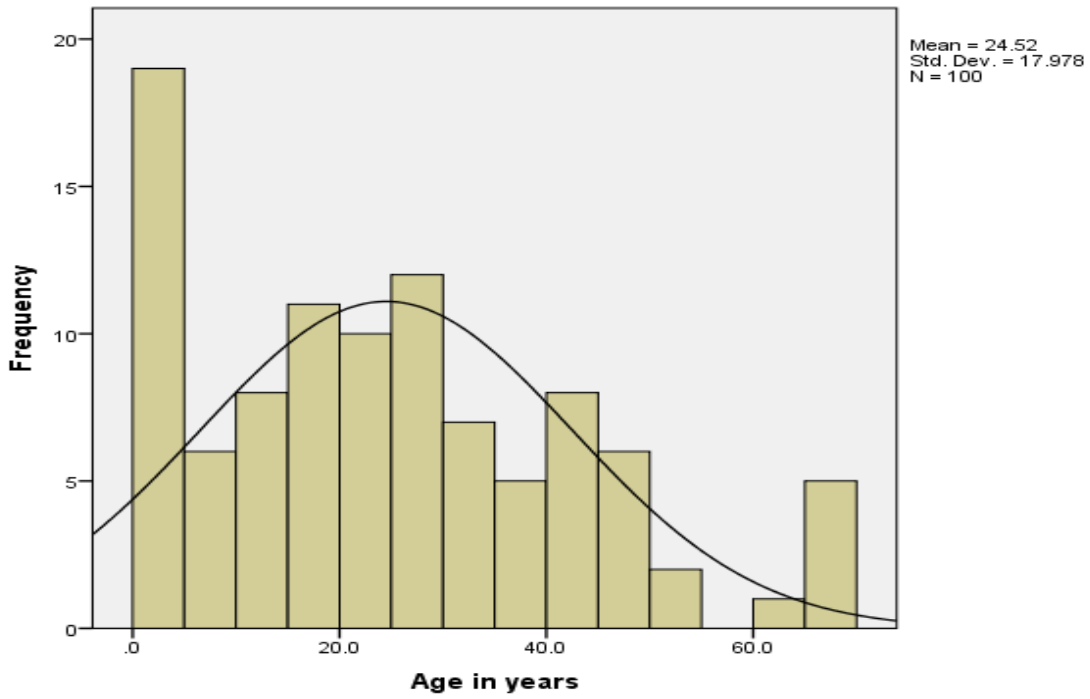

Figure1: Age distribution of respondents

Characteristic	Category	Frequency	Percent	P-value
Gender	Male	57	57.0	0.194
	Female	43	43.0	
Level of education of adult patients	Tertiary education	23	34.3	<0.001
	Primary school	15	22.4	
	Junior secondary school	15	22.4	
	High school	12	17.9	
	Illiterate	2	3.0	
Occupation of patient	Unemployed	34	34.0	<0.001
	Employed	29	29.0	
	Casual worker	4	4.0	
Occupation of parent	Employed	21	21.0	0.001
	Unemployed	6	6.0	
	Casual worker	6	6.0	
Residence	Urban	19	19.0	<0.001
	Peri urban	81	81.0	
Size of household population	<6	55	55.0	<0.001
	6-10	40	40.0	
	>10	5	5.0	
Type of cooking fuel used	Charcoal	63	63.0	<0.001
	Electricity	35	35.0	
	Firewood	2	2.0	
House hold member smokes	Does not smoke	83	83.0	<0.001
	Smokes	17	17.0	

Table 2: Demographic characteristics of CSOM patients

4.1 Medical History Findings

Of the 100 CSOM patients that participated in the study, 59 had unilateral CSOM while 41 had bilateral CSOM, making a total of 141 ears and specimens that were analyzed.

The commonest mode of onset for CSOM was acute ear pain in 100 (71%) ears (figure2). Upper respiratory tract infections (URTI) were associated with onset of CSOM in 19 (13%) ears, while 17(12%) reported an association of both acute ear pain and URTI. There was no history of associated foreign body or trauma in onset of CSOM. Otalgia was present in only I ear.

Duration of otorrhea was greater than 5yrs (>240 weeks) in 49(49.0%) of the patients and less than 8 weeks in 29(29.0%). It was reported by 38 adult patients (56.7% of the adults) that otorrhea was long standing and started in childhood. Ear discharge (CSOM) was common on the right side accounting for 91(64.5%) ears, and less so on the left accounting for 50(35.5%) ears. Purulent discharge was the commonest type of discharge that accounted for 132(93.6%) ears (figure 3). It was foul smelling and intermittent in 79(56.0%) ears and copious in 70(49.6%) ears.

Blood stained discharge was reported in 8 (5.7%) ears that had discharge as purulent. Other types of discharges were watery in 6 (4.3%) ears and mucoid in 3(2.1%) ears.

Hearing Loss was reported in a 100 (71 %) ears. It was said to be persistent in 97(69%) ears and fluctuant in 3(2%) ears (figure 4).

As regards treatment of CSOM, 75(75%) of the patients reported to have sought modern medical treatment for CSOM while 23(23%) consulted traditional healers (figure 5). 2% of the patients bought on the counter ear drops to treat CSOM. 65(65%) of the patients reported history of use of ear drops while 35(35%) reported no previous use of ear drops to treat CSOM.

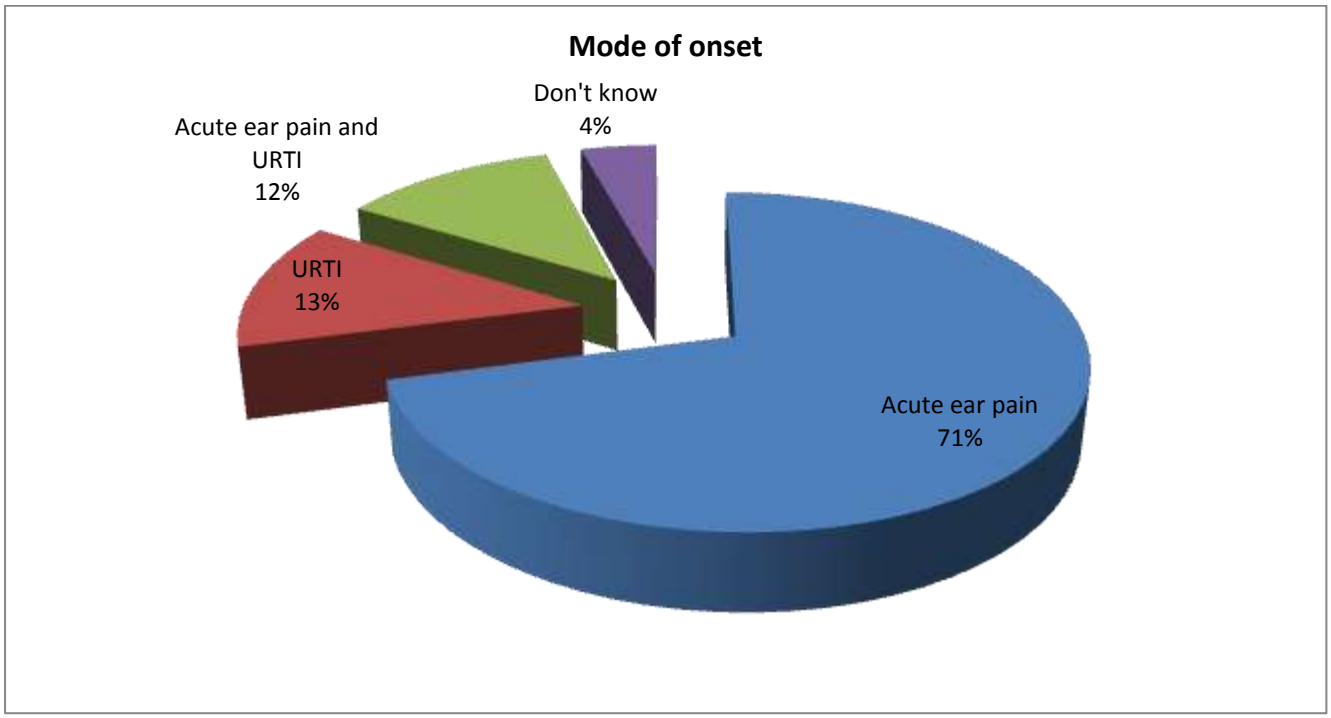

Figure 2: Mode of onset of CSOM

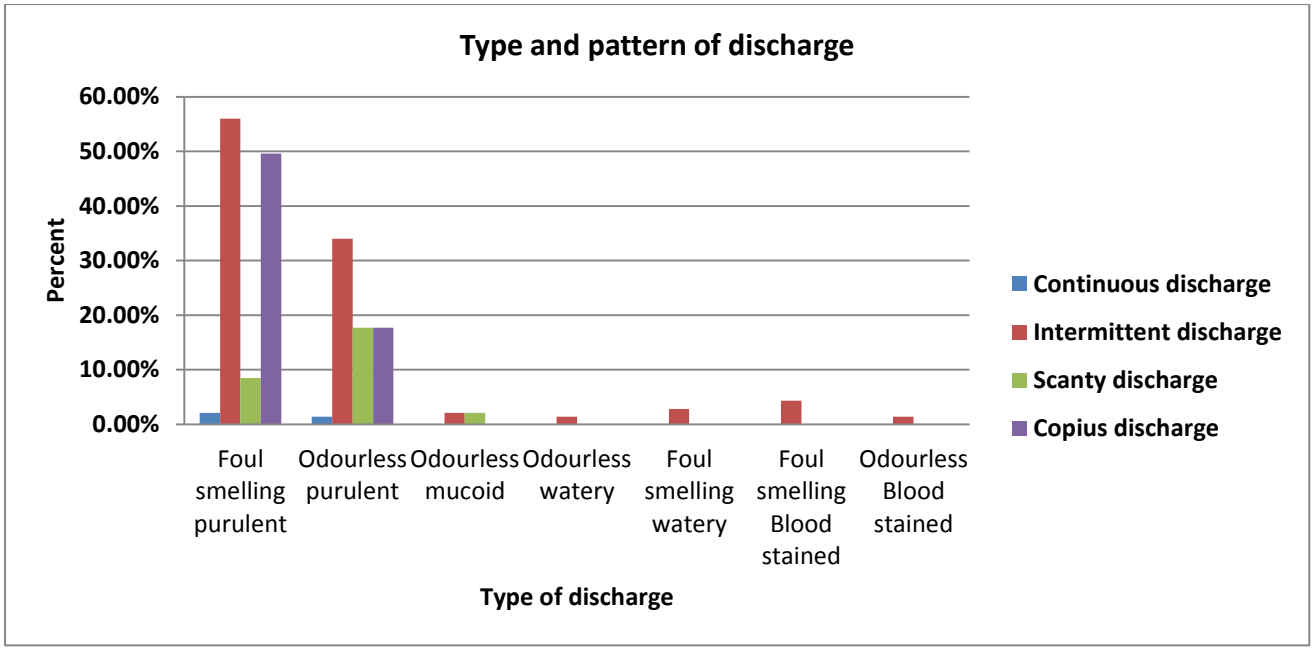

Figure 3: pattern and type of discharge

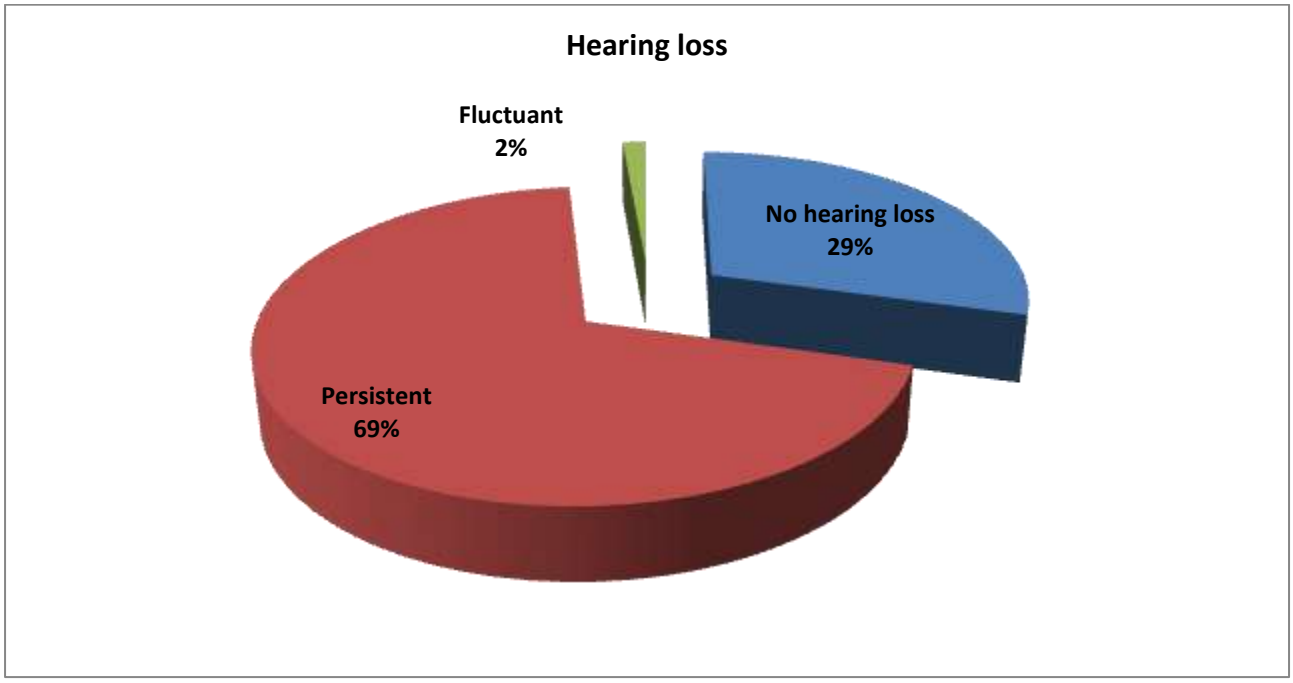

Figure 4: History of associated Hearing Loss

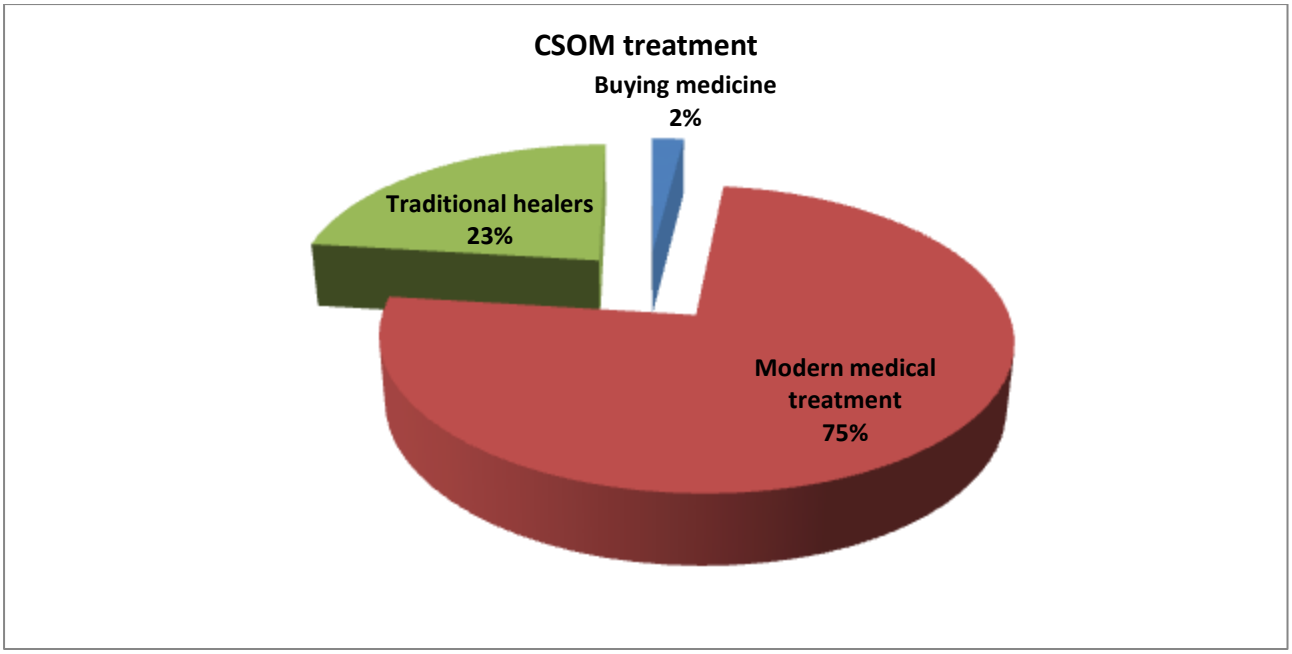

Figure 5: Respondents way of treating CSOM

4.2 Examination findings

On examination, foul smelling purulent discharge was the commonest type of ear canal discharge that was seen, accounting for 82(58.2%) ears (table 2 below).This was copious in 70(49.6%) ears and scanty in 12(8.5%) ears. Odourless purulent discharge was seen in 52(36.9%) ears which was scanty in 27(19.1%) ears and copious in 25(17.7%) ears. Mucoid discharge, in 3(2.1%) ears, and watery discharge, in 4(2.8%) ears, where the least common types of ear canal discharge that was seen.

The tympanic membrane perforation was central in 119(84.4%) ears and was subtotal in 43(30.5%). It was attic in 2(1.4%) ears, marginal in 9(6.4) ear, and total in 11(7.8%) ears (Figure 7).

In the middle ear, mucosal appearance was edematous in 52(37%) ears, Hyperplastic 44(31%) ears, atrophic in 25(18%) ears, injected in 18(13%) ears and polypoid in 2(1%) ears (figure 8). Granulation tissue was present in 20(14.2%) and cholestaetoma in 17(12.1%).

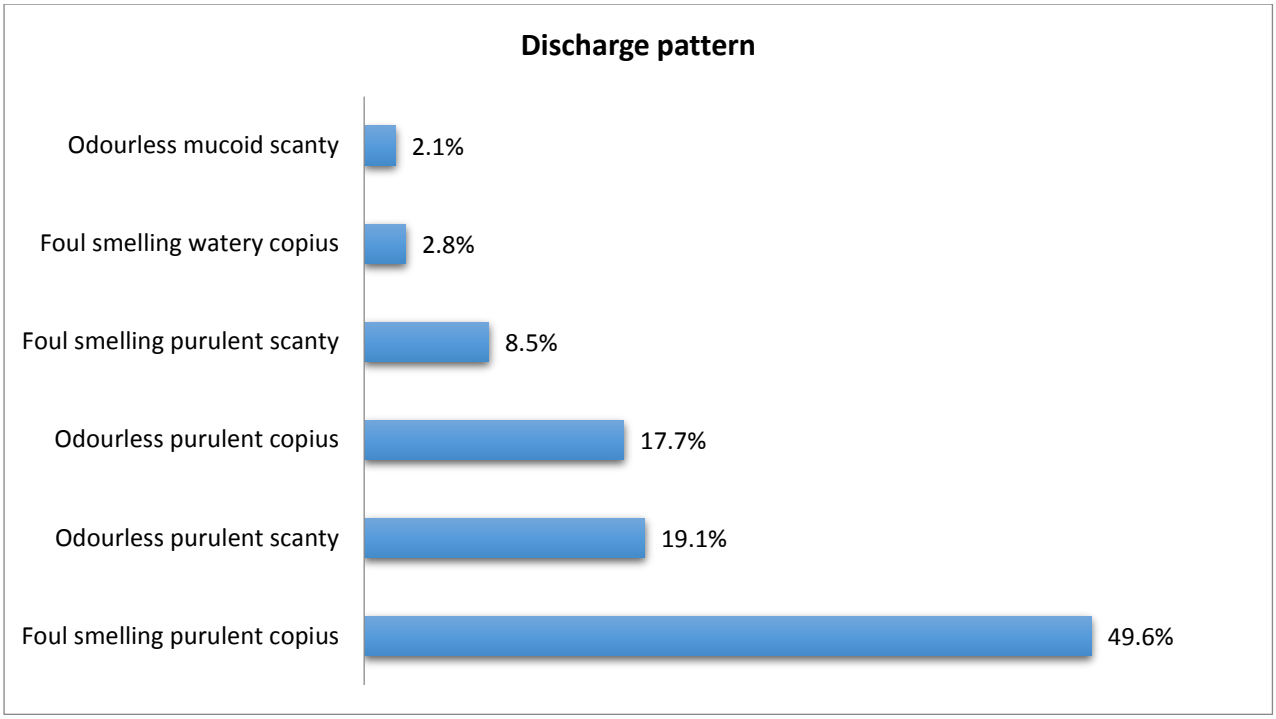

Figure 6: character of ear discharge

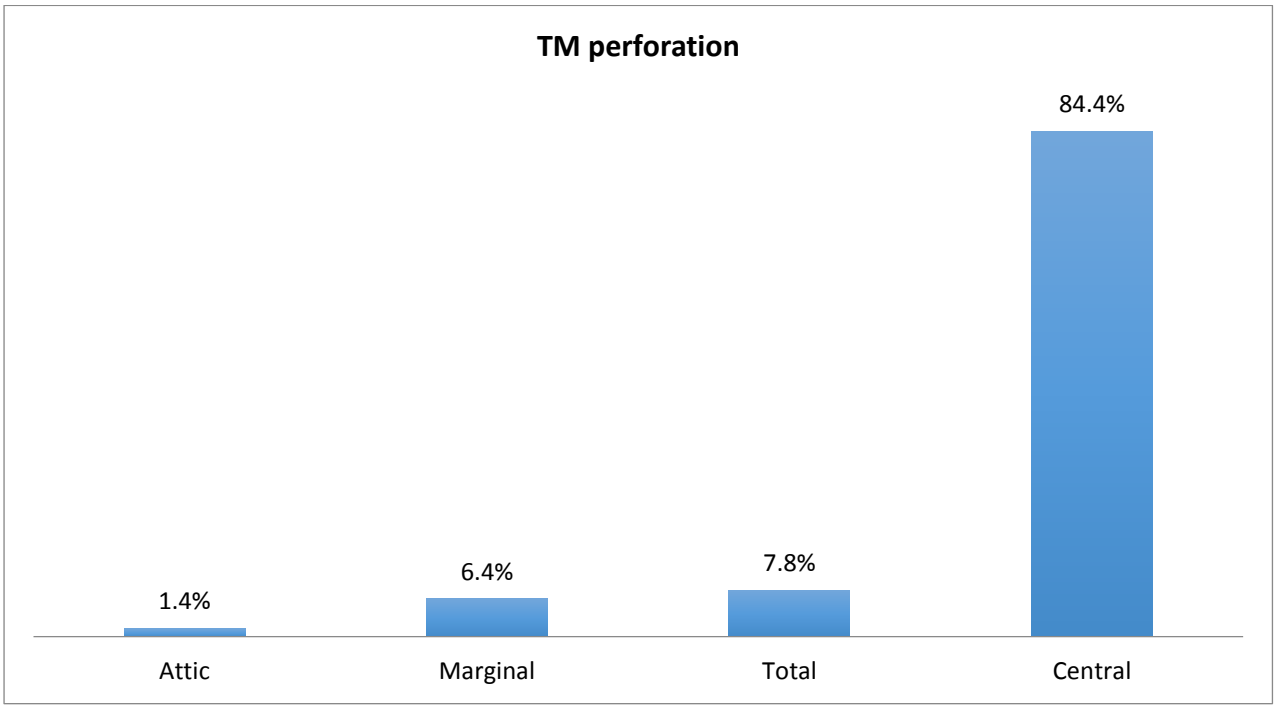

Figure 7: Location of Tympanic membrane perforation

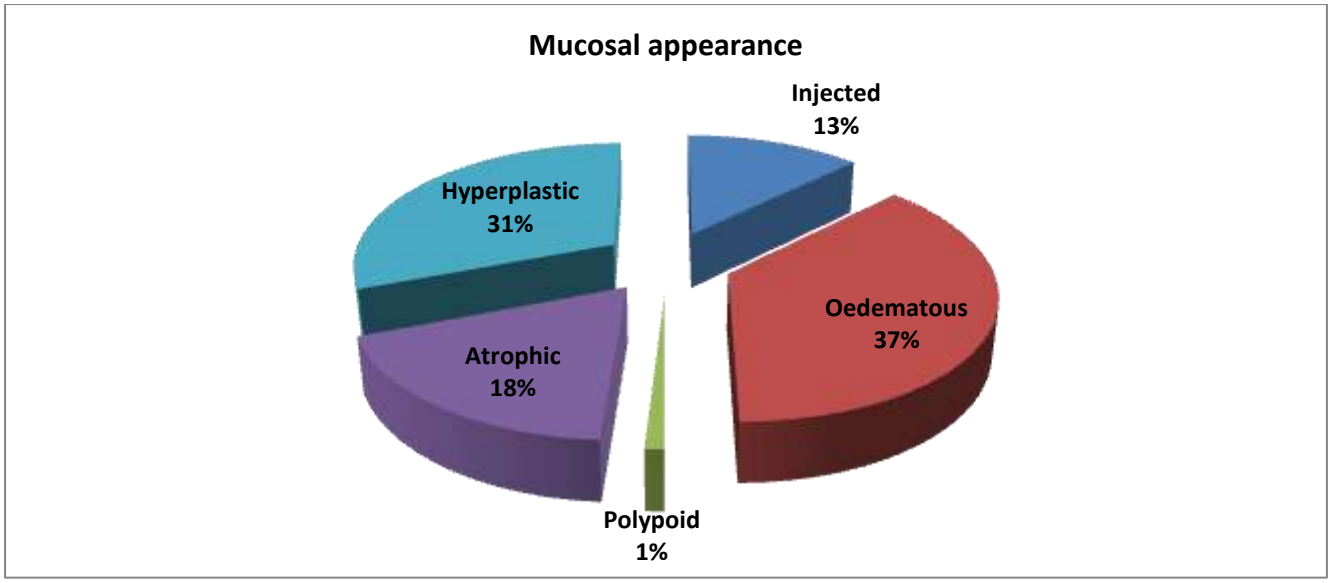

Figure 8: mucosal appearance

4.3 Laboratory findings

Of the 141 specimens analyzed, 103(73.0%) had gram negative rods. 22(15.6%) had gram positive cocci, 9(6.4%) had gram negative cocci, and 8(5.7%) had fungal elements (figure 9).

Pure cultures were 119(84.4%) and mixed cultures were 20(14.2%). 2(1.4%) specimens had no growth. A total of 169 microorganisms were isolated.

The most common organism isolated *was Proteus mirabilis*, a gram negative facultative anaerobe, accounting for 49(29.0%) isolates (table 3).This was followed by *Pseudomonas aeruginosa*, a gram negative aerobe, accounting for 32(18.9%) isolates. Coagulase negative *Staphylococcus* species were the commonest gram positive organisms that were isolated, accounting for 18(10.7%) isolates. No strict anaerobic organisms were isolated. 3(1.8%) isolates were *Aspergillus niger*, a fungus. Of the mixed cultures, *Proteus mirabillis* plus coagulase negative *Staphylococus* species, in 4(20%), were the most frequent mixed isolates (table 4 below). Other mixed isolates included coagulase negative *Staphylococus* species *plus Klebsiella pneumonia* in 2(10%) specimens, and *Proteus mirabillis plus Klebsiela pneumonia* plus *Pseudomonas aureginosa* plus *E. coli* in 1(5%) specimen.

Of the 41 patients that had bilateral CSOM, 26(63.4%) patients had different microbiological isolates on the left ear in comparison to the right ear. Only 7 had similar microbiological isolates between the right and the left ear.

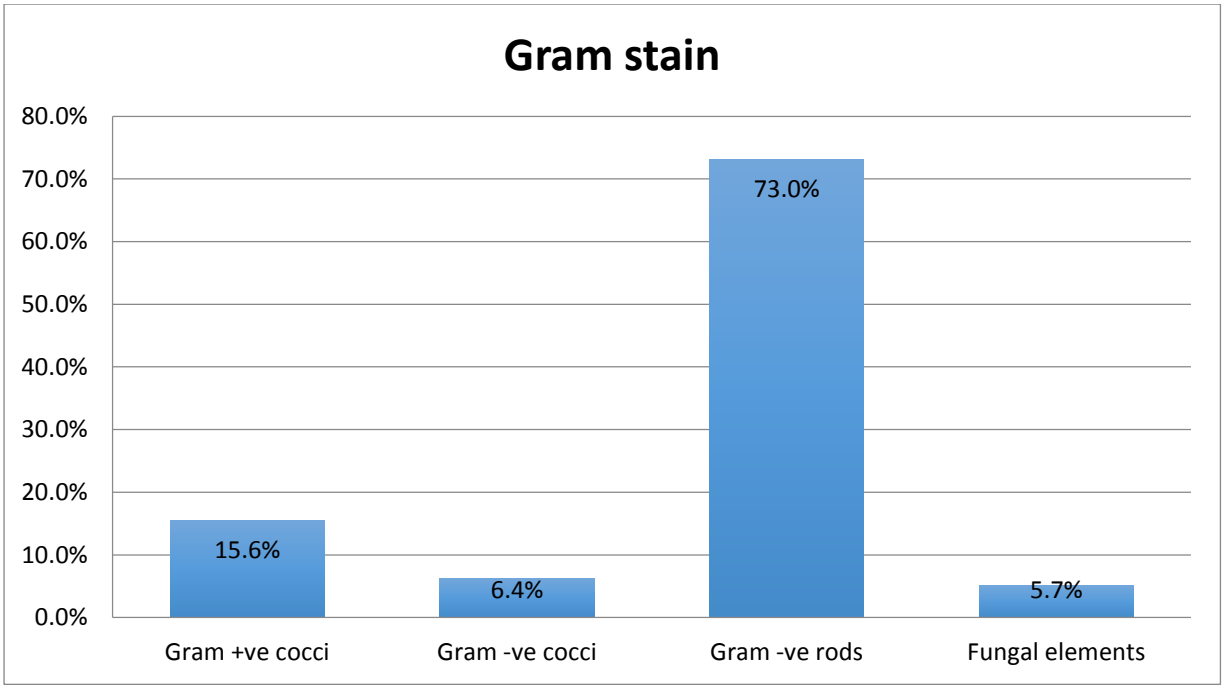

Figure 9: Gram stain.

Microbiological Isolates	**Oxygen requirement**		
Gram -ve Bacteria	**Facultative anaerobes**	**Aerobes**	**Percent**
Proteus mirabillis	49		29.0%
Proteus vulgaris	3		1.8%
Pseudomonas aeruginosa		32	18.9%
Pseudomonas spp not aeruginosa		17	10.1%
Klebsiela pneumoniae	17		10.1%
Kebsiella oxytica	2		1.2%
Corynebacterium		10	5.9%
E.coli	6		3.6%
Anterobacter agglomeraas	2		1.2%
Actinomycetes	1		0.6%
Gram +ve Bacteria			
Staphylococus coaglase -ve spp	18		10.7%
Staphylococcus aureus	6		3.6%
Alpha hemolystic strep	2		1.2%
Enteroccocus feacalis	1		0.6%
Fungi			
Aspergillus niger		3	1.8%
Total	107	62	100%

Table 3: Microbiological isolates

Mixture of isolates	Frequency	Percent
Proteus mirabillis + Staphylococus coaglase negative spp	4	2o
Staphylococus coaglase negative spp + Klebsiella pneumoniae	2	10
Staphylococcus aureus + Corynebacterium spp + Klebsiella pneumoniae	1	5
Staphylococus coagulase negative+ Corynebacterium	1	5
Enteroccocus feacalis + Proteus mirabillis	1	5
Alpha hemolystic strep + Corynebacterium + Proteus mirabillis	1	5
Pseudomonas aeruginosa + Staphylococus coagulase nagative	1	5
Pseudomonas aeruginosa + Pseudomonas not aureginosa	1	5
Kebsiella oxytica + Staphylococus coagulase negative spp	1	5
Aspergillus niger + Staphylococus coagulase negative spp	1	.5
Pseudomonas not aeruginosa+ Corynebacterium + Aspergillus niger	1	5
Proteus mirabillis + Klebsiela pneumoniae + Pseudomonas aureginosa + E. coli	1	5
Pseudomonas not aeruginosa + Proteus mirabillis	1	5
Proteus mirabillis + Klebsiela pneumoniae	2	10
Corynebacterium + Proteus mirabillis	1	5
Total	20	100

Table 4: Mixed isolates

As regards susceptibility tests, of the 46 *Proteus mirabilis* organisms that were tested, 42(91.3%) were sensitive to Gentamycin, 41(89.1%) to meropenem, 40(87.0%) to ceftazidime, 37(80.4%) to ceftriaxone, 30(65.2%) to cefoxitin, 35(76.1%) to cefotaxime, 26(56.5%) to chloramphenicol, and 31(67.4%) to ciprofloxacin (figure10). *Proteus mirabilis* species showed resistance to amoxicillin-clavulanate (77.8%), ampicillin (68.9%), cotrimoxazole (78.9%) and tetracycline (91.2%), (Figure 10).

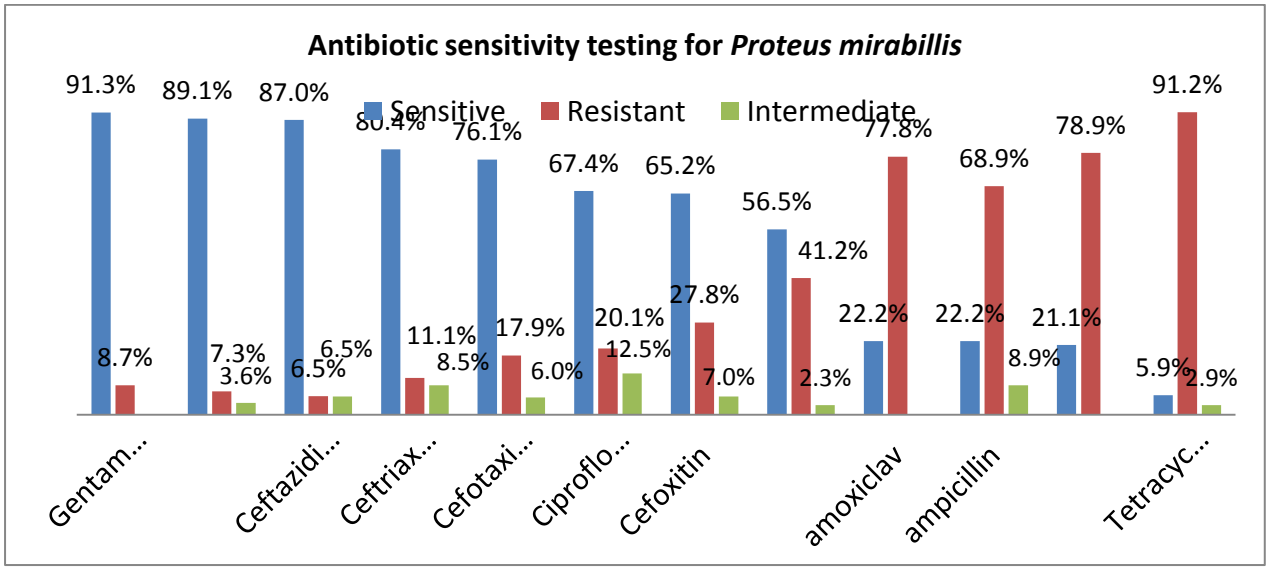

Figure 10. Antibiotic Susceptibility testing for Proteus mirabilis

Antibiotic susceptibility testing for the 25 *Pseudomonas aeruginosa* microorganisms that were isolated showed that it was sensitive to ceftazidime in 25(100%), ciprofloxacin in 22(88.0%), meropenem in 17(68.0%), and Gentamycin in 16(64%), (Figure 11). Out of 15 other *Pseudomonas species* (not aeruginosa), 14(93.3%) were sensitive to ceftazidime, 14(93.3%) to meropenem, 12(80%) to Gentamycin, and 10(66.7%) to ciprofloxacin (Figure 12).

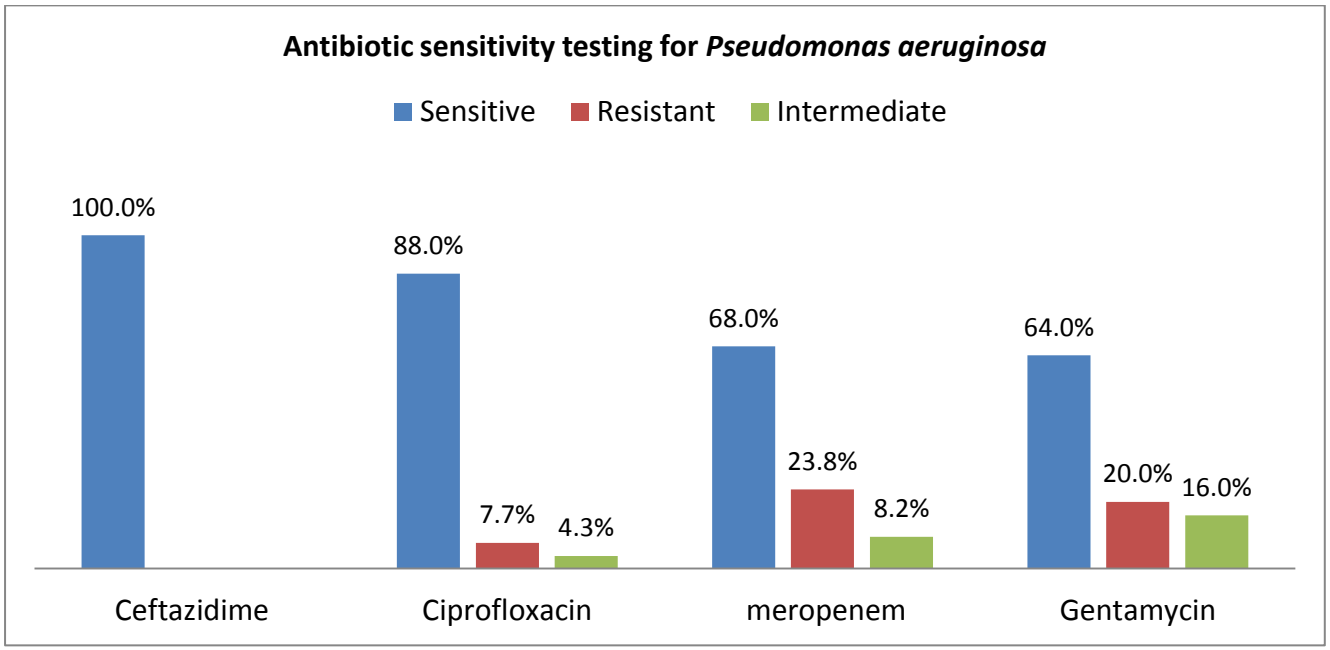

Figure11: *Pseudomonas aeruginosa* antibiotic susceptibility testing

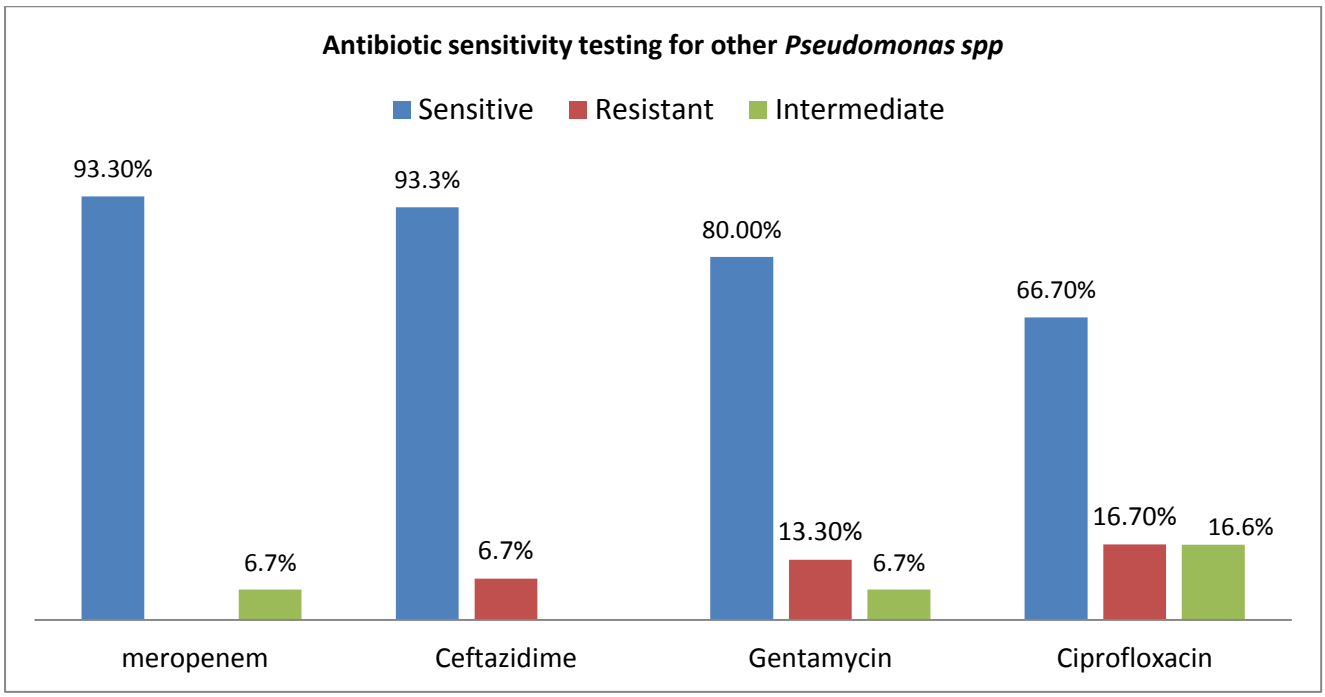

Figure 12: Antibiotic susceptibility testing for other *Pseudomonas* species

Antibiotic susceptibility testing of *14 Klebsiella pneumonia* microorganisms revealed that 14(100%) were sensitive to gentamycin and meropenem, 12(85.7%) to ceftazidime, 12(85.7%) to ciprofloxacin, 10(71.4%) to chloramphenicol and 9(64.3%) to ceftriaxone (Figure 13). It showed that 14(100%) were resistant to amoxicillin-clavulanate, 11 (78.6%) to ampicillin, 8(57.1%) to cefoxitin, 6(42.9%) to tetracycline and 6(42.9%) to cotrimoxazole.

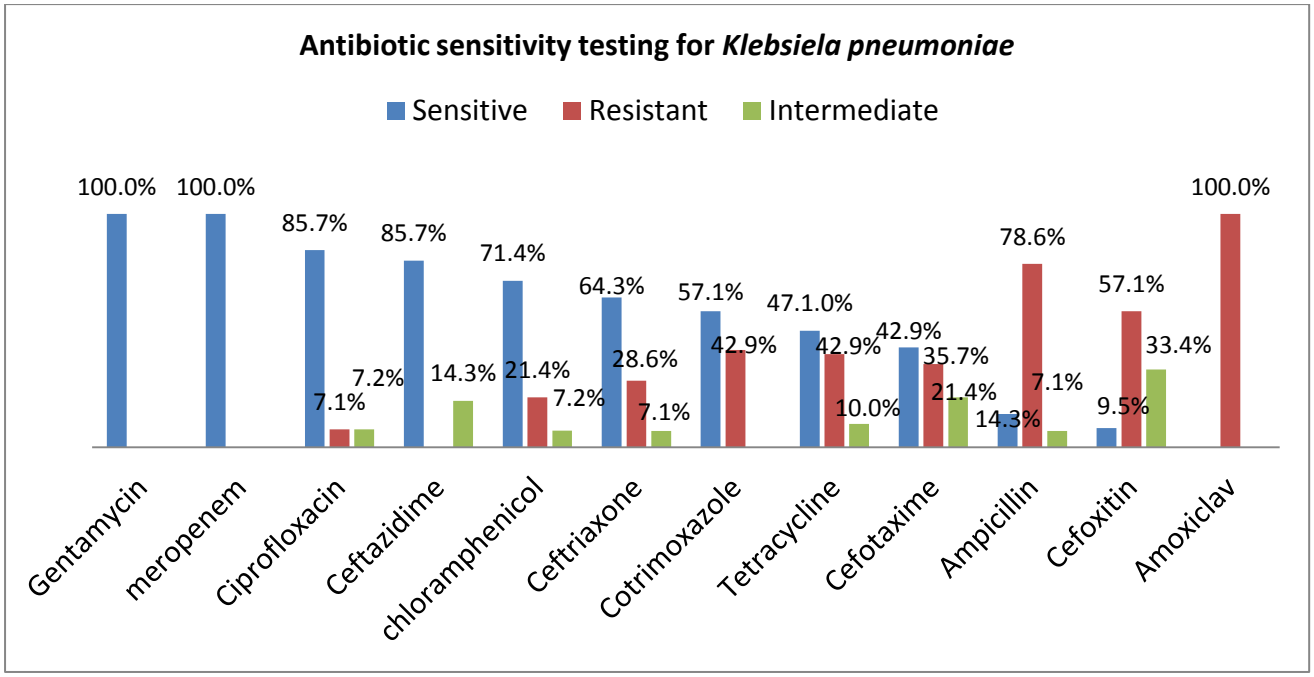

Figure 13: Antibiotic susceptibility testing for *Klebsiella pneumonie.*

Antibiotic susceptibility testing for 15 coagulase negative *staphylococcus* species revealed that 12(80.0%) were sensitive to oxacillin, 11(73.3%) to gentamycin, 12 (80%) to cefoxitin, 14(93.3 %) to chloramphenicol, 12(80.0%) to ciprofloxacin, 8 (53.3%) to erythromycin, and 13(86.7%) to clindamycin (figure 14). coagulase negative *Staphylococcus* species showed 100% resistance rates to penicillin and cotrimoxazole (Figure 14).

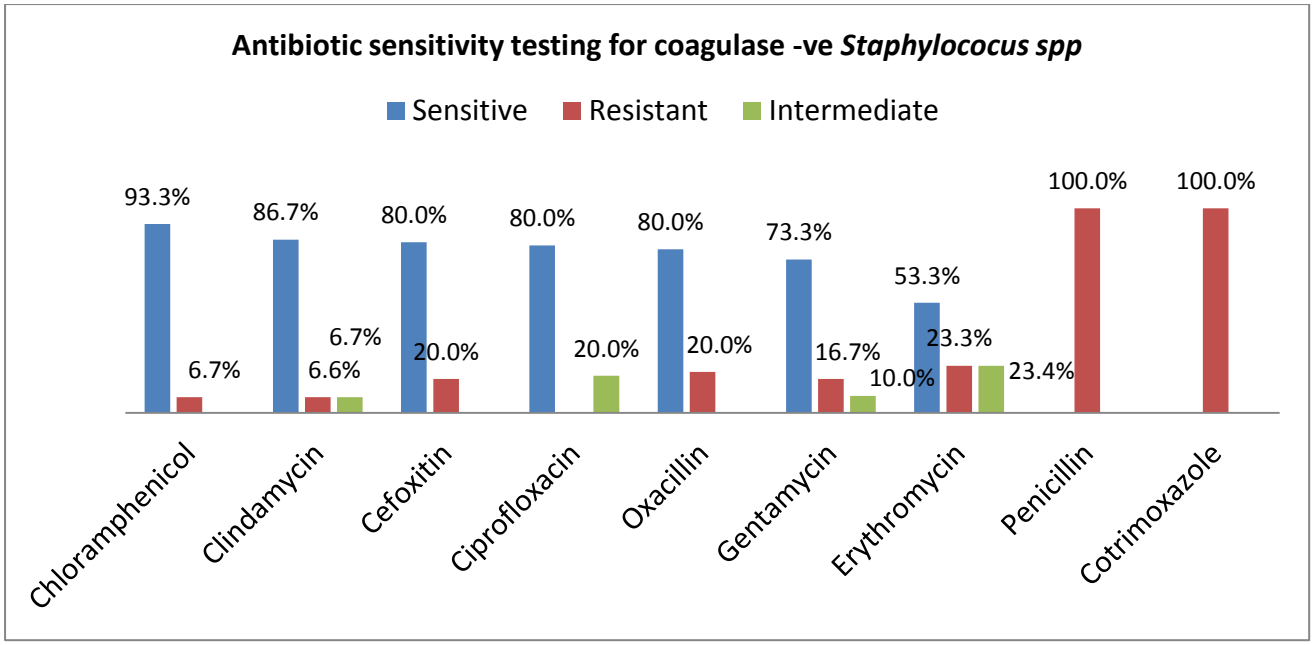

Figure 14: Antibiotic susceptibility testing for coagulase negative staphylococcus species.

4.4 Association between demographic characteristics and pattern of microorganisms

The Likelihood ratio of gender distribution with respect to pattern of etiological CSOM microorganisms was significant (p-value=0.049). This implied that Pseudomonas species was more common among males (29 versus 16 in females), while Staphylococcus coagulase negative species were more common in females (10 versus 5 in males). Proteus mirabilis was common in both males and females (Table 5)

Gender	Statistics	*Proteus mirabillis*	*coagulase negative Staphylococcus spp*	*Pseudomonas spp not aeruginosa*	*Pseudomonas aeruginosa*	*Klebsiela pneumoniae*
Male	n	24	5	**10**	**19**	9
	%	15.4%	3.2%	6.4%	12.2%	5.8%
Female	n	23	**10**	5	11	6
	%	14.7%	6.4%	3.2%	7.1%	3.8%

Table 5: Distribution of CSOM etiological microorganisms among different gender (p-value=0.049

Pseudomonas aeruginosa and coagulase negative *Staphylococcus species* were more common among the unemployed patients (17 and 6 patients respectively) than the employed (5 and 1 patients respectively). This association was statistically significant (p- value= 0.017). *Proteus mirabilis* was common in both the employed and unemployed CSOM patients (Table 6).

Occupation of patient	Statistics	*Proteus mirabillis*	*coagulase negative Staphylococcus spp*	*Pseudomonas aeruginosa*
Unemployed	n	14	**6**	**17**
	%	14.4%	6.2%	17.5%
Employed	n	10	1	5
	%	10.3%	1.0%	5.2%

Table 6: Association between patient's state of employment and CSOM etiological microorganisms (P-value=0.017).

Proteus mirabilis, coagulase negative Staphylococcus species, Pseudomonas aeruginosa and *Klebsiela pneumonia* were more common among children from households that had parents/legal guardians who were employed than those were unemployed (p-value=0.042) (Table 7)

Occupation of parent	Statistics	*Proteus mirabillis*	*coaglase negative Staphylococus spp*	*Pseudomonas aeruginosa*	*Klebsiela pneumoniae*
Unemployed	n	2	2	0	1
	%	3.4%	3.4%	0.0%	1.7%
Casual worker	n	2	0	3	1
	%	3.4%	0.0%	5.1%	1.7%
Employed	n	**16**	**6**	**5**	**5**
	%	27.1%	10.2%	8.5%	8.5%

Table 7: Association between state of employment of parent/legal guardian and etiological CSOM microorganisms (p-value=0.042)

Proteus mirabilis, coagulase negative Staphylococcus species, Pseudomonas spp, Klebsiela pneumonia and Corynebacterium were more common among peri urban dwellers as compared to urban dwellers (p-value=0.009) (Table 8)

Residence	Statistics	*Proteus mirabillis*	*Coagulase negative Staphylococus spp*	*Other Pseudomonas spp*	*Pseudomonas aeruginosa*	*Klebsiela pneumoniae*	*Corynebacterium*
Urban	n	5	5	2	10	4	1
	%	3.2%	3.2%	1.3%	6.4%	2.6%	.6%
Peri urban	n	**42**	**10**	**13**	**20**	**11**	7
	%	26.9%	6.4%	8.3%	12.8%	7.1%	4.5%

Table 8: Association between residence of patient and CSOM etiological microorganism (p-value-0.009)

The pattern of microbiological isolates did not have any significant relationship (p-value>0.05) with the discharge pattern. *Proteus mirabilis*, coagulase negative *Staphylococus spp, Pseudomonas spp, Klebsiela pneumonia* and *Corynebacterium* were highly associated with hearing loss (p-value=0.027) (Table 9). Cholesteatoma was associated with marginal and attic tympanic membrane perforations (Pearson coefficient=1).

Hearing loss	*Proteus mirabillis*	*coaglase negative Staphylococus spp*	*Pseudomonas spp not aeruginosa*	*Pseudomonas aeruginosa*	*Klebsiela pneumoniae*	*Corynebacterium*
No hearing loss	14	2	4	9	2	0
Associated hearing loss	32	12	12	17	9	5

Table 9: Association between hearing loss and CSOM etiological microorganisms (p-value=0.027)

CHAPTER FIVE

5.0 DISCUSSION

In this study of a 100 CSOM patients, the majority of the patients were adults that accounted for 67%. It was, however, reported by 38 adult patients (56.7% of the adults) that otorrhea was long standing and started in childhood. Adding these 38(38%) adult patients to the 33(33%) children that were in this study, it can be inferred that CSOM is common in childhood. This is so owing to the short, wider and relatively horizontal Eustachian tube in this population [11]. (19) 19 % of the patients were in the age group 0-5years (figure1). This finding is similar to that by Orji FT and Dike (2015) where children below the age of 5 accounted for 23.8% of the patients [44]. In a study by Wariso et al. (2006), children below 5years accounted for a relatively higher percentage, 31.5%, than that in our study [50]. The highest distribution of CSOM in our study was between the age of 15 and 35 (figure) with the least distribution after the age of 45years. In our study, the decline in the distribution of CSOM after the age of 45 can be due to an increased frequency in seeking health care from traditional healers among patients aged 50 and above as was found (80%) in a study by Stekelenburg J (2004) [53].

It was found that CSOM was slightly more common among male patients (57%) than among female patients (43%). This finding is similar to that by Chirwa (2014) [34] where 64(61.5%) were males and 40(38.5%) were females. Other studies, however, found that CSOM was common among females than among males [47]. In the study by Wariso et al (2006), the male to female ratio was 1.3: 1 [50].

The commonest mode of onset of CSOM was acute ear pain in 100 (71%) ears which supports the notion that CSOM commonly starts as acute otitis media [1]. However, recall bias on the part of the respondents could have affected the accuracy of the findings (In terms of frequency) on the mode of onset of CSOM.

Unilateral CSOM (59%) was more common than bilateral CSOM (41%). This finding is similar to other similar studies as by Orji and Dike (2015) [44] who found that unilateral cases (64.6% [133/206]) were more than bilateral cases (73/206 [35.4%]).

The majority of the patients with CSOM in this study resided in peri urban areas (81%) which is associated with a low socio-economic status. This conforms to the notion that CSOM is a disease of those with a low socioeconomic status [1, 7].
Although history findings on otorrhea correlated with physical findings, it was difficult to have the respondents give a uniform definition of copius and scanty otorhhea.

Central perforation (84.4% of the ears) was the most common type of tympanic membrane perforation. This implies that most of the patients had the safe type of CSOM, tubotympanic type [22], and may explain why there was no report of complications from the patients. A very small percentage of the ears had an attic perforation (1.4%) and a marginal perforation (6.4%). This may explain the small number of cholesteatoma (12%) that was found. In this study cholesteatoma was significantly associated with attic and marginal tympanic membrane perforation (pearson coefficient=1)

The dominant microbiological isolate in this study was *Proteus mirabilis* (29%), a gram negative facultative anaerobe (Table 2). This was followed by *Pseudomonas aeruginosa* (18.9%) a gram negative aerobe. Other isolates included coagulase negative *Staphylococcus* species (10.7%) and *Klebsiella pneumoniea* (10.1%). The finding of *Proteus mirabilis* as the most common isolate is similar to findings in other studies as by Chirwa (2014) in Malawi where *Proteus mirabilis accounted for* 28.6%, Aduba et al (2010) in Garissa (Kenya) where *Proteus mirabilis* accounted for 32.7%, and Muluye et al (2013) in Ethiopia were *Proteus mirabilis* accounted for 27.5% [16, 33, 34].

These findings are different from those of other studies where they found *that pseudomonas aeruginosa* was the most common isolate [1,3,30)].The difference in the pattern of microbiological isolates may be explained by differences in the geographical conditions and population dynamics [6,19*]*. *Proteus* species are widely distributed in places with poor sanitary conditions, being found in faeces decomposing meat and sewage [54]. This could account for its high frequency in our study where the majority of the patients (81%) stayed in peri-urban areas which are associated with poor sanitary conditions.

Proteus mirabilis, Staphylococcus coagulase negative species, *Pseudomonas aeruginosa* and *Klebsiela pneumonia* were more common among children from households that had parents/legal guardians who were employed (Table 7). This may indicate relatively poor care

of children when guardians/parents are away and therefore more exposure to infections that cause CSOM.

In this study, age distribution in association with pattern of microbiological isolates was not significant. It was however found in other studies that *Proteus* spp. were the commonest isolates in pediatrics compared to adults [48]. There were no strict anaerobes that were isolated in this study. This finding differs from that in other studies were strict anaerobes were isolated [16, 34]. Some of the anerobes isolated in other studies include *Bacteroides* species, and *Peptostreptococcus* species.

Aspergillus niger, in only 3(1.8%) specimens, was the only fungal microorganism that was isolated in this study. The finding of *Aspergillus niger* as an etiological agent for CSOM is supported by other studies as by Mwaniki (2009), Chirwa (2014) and Ibekwe (1983) [31, 32, 34]. In other studies, C*andida* species were also isolated as by Chirwa (2014) and Mwaniki (2009) [31, 34].

Antibiotic susceptibility test was carried out for all the significant isolates which were *Proteus mirabilis*, *pseudomonas species*, *klebsiella pneumonie*, and coagulase *Staphylococcus species* (figure 10, 11, 12, 13, 14). *Proteus mirabilis* showed high sensitivity rates with gentamycin (91.3%), meropenem (89.1%), ceftazidime (87.0%), ceftriaxone (80.4%), cefotaxime (76.1%, cefoxitin (65.2%) and ciprofloxacin (67.4%). The sensitivity rates of *Proteus mirabilis*, a gram negative bacilli, for ciprofloxacin (a commonly used topical antibiotic) were relatively lower(67.4%) than those found in other studies as by Bayeh *et al (*2011) where rates were as high as 93% [49]. Decreased sensitivity of Ciprofloxacin was noted among gram negative bacilli by Jeyakumari, D. et al (2015) [51]. Because Ciprofloxacin is the most commonly used otic antibiotic for CSOM, its lower sensitivity rates found in this study need to be further investigated.

Other gram negative bacilli, *Pseudomonas species* and *klebsiella pneumonie,* also showed high sensitivity rates for gentamycin (64-80%, and 100% respectively), meropenem (66-93%, and 100% respectively), ceftazidime (>90% and 80% respectively) and ciprofloxacin (66-88%, and 84% respectively).

As all the gram negative bacilli, including *proteus mirabilis*, that were isolated in this study showed high susceptibility rates (> than 80%) to Ceftazidime and meropenem, these drugs can be formulated as an empirical therapy for all gram negative bacilli in cases of complicated CSOM where an intravenous drug would be required.

High resistance rates were documented for gram negative bacilli to amoxicillin-clavulanate, ampicillin, tetracycline, and cotrimoxazole. *Proteus mirabilis* showed resistance rates of 77.8% to amoxicillin-clavunate, 68.9% to ampicillin, 91.2% to tetracycline and 78.9% to cotrimoxazole. Comparable to our study, high resistance rates were reported for *Proteus spp* to tetracycline (100%) and cotrimoxazole (52%) by Wariso (2006) in Nigeria [50]. Similar findings are recorded by Bayer et al (2011) where they found resistance rates of 89% for tetracycline and 64% for cotrimoxazole [49].

Gram positive cocci, coagulase negative *staphylococcus species*, showed high susceptibly rates to gentamycin (73.3%), oxacillin (80%), cefoxitin (80%), chloramphenicol (93.3%), clindamycin (86.7%) and ciprofloxacin (80%).). These results are comparable with those in the study by Jeyakumari, D. et al (2015) where they found high sensitivity rates for staphylococcus species to clindamycin (93%), Oxacillin (73%), and ciprofloxacin (73%) [51]. Due to the high susceptibility rates, these antibiotics can be designed as an empirical therapy for *Staphylococcus species*. Coagulase negative *staphylococcus species* showed 100% resistance rate to penicillin and cotrimoxazole. Jeyakumari D et al (2015) also documented staphylococcus species high resistance rates to penicillin (93%) [51].

5.1 Conclusion

CSOM is common in both children (33%) and adults (67%). It is more prevalent in the peri-urban areas (81%) than in the urban areas (19%). *Proteus mirabilis* (29%), a facultative gram negative bacilli, was the most dominant microbiological isolate followed by *Pseudomonas aureginosa* (18.9%), an aerobic gram negative bacilli. Other *Pseudomonas* species (not aeruginosa) (10.1%) and *Klebsiella pneumonia (10.1%)* were the other common gram negative microbiological isolates. Coagulase negative *staphylococcus* species (10.7%) were the most common gram positive microbiological isolates. The isolated microorganisms had high susceptibility rates to gentamycin (64-100%), meropenem (68-100%), ceftazidime (85-100%), ceftriaxone (64-80%), and ciprofloxacin (66-88%). High resistance rates were recorded to Amoxicillin-clavulanate (as high as 100%), ampicillin (as high as 100%), tetracycline (as high as 91.2%) and cotrimoxazole (as high as 100%) and penicillin (as high

as 100%).By virtue of having found a pattern of microbiological isolates in this study that is different from other studies, it can be inferred that culture and susceptibility testing for CSOM in a population/ geographical area is of paramount importance for appropriate antimicrobial therapy of CSOM.

5.2 Recommendations

To formulate guidelines for the appropriate treatment of CSOM which are based on the sensitivity patterns of microorganisms that are locally isolated in Zambia.

To discourage the use of tetracycline, ampicillin and cotrimoxazole, drugs that revealed high resistance patterns, from being used to treat CSOM.

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APPENDICES

APPENDIX I: GENERAL PATIENT INFORMATION AND CONSENT FORM.

Title of Study: Microbiological Isolates of Chronic Suppurative Otitis Media at the University Teaching Hospital (UTH) and Beit Cure Hospital (BCH) in Lusaka, Zambia.

Investigator: Dr Harrison Phiri, Master of Medicine in ENT, Head and Neck surgery registrar (UON),

Introduction

Long standing or chronic ear discharge (Chronic Suppurative otitis media) is associated with a perforated ear drum. It is a common cause of hearing loss which may affect the academic performance and social interactions in those affected.

You are being requested to participate or allow your child to participate in a research study that seeks to determine the pattern of organisms that cause chronic or long standing ear discharge (chronic supurrative otitis media).

We ask that you read this form and ask any questions that you may have before agreeing to participate in this study.

Purpose of Study

The purpose of the study is to determine the pattern of organisms that cause chronic or long standing ear discharge (Chronic suppurative Otitis Media) in patients with chronic ear discharge attending outpatient clinic at UTH and BCH. The information that will be gathered shall be used to improve the medical management of chronic or long standing ear discharge as far as selection of appropriate medication is concerned.

Description of the Study Procedures

Once you have given consent to participate in this study, you will be requested to undergo a medical examination of the ear, nose and throat. If pus is found in the ear(s), a sample will be obtained using sterile cotton swab for analysis in the laboratory.

The entire process will last about 30 minutes to an hour.

Benefits of Being in the Study

The results of the study will be used to improve the management of chronic ear discharge (Chronic suppurative otitis media). If chronic suppurative otitis media or any other ear disease is diagnosed in the respondent, the patient will be management accordingly.

Confidentiality

All the Information about the patient will be kept confidential including the results of the laboratory ear pus analysis.

Payments

No payments are involved in the study.

Right to Refuse or Withdraw

The decision to participate in this study is entirely up to you. You may refuse to take part in the study at any time without affecting your relationship with the investigators of this study and will not be penalized.

Right to Ask Questions and Report Concerns

You have the right to ask questions about this research study and to have those questions answered by the research team during or after the research. If you have any further questions about the study, at any time feel free to contact me using the contact details provided below.

Consent

Your signature below indicates that you have voluntarily agreed to participate/ have your child participate in this study, and that you have read and understood the information provided above.

I (Name of Patient/Guardian) **…… of..... ….....**

Do agree to participate/ have my child.....participate in the study**.** The nature of the study has been fully explained to me by Dr ……

Signature of Patient/Guardian: _____ Date: _____

Signature of Investigator(s): _____ Date: _____

Contact details

1. **Dr Harrison Phiri, (Principle Investigator)**

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APPENDIX II: GENERAL PATIENT INFORMATION AND CONSENT FORM (Nyanja Translation)

Zounikira: Zolengedwa ziri ndi moyo zamene zipatsa Matenda amafina mukhtu amene akhala opitilira patsogolo pa munthu pa chipatala cha UTH na beit cure Hospital ku Lusaka,Zambia.

Ofufudza: Adotolo Harrison Phiri, Akaswili ogwira nchito ya Za matenda ya Mukhutu, Mpuno, ndi Pakhosi (University of Nairobi).

NDONGOSOLO

Mu pempedwa kutengako mbali,mwina kulola mwana wanu kutengako mbali mu kufufuza ndikuziwa zirombo zomwe dzimapatsa antu matenda amukhutu. Aya Matenda ndi matenda amukhutu momwe muchoka mafina, ndikutuli zi mapatsa muntu wodwalayo kutsamvetsa ndipo muntuwo tere samatha kuchitabwino mumaphuziro ace mwina mukukhala ndianzace. Chonde, tapempha kuti muwerenge ndiku mvetsetsa pepala iyi,ndipo muloledwa kufunsa mukalibe kubvomereza.

CHOLINGA

Cholinga champunziro ili, ndikufuna kudziwa tirombo imene ipatsa matenda mu anthu, amene amapedza thandidzo kuchipatala cha UTH mwina ku BCH. Nkhani yomwe izaikidwa pamodzi, izathandizila kupitisa patsogolo zau moyo.

TANTHAUZO YA PHUNZIRO NDIDZOFUNIKIRA

Ngati mwabvomereza kutengako mbali,mufunika kupimiwa mkhutu,mphunondi pa nkhosi. Ngati mwapedzeka mafina mu khutu, kudzakhala kutenga mafina pang'ono ndithonje yololedwa kuti aka pime kuja kopimila komwe amaona matenda. Zonsezi dzitheka pa minetis makhumi atatu kapena olo houri alimodzi.

DZOBVUTA KAPENA ZOLIMBA ZINGAPEZE MUPHUZIRO IYI

Kulibe zolimba zomwe zingapedzeke pa kufufuza uku. Mudza mvera kusamasuka kwenikweni pomwe atenga mafina okapima,koma osadankha wachifukwa ziri chabe.

CHABWINO CHOPEZEKA MU PHUNZIRE IYI

Za mukatimwa kufufuza uku ku dzathandizira a chipatala momwe angasungire opedzeka ndimatenda a khutu.

CHISINSI

Zonse zopedzeka pa odwala, zimakhala zacisinsi, ngakhale zomwe dziza pezeka kuja kopimila.

ZOLIPIRA

Kulibe kulipira.

MULI NAIO DANGA YOKANA MWINA KUCHOKA

Inu mulindi danga ngati mukufuna kutengako mbali muphunziro iyi kapena ai.Simukakamidzidwa kutengako mbali,ndipo mungathe kusiya nthawi iri yonse kopanda vuto iri yonse.

DANGA KUFUNSA MAFUNSO NDI KUNENA ZOMWE MWADZIGANIDZIRA
Muloledwa kufunsa mafunso pa phunziro ili, ndipo otsogolera ayenera kuyankha mukati mwaphunziro kapena atathaphunziro. Ngati mungafune kufunsa dziri zonse pa punziro nthawi iliyonse, muloledwa kutero kupyolera mu pepala yi.

KUBVOMEREDZA

Mukasaina pansi pa, ndikokuti mwabvomereza kutengako mbali/mwina mwana wanuku tengako mbali muphunziro iyi, ndipo kuti mwa werenga ndikumvetsetsa bwino zonse.

Ine(Dzina la odwala/womsunga……waku……Ndabvomera/kapena mwanawanga……..kutengako mbali muphunziro.Ndipo zonse andi matsulira a Dr……..

Asaine; odwalayo/womusunga……Tsiku……..

Asaine; mtsogoleri…….....Tsiku……...

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APPENDIX III: INFORMED ASSENT FORM

ASSENT TO PARTICIPATE IN RESEARCH STUDY

Informed assent Form for Chronic suppurative otitis media patients below the age of 18 at Beit Cure Hospital or the University Teaching Hospital.

Principal Investigator: Dr Harrison Phiri

Contact details:

Beit Cure Hospital

ENT department

Cell phone Number: +260979625723

Email address: harridavis@yahoo.co.uk

Title of study: Microbiological Isolates of Chronic Suppurative Otitis Media at the University Teaching Hospital and Beit Cure Hospital in Lusaka, Zambia

Introduction: I am a Medical doctor at the University of Nairobi and I want to find out the pattern of microscopic organisms that cause long standing ear discharge. I am going to try and do that by asking you a few questions about your Ear discharge, do a physical examination and collect a sample of pus discharge from the ear which will be taken to the laboratory for examination. The process will take about 30minutes. Before I can do that I will first ask your parent/legal guardian for permission to allow me to go ahead and ask questions and examine you.

How will my privacy be protected?

Your name will not be written on the questionnaires. I will ensure your identity is concealed and keep the information obtained confidential.

Do I have to do this?

The choice to participate is yours. Your choice to participate or not will not be over-ridden by your parent's/guardian's permission to allow you to participate. Nothing bad will happen to you if you decide not to participate. If you decided you want to do the assessment, please know that you can stop at any time you want.

Will I get anything from the project?

You will not get anything for taking part in the exercise. However, by participating assessment, you can help me to learn the pattern of microorganisms that cause ear long standing ear discharge so that it can be treated adequately.

What should I do if I have questions?

If you have any questions about this study, either you or someone at home can contact me. My contact derails are as written above on the front page of this form.

SIGNATURE:

I understand what this research is about and what I am asked to do if I decide I want to take part in it. I know that I can ask any questions that I have at any time. I also understand that I can stop participating at any time that I want. I am writing my name below after I have been read information about the study and have agreed to be a participant.

Participant's Signature……
Date…….

Name of Participant……..

Researcher's Signature……
Date…….

Name of Researcher……..

APPENDIX IV: PATIENT PROFORMA.

Proforma Number: _____

AGE: _____, SEX:_____

SECTION A: DEMOGRAPHIC PROFILE

I) Physical address……...

II) Age of Patient.....

III) Level of education of patient

Illiterate ☐

Primary school ☐

Junior secondary school ☐

High school ☐

Tertiary Education ☐

IV) Occupation of Patient----------

V) Level of Education of Guardian/parent----------

VI) Occupation of Legal guardian/parent----------

VII) **Sizes of House hold population_____**

VIII) **Guardian/ Household member smokes at Home** Yes ☐ No ☐

IX) Type of cooking fuel used

Gas ☐

Kerosene ☐

Firewood ☐

SECTION B: MEDICAL HISTORY

A) Otorrhea (tick response**)**

	Right	**Left**
Yes	☐	☐
No	☐	☐

I) **Duration of Ear discharge**: ……..

II) Type of discharge

	Right	**Left**
Watery:	☐	☐
Purulent:	☐	☐
Blood stained:	☐	☐
Mucoid:	☐	☐

III) Pattern of discharge

	Right	**Left**
Continuous:	☐	☐
Intermittent:	☐	☐
Scanty:	☐	☐
Copius:	☐	☐

IV) Odour

Not foul smelling	☐	☐
Foul smelling	☐	☐

V) Onset preceded by:

Acute ear pain	☐	☐
Foreign body	☐	☐
Trauma URTI	☐	☐
URTI	☐	☐

B) Current Otalgia (Tick response) **Right** **Left**

Yes	☐	☐
No	☐	☐

C) Hearing Loss (tick response) **Right** **Left**

YES	☐	☐
NO	☐	☐

If Yes,

Persistent	☐	☐
Fluctuant	☐	☐

D) How is the patients CSOM treated?

Sought modern medical treatment	☐
Buying medicine	☐
Consulting traditional healers	☐

E) History of previous use of antibiotic ear drops: ……..

I) Name of Ear drops used (If pt can remember)

SECTION C: Examination

	Right	Left
A) Discharge		
Yes	☐	☐
No	☐	☐
I) Quantity of pus		
Scanty	☐	☐
Copious	☐	☐
ii) Character of pus	**Right**	**Left**
Foul smelling	☐	☐
Odourless	☐	☐
Mucoid	☐	☐
Purulent	☐	☐
Bloody	☐	☐

B) TM perforation **Right** **Left**

Marginal	☐	☐
Attic	☐	☐
Central	☐	☐
Total	☐	☐
Subtotal	☐	☐
Percentage	☐	☐

C) Mucosal Appearance

Injected	☐	☐
oedematous	☐	☐
Polypoid	☐	☐
Atrophic	☐	☐
Hyperplastic	☐	☐
Sclerotic	☐	☐

D) Granulation tissue

Present	☐	☐
Absent	☐	☐

E) Cholesteatoma

	Right	Left
Present	☐	☐
Absent	☐	☐

F) Other findings_____

G) Complications

Present	☐	☐
Absent	☐	☐

If Present, Which ones?

1.
2.
3.

SECTION D: Laboratory Findings

i) Gram stain

Gram positive

Gram negative

ii) Morphology

Cocci

Rods

iii) Culture results

Pure

Mixed

Number of isolates if mixed

iv) Species isolated

1.

2.

3.

Aerobes

Anaerobes

Fungi