

Remedial Effects of Homeopathic Drugs against Chronic Suppuration of Ear Caused by Pathogenic Microorganisms

A DISSERTATION SUBMITTED TO THE DEPARTMENT OF GENETIC ENGINEERING AND
BIOTECHNOLOGY, UNIVERSITY OF DHAKA FOR THE PARTIAL FULFILLMENT OF THE
REQUIREMENT FOR THE DEGREE OF MASTER OF PHILOSOPHY (M.PHIL) IN
GENETIC ENGINEERING AND BIOTECHNOLOGY



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Certificate

This is to certify that the thesis entitled “Remedial Effects of Homeopathic Drugs against Chronic Suppuration of Ear caused by Pathogenic Microorganisms” submitted by Nazmul Hasan (Roll No. 01, Registration No. 063-2015-16), incorporates original research work carried out by him under my supervision. I am hereby forwarding his thesis report being submitted for the award of the degree of Master of Philosophy (MPhil.) in Genetic Engineering and Biotechnology, University of Dhaka. This work or any of its part has not been submitted elsewhere previously for awarding any degree.

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Dedicated...

To My beloved Parents & Family

To My Respected Supervisor

&

To the Fellow Homeopath of Bangladesh

Who Inspire Me Always

Acknowledgements

At first, I express my gratefulness to Almighty ALLAH who facilitated me to perform this research work and submit this thesis paper.

I am thankful to my supervisor, **Dr. Md. Anwarul Azim Akhand**, Professor, Dept. of Genetic Engineering and Biotechnology, University of Dhaka, for giving me an opportunity to work with him. I would like to express my heartfelt gratification for his scholastic guidance, constructive criticism, constant encouragement and inspiring suggestions for completing this work successfully. Undoubtedly, his supervision turned me more successful in daily life.

I express my earnest thanks to my esteemed co-supervisor **Dr. Latiful Bari**, Principal Scientist and Head, Food Analysis and Research Laboratory, Centre for Advanced Research in Sciences, University of Dhaka for his valuable guidance, steadfast support and boosting up confidence during the work in his laboratory to conduct smooth research within the fixed time.

I would like to give my heartiest thanks to **Dr. Mohammed Nazmul Ahsan**, Professor and Chairman, Dept. of Genetic Engineering & Biotechnology, University of Dhaka, for his continuous support, teachings and assistance to reach my goal.

I am thankful to **Dr. Sharmin Zaman Emon**, Research Fellow and **Sunzid Ahmed**, former Research Associate, Food Analysis and Research Laboratory, Centre for Advanced Research in Sciences, University of Dhaka. I am in debt to for his persistent support and advices, above all for his borderless mind for giving me free hands on working experience throughout the course of investigation.

I would like to thank the entire respected '**Teachers**' of the Dept. of Genetic Engineering & Biotechnology, University of Dhaka for their constant encouragement.

I am grateful to the fellow students of Dept. of Genetic Engineering & Biotechnology, University of Dhaka for receiving me warm heartedly; especial thanks to **GEB-12th** batch for their endless care and guidance.

Finally, I must express my very profound gratitude to my parents and to my wife for providing me with unfailing support and continuous encouragement throughout my

years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them.

Abstract

Chronic Suppurative Otitis Media (CSOM) is known as one of the most common infectious disease and is characterized by a persistent discharge from the middle ear through a perforated tympanic membrane. CSOM is considered as one of the most common cause of hearing impairment in the developing countries. Use and misuse of antibiotics for treating CSOM promotes antibiotic resistance leading to accelerated public health risks. Homeopathic medicines are mostly free from side effects, and therefore, this study was performed to evaluate the effects of homeopathic medicines for remedies of CSOM symptoms. A total of 70 subjects were included in this study; among them, 40 were suffering from CSOM and 30 were healthy control. The CSOM patients were randomly assigned for daily administration of homeopathic medicines such as tellurium metallicum in 6C potency (n=17), mercurius solubilis in 200C potency (n=13) and calcarea sulphurica in 30C potency (n=10) for 8 weeks. Aural swab of the patients were examined to assess microbiological infection. Identification of the isolated microorganisms such as *Staphylococcus sp.*, *E coli*, *klebsiella sp.* was confirmed with Analytical Profile Index (API). The homeopathic medicines did not show significant antibacterial activity when assessed by agar disc diffusion; however, they reduced average microbial load significantly. Ear suppuration was prevented in all of the patients treated with the medicines. The patients were also examined with otoscope to observe the level of their tympanic membrane perforation and the healing of the perforated membrane after treatment. Among the seventeen (17) patients suffering from CSOM associated with membrane perforation, 9 patients' (52.9%) membranes were healed when treated with tellurium metallicum. Calcarea sulphurica also healed perforated tympanic membranes of 50% patients, however, mercurius solibulis failed to trigger membrane healing in treated patients. It was next examined whether the patients also had hearing impairment compared to healthy control subjects. The average hearing thresholds of the control subjects (n=30) at 1, 4, 8 and 12 kHz frequencies were 13.55 ± 1.57 , 15.58 ± 1.12 , 27.58 ± 2.00 and 32.57 ± 2.45 dB SPL, respectively. When the average hearing thresholds of the CSOM patients (n=40) were measured at all of the above frequencies, the values became 30.25 ± 1.75 , 36.80 ± 3.25 , 50.75 ± 2.35 , and 59.50 ± 2.96 dB SPL, respectively. This result indicated that the CSOM patients were suffering from hearing loss as the average hearing thresholds of the CSOM patients at all the frequencies tested were significantly higher ($p < 0.05$) than that of the control subjects. To our surprise, treatment for 8 weeks with all three homeopathic medicines significantly reduced ($p < 0.05$) hearing thresholds of the patients at all the frequencies. This result clearly indicated that the patients experienced dramatic improvement in hearing by the homeopathic medicines. This study, therefore, provides conclusive evidence that

homeopathic medicines prevent ear suppuration in CSOM patients as well as reduce microbial load, heal perforated membrane and improve hearing.

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Abbreviations

AOM	Acute Otitis Media
ASOM	Acute Suppurative Otitis Media
CSOM	Chronic Suppurative Otitis Media
CFU	Colony Forming Unit
DW	Distilled Water
dB	Decibel
MHA	Mueller Hinton Agar
MEE	Middle Ear Effusion
NaCl	Sodium Chloride
NS	Normal Saline
OME	Otitis Media with Effusion
TSA	Tryptic Soya Agar
TSB	Tryptic Soya Broth
SDA	Sabouraud Dextrose Agar
sAOM	Sub-Acute Otitis Media
WHO	World Health Organization
µg	Microgram
µl	Microliter
µm	Micrometer

Chapter One

Introduction

1 Introduction

1.1 Background

Infection in the ear is known as otitis, classified in externa, media and interna; named according to the site of lesion. Commonly ear infection refers to middle ear infection or otitis media characterized by effusion, pain, redness and rise of temperature in the middle ear region; this clinical condition may associate with discharge from the site, which indicates the perforation of tympanic membrane (Berman, 1995; Pediatrics, 2004; Smith et al., 2010). This inflamed feature may associated with or followed after local infection including tonsillitis and pharyngitis (Berman, 1995; Pediatrics, 2004).

Middle ear effusion (MEE) is the initial state of developing complaints in the middle ear which may derived by local irritation, change of body temperature and air pressure etc. Increased humidity in habitual environment, drought of air during shifting monsoon and allergy triggered by inhaled air also facilitate MEE (Padia et al., 2017, Kong et al., 2017). Dysfunction of the cartilaginous part of eustachian tube could be another pathway to produce MEE; malfunction will hamper the hygiene of the middle ear cavity as eustachian tube maintains the connection between oral cavity and middle ear. Though this etio-pathogenicity is not established yet it is widely accepted as a major contributing factor in MEE (Rezes et al., 2007).

According to clinical severity and duration of lasting otitis media is divided into Acute Otitis Media (AOM) which get healed within three weeks, Sub-acute Otitis Media (sAOM) what lasts more than three weeks but less than three months and Chronic Otitis Media (COM) lasts more than three months. Considering the clinical feature, otitis media could be classified in AOM, Otitis media with effusion (OME), COM and cholesteatomatous otitis media (ChOM). However, in daily medical practice, OM is generally categorized in OME (Includes AOM, MEE) and Suppurative Otitis Media (SOM) includes chiefly COM. OME presenting all features of inflammation including pain, rise of local temperature, tenderness, generalized fever, partial hearing loss with intact tympanic membrane. Acute otitis media (AOM) is one of the most common diseases among children (Rettig and Tunkel, 2014). More than half of all children suffer at least one (1) episode of AOM by the age of three (3) and one-third suffers from recurrent episodes (Le Saux et al., 2005). On an average,

suffering from middle ear effusion (MEE) is about 2.5 months during the first year of life and 2 months in the second (Paradise et al., 2005; Teele et al., 1989). MEE causes hearing loss of almost 30 dB (Bluestone, 2003) and may impact negatively on speech development, education, and behavior (Roberts et al., 2004; Rovers et al., 2004).

On the other hand, SOM has all the features of OME including Otagia, tinnitus and history of MEE for long; furthermore here a distinct intermittent or continuous discharge present from the perforated tympanic membrane which distinguishes with OME (Teale et al., 1989). Sudden onset of otalgia in high degree followed by mucoid or serous discharge perforating the tympanic membrane, may associated with partial hearing loss are cardinal feature of Acute Suppurative Otitis Media (ASOM). In Chronic Suppurative Otitis Media (CSOM) Otagia and features of inflammation presents in less severe degree with continuous or intermittent otorrhoea, partial to moderate hearing loss and tinnitus are common (Qureishi et al., 2014).

CSOM is characterized as low grade Otagia, the rise of local temperature may present or not, intermittent or continuous otorrhoea and noticeable conducting hearing impairment may present; tinnitus is occasional complaints and low grade headache may found along with feature of common cold. According to WHO, CSOM is the inflammation of the middle ear and mastoid cavity, which presents with recurrent ear discharges or otorrhoea through the tympanic membrane perforation (Acuin and Organization, 2004). The perforation may present as a spontaneous damage due to an acute infection of the middle ear or as a sequel of less severe forms of otitis media (Daly et al., 1998, Tos, 1990). The point in time when AOM becomes CSOM is still controversial. Generally, patients with tympanic membrane perforations which continue to discharge mucoid material for periods, from six (6) weeks to three (3) months, despite medical treatment, are recognized as CSOM cases (Kenna, 1994). The WHO definition requires only two (2) to six (6) weeks of otorrhoea (Smith et al., 1996), but otolaryngologists tend to adopt a longer duration, e.g. more than 3 months of active disease (Goycoolea et al., 1991).

Hearing loss is an unavoidable reality in otitis media, though it is somewhat reversible in AOM. However, in CSOM patients, conductive type of hearing loss may improve but sensorineural type of hearing loss has very limited hope in improving hearing impairment. This infection is a common disease in school going children causing

hearing loss and resulting learning disabilities (Reichman and Healey, 1983); people who are prone to eustachian tube infection (Gibson et al., 1996), have a smoking habit (Pezzoli et al., 2017), used to prick ear with matchsticks and low-socioeconomic level are more vulnerable to CSOM and hearing impairment (Chandrashekharayya et al., 2014).

1.2 Ear

It is the special organ concerned with hearing and balance; with three different parts consists of external, middle (Medial) and inner ear (Figure 1.1). Pinna, one of the parts of external ear, the only visible part remains outside and commonly refers as 'EAR'.(Dictionary, 1989; Gray and Standring, 2008).

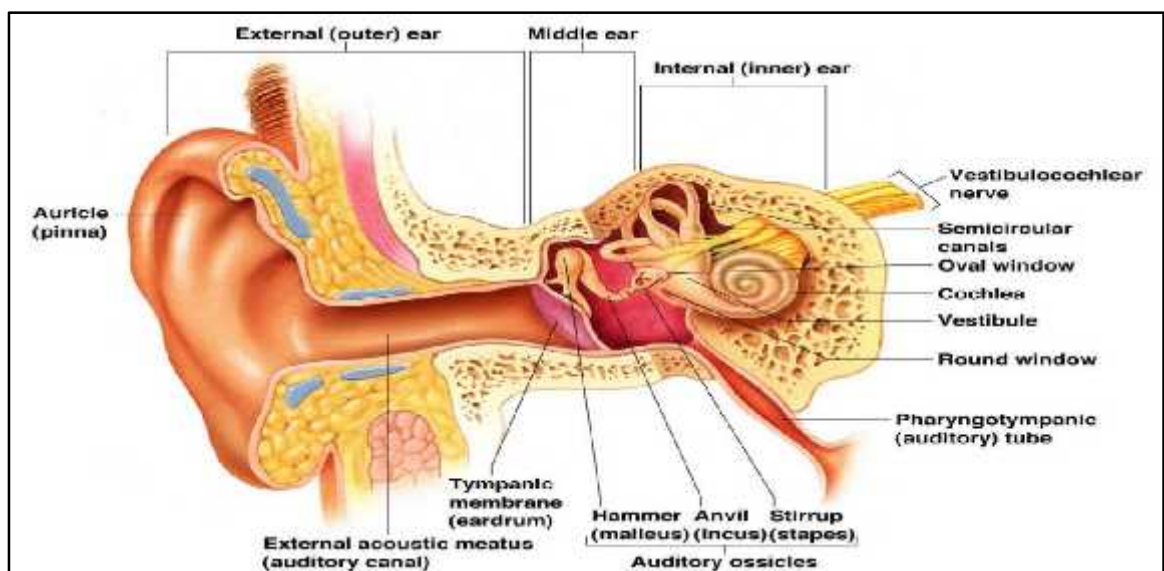


Figure 1.1 Parts of ear. External ear consists of auricle or pinna and auditory canal; middle ear consists of tympanic membrane and three bones, malleus, incus and stapes; internal ear contains cochlea, semicircular canals and eustachian tube or pharyngotympanic tube.

1.3 External ear

Pinna, the external auditory canal (meatus) and the outer (lateral) surface of the tympanic membrane have formed this (Figure 1.2). The cuticle of the outer third of the external auditory meatus contains hair, sebaceous and ceruminous glands. Wax is formed with secreted cerumen, sebum and squamous debris from the outer part of the drum, which migrates to the outside (Gray and Standring, 2008; Drake et al., 2009; Moore et al., 2013).

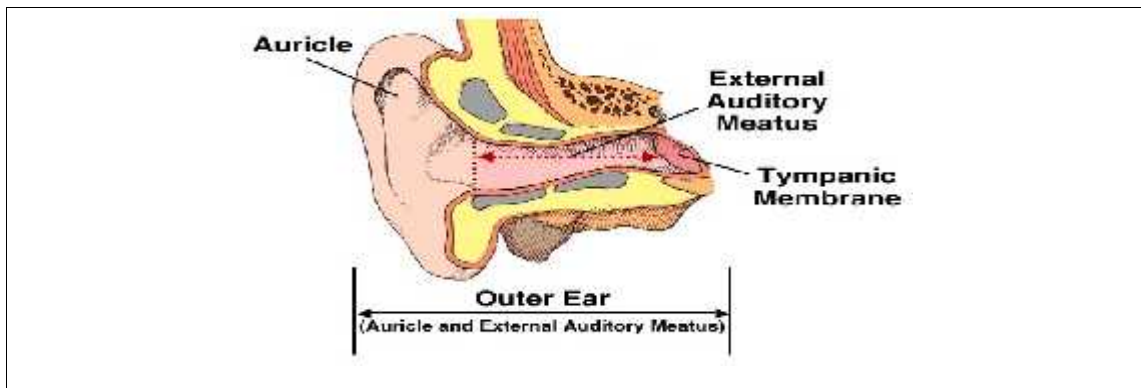


Figure 1.2 External ear. Auricle or pinna (in pink color), the most outer part & external auditory canal, extends from the opening of the ear canal to the tympanic membrane (shown by the horizontal dotted line), ends with Tympanic Membrane

1.4 Middle ear

It is formed by the medial surface of the tympanic membrane (lateral border), the tympanic cavity filled with air and the Eustachian tube which communicates with the pharynx (Figure 1.3). Three bones - the malleus, incus and stapes (the ossicles) occupying the tympanic cavity and transmit sound from the external ear to the inner ear (Gray and Standring, 2008; Drake et al., 2009; Moore et al., 2013).

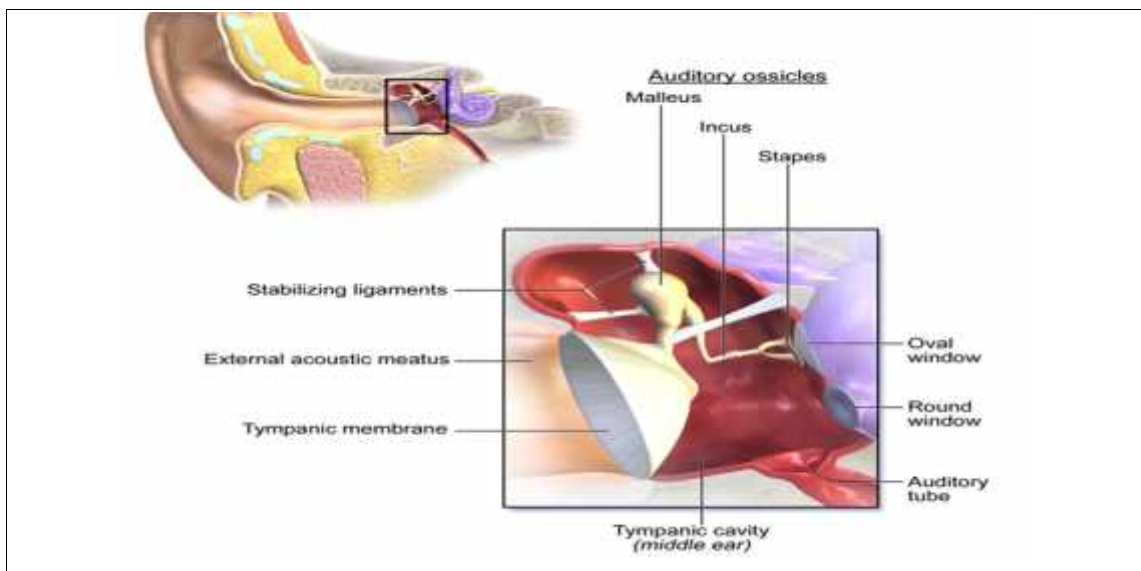


Figure 1.3 Middle ear. It consists of malleus, adjacent to tympanic membrane, incus, the second bone, making bridge and steps, the smallest one, connecting with the oval window of cochlea. The three bones are stabilized with three different ligaments. Auditory tube or eustachian tube opens lower to middle ear cavity

The tympanic membrane, lies obliquely across the external auditory meatus forming the divider between the external and middle ear (Figure 1.4). Healthy membrane is

usually grey in color and semi-translucent in appearance; consists of fibrous; largest part lower pars tensa, and small, upper part is pars flaccida. The handle of the hammer (malleus) remains attached on to the fibrous layer of the pars tensa. Using an otoscope the membrane and the part of hammer could be visualized (Gray and Standring, 2008; Drake et al., 2009; Moore et al., 2013).

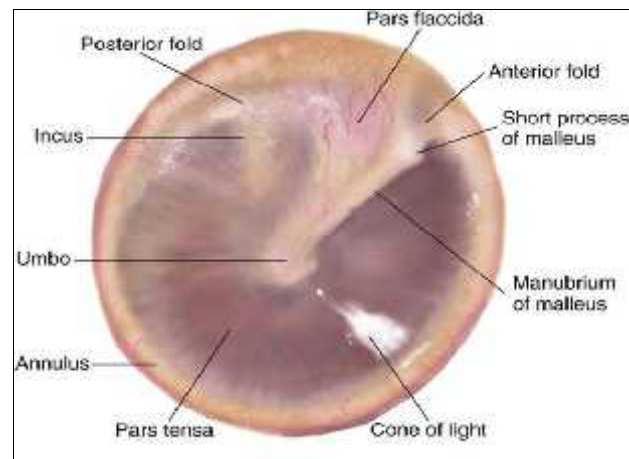


Figure 1.4 Tympanic membrane. An ideal tympanic membrane consists of short process of malleus, manubrium of malleus, pars flaccida, pars tensa, umbo, annulus, anterior and posterior fold

1.5 Inner ear

Most inner part, also called labyrinth, lies in the petrous part of the temporal bone; consists of bony labyrinth, externally separated by perilymph from endolymph fluid filled membranous labyrinth internally which is separated by perilymph (Figure 1.5). There are three parts of bony labyrinth, the cochlea anteriorly, the vestibule in the middle and the semicircular canals posteriorly. Parts of the epithelium of membranous labyrinth are specialized in forming receptors for sound organ of Corti, macule for static balance and cristae for kinetic balance (Gray and Standring, 2008; Drake et al., 2009; Moore et al., 2013).

Cochlea: It is the boney part appears like shell of common snail. The transmitted sound waves travel into the cochlea through oval window and runs throughout the perilymph. Conversion of sound, from mechanical form to electrical form take place here in the hair cells, which are transmitted to auditory region of brain through cochlear branch of vestibule-cochlear, the 8th cranial nerve (Kehr, 2010; Moore et al., 2013; Ehret, 1978).

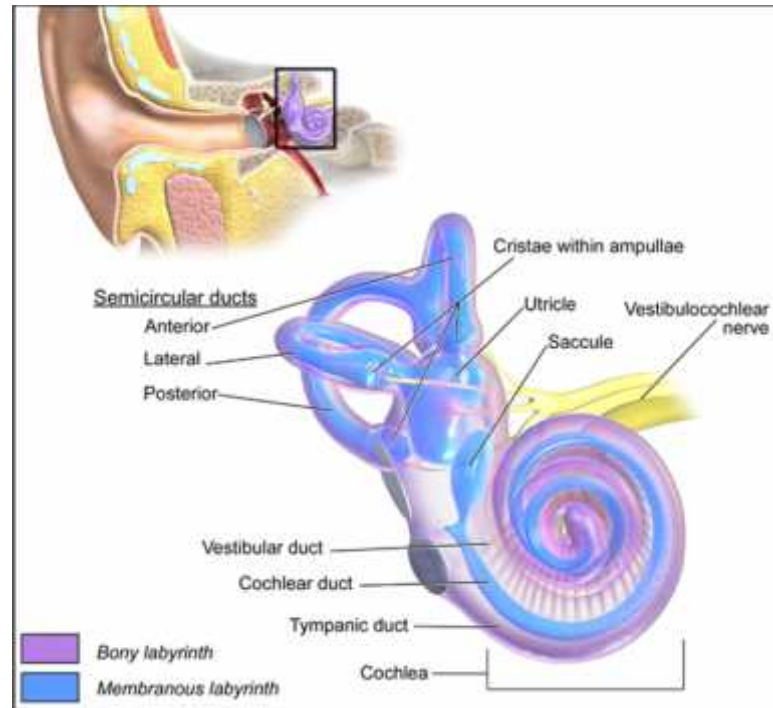


Figure 1.5 Inner ear. Consists of bony labyrinth (colored in violet), cochlea anteriorly, vestibula in middle and three semi-circular ducts posteriorly. Membranous labyrinth remains within the bony part (colored in blue)

Vestibule and Semicircular canals: There are three distinguished semicircular canals lateral, superior and posterior, appeared at right angle to each other and opening into the vestibule. Vestibule contains endolymph filled utricle and saccule which are responsible to form vestibule-ocular reflex, maintains head movement and helps conjugate eye motion to preserve macular fixation (Moore et al., 2013; Boron and Boulpaep, 2005; Spoor et al., 2007).

1.6 Hearing

Perception of sound is a special sense which is generated by vibration over the tympanic membrane. Normal human ear can detect sounds with frequencies ranging from about 20 Hz to 20,000 Hz, though most sensitive range of sound is between 1500-Hz to 3000-Hz frequency, which is mostly used in speech (Venes, 2009b).

The mechanism of hearing is a series of chronological action where all the three parts of ear contribute. Sounds from surrounds collected by external meatus and facilitates to enter into the auditory canal, part of external ear (Figure 1.6). This accumulated sound energy creates vibration on the tympanic membrane, according to variation of

frequency and convey forth. In the middle ear part, tympanic membrane converts this sound energy to mechanical energy through the variable motion of three consecutive small bones (i.e. malleus, incus & stapes), where stapes open into the oval opening and creates waves in the fluid of inner ear. The presence of these small bones is to facilitate the sound to get through from air medium to water medium and this transformation mechanism is also known as ‘Impending Mechanism’. (Venes, 2009b; Gray and Standing, 2008).

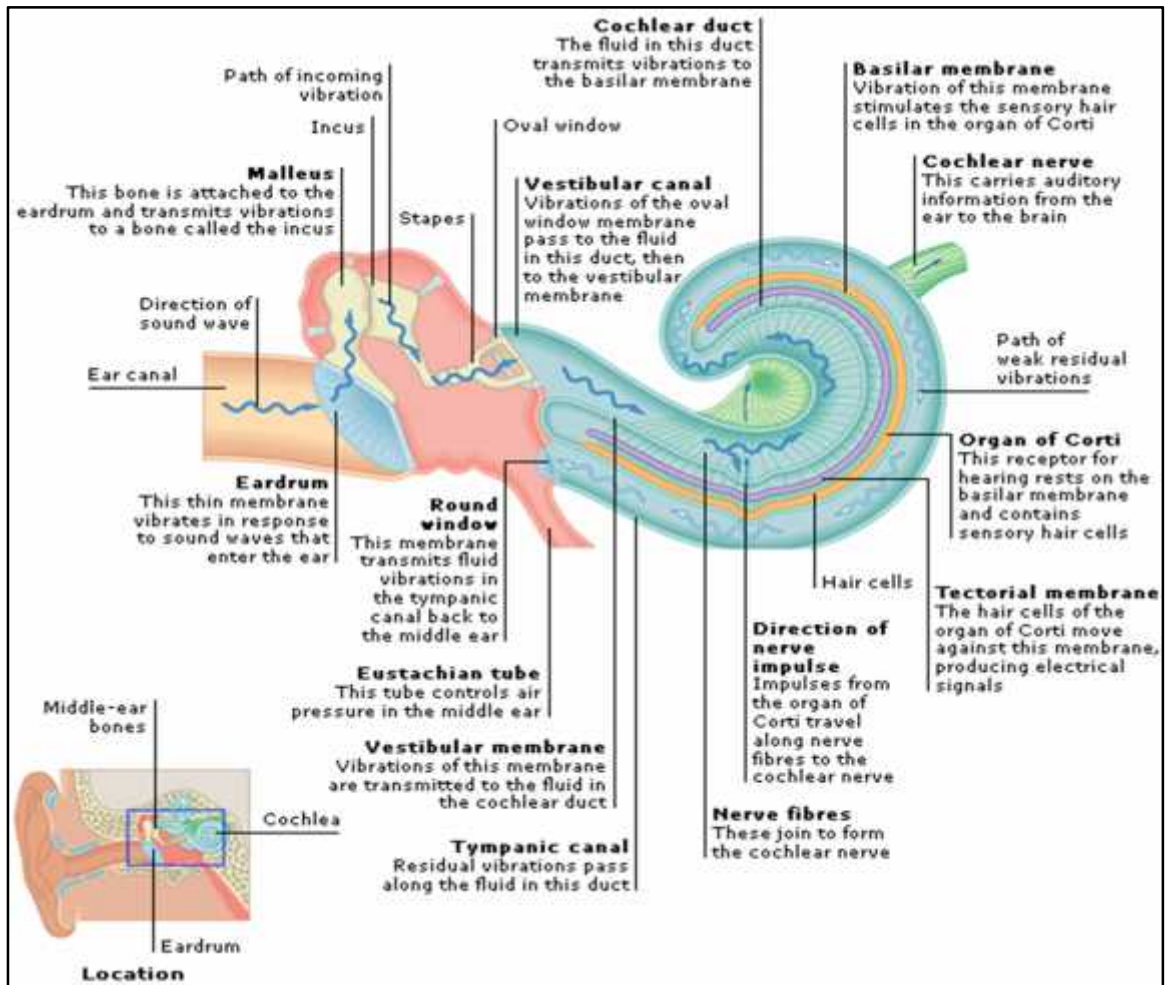


Figure 1.6 Motion of sound wave. Sound waves from outer ear fluxing into the middle ear through TM, transporting sound wave towards the inner ear-cochlea though oval window. This mechanically transported sound wave then conveys into the cochlear fluid, turns into electrical energy which is collected and processed by hair cell and send to auditory region of brain

After being carried by the three bones, sound waves passed over the fluid of the cochlea, the inner ear, a spiral-shaped, fluid-filled tube. Transferred sound energy runs in wave motion though perilymph, mostly sodium based, positively charged

extracellular fluid runs through the scala tympani and scala vestibuli, two outer compartment of cochlea tube (Bosher and Warren, 1968; Alberti, 2001).

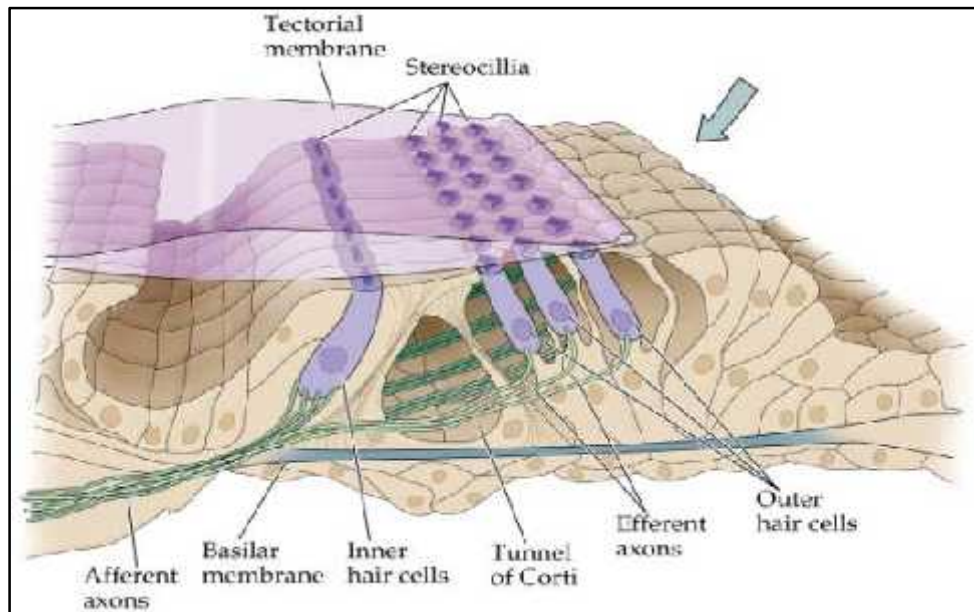


Figure 1.7 Hair cell (colored in violet). It collects the mechanical sound wave from tectorial membrane, converts into electrical energy and conveys into the brain through auditory nerve

This wave continues to oval window to round window, which opens in the middle ear. On this continuous motion sound wave creates rhythmic motion in the endolymph, contents of scala media, more positively charged than perilymph due to presence of more potassium, membranous like (Konishi et al., 1978); the produced vibration transferred through this tectorial membrane into the hair cells, the special type of auditory receptor cell (Figure 1.7) where the resonance causes depolarization converts mechanical sound wave in to neural transduction following spatiotemporal patterns of firings which transmits sound information to brainstem through auditory nerve (Ashmore, 1987); recent researches regarding hearing re-proved various animal model data in human hearing mechanism (Stamper and Johnson, 2015).

Many ear diseases are due to mutations in gap junction proteins, including the most common form of autosomal recessive hearing loss, e.g. GJB2 (Marziano et al., 2003). Genes from POU family, POU3F4 and POU4F3 are known transcription factors, in which, POU4F3 gene only expressed in hair cells (Willems, 2000).

Chapter Two

Literature review

2 Literature Review

2.1 Background

Ear infection is a common childhood disease with higher rate of recurrence (Jahn, 1991; McPherson and Holborow; 1985; Krueger et al., 2017) which also common in adolescence and adults (Nondahl et al., 2002; Hinchcliffe, 1961). The infection may occur during the first 6 years of a child's life, with a peak around 2 years (Mahoney, 1980). Infants are more prone to this disease due to many issues (Jacobs et al., 1998) including mouth-ear hygiene (Nelson et al., 2005), decubitus induced failure to burping during breast and bottle feeding (Garcia et al., 2012; Avital et al., 2018), repeated episodes of nasopharyngeal infection (Dhooge et al., 1999; Qureishi et al., 2014) along with common cold in both winter and rainy season (Kumari et al., 2016).

Various pathogenic bacterial species are responsible for ear infection as isolated and identified from middle ear namely *Staphylococcus aureus*, *Haemophilus influenza*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Proteus mirabilis*, *Klebsiella* sp., *Escherichia coli*, *Micrococcus catarrhalis*, *Serratia* etc. (Ayub et al., 2015).

Primary diagnosis is usually done by examining the ear canal using an otoscope. Examination of tympanic membrane and its surrounding area is done with this apparatus. Any local lesion, ulcers or any sign of inflammation is noted which are usually seen in otitis media or externa. Inflamed ear swab will be sent for culture test to exclude causative organisms and sensitivity test to find out suitable and sensitive antibiotics. Presentation of local mucosa changes in early otitis media and related bones also faces pathological changes which are essentially reversible; repetition of these changes continues a series of long chronic phase which establishes an intractable muco-periosteal disease. Frequent course of otorrhoea and local mucosal changes followed by osteo-neo-genesis, bony erosions, and osteitis that include the temporal bone and ossicles (Acuin and Organization, 2004). This chronological features results ossicular destruction followed by shift of bony joints (Ankylosis) and association of tympanic membrane perforation contribute to conductive type of the hearing loss (Flint et al., 2010, Paparella and Djalilian, 2002, Acuin and Organization, 2004). Rout of infection is variable including eustachian tube, external ear and blood (Daly et al., 1997).

Hearing impairment tested using tuning fork test or audiogram machine. Here hearing threshold level measured at various frequencies and decibels. Antibiotics are commonly used in the treatment of OM, which is the most frequent reason for antimicrobial treatment among children (McCaig et al., 2002; Schappert, 1992). Antibiotic overuse and the threat of emerging multi-resistant bacterial strains are of concern. On the other hand, perforated middle ear surgery or grafting is another expensive and complex way of OM management (Santos *et al.*, 2005).

Antibiotic treatment causes side effects, mostly diarrhea, rash or dermatitis, in children. Other disadvantages of antibiotic use include cost of therapy, allergic reactions, toxicity and interaction with other drugs. Recently it has been suggested that 2- year-old children exposed to antibiotics were heavier than unexposed children (in boys $P < 0.001$ and in girls $P < 0.05$) (Saari et al., 2015). Antibiotic resistance of bacteria is a serious recognized threat related to the use of antibiotics (Oldfield and Feng, 2014).

To find out an alternative to this hostile condition, homeopathic medicine could be a good solution. Homeopathic medicine is well known for its reputation of 'no side effect' which encourages its potentiality in medicine. In this current study 40 (forty) CSOM patients were included to justify the effectiveness of homeopathic medicines. There are few homeopathic medicines including mercurius solubilis, silicea, pulsatilla nigricans, tellurium, calcarea sulphurica etc. which are reputedly known to manage CSOM. This current study designed to prescribe tellurium metallicum, mercurius solubilis and calcarea sulphurica based on some specific clinical condition, i.e. CSOM with hearing impairment due to damaged tympanic membrane, pungent smelling in the pus indicates tellurium metallicum; serous, yellowish pus, pain in eustachian tube origin, with partial hearing loss indicates mercurius solubilis and mucoid pus, yellow-green pus, recurrence of inflammation, injured tympanic membrane with partial hearing loss indicates calcarea sulphurica. Depending on these clinical appearances participated patients will be prescribed and will be kept under keen follow up for 8 weeks onwards.

2.2 Epidemiology of ear infection

Acute otitis media (AOM) is a common health problem both in under-developed, developing and developed countries, though prevalence is high in developing countries yet it is at significant rate in the developed countries (Schilder et al., 2016). Approximate 30 in 100 people, of mid Africa continent are suffering from AOM, and less than 4 out of 100 people in developed countries of Europe are suffering from this disease. Around 4-5 in USA and 9-15 people in 100 people in India and Bangladesh are suffering from AOM (Figure 2.1).

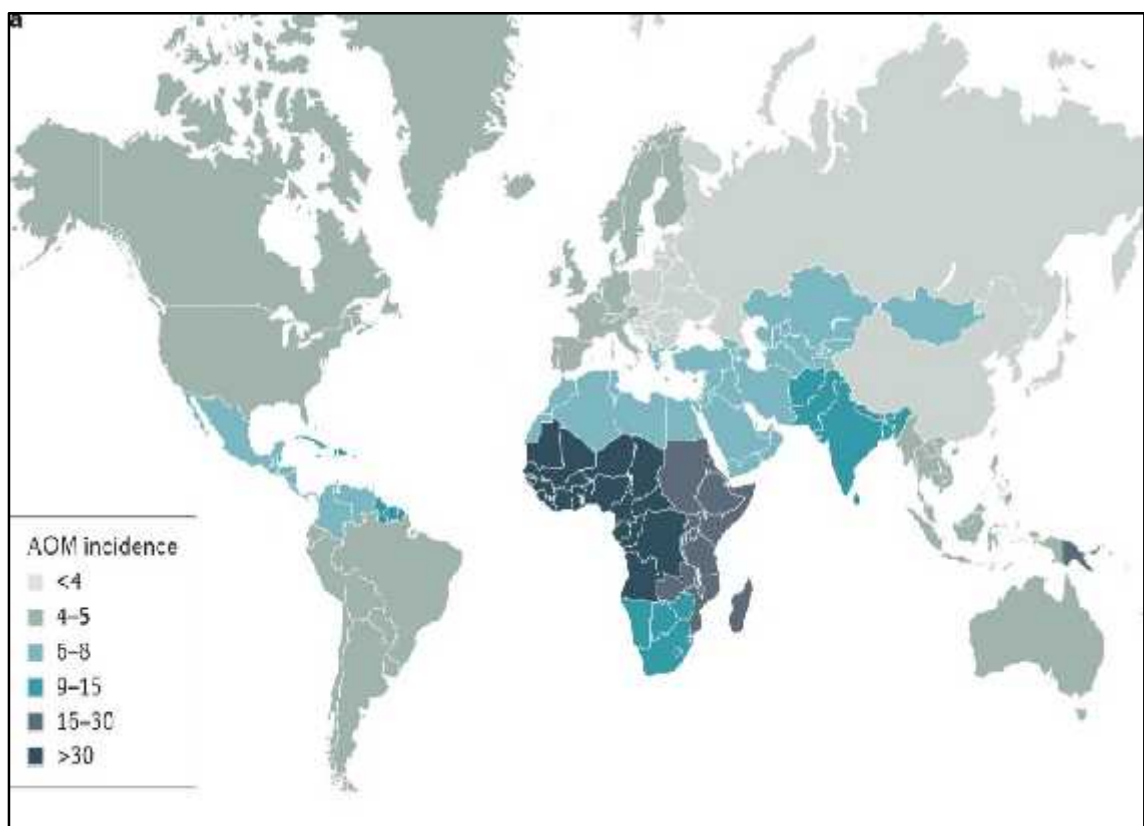


Figure 2.1 Geographical distribution of AOM incidence; Most in mid-west Africa region with >30, followed by mid-east Africa region with 16-30, south Asia region and southern region of Africa continent with 9-15, north Africa, Arab and mid Asia region with 6-8, most part of north America, south America, Australia and western coast of Europe region with 4-5 and rest of the region with less than 4 out of 100 people are suffering from AOM

The whole world is facing this common enemy with significantly high prevalence; CSOM prevalence is higher in underdeveloped countries than developing and developed countries (Schilder et al., 2016). The incidence rate of CSOM is most in

mid-west Africa region with more than 8, followed by 7-8 in few countries in Africa, 5-6 in mid-east Africa and south Asia region (Figure 2.2).

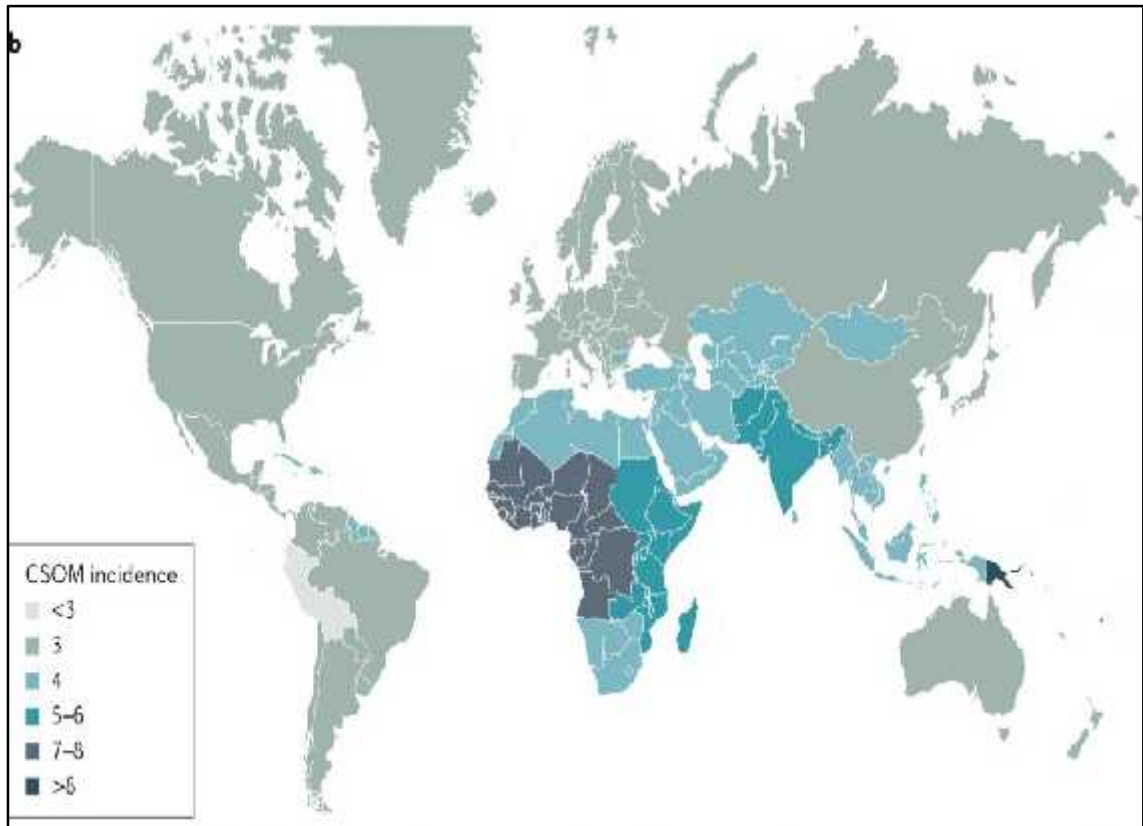


Figure 2.2 Geographical distribution of CSOM incidence; It is highest >8 in mid-west Africa, 7-8 in few countries in Africa, 5-6 in mid-east region of Africa and south Asia. In the north and south region of Africa continent, Arab, part of Europe incidence is 4 and rest have around 3 out of 100people

According to severity of disease condition and degree of urging for immediate help countries like Tanzania, Solomon Islands, Australian aborigines, India etc. grouped in highest attention seeking group in a classification of countries done by world health organization, However highly developed countries including Saudi Arabia, Denmark, Australia, united states of America and Gambia from Africa, were placed in the least need group (Table 2.1).

In school going children ear infection is one of the commonest complaints of absence of school (Mukara et al., 2017, Minovi and Dazert, 2014). In most cases the history of infection continuous from infant age with multiple episodes (Krueger et al., 2017), in addition infection in tonsils, allergic rhinitis increases the chances of infection in the eustachian tube which is directly opens into the middle ear (Maunsell et al., 2012;

Marseglia et al., 2009). Ear infection is not uncommon in adult though incidence is lower than early period of life (Sone et al., 2013; Pearson et al., 2015). It is more commonly found in the individuals who had a history of repeated MEE (Jensen et al., 2017).

Table 2.1 Worldwide classification of countries according to CSOM prevalence

Group	Populations
Highest (>4%) – urgent attention needed to deal with a massive public health problem.	Tanzania, India, Solomon Islands, Guam, Australian Aborigines, Greenland.
High (2–4%) – avoidable burden of disease must be addressed	Nigeria, Angola, Mozambique, Republic of Korea, Thailand, Philippines, Malaysia, Vietnam, Micronesia, China, Eskimos
Low (1–2%)	Brazil, Kenya
Lowest (<1%)	Gambia, Saudi Arabia, Israel, Australia, United Kingdom, Denmark, Finland, American Indians

Prevalence of CSOM measured in school going children by different researcher in different region of Bangladesh and found rural children are more affected. In a study of 225 children, age between 4-13 years from Mgura district and Dhaka city, showed 12.44% rural and 2.22% urban children found CSOM (Biswas et al., 2005). Use of clean cotton bud found only in 5.78% rural and 47.55% urban sample (Biswas et al., 2011). Another study conducted at Norshingdhi district in 4280 primary school student in rural area where 48% were boys and 52% were girls with mean age of 8.8 years showed that girls (6.6%) were more sufferer than boys (4.5%) (Shaheen et al., 2012). A study consists of 200 individual in Rangpur district, where 58.33% of CSOM individuals were in 11-20 years age group and prevalence was 6%. (Al-Robbani AM, 2012).

2.3 Predisposing factors

2.3.1 Pathological

Numbers of pathogenic microbes are involved in causing infection in the ear; many of them are common upper respiratory pathogens that may have been puffed from the

naso-pharynx into the middle ear through the Eustachian tube during bouts of upper respiratory infections. Most of the microbes are aerobic type and few are anaerobic (e.g. *Bacteroides*) reported (Brobby and Zadik, 1987; Brook and Frazier, 1996; Fairbanks, 1981). These pathogenic bacteria e.g. *Staphylococcus sp.*, *Klebsiella sp.*, *E. coli* and some other which are commonly present in normal ear flora (Broides et al., 2009). Also infrequently found in the skin of the external canal and may proliferate in the presence of trauma, inflammation, lacerations or high humidity (Pollack, 1988). These bacteria may gain entry into the middle ear through a chronic perforation. Among these bacteria, *P. aeruginosa* has been particularly blamed for the deep-seated and progressive destruction of middle ear and mastoid structures through its toxins and enzymes (Pollack, 1988). Colonization of microorganism in aural flora may found from 3 months of age of a child which may increase the incidence of OM (Faden et al., 1997). Presence of these pathogens may differ according to age though it remains highest in childhood (Casey et al., 2010; Faden et al., 1997; Syrjänen et al., 2001).

Like nonpathogenic bacterial flora colonizing the naso-pharynx, pathogenic bacteria do not cause symptoms until there are changes in the nasopharyngeal milieu. During periods of upper respiratory tract infection (URI), AOM particularly, colonization of middle ear pathogens increases significantly (Faden et al., 1991; Syrjänen et al., 2001). This increase is especially prominent among children in day-care, or prone to AOM (Aniansson et al., 1992; Faden et al., 1991). Chronic biofilm colonization of the adenoids may act as a reservoir for pathogens, entering the middle ear in OM (Saafan et al., 2013). Almost all middle ear pathogens derive from the pathogens colonizing in the naso-pharynx, but not all nasopharyngeal pathogens enter the middle ear to cause OM. Common nasopharyngeal or nasal inflammation caused by many viruses including influenza virus and rhino viruses, which inhibit ciliary function resulting facilitating entrance of number of bacteria into the eustachian tube and followed by ear infection (Chung et al., 1993). Various bacteria including *staphylococcus sp.*, *streptococcus sp.* etc. infect tonsils and surroundings in variably resulting chocking and hawking which mediate infiltration of those causative agents into the middle ear (Bosch et al., 2013). Clinical condition like nasal polyps, hypertrophy of inferior turbinate (HIT) and deviation of nasal septum (DNS) are very much influenced by unknown allergies; which have both direct and indirect impact over eustachian tube.

Local inflammatory clinical condition like rhinitis and sinusitis results sneezing followed by draining of bacteria into the middle ear through eustachian tube, which facilitates ear infection (Lee et al., 2016). Anatomically short, straight and wide eustachian tube in young children, facial nerve paralysis, inappropriate surgery in the maxillo-facial and anomaly in TLR4 gene may have role in susceptibility of ear infection (Luers and Hüttenbrink, 2016; MacArthur et al., 2006).

2.3.2 Lifestyle mediated influence

Ear is exposed to surrounding environment through external ear so it is prone to opportunistic infection facilitated by various agents including bathing in unsafe water, insertion of water into the ear, using earphone for long, exposure to house hold smoking (Mukara et al., 2017), cigarette smoking, pricking ear, living in loud sounds and low nutrition (Zhang et al., 2014). Smoking has affinity to produce middle ear effusion easily (Figure 2.3).

Rivers or ponds are very large reservoir of open water which is good place for bathing to men around the world. Open water contains large quantity of various pathogenic microbes including *Staphylococcus* sp., *E. coli*, *Salmonella* sp. *klebsiella* sp. etc. which are also known pathogen causing CSOM. Swimmers are always in risk of draining ear caused by various pathogenic microbes both in open water and in swimming pool. Using ear phone for long causing much humid environment in the auditory canal which facilitate microbial growth and repeated high frequency in short range causing trauma in the TM and distortion of ear following local inflammation resulting increased hearing threshold level than normal level (Harrison, 2008; Widén et al., 2017).

Smoking is a life threatening social problem causing various health issues including bronchitis, upper respiratory tract infection, hearing loss and chronic cough (Yanbaeva et al., 2007). Number of passive smoker is much higher than active smokers and more vulnerable in the society (Sumit et al., 2015). Chemicals like arsenic has also negative impact in people who are taking arsenic mediated drinking water (Li et al., 2017).

People with low nutrition and lack of necessary nutrition are relatively in risk of various health issues including hearing impairment (Shargorodsky et al., 2010; Spankovich and Le Prell, 2014).

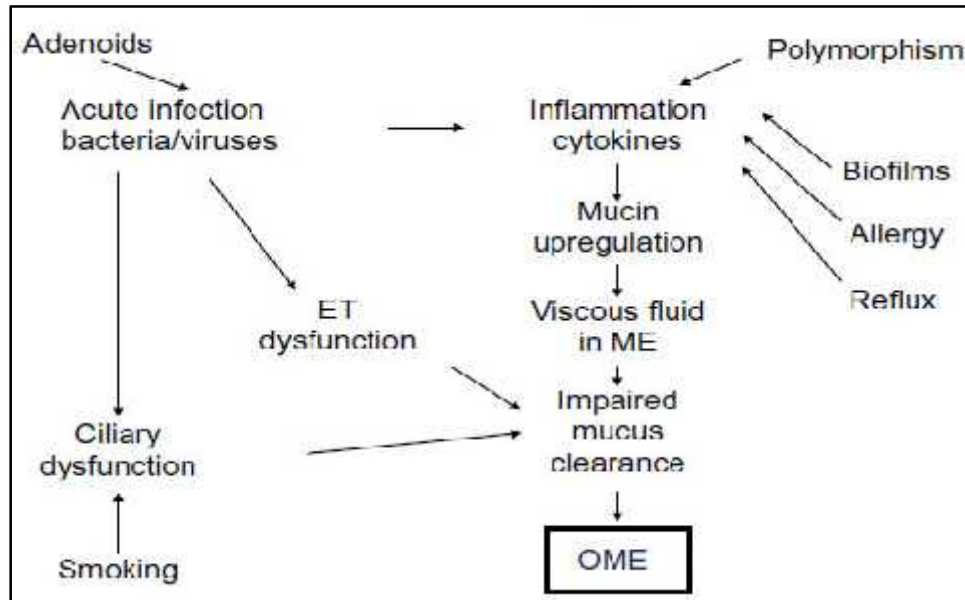


Figure 2.3 Pathway shows smoking facilitate effusion. ME - middle ear effusion. ET- eustachian tube; ME- middle ear; OME- otitis media with effusion

Socioeconomic condition is a major concern in various health issues and in case CSOM it is highly related as lots of factor are involved in hearing impairment, are directly controlled by family-society-national socioeconomic status including primary health care, major health service provider (Curhan et al., 2010; Helvik et al., 2009).

2.4 Various sign and symptoms of ear infection

Symptoms and its definition:

Distinct symptoms are expressed for each complaint in various clinical medicine and practice of medicine books. In the ear, there are few symptoms found those are widely presented in most of the ear complaints (Table 2.2) including otalgia, pruritus, otorrhoea, deafness, tinnitus, vertigo and unsteadiness.

Table 2.2 Commonly found symptoms in ear infection and their definition

<p>Pain (Ootalgia): Common in almost every complaints e.g. Otitis</p>	
<p>Itching (Pruritus): Sensation of irritation in the canal or inside of the ear is found invariably. Most common in otitis externa.</p>	
<p>Discharge (Otorrhoea): Purulent, mucoid or blood stained, followed by tympanic membrane perforation, granulation from infection, trauma etc.</p>	
<p>Hearing loss (Deafness): Conductive type: Hearing reduced due to lack of conduction in between ear canal, middle ear and inner ear, by various cause including middle ear effusion (MEE) and CSOM Sensorineural type: Hearing impaired due to insufficiency of auditory nerve by multiple causes including Alport's syndrome, birth injury etc.</p>	
<p>Noise (Tinnitus): Imaginary sounds in the ear mostly in the form of humming and heaviness found eat drum and inner ear complaints.</p>	
<p>Vertigo: It is the hallucination of motion usually found in inner ear complaints.</p>	
<p>Unsteadiness: Sensation as if will fell down from a posture, with or without motion, commonly seen in inner ear complaints.</p>	

2.5 Hearing Impairment

Difficulty in hearing implies hearing impairment, commonly human hearing limit is from 20 to 20000 Hz (Rosen and Howell, 2011); hearing threshold level is the least lowest level of frequencies with what human ear can press presence of sound and considered level is 20 dB in 1 kHz and 4 kHz frequencies; at 8 kHz and 12 kHz frequencies this level is considered up to 40 dB.

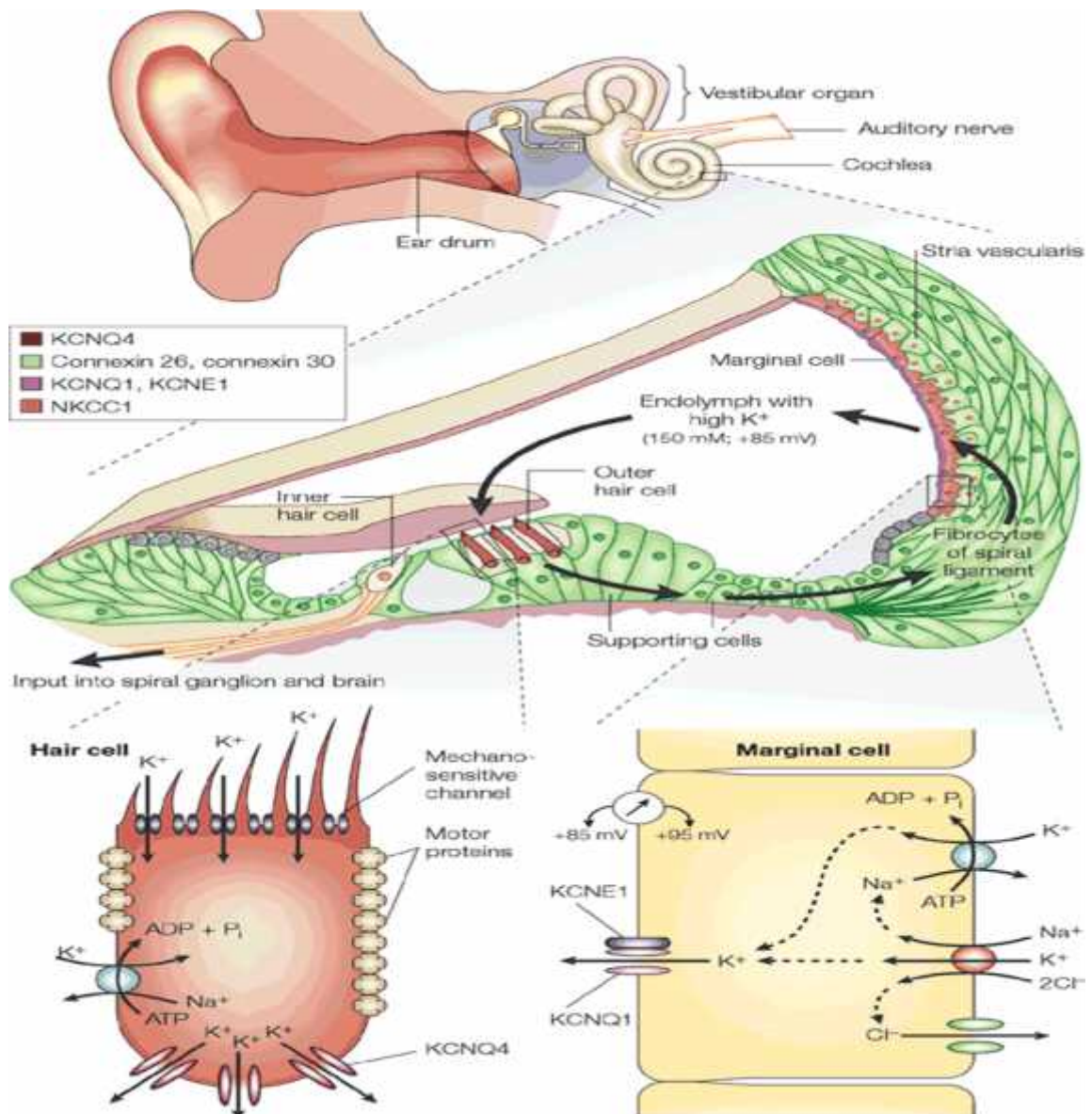


Figure 2.4 Mechanism of hearing. A basolateral Na/K-ATPase pumps K and creates a Na gradient to drive K and Cl into the cell in a co-transport process. Chloride is recycled by basolateral Cl channels, and K is secreted apically by KCNQ1/KCNE1 K channels, which are open at the unusual apical membrane voltage of marginal cells. This allows for a net secretion into the endolymph in spite of its high K concentration. KCNQ proteins have six trans-membrane domains and a pore-forming P-loop

Any alternation of K channels, as if KCNQ1 were down regulated in stria vascularis may result presbycusis or age related hearing loss. A reduced KCNQ4 may lead to gradual degeneration process (Figure 2.4).

Hearing loss or inability to hear is a common complication in ear infection irrespective to ASOM and CSOM. As the inflammation remains for long the complicity become much deeper. Hearing impairment is divided into two major segments, one is conductive type, and other one is sensorineural type (Paparella et al., 1984). Conduct type of hearing loss caused by failure of transport and conversion of sound wave from mechanical energy to acoustic energy due to lack or loss of conduction in between the hearing apparatus including wax in the external ear, perforation in the tympanic membrane, disturbance is bony chain, degenerative bone diseases in the related bones, fluid collection in the middle ear and dysfunctional eustachian tube.

Sensory type of hearing impairment is due to lack of transport or relay of acoustic energy into auditory region of the brain through auditory nerve root.

2.6 Treatment

Like any other bacterial infection, suppuration of ear is also required medicinal treatment; acute infection of ear in children is common with spontaneous healing yet number of patients needs recurrent antibiotics and analgesics. Many studies shown that fast prescription is not always advised in acute ear infection (Worrall, 2011). However, doctors are prone to advice medicines both oral and topical including antibiotics, from the age of 6 (six) months, sometimes even from less (Le Saux and Robinson, 2016; Hoberman et al., 2011). There are two major type of treatment policy available, medicinal and surgical. Medicinal treatments consists of analgesic, antibiotics and in some cases steroids. Condition like damage of parts of ear, rupture and perforation of tympanic membrane may need surgical reconstruction (Holmes, 2017).

2.6.1 Conventional treatment

Choice of antibiotic in treatment is an automatic picking in any kind of infection. Number of antibiotics of various types had been applied in ear infection. Usually

antibiotics are prescribed after 6 month of age, as till then mother immune system helps to fight against various pathogen (Bar-Oz et al., 2003; Sakulchit and Goldman, 2017). Though watchful waiting without any antibiotics an option to the respective physicians and noticed that early treatment outcome is limited (Siegel, 2010). Some studies shown acute otitis media may resolved spontaneously within 24-48 hours, though need of antibiotics also shown by number of studies (Venekamp et al., 2013). To reduce pain sometimes NSAIDs applied with satisfactory outcome and various antibiotics had been deployed in otitis correction including amoxicillin, ciprofloxacin, and cefixime with success. In course of time, much effective antibiotic combination of amoxicillin with clavulanic acid is introduced recently (Tancawan et al., 2015). Application of local antibiotics like as Chloramphenicol and Ciprofloxacin ear drops also an option used by the physicians, may or may not along with oral medicine therapy (Ahmad, 2013).

Vaccination with Streptococcal vaccines is thought to be an effective way under process of protective action to control the occurrence of OM (Briles et al., 2000). However, numerous reports emphasized that association of several pathogenic bacteria or biofilms rather than a single pathogenic species is mostly responsible for OM. In such cases, vaccination may not bring positive outcome in preventing OM (Brook et al., 2000; Saylam et al., 2010). All these existing treatment or preventive measures are not adequate in curing OM. Furthermore, many researchers suggested that AOM can be resolved without antibiotics within three to twelve months and guidelines for the treatment of AOM now included observation options (Qureishi et al., 2014). However, most of these studies have not recorded the duration of MEE and thus hearing loss. The main aim of treating AOM should be to eradicate bacteria from the middle ear and to normalize hearing (Burton et al., 2016).

In Bangladesh, use of antibiotics is much higher as prevalence of various bacterial diseases has increased. Self-medication is a popular choice of selecting antibiotic in treatment of ear infection and approximately 2.3% prescription order this (Biswas et al., 2014a; Biswas et al., 2014b). Another study showed around 50% physician prescribes antibiotics in upper respiratory infection including pain in throat and eustachian tube where 10% physician prescribe antibiotics for specific infection in ear i.e. otitis media (Rahman and Huda, 2014). Pattern of antibiotic prescribing is

different in Bangladesh than other countries as there are few factors influencing this phenomenon including diagnostic uncertainty, lack of training about appropriate application guideline, practice of prescribing inappropriate antibiotics and lack of knowledge of antibiotic resistances (Saha and Promite, 2017).

2.6.2 Preventive strategies

Knowledge of source of infection in ear may help in avoiding various complications (Prakash et al., 2013). Cleaning the ear canal with 2% acetic acid to remove debris can be a useful adjunct to therapy (Cole et al., 2003). Prevention may be necessary for those patients who suffer from recurrences. Dilute alcohol or acetic acid (2%) can be instilled promptly after swimming or bathing. A preparation of 50% white vinegar and 50% rubbing alcohol could be a good choice for this (Acuin and Organization, 2004). Patients should protect their ears from water when bathing (by placing a cotton ball with petrolatum jelly into the ear canal) and should avoid swimming until their otitis externa resolves. Wearing ear plugs, shaking the ears dry after swimming, and using a blow dryer are considered as some other preventive methods. Though use of ear drops, with or without antibiotic properties, after surgery is not advised as the otorrhea is a common feature for two weeks from the day of incision and suture event (Browning, 2013). Chronic cough and itching in the eustachian tube is a common feature in allergic rhinitis which is reasonably reduced after taking warm water, and rhinorrhea may also has an entry through middle ear infection (Eskeland et al., 2017). Researchers are not convincingly agree with which rout of medicine should be used as both oral and topical use shows significant result (McVicar, 1999). Low dose X-rays have potential in controlling and preventing ear infection, it also known agent in managing mastoiditis, cervical adenitis and related hearing impairment (Calabrese and Dhawan, 2014).

Chewing gums may have potentials in preventing prevalence of ear infection, mostly in school going children, during in their classes or play grounds (Danhauer et al., 2011). Breastfeeding helps in preventing ear infection, as well as essential in early life due to its known supportive immunological properties; Smoking should be stopped by parents as because passive smoking can cause repeated upper respiratory tract infection, more over smoking has affinity to cause otitis media and related hearing impairment both in children and adult (Sumit et al., 2015; Granath, 2017).

2.7 Disadvantages of antibiotic treatment

Antibiotic-resistant bacteria develop as a result of natural adaptations, spontaneous changes in DNA, or inter bacterial plasmid exchange (Blair et al., 2015; Tenover, 2006). Number of antibiotics including ampicillin, augmentin and cephalothin have been found full resistant to MRSA (Ahmad, 2013). Antibiotics also affect the normal flora and interfere with the human bacterial balance, the effects of which could last minimum for a year. Since the normal flora guides the development of the infant's immune system, any changes can impose a lasting impact on a child's life (Groer et al., 2014). Invention of new antibiotics and their distribution is eventual and unfortunately, the related exchange price proportionately may rise in compare to worldwide socioeconomic condition which endangered a huge number of population (Falagas et al., 2008).

Use of drugs during pregnancy takes extra care, however, application of antibiotics is not encouraged during gestational period as the vertical transmission of unfavorable microbiom could not be excluded (Pedersen et al., 2017). Antibiotic application is gradually discouraging not only for its lack of novelty on pathogen but also for its adverse effects on environment specially on soil and water; excessive or unwanted use of antibiotics are common in world-wide which initiates a direct impact over the environment by interfering the growth of many microbes functioning ecologically; this phenomenon indirectly hampering in various metabolic or co-metabolic process and biodegradation process (Grenni et al., 2018).

One of the major use of antibiotic is 'IF' or 'presumptive' in any slightest infection including otitis media, upper respiratory tract infection, viral infection etc. to avoid opportunistic infection by various pathogenic bacteria. Surgeons are in top in this run by prescribing antibiotics as prophylaxis and CDC estimates fifty percent of this misuse could be stopped by a single step by engaging surgeons (Goff and File Jr, 2018).

Moreover, introduction of antibiotics in various chronic infection like rhino-sinusitis, usually caused by mixed both aerobic and anaerobic pathogen, dominated by *Staphylococcus* sp. shown no significant difference in clinical features versus placebo in a randomized controlled study which conveys a message that reduction of number

of pathogen is not the treatment (Barshak and Durand, 2017). In chronic suppurative otitis media applied antibiotics found with no significant benefit in controlling infection or hearing threshold level; in addition related surgery like adenoidectomy and tympanostomy is controversial and age dependent which brings these patients in deep ambiguity in treatment policy (Schilder et al., 2017).

2.8 Homeopathy

It is a school of treatment policy what Dr. Samuel Christian Friedrich Hahnemann (1755-1843) introduced (Kuzniar, 2017), the dogma of activity of drugs substances upon the healthy individual when administered in a certain law where those drugs are being prepared following a series of specific regulation. The idea of Like Cures Like was expressed by Hippocrates; the theory of ‘Doctrine of Signature’ or ‘like cures like’ also denoted by Paracelsus (Boyd, 1936). Hahnemann studied this theory and added some more regulation including use of minimum quantity and dose of medicine and named the system ‘Homeopathy’ in 1796 (Jonas and Jacobs, 2009). Hahnemann named this concept from two Greek words *hómoios- ὅμοιος* and *pátheia- πάθεια*, meaning ‘like’ or ‘similar’ and ‘disease’ respectively, conjointly obtained. He described his concepts of proving drugs in healthy human being and documented the changes in a written manner in *materia medica pura*; he also conceptualized the procedures to prepare the drugs, philosophy to administer these medicine to diseased, how a single drug should be selected and administered etc. in ‘Organon of Medicine’(Hahnemann, 1982). Medicine should be selected on the overall condition of the patient, should not be selected on the basis of organ/site/ same symptoms previously cured by this remedy etc.(Baehr, 1869). Homeopathic medicine works on and with vital force, it helps vital force to flow in its own pathway. And with it vital force itself become strong and get healed spontaneously. During selecting a medicine, physicians need to keep an eye on some special but individual symptoms which very important to selecting a homeopathic medicine (Bell et al., 2004). Various clinical evidences proving efficacy of homeopathic medicine are gradually increasing, not only in case studies but also in double blind randomized studies. Homeopathic medicine is well proved for pediatric and female cases including managing premenopausal syndrome rather than conventional medicine (del Carmen Macías-Cortés et al., 2015). Homeopathic medicine have preventive effects on upper respiratory tract diseases, gradually it increases health status in positive manner and not being

interfered with cigarette smoking or other environmental factors (Beghi and Morselli-Labate, 2016).

Homeopathic medicine comprises some conceptual principal and regulations which are distinct from conventional theory, are described here:

- 1) Concept of vital force
- 2) Concept of disease
- 3) Concept of source of symptoms
- 4) Concept of simi-mono-mini
- 5) Concept of potentization.
- 6) Concept of potency.
- 7) Concept of prescription method.

2.8.1 Concept of vital force

Cell is the structural and functional unit of an organism which contains a hypothetical force also known as vital force, elan vital or vitality to cause the evolution and development of that organism. It is called by the name Chi by Traditional Chinese Medicine, Prana by Ayurveda and in plain language 'Atman' or soul (Pandya, 2011). Human body is a bundle of cell, possessed of various tissues; it is more over a bundle of energy consists by numerous living cells and complex substances constituting the body. Hahnemann called that vital force governs the mind, body, emotions and mental state of a person. This omnipotent vital force or which pervades the whole word, in its animate and inanimate states and maintains harmony in them, is also equally present in human beings, recently researchers mentioning in biofield hypothesis (Rubik, 2002). Treatment with potentized medicine selected on the basis of the law of similarity, given in minimum dose just sufficient to restore the vital force to its original state of dynamic equilibrium in shortest possible time, which is called cure (Bellavite et al., 2006). As 'individual' forms the basis of treatment, it has to be highly elicit and therefore a rule of thumb can hardly exist in homeopathic treatment though it is possible to envisage near specifics in some acute and endemic cases (Nuzzo, 2014).

2.8.2 Concept of disease

In conventional medical science disease defined as altered condition marked by subjective complaints, a specific history, and clinical signs, symptoms, and laboratory or radiographic findings. Manifestation of disease depends on individual person and/or definite conditions related disease, e.g. a person with hypertension may not have significant discomfort, yet he is in a serious disease condition (Venes, 2009a). But in homeopathy, concept of disease is just not only a set of symptoms caused by some random pathogen resulting alternation of equilibrium but also involves the alternation of characteristic modules of individual such as diet, habitat, responds to both physical and mental stress, changes that take placed along with current disease (Kent, Reprint: 2001).

In homeopathy, wellbeing of mind, physical and emotion is collectively named as health and there is a continuous balance between the building up of complex substances and tissues, when energy is consumed and their breakdown, then energy is liberated (Abbasi, 2017). The former process is called anabolism and latter catabolism. They together constitute what is known as metabolism which represents the net energy used up by the body for the fulfillment of its functions. In the growing stage of the body, the anabolic effect is more than the catabolic effect, when the growth stops there appears to be a balance between these effects and the body's equilibrium is maintained with vital force. According to biofield or bioenergy medicine concept i.e. acupuncture, homeopathy & ayurveda, disturbance of free flow of energy around the living body manifests some disorientation also known as symptoms and all these symptoms collectively called a disease (Rubik et al., 2015).

2.8.3 Concept of symptoms and their sources

Symptoms form the very basis of homoeopathic treatment. An ailing person gives out symptoms of the disease he is suffering from, his curative reaction to the morbidic stimulus. These are called the Disease Symptoms. According to the Law of Similar, if the disease has to be cured, a drug must be found which gives symptoms as similar as possible to the disease symptoms. Symptoms belonging to the drug are called the Drug Symptoms. So, mere potentized drugs will not serve the purpose of treating ailing persons, unless further data are made available regarding detailed aspects of each drug, such as its general characteristics, the nature of its action on each organ of

the human system, its effect on the human mind, the modalities of its action, its relation to other remedies and so on. Just as homeopath would like to have detailed symptoms of the patient in his entirety, similarly, he must have details of the drug to assess its similarity with those of the patient (Kent, Reprint: 2001).

There are three methods of obtaining details of symptoms caused by the drug. The first is the method of proving under which specified medicinal drugs are given in mother tincture or potentized form to healthy volunteers more frequently for a period sufficient to produce symptoms. These symptoms are carefully recorded under various heads for subsequent consideration and prescribing of remedies (Teixeira, 2003). The second source is toxicology. Some of the homeopathic drugs in crude form are deadly poisonous such as Conium (Hemlock), Lachesis (Bushman snake), Arsenic, Cyanide compounds etc. obviously, such poisons or toxins cannot be used as proving's on healthy individuals to get symptoms. In such cases, accidental or deliberate poisonings help to get the related symptoms. Socrates, the Greek Philosopher, was poisoned by Conium and the description of symptoms left by Plato enabled Conium to have an important place in the hierarchy of homeopathic drugs (Bostock, 1986). The third source is clinical experience (Hahnemann, 1996). Today's progress of Homoeopathy, though halting, has contributed not a little to the storehouse of symptoms through clinical experience. Not all proving are completed; quite a number of drugs are listed in materia medica on the basis of partial proving. In such cases, data were collected from clinical experience to fulfill some of the blank space left. Even where the proving is supposed to be completed, new light has been thrown through additional data that were collected from clinical experience. It lies scattered in published journals and in books on clinical experiences of experts. Such information have been collected, collated and published as a single compendium for future physicians (Kent and Loos, 1912).

Number of materia medica gives the totality of only frequently recurring symptoms of each proved drug. Various writers and analyst including Bonnégossain, Kent, C Hering, HC Allen etc. wrote number of huge materia medica contains many details of such drugs and are helpful when a particular case demands a detailed enquiry in respect of a drug. Even otherwise, these should be consulted for getting the broad picture of a drug with its peculiar, uncommon, red line and single symptoms (Murphy,

2003). It needed to be mentioned that a "drug" becomes a "remedy" when it satisfies the Law of Similar, though loosely, they are used in the same sense (Bowman et al., 1986).

Homeopathic medicine still looking for FDA approval due to lack of proper and sufficient scientific evidence and tests to pass in the accreditation (Neldner, 2000). Most authentic scientific evaluation technique to get approval of a drug, every single drug must go through 'Double blind' or 'Single Blind' research method to prove its efficacy and its safety; for an example, a group of people suffering from common cold, having some common complain like low grade temp, malaise, anorexia and mild rhinorrhea; and to remove these entire symptoms researcher uses a drug, an NSAID agent. After a successful procedure researcher get a statistics and present a result. But in homeopathy it is quite impossible to give a single medicine to a group of people having some common symptoms. Because, with the same set of symptoms those patients have red tip of tongue will be given *Rhus tox*; rhinorrhea with blend discharge and corrosive lachrymation will be given *Euphrasia*; with corrosive nasal discharge will be given *Allium cepa*, following aphorism 153, Organon of Medicine (Hahnemann, 1982).

Due to complex selection procedure, it is hard to treat a single clinical case in many individual with the very same homeopathic medicine as the selection should be according to individual presentation (Kent, Reprint: 2001; Hahnemann, 1982).

2.8.4 Concept of simi-mono-mini

'Similarity' is homeopathic medicines another name, shortly known as 'Simi'. During proving phase it has shown that every single prover manifested with a set of common symptoms which were graded highest rank as this specific set of symptoms are the guiding symptoms of that very medicinal substance namely modalities of symptoms, likings-disliking, temperament etc. In therapeutic phase, a homeopath keenly search for this set of symptoms and only with this specification an individual could be separated from ambiguity (Hahnemann, 1996; Vithoukas, 2017). Every single patient should be advised medicine only after being screened matched with similar symptoms as written or mentioned in materia medica. It is the principle commandment that

should be followed in every prescription. Preserving this fundamental confirms the purity and mastery of homeopathy (Hahnemann, 1982; Lüdtke and Rutten, 2008).

At a time, only one medicine should be given to the patients. Use of multiple drugs, combined medicines, application of many drugs in a bottle etc. is prohibited. The word 'Mono' defines its drug application equity and it's always in single form, the very same form which manifests symptoms when standardized. There are few drugs in combine form, which had been included in the drug list after being proved as a single entity (Lüdtke and Rutten, 2008).

Very small amount of medicinal substance may evolve a large amount of inner dynamic energy which heals the diseased, otherwise large amount of medicine could cause many complications including death (Woodward, 2005). So, the quantity of drugs always an important feature of an well selected remedy, as it carries the medicinal property shouldn't be taken as food or in large dose, otherwise many serious complications may cause. It is one of the major bright sight of homeopathic medicine that administered medicine should be in minimum of quantity to avoid any unwanted side effects (Shah et al., 2010).

2.8.5 Concept of potentization

Potentization of drugs is an indispensable feature of homeo-treatment. It means bringing out the latent medicinal properties of a drug by successive friction by means of multiplied and continued trituration and succussion of a small portion of the drug. The transformation of the drug is so dynamic, extraordinary and astonishing that a minute quantity of the potentized drug cures various ailments that the human body suffers from (Czerlinski and Ypma, 2011; Schulte, 1999). Indeed, the remedy is equally applicable to ailments of animals and plants. But, how this happens remains a mystery. It has baffled scientific investigation till to-day (Czerlinski and Ypma, 2010; Molski, 2011).

The three systems under which the potentized medicines are available are: (a) The Centesimal System (1:100), (b) The Decimal System (1:10) and (c) The 50 Millesimal Potencies (1:50,000). In Centesimal System '6', '30' etc. are suffixed to the name of the medicine such as Aconite 6, Bell 30, Rhus tox 200 etc. Under the Decimal System we have suffixes such as 1x, 2x... 30x etc., "x" signifying the Decimal System. A new

system of potencies was suggested by Dr. Hahnemann in aphorism 270 of the 6th edition of his Organon has been developed the 3rd type, but in practice not so popular, like the centesimal or the decimal potencies. The potencies in this system are denoted by 0/1, 0/2 etc. Few more advantages claimed over the centesimal and the decimal systems including more powerful in action, safe, avoids aggravation, permits repetition as often as necessary and cuts short the period of suffering of the patient. But the experience of practitioners differs, particularly in respect of expeditious cure. The ultra-potencies, e.g. MM, LMM, CMM, DM etc. though proved to be most effective and curative in some desperate chronic cases, are rarely available as they are not in common use (Jütte and Riley, 2005; Lobyshev and Tomkevitch, 2001; Rossi et al., 2012).

2.8.6 Concept of selecting dose and potency

The selection of proper potency is an important step after the remedy has been selected. Various opinions differ greatly in this matter as to which potency one should prescribe, though there are few broad division of potency, namely (a) low : potencies below 30, (b) medium : potencies between 30 and 1M and, (c) high : potencies above 1M (Rawat, 2002). Experience has shown that even if a remedy has been correctly selected on the basis of totality of individualizing symptoms, it may not act curatively unless it is given in proper potency. Proper potency may be defined as the optimum potency of the respective drug which, when given in minimum dose at specified intervals depending upon the nature of the disease and the response of the patient, would cure him of his illness in minimum of time. It is a flexible concept allowing one to use any potency from the lowest to the highest according to the severity of a case (Dantas and Rampes, 2000; Fisher et al., 2002).

From ancient to till date various physicians including Hahnemann used lower potency in both acute and chronic condition. Although Hahnemann spoke about LM potencies in the sixth edition of his Organon, it was only after Kent, an eminent homeopathic philosopher, spoke consistently in favor of high potencies that high potencies came to be used frequently. Researchers have found significant out come in various studies using higher dilution like 30C in rat models (Khuda-Bukhsh, 1997).

2.8.7 Methods of prescribing

This is one of the most complicated section of homeopathic medicine system as there is no specific single rule to follow, however, according to aphorism one to eight, the objective of prescribing, by a physician, is to cure the patient in most convenient way including within short time, without any delay, convenient to understand the prognosis and long lasting (Hahnemann, 1982). Following this there are three major methods developed to help the vital force in course of healing namely a) on the basis of the totality of symptoms, b) the snap –shot prescriber and c) the pathological methods. These concepts are to select the remedy to help the vital force to get in regular shape in no time. As per aphorisms 153 and 154 of the Organon of medicine, peculiar (P), uncommon (Q), red line (R) and singular (S) symptoms will be ranked highest as they make the distinguished contrast among the medicines in the materia medica(Hahnemann, 1982). Selecting medicine following totality of symptoms means, a medicine is selected counting his back ground of the individual patient, current status of the health, characteristic symptoms, PURS and miasm as revealed in the Materia Medica (Kent, Reprint: 2001). While the modern diagnosis is confined only to the determination of the disease producing the symptoms, the homoeopathic diagnosis covers the entire gamut of the disease, not merely its symptoms but also the field producing the symptoms, i.e. , the individual and the fundamental, exciting and maintaining causes on which the disease thrives, as summed up in the dynamic concept of the totality of symptoms (Cummings and Ullman, 1991).

Concentrating on keynote symptoms, redline symptoms, PURS, modalities and various stonewort’s instructions on clinical experience homeopathic medicine could be selected and this system is known as Snap shot system of selection. Medicine could be selected on the basis of cause, organ, and specific clinical condition, are included in this group.

Every symptom derived by alternating of normal physiological status though etiology may differ and these changes known as pathological symptoms. Now a days these symptoms play an important role in case analysis and selection of drugs (Bellavite, 2015). There are many pathological indications, which have been included in various repertories-the dictionary of symptoms. Moreover, critical cases like malignancy,

complicated abscess in internal organs, tissue changes in various diseased organ etc. are precisely being advised to be treated by experts (Unlu et al., 2017).

2.9 Worldwide status of homeopathy

Most commonly used medical service is Allopathic medicine, also called the western medicine, conventional medicine etc. which has increased tremendously after discovery of penicillin, since 1940. However, homeopathy faced tremendous threat from orthodox medicine from the very beginning of its venture as people accepted it's philosophical and simultaneously experimented concept rather than orthodox medicine's scientific concept (Starr, 2008). As a matter of fact the exact reason to oppose homeopathy was not its philosophy or its lack of scientific evidence but cutting into their health business (Ullman, 2017). Homeopathy passed through difficult bumpy time and still existing into the health system in all over the world including countries England, France, Netherland in Europe and many countries in Asia. Among these countries homeopathic medicine is practiced as alternative medicine to conventional medicine. Homeopathic medicine has a distinct medal of 'No Side effect' which encourages people all over the world and gradually increasing the acceptance of homeopathic medicine as an alternative medicine (Dantas and Rampes, 2000). In southern Europe, homeopathy has earned peoples trust due its clinical evidences over the conventional pharmaceutical medicines (Avello et al., 2009). At the edge of end of twentieth century, homeopathy has make its own position in the health service; about 500% increases in USA from the age of mid twenty especially in chronic condition including back problems, headaches and anxiety while in European countries it has become more institutionalized. (Eisenberg et al., 1998).

In the nineteenth century, homeopathy was introduced into Bengal, the eastern part of indo-pak subcontinent. It was a practice by amateurs among the both civil and military services, in course of time it flourished and spread out all over the this geographical region. Since 1881, homeopathic medicine has been institutionalized in India whereas, in the year of 1973, government of India has declared homeopathy as a part of national system of medicine and set up a council 'Central Council Homeopathy' to guide and regulate its education, research and practice. In India, Homeopathy is the third most taken medical services, following Allopathy and Ayurveda (Ghosh, 2010). Approximately 14% of total sick population of India, are

taking alternative medicine i.e. homeopathic medicine and their main reason to choosing over the conventional medicine is lack of availability and high price of allopathic medicines along with low price and 'no side effect' concept of homeopathic medicine; the main accusation was slow progress, what represses the acceptance of homeopathy in somewhat (Singh et al., 2005). In Nepal a randomized, double blind and placebo-controlled study evidenced the efficacy of homeopathic medicine in diarrhea (Jacobs et al., 2000). A study revealed that, in Pakistan, use of homeopathic medicine is more popular in women than men in various chronic disease including skin lesions and rheumatism (Shah et al., 2010).

2.10 Homeopathy in Bangladesh

Status of around thirty one percent (31%) of Bangladeshi diseased people prefers homoeopathic medicine instead or as an alternative option (Elahee et al., 2008) ; a large portion of patients believe that in homeopathy they will get relief for a long time in chronic disease; its low cost and 'no side effects' theory are also came up with its study. Patients here seeking help for various diseases including skin disease, gastrointestinal disease, genital and sexual disease in sexes, ENT diseases and musculo-skeletal diseases. More importantly it was observed that, people from higher economy group and young aged patients are fond of taking homeopathic medicine instead of low economy group and aged patients (Elahee et al., 2008). Choosing homeopathic medicine is also provoked by low services in conventional medicine service provider and lack of satisfaction with the given services; as a result, frustrated patients inclined to take health services from abroad and seek help from alternative medicine (Andaleeb et al., 2007). Another study revealed that around 79% of patients are comfortable to use complementary and alternative medicines in contrary to conventional medicine (21%), among them homeopathic medicine found with 23% of patients (Karmakar et al., 2012). Around 70-75% of Bangladeshis are fond of homeopathic medicine and the availability of homeopath is almost 33 homeopaths per 10,000 population, which helps the patients to get this service easily (Rashid et al., 2011). Surprisingly, only 5% of patients get mainstream health services revealed by a researcher and anxiously observed that a large number of 44% is served by traditional healers. Statistical stance of homeopathy in Bangladesh was not measured in recent past yet its popularity in various diseases are evidence based; among them female diseases, sexual diseases of both sexes, tumors and interestingly cancer are in the list

(Rashid et al., 2011). It was thought that homeopathic medicine is cheap and very low economic class people could get health services easily, interestingly it was found that patients from various classes came for treatment including middle, upper-middle and high class patients, this phenomenon also observed in mid-Europe too (Trichard et al., 2005).

The statistical analysis of the patients who are fond of homeopathic medicine, types and distribution of diseases are treated with this medicine and more importantly comparative status of healing percentage in various diseases between homeopathic and conventional medicine are not revealed yet. Many epidemiological studies found to be conducted in many countries including Israel, Pakistan and India; unfortunately, in Bangladesh this sort of studies were not performed in homeopathic services (Organization, 2015).

2.11 Rationale of the study

Otitis media is a serious health concern for developing countries. Moreover, chronic otitis media has drawn major attention for its recurrence and length of sufferings in the children as well as in adults. In addition, CSOM causes hearing impairment which interfere mental growth from childhood. Partial hearing impairment or inability to hearing turns those affected persons mostly deaf causing them avoided socially and affects their scholastic virtue. Conventional treatment using antibiotic is a common practice in CSOM with immense failure due to lack of effective antibiotics. Most of the antibiotics, due to indiscriminate prescription, have become resistant to most known pathogens. Finding an effective alternative medicine for CSOM and CSOM-induced disorders has become a general demand. In this study, homeopathic medicines were used to treat CCSOM patients with an aim to reduce cost as well medicine-related adverse side effects.

2.12 Objective of the study

Specifically the objective of the present study is several folds. These are:

-) Isolation of pathogenic microorganism from the selected patient's aural swab causing CSOM.
-) Identification of the pathogenic microorganism with conventional methods.

-) Evaluating the sensitivity of the isolated microorganisms to homeopathic drugs
-) Identification of potential homeopathic drugs having antibacterial activity for remedies of CSOM.
-) Comparing hearing thresholds between healthy and CSOM patients.
-) Measuring whether CSOM patients undergoes hearing loss.
-) Examining the effects of homeopathic drugs for remediation of hearing impairment.

2.13 Possible outcome from this study

After completion of the study we hypothesize that a number of homeopathic medicines would be found effective for reducing and curing CSOM symptoms. We are also hopeful that perforation of tympanic membrane and hearing impairment associated with CSOM would be ameliorated. Homeopathic medicine is cheaper and mostly devoid of side effects which would encourage people to use as an effective alternative medicine for remediation of CSOM.

Chapter Three

Methods and Materials

3 Methods and Materials

All the participated patients were being included with fulfilling a 'Self-Reporting Questionnaire' form (Annexure-). Patients, who have a history of CSOM for more than 1 year or so, and no antibiotic was taken in last six (6) months, were precisely scrutinized and included in this study. This study was conducted among seventy (70) subjects, who agreed in writing to be a part of this study and continue till its end without any interruption, unless it was obvious. This study was designed to conduct within Dhaka, Bangladesh. Three particular tests were done in all those participants, a) captured images of TM, b) measuring the hearing threshold level of the infected ear and c) microbiological analysis of aural swab collected from the infected ear. The first two tests were done as a part of regular check or examination on every visit, following the very first visit, and continued till the end of eight weeks of homeopathic medication. The third test, microbiological analysis was designed to perform two times, first ear swab sample should be collected from the diseased ear on the very first visit and second sample should be collected from the very same ear, after eight (8) weeks of homeopathic medication.

All the selected patients went through these three distinct tests were done initially at the first visit, before taking homeopathic medicine. Otoscopic images and audiograms were collected on every follow up visit and compared with previous; this was followed till 8th weeks of treatment. And at the end of eight (8) weeks of medication, second aural swab collected from the respected ear, analyzed and compared with first microbiological analysis.

3.1 Ethical permission

Ethical issues were considered as the research involved human subjects. The study was approved by the Ethical Review Committee of the Faculty of Biological Sciences, University of Dhaka (Ref. no. 55/BioSci/2017-2018).

3.2 Selection of CSOM patients for our study

The visiting patients were selected clinically in the health facility, on their first visit, through presenting clinical features, examination of the ear using a digital otoscope

and measurement of hearing threshold level using an iPod, at 1, 4, 8 and 12 kHz frequencies.

3.3 Clinical examinations of the selected patients

The selected patients were suffering from pain in the ear, discharge from the affected ear, fever, redness of the ear with heaviness of the ear.

3.3.1 Microbiological analysis of aural swab

From patients aural swab was collected two times; first collection was done during the first visit of the patient, before taking any homeopathic medicine and the second one was collected at the end of eight weeks of homeopathic treatment.

Aural swab was taken using a cotton swab stick and put in sterile normal saline (0.85% NaCl) solution. The samples were then carried in a cool box and transferred to the laboratory. Sample was stored at 4 °C until microbiological analysis was done.

Saline containing the swab samples were vortexed and 100 µL of each sample was plated on the Tryptic Soy Agar (Oxoid, England) for total count, Mannitol Salt Agar (Merck, Germany) for *Staphylococcus s.*, Cetrimide Agar (Oxoid, England) for *Pseudomonas aeruginosa*, Sorbitol MacConkey (Oxoid, England) agar for *E. coli*, Chromocult Agar (Merck, Germany) for coliform, Bismuth Sulfite Agar (BSA; Oxoid, England) for *Salmonella sp.* and *Klebsiella sp.*, Sabouraud's Dextrose Agar (Active Fine Chemicals Ltd., Bangladesh) for total count of fungus, yeast and mold. Plates were incubated at 37°C for 24 to 48 hrs. For specific identification of the isolated microorganisms biochemical tests were performed using specific API 20E kit

3.3.1.1 Antimicrobial sensitivity assay of the isolated pathogenic microorganisms with conventional antibiotics and homeopathic medicine

Antimicrobial sensitivity assay of the isolated pathogenic microorganisms was done with antibiotics and homeopathic drugs by agar diffusion well method. Individual isolates were cultured up to 0.5 MacFarland standards in nutrient media and 100 µL of the isolates were spread on Muller Hinton agar (Difco, USA). Antibiotic discs were then placed and incubated overnight at 37°C. After that, zone of inhibition was measured (in mm) and compared with the standard chart to determine their sensitivity.

Antibiotic discs (Oxoid, England) of Cefixime (5µg), Ciprofloxacin (5 µg), Azithromycin (15 µg), Ceftazidime (30 µg), Erythromycin (15 µg), Tetracycline (30 µg), Streptomycin (10 µg), Kanamycin (30 µg), Aztreonam (30 µg), Gentamicin (10 µg), Bacitracin (10 µg), Nitrofurantoin (300 µg), Chloramphenicol (30 µg), Pipracilin/Tazobactam (110 µg), Amoxicillin (25 µg), Rifampicin (30 µg) were used. Homeopathic drugs of *Tellurium metallicum* 6C), *Mercurius solubilis* (200C) and *Calcarea sulphurica* (30C) were used.

3.3.2 Ear examination with otoscope

The study subject’s ear canal and tympanic membrane was examined with a digital endoscopic otoscope (Blueskysea, Guangdong-China) and images were captured time to time till the end of eight weeks of treatment. This procedure helps to differentiate between physiological and pathological appearance.

Procedure followed during the examination of tympanic membrane using otoscope:

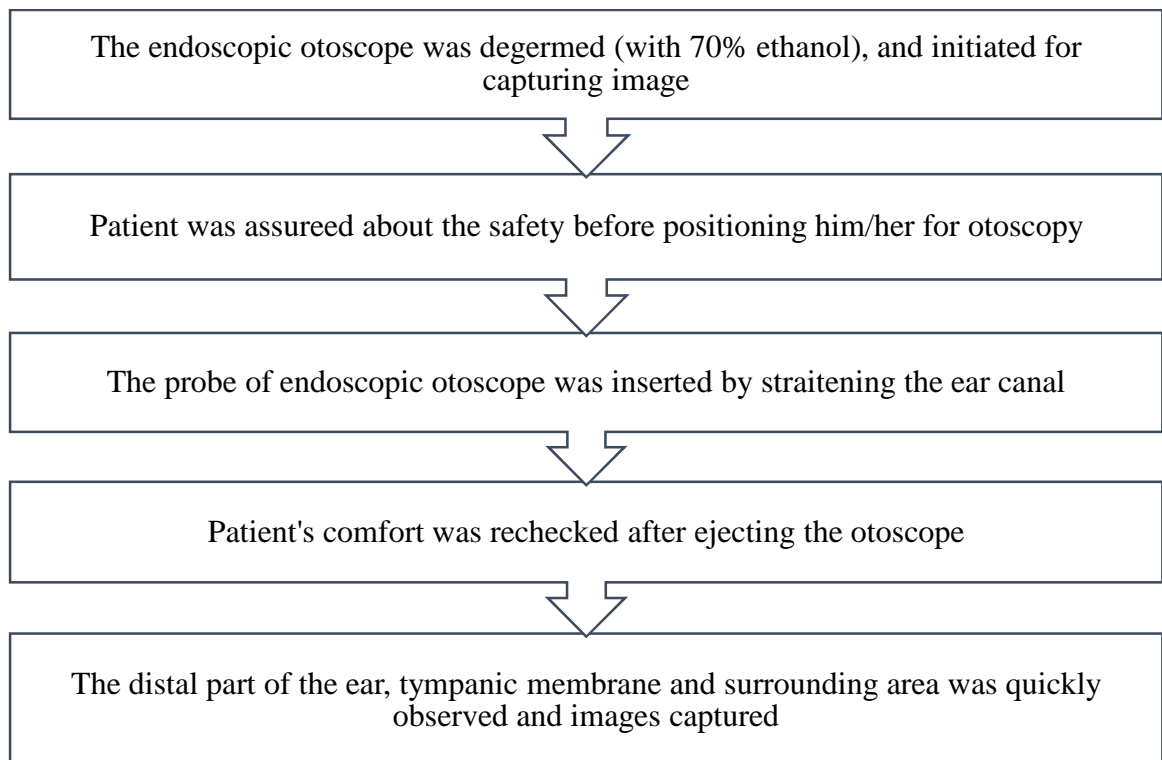




Figure 3.1 Examination of ear using a digital endoscopic otoscope. With aseptic precaution examining the ear canal and tympanic membrane with a digital endoscopic otoscope, images captured and stored.

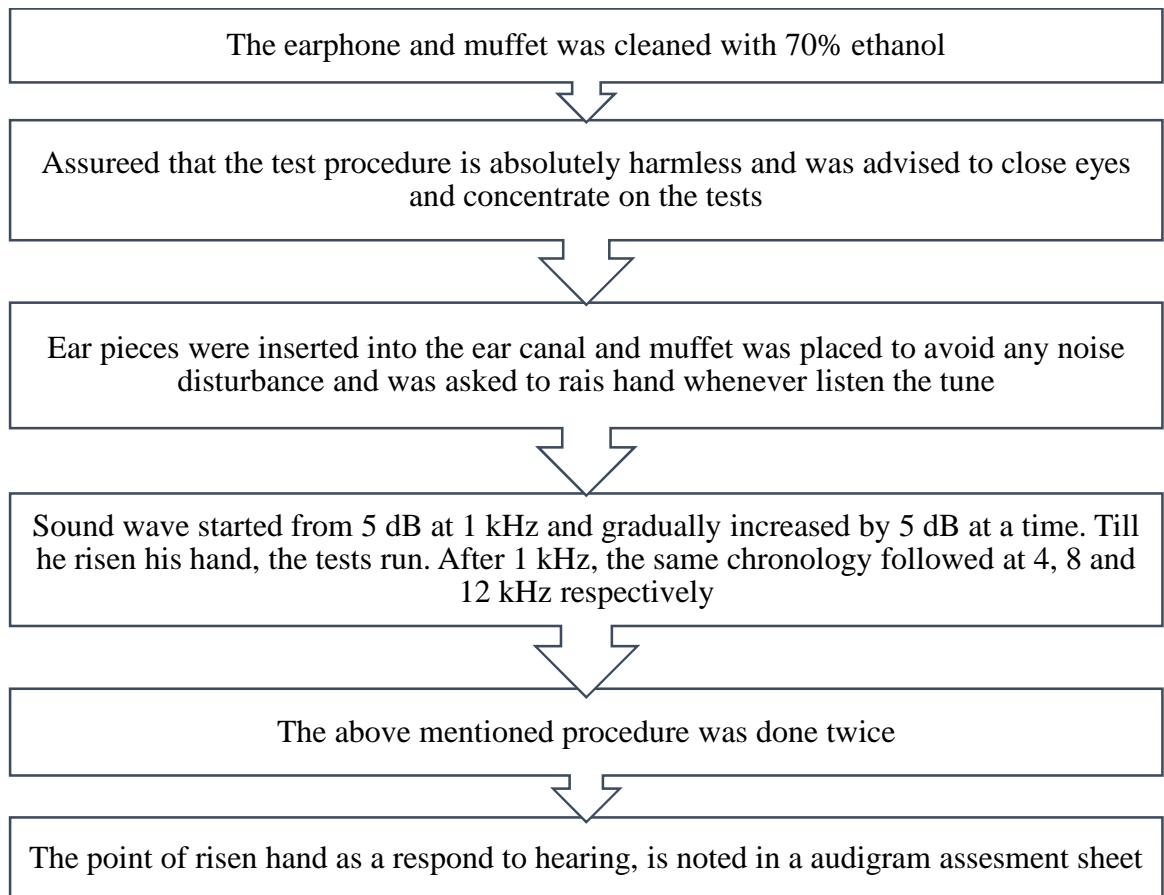
3.3.3 Measuring hearing threshold level of the patients

It is a recognized examination process of presumption of hearing threshold level using a sophisticated iPod with earphones in a sound proof room (Van Tasell and Folkeard, 2013; Sumit et al., 2015; Das et al., 2018). All participated patient's hearing threshold level were measured at 1, 4, 8 and 12 kHz frequencies in various decibels (dB), started from 5 dB and progressively increased by 5 dB each time. To avoid perception error on patient and physician end, the test was done twice. From the beginning to the end of eight weeks of treatment using homeopathic medicine this same procedure was followed for few times.



Figure 3.2 Presuming hearing threshold level. Using an iPod at 1, 4, 8, and 12 kHz frequencies. The. Patient was asked to raise his hand in response to hearing the tone

The procedure followed in presuming hearing threshold level:



3.4 Prescribed homeopathic drugs and doses to the patients

We divided our patient sample into three groups 1. TM (Tellurium metallicum advised to 17 individuals) 2. MS (Mercurius solubilis prescribed to 13 individuals), and 3. CS (Calcarea sulphurica dispensed to 10 individuals) according to the following table (Table 3.1).

In case of group TM, within 2 ounces (60 ml) distilled water 0.5 ml tellurium metallicum 6C dissolved and advised to take orally, 2 ml/24 hrs, before meals, for four weeks. After that, the development of tympanic membrane was assayed through otoscopy and measuring the hearing threshold level. They were given the same medicine for the next four weeks. Whereas in case of MS group, mercurius solubilis, (0.5 ml of 200C potency), added in 60 ml distilled water was prescribed. For another group named CS, the Calcarea sulphurica (0.5 ml of 30C potency) mixed with 60 ml

distilled water was prescribed. The duration and dose of MS and CS group were similar as describe above for TM group.

Table 3.1 Selective characteristics of the CSOM patients

Group	No. of patients treated	Inclusion Characteristics
group TM	17	# CSOM with constant thin pus with pungent or garlicky odor # Tympanic membrane perforation # Hearing impairment (due to insufficient transmission of sound wave to cochlea)
group MS	13	# CSOM with yellow thick, pus # Pain with suppuration in the ear drum and Eustachian tube # Hearing impairment with tinnitus, better on deglutition (due to pus in the middle ear cavity)
group CS	10	# CSOM with pus, may be thick or thin, greenish-yellow in color # Occasional balance issue with tinnitus # Hearing impairment with slow tendency to heal

Chapter Four

Results

4 Results

The study was conducted with patients who were suffering from CSOM and underwent a treatment procedure. The treatment group was sub-divided in three distinct groups based on the type of medicines provided. More specifically, 17 patients were in 'TM' group who were treated with Tellurium metallicum; 13 patients were given Mercurius solubilis who were grouped as 'MS'; and 10 patients were treated with Calcium sulphurica, who were under 'CS' group. Apparently healthy thirty (30) subjects were also included in this study as controls.

4.1 Characteristic profile of the study participants

A total of 70 subjects was included in this study, among them, 30 (42.85%) were healthy control and 40 (57.14%) were patients who were treated with homeopathic medicine (Table 4.1). The number of male and female participants were 42 (60%) and 28 (40%), respectively. Among the male participants, 18 (42.85%) were in the control group and 24 (57.14%) in the treated group; whereas among the female participants, 12 were (42.85%) in control and 16 (57.14%) in the treated group. Average age of male was calculated 34.96 ± 2.66 years and that of female was 28.25 ± 2.33 years. Mean body mass index (BMI) of all participants was 24.41 ± 0.69 and for control and treated groups it was 25.46 ± 0.92 and 24.13 ± 0.82 , respectively. The participating subjects were further categorized as under-, normal- and over-weight based on their BMI value of < 18.5 , $18.5-25$ and > 25 kg/m^2 , respectively. The number of treated patients belonging to under-, normal- and overweight was 4 (10%), 19 (47.5%) and 17 (42.5%), respectively, while that of the control subjects was 0 (0%), 22 (73.33%) and 8 (26.66%), respectively. The least number of subjects was found to be under-weight in the treated group and no-one was in control. Among the 40 CSOM patients, 8 (20%) were suffering from the disease for ≤ 2 years and the remaining 32 (80%) for > 2 years.

4.2 Clinical features of the study participants

Most of the patients were having similar clinical features. All of the attending patients were experiencing pain in the ear (otalgia), and some were experiencing mild to moderate hearing impairment, discharge from ears (otorrhoea), fever, heaviness and reddish ear (Figure 4.1).

Table 4.1 Baseline characteristics of the study participants

Variable		Participants	Control	Treated
Total No.		70	30 (42.85%)	40 (57.17%)
Gender				
	Male: n (%)	42 (60%)	18 (60%)	24 (60%)
	Female: n (%)	28 (40%)	12 (40%)	16 (40%)
Age				
	Male	34.96±2.66		
	Female	28.25±2.33		
BMI Kg/m ² (Mean ± S.E.)		24.41 ± 0.69	25.46 ± 0.92	24.13 ± 0.82
BMI category*				
	Underweight	4 (5.71%)	-----	4 (10%)
	Normal weight	27 (38.57%)	22 (73.33%)	19 (47.5%)
	Overweight	39 (55.71%)	8 (26.66%)	17 (42.5%)
Duration of Disease				
	2 years			8 (20%)
	> 2 years			32 (80%)

B The subjects were categorized as underweight, normal weight and overweight when the BMI was found <18.5, 18.5-25 and >25 kg/m², respectively.

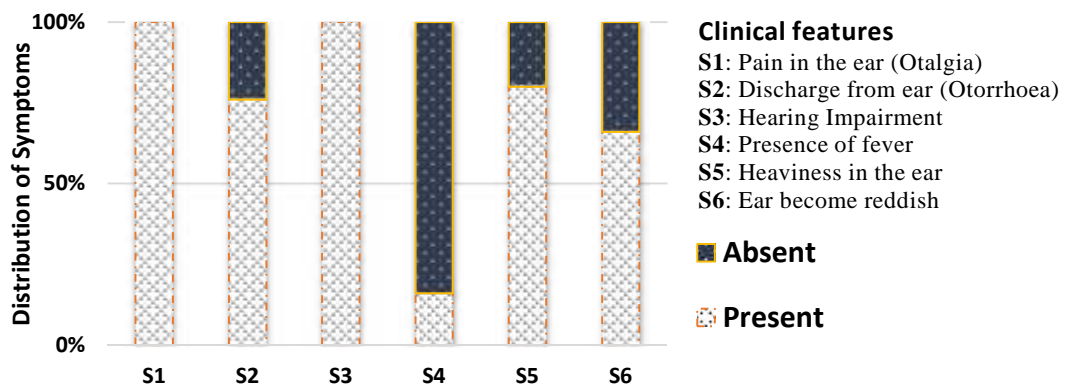


Figure 4.1 Clinical features of the study participants. S1 (Otalgia) was present in 100% participants, S2 (Otorrhoea) was present in 75% patients, S3 (hearing impairment) was present in 100% patients, S4 (Fever) was presented in 15% patients, S5 (heaviness in the ear) was in 80%, S6 (Reddish ear) was in 65% patients

4.3 Characteristics of the discharge from the patient's ear

During observation of the ear canal, characteristics of the aural discharge of all 40 patients were examined in three different parameters i.e. odor, quantity and type of discharge (Table 4.2). When examining odour the odor of discharge, around 76% patient was found to contain discharge with malodors and 24% odorless. When the quality of discharge was examined, profuse discharge was found in 80% cases, while scanty discharge was observed in 20% cases. Lastly, mucoid type discharge was seen in 52% cases, serus type 32% and purulent type 15%.

Table 4.2 Characteristic of ear discharge

Total no. of patients	Odor of discharge		Quality of discharge		Type of discharge		
	Odorless (%)	Malodorous (%)	Scanty (%)	Profuse (%)	Muroid (%)	Serous (%)	Purulent (%)
40	10 (25%)	30 (75%)	8 (20%)	32 (80%)	21 (52%)	13 (32%)	6 (15%)

4.4 Findings of microbiological analysis of the sample aural swab

Various agar plates were used and standard procedures were followed to sort out the possible causative pathogenic microorganisms. Microbial colony was revealed with TSA plate (Figure 4.2A). *Staphylococcus sp.* was observed in MSA plate (Figure 4.2B), and black colonies were observed in BSA plate (Figure 4.2C).

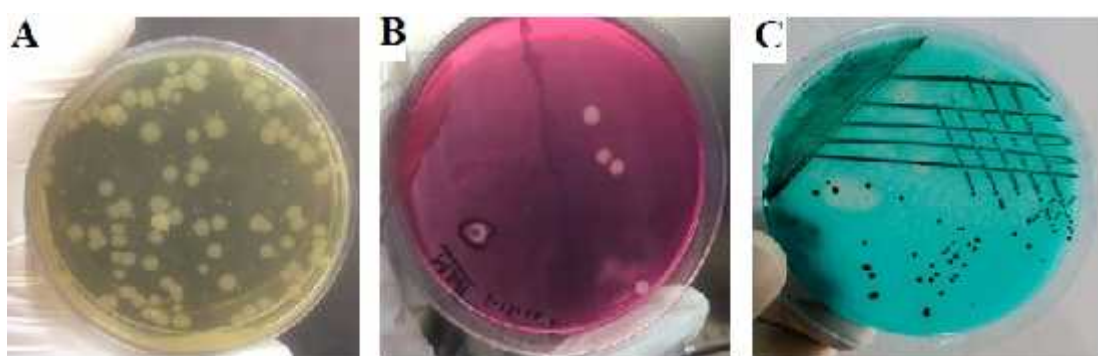






Figure 4.2 Representative images of microbial colonies on different agar media plate. Whitish colonies on the TSA plate (A), white colonies on MSA plate (B) and (C) black colonies on BSA plate

4.4.1 Isolation and identification of microorganisms from the collected aural swab

The aural swabs positive for microbial growth were primarily selected according to their cultural characteristics. It was presumed that yellow, convex, small to medium size colony on MSA media was *Staphylococcus sp.*; deep purple medium sized flat colony on CHR agar was *E coli*; yellow gummy medium sized colony on XLD was *klebsiella sp.*, (Table 4.3). After preliminary selection, identification of the isolated colonies was confirmed with Analytical Profile Index (API). API 20E was used for identification of gram negative bacteria i.e. *E coli*, *klebsiella sp.*, and *salmonella sp.*; identification of *Staphylococcus sp.* was done using API *Staph.* (Table 4.3).

Table 4.3 List of microbes isolated from the sample aural swab. Cultural characteristics of various microbes and representing selected API stipe images

Name of the bacteria	Cultural Characteristics		Representing selected API Image.
<i>Staphylococcus sp.</i>	Color	Yellow, golden yellow on MSA	
	Size	Small to Medium	
	Shape	Convex	
<i>E coli.</i>	Color	Pink on Sorbitol MacConkey	
	Size	Medium	
	Shape	Flat	
<i>Klebsiella sp.</i>	Color	Yellow (Gummy Yellow) on XLD	
	Size	Medium	
	Shape	Convex	
<i>Kluyvera sp.</i>	Color	Violate on CHR	
	Size	Small	
	Shape	Round, irregular edge.	

4.4.2 Understanding the conventional antibiotic sensitivity of the selected isolated microbes

After identification of various pathogenic microbes, their anti-biogram was done with conventional antibiotics in agar disc diffusion method and the following results were obtained. In this study, the most found pathogenic microbes were *K. pneumoniae*, *E. coli* and *K. oxytoca*, few of them were randomly selected for anti-biogram with conventionally used antibiotics. 'Rifampicin' was used as 'control' for antibiotic

resistance. According to this study, seven antibiotics such as cefixime, ceftazidime, erythromycin, tetracycline, bacitracin, amoxicillin and rifampicin had been found resistant against the selected microbes. Only few antibiotics were found sensitive including ciprofloxacin, aztreonam and chloramphenicol (Table 4.4). Other antibiotics mostly showed intermediate activity.

Table 4.4 Antibigram assay of pathogenic microorganisms isolated from CSOM patients

Antibiotic	Diameter of zone of inhibition (mm) for the strain		
	<i>E. Coli</i>	<i>K. pneumoniae</i>	<i>K. oxytoca</i>
Cefixime	09 mm	06 mm	06 mm
Ciprofloxacin	26 mm	12 mm	24 mm
Azithromycin	15 mm	12 mm	11 mm
Ceftazidime	06 mm	06 mm	06 mm
Erythromycin	06 mm	07 mm	06 mm
Tetracycline	06 mm	07 mm	08mm
Streptomycin	10 mm	18 mm	15 mm
Kanamycin	12 mm	15 mm	15 mm
Aztreonam	22 mm	20 mm	18 mm
Gentamicin	15 mm	17 mm	13 mm
Bacitracin	06 mm	06 mm	06 mm
Nitrofur	14 mm	12 mm	12 mm
Chloramphenicol	24 mm	13 mm	24 mm
Pipracilin/Tazabactum	13 mm	10 mm	10 mm
Amoxicillin	06 mm	06 mm	06 mm
Rifampicin	06 mm	06 mm	06 mm

4.4.3 Assessment of antimicrobial activity of homeopathic medicine on isolated microbes

As a part of our study, we tried to find out the antimicrobial property of homeopathic medicine in conventional agar disc diffusion method. As shown in Figure 4.4, Tellurium metallicum and mercurius solubilis (dissolved in 90% ethanol) showed a little larger zone of inhibition than the '90% Ethanol Control'. Bacteria were sensitive to the antibiotic ciprofloxacin; however, no significant antibacterial activity was shown by the homeopathic drugs used in this assessment. As homeopathic drugs were used in much diluted form, bacteria were probably weakly sensitive.

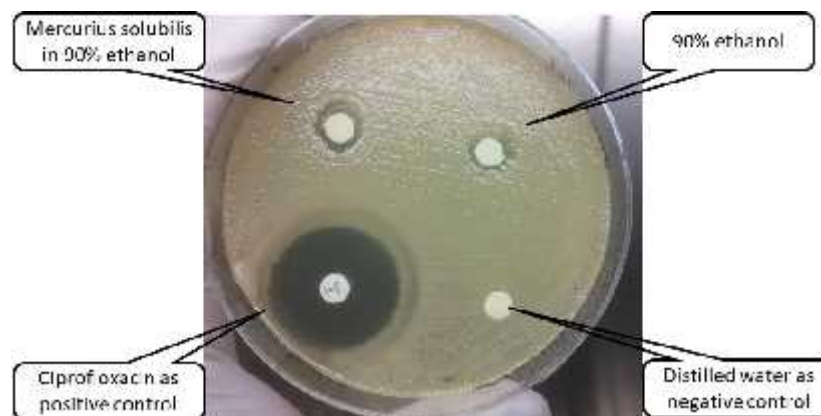


Figure 4.3 Antimicrobial activity of homeopathic medicine on agar disc diffusion. *Klebsiella pneumoniae* was cultured in presence of ciprofloxacin and different homeopathic medicine as indicated

4.5 Homeopathic medicines reduced total microbial count

Aural swab of the study patients before and after treatment with homeopathic medicine was analyzed for assessing microbial counts. Significant reduction of average microbial load was observed after homeopathic treatment.

Three medicines that were applied to the patients are Tellurium metallicum, Mercurius solubilis and Calcarea sulphurica. Among the three treated groups, the TM group was the largest group consisting of seventeen (17) patients. The total aerobic bacterial colony count (TABC) of the aural swab before applying Tellurium metallicum was 7.25 ± 0.45 log CFU/ml.

A significant reduction ($p < 0.05$) of TABC (5.11 ± 0.23 log CFU/ml) was observed after applying Tellurium metallicum. Average load of *Staphylococcus* sp. was also reduced from 4.65 ± 0.19 log CFU/ml to 3.68 ± 0.12 log CFU/ml, and this reduction was also statistically significant ($p < 0.05$). Total coliform counts (TCC) before and after

Tellurium metallicum treatment were 5.52 ± 0.58 and 3.27 ± 0.20 log CFU/ml, respectively; and again average TCC was significantly reduced ($p < 0.05$). Similar significant reduction of total fungal count (TFC) was also observed after applying Tellurium metallicum (Figure 4.4).

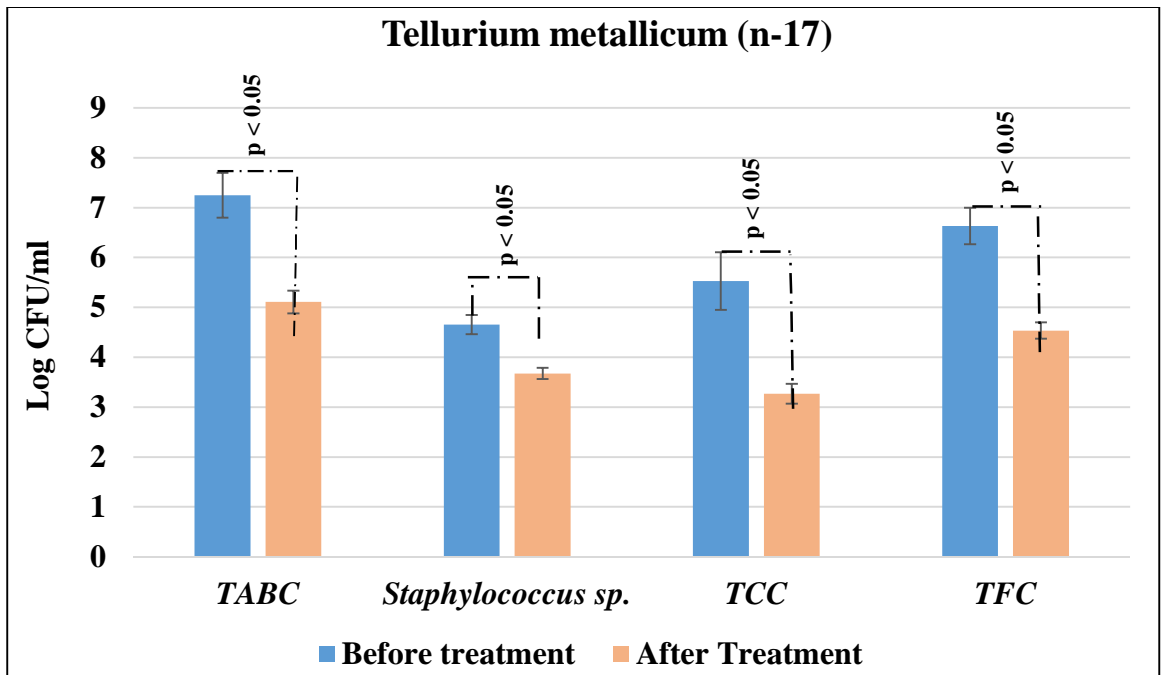


Figure 4.4 Tellurium metallicum reduces microbial load significantly. TABC: Total aerobic bacteria count, TCC: Total coliform count, TFC: Total fungal count

MS and CS also reduced TABC, *Staphylococcus sp.*, TCC and TFC load significantly (Figure 4.5 and 4.6)

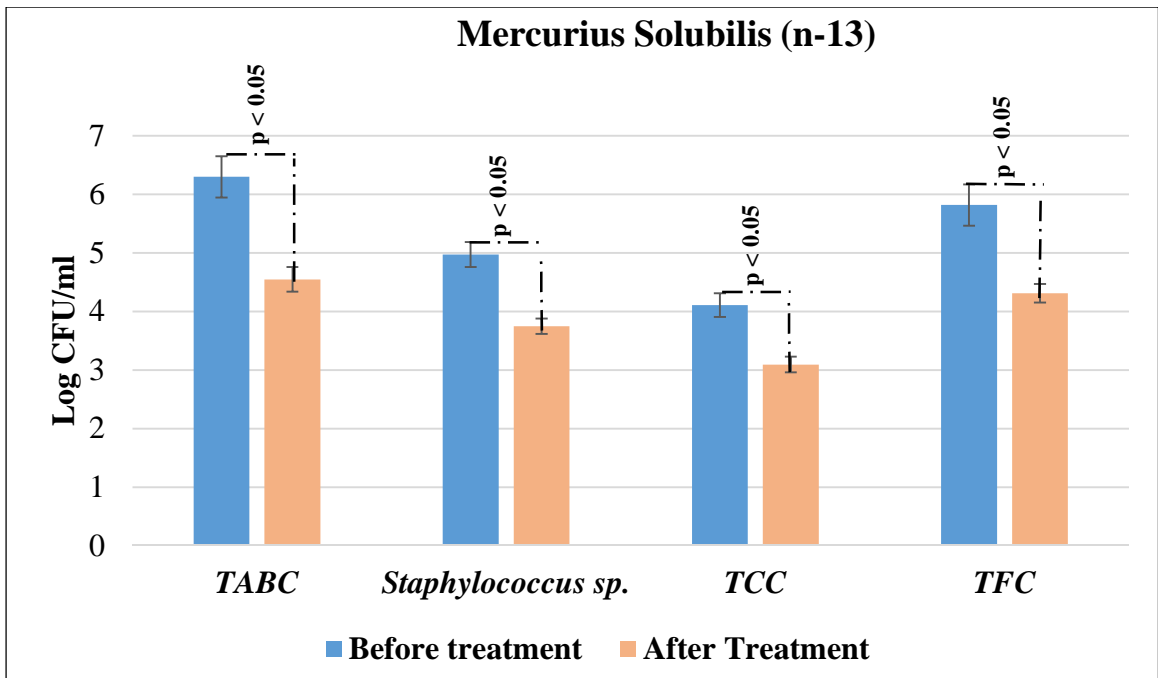


Figure 4.5 Mercurius solubilis proved its efficacy in reduction of total microbial load. TABC: Total aerobic bacteria count, TCC: Total coliform count, TFC: Total fungal count

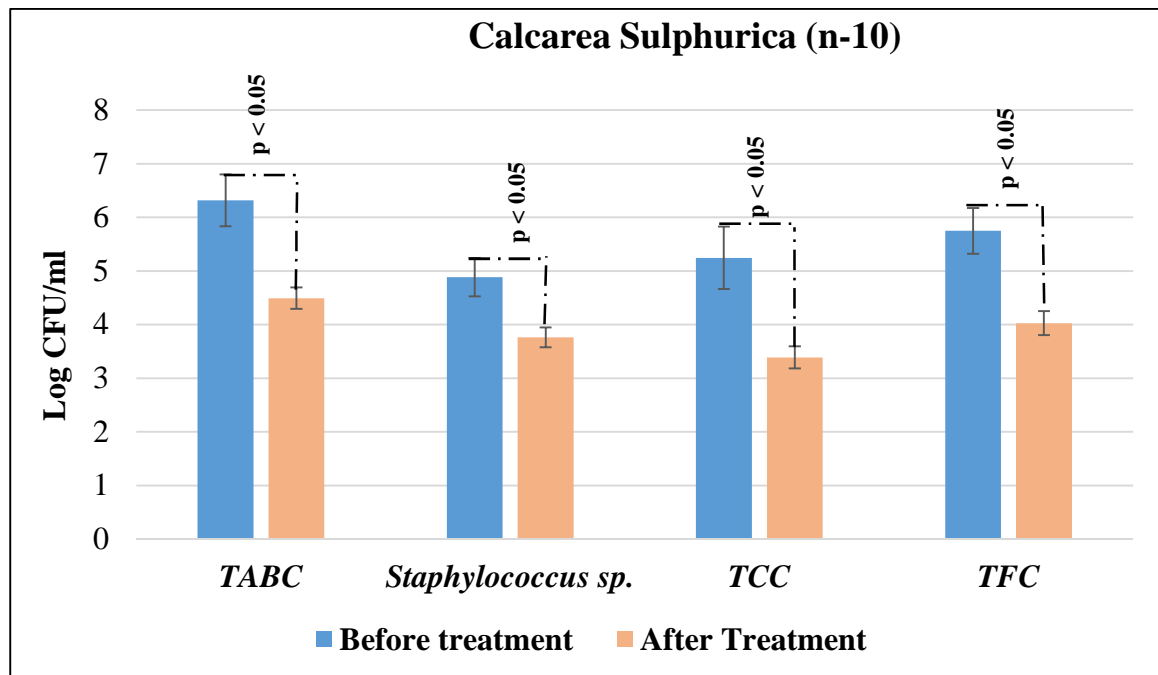


Figure 4.6 Calcarea sulphurica announces its property in reduction of microbial load. TABC: Total aerobic bacteria count, TCC: Total coliform count, TFC: Total fungal count

4.6 Homeopathic medicine prevented suppuration and tympanic membrane perforation in the ear

In most cases, CSOM involves discharge from the middle ear through a perforated tympanic membrane. Perforation or structural changes of tympanic membrane mainly occurs due to chronic inflammation associated CSOM. Therefore, the ear canals of the CSOM patients were examined using an otoscope to observe any structural changes/perforation of tympanic membrane associated with middle ear effusion.

Seventeen (17) patients suffering from CSOM were given Tellurium metallicum and their ear canals were examined every 4 week with otoscope. Invariably all the patients were experiencing middle ear effusion associated with tympanic membrane perforation. However, the degree of membrane perforation varied among those patients. Seventeen (17) patients were treated with Tellurium metallicum, all of whom were suffering from ear suppuration and having tympanic membrane perforation (Table 4.5). Ear suppuration was prevented in all the patients with the drug; however, the perforated membranes of 9 patients (52.9%) were healed. Here the otoscopic results of three representative patients are shown (Table 4.5). In the first case, two distinct sites with perforations (indicated by red arrow) were visualized at the right tympanic membrane of the patient (Figure 4.7A). Healing of these perforations gradually occurred with time as the patient completed the course of the drug in 8 weeks (Figure 4.7 B and C). The cicatrized or healed site is indicated with red arrow.

Table 4.5 Effect of homeopathic medicine on ear suppuration and healing of membrane perforation

Homeopathic medicines used for treatment	Total no. of patients treated	Ear suppuration		Tympanic membrane perforation	
		Before treatment	Prevented after treatment	Before treatment	Healed after treatment
Tellurium metallicum	17	17	17	17	9
Calcarea sulphurica	10	10	10	10	5
Mercurius	13	13	13	13	0

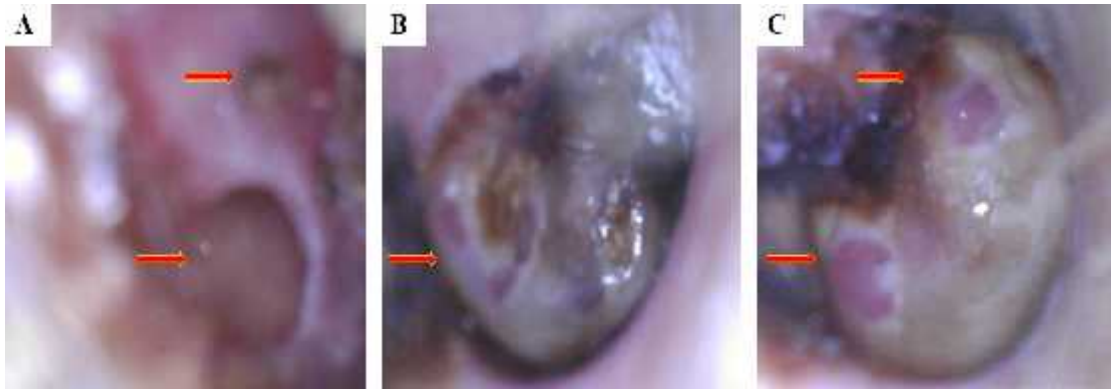


Figure 4.7 Healing of perforated tympanic membrane by Tellurium metallicum. Patient's ear was examined using a digital otoscope. Images of tympanic membrane were captured before the treatment started (A). Images were again taken after 4 weeks (B) and 8 weeks (C) of tellurium metallicum medication. In image B, aggregation of pus also observed

The otoscopic ear views of another patient (2nd case) are shown in Figure 4.8. The pars flaccid portion of the tympanic membrane of this patient was associated with perforation (indicated with arrow) (Figure 4.9A). Healing of this perforated membranes gradually occurred due to intake of tellurium metallicum (Figure 4.9B and C)

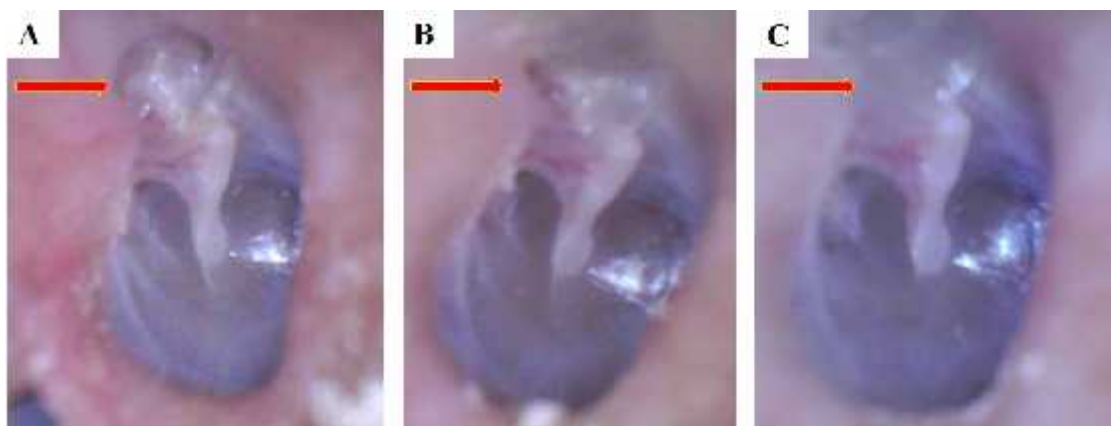


Figure 4.8 Healing of perforated 'Pars Flaccida' by tellurium metallicum. Using an endoscopic otoscope, pictures of the tympanic membrane were taken before initiating treatment (A). Follow up images were taken in 4 weeks (B) and 8 weeks (C) of tellurium metallicum treatment

It was next examined whether calcarea sulphurica and mercuris solibulis could also be able to heal membrane perforation and ear supuration. Among the 10 patients treated with calcarea sulphurica, ear supuration was prevented in all patients, however, perforated membranes of 5 (50.46%) patients were healed (Table 4.5).

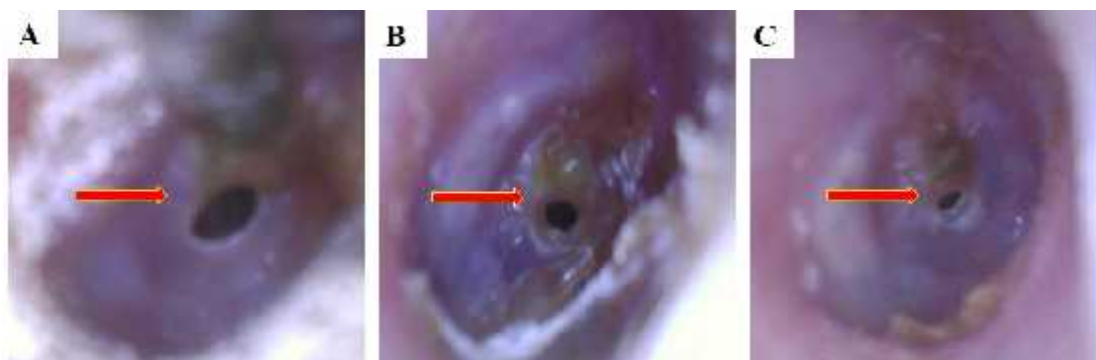


Figure 4.9 Gradual improvement of tympanic membrane perforation by tellurium metallicum. Otoscopic pictures showing tympanic membrane before treatment (A), after 4 weeks (B) and 8 weeks (C) treated by tellurium metallicum

On the other hand, mercurius solubilis could not trigger healing of membrane perforation, although it controlled ear suppuration (Table 4.5).

4.7 CSOM patients underwent hearing impairment

In most cases, CSOM patients also experience hearing impairment due to inflammation in their middle ear. It was examined whether the patients also had hearing impairment compared to healthy control subjects. The average hearing thresholds of the control subjects (n=30) at 1, 4, 8 and 12 kHz frequencies were 13.55 ± 1.57 , 15.58 ± 1.12 , 27.58 ± 2.00 and 32.57 ± 2.45 dB SPL, respectively. When the average hearing thresholds of the CSOM patients (n=40) were measured at all of the frequencies mentioned above, we found the values as 30.25 ± 1.75 , 36.80 ± 3.25 , 50.75 ± 2.35 , and 59.50 ± 2.96 dB, respectively (Figure 4.10). The threshold of hearing is known to be frequency-dependent. In our study, we observed an increase in mean hearing thresholds with increasing sound frequency in both cases of control and CSOM patients. The hearing level is measured in dB; and the values exceeding 20 dB at low frequencies (1 and 4 kHz) and values exceeding 40 dB at high frequencies (8 and 12 kHz) indicate hearing impairment. The higher values of dB indicate higher degree of hearing impairment. When compared with the control subjects, the average hearing thresholds of the CSOM patients at all the frequencies tested were significantly higher ($p < 0.05$). These results suggest that the control subjects had better hearing overall, whereas the CSOM patients experienced deterioration of hearing at all the frequencies tested.

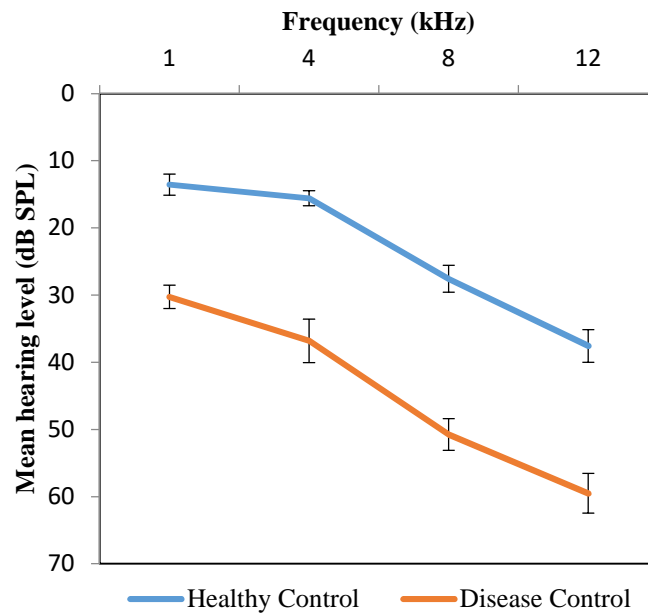


Figure 4.10 Hearing threshold level measured by using iPod. Average hearing thresholds (mean \pm SEM) measured in 1, 4, 8 and 12 kHz frequencies of control (n-30) and CSOM patients (n-40)

4.8 Homeopathic medicines improved hearing thresholds in CSOM patients

The average hearing thresholds of the 'TM' group patients (n=17) (before they started taking tellurium metallicum) at 1, 4, 8 and 12 kHz frequencies were 31.91 ± 2.11 , 41.32 ± 2.43 , 54.85 ± 2.51 and 65 ± 2.56 dB SPL, respectively (Figure 4.11). These values of the average hearing thresholds of the patients indicated that the patients were experiencing hearing loss both at low and high frequencies. After eight weeks of tellurium metallicum medication, the hearing threshold levels at all the frequencies were measured again and the obtained values were 17.94 ± 1.66 , 23.97 ± 1.86 , 39.11 ± 2.15 and 44.70 ± 2.25 dB SPL, respectively. The hearing thresholds at all the frequencies after 8 weeks of medication were significantly reduced ($p < 0.05$). This result clearly indicated improvement of hearing thresholds by homeopathic medicine at all the frequencies tested.

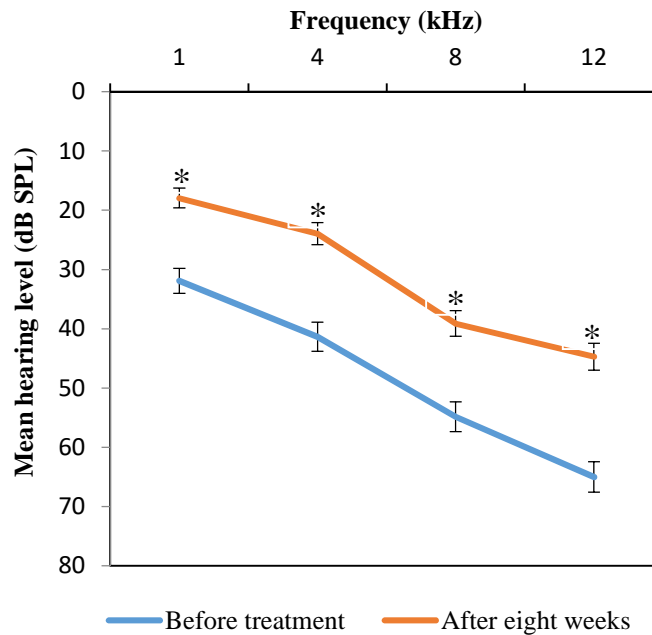


Figure 4.11 Tellurium metallicum-mediated improvement of hearing threshold. Average hearing thresholds (mean \pm SEM) at 1, 4, 8 and 12 kHz frequencies of CSOM patients before and after 8 weeks of Tellurium medication. *Significantly different ($p < 0.05$)

Another homeopathic medicine, mercurius solubilis, was also prescribed to the patients (MS group) to observe its effect on hearing improvement. The average hearing thresholds of the patients ($n=13$) (before they started taking mercurius solubilis) at 1, 4, 8 and 12 kHz frequencies were 32.11 ± 1.24 , 41.15 ± 1.34 , 52.88 ± 0.80 and 62.5 ± 1.60 dB SPL, respectively (Figure 4.12). After eight weeks of medication, the values of the hearing threshold became 14.80 ± 1.16 , 21.53 ± 1.52 , 34.42 ± 1.12 and 41.73 ± 1.16 dB SPL, respectively. It was clearly observed that mercurius solubilis caused significant reduction ($p < 0.05$) of the hearing thresholds at all the frequencies after 8 weeks of medication.

Similar results were obtained when calcarea sulphurica were used for eight weeks in CS group patients ($n=10$) (Figure 4.13). All of the above medicines significantly improved hearing thresholds in CSOM patients. These results are particularly encouraging because CSOM-mediated hearing loss is treatable with homeopathic medicines cost effectively.

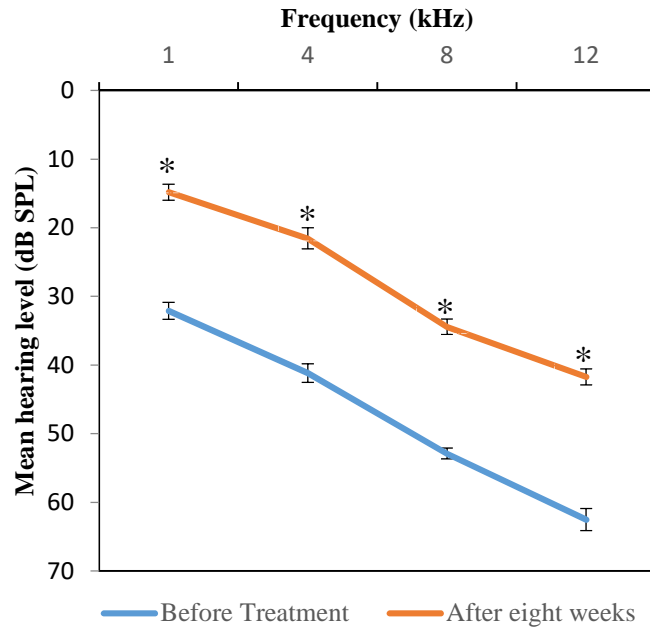


Figure 4.12 Mercurius solubilis enhanced hearing threshold. Average hearing thresholds (mean \pm SEM) at 1, 4, 8 and 12 kHz frequencies of CSOM patients before and after 8 weeks of mercurius solubilis medication. *Significantly different ($p < 0.05$)

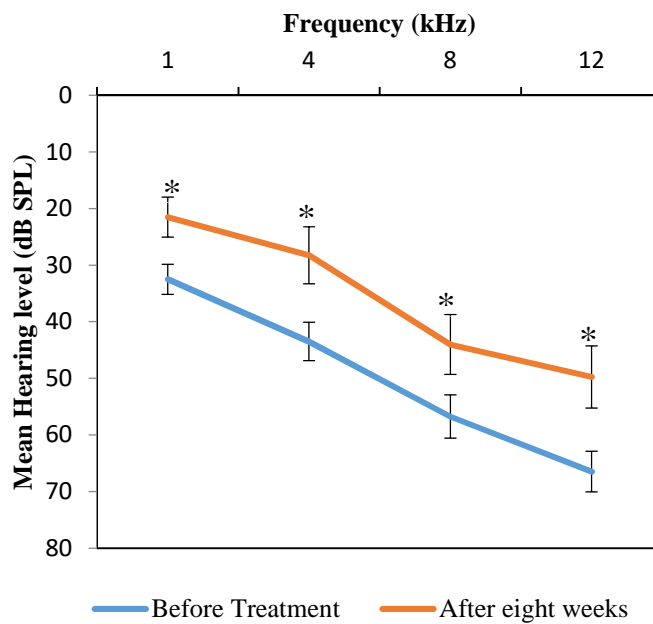


Figure 4.13 Calcarea sulphurica improved hearing threshold. Average hearing thresholds (mean \pm SEM) at 1, 4, 8 and 12 kHz frequencies of CSOM patients before and after 8 weeks of calcarea sulphurica. *Significantly different ($p < 0.05$)

Chapter Five

Discussion

5 Discussion

Adult with CSOM is common in developing countries like Bangladesh, though the actual prevalence of this disease is not determined yet (Merkus, 2017, Akinpelu et al., 2008). Usually antibiotics are prescribed for the treatment of this disease. But drug resistant microorganisms are developing day by day, making the infection scenario worsen. Moreover, complicity arising from tympanic membrane perforation and hearing impairment is not recovered from this treatment procedure. This study, for the first time, demonstrated that the various homeopathic medicines work well for the treatment of CSOM. Here, we showed the healing of perforated tympanic membrane and improvement of hearing threshold levels using homeopathic medicines.

The incidence of CSOM is not figured out in Bangladesh, however, among the patients participated in this study, males are more prone than females (ratio is 3:2) for this chronic infection. The average age of the male and female patients in our study was 34.96 ± 2.66 and 28.25 ± 2.33 years, respectively and the average BMI was within normal level (Table 4.1).

It is sometimes difficult to choose proper remedial actions for a group of patients due to lack of similar symptoms as well as response to similar stimuli (Hahnemann, 1982). In this study, a set of common symptoms were analyzed and prescribed accordingly (Table 3.1). CSOM patients with thin, pungent or garlicky odorous pus, perforation of tympanic membrane and impaired hearing due to lack of transmission of sound wave into the cochlea, were treated with tellurium metallicum (Boericke, 2002; Murphy, 2003; Vermeulen, 1997; Hering, 1879). Patients suffering from CSOM, discharging thick yellow pus, pain in the eustachian tube and partial deafness relieved on deglutition were treated with mercurius solubilis. Calcarea sulphurica was selected for CSOM with yellow, greenish-yellow lumpy pus, thin or thick, long lasting suppurative lesion, partial deafness with humming in the ear and associated with balance issue (Murphy, 2003; Boericke, 2002; Vermeulen, 1997; Hering, 1879).

In our study, we found that different types of pathogenic microorganisms were isolated from each patients samples indicating a group of pathogens were responsible for this disease (Abdelshafy et al., 2015). Among the isolated pathogens the most common was *Klebsiella pneumoniae*, *K.oxitoca* and *E coli*. Besides these pathogens,

Staphylococcus sp. and *Kluyvera* sp. was also found. In antibiotic sensitivity assay, we observed that isolated organisms were resistant almost 50% of the antibiotic tested. Isolates showed weak sensitivity against cefixime and azithromycin. However, ciprofloxacin and chloramphenicol were found sensitive to *E. coli*. and *K. oxitoca* but not against *K. pneumoniae* (Table 4.4).

Tellurium is known to act against *E. coli*, *K. pneumoniae* and *S. aureus*. (Gupta et al., 2016). A recent study demonstrated that metallic compounds like tellurium can induce effective antimicrobial activity when used in very low concentrations (Jassim et al., 2015). Tellurium showed less cytotoxicity and enhance anti-oxidant property in mammalian cell (Zhong et al., 2013). On the other hand, homeopathically prepared mercurius solubilis was shown to control bacterial growth (de Araújo et al., 2009), and inflammation effectively (Vangoori et al., 2013). In addition, mercurius solubilis was also shown to reduce genotoxic effects in human cells (Das et al., 2015, Datta et al., 2004) and control scopolamine-induced damage of brain cells and memory loss (Kaur et al., 2018). Calcarea sulphurica, in contrast, was reported to help bone-tissue regeneration and to control circulatory disturbance and chronic inflammation (Jaffe et al., 2014). In this study, CSOM patients were treated with all three homeopathic medicines in separate groups for 8 weeks. Our results clearly demonstrated that tellurium metallicum, mercurius solubilis and calcarea sulphurica prevented ear suppuration in all the patients (Table 4.5). In addition, microbial load in ear discharge was significantly reduced. Moreover, tellurium metallicum and calcarea sulphurica induced healing of perforated tympanic membrane (Table 4.5). More importantly we observed that all the medicines improved hearing thresholds significantly in all of the patients. All these results are very encouraging because frequently occurring CSOM and related disorder can be treated cost effectively without having any side effects.

It has been observed over the last few decades that use of homeopathic medicines has substantially increased worldwide as an alternative medicine (Organization, 2001). In recent years, several clinical trials have evidenced the effectiveness of homeopathic medicines for treatment of various serious illnesses. An earlier study showed significant improvement of patients with homeopathic treatment, where conventional treatment had been unsatisfactory or contraindicated (Sevar, 2000). In Bangladesh, homeopathy dug treatment co-exists strongly with other forms of treatment. However,

no significant basic research or research involving treatment of patients with homeopathic medicines is so far carried out. In this study, we tried to thoroughly examine the effects of three homeopathic medicines in a group of CSOM patients that produced valuable and effective results. We strongly believe that the results obtained in this study will act as a reference source for the effectiveness of homeopathic medicines and also encourage us to prefer homeopathic treatment for CSOM and other disorders.

The exact mechanism, by which the homeopathic medicines used in this study, repaired damaged tympanic membrane and improved loss of hearing is still unclear. However, some previous studies demonstrated that cochlear damage in patients with CSOM might be due to the toxins released by infectious microorganisms that diffuse through the damaged tympanic membrane (Spandow et al., 1989; Goycoolea et al., 1980). Subsequently, these toxins might cause damage to the hair cells at the cochlear base; where the hair cells are sensitive to sound frequencies. The homeopathic medicines that we have used in this study might interfere in any of the above plausible mechanisms that might be associated with their remedial actions.

We acknowledge some limitations that may be associated with this study. The most important limitation seems to be the relatively small number of study participants. Demographic data were collected using a self-reporting questionnaire and were adopted directly without testing their authenticity by any other means. We also acknowledge that this study lack proper control for the possible effect of a confounding factor—especially the use of antibiotics. Although the patients were advised not to take any other medicines or medicinal supplements while under this treatment period, we could not assure whether this advice was maintained strictly or not. Nonetheless, these limitations do not prevent us to conclude that homeopathic medicines reduced ear suppuration, healed damaged tympanic membrane and caused improvement of hearing in CSOM patients.

Conclusion

CSOM is a common non-communicable disease in the developing world in which antibiotics are frequently prescribed. In addition, frequent and unjustified use of antibiotics is rendering various microorganisms resistant to antibiotics creating

serious health problems. Moreover, correction of perforated tympanic membrane with surgery like tympanoplasty and improvement of hearing loss with cochlear implant or hearing aid devices are far beyond the reach of mass people. Even the risk of recurrent infection in those cases is still unavoidable. Under these circumstances, a cost effective alternative treatment of CSOM would be well appreciated to control infections and related disorders. Current study presents a light of hope of using homeopathic medicines as an alternative to antibiotics and other related treatment process. In this study, we provided conclusive evidences that homeopathic medicines prevent ear suppuration in selected CSOM patients as well as reduce microbial load, heal perforated membrane and improve hearing. More extensive researches involving large population size are needed to justify the results and outcome of this study.

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Annexure



Annexure

Questionnaire

A Survey of CSOM Mediated Hearing Impairment for Research Work

অংশগ্রহনকারীর নাম:.....

রোজ: নং

বয়স:..... বছর; লিঙ্গ: পুরুষ / মহিলা; উচ্চতা:..... ফুট..... ইঞ্চি;

তারিখ:

ওজন:.....কোজ রক্ত চাপ:.....mmHg; টেলিফোন নং-.....

শিক্ষাগত যোগ্যতা: প্রাইমারি মাধ্যমিক উচ্চমাধ্যমিক উচ্চতর

পেশা:.....সময়-কাল:.....ঘন্টা/দিন,বছর

আবাসস্থল: ক) পাকা দালান কাচা-পাকা দালান কাচা বাড়ি
খ) বাড়ির পাশে পুকুর বড় ড্রেন জলাশয় নদী আছে
গ) বাড়ির পাশে রাসায়নিক কারখানা প্লাস্টিক কারখানা
ভারী শিল্প-কারখানা আছে

পুরাতন রোগের বিবরণ এবং এর চিকিৎসা: টাইফয়েড ম্যালেরিয়া যক্ষ্মা
মেনিনজাইটিস ক্রনিক টনসিল প্রদাহ অন্যান্য.....
..... চিকিৎসা নিয়েছি।

বংশগত রোগের বিবরণ (মাতৃ এবং পিতৃ, উভয়); উচ্চরক্তচাপ হাঁপানি / শ্বাসকষ্ট ডায়াবেটিস
আর্থ্রাইটিস যক্ষ্মা অন্যান্য:

আসক্তি: তামাক - হ্যাঁ না ; 'হ্যাঁ' হলে ধূমপান শলাকা/দিন; চিবানোবার/দিন
পান: হ্যাঁ না 'হ্যাঁ' হলে কত দিন যাবত?.....দিন;
অন্যান্য:.....

প্রধান সমস্যা সমূহ:

- ১) কান ব্যথা করে? হ্যাঁ না ; 'হ্যাঁ' হলে কত দিন যাবত?.....দিন, ডান বাম উভয়
- ২) পুঁজ হয় / পড়ে? হ্যাঁ না ; 'হ্যাঁ' হলে কত দিন যাবত?.....দিন, ডান বাম উভয়
- ৩) কানে কম শোনে / কানে শ্রবনে অসুবিধা হয়? হ্যাঁ না ; 'হ্যাঁ' হলে কোন কানে? ডান বাম
উভয়
- ৪) কানে কখনো আঘাতের ইতিহাস আছে কি? 'হ্যাঁ' হলে কত দিন আগে?.....দিন, ডান বাম
উভয়
- ৫) কান ব্যথার কারণে জ্বর আসে? হ্যাঁ না ; 'হ্যাঁ' হলে কত দিন যাবত?.....দিন
- ৬) কানে দপদপ / শোঁ শোঁ / চি - শব্দ করে? হ্যাঁ না ; 'হ্যাঁ' হলে কত দিন যাবত?.....দিন, ডান
 বাম উভয়
- ৭) কান ভারী অনুভূত হয়? হ্যাঁ না ; 'হ্যাঁ' হলে কত দিন যাবত?.....দিন, ডান বাম
 উভয়



৮) কান লাল হয়ে যায়? হ্যাঁ না ; 'হ্যাঁ' হলে কত দিন যাবত?.....দিন, ডান বাম

উভয়

রোগ ভোগের সময়-কাল:দিনমাসবছর

আনুসঙ্গিক লক্ষণ

সমূহ:.....

.....

.....

কি পানিতে গোসল করেন? নদী পুকুর জলাশয় টিউবয়েল ট্যাপের পানি

জমানো পানি

ইয়ারফোন ব্যবহার করেন? হ্যাঁ না ; 'হ্যাঁ' হলেঘন্টা / দিন,মাস / বছর যাবত

নিয়মিত কান পরিষ্কার করেন? হ্যাঁ না ; 'হ্যাঁ' হলেবার / মাসে; কটন বাড

ধাতব কাঠ অন্যান্য.....

কান খোচানোর অভ্যাস আছে? হ্যাঁ না ; 'হ্যাঁ' হলে কটন বাড ধাতব কাঠ কাঠ/বাঁশের

কাঠ অন্যান্য.....

ঘোষণা

আমি এতদ্বারা ঘোষণা করিতেছি যে, উপরে উল্লিখিত তথ্যসমূহ সঠিক এবং আমি স্বৈচ্ছায় এই গবেষণায় অংশ গ্রহণ করেছি।

স্বাক্ষর / টিপসই

Audiogram Sheet

Department of Genetic Engineering and Biotechnology
University of Dhaka



A Survey of Hearing Level for Research Work

Hearing examination sheet

Subject ID: _____ Date: / / (dd/mm/yyyy)

Frequency	1 kHz	4 kHz	8 kHz	12 kHz	Frequency	1 kHz	4 kHz	8 kHz	12 kHz
Hearing level (dB)					Hearing level (dB)				
5 dB					5 dB				
10 dB					10 dB				
15 dB					15 dB				
20 dB					20 dB				
25 dB					25 dB				
30 dB					30 dB				
35 dB					35 dB				
40 dB					40 dB				
45 dB					45 dB				
50 dB					50 dB				
55 dB					55 dB				
60 dB					60 dB				
65 dB					65 dB				
70 dB					70 dB				
75 dB					75 dB				
80 dB					80 dB				
85 dB					85 dB				
90 dB					90 dB				
95 dB					95 dB				

Homeopathic potency preparation

Available at : <https://www.powerpak.com/course/print/115139>

In homeopathy, the minimum dose principle holds that only the very minimum amount of medication should be given to elicit a response. This is the rationale for using highly diluted and succussed (i.e., vigorously shaken) potencies of homeopathic medications. As figure-1 shows, these medicines are prepared according to specifications by their degree of dilution: X potencies are factors of 10 (decimal) and C potencies are factors of 100 (centesimal). The roman numerals denote the factor by which the substance has been diluted (X is the process of dilution by a factor of 1:9; C is the process of dilution by a factor of 1:99).

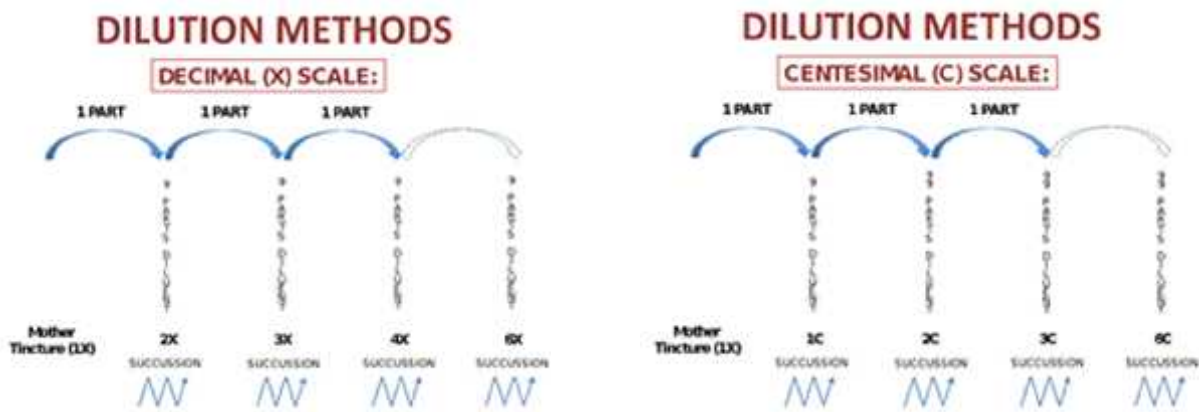


Figure 1. Homeopathic medicine dilution. (a) X potency medicines are diluted by factors of 10. (b) C potency medicines are diluted by factors of 100.

A homeopathic medicine is made with carefully delineated and controlled successive homeopathic dilutions, each followed by precisely directed succussion. For C potencies, the process begins by taking 1 part of 1C potency and adding it to 99 parts diluent (water or alcohol), followed by succussion, which creates the 2C potency; then 1 part of 2C is added to 99 parts diluent to make 3C. This process continues to make the common C-potencies used in community pharmacy practice: 6C, 9C, 15C, and 30C.

The concepts of potency and dilution are important for pharmacists and pharmacy technicians to understand: homeopathic medicines are sufficiently dilute to encourage innate healing responses and yet pose little risk of side effects or pharmaceutical interactions when used at the doses described above.