DISSERTATION ON

HEARING LOSS IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

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CERTIFICATE

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CONTENTS

Introduction

1. INTRODUCTION

Diabetes mellitus comprises of a group of common metabolic disorders that share the phenotype of hyperglycemia. It is the most common endocrine metabolic disorder affecting both children and adults. The worldwide prevalence of type 1 and type 2 diabetes mellitus is increasing worldwide, with especially type 2 diabetes mellitus rising more rapidly both in children and adults due to the recent epidemic of obesity and also due to lifestyle changes. In 2000, the prevalence of diabetes mellitus was estimated to be 0.19% in people <20 years and 8.6% in people >20 years[1].

Type 1 diabetes mellitus, the most common form of diabetes mellitus encountered in childhood, accounts for approximately two thirds of all cases of diabetes mellitus in children[2]. Incidence of the disease varies from as high as 50 per 100,000 population in European countries like Finland to as low as 0.1 per 100,000 population in Asian countries like India[2]. The incidence of the disease is increasing especially in countries with a previous low incidence of autoimmune diseases[3]. It is predicted that the overall incidence of type 1 diabetes will be 40% higher in 2010 than in 1997[3].

Magnitude of the Problem in India:

Though this disease has a low incidence in our country of only 0.1 per 100,000 populations the magnitude of the problem is indeed huge considering the chronicity of the illness, its effect on growth and development and long-term complications on the various organ systems causing considerable morbidity and mortality. The disease also brings about with it a change in lifestyle for the young diabetics with the need for daily exogenous insulin therapy, blood glucose monitoring and dietary changes. Due to the same reasons, diabetes mellitus imposes a great drain on the economy.

In India, Government health expenditure accounts for just 2% of the total budget and 0.8% of the Gross Domestic Product (GDP) (World bank Development indicators). The per capita expenditure on health care is only 6.4% of the average global figure, while India accounts for 23.5% of the world's disability- adjusted life years lost due to diabetes[4]. Given the very limited resources available, the main thrust of health care provision is on the eradication of communicable diseases. There are also services provided by private medical practitioners for those who can afford the cost.

Shobana et al[5] studied the direct cost of diabetes in patients attending secondary care facilities in Chennai, in the private sector.

The median direct cost for patients receiving diabetes care in the private sector was US$107. They have reported that median direct cost to the family of an individual with type 1 diabetes is US$310 (range US$45-1936). The percentages of family income spent on diabetes care were 59%, 32%, 18% and 12% in low, middle, upper-middle and upper socio economic groups, respectively. Thus, the disease has its effects not only on the growth, development and emotional aspects of a child; it also carries the risk of long term complications with its associated morbidity and mortality with a significant effect on the economy as well.

ICH experience:

The Diabetic clinic at the Institute of Child Health and Hospital for Children was started in the year 1999 and has about 300 registered patients. The services provided at the clinic include:

a) Monitoring of blood glucose and insulin therapy

b) Monitoring of glycemic control

c) Growth monitoring

d) Monitoring for complications:

- Injection site assessment for atrophy/hypertrophy/abscess
- Annual ophthalmologic review
- Periodic monitoring of urine miciroalbuminuria for risk of diabetic nephropathy.
- Blood pressure monitoring.
- Evaluation of hands, feet and peripheral pulses for signs of neuropathy or peripheral vascular disease.
- Evaluating for associated autoimmune disorder like thyroiditis in suspected cases.

Hearing loss is more common in diabetic children than non-diabetic children[9]. Hearing loss starts earlier in diabetic children than other chronic complications of diabetes[21]. During the onset, with mild degrees of hearing loss, it won't cause much clinically recognizable impairment in children. Once if it is missed to be screened earlier, it will progress to higher degrees of hearing loss causing significant morbidity in children.

Literature did not provide much data on the incidence, type and degree of hearing loss, hearing loss at various frequencies. Limited studies only available in Indian literature to enlighten this problem21. So this study was conceived to look in to the association between hearing loss and type 1diabetes in children.

Immunopathology of Hearing Loss in Diabetes Mellitus

2. IMMUNOPATHOLOGY OF HEARING LOSS IN DIABETES MELLITUS

Diabetes Mellitus is a common chronic metabolic disorder affecting both children and adults. It is characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin action or insulin secretion or both. It can have long-term effects on the various organs of the body like the eye, kidneys, heart, peripheral vessels and nerves.

The disease was first mentioned in the Eber's papyrus as early as 1500 B.C. The discovery of insulin by Banting et al was a significant breakthrough in the history of diabetes. They were followed by many such researchers, who have helped us to understand this disease better. And hence there has been a shift of terms from the older 'Non insulin dependent diabetes mellitus' and Insulin dependent mellitus' to the newer 'type 1 diabetes mellitus' and 'type 2 diabetes mellitus'.

Type 1 Diabetes Mellitus:

Type 1 Diabetes Mellitus is a T cell mediated autoimmune disease involving β cell damage form inflammatory cytokines and auto-aggressive T-lymphocytes. In Type 1 DM, there is absolute insulin deficiency leading on to symptomatic hyperglycemia and immediate need for exogenous insulin replacement.

Epidemiology:

Type 1 diabetes mellitus, the most common form of diabetes mellitus encountered in childhood, accounts for approximately two thirds of all cases of diabetes mellitus in children[2].

The incidence and prevalence of Type 1 DM varies dramatically around the world, with more than 400 fold variation in the incidence in reporting countries[2]. Type 1 DM is uncommon in India, China with an incidence of only 0.1/100, 000[2]. It is more common in Finland & Sardinia with an incidence of 510 cases per 100,000 populations per year[2]. The incidence of Type 1 DM is increasing throughout the world especially in nations with a previous low incidence of autoimmune diabetes. It is predicted that the overall incidence of Type 1 DM will be 40% higher in 2010 than in 1997[3]. Also the disease has a younger age of onset now than earlier[3].

Complications of Diabetes Mellitus:

Diabetes Mellitus is a chronic metabolic disorder characterized by both acute and chronic complications.

Acute complications of Diabetes Mellitus:

These include DKA, hyperglycemia and hypoglycemia, which occur due to the imbalance between insulin therapy and dietary intake or exercise. These are often encountered in Type 1 DM.

Diabetic Ketoacidosis:

It is an important complication of childhood diabetes mellitus and the most frequent diabetes related cause of death in children. It is a syndrome characterized by hyperglycemia, ketosis and acidemia. Diabetic Ketoacidosis (DKA) in diabetes mellitus can be the initial presentation, an acute metabolic compensation or the cause of mortality. In established diabetics, it can be precipitated by infections, intercurrent illness or by omission of insulin.

Chronic complications of Diabetes Mellitus:

These include retinopathy, cataracts, hypertension, nephropathy, neuropathy, coronary artery disease, peripheral vascular disease etc., These occur due to the effects of hyperglycemia or insulinopenia on the various tissues and can be prevented by proper glycemic control as was established by the Diabetes Control and Complications Trial (DCCT)[6].

Hearing loss is an important complication of diabetes. Initially it doesn't produce self recognizable hearing impairment by the children or by the parents. It can manifest initially as poor school performance in children to speech and learning disturbances later. So it can progress to significant morbidity, unless it is screened earlier in mild degree by audiometry.

Hearing loss and Diabetes Mellitus:

It has been a time honored concept that incidence of hearing loss is higher in persons with diabetes[25].

Hearing loss occurs by three possible pathophysiological Mechanisms

1. Diabetic Microangiopathy of Cochlea
2. Diabetic Neuropathy of Cochlear nerve
3. Combination of above

I. Diabetic Microangiopathy of Cochlea:

(i) Thickness of walls of capillaries in striavascularis:

Major immuno pathology in diabetic Microangiopathy is increasing in thickness of capillary wall in striavascularis. Hisakifuskushema et al[8] studied in 1985 with temporal bones of 13 diabetic patients with type 1 DM and showed that the mean thickness of

capillary walls under basilar membrane in all turns of cochlea combined ,in diabetics (2.27μm+SD 0.60) was significantly higher than that of controls (1.60 μm + SD 0.32).

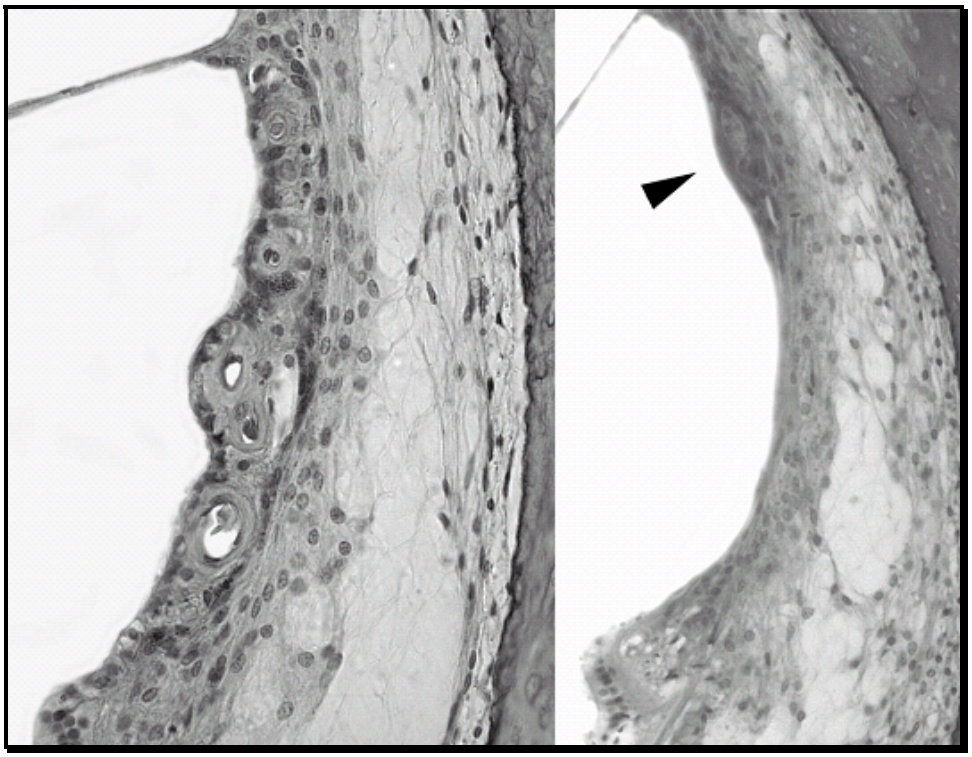


Figure 1-a. There is thickening of the capillary walls in the stria vascularis in lower middle turn of the cochlea from a 39-year old female with a 33-year-history of type 1 diabetes mellitus.HE, x200.

Figure 1-b. There is total occlusion of a capillary (arrow head) and complete loss of stria vascularis in lower middle turn of the cochlea from a 38-year old female with a 19-year-history of type 1 diabetes mellitus. HE, x200.

(ii) Loss of outer hair cells:

Loss of outer hair cells in basal turn of cochlea is another proposed pathological changes in cochlea causing hearing loss in diabetes. Wackym-pa et al[9] studied temporal bones of 68 type 1 diabetic patients and found that significant loss of outer hair cells in diabetics (24.3%+SD 16.6) compared with controls (15.4%+SD 4.1) in the lower basal turn. Finally he concluded that there was a correlation between loss of outer hair cells in lower basal turn and increased thickness of capillary wall in basilar membrane in diabetics.

(iii) Atrophy of Striavascularis:

Atrophy of Striavascularis is another important histopathological change in microangipathy of cochlea causing hearing loss in diabetes. Makishima K, etal[10] conducted a study in 1996 and showed that total area of all five turns of Striavascularis in diabetics (19808 μm^2+ SD 6910) was significantly lower than controls (32113 μm^2+ SD 4302) . He also correlated the thickness of capillary wall in basilar membrane and atrophy of Striavascularis.

(iv) Loss of Spiral Ganglion cells:

Loss of Spiral Ganglion cells in cochlea can cause hearing loss, and it was proved by Costa OA et al[11] in 1993. From his study, he observed that there is significant loss in number of spiral Ganglion cells in any segment of cochlea between Diabetics and controls.

II) Diabetic Neuropathy of Cochlear Nerve:

This is another pathophysiology of hearing loss in diabetes next to diabetic microangiopathy.

Like other Neuropathy occurring in diabetes, auditory Neuropathy can cause hearing loss[12]. Friedman et al showed in his study that his diabetic patients with peripheral neuropathy had high threshold of hearing secondary to auditory neuropathy.

Doyle KJ et al[24] concluded from his study with 58 diabetic children, that auditory neuropathy caused prolonged inter wave latencies in BERA. He also positively correlated the high threshold of hearing for his study population with auditory neuropathy.

Even though both diabetic microangiopathy and cochlear neuropathy can cause hearing loss, most studies[21,26] favors microangiopathy theory as a major pathophysiology of hearing loss.

Literature Review

LITERATURE REVIEW

Apart from the well described association between congenital deafness and the maternally inherited type of diabetes mellitus in the wolfram syndrome[13], the relationship between type 1 DM and hearing impairment has been a subject of debate since Jordao et al[14] reported a case of hearing loss with incipient diabetic coma almost 150 years ago.

Incidence of hearing loss in diabetes:

Kakal Paudi et al[15] on May 2003 conducted a retrospective data base review from 1989 to 2003, concluded that sensorineural hearing loss was more common in patients with diabetes than in the control nondiabetic patients. He also observed that the severity of hearing loss seemed to correlate with progress of disease as reflected in Sr. Creatinine and glycosylated Hb level (HbA1c). This may have been due to microangiopathic disease in inner ear.

Incidence of hearing loss in various studies

Limited studies are available in literature to show the actual incidence of hearing loss in diabetes. Most of studies quoted that incidence of hearing loss in type1 diabetes ranging from 25 to 35%.

Incidence of hearing loss

Authors	*Incidence of hearing loss*
Elamin et al[20]	30%
Virtaniemi J et al[24]	32%
TayHL et al[30]	36%
De espana et al[34]	28%
DCCT[17]	26%
Lisowska et al[16]	24%
Kurion M et al[14]	29%
Celik O et al[28]	32%

Pathogenesis of hearing loss in diabetes:

i) Microangiopathy and hearing loss

Hearing loss occur in diabetes secondary to diabetic microangiopathy and auditory neuropathy as evidenced by the study of Hisakifuskushema et al[8]. He studied with temporal bones of 13 type 1 diabetic children and concluded that hearing loss in diabetes is due to diabetic microangiopathy.

ii) Auditory neuropathy and hearing loss

Auditory Neuropathy can cause hearing loss. It is evidenced by the study of Durmus C etal[16].He Showed that absolute latencies of waves I, III, V, and Interwave latencies between III & V by Brainstem evoked auditory response were significantly higher in diabetics compared to controls. He concluded that prolongation of latencies of ABER in patients with DM is due to damage of cochlear nerve.

Hearing loss and age of diabetic patients:

Hearing loss occurs in diabetics more frequently as age advances. In adults, diabetes influences age related hypoacuosis, evidenced by the study of Ferrer et al[17] on 1991 with 46 diabetic patients using pure tone audiometry. He observed that the threshold of hearing in all frequencies was quiet higher and it was associated with age, duration of disease as well as retinopathy. He concluded that age related hypoacuosis, is influenced by diabetes.

Hearing loss and diabetic age:

Hearing loss occurs more frequently as diabetic age advances. Tay et al[18] shows in his study of 102 type 1 diabetic children, that the threshold of hearing was higher in low and mid frequencies and it was

positively correlated with diabetic age. He observed that the diabetic age advances by more than 5 years, there is higher incidence of hearing loss.

Hearing loss in various frequencies:

Hearing loss in diabetes occurs commonly in mid and high frequencies as the basal turn of cochlea is more affected. De epsana et al[19] conducted a study in Barcelona university spain with two groups (Group I: early diabetics, group II: chronic diabetics). In group 1 (17/47) patients developed hearing loss at high and mid frequency, in group II (30/47) patients developed hearing loss at all frequencies. He concluded that a diabetes initially affects basal turn of cochlea as evidenced by mid and high frequency hearing loss in early diabetics. As diabetic age advances with involvement of apical turn of cochlea, there will be hearing loss at all frequencies in chronic diabetics.

Hearing loss and Metabolic Control:

Hearing loss in diabetes significantly correlated with degree of metabolic control (Glycosylated Hb).

Elamin et al[20] conducted a study in 2005 with 63 sudansi diabetic children below the age of 18 years and concluded, that hearing loss

occurs earlier in diabetic children and is related to duration of diabetes and the degree of metabolic control.

Hearing loss and acute complications:

Hearing loss in diabetes is a chronic complication. Celik et al[21], elamin et al[20], studied with 75 patients with IDDM and observed that hearing loss positively correlated with chronic complications like retinopathy and nephropathy, not with acute complications like Hypoglycemia and DKA.

Hearing loss and retinopathy, nephropathy:

Microangiopathic complications like nephropathy and retinopathy are correlated with hearing loss. Ferrer et al[22] and Elemin et al[20] performed a study with 98 diabetic children in 1991. They observed that hearing loss was positively correlated with background and proliferative diabetic retinopathy and nephropathy, because all of this three complications are different spectrum of diabetic microangiopathy.

Peripheral neuropathy and hearing loss:

Cochlear neuropthy is another important cause of hearing loss in diabetes. Cochler neuropathy in diabetes is either due to direct inositol induced injury by chronic hyperglycemia or by microangipathy of

vasanervosa of cochlear nerve was not clearly known. Celik O et al[22] and Huyang et al[23] observed from their studies that cochlear neuropathy identified by BERA causing hearing loss was positively correlated with peripheral neuropathy identified by Nerve conduction studies (NCS).

Thyroid dysfunction and hearing loss:

Significant numbers of studies are available in literature to show the auto immune dysfunctions in diabetes including auto immune thyroiditis, celiac disease, addisions disease and multiple sclerosis.

Mjmekenna et al[21] screened 371 diabetic children for thyroid microsmal antibodies and noticed that 7% of children had thyroid dysfunction. So he recommended that all the diabetic children should be screened for thyroid dysfunction shortly after diagnosis of IDDM.

None of the study positively correlated the hearing loss and thyroid dysfunction in diabetes[13], probably because hearing loss in diabetes is due to microangiopathy and not secondary to auto immune problem.

Study Justification

STUDY JUSTIFICATION

Hearing loss is more common in diabetic children and also occurs much earlier than expected[13]. Though Hearing loss in adult diabetes have been extensively studied[22], literature does not provide much data on hearing loss in childhood diabetics[17] especially in India as research data on diabetes in children is scarce.

Most of western literature[20-24] shows that hearing loss occurs earlier in diabetic children and positively correlates with poor glycemic control. By early detection of hearing loss in diabetic children and maintaining them on strict glycemic control, we can prevent the occurrence and progression of hearing loss[14]. Hence there is an urgent need to study the actual incidence of hearing loss in diabetic children and when to screen the diabetic children for hearing loss, also how hearing loss is correlating with metabolic control and the acute and chronic complications of diabetes.

So this study is expected to be very helpful in identifying the presence of hearing loss in diabetic children, in order to prevent its occurrence.

Objectives of the Study

OBJECTIVES OF THE STUDY

i. To examine the auditory function in a group of children more than 5 years of age with type 1 diabetes mellitus.

2. To know the incidence of hearing loss in diabetic and non diabetic children.

3. To assess the degree of hearing loss and its distribution in various frequencies.

4. To analyze the various risk factors like metabolic control and complications of diabetes for hearing loss.

5. To compare the threshold of hearing in diabetic children without hearing loss and non diabetic children.

Materials and Methods

MATERIALS AND METHODS

The study was conducted at Institute of Child Health and Hospital for Children, Madras Medical College, a Tertiary care Children's Hospital in Chennai during the period between Nov 2005 and Aug 2007. It was carried out with case control study design.

Study population was classified in to two groups. Children with diabetes attending the diabetic clinic at the Institute of Child Health and Hospital for children (Group I) were enrolled as cases. An equal number of age and sex matched Children without diabetes mellitus from school health cell and near by Govt. Higher Sec. School during school visit conducted by School Health Cell were enrolled as comparison group (Group II).

Diabetic and non diabetic children were selected with following inclusion and exclusion criteria for study enrollment.

Inclusion Criteria:

For Group I - Children of age more than 5 years with diabetes mellitus attending diabetic clinic and on regular follow up and willing to participate in the study.

For Group II: Age and Sex matched children free of diabetes mellitus and willing to participate in the study.

Exclusion Criteria:

- Children with CSOM
- H/O Head or ear trauma
- Family H/O Congenital deafness
- Features of Wolfram syndrome
- Known Ototoxic drug exposure

Sample Size:

From the previous studies it was found that the incidence of hearing loss in diabetic children was about 30%[21-23]. Among normal children, the incidence of Sensorineural Hearing Loss is almost 0.1% [14, 19] (1 in 1000). With an α error of 5% and a power of 90%, the sample size is calculated to be 31 in each group.

Since in the diabetic clinic about 300 children are registered, it was considered to perform the study with twice the number of calculated study sample.

So the study was conducted with 62 diabetic children (Twice the number of calculated sample) and 62 age and sex matched non diabetic children

Manoeuvre:

The study was conducted at the Institute of Child Health and Hospital for Children between the period of November 2005 to August 2007. The cases were enrolled for the study from the diabetic clinic at the institute.

Though 300 diabetic children are registered, those children aged more than 5 years were only enrolled in this study. As it is essential to understand and perform the exercises of pure tone audiometry, those children aged more than 5 years who are capable of understanding and reciprocating the tasks involved in audiometry were selected and enrolled.

Out of the 300 children registered in our diabetic clinic, only 142 children were on regular follow up. Of these 142 children, 128 were more than 5 years of age. 62 children were selected randomly from this group and were enrolled into the study.

All patients are treated with human insulin provided by our diabetic clinic. Blood glucose was estimated every time when the child was attending the diabetic clinic.

Their glycemic control was assessed by measuring glycosylated Hb once in 3 months. Children were subjected to undergo hearing assessment once in every three months while taking blood for glycosylated Hb measurement.

Before doing hearing assessment, age at onset of Diabetic Mellitus was noted to calculate the exact diabetic age of the children. Previous history of hearing impairment, ear discharge, head or ear trauma and family history of congenital deafness were enquired. Other associated acute complications like hypoglycemia, diabetic ketoacidosis and chronic complications like nephropathy, retinopathy were assessed.

Hypoglycemia was considered only when it required assistance from the parents or by hospital. Diabetic ketoacidosis was considered only when confirmed and treated in hospital. Retinopathy was assessed by periodic retinal examination. Nephropathy was assessed by albumin excretion rate and by estimation of blood urea, serum creatinine and

electrolytes. Then clinical assessment of hearing was done in all children by doing Rinnes test, Webers test, ABC conduction test.

Those who were able to understand and reciprocate the above clinical tests were subjected to undergo otoscopic examination and Puretone audiometry using Amplaid 300 clinical audiometer. None of the study population had any ear pain or hearing loss following an exposure of excessive noise or sound.

Following a thorough ENT examination, pure tone audiometry was performed in a sound proof room for both cases and controls. Both air and bone conductions were tested at low, mid and high frequencies.

Out of 62 diabetic children, 13 children had hearing loss during the study period. Those 13 children were subjected to hearing assessment for at least more than twice during the study period. Controls were also subjected to hearing assessment by puretone audiometry. As none of them had hearing loss in the initial visit, they were not followed up.

Definition of Hearing Loss:

Any children with average threshold of hearing more than 25 db in any frequency by pure tone audiometry were considered to have hearing loss.

Audiometry was done in 3 different frequencies.

1. Low frequency (250 to 1000 Hz)
2. Mid frequency (1000 to 4000 Hz)
3. High frequency (4000 to 8000 Hz)

Degree of hearing impairment were analyzed according to WHO classification.

DEGREE OF HEARING LOSS

1.	Mild :-	26 to 40 db
2.	Moderate :-	41 to 55 db
3.	Moderately severe :-	56 to 70 db
4.	Severe :-	71 to 91 db
5.	Profound :-	>91 db

All the diabetic children completed the one year follow up period. There were no deaths in either group. The results are discussed subsequently.

Results

RESULTS

A total of 62 diabetic children were enrolled in the study and same number of age and sex matched non-diabetic children were identified with same exclusion criteria from school health cell of ICH&HC and from nearby government higher secondary school during school visit by school health cell of ICH&HC Chennai were enrolled as a comparison group.

Diabetic children who were diagnosed to have hearing loss at the beginning of the study were followed for 2 years and hearing was assessed once in 3 months, when they were assessed for glycemic control by estimating Glycosylated Hemoglobin. The data was analyzed using SPSS software version 11.0 for windows.

The results were analyzed as follows:-

1. Presence of hearing loss in diabetic and non diabetic children**.**
2. Profile of hearing loss
3. Risk factor for hearing loss
4. Co morbidities of diabetes and hearing loss
5. Hearing loss in various frequencies with metabolic control.
6. Threshold of hearing in diabetic and non diabetic children.

1. PRESENCE OF HEARING LOSS IN DIABETIC AND NONDIABETIC CHILDREN

Comparing to non diabetic children hearing loss is more common in diabetic children.

Study Population	***Hearing Loss Present***		***Hearing Loss Absent***	
	n	***%***	***n***	***%***
Diabetic Children	13	20.9	49	79.1
Non diabetic Children	0	-	62	100.0

χ^2 value = 14.5 (p-value = 0.00)

*(chi square test)

In this study 13 (20.9%) diabetic children had hearing loss. None of the non diabetic children had hearing loss.

Analysis shows that there is significant difference in incidence of hearing loss between diabetic children and non diabetic children.

2. PROFILE OF HEARING LOSS IN DIABETIC CHILDREN

a) Sensory Neural Hearing Loss in Various Frequencies

In pure tone audiometry hearing is assessed for both air and bone conduction between 250 to 8000 Hz and 250 to 4000 Hz respectively. On the air conduction, tested between 250 to 8000 Hz, hearing is assessed in 3 different ranges of frequencies.

1. Low frequency (250 to 1000 Hz)
2. Mid frequency (1000 to 4000 Hz)
3. High frequency (4000 to 8000 Hz)

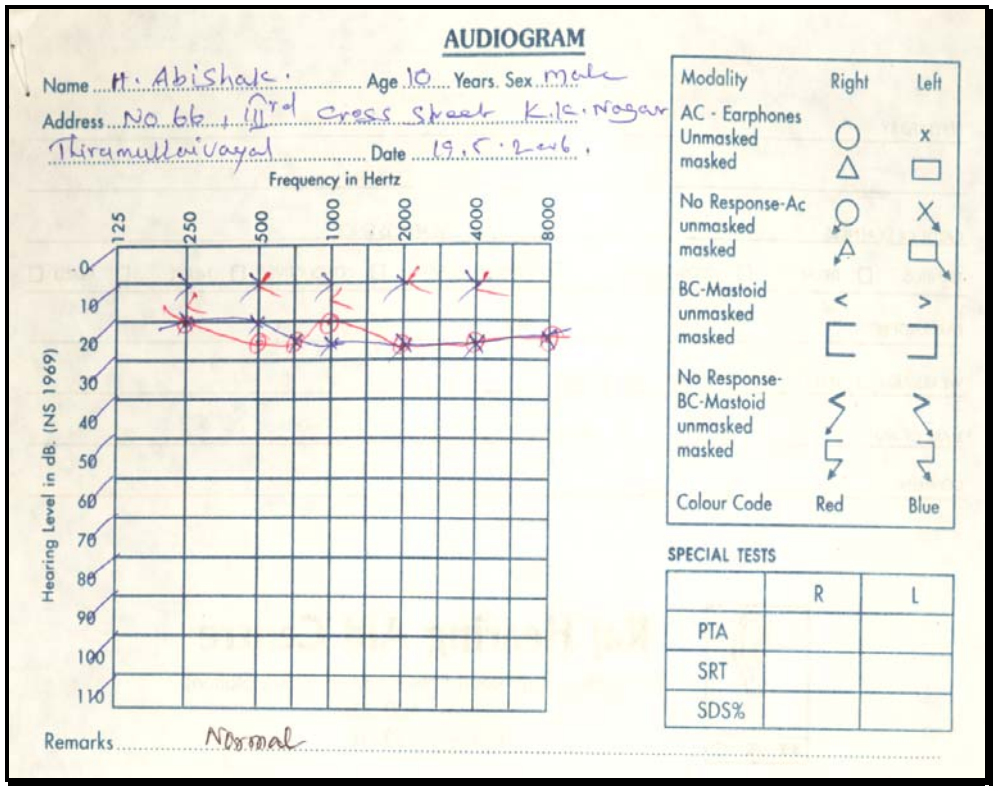
Sensory Neural Hearing Loss in Various Frequencies

Sex	***Sensory Neural Hearing Loss***		***Total***
	All frequencies (low, mid and high)	***Mid and high frequencies***	
Male	2	4	6
Female	2	5	7
Total	4 (30.7%)	9 (69.2%)	13 (100%)

Out of 13 diabetic children with hearing loss, 4 children (30.7%) developed hearing loss at all frequencies, 9 (69.2%) children developed hearing loss at mid and high frequencies.

SOME PURE TONE AUDIOMETRIC GRAPHS OF THE STUDY DEPICITED BELOW TO REPRESENT THE DEGREE OF HEARING IMPAIRMENT

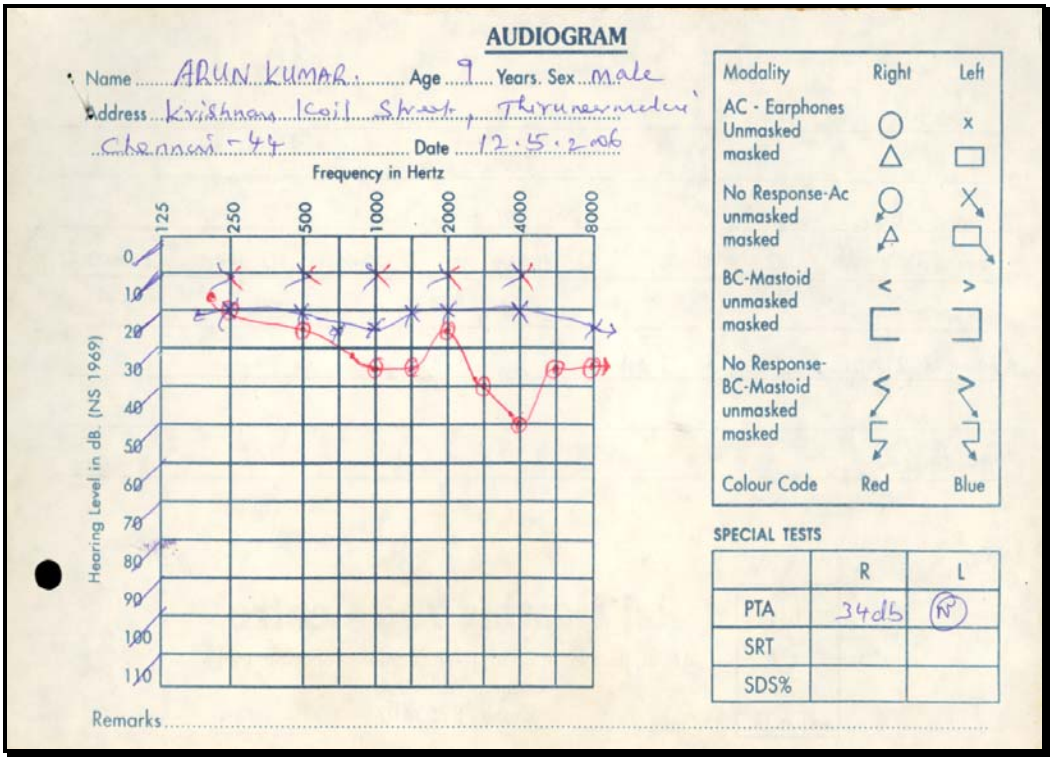
NORMAL HEARING ASSESSMENT



Threshold of Hearing in both ears at all frequencies is 25 db.

Impression: Normal hearing assessment in both ears. No hearing loss

SENSORY NEURAL HEARING LOSS AT MID AND HIGH FREQUENCIES

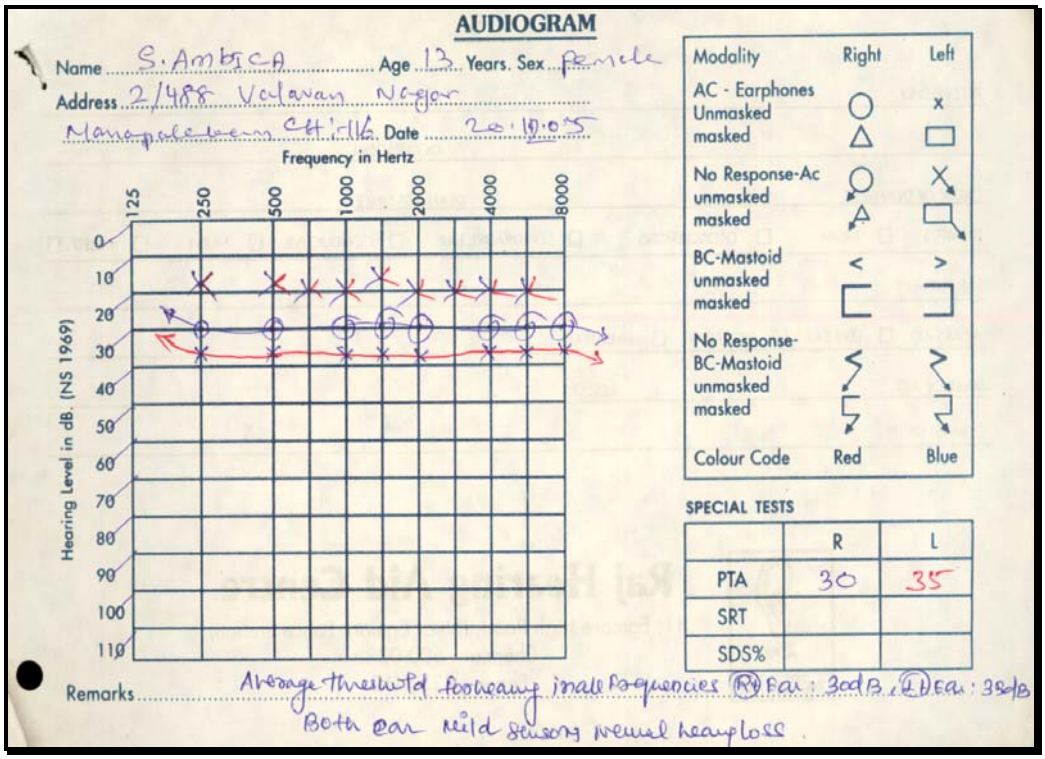


Average threshold of hearing in right ear is 35db at mid and high frequencies.

Average threshold of hearing in left ear is 20db at all frequencies.

Inference: Mild degree of sensorineural hearing loss at mid and high frequencies in right ear, hearing assessment in left ear normal.

SENSORY NEURAL HEARING LOSS AT ALL FREQUENCIES



Average threshold of hearing in right ears at all frequencies is 35db.

Average Threshold of hearing in left ear at all frequencies is 30 db.

Impression: **Mild degree of Sensory Neural Hearing Loss at all frequencies in both ears.**

b) Degree of Sensorineural Hearing Loss in Diabetic Children

Degree of hearing loss (WHO classification)

WHO recommends the following classification on the basis of pure tone audiometry taking the average threshold of hearing for frequencies 500, 1000, 2000 Hz with reference to ISO: R 389-1970.

Degree of Hearing Loss

1. Mild	:-	26 TO 40 db
2. Moderate	:-	41 to 55 db
3. Moderately severe	:-	56 to 70 db
4. Severe	:-	71 to 91 db
5. Profound	:-	>91 db

c) Degree of sensorineural hearing loss in diabetic children

Sex	***Sensorineural Hearing Loss***				
	Mild	***Moderate***	***Moderately severe***	***Severe***	***Profound***
Male	6 (21.42%)	0	0	0	0
Female	7 (20.58%)	0	0	0	0
Total	13 (20.96%)	0	0	0	0

All the 13 diabetic children developed hearing loss in mild degree.

All the 13 children of mild sensorineural hearing loss identified at the beginning of the study were followed up with strict glycemic control over 2 years of study period, neither of them progressed from mild to higher degrees of hearing loss, nor regressed to normal threshold of hearing (<= 25 db) even after good glycemic control.

3. RISK FACTORS FOR HEARING LOSS IN DIABETIC CHILDREN

i) Gender of diabetic children.

ii) Age of diabetic children

iii) Diabetic Age (duration between the date of diagnosis of diabetes and date of first hearing assessment)

iv) Age at onset of diabetes

v) Glycosylated hemoglobin

vi) Co morbidity relating to management of diabetes

a. Diabetic ketoacidosis

b. Hypoglycemia

vii) Co morbidity relating to involvement of other organ systems in diabetes

a. Thyroid dysfunction

b. Nephropathy

c. Retinopathy

(i) Gender and hearing loss

Gender	***Hearing Loss***		***Total***	***p-Value***
	Present	***Absent***		
Male	6(46.1%)	49(100%)	28(45.1%)	0.42
Female	7(53.8%)	27(55.1%)	34(54.9%)	
Total	13(100%)	49(100%)	62(100%)	

*(Chi square test)

χ^2 value 0.62

Out of 13 diabetic children with hearing loss 6 (46%) are males and 7 (54%) are females.

There is no significant difference in incidence of hearing loss according to gender.

ii) Age of diabetic child and hearing loss

Incidence of total hearing loss were analyzed with respect to age as 5-10 yrs, 11-15 yrs, since the children more than 5yrs of age only can understand and perform the exercise of pure tone audiometry.

Age (Yrs)	***Hearing loss Present***		***Hearing loss Absent***		***Total n***	***p-Value****
	n	*%*	*n*	*%*		
5 – 10	4	30.7	10	20.4	14	0.43
11 - 15	9	69.2	39	79.5	48	
Total	13	100	49	100	62	

*(chi square test)

χ^2 value: 0.63, OR: 1.7(95% CI: 0.36, 8.13)

Under age group between 5-10 yrs, 4(30.7%) children had hearing loss between 11-15 yrs, 9(69.2%) children had hearing loss

Analysis of chi-square test, showed there is no significant association between age and hearing loss, since p-value is > 0.05

iii) Diabetic age and hearing loss

Incidence of hearing loss in diabetic children were analyzed with respect to diabetic age less than 5 yrs and between 5-10 yrs, Since diabetic age in the study population ranging from 1 yr to maximum of 8 yrs.

Diabetic Age	***Hearing loss Present***		***Hearing loss Absent***		***Total n***	***p-Value****
	n	***%***	***N***	***%***		
< 5 yrs	9	69.2	45	91.8	54	***0.03***
5-10 yrs	4	30.7	4	8.1	8	
Total	13	100	49	100	62	

*(chi square test), χ^2 value: 4.7, OR : 5.0(95% CI : 0.8, 30.9)

Among 13 diabetic children with hearing loss, 4(30.7%) children were between diabetic age of 5-10 yrs, 9(69.2%) were diabetic age <5 yrs.

Analyses of chi-square test showed that **there is a significant association between diabetic age and hearing loss.** Since odds ratio calculated was 5, children between 5-10 yrs of diabetic age had 5 times more risk of developing hearing loss as compared to children <5 yrs of diabetic age.

This shows that as diabetic age increases more than 5 yrs, there will be an increase in incidence of hearing loss.

iv) Age at onset of diabetes and hearing loss

Incidence of hearing loss in diabetic children were analyzed with respect to the age at onset of diabetes between less than 5yrs and 6-10yrs, since all the diabetic children under study had age at onset of diabetes less than 10yrs.

Age at on set of diabetes	***Hearing loss Present***		***Hearing loss absent***		***Total***	***p-value****
	n	***%***	***n***	***%***		
<5yrs	7	53.8	34	69.38	41	0.3
6-10yrs	6	46.1	15	30.6	21	
Total	13	100	49	100	62	

*(chi square test)

χ^2 value: 1.1, OR : 1.9(95% CI : 0.5, 8.0)

Among 13 diabetic children, 7 (53.8%) had age at onset of diabetes less than 5 yrs and 6 (46.1%) had age at onset of diabetes between 6-10 yrs.

Analysis of chi-square test shows that there is no significant association between age at onset of diabetes and hearing loss, since p-value is > 0.05.

v) Glycosylated Hb and hearing loss

Metabolic control of diabetes was assessed by estimating glycosylated Hb once in 3 months. Incidence of hearing loss in diabetic children were analyzed with respect to Glycosylated Hb (HbA1c) between < 7 and >7, since the goal of mean HbA1c as per PCNA (Pediatric clinics of North America) guidelines for age group between 5-10 yrs is <7.5 and <7 for children aged more than 10 years to get strict glycemic control.

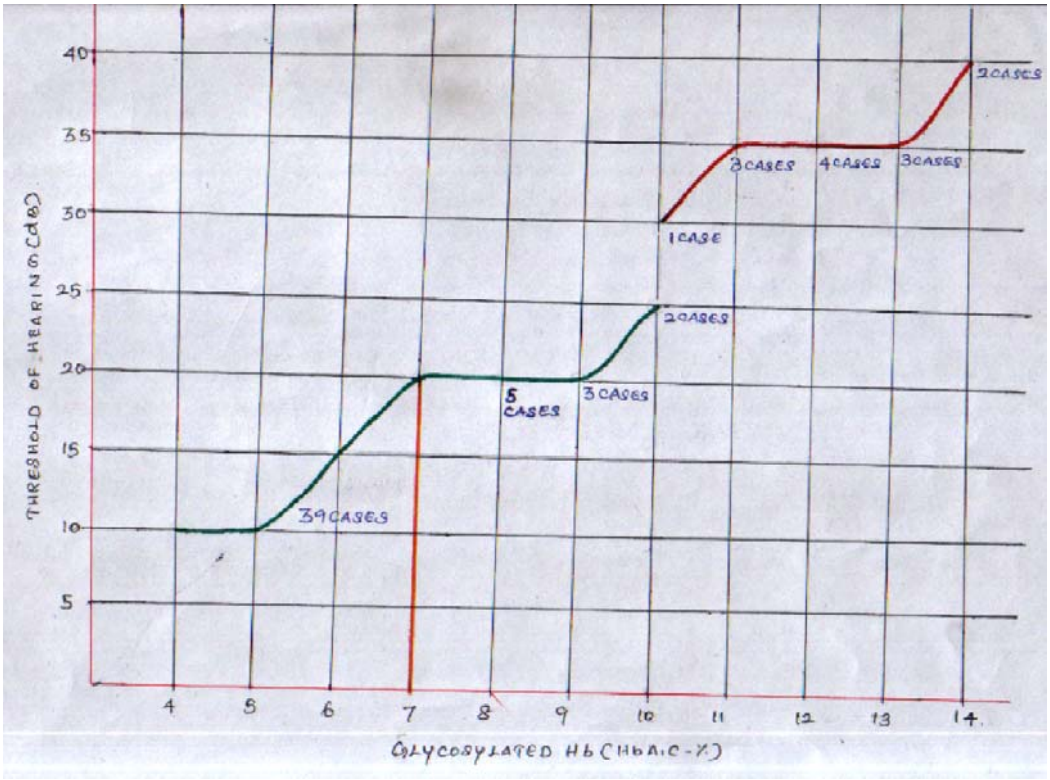
HbA1c	***Hearing Loss***		***Total***	***p-Value****
	Present	***Absent***		
>7	13	35	48	0.03
<7	0	14	14	
Total	13	49	62	

*(chi square test), χ^2 value: 4.8

All 13 diabetic children had HbA1c level >7.

Analysis of chi-square test showed **that there is a significant association between hearing loss and Glycosylated Hb**, since p-value is <0.05. It shows that hearing loss occurs more frequently in diabetic children with poor glycemic control.

THRESHOLD OF HEARING AND METABOLIC CONTROL



Red Curve Shows Diabetic children with hearing loss (13 Children)
Green Curve Shows Diabetic children without hearing loss (49 Children)

Threshold of Hearing and Metabolic Control

As previously mentioned there is a positive correlation between Hearing Loss and Metabolic Control (Glycosylated Hb).

Threshold of Hearing by Puretone audiometry more than 25 db was considered as hearing loss. Out of the 62 diabetic children, 49 children had normal threshold of hearing (No hearing loss), and 13 diabetic children had hearing loss.

As per PCNA guidelines, the ideal goal of mean glycosylated Hb is less than 7 % to get good glycemic control.

Out of 49 children without hearing loss, 39 children had Glycosylated Hb value less than 7% and remaining 10 children had value more than 7%. These 10 children are at risk of developing hearing loss at any time if they are not maintained with strict glycemic control.

All the 13 diabetic children with hearing loss had Glycosylated Hb value, invariably more than 10%. So the hearing loss occurs more frequently, when there is a poor metabolic control.

4. COMORBIDITY OF DIABETES AND HEARING LOSS

Acute and Chronic complications are considered as comorbidity of diabetes. Acute complications like hypoglycemia, and diabetic Ketoacidosis (DKA) are considered as co-morbidity relating to management of diabetes. Chronic complications like nephropathy, retinopathy and thyroid dysfunction are considered as co-morbidity in relation to the involvement of various organ systems.

Comorbidity		***Hearing Loss Present***	***Hearing Loss Absent***	***P Value***
Hypoglycemia	Present	13	41	0.12
	Absent	0	8	
DKA	Present	13	3	0.15
	Absent	0	46	
Nephropathy	Present	0	2	0.5
	Absent	13	47	
Retinopathy	Present	0	28	-
	Absent	0	34	
Thyroid Dysfunction	Present	0	2	0.16
	Absent	13	47	

i) Hearing Loss and Acute Complications:-

All the 13 Diabetic children with hearing loss developed at least one episode of hypoglycemia and DKA during the study period. Analysis of Chi square test shows that there is no significant association between hearing loss and hypoglycemia and DKA as Calculated p value is > 0.05.

ii) Hearing Loss and Chronic Complications:-

In the present study two diabetic children had diabetic nephropathy as evidenced by persistent microalbuminuria during the study period, but none of them developed hearing loss.

Among 62 diabetic children of the present study, neither of them had retinopathy at the beginning, nor they developed during the 2 years of followup period.

In this study 2 diabetic children had thyroid dysfunction but none of them had hearing loss. Analysis of Chi Square test shows that there is no significant association between thyroid dysfunction and hearing loss because of both of them had different pathogenesis. Thyroid dysfunction is due to autoimmune problem, hearing loss is due to diabetic microangiopathy.

5) HEARING LOSS AT VARIOUS FREQUENCIES WITH METABOLIC CONTROL

In this study Hearing assessment was done at three different frequencies using pure tone audiometry.

- Low Frequency – 250 to 1000 Hz.
- Mid Frequency – 1000 to 4000 Hz.
- High Frequency – 4000 to 8000 Hz

Hearing Loss at different frequencies was correlated with metabolic control (Glycosylated Hb) as shown below.

a) Glycosylated Hb and Hearing loss at low frequency

Hb A1C	***Hearing Loss at Low Frequency Present***	***Hearing Loss at Low Frequency Absent***	***p value****
>7%	4	44	0.04
<7%	0	14	

*(Chi Square test), $\chi^2 = 4.2$

In this study out of 13 diabetic children with hearing loss, 4 children developed hearing loss at low frequency and all the 4 children with hearing loss at low frequency had HbA1C values >7. Analysis of chi square test showed that there is a significant association between hearing loss at low frequency and glycosylated Hb (HbA1C).

b) Glycosylated Hb and Hearing Loss at Mid and High frequency

Hb A1C	***Hearing Loss at Mid and High Frequency Present***	***Hearing Loss at Mid and High Frequency Absent***	***p value****
>7%	9	39	0.03
<7%	0	14	

*(Chi Square Test), $\chi^2 = 4.8$

In our study out of 13 diabetic with Hearing Loss, 9 children developed hearing loss at Mid and High frequencies and all these 9 children with hearing loss at Mid and High frequencies had HbA1C values >7. Analysis of chi square test showed that **there is a significant association between hearing loss at Mid and High frequencies and glycosylated Hb (HbA1C).**

c) Correlation between Glycosylated Hb (HbA1C) and threshold of hearing

Threshold of Hearing	*Correlation (r)*	*p-value*
Low Frequency	0.34	0.01
Mid Frequency	0.42	0.001
High Frequency	0.40	0.001

The above table shows that there is a positive correlation between threshold of hearing at all frequencies with glycosylated Hb. There is a more positive correlation between threshold of hearing at mid and High frequencies than at low frequency in relation with HBA1C.

Since diabetic microangiopathy of Cochlea affects mainly the basal turn of cochlea, hearing loss occurs more at mid and high frequencies initially. As the diabetic age advances, it will affect apical turn also producing hearing loss at low frequency.

6) THRESHOLD OF HEARING BETWEEN NON DIABETIC CHILDREN AND DIABETIC CHILDREN WITHOUT HEARING LOSS

Threshold of hearing is higher in diabetic children than non diabetic children.

Threshold of Hearing	***Non Diabetic Children***		***Diabetic Children without Hearing Loss***		***p-value***
	Median	***Range***	***Median***	***Range***	
Low Frequency	10	5 to 20	20	10 to 25	0.00
Mid Frequency	10	5 to 20	20	10 to 25	0.00
High Frequency	15	5 to 20	20	15 to 25	0.00

Mann-Whitney U test

Analysis of Mann - Whitney U test showed that the threshold of hearing for Diabetic children without hearing loss was higher than non diabetic children even though they have not developed hearing loss during the study period.

Diabetic children without hearing loss already developed evidences of diabetic micorangiopathy of cochlea as evidenced by high threshold of hearing compared to non diabetic children.

So if the diabetic children without hearing loss, not maintained with good glycemic control anytime they may develop hearing loss and can progress from mild degree to higher degrees of hearing loss

Summary of the Study

SUMMARY OF THE STUDY

From the analysis of hearing loss in diabetic children, 13 (20%) diabetic children were identified to have Sensorineural hearing loss. All these children had mild degree of hearing impairment (26-40 db). Neither of them had progressed to higher degrees of hearing impairment, nor regressed to normal threshold of hearing on follow up for 2 years.

Out of the 13 diabetic children with hearing loss, 2/3rd of them were identified to have hearing impairment at mid and high frequencies and less than 1/3rd had hearing impairment at low frequency.

Associations of various risk factors and co morbidities with hearing loss were analysed. There is statistically significant association between hearing loss and diabetic age and metabolic control (Glycosylated Hb). There is no statistically significant association between gender, age, age at onset of diabetes mellitus, acute complications like hypoglycemia, diabetic ketoacidosis, chronic complications like nephropathy, retinopathy, thyroid dysfunction and hearing loss.

In our study only 2 diabetic children were diagnosed to have diabetic nephropathy. Neither of them had hearing loss at beginning, nor developed during the whole study period.

In our study only 2 diabetic children were diagnosed to have thyroid dysfunction. Neither of them had hearing loss at beginning, nor developed during the whole study period.

Hearing loss in all frequencies positively correlated with degree of metabolic control (HBA1c) especially in mid and high frequencies (1000-8000 Hz).

Threshold of hearing in all diabetic children even without hearing loss were statistically higher, when compared to non diabetic children.

Discussion

DISCUSSION

Comparison with other Studies and Literature Review:-

Most of the studies on hearing loss in DM have been done only in adults with either type 2 or type 1 diabetes[12]. There is paucity of data on hearing loss in diabetic children. Review of literature shows that hearing loss is more common in diabetics[18]. Hisaki fuskushima et al[8] concluded from his study that there are three main theories are available to explain the pathogenesis of hearing impairment in DM[8, 21, 32].

These are

1. Micro angiopathy of cochlea
2. Auditory Neuropathy
3. Combination of the above.

Elamin et al[20] favours microangipathic theory, which is supported by histopathological findings on temporal bones and inner ear[8, 10]. Thickening of capillary wall with secondary ischemia in the cochlea and the 8th cranial nerve[16] have been demonstrated in diabetic patients and experimental animal models by Durmus et al on 1980[16].

Elamin et al[20] studied 63 Sudensi diabetic children using bovine insulin and showed that there is 30% incidence of hearing impairment in diabetic children with mild, moderate and severe degrees of hearing loss.

Since in our hospital we are using human insulin and maintaining the diabetic children with strict glycemic control and advising them on regular follow up with compliance in insulin usage and meal plan, our study revealed that decreased incidence of Sensorineural hearing loss in diabetic children as 20% when compared to 30% in other studies[29.]

With the same reason mentioned above all of our study population developed only mild degree of hearing impairment and none of them progressed to higher degrees of hearing loss.

Since micro-angiopathy of cochlea is an irreversible damage proved by Virtanemi et al[24], all children with hearing loss in this study population were not regressed to normal threshold of hearing, even after maintenance of strict glycemic control. But we can prevent further progression of hearing loss by maintaining them on good glycemic control.

Since diabetic micro-angiopathy mainly affecting the basal turn of cochlea evidenced by the study of De espanas et al[11], in the present study

also hearing loss occurs more at mid and high frequencies. In this study 2/3rd of diabetic children with Sensorineural hearing loss had hearing impairment at mid and high frequencies and the remaining 1/3rd at low frequency. This is evidenced in this study by statistically significant association between hearing loss at mid and high frequency with glycemic control than at low frequency.

Elamin et al[20] concluded that hearing loss is associated with degree of metabolic control. Present study also shows that hearing impairment occurs earlier in diabetic children with high HBA1C levels. Ideal HBA1c level is considered as a tool for good metabolic control.

GOAL OF MEAN HBA1c % AS PER PCNA GUIDELINES:

1. Infants and toddlers …. <8%
2. Children between 5 – 10 years …. <7.5%
3. Adolescent …. <7%

Hearing loss occurs more frequently as diabetic age advances. Ferrer J.P et al[17] shows in his study that when the diabetic age increases, the hearing loss occurs more frequently. His calculated mean diabetic age to develop hearing loss was 7 years, and it is 5 years for the study

population of Elamin et al. In the present study also the hearing loss is positively correlated with mean diabetic age. The observed mean diabetic age to develop hearing loss in the present study is 5 years. As the odds ratio calculated in the present study is 5, there is 5 times increase in risk of developing hearing loss when diabetic age increases by more than 5 years.

Celik et al[20] studied 205 adult diabetic patients and observed that the hearing loss at high frequency is positively correlated with nephropathy and retinopathy. In pediatric age group retinopathy occurs by late adolescence[21] and nephropathy develops at early or mid adolescence[14]. In the present study all the children studied comes under early adolescent period. Two of the study population had nephropathy as evidenced by persistent microalbuminuria but neither of them developed hearing loss. None of the study population developed retinopathy which is a chronic complication of diabetes mellitus.

Conclusion

CONCLUSION

- Hearing loss occurs earlier in type 1 diabetic children.
- Sensorineural hearing loss in diabetic children occurs predominantly at mid and high frequencies.
- Hearing loss is positively correlated with degree of gylcemic control.
- There is significant association between hearing loss & diabetic age.
- If diabetic age increases by more than 5 yrs, there is an increase in Incidence of hearing loss
- It is mandatory to perform hearing assessment after 5 years from the onset of diabetes, at least once in 3 months when they are subjected to undergo glycosylated hemoglobin estimation to assess metabolic control.
- It is necessary to perform hearing assessment even before 5 years of diabetic age, if the children show poor metabolic control.
- There is no significant correlation between hearing loss and acute complications of DM.
- By maintaining strict glycemic control we can prevent occurrence and progression of hearing loss
- Hence there is an urgent need to create awareness in children and their parents regarding maintenance of good glycemic control.

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Annexure

ANNEXURE - I

DATA COLLECTION FORM

Sl. No :

Name :

Age :

Sex :

Date of registration :

Age at onset of diabetes :

Diabetic age as on registration :

H/O hearing impairment :

H/O ear discharge :

H/O head / ear trauma :

Family H/O congenital deafness :

H/O known ototoxic drug exposure :

Associated complications

Hypoglycemia :

DKA :

Nephropathy :

Retinopathy :

Present blood glucose level :

Clinical assessment of hearing &

Otoscopic examination :

Pure tone audiometry :

Level of glycemic control :

(HBA1C level)