Original Article

Hearing Loss in Children with Type 1 Diabetes

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Objective: *To examine the auditory function in a group of children with type 1 diabetes, and to study the association between hearing impairment and duration of illness, metabolic control and diabetic complication.* ***Methods:*** *Sixty-three diabetic patients below the age of 18 attending the university hospital in Khartoum, Sudan were investigated together with 63 age and sex matched non-diabetic controls. Pure-tone audiometric tests were performed using an Amplaid 300 clinical audiometer in a soundproof room. Both air and bone conduction were tested at frequencies between 250-8000 Hz and 250-4000 Hz respectively. Hearing impairment was noted at auditory threshold above 25 dB in any frequency and the magnitude of hearing loss was assessed according to auditory threshold in conversational frequencies only.* ***Results:*** *The hearing acuity was lower in the diabetic patients than in the control subjects in all tested frequencies, but the differences achieve statistical significance only at middle and high frequencies. The hearing loss was symmetrical, generally mild, and affects both sexes equally. Duration of diabetes, HbA1c concentration, and angiopathic complications showed positive correlation with the increased hearing thresholds; while, age at onset, insulin dose per day, presence of neuropathy, and frequency of DKA and hypoglycaemic episodes were not associated.* ***Conclusion:*** *Hearing loss occurs early in diabetic children and is related to the duration of the disease and the degree of metabolic control. Strict glycemic control might prevent or delay this complication.*

Keywords: *Africa, Angiopathy, Bovine insulin, Deafness, Diabetes mellitus, Insulin shortage.*

APART from the well-described association between congenital deafness and the maternally inherited type of diabetes mellitus in the Wolfram syndrome(1), the relationship between type 1 diabetes mellitus and hearing impairment has been a subject of debate since Jordao reported a case of hearing loss with incipient diabetic coma almost 150 years ago(2). Previous studies have reported contradicting results regarding hearing impairment in diabetic patients and its relationship to other diabetic complications and to metabolic control. Several earlier studies have documented presence of bilateral sensori-neural hearing loss affecting mainly the high and middle frequencies, quoting widely different incidence ranging from 15 to 85 percent(3-5). Majority of these studies have included adult patients with non insulin-dependent diabetes mellitus, and described a characteristic audiometric profile that simulates presbyacusis, which is known to occur with old age(6). On the other hand, many studies, which involved both type 1 and type 2 diabetic patients, have failed to detect any significant difference in audiometric functions between the diabetic patients and non-diabetic controls(7-9). Only few studies to date have documented presence of significant hearing loss in young patients with type 1 diabetes mellitus particularly in children who have relatively short duration of illness. The aim of the present study was to examine the auditory function in a group of children and adolescents with type 1 diabetes mellitus and to evaluate its relationship with the duration of the disease, the tightness of metabolic control, and the acute and chronic diabetic complications.

Subjects and Methods

The study is one of a series of studies that address complications in young Sudanese diabetic patients. The cohort included sixty-three children and adolescents below the age of 18 years with type 1 diabetes mellitus. The patients were seen regularly at the diabetes clinic of the university hospital in Khartoum, Sudan on monthly basis for clinical follow-up and insulin prescription. All patients were treated with a mixture of short acting and intermediate-acting purified bovine insulin given in two daily injections. Human insulin was not available in government hospitals, but the bovine insulin was given free of charge to all patients. The onset of diabetes was noted on the day of commencement of insulin therapy. The data recorded included age and sex, duration of diabetes, insulin dose and frequency of acute complications: diabetic ketoacidosis (DKA), and severe hypoglycemia. The glycated haemoglobin (HbA1c) concentration was measured every two months and the average of one-year readings was used to reflect the degree of glycemic control. Reference values for non-diabetic Sudanese children are below 6.3 % as we have described before(10). Severe hypoglycemia was defined as an episode that required assistance from another person or hospital care and DKA was rated significant only when confirmed and treated in a hospital. The mean number of such episodes in the year preceding the study was utilised for data analysis. Patients with a history of ear infection, head or ear trauma, thyroid disease, use of ototoxic drugs, or a family history of congenital deafness, were excluded. None of our patients had exposure to excessive noise or showed features of Wolfram syndrome. All patients were ketone-free and had used no medication other than insulin in the 72 hours that preceded the tests. Sixty-three healthy non-diabetic school children, matched for age and sex, were recruited to serve as a control group. The same exclusion criteria of patients were applied for the controls. Written informed consents were obtained from the guardians and from the participants when appropriate.

Following a thorough ENT examination, pure-tone audiometric tests were performed using an Amplaid 300 clinical audiometer in a soundproof room. Both air and bone conduction were tested at frequencies between 250-8000 Hz and 250-4000 Hz respectively. Results are expressed as mean air conduction auditory threshold of both ears. Hearing impairment was noted at auditory threshold above 25 dB in any frequency and hearing loss was quantified employing a formula that takes into account only the auditory threshold in conversational frequencies (500-4000 Hz). Independent evaluation of each patient to ascertain the presence of late-onset complications was carried out using standardised ophthalmoscopy and retinal photography for retinopathy, serum creatinine and 24 h urinary protein concentration for nephropathy, and clinical evaluation and nerve conduction studies for peripheral neuropathy. Cardiac autonomic nerve function was assessed by standard heart rate variability tests and postural hypotension.

Medians and ranges were used for variables, which are not normally distributed, while means and standard deviations (SD) were used for normally distributed variables. Student's t-test and ANOVA were used to compare the auditory threshold between the right and left ears initially and between the means of patients and the control group. Chi-square distribution, linear regression, and Spearman rank correlation were also used as appropriate. Statistical significance was set at the 5% level.

Results

The demographic and clinical characteristics of the study population are displayed in *Table I.* Because there was no significant difference in parameters between boys and girls results were combined for analysis. Most of our patients (88%) had DKA at the time of diagnosis and the initial transient period of decreased exogenous insulin requirement often described in newly diagnosed diabetic children "the honeymoon phase", was not noticed in this group of patients. Both observations suggest delayed diagnosis. The median duration of diabetes in the cohort was 5 years, which is pretty short, but nevertheless 21% of them showed evidence of micro-vascular and/or neuropathic complications. The metabolic control of this group of patients was not good with a median HbA_{1c} of 11.5 % (range 7.3-18.6%) and median insulin dose of 1.6 U/kg/day (range 0.9-2.3).

Air and bone conduction thresholds were almost similar and none of the patients or the control subjects showed evidence of conductive hearing loss on audiometry. The mean air conduction thresholds of both ears at each frequency were used in the analysis because no significant difference existed between the thresholds of the right and the left ears. The auditory threshold of the diabetic patients was uniformly higher than that of the control group in all frequencies, but the difference assumes statistical significance only in middle and higher frequencies from

TABLE I–*Demographic and Clinical Characteristics of the Diabetic cohort*

Parameter	Diabetic patients	
	Boys	Girls
Number	30	33
Age at onset yrs (mean ± SD)	8.9 ± 2.5	9.3 ±2.7
Duration of diabetes yrs (median & range)	4.8 (1.5-8.4)	5.4 (2.0-9.0)
HbA_{1c} level % (median & range)	11.2 (7.3-17.5)	11.9 (7.7-18.6)
Insulin dose U/day (median & range)	1.6 (1.0-2.2)	1.7 (0.9-2.3)
DKA at first diagnosis (%)	87%	89%
Neuropathy	3	2
Retinopathy	–	1
Nephropathy	3	4

2000 to 8000 Hz. Twenty-one patients (33%) had satisfied our definition of significant hearing loss with auditory threshold above 25 dB in at least one frequency. The hearing loss was symmetrical, sensori-neural in nature, and affecting mainly the middle and high frequencies. When the degree of hearing impairment was quantified, fourteen of the 21 patients (67%) had mild hearing loss (range 25-30%), four patients (19%) had moderate hearing loss (range 31-39%), and three patients (14%) had severe hearing loss >40%. Symptomatic hypoacusia was not complained of even by the seven patients who had more than mild degree of hearing impairment. The auditory threshold was not correlated with the age or sex of the patient, stage of pubertal development, daily insulin dose, and number of hospital admissions because of DKA or hypoglycemic episodes. But it was positively correlated with the average HbA_{1c} concentrations and the duration of diabetes at all frequencies above 500 Hz ($P < 0.001$). At conversational frequencies (500-4000 Hz) no significant difference was noticed between the diabetic patients with microangiopathic complications (nephropathy and retinopathy) and/or neuropathy and those patients without complications. Only at high frequencies (6000-8000 Hz) does a positive correlation appear between these microangiopathic complications and hearing loss ($P < 0.01$). Neuropathy, peripheral or autonomic was not associated with hearing impairment in this cohort of patients.

Discussion

Hearing impairment has long been observed in patients with diabetes mellitus, but its casual relationship with the disease has been disputed. Several studies have addressed the questioned association in adults; screening both type 1 and type 2 diabetic patients. Most of these reports have documented presence of significant hearing loss in patients with either type of diabetes, being more prevalent in non-insulin treated patients, and is related to age and microvascular complications(3-5). However, similar findings have also been reported from the studies, which examined hearing loss in patients with insulin-dependent diabetes mellitus indicating that it is not only the type of treatment, which dictates the degree of hearing impairment in diabetics, but some other additional factors (11-13). Although there is no consensus among researchers regarding the exact etiology of hearing impairment in diabetic patients, a large body of evidence is accumulating in favor of a strong relation-ship between poor glycemic control and hearing loss. Axelsson, *et al.*(14) studied 205 adult diabetic patients and found marked hearing loss in 37% of them. They observed that insulin treated patients have a better auditory threshold than those of the same age group who received oral hypoglycemic agents and attributed the finding to the better metabolic control exhibited by the former group. Taylor and Irwin(15) reported that almost 70% of their adult diabetic patients had hearing impairment. This occurred more commonly in older patients and when retinopathy was present. Kurien, *et al.*(16) found that the auditory threshold was significantly higher at all frequencies in the diabetic patients when compared with healthy controls. This hearing impairment was not related to age or duration of diabetes, but was related to the degree of glycemic control being more profound in poorly controlled diabetic patients.

Only few studies to date had examined the question of hearing impairment in children and adolescents with type 1 diabetes mellitus (17). Of the studies we have reviewed, only that of Ferrer, *et al.*(18) found significantly higher auditory thresholds in children with type 1 diabetes mellitus when compared to those of non diabetic children over all frequencies from 250 to 8000 Hz. The loss of hearing was positively correlated to age at onset of diabetes, duration of the disease and presence of retinopathy. Three studies by Sieger, *et al.*(19), Osterhammel, *et al.*(20), and Parving, *et al.*(21) failed to show any ill effect of diabetes on hearing as tested by clinical and audiologic methods. However, many recent studies, which utilize modern electro-physiological tests, have succeeded in demonstrating impaired auditory brain stem responses and absence of otoacoustic emissions in the diabetic patients who have no clinical hypoacusia and who showed normal pure tone audiometric tests(22-26). These findings support the assumption that sub-clinical hearing loss occurs early in diabetic patients and progressed slowly over time. The present study showed that the auditory threshold was significantly higher in the diabetic patients in all middle and high frequencies when compared to the control group. Levels considered to denote significant hearing loss were observed in one third of the studied group of diabetic children, which is a sizable proportion. The majority of children with hearing defect have mild hearing impairment, but 14% of them had profound hearing loss. Poor auditory function was significantly correlated with metabolic control and presence of microvascular diabetic complications. Our findings support those of Ferrer, *et al.*, and indicate presence of hearing loss in children with type 1 diabetes mellitus of relatively short duration. However, we failed to show a positive correlation between the auditory threshold and the age and sex of the patient, age at onset of diabetes, insulin dose/day, and frequency of acute diabetic complications. Some of these observations are in accordance with previous reports, and in contrast to others, which showed hearing loss to be more common in boys and when diabetes starts in the pubertal years(27). Of the chronic diabetic complications, only neuropathy was not correlated to auditory thresholds in our diabetic population. Retinopathy and nephropathy, both showed significant correlation at high frequencies. This finding agrees with the described association between retinopathy and hearing loss in diabetic patients(18), and in contrast to the studies, which related the hearing impairment to diabetic neuropathy alone(28), and those, which, astonishingly, found no association between the microvascular and neuropathic complications of diabetes mellitus and impaired hearing(29-31). Few studies have described positive correlation between hearing impairment and both neuropathy and angiopathy(32-33). The significant correlation observed between auditory thresholds and HbA_{1c} concentration, in the present study and several previous reports, indicates that glycemic control is the most crucial factor for development of hearing loss in type 1 diabetic patients. The Diabetes Control and Complication Trial(34) has proved beyond doubt the casual relationship between poor glycemic control and development of microvascular complications in diabetic patients, and hearing loss irrespective of its precise etiology and pathogenesis should not be an exception. However, it is note worthy that the studies reported by Viraniemi, *et al.*(13), Ferrer, *et al.*(18), and Kasemsuwan, *et al.*(31), have failed to show any association between glycemic control as judged by HbA_{1c} concentration and development of hearing impairment. Duration of diabetes is an important factor in relation to the appearance of microvascular complications of diabetes and it seems equally important for development of deafness in many previous studies as well as in our diabetic population. However, mild degree of hearing impairment was detected in many children with diabetes duration of less than four years. Such observation is extremely unusual and might be explained by the poor glycemic control in this group of patients. In sub-Saharan Africa where bovine insulin is still commonly used, with occasional periods of insulin shortage or non-availability, poor compliance with diet and meal plan because of poverty and subsistence living, and home blood glucose monitoring almost not heard of, this is not a surprise.

Three main theories were postulated to explain the pathogenesis of hearing impairment in diabetes mellitus. These are: neuropathy, microangiopathy or a combination. The majority of researchers go for the microangiopathy theory, which is supported by histopathological findings on temporal bones and inner ear. Thickening of capillary wall with secondary ischemia in the cochlea and the 8th cranial nerve have been demonstrated in diabetic patients and experimental animal models(35-37).

In conclusion, children and adolescent with type 1 diabetes have hearing loss at middle and high frequencies, which is not present in their matched controls. Such changes are not related to age and appear to start early in type 1 diabetic patients who are treated with conventional insulin therapy using bovine insulin. This complication can be prevented or delayed by strict glycemic control.

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