PREVALENCE OF HEARING LOSS AMONG SICKLE CELL PATIENTS AT THE KORLE-BU TEACHING HOSPITAL

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THIS DISSERTATION IS SUBMITTED TO THE UNIVERSITY OF GHANA, LEGON IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF MSC AUDIOLOGY DEGREE

JULY 2015

DECLARATION

I **ROGER BOAKYE-AKUFFO** do hereby declare that this dissertation being submitted in partial fulfillment of the requirement for the degree of Master of Science in Audiology is the result of my own research performed under supervision and that except where otherwise, other sources are acknowledged and duly referenced, this work has not been accepted in substance for any degree and is not being currently submitted in candidature for any degree.

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DEDICATION

This work is dedicated to my late Father Stephen Boakye-Akuffo.

ACKNOWLEDGEMENT

I am grateful to the Almighty God for giving me the strength to come this far. I am indebted to my supervisors, Dr. Neal Boafo and Dr. George A. Asare for their invaluable support, encouragement, patience and wonderful guidance to make this project successful.

I would also like to thank Dr. S. Anim-Sampong, Mrs. Jemima Fynn, Dr. E. Olayemi and Prof. G. Amedofu who encouraged and supported me through this academic journey.

Also, a big thank you to all my lecturers and Mr. Ronald N. Agyekum for their wonderful support. May God bless you for the wonderful time you spent with us.

Also to the staff of the Adult Sickle Cell Disease Clinic and the Hearing Assessment Centre of Korle-Bu Teaching Hospital for their immense support and cooperation to make this work become a reality.

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LIST OF ABBREVIATIONS

ANSI	American National Standards Institute
ASHA	American Speech-Language-Hearing Association
BSA	British Society of Audiology
CHL	Conductive Hearing Loss
dB	Decibels
Hb	Haemoglobin
KBTH	Korle-Bu Teaching Hospital
kHz	Kilo Hertz
MHL	Mixed Hearing Loss
SCA	Sickle Cell Anaemia
SCD	Sickle Cell Disease
SNHL	Sensorineural Hearing Loss
WHO	World Health Organization

ABSTRACT

Background: Sickle Cell Disease (SCD) is one of the commonest blood and genetic disorders in the world. It results when abnormal haemoglobin (Hb S, Hb C, Hb β-thalassemia) is found either in the homozygous or heterozygote state. Sickle cell disease causes painful vascular occlusion crisis, anoxia and ischaemia which sometimes lead to tissue or organ damage including the auditory system especially the blood rich cochlear. Damage to the auditory system eventually causes hearing loss.

Aim: The study assessed the hearing status of the sickle cell disease patients reporting to the Adult Sickle Cell Clinic of the Korle-Bu Teaching hospital.

Methods: A case control study involving 100 known genotyped sickle cell patients from the adult SCD Clinic at the Ghana Institute of Clinical Genetics, Korle-Bu Teaching hospital and age-matched 100 confirmed haemoglobin AA genotyped participants (staff and students of School of Biomedical and Allied Health Sciences, University of Ghana) constituted this study. Subjects were selected based on inclusion and exclusion criteria. A structured questionnaire was administered to obtain basic information on socio-demographic parameters and case history of the participants. Their hearing was assessed by pure tone audiometry in a sound treated booth.

Results: A significant association between hearing status and hemoglobin genotype for air and bone conduction thresholds was observed. This was evidenced by relatively higher prevalence of hearing loss among participants with Hb SS and Hb SC genotypes (cases) compared to respondents with Hb AA genotype (control) at the respective tested frequencies.

Conclusion: There is significant difference in hearing thresholds in persons living with SCD and the control group. Results from this study showed one type of loss (sensorineural hearing loss)

among Ghanaian adult SCD patients. Likewise, the degree of hearing loss among the SCD patients ranged from mild to profound from 2000 Hz to 8000 Hz. Finally, sensorineural hearing loss presented more among the Hb SS genotype group than the Hb SC group.

Keywords: Sickle cell disease, vascular occlusion, haemoglobin, haemolysis, hearing loss.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

The origin of sickle cell disease (SCD) is not known, but it is believed to have started from Africa. According to Herrick (1910), this belief is based on the claim that SCD has the ability to protect people against malaria (a deadly disease found in countries of warm weather conditions). It is reported that symptoms associated with SCD crises were known by other different names in Africa way before they were identified in other continents. It is further indicated that symptoms of sickle cell anaemia (SCA) could be tracked back to one Ghanaian family as far back as 1670 (Konotey-Ahulu, 1973).

Since then various studies have described different types of the disease conditions and its associated complications. The sickle-cell trait haemoglobin (Hb) S is now known to be widespread and vastly distributed, reaching its highest prevalence in parts of Africa as well as among people with origins in Equatorial Africa, Middle East, Central India, and countries bordering the Mediterranean Sea, especially Italy and Greece (Vedro & Morrison, 2002). The disease is currently found all over Europe and in large regions of Asia besides Africa and the Americas (Burch-Sims & Matlock, 2005). It is a multisystem disease, associated with episodes of acute illness and progressive organ damage (Rees, Williams & Gladwin, 2010) and is primarily an inherited blood disorder which affects the red blood cells. However Hb SS is the commonest type of SCD throughout the world (Grosse et al., 2011).

According to the World Health Organization (WHO), over 300 000 babies with SCD are born each year throughout the world. It has been indicated that, there are approximately 5% (356,250,000 million) carriers of the SCD trait worldwide. Furthermore it is intimated that, SCD is widespread in the tropical regions, with a prevalence of 25% (WHO 2013).

Ghana and other countries in West and Central Africa have the highest prevalence of SCD and related disorders in the world (Owusu, 2010). The common forms of SCD in Ghana are Hb SS, Hb SC, and Sickle B^0 and B^+ thalassaemia. There are very few families in Ghana who are not affected by this disease (Konotey-Ahulu, 1974). Statistics from the newborns screening for SCD Project in Kumasi and its environs indicate that approximately 2% of newborns have SCD. This translates to about 16, 000 annual births with SCD in Ghana (Owusu, 2010). Sickle cell disease SS and SC constitute over 90% of SCD in Ghana. About 20% of southern Ghanaians have (Hb S) trait and 10% have (Hb C) trait while 20% of northern Ghanaians have (Hb C) trait and 10% have (Hb S) trait (Konotey-Ahulu, 1974).

Sickle cell disease is associated with painful vascular-occlusive crises and inflammation which results in damage to major organs such as the brain, kidneys, lungs, bones, cardiovascular system and increased vulnerability to severe infections. Vascular-occlusive crises also affect the effective functioning of the auditory system especially the cochlea, thereby causing hearing loss. The prevalence of hearing loss is higher among SCD patients ranging from 11% to 41% than the general population with a prevalence rate of 10% (MacDonald et al., 1999).

Similarly, Castro Silva et al., (2010) associated hearing loss with SCD with a prevalence of 3.5% to 57% depending on the region of study, age group and severity of the disease. It was further

indicated that hearing loss in SCD patients can be conductive with variable degrees of obstruction to sound transmission either in the outer ear or the middle ear, and would likely be due to susceptibility to infections in such patients. Considering the delicate nature and function of the cochlea vasculature (high metabolic demand and high rate of gaseous exchanges needed for its activities), vaso-occlusion in SCD crisis can affect its functionality thereby causing sensorineural hearing loss (SNHL). Hearing loss could also be neural in nature due to abnormal transmission of nerve impulses to the acoustic nerve and central auditory process (Castro Silva et al., 2010). However, the effect of vascular occlusion on hearing is normally underrated as management of SCD crisis mostly focuses on other dysfunctions of the body in Ghana.

1.2 STATEMENT OF THE PROBLEM

Sickle cell disease is characterized by vascular occlusive crises. Vascular occlusion can lead to compression of the auditory canal, cause damage to the hair cells of the organ of corti, stria vascularis, the basal turn of the cochlea and eventually impaired auditory function (Mgbor & Emodi, 2004). Moreover, the sickle cell trait is extremely common in Ghana. One in every three healthy Ghanaians is either Hb AS or Hb AC (Konotey-Ahulu, 1974). Furthermore, 2% of newborn births in (16000 annual births) present with SCD every year (Owusu 2010). However, only one study has investigated SNHL among sickle cell anaemia patients in Ghana, with a prevalence rate of 29% over 25 years ago (Atsina *et al*., 1988). Though many studies on SCD have been done in Ghana, there is however no study done on the types of SCD and their associated effects on hearing among SCD patients.

At present there is no up-to-date data on the hearing status of SCD patients in the country. Given the relatively large number of SCD patients in the country, it is likely that its effect on their hearing will have a negative impact socially, economically and health wise.

The lack of research on this condition coupled with unavailability of scientific and technical solutions to alleviate the problems also pose a challenge. It is therefore imperative that a study is carried out to make available, data on the prevalence, types and degrees of hearing loss that exist among SCD patients, as well as programmes for frequent monitoring of hearing abilities of SCD patients.

1.3 SIGNIFICANCE OF STUDY

This study will be significant in:

- Establishing the prevalence of hearing loss among SCD patients in Ghana.
- Making available relevant information on the types of hearing loss that exist among sickle cell patients in the country.
- Establishing the genotypic distribution of hearing defects among SCD patients in Ghana.
- Serving as a baseline data for the holistic management of SCD patients in the country.

1.4 AIM OF THE STUDY

The aim of the study is to determine and establish the prevalence of hearing loss among SCD patients at the Korle-Bu Teaching Hospital (KBTH).

1.5 OBJECTIVES OF THE STUDY

The specific objectives set out for the study were as follows:

1. Determination of the prevalence of hearing loss among SCD patients in KBTH.
2. Determination of the types of hearing loss among SCD patients.
3. To examine the degrees of hearing loss among SCD patients.
4. To determine the genotypic distribution of hearing defects.

1.6 HYPOTHESES

The following hypotheses were set and tested in line with the specific objectives.

H_1: There will be a significant association between Ghanaian SCD subjects and hearing loss.

H_2: There will be an association between the degree of hearing loss and the type of SCD.

CHAPTER TWO

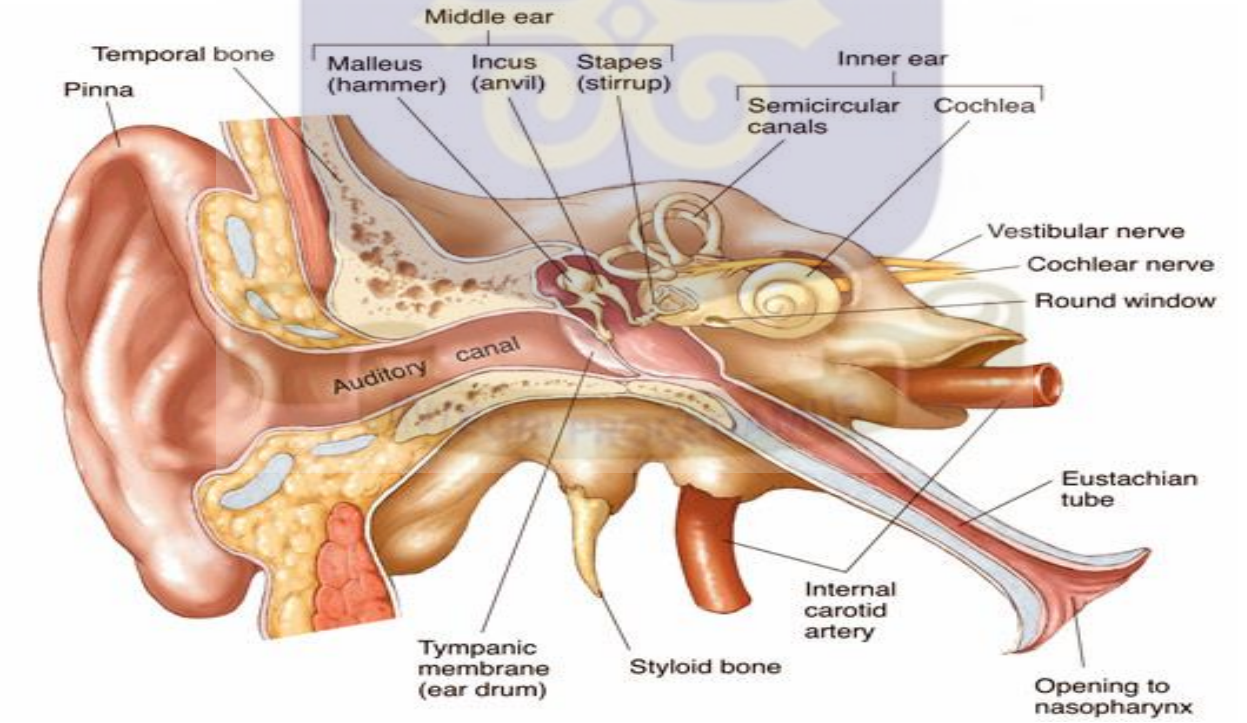
LITERATURE REVIEW

2.1 INTRODUCTION

The review of the anatomy and physiology of the auditory system, hearing loss and SCD is presented in this Chapter. Particular emphasis is placed on the prevalence of hearing loss among SCD patients across the world.

2.2 ANATOMY AND PHYSIOLOGY OF THE EAR

The hearing mechanism consists of the outer ear, the middle ear and the inner ear as depicted in Figure 2.1.



Source: Irregular Anatomists (2014).

Figure 2.1: Major parts of the auditory system.

2.2.1 Outer Ear

The most noticeable portion of the outer-ear mechanism is the auricle or pinna. The anatomy of the auricle is more efficient at delivering high frequency sounds than low-frequency sounds, and it helps in the localization of sounds delivered to the head. It is made up of the external auditory canal (EAC) and the tympanic membrane (Stach, 2010, Martin & Clark, 2012).

The EAC has several important functions. In particular, it serves as a filter to reduce low frequencies and as a tube resonator for frequencies between 2000 and 7000 Hz, thereby creating efficient energy transfer to the tympanic membrane (Stach, 2010, Martin et al., 2012).The tympanic membrane is made of several layers of skin embedded into the bony portion of the canal. It is an extremely efficient vibrating surface. Movement of one billionth of a centimeter is sufficient to produce a threshold response in normal-hearing individuals in the 800 to 6000 Hz range. The entire area of the tympanic membrane lies between the outer ear and the middle ear. It is very rich in blood supply and accounts for its reddish appearance when infection is present and blood is brought to that area (Martin et al., 2012).

2.2.2 Middle Ear

Beyond the tympanic membrane lies the middle-ear cavity. Air in the cavity is kept at atmospheric pressure via the Eustachian tube. The ossicular chain is attached to the tympanic membrane and consists of a series of three small bones or ossicles called the malleus, incus, and stapes. These ossicles transfer the vibration of the tympanic membrane to the inner ear or cochlea (Stach, 2010, Martin et al., 2012).

The middle ear acts as an impedance matching transformer. The mechanical energy of the middle ear serves as an efficient energy converter from air to fluid. First, there is a substantial area difference between the tympanic membrane and the oval window. Pressure applied on the large end results in substantially greater pressure at the narrow end. The ossicles also act as a lever, pivoting around the incudo-malleolar joint, which contributes to an increase in vibrational amplitude at the stapes (Stach, 2010, Martin et al., 2012).

2.2.3 Inner Ear

The inner ear consists of the auditory and vestibular labyrinths. The auditory labyrinth is called the cochlea and is the sensory end-organ of hearing. It consists of fluid-filled membranous channels within a spiral canal that encircles a bony central core. Here the sound waves, transformed into mechanical energy by the middle ear, set the fluid of the cochlea into motion a manner consistent with their intensity and frequency. Waves of fluid motion impinge on the membranous labyrinth and set off a chain of events resulting in generation neural impulses at the VIIIth cranial nerve Stach (2010).

The cochlea is a fluid-filled space within the temporal bone which resembles the shape of a snail shell with 2.5 turns. The cochlea partition separates the scala vestibuli from the scala tympani. The scala vestibuli is the uppermost of two perilymph-filled channels of the cochlea duct and terminates basally at the oval window. The scala tympani is the lowermost channel and terminates basally at the round window. Both of these channels terminate at the apical end of the cochlea at the helicotrema. The cochlea partition or scala media is an endolymph-filled channel that lies between the scala vestibuli and scala tympani and cordoned off by two membranes.

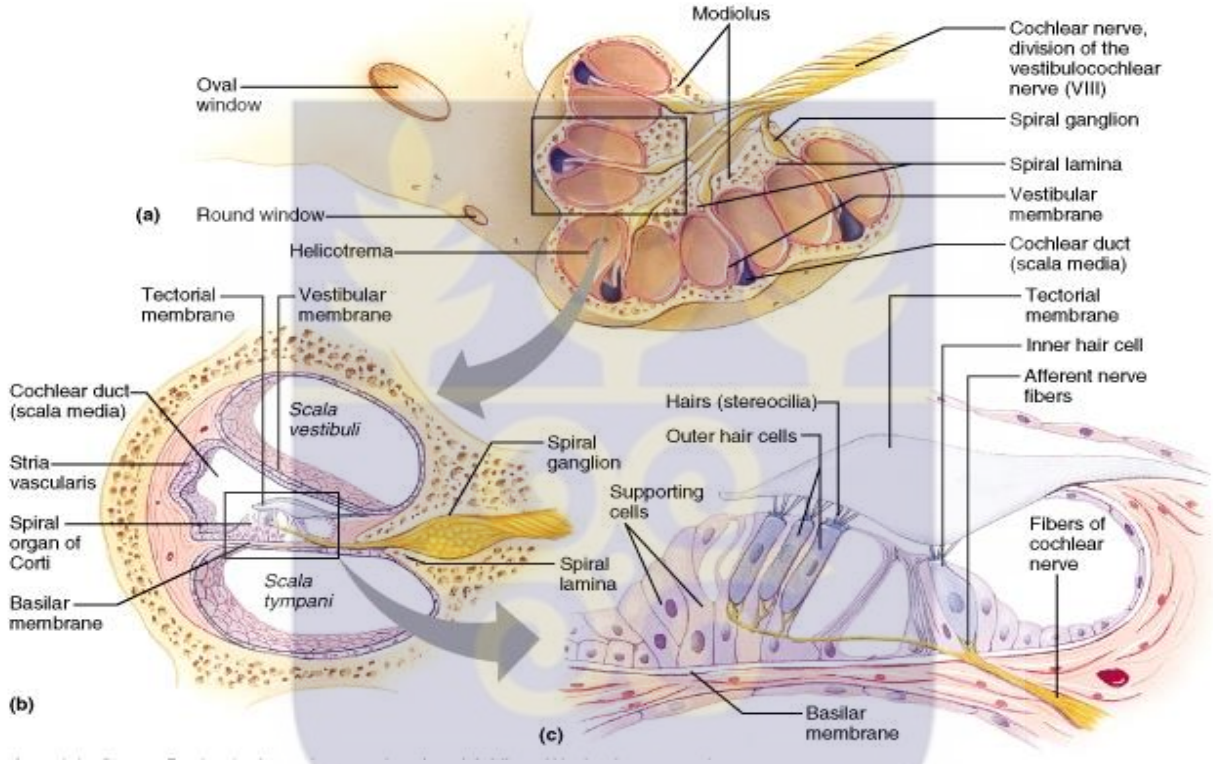
The Reissner's membrane serves as the cover of the partition, separating it from the scala vestibule, while the basilar membrane serves as the base of the partition, separating it from the scala tympani. Riding on the basilar membrane is the organ of Corti, which contains the sensory cells of hearing.

There are two types of sensory cells, both of which are unique and very important to the function of hearing. These are termed the outer hair cells and inner hair cells. Outer hair cells are elongated in shape and have small hairs, or cilia, attached to their top. These cilia are embedded into the tectorial membrane which covers the organ of Corti. There are three rows of outer hair cells throughout most of the length of the cochlea. The outer hair cells are innervated mostly by efferent or motor fibers of the nervous system. There are about 13,000 outer hair cells in the cochlea. Inner hair cells are also elongated and have an array of cilia on top. Inner hair cells stand in a single row, and their cilia are in proximity to, but not in direct contact with, the tectorial membrane. The inner hair cells are innervated mostly by afferent or sensory fibers of the nervous system. There are about 3,500 inner hair cells in the cochlea (Stach 2010).

2.2.4 Functions of the Outer and Inner Hair Cells

Vibration of the stapes in and out of the oval window creates fluid motion in the cochlea, causing the structures of the membranous labyrinth to move, resulting in stimulation of the sensory cells and generation of neural impulses. The outer hair cells are active and move in response to sound and amplify travelling wave. The outer hair cells also produce sounds that can be detected in the external auditory canal by sensitive microphones. The basilar membrane is arranged tonotopically in that each frequency stimulates a different place along its course. When the traveling wave reaches its point of maximum displacement, the inner hair cells are stimulated,

sending neural impulses to the auditory nerve. The sensitivity of the inner hair cells is controlled to some extent by the outer hair cells. When the traveling wave reaches its maximum displacement, the inner hair cells are stimulated, resulting in the secretion of neurotransmitters that stimulate the nerve endings of the cochlea branch of the VIIIth nerve (Stach, 2010).



Source: Cummings (2006).

Figure 2.2: Parts of the Cochlea

2.2.5 Cochlea Blood Supply

The cochlea and the vestibule are supplied by arteries from the same source, namely, the internal auditory artery (labyrinthine artery). The internal auditory artery usually arises from the apex of the meatal loop of the middle cerebral artery which is consistently present and penetrates more or less deeply within the internal acoustic meatus. The meatal loop usually sits on the cochlea nerve and is often sandwiched between this nerve and the facial nerve. It also gives off the subarcuate

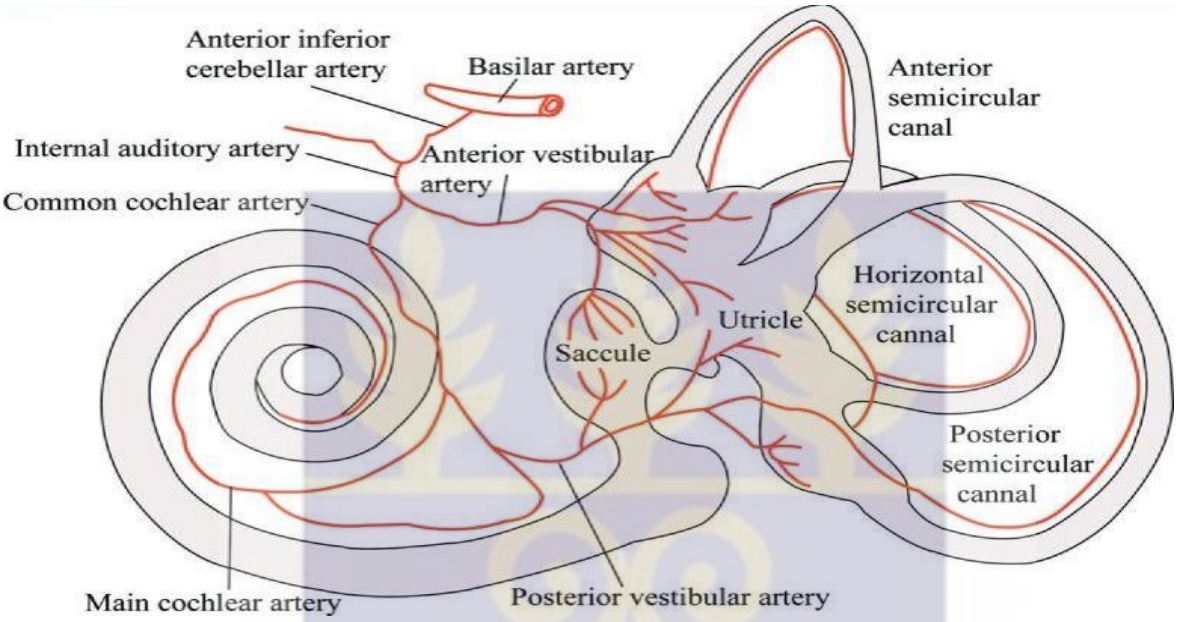
artery which runs in the petromastoid canal, passing through the arch of the superior semicircular canal. The portion of the internal auditory artery located within the meatus gives off several branches. The first branch is the anterior vestibular artery which supplies the posterior and lateral semicircular canals, the utricle, and the posterior part of the saccule with blood (Mom et al., 2005).

The spiral modiolar artery and vestibulocochlea artery from the cochlea artery, supply the cochlea with blood. The apex of the cochlea, the second turn, and part of the basal turn are supplied blood. The vestibulocochlea artery arises after the spiral modiolar artery and travels to the vestibule, where it gives off a vestibular branch and a cochlea branch. The vestibular branch supplies the posterior semicircular canal and the saccule, whereas the cochlea branch feeds the proximal part of the base of the cochlea.

This distribution suggests that the clinical features may vary according to the site of arterial obstruction (Tange, 1998). Thus, obstruction of the spiral modiolar artery would be expected to cause hearing loss predominantly in the low frequencies and obstruction of the vestibulocochlea artery, hearing loss predominantly in the high frequencies and accompanied with vertigo (Mom et al., 2005).

Risk is posed to the auditory system due to ischemia of the stria vascularis and hypoxia of the secondary organ of Corti as a consequence of sickle cell crisis. The very large and detailed arrangement of the vascular system of the inner ear reflects abundant blood supply to the cochlea. This tiny organ receives large amount of the body's blood despite its small size, which is very essential for the high metabolic activity required to maintain both ionic and electrical

characteristics of the endolymph. In view of this, secure and extensive cochlea blood flow is critical due to the highly dependent evoked responses of the inner ear (Burch-Sims et al., 2005).



Source: (Kim, 2009).

Figure 2.3: Arterial Supply to the Inner Ear.

2.3 SICKLE CELL DISEASE

Sickle cell disease is primarily a hematologic and genetic disorder with multi-organ manifestations (Herrick, 1910). It is a change brought about genetically which affects the manufacture of a significant protein called haemoglobin. It is reported to be one of the significant health care and social problems that affect millions of people globally by Center for Disease Control, (2008). It is further described as a multisystem disease, characterized by episodes of acute illness and increasing organ damage, and is one of the most common severe genetic disorders in the world (Rees et al., 2010). The disease is not just a regional or continental problem but a worldwide menace that must be given the needed global attention. In short SCD is

an inherited blood disease. Disease is applied to this condition because the inherited abnormality causes a pathological condition that can lead to death and severe complications (Kaur, Dangi & Singh, 2013).

2.3.1 Classification

Sickle cell disease is described as all the different genotypes that cause the characteristic clinical syndrome. Sickle-cell anaemia is the most common form of SCD, which refers specifically to homozygosity for Haemoglobin S (Hb SS) (Rees et al., 2010). Another study also grouped SCD under three different headings; sickle cell disorder, sickle cell disease and sickle cell anaemia (Kaur et al., 2013).

Sickle cell disorder includes all states in which a sickle gene is inherited. This group includes all patients with a positive sickle preparation smear. The patient may or may not be symptomatic.

Sickle cell disease is a disorder in which significant morbidity, such as organ failure or vascular occlusive pain crises (VPC), results from the sickling of red blood cells.

Sickle cell anaemia is usually reserved specifically for patients who are homozygous for haemoglobin S (Hb SS) (Kaur et al., 2013).

2.3.2 Pathophysiology

Sickle cell disease is a disorder of the erythrocytes caused by an autosomal recessive single gene defect in the β-globin chain of adult haemoglobin (Hb A) that produces a mutant form of haemoglobin known as sickle haemoglobin (Hb S). The sickle cell trait (Hb S) occurred as a natural mutation to the haemoglobin gene. It is further indicated that the trait offer protection against malaria (a deadly disease found in the countries near the equator) (Vedro et al., 2002).

This explains why the sickle cell trait is mostly found in places where malaria is prevalent (Ferreira et al., 2011).

The Hb S trait is caused by a mutation in the beta (β) globin gene in which the 17th nucleotide is changed from thymine to adenine and the sixth amino acid in the β-globin chain becomes valine instead of glutamic acid. The mutant β-allele (β^s) codes for the production of the variant haemoglobin, Hb S and the sickle cell gene mutation occurs in the sixth codon of exon 1 in the β-A gene, replacing adenine with thymine (Kaur et al., 2013).

The valine is produced as a result of the mutation on the β-globin chain of one haemoglobin molecule, and can bind with another haemoglobin molecule in the hydrophobic pocket. Once this process starts, the haemoglobin polymerizes within the erythrocyte as a result of this bond, thus, affecting the shape of the erythrocyte to change into sickle shape. The bond formed produces a polymer nucleus, which grows and fills the erythrocyte, changing its structure and flexibility and enhancing cellular dehydration, with physical and oxidative cellular stress. This polymerization therefore alters the shape of the normal haemoglobin (Hb A) from a disc shape to a mutated Hb S sickle shaped. The severity of SCD may be dependent on the degree of Hb S polymerization (Brittenham, Schechter & Noguchi, 1985).

2.3.3 Types of Sickle Cell Disease

There are different types of SCD depending on the type of bond they form after mutation and polymerization of the mutated haemoglobin. This bond then determines the severity of the disease as expressed among the different types of the SCD. If two β^s (beta globin S) genes interact, the resulting sickling disorder is known as Hb SS disease. Also when the β^s (beta globin

S) gene interacts with the β^c (beta globin C) gene, the resulting sickling disorder is known as Hb SC disease which is identified as mild. This interaction and bonding applies to the other SCD genotypes. If the mutation is mild the disease will be clinically mild. On the other hand if the mutation is severe the disease will be clinically severe as seen in Mediterraneans and populations of African descent (Serjeant et al., 1973).

2.3.4 Genetics of the Disease

Mutations in the haemoglobin beta chain cause of all forms of SCDs. In a pregnancy between two carriers of sickle cell trait, there is a 25% chance of producing an affected child (Hb SS or SC), a 50% chance of producing an unaffected carrier (Hb AS or AC), and a 25% chance of producing an unaffected child who is not a trait carrier (Hb AA). There are also the heterozygous states where children are born with two different forms of variant haemoglobin. Haemoglobin SC disease and haemoglobin S B-thalassemia are examples of SCD resulting from compound heterozygous states (Smith, Tancabelic & Reddy, 2011).

2.3.5 Epidemiology

The origin of sickle cell anaemia is not known, but it is believed to have started from Africa. According to Herrick (1910), this belief is based on the claim that SCD has the ability to protect people against malaria (a deadly disease found in countries of warm weather conditions). The first case of SCD was described in contemporary medicine literature in 1910. Since then various studies have described different types of the disease conditions and its associated complications. Distribution of Hb S trait globally is dependent on two factors: choice for people with the Hb S trait as an advantage in surviving in regions endemic with malaria and secondly migration (Flint et al., 1998). The sickle-cell trait is now known to be widespread, reaching its highest prevalence in parts of Africa as well as among people with origins in equatorial Africa, Middle East, Central

India, and countries bordering the Mediterranean Sea, especially Italy and Greece (Vedro et al., 2002). Sickle cell disease is currently found all over Europe and in large regions of Asia besides Africa and the Americas (Burch-Sims et al., 2005). However Hb SS is the commonest type of SCD throughout the world (Grosse et al., 2011).

It is reported that, there were three different β-globin mutations in different parts of Africa and the resultant β-globin haplotypes were named after the areas where these mutations took place (Benin, Senegal, and Central African Republic or Bantu) (Pagnier et al., 1984). Another study asserts that mutation resulting in Hb S has occurred leading to the definition of four region-specific African haplotypes (the Senegal, Benin, Bantu, and Cameroon haplotypes) and one Asian haplotype (the Arab-India haplotype) (Flint et al., 1998). Furthermore, it is indicated that, the Hb C allele occurs exclusively among West Africans with a high occurrence of the trait in northern Ghana and Burkina Faso (Grosse et al., 2011). Again, the Hb C trait is believed to have been a recent mutation peculiar to West Africa. It is found at high frequencies 20% in central Ghana and Burkina Faso, and only 2% in Nigeria (Serjeant, 2013).

In Africa, the sickle cell trait is spread over a large area. The trait has high but different frequencies in equatorial Africa with low frequencies (1%–2%) in the north and south of the African continent (Serjeant, 2013). The prevalence of SCD is highest in sub-Saharan Africa. Although the scarcity of diagnostic facilities means that precise data are not available, a recent estimate suggests that more than 230 000 affected children are born in this region every year (0·74% of the births in sub-Saharan Africa), which is about 80% of the global total. By comparison, the yearly estimate of affected births in North America is about 2600 and 1300 in Europe (Rees et al., 2010). The highest prevalence of sickle-cell trait occurs between latitudes

15° North and 20° South, ranging between 10% and 40% of the population in some areas. Prevalence levels decrease to between 1% and 2% in north-Africa and to less than 1% in southern Africa. In countries such as Cameroon, Republic of Congo, Gabon, Ghana and Nigeria, the prevalence is between 20% and 30% while in some parts of Uganda it is as high as 45%. In countries where the trait prevalence is above 20% the disease affects about 2% of the population. The geographic distribution of the sickle-cell trait is very similar to that of malaria as it has a partial protective effect against malaria, and this may explain why it has been maintained at such high prevalence levels in tropical Africa (Sambo, 2014). Statistics from newborn screening for SCD project in Ghana and its environs indicate that approximately 2% of newborns have SCD (SS and SC), translating to about 16, 000 annual births with SCD in Ghana (Owusu, 2010).

2.3.6 Vascular Occlusion and Haemolysis

Sickle cell disease is usually associated with painful episodes among those with the disease. When the sickled cells are unable to flow through small blood vessels they obstruct blood flow causing vascular occlusion (vaso-occlusion). Vaso-occlusion reduces blood flow to an area of the body resulting in pain. This can occur anywhere in the body, including fingers, arms, legs, ribs, abdomen, and organs such as the spleen, brain, and eyes (Vedro et al., 2002). Vaso-occlusion with ischemia-reperfusion injury and hemolytic anaemia are the two main physiological processes that drive the clinical manifestations of the SCD (Rees et al., 2010). Similarly, it is indicated that, vaso-occlusion result from a constant interaction between erythrocytes and the vascular endothelium, which eventually leads to micro-vascular occlusion and ischemia and after this blood flow is restored leading to tissue injury mediated by reperfusion.

Hemolytic anaemia another cause of major complications in SCD is brought about by Hb S polymerization. Rees et al., (2010) indicated that hemolysis causes fatigue, anaemia and cholelithiasis, and can also initiate vascular disorders. Kaur et al., (2013) also explained that a combination of hemolysis and vaso-occlusion is the main cause of complications in SCD. Patients with SCD are common victims of recurrent attacks of hemolytic and thrombotic crises, which are well documented to impair the hearing thresholds of these patients during their crisis attacks (Ezzat et al., 2013).

2.4 HEARING LOSS

The most common form of hearing disorder is hearing loss. It is described as "a reduction in the sensitivity of the auditory mechanism so that sounds need to be of higher intensity than normal before they are perceived by the listener" (Stach, 2010). The ear is separated into two parts. The conductive portion is made up of the outer and middle ear and, the sensory/neural portion is made up of the inner ear and the auditory nerve. Hearing loss occurs when either or both of these two portions do not function well due to reduction in the sound energy that is being transmitted. There are different types of hearing loss depending on the part of the ear that is affected or not functioning efficiently (Martin et al., 2012).

Conductive hearing loss occurs when there is attenuation or reduction of sound by the outer or middle ear as sound travels from the outer ear to the cochlea (Stach, 2010; Martin et al., 2012). Sensorineural hearing loss occurs when either the inner ear or the auditory nerve and sometimes both are not functioning properly. Hence the cochlea is not able to transduce sound from mechanical energy from the middle ear to nerve impulses in the VIII nerve, (Stach, 2010; Martin

et al., 2012). Mixed hearing loss (MHL) occurs when there is both conductive component and a sensorineural component which contributes to the loss of hearing sensitivity (Stach, 2010).

2.4.1 Diagnosis and Degrees of Hearing Loss

To evaluate the type of hearing loss, hearing sensitivity is measured by presenting sounds in two ways. The most common way is to present sound through an earphone or insert phone to assess hearing sensitivity of the entire auditory mechanism. This is referred to as air-conduction testing. The other way to present sound to the ear is by placing a vibrator in contact with the skin, usually behind the ear or on the forehead. Sound is then directed to the vibrator which transmits signals directly to the cochlea via bone conduction.

The difference between hearing sensitivity via air conduction and the sensitivity as determined by bone conduction represents the contribution of the function of the outer and middle ear (Stach, 2010). A summary of the degrees and ranges of hearing loss is presented in Table 2.1.

Table 2.1: Degrees and ranges of hearing loss

Degree of Hearing loss	Hearing loss Range in (dB HL)
Normal	0 to 25
Mild	26 to 40
Moderate	41 to 55
Moderately severe	56 to 70
Severe	71 to 90
Profound	91+

Source: Clark, (1981).

2.5 HEARING LOSS IN SICKLE CELL DISEASE PATIENTS

Hearing loss has been established to be a known complication of SCD. An experimental study by Perlman, Kimura & Fernandez (1959) affirmed in writing that, ischemia caused changes in the functioning and structure of the cochlea. Another study also proposed a theory that compression of the auditory canal by the expanded bone marrow of the petrous temporal bone due to thrombotic process could contribute to hearing loss (Morgenstern & Menace, 1969). Hearing loss is again described as one of the complications which occur as a result of vascular occlusion among SCD patients (Ogawa & Kanzaki, 1994).

Vascular occlusion resulting from obstruction of blood flow due to sickled red blood cells lead to anaemia and finally organ (including the cochlea) damage, which may lead to hearing loss among SCD patients (Whitehead et al., 1998). It is also reported that there is a high prevalence rate of hearing loss among SCD patients compared to the general public. Furthermore, it has been indicated that among those with SCD the prevalence rate of hearing loss ranges from 12% to 41% (Downs, Stuart & Holbert, 2000). It further emphasized that vascular occlusion affects the function of the labyrinthine artery (the single artery which supplies the cochlea), thereby causing hearing deficit due to changes in the function of the inner ear (Ondzotto et al., 2002). According to the report of Schneider et al., (2002), local homeostasis and cochlea function are affected when oxygenated blood supply is in short.

A regular pattern of hearing loss observed among those with SCD has also been explained. It is identified that the basal turn to the cochlea is very sensitive to anoxia (absence of oxygen in a tissue) which results from hemolysis. Anoxia affects the basal turn which records high frequencies and secondly the apical turn which records low frequencies. Hence, hearing loss

among SCD patients starts from the basal turn to the apical turn which are responsible for recording the high and low frequencies respectively and finally the whole cochlea (Mgbor et al., 2004). Moreover hearing deficit is reported to occur as an immediate consequence of cochlea ischemia (Mom et al., 2005).

Moreover, there are several case findings in literature that supports the presence of SNHL among SCD patients with a prevalence rate of 11–41% (Todd & Larson, 1973; Freidman et al., 1980; Foramen-Franco et al., 1982; Ashoor & Al-Awamy, 1985; Odetoyinbo & Adekile, 1987; Atsina et al., 1988; Crawford et al., 1991; Gould et al., 1991, and MacDonald et al., 1999). Sickle cell disease patients experience repetitive haemolytic and thrombotic crises and these crises are also known to damage tissues in the cochlea which eventually affects the hearing of these patients. However, most of these patients regain their hearing within two weeks after they recover. As a result of this recurrent hearing threshold impairment due to hemolytic and thrombotic crisis, SCD patients develop SNHL in the long term (Ashoor et al., 1985). Slow blood flow in the vertebra-basilar system is associated with SNHL in humans (Yamasoba et al., 1993).Vascular occlusion and haemolysis affects the (stria vascularis, the basal and apical turn, hair cells of the organ of Corti) of the cochlea, resulting in a SNHL (Mbgor et al., 2004).

Furthermore, a study among 100 sickle cell anaemia patients in Quatif, Saudi Arabia indicated that, tympanometry was the same for the SCD patients and the control group except for slight differences in the compliance (Al-Dabbous et al., 1996). Hearing loss is also associated with vascular occlusive events which affect the delicate vasculature of the auditory system, causing conductive, sensorineural and central process hearing loss (Downs et al., 2000). In addition to the above Otitis media externa (OME) was demonstrated in 22 SCD subjects in a study that

investigated the prevalence of hearing loss among 80 sickle cell anaemia (SCA) patients (Alibi et al., 2008). It was further indicated that hearing loss in SCD can either be Conductive with variable degree of obstruction of sound transmission either in the outer ear or the middle ear, likely due to susceptibility to infections in SCD patients (Castro Silva et al., 2010).

2.6 PREVALENCE OF HEARING LOSS AMONG SCD PATIENTS

2.6.1. Prevalence in Developed Countries

Sensorineural hearing loss is reported to be the most occurring type of hearing loss among SCD patients, and the prevalence of hearing impairment ranges from mild to profound, with bilateral hearing loss occurring the most (Da Silva, Nova & Lucena, 2012). The incidence of peripheral and central auditory dysfunction is further described in SCD patients. The peripheral auditory function of 58 Hb SS and the central auditory function of 28 of these patients were examined in USA. Six (11%) of the SCD patients had peripheral hearing loss while 13 (46%) of them had mild central auditory dysfunction (Forman-Franco et al., 1982).

A study conducted in the United Kingdom among 52 sickle cell anaemia patients also associated SNHL with SCD. Seven (13.5%) sickle cell anaemia patients were reported to have SNHL greater than 20dB at two or more frequencies. None of the 36 control group with genotype AA presented with a hearing loss. It was further indicated that the crucial period for the development of SNHL in SCD may be during the first few years of life (Ajulo, Osiname & Myatt, 1993). Eighty-four (84) subjects out of 250 children with SCD in Boston (USA) as part of their annual audiometry and otolaryngologic examinations of their routine care provided a study group who underwent hearing tests. Hearing evaluation was by age appropriate protocol, including auditory evoked brainstem response (ABR), visual reinforcement audiometry (VRA), conventional

audiometry and where possible speech reception threshold and word recognition. Three children (3.5%) out of the 84 had mild SNHL which was found to be in the high frequency range. Two out of the three children who presented with SNHL have Hb SS and one has Hb SC (MacDonald et al., 1999).

Otoacoustic emissions (OAEs) among 20 African-American children with Hb SS were investigated in East Carolina (USA). The findings of the study showed that distortion product otoacoustic emission (DPOAE) have larger amplitudes in children with SCD than in children with normal haemoglobin (Downs et al., 2000).

Hearing loss among SCD patients is known to be a likely occurrence due to vascular occlusive crisis associated with the disease. Hearing impairment prevalence of 0 to 60% with different patterns and degrees of hearing loss was reported. The hearing loss ranged from profound bilateral losses with partial recovery overtime to, mild to moderate unilateral loses mostly in the high frequencies (Burch-Sims et al., 2005).

A study was conducted to investigate the relationship between SCD and hearing loss among 183 SCD patients (Hb SS, Hb SC and Sβ-thalassemia or EF) in Tennessee (USA). All of them underwent routine audiological and electrophysiological assessments. Out of the 183 SCD patients, 80% of those with Hb SS had hearing deficit while 59% of them had normal hearing. Among those with Hb SC 7% of them had hearing deficit while 25% of them had normal hearing. Again 7% of those with Sβ-thalassemia had hearing impairment while the 12% of them had normal hearing. Among those with the hearing deficit, 78% of them had high frequency

SNHL. A significant relationship between DPOAE results and high frequency SNHL was established (Burch-Sims et al., 2005).

A prospective study in Guadeloupe, France involving 79 SCD patients and a control group of 40 people aged 15 to 60 years was done to determine the incidence of SNHL, identify changes in cochlea nerve and central pathways and to determine the most vulnerable group. The study was done via ENT, audiological and brainstem auditory evoked responses examinations. A hearing loss of more than 20 dB in two or more frequencies was reported in 36 (45.57%) of SCD patients, with 19 (47.22%) in Hb SC, 17 (43.59%) in Hb SS, and 3 (7.5%) members of the control group. Bilateral hearing loss occurred in 19 (52.78%) patients, unilateral right-sided hearing loss in 5 (13.89%) patients and unilateral left-sided hearing loss in 12 (33.33%) patients. A prolonged wave I-V (III-V) inter-peak latency was observed in 13 (25.35%) SCD patients (11 men and 2 women) in a brainstem auditory evoked potential. Those with Hb SS demonstrated neural hearing loss of earlier onset while, the hearing loss in Hb SC patients was cochlea in nature and of later onset (Jovanovic-Bateman & Hedreville, 2006).

2.6.2. Prevalence in Developing Countries

Another study was carried out to investigate the frequency and pattern of hearing loss among 100 Hb SS sickle cell disease patients aged 5 to 40 years in Qatif, Saudi Arabia. The subjects included 41 children and 59 adults. Tympanometry was the same for the SCD patients and the control group except for slight differences in the compliance. Sensorineural hearing loss was recorded in 19 (19%) of the SCD patients and in none of the control individuals. Five pediatric patients (less than 12 years) and 14 adults (above 12 years) included those who had the hearing loss. Most of them had a moderate SNHL with 3 of them having high frequency losses. Nine

(47.4%) of them had bilateral SNHL with 10 (52.6%) of them having a unilateral hearing loss. Four out of the 19 with SNHL recovered their hearing in within 18-22 months. Again 15- 40 dB hearing improvement was found in 7 (36.8%) between 6 to 21 months (Al-Dabbous et al., 1996).

A case control study was carried out to ascertain the prevalence of SNHL among SCA patients in Southern Brazil. Twenty-eight SCA patients and a matched control group constituted the study. Of the SCA group 6 (21.4%) had SNHL as against 1 (3.6%) in the control group (Piltcher et al., 2000). Twenty-four SCD patients underwent ENT and audiometric assessment to determine the Presence, type and degree of hearing loss presented among them in Greece. Only 1 (4.6%) patient had a unilateral hearing loss in the high frequencies above 70 dB with a prolonged III-V inter-peak latency in brainstem auditory evoked potentials (Koussi et al., 2001).

In addition to the above, another study was conducted in Sicily (Italy) to investigate the prevalence of SNHL among 50 Hb S/beta thalassemia (37Hb S/β^0-thalassemia and 13 Hb S/β^+-thalassemia) and 23 SCA patients. According to the study 24% of subjects with Hb S/β^0-thalassemia, 23% of subjects with Hb S/β^+-thalassemia and 30% of subjects with SCA demonstrated a SNHL of more than 25 dB. Frequency of hearing loss in increasing age was also reported (Samperi et al., 2005).

A study was conducted to ascertain the integrity of the peripheral and central auditory systems of SCD patients using brainstem auditory evoked response (BAER) an electrophysiological evaluation. The study described the auditory system to have abundant vascular supply especially in the stria vascularis which is located in the organ of corti responsible for the ionic exchanges that promotes the activation and deactivation of outer and inner hair cells, the sensory cells for

hearing. This region is known to have high consumption of oxygen and a poor capacity for anaerobic respiration, making the vestibular apparatus and the cochlea sensitive to anoxia (Castro Silva et al., 2010).

Forty SCD patients with age and gender matched non-SCD subjects between 8 to 20 years constituted the study in Brasilia, Brazil. Of these, 34 (85%) had Hb SS, 3 (7.5%) had Hb SC and 3 (7.5) had Hb Sb-thalassemia with 40 Hb AA genotype presenting in the control group. The results of the study indicated that 11 (27.5%) children were affected. Six of them had unilateral hearing loss whiles 5 had bilateral hearing loss. Out of the 80 ears, 16 (20%) presented with hearing thresholds worse than, 20 dB. However, in the control group, 2 (5%) children presented with hearing thresholds worse than 20 dB, with 1 child having a unilateral loss and the other child having a bilateral loss. That is 3 (3.8%) out of 80 ears. The distinct SCD genotypes showed slight differences in the threshold averages (Hb SB 26.6 dB, Hb SS 23.5 dB and Hb SC 20 dB). The type of hearing loss presented in the study was sensorineural in nature with cochlea abnormalities mostly of mild degree (Castro Silva et al., 2010).

Another study was carried to determine the prevalence and pattern of hearing loss in 46 SCD patients and 29 controls aged 16 to 45 years in Oman. The average hearing thresholds of SCD patients were higher than that of the controls (which had normal hearing thresholds) across all frequencies tested in both ears. Sensorineural hearing loss presented in 29.34% of the 92 ears tested the SCD patients. Ten had bilateral hearing loss while 3 and 4 showed unilateral SNHL in the left and right ears respectively. The hearing loss was worse in the right ears mostly among females. The high frequencies were mostly affected (Al-Okbi et al., 2011).

2.6.3. Prevalence in Africa

A study carried out in Kenya assessed the auditory function of 62 SCA patients aged 7 to 30 years with age matched 55 healthy controls with Hb AA. Twenty-five (40%) of the SCA patients and 3 (5.5%) of the controls had SNHL of 30 dB or worse. The high frequencies were mostly affected with hearing loss of 30-40 dB which was equally presented in both gender. Bilateral lesion was found in 10 (16%) while 2 (3.2%) cases of severe unilateral deafness at all frequencies were reported (Tsibulevskaya, Oburra & Aluoch, 1996).

Hearing loss among Angolan children with SCD was also investigated. The study asserted that bacterial infections and recurrent inadequate blood supply due to vascular occlusion in the cochlea region could lead to gradual loss of hearing. Bilateral hearing loss with a prevalence rate of 6% - 27.5% was reported among children with SCD in the developing countries. In addition to the hearing loss they also suffer splenic dysfunction and other infections that can increase the prevalence of otitis media (Taipale et al., 2012). Sixty-one children with SCD and a matched control group participated in the study. After audiometric evaluation participants were diagnosed of acute otitis media (AOM), chronic suppurative otitis media (CSOM) and middle ear effusion (MEE). Tympanograms were also interpreted as type (A, B or C) depending on tympanometry results. The results of the study indicated that 3% of the SCD patients presented with AOM, none with CSOM and 2% with MEE. Moreover, 36% of the SCD patients presented with mild bilateral hearing loss as against 11% in the control group (Taipale et al., 2012).

2.6.4. Prevalence in West Africa

Audiometric assessment was done for 56 Nigerians with SCA aged 6 to 15 years to ascertain the presence, types and degrees of hearing loss presented among them as various degrees of hearing

loss have been associated with the disease. Of the 56 SCA patients 12 (21.4%) were found to have SNHL greater than or equal to 25 dB in two or more frequencies. However tympanometry was normal for all patients. A significant association between hearing loss and early occurrence of vaso-occlusive crisis was established (Odetoyinbo et al., 1987).

Hearing assessment of 167 SCA patients and a matched 100 Hb AA adults aged between 15 and 56 years and 15 to 65 years respectively was done in a prospective study in Ibadan, Nigeria. Sensorineural hearing loss was presented in 178 ears in 110 SCA patients with a prevalence rate of 66% while 68 ears in 47 controls presented with SNHL representing 47% was reported. Sixty-eight SCA patients (62%) and (21) controls (44.7%) had bilateral hearing loss. The high frequencies 4000 to 8000 Hz were commonly affected in both SCA patients and the control group compared to the low frequencies. Most of them had mild hearing loss ranging from (26 - 40 dB HL) and a severe to profound SNHL in 5 patients. It was also observed that hearing level of patients got worse with increasing age especially among the sickle cell patients. However, there was no significant correlation between the severity of the hearing loss and frequency of vaso-occlusive crises (Onokoya, Nwaorgu & Shokunbi, 2002).

Another study was carried out to investigate the prevalence and pattern of hearing loss among 52 children in Enugu, Nigeria. A regular pattern of hearing loss observed among those with SCD was reported. The basal turn which records high frequencies and secondly the apical turn which records low frequencies are affected by anoxia. Hearing loss among SCD patients starting from the basal turn to the apical turn which are responsible for recording the high and low frequencies respectively and finally the whole cochlea were reported. All the 52 subjects were (Hb SS) SCA patients. Seven (13.1%) out of 52 SCD patients had bilateral SNHL. Two out of the 7 presented

with high frequency loss at 8000Hz ranging from 35 to 45 dB, and the remaining five (71.4%) had a SNHL at 500 Hz – 6000Hz greater than 35 dB (Mgbor et al., 2004).

The presence and severity of SNHL among 46 SCA patients in Ilorin, Nigeria was also investigated in a study. It was reported from the study that, 95.7% of the 92 tested ears exhibited normal hearing thresholds while 4.3% had mild hearing loss. All the 84 ears of the control exhibited normal hearing thresholds. There were higher average hearing thresholds among the Hb SS group than in the controls. It was further indicated that hearing in the left ears was better than the right ears (Aderibigbe, Ologe & Ouejola, 2005).

Eighty SCA patients and a gender matched 60 control patients of Hb AA genotype aged 4 to 15 years underwent audiological assessment and tympanometric evaluations in a prospective study to determine the prevalence of hearing loss among this group. Among the SCA patients, 25 subjects (50 ears) had abnormal audiograms. Otitis media externa (OME) was demonstrated in 22 subjects and 3 had bilateral SNHL. Fifteen subjects from the control group had abnormal audiograms resulting from OME while 19 subjects with SCA had bilateral OME with 2 and 1 in the left and right ears respectively. A 3.8% prevalence was presented among the 80 SCA patients (Alabi et al., 2008).

The auditory function of 112 SCD patients and a matched 112 healthy controls aged between 5 to 40 years were assessed to ascertain the impact of SCD on their hearing in Yopougon, Côte d'Ivoire. Hearing loss from 30 dB to 65 dB was found in 17% of the SCD patients as against 4% in the control group. From the study, 47% of hearing loss was seen in those with Hb SC while 37% and 16% were presented in those with Hb SS and Hb S/β^{+}-thalassemia respectively. Hb

S/β^+-thalassemia had the highest attack rate of hearing impairment 25% followed by Hb SC 21% and Hb SS 14%. Bilateral loss was demonstrated in 52.6% of the cases affecting both extremes of the hearing range, but was more significant in the lower frequencies (58% of the cases). Mixed hearing loss presented in 42% of the cases while SNHL presented in 58% of the cases (Elola et al., 2009).

A detailed investigation of hearing loss among SCD patients with haemoglobin SC genotype was conducted in Ibadan Nigeria. The aim of the study was to ascertain the incidence of SNHL and also to determine if hearing loss among these subjects correlated with age or gender. Forty-three Hb SC patients between 16 to 65 years and a matched control group of hundred Hb AA genotype individuals constituted the study. Hearing loss was reported to be one of the complications of Hb SC which is similar to Hb SS due to vascular occlusion and subsequent ischemic tissue damage in all organs including the cochlea (Onokoya et al., 2010).

More high frequency losses than low frequency losses among SCD patients were recorded. It was again indicated that hearing loss among Hb SC patients was cochlea in nature whiles hearing loss among Hb SS patients was neural in nature. The SCD group was made up of 17 males and 26 females, while the control group consisted of 48 males and 52 females. SNHL was defined as a loss of more than 25 dB HL at two or more frequencies in the same ear or at one or more frequencies in both ears. The degree of loss as defined by the study was according to that of the WHO (Onokoya et al., 2010). Sensorineural hearing loss presented in 12 (27.9%) out of the 43 Hb SC patients and 17 (19.8%) out of the 86 ears. Hearing loss was present in 17 (17%) of the hundred subjects and 21 (10.5%) of the 200 ears. Hearing loss was more common in the right ear than in left and was more of unilateral SNHL than bilateral loss.

The degree of loss ranged from 26 to 60 dB with most losses recorded between 26 to 40 dB. Of the 43 Hb SC patients, 14 (32.6%) had slight hearing loss while 3 (7.0%) had moderate loss. The prevalence in the control group were 19 (19%) and 2 (2%) respectively. Sensorineural hearing loss was over three times more in the females (38.5%) than in the males (11.8%) among the Hb SC group. In the control group, prevalence of SNHL among the females and males were 15.4 and 18.8% respectively. The occurrence of SNHL was higher among older participants in both groups. Again in the Hb SC group high frequency SNHL presented in 48 (55.6%) of the 86 ears and 62 (31.0%) out of 200 ears in the control group (Onokoya et al., 2010).

2.6.5. Prevalence in Ghana

The hearing levels of 55 SCA patients and a matched control group between the ages of 14 to 40 years were assessed to ascertain the extent of SNHL among this group at the Korle-Bu Teaching Hospital in Accra, Ghana (Atsina et al., 1988). The study indicated that all those within the control group had normal hearing thresholds while those with SCA presented with a SNHL of 29.1% ranging from 30 to 60 dB in the high frequencies (4000 to 8000 Hz) in 15 patients. Nine patients had bilateral hearing losses whereas 6 were found to have unilateral hearing losses (Atsina et al., 1988). A summary of the group studies is presented in Table 2.2

Table 2.2: Review of literature: summary of group studies

Investigator(s)	Year	No.	Procedure	Hearing Loss
Todd, Serjeant and Larson	1973	83	PT	22%
Sharp and Orchik	1978	09	HE	1/9
Friedman et al.	1980	43	HE	12%
Forman-Franco et al.	1982	54	HE	11%

Table 2.2 cont'd: Review of literature: summary of group studies

Investigator(s)	Year	No.	Procedure	Hearing Loss
Odetoyinbo and Adekile	1987	56	HE	21%
Elwany and Kamel	1988	10	HE,ABR	Abnormal
Wiliams et al.	1988	22	CAP	0%
Atsina et al	1988	55	PT	29.1%
Crawford et al.	1991	75	HE	41%
Gould et al.	1991	34	HE, ABR	13/34, 6/25
Ajulo, Osiname and Myatt	1993	52	PT	13.5%
Al-Dabbous et al.	1996	100	HE, ABR	19%
Chiodo et al.	1997	75	PT	57%
Gentry, Davis and Dancer	1997	100	PT	12%
MacDonald, Bauer and McMahon	1999	84	PT	22%
Piltcher et al.	2000	28	PT, Tym	21.4%
Downs, Stuart and Holbert	2000	20	DPOAE	Significantly large amplitudes
Koussi et al.	2001	24	HE, ABR	4.6%
Onakoya et al.	2002	167	PT	66%
Mgbor and Emodi	2004	50	PT	13.4%
Burch-Sims et al.	2005	113	HE, ABR	21%
Aderibigbe et al.	2005	46	HE	4.3%
Samperi et al.	2005	73	HE	13.8%
Jovanovic et al.	2006	79	HE, BER	45.57%
Alabi et al.	2008	80	HE	31.3%
Elola et al.	2009	112	HE	17%
Onokoya et al.	2010	43	PT	19.8%
Castro Silva et al.	2010	40	HE	27.5%

Pure tone thresholds (PT); hearing evaluation (HE); auditory brainstem response (ABR); central auditory processing (CAP); distortion product otoacoustic emissions (DPOAE); brainstem evoked response (BER).

2.7 RESEARCH GAP

Although a lot of studies have been done on SCD and its effect on hearing across different parts of the world and in Africa especially in Nigeria, there are limited data on this subject in the country. As far as this research study is concerned, only one study investigated SNHL among SCA patients in the country over 25 years ago (Atsina et al, 1988). The study was limited to and focused on only SNHL and one type of SCD (Hb SS). Presently there are limited data on the prevalence of hearing loss among the different types of SCD and the types of hearing loss that exist among SCD patients in the Country. Concurrently, the distributive effect of the different genotypes of SCD on hearing in the country is also not known. It is a result of this necessity that the current study was designed to determine the prevalence of hearing loss among SCD patients at the Korle-Bu Teaching Hospital in Accra, Ghana.

CHAPTER THREE

METHODOLOGY

3.1 INTRODUCTION

This Chapter describes the methodology and techniques used in the study. These include research design, study population, sample size and sampling technique, study sites, data collection procedure, data analysis and ethical consideration.

3.2 RESEARCH DESIGN

A case control study design was adopted for the study. The design was found suitable in achieving the stated objectives of the study. Scientific and demographic information of SCD patients were gathered within six (6) months at a study site and findings from the data were utilized to establish association between SCD and prevalence of hearing loss. Data was collected through hearing evaluation of participants using standardized pure tone audiometer and a tympanometer.

3.3 SAMPLE POPULATION

The population consisted of SCD patients within the age bracket of 13 to 60 years reporting to the Sickle Cell Clinic in Korle Bu Teaching Hospital (KBTH). The age range allowed for admission to the adult sickle cell clinic is 13 years and above. Secondly people above age 60 were excluded due to confounding factors associated with age like SNHL among this group known as presbycusis. Patients were referred to the audiology clinic of the KBTH where they were evaluated using a structured questionnaire.

3.4 SAMPLE SIZE AND SAMPLING TECHNIQUE

A purposive sampling technique was used in recruiting participants into the study because it offered easy accessibility to research participants. A total number of 200 participants aged 13-60 years were selected for the study. The participants were divided into two groups, consisting of 100 SCD patients and a control group of 100 individuals with normal haemoglobin electrophoresis with AA pattern. Participants were selected based on inclusion criteria defined in Section 3.5 and were drawn from the Sickle Cell Clinic at KBTH.

3.5 INCLUSION AND EXCLUSION CRITERIA

3.5.1 Inclusion Criteria

Participants between the ages of 13 to 60 years who had no history of exposure to excessive noise, hypertention, and were not on ototoxic medication were included in the study.

The criteria used to select sickle cell disease patients included:

- Those diagnosed by the sickle cell clinic as presenting with SCD.
- SCD patients aged 13 to 60 years.

For the control group, the following criteria were used:

- Subjects with haemoglobin AA genotype in the age range of 13 and 60 years.
- Subjects without any history of ototoxic medications within the last three months.
- Subjects with no chronic diseases such as diabetes, hypertension, renal impairment, rheumatoid diseases.

3.5.2 Exclusion Criteria for both SCD patients and control group

- Subjects who fall outside the required age range (i.e. 13 years and 60 years).
- Subjects with history of ototoxic medications within the last three months.
- Subjects with chronic diseases such as diabetes, hypertension, renal impairment, rheumatoid diseases

3.6 INSTRUMENTATION

The auditory status of participants was determined using a calibrated AC33 interacoustics audiometer and GSI TYMPSTAR version 2 tympanometer.

3.6.1 Interacoustics AC33 Audiometer

The AC33 clinical audiometer is a device for diagnosing hearing loss. This instrument is operated within an ambient temperature range of 15-35 ^{0}C (59-95 degrees ^{0}F) and has two independent channels. The AC33 audiometer and its accessories such as the TDH39 audiometric headset and the B71 bone conductor are all calibrated to meet the American National Standards Institute (ANSI) S3.6.) standards. The AC33 audiometer can be connected to a computer to store the test results in a database. It is able to do different test types ranging from pure tone, speech, ABLB, SISI, Stenger and Auto threshold tests. Figure 3.1 shows a block diagram of the pure tone audiometer which was used for the study.

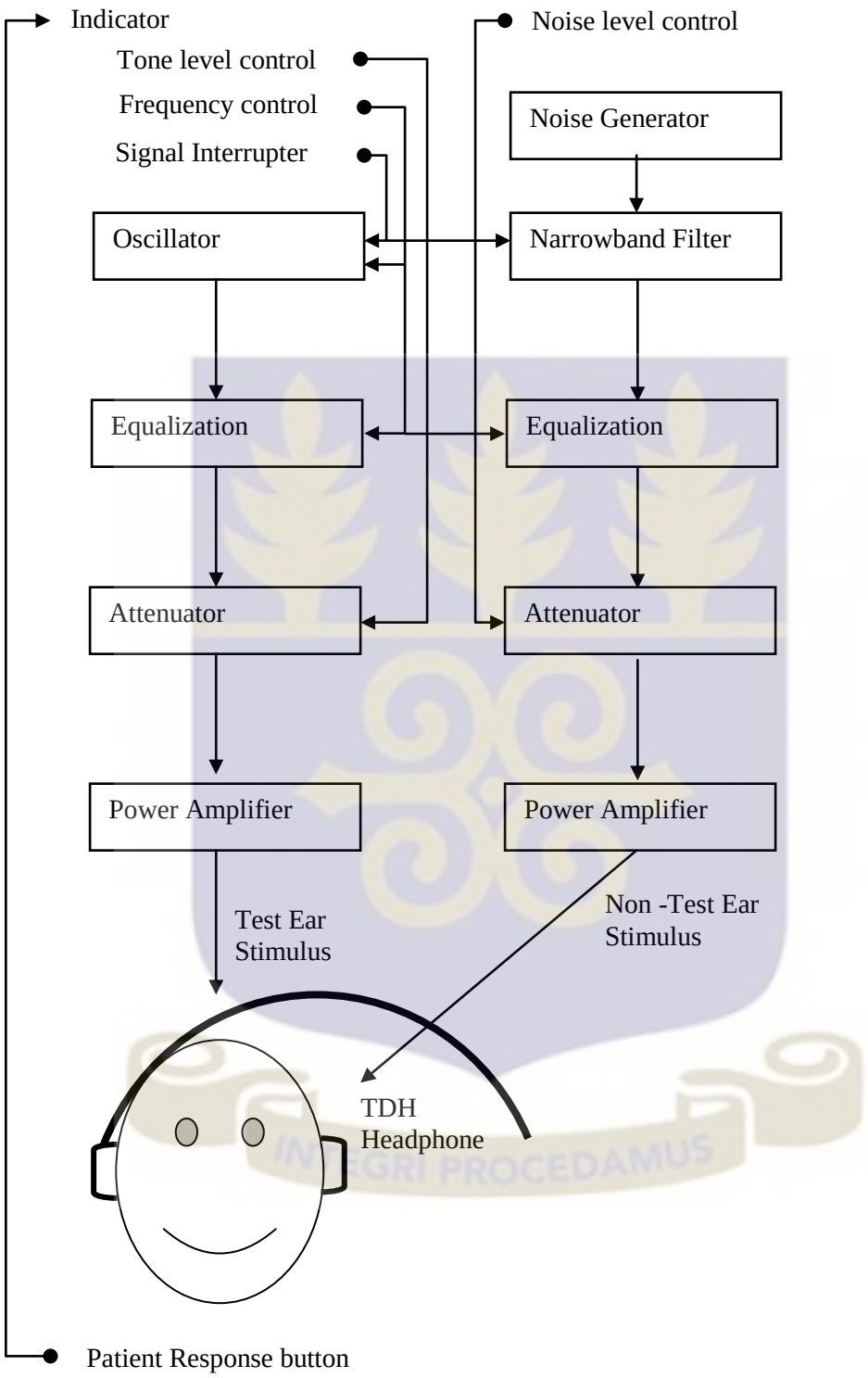


Figure 3.1: Block diagram of the pure tone audiometer

Table 3.1: AC 33 Audiometer technical specifications

Technical Variable	Specification
Standards	Audiometer: EN 60645 -1, EN60645-2, ANSI S3.6, Type 2 Speech: EN60645-2/ANSI S3.6 type A or A-E. Safety: EN 60601-1, Class I, Type B.
Calibration	AC: ISO 389-1 (TDH39), ISO 389-2 (EAR-Tone5A), BC: ISO 389-3, ISO 389-4, NB: ISO 389-4.
Channels	Two independent channels.
Modulation	+ 5% 5Hz. True sine wave.
Transducers	TDH39 Audiometric Headset. EAR-Tone 5A Insert Phones (optional). B71 Bone Conductor. CIR22 Insert Earphone for masking.
Power	AC 50-60 Hz. 100-120 V, 200-240 V.
Consumption	Max. 140 VA.
Dimensions (LxWxH)	48x40x15 cm / 19x16x6 inches.
Weight	9 kg / 20lbs.

3.7 PURE TONE AUDIOMETRY

Pure-tone threshold audiometry is defined as the measurement of an individual's hearing sensitivity for calibrated pure tones (American Speech-Language Hearing Association, 2005). This is done to find out the degree and type of a person's hearing loss. Pure tone audiometry was

carried out using calibrated Interacoustics AC33 audiometer in a sound treated booth to ANSI, (1996) standards. Headphones and bone vibrator were used to check air and bone conduction respectively. Air- and bone-conduction audiometry were done with an audiometer and transducers calibrated to required ANSI S3.6 specifications (ANSI, 1996).

Biological calibrations, functional inspection and performance checks were done daily before the beginning of hearing assessment to ensure the equipment were functioning properly (ASHA, 2005). Air and bone conductions were done for each ear across all conventional frequencies with the same audiometer and by the same examiner. For diagnostic purposes, air conduction hearing thresholds were assessed for tones 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz whereas bone conduction thresholds were tested for tones 500, 1000, 2000, 3000 and 4000 Hz.

3.7.1 Examiner and Participants Role in Pure Tone Audiometry

Ear examination: Visual inspection of the pinna and ear canal, including otoscopy, was done before audiometric testing to ensure each ear was in good condition for the test. Testing began with the better ear when it was identified, otherwise it was arbitrary.

Participant seating: Participants were seated in a way that the examiner's hand movement could not be observed and also in a comfortable and safe manner.

Instructions: Instructions for the test were given in a language the participant understood very well. Instructions included:

- Purpose of the test (to determine the faintest tone that could be heard).
- Participants were asked to sit quietly during the test.
- Participants were asked to respond by raising and lowering the hand whenever the tone was heard.

- Participants were asked not to hold or change the position of headset after checking with them if there was no discomfort (ASHA, 2005).

3.7.2 Pure Tone Audiometry: Air Conduction

Air-conduction audiometry is done to determine the level of a patient's hearing sensitivity at various frequencies. Air-conduction test results can identify the degree of loss but not the type of loss (Martin et al., 2012).

3.7.3 Determination of Pure Tone Threshold

An ascending technique which is the recommended standard procedure for manual pure-tone threshold audiometry was used. Pure-tone stimuli were presented between 1 to 2 seconds, with varied intervals between tone presentations. The level of the first presentation of the test tone was better than the expected threshold and the level of each succeeding presentation was established by the preceding response. After each failure to respond to a signal, the level was increased in 5dB steps until the first response occurred. The intensity was then decreased by 10 dB and the process repeated for higher steps.

Hearing threshold is defined as the lowest decibel hearing level at which responses occur at least one half of a series of ascending trials. Two responses out of three presentations are needed to determine the threshold of hearing at a single level (ANSI, 1996). The initial test frequency was 1000 Hz. Following this, tests were conducted across the 2000Hz, 3000Hz, 4000Hz, 6000Hz, and 8000 Hz, followed by a retest of 1000 Hz before testing 500 Hz, and 250 Hz. A retest at 1000 Hz was not necessary when the second ear was tested. The other ear was tested in the same way (ANSI, 1996).

3.7.4 Pure Tone Audiometry: Bone Conduction Threshold Determination

Pure tone bone conduction involves placing the bone vibrator on the mastoid process behind the ear to test the cochlea directly bypassing the middle ear. It compliments air conduction method and provides reliable information on conductive element of hearing loss. Ascending method was used (up 5 and down 10) across the 500Hz to 4000Hz frequency range. Maximum and minimum intensities at 60dB from 1000 Hz to 4000 Hz and 50 dB at 500 Hz were set (British Society of Audiology, 2011).

Based on the report of Boothroyd & Cawkwell (1970), bone conduction testing was not done at 250 Hz because vibrotactile threshold occurred at 25 dB which was not a hearing threshold. Furthermore, bone vibrator radio ear B71 has poor distortions performance at low frequency (Lightfoot, 2000) and such testing was not done at frequencies lower than 500 Hz because participants hearing threshold may relate to second or third harmonic instead of fundamental (BSA, 2011). In addition, testing was not done at 6000 Hz and above due to transducer limitations (Lightfoot & Hughes, 1993).

Standard bone-conduction vibrator was placed on the mastoid with the proper force applied (Dirks, 1964; ANSI, 1996). The test ear was not covered during standard bone conduction measurements. Participants were instructed to sit quietly, avoid movement that will dislodge the bone vibrator from the proper position and to notify the audiologist when the bone vibrator slipped or moved in any way from the original placement (ASHA, 2005).

3.7.5 Masking Air and Bone Conduction

Cross hearing may occur when the difference in the thresholds of the two ears is greater than the transcranial transmission loss. Cross-hearing is often overcome by temporarily raising the hearing threshold of the non-test ear by a known amount in order to enable a proper assessment of the test ear threshold to be made. This was accomplished by presenting a masking noise into the non-test ear at the correct intensity to hinder it from detecting the test signals, and at the same time measured the actual threshold of the test ear with the test signals.

Masking was needed where the difference between the left and right unmasked air conduction thresholds either exceeded 40 dB using supra- or circum-aural earphones, or 70 dB using insert earphones. Masking was also required at any frequency where the unmasked bone conduction threshold exceeded was more than the air-conduction threshold of either ear by 10 dB or more. The worse ear (by air conduction) was then classified as the test ear and the better ear as the non-test ear for masking. Narrow band noise was used for the masking. Participants were instructed to lift up their hands in response to the tones as described earlier. They were also instructed to ignore any steady rushing noise they heard but only respond by raising up the hand when they heard the tones (BSA, 2011). Air conduction threshold of non-test ear (NTE) plus occlusion effect and safety factor making 15 dB HL initial masking level was used.

3.8 GSI TYMPSTAR VERSION 2 MIDDLE EAR ANALYZER

The GSI TympStar version 2 Middle-Ear Analyzer is a technically advanced computer based instrument designed for examining of middle ear function. Admittance and its susceptance and conductance components may be measured with probe tone frequencies of 226Hz, 678Hz, and 1000Hz.

The extensive battery of test mode choices of this device includes:

- Diagnostic Tympanometry
- Acoustic Reflex Threshold and Decay Measurements
- Eustachian-Tube Function Testing (Both intact and perforated eardrums)
- Screening Tympanometry/Reflex (Automatic Only)
- Acoustic Reflex Latency Testing
- Acoustic Reflex Sensitization
- Multiple Frequency Tympanometry (250 Hz to 2000 Hz)

A schematic of the immitance device and the technical specifications of the GSI TympStar device are shown in Figure 3.2 and Table 3.2 respectively.

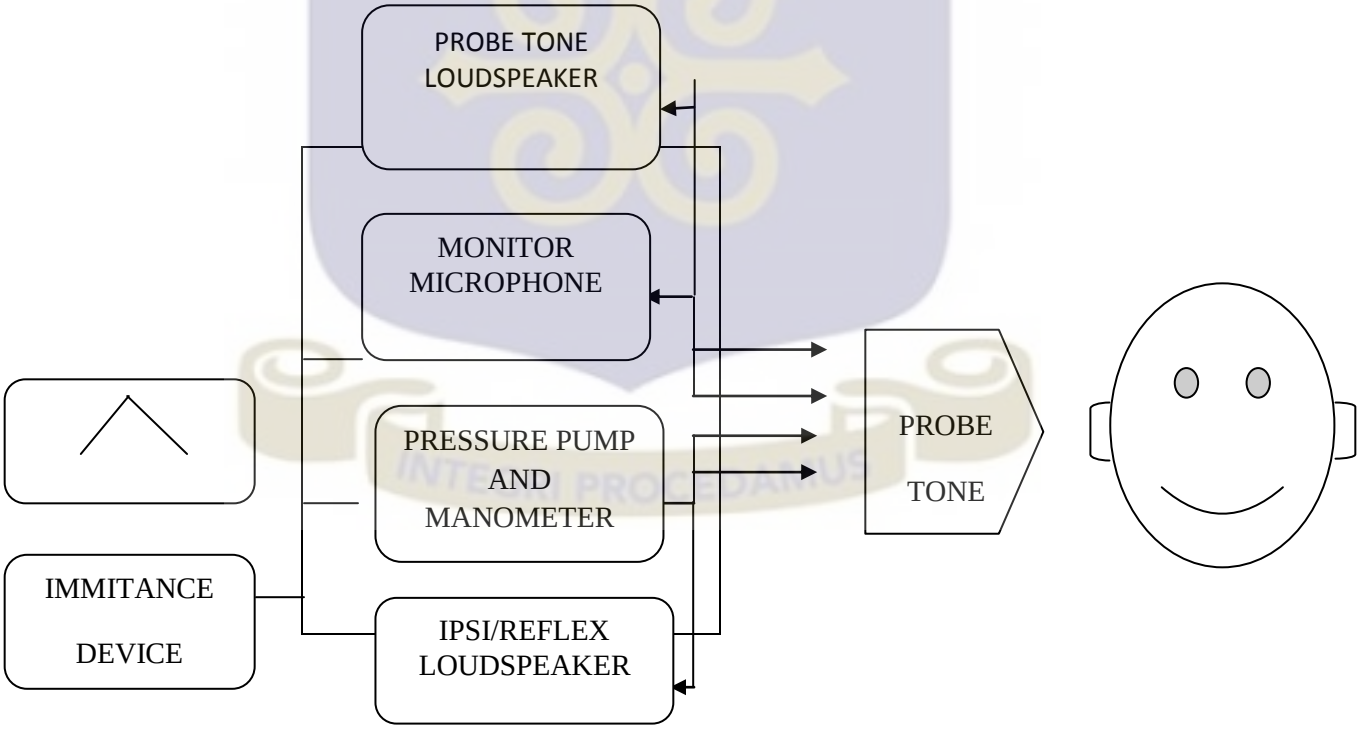


Figure 3.2: Block diagram of the immitance device

Table 3.2: GSI TympStar Version 2 Specifications

Technical Variable	Specification
Test standardization	IEC 1027 1991-03, ANSI S3.39-1987, ANSI S3.6-1996, ANSI S3.7-1995, IEC 645-1 1992, IEC 126-1973, BS ISO 389-2-1994
Probe tone frequencies	226, 678 & 1000 Hz
Acoustic reflex tones	Pure-tones, broad band & narrow band noise
Pressure range	+400 to -600 daPa

3.8.1 Physical Examination and Tympanometry

Physical examination was done with an otoscope to rule out middle ear infection, impacted wax and ear perforation. Tympanometry was performed using the GSI TympStar Version 2 Middle-Ear Analyzer. A stimulus tone of 226 Hz protocol was used. Normal ear canal volume, middle ear compliance or admittance peak value and a middle ear pressure ranged from 0.4 – 1.5 cm^3, 0.2 – 1.6 cm^3 and -100 to +100 daPa respectively (BSA, 2013).

3.9 STATISTICAL ANALYSIS

The result of the study was summarized in descriptive and inferential statistics. Measures of central tendency and range were used to depict average thresholds at all tested frequencies. Test of associations between SCD and hearing loss were conducted with the chi-square test at 95 and 99 % confidence levels.

3.10 ETHICAL CONSIDERATION

Ethical clearance was sought from the Ethics and Review Committee of the School of Biomedical and Allied Health Sciences for the commencement of the study (Appendix V). In addition permission was obtained from the Sickle Cell Clinic and Korle –Bu Teaching Hospital Hearing Assessment Centre (Appendix VI). Participants were informed about the study and informed consents were obtained from all participants (Appendix III, IV). Methods and objectives of the study, the process of assessment were fully explained to participants. Confidentiality of information with respect to their bio data and any data generated during the study was assured.

CHAPTER FOUR

RESULTS

4.1 INTRODUCTION

The results of the study are presented in this Chapter. Details of the results include demographics, distribution of pure-tone and impedance audiometry results, type and degree of hearing loss and tests of associations.

4.2 DEMOGRAPHIC CHARACTERISTICS

The age, gender, and haemoglobin genotype distributions of the 200 respondents (100 each in the case and control groups) are presented in Table 4.1.

Table 4.1: Demographic characteristics of respondents

Demographic Variable		Cases Group		Control Group		Total number
		Number	Percent, %	Number	Percent,%	
Gender	Male	45	45.0	48	48.0	
	Female	55	55.0	52	52.0	
	Total number	100		100		200
Age (years)	13 - 19	11	11.0	6	6.0	
	20 - 29	41	41.0	51	51.0	
	30 - 39	28	28.0	27	27.0	
	40 - 49	7	7.0	9	9.0	
	50 - 59	11	11.0	7	7.0	
	60	2	2.0	0	0.0	
	Total number	100		100		200
Haemoglobin genotype	SS	50	50.0	-	-	
	SC	50	50.0	-	-	
	AA	-	-	100	100.0	
	Total number	100		100		200

The mean ages of the participants (age range: 13-60 years) were 31.9 ±15.21 years for the case group and 30.61 ± 9.01 years for the control group. Participants aged 20-29 years were the most prevalent for both case (*n*=41, 41.0%) and control (*n*= 51, 51.0%) while the least prevalent age group was 60 years for both case (*n*=2, 2.0%) and control (*n*=0, 0.0%) groups.

All the subjects presented with Type A tympanograms in 400 ears.

Pure-tone air-conduction thresholds at test frequencies in the right and left ears were estimated for case and control groups. The results of the maximum, minimum and mean thresholds are shown in Table 4.2. The maximum air-conduction threshold for cases and controls were 95 dB at 3 and 6 kHz for right ears, 100 dB at 250 and 500 Hz for left ears and 55 dB at 6 kHz for right ears, 50 dB at 4 kHz for left ears respectively. A minimum air-conduction threshold of 0 dB was recorded at 500 Hz (left ears) and 8 kHz (both ears) for the case group. Similarly, a minimum of 0 dB air-conduction threshold was recorded for both right and left ears at all frequencies.

The distributions of the maximum and minimum pure-tone air-conduction and bone conduction thresholds at test frequencies are shown in Tables 4.2 and 4.3 respectively. The range of mean air-conduction thresholds for the case group (14.20 ± 9.15 dB to 22.55 ± 18.85 dB) was higher than the control group (8.54 ± 6.40 dB to 12.05 ± 8.96 dB) across the test frequencies.

With respect to the pure-tone bone-conduction threshold measurements (Table 4.3), maximum thresholds of 55dB in the right ear at 1, 2 and 4 kHz and the same at 2, 3 and 4 kHz in the left ear were registered for the case group. For the control group, maximum thresholds of 35 and 30 dB at 4 kHz were measured the right and left ears respectfully. A minimum bone-conduction threshold of 0 dB was recorded for cases (right and left ears) and controls (right and left ears).

The mean bone-conduction thresholds ranged from 7.70 ± 7.54 dB to 11.12 ± 12.00 dB for cases and 2.20 ± 4.22 dB to 3.00 ± 6.28 dB for controls across the tested frequencies.

Table 4.2: Distribution of maximum and minimum pure-tone air-conduction thresholds at test frequencies

Frequency (Hz)	Ears	Air-conduction thresholds (dB HL)					
		Case Group			Control Group		
		Maximum	Minimum	Mean ± s.d	Maximum	Minimum	Mean ± s.d
250	Right	50	5	15.40 ± 8.03	30	0	10.50 ±5.44
	Left	100	5	15.35 ±11.28	25	0	9.70 ± 4.97
500	Right	55	0	14.20 ± 9.15	25	0	10.15 ± 5.44
	Left	100	5	14.20 ± 12.39	25	0	9.70 ± 5.16
1000	Right	65	5	17.90 ± 9.70	25	0	11.50 ± 5.20
	Left	50	5	16.48 ± 7.15	25	0	10.20 ± 5.27
2000	Right	55	5	16.05 ± 8.24	25	0	9.75 ± 5.70
	Left	70	5	15.26 ± 9.40	25	0	8.80 ± 5.65
3000	Right	95	5	16.20 ± 12.85	35	0	8.90 ± 6.87
	Left	65	5	15.26 ± 10.75	30	0	8.54 ± 6.40
4000	Right	85	5	17.55 ± 13.95	40	0	8.70 ± 7.67
	Left	55	5	17.30 ± 11.24	50	0	9.60 ± 8.43
6000	Right	95	5	21.25 ± 16.16	55	0	11.45 ± 9.16
	Left	85	5	21.68 ± 13.18	35	0	10.75 ±7.63
8000	Right	85	0	21.77 ± 15.52	40	0	12.05 ± 8.96
	Left	70	0	22.55 ± 18.85	35	0	11.95 ± 8.79

Table 4.3: Distribution of maximum and minimum pure-tone bone-conduction thresholds at test frequencies

Frequency (Hz)	Ears	Bone-conduction thresholds (dB HL)					
		Case Group			Control Group		
		Maximum	Minimum	Mean ± s.d	Maximum	Minimum	Mean ± s.d
500	Right	50	0	8.40±9.32	20	0	2.55 ± 4.05
	Left	40	0	7.70 ± 7.54	15	0	2.37 ± 4.00
1000	Right	55	0	9.60 ± 9.50	20	0	2.80 ± 4.04
	Left	50	0	9.33 ± 8.63	15	0	2.50 ± 3.99
2000	Right	55	0	9.25 ± 9.70	20	0	2.55 ± 4.58
	Left	55	0	8.62 ± 9.27	20	0	2.20 ± 4.22
3000	Right	40	0	8.47 ± 9.64	30	0	2.75 ± 5.48
	Left	55	0	9.39 ± 10.70	25	0	2.30 ± 4.41
4000	Right	55	0	10.30 ± 11.00	35	0	3.00 ± 6.28
	Left	55	0	11.12 ± 12.00	30	0	2.95 ± 6.08

Table 4.4 shows that 86.25% (n=345) of the ears presented with normal hearing while 13.75% (n=55) presented with hearing loss among the tested population with Hb SS, Hb SC and Hb AA haemoglobin genotypes. All (14%) measured hearing loss were sensorineural.

The prevalence of hearing loss among subjects presenting with Hb SS, Hb SC and Hb AA haemoglobin genotypes were 30, 24 and 8 % respectively.

Table 4.4: Type and Prevalence of hearing loss among haemoglobin genotypes

Variable	Haemoglobin genotype			
	Hb SS (cases)	Hb SC (cases)	Hb AA (controls)	Total
Type of hearing loss (Ears)				
Normal hearing	73	84	188	345
Conductive hearing loss	-	-	-	-
Sensorineural hearing loss	27	16	12	55
Mixed hearing loss	-	-	-	-
Total	100	100	200	400
Prevalence of hearing loss				
Ears	27% (n=27)	16% (n=16)	6.0% (n=12)	49%
Subjects	30% (n=30)	24% (n=24)	8% (n=16)	62%

From Table 4.5 35 (70 ears) subjects with Hb SS genotype presented with normal hearing while the Hb SC and Hb AA groups recorded 38 (76 ears) and 92 (188 ears) normal hearing subjects.

Table 4.5: Hearing status according to genotype

Status	Hb SS n (%)		Hb SC n (%)		Hb AA n (%)	
	Subjects	Ears	Subjects	Ears	Subjects	Ears
Normal hearing	35 (70)	70 (70)	38 (76)	76 (76)	92 (92)	188 (94)
Hearing loss	15 (30)	27 (30)	12 (24)	16 (16)	8 (8)	12 (6)
Right	1 (2)	1 (1)	4 (8)	4 (4)	3 (3)	3 (1.5)
Left	2 (4)	2 (2)	4 (8)	4 (4)	1 (1)	1 (0.5)
Both	12 (24)	24 (24)	4 (8)	8 (8)	4 (4)	8 (4)

Furthermore, the Hb SS, Hb SC and Hb AA genotypic groups presented the respective subjects of 15 (27 ears), 12 (16 ears), and 8 (12 ears) with a hearing loss. Among the subjects with a hearing loss at the various genotypic conditions, Hb SS presented with 3 (3 ears) unilateral and 12 (24 ears) bilateral hearing loss while Hb SC and Hb AA registered 8 (8 ears) unilateral, 4 (8 ears) bilateral and 4 (4 ears) unilateral and 4 (8 ears) bilateral hearing loss respectively.

Table 4.6 depicts the degree of hearing loss at the various genotypes. There were 16, 4 and 11 ears with mild hearing loss for Hb SS, Hb SC and Hb AA groups respectively while the same genotypic conditions registered 7, 4 and 1 moderate hearing loss respectively. At the degree of moderately severe, there were 2 ears at the Hb SS group and 3 ears at the Hb SC group. None of the subjects with Hb AA genotype presented with a moderately severe degree of hearing loss. Only the Hb SC group presented 3 ears with a severe degree of hearing loss. At the profound degree of hearing loss, there were 2 and 1 ears at the Hb SS and Hb SC groups respectively.

Table 4.6: Degree of hearing loss in each ear

	Hb SS (n=50) (%)		**Hb SC (n=50) (%)**		**Hb AA (n=100) (%)**	
Degrees	**Right Ear**	**Left Ear**	**Right Ear**	**Left Ear**	**Right Ear**	**Left Ear**
Normal	37 (74)	36 (72)	42 (84)	42 (84)	93 (93)	95 (95)
Mild	10 (20)	6 (12)	1 (2)	3 (6)	6 (6)	5 (5)
Moderate	2 (4)	5 (10)	2 (4)	2 (4)	1 (1)	
Moderately Severe		2 (4)	2 (4)	1 (2)		
Severe			3 (6)	1 (2)		
Profound	1 (2)	1 (2)		1 (2)		

4.3 TEST OF ASSOCIATION

Tables 4.7 showed a significant association between hearing status and haemoglobin genotype for air-conduction thresholds [χ^2 (2, *n*= 304) = 68.74, 68.57, 108.59, 115.22, 105.67, 115.14, 125.52, 120.93; $p < 0.01$].

Table 4.7: Association between hearing status (AC) at test frequencies and haemoglobin genotype

Frequency (Hz)	Hearing status (Ears)	Haemoglobin genotype Hb SS N0. (%)	Hb SC No. (%)	Hb AA No. (%)	χ^2	*df*	p-value (2-tailed)
250	Normal hearing	92 (92.0)	91 (91.0)	197 (98.5)	68.74	2	0.00
	Hearing loss	8 (8.0)	9 (9.0)	3 (1.5)			
500	Normal hearing	93 (93.0)	93 (93.0)	200 (100)	68.57	2	0.00
	Hearing loss	7 (7.0)	7 (7.0)	0 (0.0)			
1K	Normal hearing	93 (93.0)	95 (95.0)	200 (100)	108.59	2	0.00
	Hearing loss	7 (7.0)	5 (5.0)	0 (0.0)			
2K	Normal hearing	90 (90.0)	91 (91.0)	200 (100)	115.22	2	0.00
	Hearing loss	10 (10.0)	9 (9.0)	0 (0.0)			
3K	Normal hearing	85 (85.0)	88 (88.0)	197 (98.5)	105.67	2	0.00
	Hearing loss	15 (15.0)	12 (12.0)	3 (1.5)			
4K	Normal hearing	81 (81.0)	88 (88.0)	192 (96.0)	115.14	2	0.00
	Hearing loss	19 (19.0)	12 (12.0)	8 (4.0)			
6K	Normal hearing	77 (77.0)	85 (85.0)	191 (95.5)	125.52	2	0.00
	Hearing loss	23 (23.0)	15 (15.0)	9 (4.5)			
8K	Normal hearing	73 (73.0)	85 (85.0)	190 (95.0)	120.93	2	0.00
	Hearing loss	27 (27.0)	15 (15.0)	10 (5.0)			

Significant at 0.01 level **AC=Air-conduction**

The prevalence of hearing loss at the respective test frequencies for Hb SS (8%, 7%, 7%, 10%, 15%, 19%, 23%, 27%) and Hb SC [(air-conduction= 9%, 7%, 5%, 9%, 12%, 12% 15%, 15%)]

compared with Hb AA [(air-conduction= 1.5%, 0%, 0%, 0%, 1.5%, 4%, 4.5%, 5%)] supports the significance of the association between air-conduction hearing status and haemoglobin genotype.

Table 4.8: Association between Hearing status (BC) at test frequencies and haemoglobin genotype

		Haemoglobin genotype					
Frequency (Hz)	Hearing status (Ears)	Hb SS No. (%)	Hb SC No. (%)	Hb AA No. (%)	χ^2	*df*	p-value
500	Normal hearing	94 (94.0)	95 (95.0)	200 (100)	155.07	2	0.00
	Hearing loss	6 (6.0)	5 (5.0)	0 (0.0)			
1K	Normal hearing	94 (94.0)	97 (97.0)	200 (100)	170.65	2	0.00
	Hearing loss	6 (6.0)	3 (3.0)	0 (0.0)			
2K	Normal hearing	94 (94.0)	94 (94.0)	200 (100)	171.39	2	0.00
	Hearing loss	6 (6.0)	6 (6.0)	0 (0.0)			
3K	Normal hearing	91 (91.0)	90 (90.0)	188 (94.0)	132.41	2	0.00
	Hearing loss	9 (9.0)	10 (10.0)	2 (6.0)			
4K	Normal hearing	85 (85.0)	89 (89.0)	187 (93.5)	145.45	2	0.00
	Hearing loss	15 (15.0)	11 (11.0)	3 (3.0)			

Significant at 0.01 level **BC=Bone-conduction**

Similarly, Table 4.8 showed a significant association between hearing status and haemoglobin genotype for bone-conduction thresholds [χ^2 (2, *n*= 304) = 155.07, 170.65, 171.39, 132.41, 145.45; $p < 0.01$]. This was supported by the prevalence of bone-conduction hearing loss at the respective test frequencies for Hb SS (bone-conduction= 6%, 6%, 6%, 9%, 15%) and Hb SC (bone-conduction= 5%, 3%, 6%, 10%, 11%) compared with Hb AA (bone-conduction= 0%, 0%, 0%, 1%, 1.5%)].

Additionally, a post hoc test between Hb SS and Hb SC respondents thresholds revealed a non-significant mean difference for air ($p > 0.01$) and bone ($p > 0.01$) conduction thresholds across the tested frequencies as depicted in Tables 4.9 and 4.10.

Table 4.9: Post hoc test (LSD) on mean differences between Hb SS and Hb SC Respondents Thresholds

	Frequency	**SS (Air-conduction)**							
		250Hz	500Hz	1kHz	2kHz	3kHz	4kHz	6kHz	8kHz
SC	250Hz	-0.45							
	500Hz		-0.95						
	1kHz			-0.10					
	2kHz				-8.80				
	3kHz					0.65			
	4kHz						1.35		
	6kHz							-0.25	
	8kHz								-0.64

***Significant at 0.01 level**

Table 4.10: Post Hoc Test (LSD) on Mean Differences between Hb SS and Hb SC Respondents Thresholds

	Frequency	**SS (Bone-conduction)**				
		500Hz	1kHz	2kHz	3kHz	4kHz
SC	500Hz	0.05				
	1kHz		0.24			
	2kHz			2.45		
	3kHz				1.40	
	4kHz					1.35

***Significant at 0.01 level**

CHAPTER FIVE

DISCUSSION OF RESULTS

5.1 INTRODUCTION

Hearing loss has been described to be one of the complications of SCD by numerous studies. Different types, degrees and pattern of hearing losses have been published in literature among SCD patients. Conductive and SNHL have been described among younger and older SCD patients respectively, with degree of losses ranging from mild to profound. This study investigated and evaluated the hearing thresholds of 100 SCD patients with Hb SS and Hb SC genotypes through pure tone audiometry and tympanometry to ascertain the prevalence of hearing loss among this group. The aim of the study was to investigate the types of hearing loss that exist among the SCD patients and the type of SCD which impacted more on hearing.

5.2 HYPOTHESIS 1

There will be a significant association between Ghanaian SCD subjects and hearing loss.

A significant difference in the hearing thresholds of SCD patients and non SCD patients have been reported in literature (Atsina et al., 1988; Ajulo et al., 1993; Tsibulevskaya et al., 1996; Chiodo et al., 1997; Ambrosetti et al., 2000; Piltcher et al., 2000; Koussi et al., 2001; Burch-Sims et al., 2005; Farid & Said, 2009). The result this study showed that, people living with SCD have high hearing thresholds compared with non SCD patients. This observation is in agreement with literature where several explanations were adduced for the varying prevalence rates of hearing deficit among the SCD patients. These include age, locality and type of haemoglobin gene of the

patient (Mgbor et al., 2004). However, 27% of SCD patients assessed in this study had hearing loss compared to 8% of the control group. Findings from other studies that used different methods between 1988 and 2009 showed percentage hearing deficit incidences with a prevalence rate of 12% to 66% among the SCD populations (Da Silva et al., 2012).

Contrary to expectation, only SNHL was observed in this study. This may be attributed to the age range of the study population. Most of the studies that reported conductive hearing losses among persons living with SCD had a much younger population as compared to this study (Brooks, 1986; Minja et al., 1996; MacDonald et al., 1999; Taipale et al., 2012). Furthermore, several studies have reported otologic findings in SCD with advanced different rationales for the development of SNHL in persons living with SCD. It is reported that, sickling of the red blood cells results in vascular occlusion that leads to tissue ischemia and necrosis which is accentuated by decreased blood flow and low oxygen supply (Berry, 1975; Serjeant et al., 1975; Marcus & Lee, 1976).

The increase in hearing thresholds of the SCD patients could result from sickling and slugging of blood in the cochlea (Diggs, 1956; Morganstein & Manace, 1969; Odetoyinbo et al., 1987; Todd et al., 1973). It is further suggested that vascular occlusion of the cochlea is the cause of hearing loss among SCD patients (Koide et al., 1964; Serjeant et al., 1975, MacDonald et al., 1999).

Statistical analysis of the results showed a significant difference in hearing thresholds of SCD patients and control group across all frequencies for both right and left ears. While the control group had normal hearing thresholds better than 25 dB, the SCD patients showed high hearing thresholds in the low and mid frequencies, albeit within the normal range. The observation of

significant SNHL in the mid to high frequencies from (2000 Hz to 8000 Hz), is consistent with findings from Onakoya et al., (2002), Burch Sims et al., (2005), Al Okbi et al., (2011), that high frequency SNHL was dominant among SCD patients. On the contrary Frisina et al., (2006) found hearing loss in persons living with SCD to be at the low frequencies.

The bone conduction hearing thresholds for both ears increased from 2000 Hz to 4000 Hz was higher among SCD patients. This is suggestive that SCD patients have higher chances of developing SNHL than non–SCD patients. The audiograms of SCD patients did not show any significant air-bone gap indicating the presence of SNHL.

Increases in the frequency of hearing loss with increasing age have been suggested by Friedman et al., (1980) and Ajulo et al., (1993). This suggestion which is contrary to the findings of Todd et al., (1973) was not found in this study.

5.3 HYPOTHESIS 2

There will be an association between degree of hearing loss and the type of SCD.

The results from the study showed that 27% of SCD patients exhibited some degree of hearing loss. Hearing loss was more common in patients with Hb SS representing 55.6% of the total SCD group that presented with hearing deficit than those with Hb SC. A similar finding was reported by Burch-Sims et al., (2005) in which 80% of SCD patients with hearing deficit had Hb SS. The degrees of hearing losses presented ranged from mild to profound SNHL in both SCD groups. However, the deficit was worse in patients with Hb SC disease with most of them exhibiting moderate to profound hearing losses. These findings agree with previous studies by Friedman et al., (1980); Crawford et al., (1991).

Unilateral and bilateral SNHL was common in both groups. However, bilateral SNHL was more common in the Hb SS group and both ears were equally affected. Nevertheless, the Hb SC group had more unilateral losses representing 30% of the total SCD group that was observed with hearing deficit. The few bilateral hearing losses showed by the Hb SC group, did not affect both ears equally. It was observed that hearing deficit was always worse in one ear than the other.

The prevalence of hearing loss in adult patients was investigated, correlating the degree of auditory deficit with the type of SCD by Crawford et al., (1991). In that study 41% of the patients exhibited some degree of hearing loss, the deficit being worse in patients with Hb SC disease, Sb-thalassiemia, and Hb SS group in that order. However, in this study 30% (15/50) of the Hb SS group presented with hearing loss compared to 24% (12/50) of the Hb SC group.

Furthermore, there was no significant difference in the degree of hearing loss presented in both the Hb SS and Hb SC groups. The two SCD groups (Hb SS and Hb SC) did not impact differently on the auditory function of its patients. Both SCD groups presented with degree of loss ranging from mild to moderately- severe except for one profound loss in the Hb SS group.

CHAPTER SIX

CONCLUSIONS, RECOMMENDATIONS AND LIMITATIONS

6.1 INTRODUCTION

This section presents the conclusions drawn from the outcome of results, recommendations for future research consideration and limitations of the study.

6.2 CONCLUSION

The findings from the study showed that:

- There is significant difference in hearing thresholds in persons living with SCD and the control group. Sickle cell disease participants had mild to profound sensorineural hearing loss in the high frequencies from 2000 Hz to 8000 Hz. Although there were slight increase in hearing thresholds of SCD participants in the low frequencies, the increases were not significant to be classified as hearing loss. The study however established that, persons with SCD are at higher risk to experience hearing loss than the general population.
- One type of loss (SNHL) among Ghanaian adult SCD patients.
- The degree of hearing loss among the SCD patients ranged from mild to profound.
- Sensorineural hearing loss was more prevalent among the Hb SS genotype group than the Hb SC group.
- Subjects with Hb SS genotype showed more bilateral sensorineural hearing losses as compared with the Hb SC group.

Results from this study are very appropriate and can be used to schedule hearing evaluation programmes for persons living with SCD as it reflects actual hearing thresholds of SCD patients at the Korle-Bu Teaching Hospital.

6.3 RECOMMENDATIONS

From the findings of this study, it is recommended that:

- All SCD patients should have regular hearing assessment irrespective of whether the patient presents with hearing problems or not.
- Health care institutions should have at least one visiting audiologist to screen all SCD patients for early identification of any potential hearing problem.
- More research should be done in this area using objective and physiological assessment like ABR to ascertain the integrity of the auditory pathway up to the brainstem, and OAE to check the effect of SCD on the outer hair cells.
- Also, longitudinal study should be done to check if indeed frequency of hemolytic crisis has effect on hearing of SCD patients.

6.4 LIMITATIONS

The lack of equipment and resources could not allow for the use of other test batteries such as ABR, CAP, DPOAE, and BER in the determination of hearing loss among SCD patients for this study.

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APPENDIX I

DEPARTMENT OF AUDIOLOGY, SPEECH AND LANGUAGE THERAPY
SCHOOL OF BIOMEDICAL AND ALLIED HEALTH SCIENCES
COLLEGE HEALTH SCIENCES, UNIVERSITY OF GHANA

STUDY QUESTIONNAIRE
PREVALENCE OF HEARING LOSS AMONG SICKLE CELL DISEASE PATIENTS AT THE KORLE BU TEACHING HOSPITAL

DEMOGRAPHICS:

1. AGE…….. 2. GENDER M /F 3. OCCUPATION……
4. HAEMOGLOBIN GENOTYPE……..

QUESTIONS:

1. Have you taken any ototoxic medication such as aminoglycosides (gentamicin, streptomycin, kanamycin, quinine etc) in the last three months? (YES) (NO) (DON'T KNOW)
2. Are you hypertensive? (YES) (NO) (DON'T KNOW)
3. Do you have history of exposure to excessive noise i.e. ≥ 85dB (NIOSH 1998)? (YES) (NO) (DON'T KNOW)
4. Have you had head injury before? (YES) (NO) (DON'T KNOW)
5. Have you had ear surgery before? (YES) (NO) (DON'T KNOW)
6. Have you had severe Jaundice (Yellowing of the skin due to an excess of bile pigments in the blood) before? (YES) (NO) (DON'T KNOW)
7. Have you had meningitis before? (YES) (NO) or (DON'T KNOW)
8. Do you have any renal disease? (YES) (NO) (DON'T KNOW)
9. Do have history of hearing loss in your family? (YES) (NO) (DON'T KNOW)
10. Do you have any history of ear discharge or pain? (YES) (NO) (DON'T KNOW)

APPENDIX II

DATA COLLECTION FORM

DEPARTMENT OF AUDIOLOGY, SPEECH AND LANGUAGE THERAPY-SBAHS

COLLEGE OF HEALTH SCIENCES, UG-KORLE BU

PREVALENCE OF HEARING LOSS AMONG SICKLE CELL DISEASE PATIENTS AT THE KORLE BU TEACHING HOSPITAL

Age…… **Gender……** **Haemoglobin Genotype……**

	AUDIOMETRIC RESULTS							
	250Hz	500Hz	1KHz	2KHz	3KHz	4KHz	6KHz	8KHz
Right AC								
Left AC								
Right BC								
Left BC								

TYMPANOMETRY	RIGHT	LEFT
ECV (0.4-1.5 ml)		
Peak Compliance (0.2 - 1.6 ml)		
Peak Pressure (-100 - +100 daPa)		

APPENDIX III

PARTICIPANT INFORMATION FORM

Title of research: Prevalence of Hearing Loss among Sickle cell disease Patients at Korle-Bu Teaching Hospital

Principal Investigator: Roger Boakye-Akuffo
Department of Audiology, Speech and Language Therapy
Professional MSc Audiology
Mob: 0208360405; email: rogerbky@yahoo.com

General Information about Research

Under the supervision of Dr. Neal Boafo. and Dr. George Asare of the University of Ghana School of Biomedical and Allied Health Sciences, I Roger Boakye-Akuffo, a graduate student of the Department of Audiology, Speech and Language Therapy, am conducting research on prevalence of hearing loss among SCD patients at Korle –Bu Teaching Hospital. The purpose of the study is to assess the hearing thresholds of SCD patients and find the relationship between SCD and hearing loss.

Possible Risks and Discomforts

There are no risks for participation in this study since the testing equipment and procedure does give any side effects.

Voluntary Participation and Right to Leave the Research

Participation in this study is voluntary. You have the right to withdraw at any time or refuse to participate entirely without any jeopardy to you whatsoever.

Contacts for Additional Information

For any information, clarification or questions about the study, please contact the principal investigator, Roger Boakye-Akuffo on 0208360405.

Confidentiality

All information provided will remain confidential and will only be reported as group data with no identifying information. All data, including test results will be kept in a secure location and only those directly involved with the research will have access to them.

Possible Benefits

Participating in the study provides you with the opportunity of knowing your hearing status and the presence or not of any hidden hearing problem without any cost.

Alternatives to Participation

In the event of any noticed problem the participant will be referred for further testing and the necessary action as needed.

Your rights as a Participant

This research has been reviewed and approved by the Ethics and Protocol Review Committee of the School of Biomedical and Allied Health Sciences, College of Health Sciences, University of Ghana. If you have any questions about your rights as a research participant you can contact the EPC Office between the hours of 8am-5pm through the landline +233-302-687974/5 or postal addresses: Box KB 143, Korle-Bu, Accra.

APPENDIX IV

INFORMED CONSENT FORM

The document describing the benefits, risks and procedures for the research: prevalence of hearing loss among SCD patients at Korle –Bu teaching hospital has been read and / or explained to me. I have been given an opportunity to have any questions about the research asked and answered to my satisfaction. I agree to participate as a volunteer.

_____ _____

Date Signature or mark of volunteer

If volunteers cannot read the form themselves, a witness must sign here:

I was present while the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

_____ _____

Date Signature of Witness

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

_____ _____

Date Signature of Person Who Obtained Consent

APPENDIX V

UNIVERSITY OF GHANA
SCHOOL OF BIOMEDICAL AND ALLIED HEALTH SCIENCES
DEPARTMENT OF AUDIOLOGY, SPEECH AND LANGUAGE THERAPY

October 7, 2014

Mr. Roger Boakye-Akuffo
Dept. of Audiology, Speech and Language Therapy
SBAHS,
Korle Bu

Dear Mr. Roger Boakye-Akuffo

ETHICS CLEARANCE

Following a technical and professional review of your research proposal by the Department Ethics and Protocol Review Committee and by your supervisors, I am pleased to inform you of the Committee's approval your research proposal entitled:

"Prevalence of Hearing Loss Among Sickle Cell Patients a Korle Bu Teaching Hospital"

This is an initial approval. You are therefore required to obtain a final approval from the School's Ethics and Protocol Review Committee per the Schools regulations.

You are required to work closely and in collaboration with your supervisors. Please report all serious adverse events related to this research to the supervisors and this Committee in writing.

Thank you.

Yours sincerely,

DR. S. ANIM-SAMPONG

For: Chairman DASL&T Ethics and Protocol Review Committee

DEPARTMENT OF AUDIOLOGY
SPEECH & LANGUAGE THERAPY
SCHOOL OF BIOMEDICAL AND ALLIED
HEALTH SCIENCES

APPENDIX VI

UNIVERSITY OF GHANA
SCHOOL OF BIOMEDICAL AND ALLIED HEALTH SCIENCES
DEPARTMENT OF AUDIOLOGY, SPEECH AND LANGUAGE THERAPY

November 3, 2014

The Head
Hearing Assessment Centre
ENT Department
Korle Bu Teaching Hospital

Dear Sir/Madam,

PERMISSION TO CARRY MSc AUDIOLOGY RESEARCH PROJECT AT THE HEARING ASSESSMENT CENTRE, KBTH

The Department of Audiology, Speech & Language Therapy (DAS&LT) of the University of Ghana School of Biomedical and Allied Health Sciences (SBAHS) presents its compliments to you and has the pleasure requesting your kind consideration of the above subject.

Mr. Roger Boakye-Akuffo is a 2nd year MSc Audiology student of the Department of Audiology, Speech and Language Therapy of SBAHS, University of Ghana. He is conducting a research project in "Prevalence of Hearing Loss Among Sickle Cell Patients" under the supervision of Dr. N. Boafo (Clinical Audiologist), and Dr. G. A Asare (Chemical Pathologist). His research study has been reviewed and passed by the Department's Ethics and Protocols Review Group of the School as meeting all ethical requirements.

The Department would be most grateful if you could kindly grant him permission to carry out this important research project for the common good of the University and your Centre. Thank you.

Yours faithfully,

Dr. S. ANIM-SAMPONG
For: (Head of Department)
cc: Dean (SBAHS)
Dr. N. Boafo
Dr. G. A Asare

DEPARTMENT OF AUDIOLOGY
SPEECH & LANGUAGE THERAPY
SCHOOL OF BIOMEDICAL AND ALLIED
HEALTH SCIENCES

HEARING ASSESSMENT CENTRE

In case of reply the number
And the date of this
Letter should be quoted

My Ref. No.....
Your Ref. No.....

KORLE BU TEACHING HOSP.
P.O. BOX 77
KORLE BU, ACCRA

Tel: 233-21- 673033-6
Fax: 233-21- 667759
Email: korlebu@ghana.com
Web Site: www.korlebu.com

17th November, 2014

The Head
Dept. of Audiology, Speech and Language Therapy
School of Biomedical and Allied Health Sciences
College of Health Sciences
University of Ghana

Dear Sir,

RE:PERMISSION TO CARRY MSc AUDIOLOGY RESEARCH PROJECT AT THE HEARING ASSESSMENT CENTRE, KORLE BU TEACHING HOSPITAL

Permission has been granted Mr. Roger Boakye-Akuffo to carry out a research project on the "Prevalence of Hearing Loss among Sickle Cell Patients".

It is recommended that he works closely with the Audiologists at the Centre to ensure all protocols are observed.

Yours Sincerely,

E. N. T. CLINIC
KORLE BU TEACHING HOSPITAL

JEMIMA A. FYNN (MRS.) FWACN
MSc AUDIOLOGICAL SCIENCE

Cc: Head, ENT UNIT