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The effects of diabetes mellitus type 1 on children's audiovestibular system: a randomized case control study

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Abstract

Background: Children with diabetes mellitus type 1 have many deficits, including neuropathy, retinopathy, and nephropathy, all of which compromise their activity and daily functional status. Vestibular dysfunction is another possible complication of diabetes and may increase the risk of falls. Despite diabetes mellitus prevalence, few studies evaluated its effect on hearing, and even fewer examined the effect on the audiovestibular system. A randomized case control pilot study design was implemented to evaluate the effect of type 1 diabetes mellitus on the audiovestibular system of children.

Results: The study included 50 children divided into 2 groups; the study group included 25 children suffering from type 1 diabetes mellitus, and the control group included 25 patients who were known to be nondiabetics. Both groups underwent basic audiological and vestibular test battery. Only 16% showed different degrees of hearing loss. Regarding vestibular assessment, saccadic eye tracking showed the highest degree of abnormal results within the study group (80%). Correlation between saccade findings among cases and the risk factors of diabetes like duration, glycated hemoglobin level, diabetic ketoacidosis, and hypoglycemic coma attacks indicated statistically significant positive correlation between saccade latency and glycated hemoglobin level.

Conclusion: This study proposed that type 1 diabetes mellitus can affect the audiovestibular system of children even in the absence of symptoms. Accordingly, appropriate early rehabilitative management should be planned in an attempt to avoid further complications.

Keywords: Type 1 diabetes mellitus, Hearing loss, Dizziness, Audiovestibular assessment

Background

Diabetes is a heterogeneous complex metabolic disorder characterized by elevated blood glucose concentration secondary to either resistance to the action of insulin, insufficient insulin secretion, or both [1]. Diabetes mellitus is a complex, chronic illness requiring continuous medical care with multifactorial risk reduction strategies beyond glycemic control to prevent acute complications and reduce the risk of long-term complications [2].

People with diabetes have many deficits, including neuropathy, retinopathy, and nephropathy, all of which compromise their activity and daily functional status. Vestibular dysfunction is another possible complication of diabetes and may increase the risk of falls [3]. The inner ear does not store energy, so minor variations in blood glucose affect its function and cause balance disorders. Altered inner ear metabolism may lead to potassium transfer from the endolymph to the perilymph and an opposite movement of sodium. This mechanism may cause vertigo, tinnitus, hypoacusis, and ear fullness [4]. It is likely that patients with type 1 diabetes mellitus could encounter audiovestibular dysfunction. Despite diabetes mellitus prevalence, few studies evaluated its effect on

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hearing, and even fewer examined the effect on the audiovestibular system [5, 6]. So the present study was designed to study the effect of T1DM on the audiovestibular system of children.

Methods

A randomized case control pilot study design was implemented to evaluate the effect of T1DM on children's audiovestibular system. This study was conducted from February 2018 till December 2018, at the Audiovestibular clinic. A written consent was obtained from all patients and their guardians and was approved by the local Ethics Committee. The study included 50 children divided into study and control groups. The study group included 25 children suffering from T1DM randomly included from children attending the pediatrics Endocrinology clinic. Inclusion criteria for all cases were: patients who were diagnosed according to WHO guidelines [2] with any duration of T1DM, both males and females, and age range from 6 to 18 years old. Exclusion criteria included those that have any other causes of elevated blood sugar (such as Cushing syndrome, hypothyroidism), those having severe neurological or psychological conditions, children having any other otological diseases, and those with family history of craniofacial anomalies. The control group included 25 patients who are known to be nondiabetics, at the same age range of the study group, and were randomly selected from the pediatrics clinic.

All children underwent the following: full history taking which included history of diabetes duration, HbA1C level, DKA, and hypoglycemic coma attacks. Full description of the hearing shall be added and dizziness complaints (if present) regarding frequency, duration, character, and progression. Otological examination: otoscopic examination. Basic audiological evaluation: acoustic immittance testing included tympanometry and acoustic reflexes (ipsilateral) using tone stimuli at 500, 1000, 2000, and 4000 Hz. The frequency of the probe used is 226 Hz. Pure tone audiometry: air conduction threshold was tested at frequencies between 250 and 8000 Hz at octave interval; bone conduction threshold was tested at frequencies between 500 and 4000 Hz, also at octave intervals with contralateral masking using narrow band noise. Speech audiometry included speech reception threshold (SRT), using Arabic spondaic words and word discrimination score (WDS), using Arabic phonetically balanced (PB) words [7] and word discrimination score (WDS), and using Arabic phonetically balanced (PB) words [8].

Vestibular evaluation

Bedside tests include Romberg test and Fukuda test. Videonystagmography (VNG) subtests included

spontaneous nystagmus, gaze-evoked nystagmus, oculography tests (smooth pursuit, saccade, and optokinetic), positional tests (both head and body testing), positioning tests (Dix-Hallpike maneuver), and bithermal caloric testing. The caloric test was in the following sequence: right cool, left cool, right warm, and left warm. The irrigation lasted for 40 s using an air caloric irrigator. Temperatures were 25 °C for cold air and 49 °C for warm air; the air flow-rate was maintained at 8 L/min. Patients were asked to perform a mental task during the recording to maximize the response. A software algorithm was used to automatically calculate unilateral weakness, directional preponderance, and total eye velocity using standard formulae.

Equipment

Immittancemeter: Madsen Zodiac 901 middle ear analyzer, GN Otometrics, Denmark, calibrated according to the ISO standards. Pure tone audiometer: the audiometer Interacoustics AC40. Computerized two channel videonystagmography (VNG): Micromedical computerized 2-channel VNG mobile eyes spectrum 8.6, two-channel equipment, Micromedical (Springfield, Illinois, USA).

Statistical analysis of data

The collected data was organized, tabulated, and statistically analyzed using the SPSS software statistical computer package version 18 (SPSS Inc, USA). For quantitative data, the mean and standard deviation were calculated. Independent *t* test was used to test the difference about mean values of age among patients with and without vestibular dysfunction. For qualitative data, the number and percent distribution was calculated; Chi squared test was used as a test of significance and correlations. For interpretation of results of tests of significance, significance was adopted at $P < 0.05$.

Results

The study group age ranged from 6 to 18 years with a mean age of 10.4 ± 2.7 years. It included 9 males and 16 females. The control group age ranged from 6 to 18 years with a mean age of 10.1 ± 2.6 years, 11 males and

Table 1 Socio-demographic characteristics of study groups ($N = 50$)

Variable	Cases ($N = 25$) Mean \pm SD	Controls ($N = 25$) Mean \pm SD	<i>P</i> value
Age (years)	10.4 \pm 2.7	10.1 \pm 2.6	0.753
Variable	<i>N</i> (%)		
Sex			
Female	16 (64.0)	14 (56.0)	0.564
Male	9 (36.0)	11 (44.0)	

14 females as shown in Table 1, and there is no statistically significant difference between the two groups which indicated proper matching between them.

The study group consists of 25 children, in which the mean duration of diabetes mellitus type 1 in years is 2.7 ± 2.66 , and the mean value of their HbA1C is 8.72 ± 2.05 . Thirteen patients (52%) complained of attacks of diabetic ketoacidosis (DKA); the mean of number of attacks is 1.55 ± 1.51 ; however, 7 patients (28%) complained of bouts of hypoglycemic comas; the mean number of attacks is 1.57 ± 0.54 as shown in Table 2.

Regarding symptomatology, two patients (8%) complained of hearing loss, 5 patients (20%) complained of tinnitus, four patients (16%) complained of true vertigo, and 8 patients (32%) complained of dizziness. While among controls, one child (4%) complained of hearing loss, two children (8%) complained of tinnitus, one child (4%) complained of true vertigo, and one child complained of dizziness. Dizziness was the only statistically significant symptom between cases and controls (Table 3).

Regarding audiological assessment, immitancemetry and pure tone audiometry were performed for both cases and controls according to the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) foundation guidelines.

Immitancemetry results among the 25 cases showed 23 patients (92%) with type A tympanogram, two patients (8%) with type C tympanogram, and four patients (16%) with absent ipsilateral acoustic reflexes while among the 25 controls, 22 showed (88%) type A tympanogram, two (8%) type B tympanogram, 1 (4%) type C tympanogram, and four (16%) absent ipsilateral acoustic reflexes as shown in Fig. 1.

Table 2 Characteristics related to diabetes among cases (N = 25)

Variable	Mean ± SD	Median (range)
Duration of diabetes (years)	2.70 ± 2.66	2 (0–9)
HbA1C	8.72 ± 2.05	9 (5–13)
Attacks of DKA	1.55 ± 1.51	1 (1–6)
Bouts of hypoglycemia	1.57 ± 0.54	2 (1–2)
Variable	N	%
DKA		
Yes	13	52.0
No	12	48.0
Hypoglycemic coma		
Yes	7	28.0
No	18	72.0

DKA diabetic ketoacidosis, HbA1C glycated hemoglobin which refers to glycemic control

Table 3 Comparison between both study groups regarding symptoms (N = 50)

Variable	Cases (N = 25) N (%)	Controls (N = 25)	P value
Hearing loss			
Present	2 (8.0)	1 (4.0)	1.000
No	23 (92.0)	24 (96.0)	
Tinnitus			
Present	5 (20.0)	2 (8.0)	0.417
No	20 (80.0)	23 (92.0)	
Vertigo			
Present	4 (16.0)	1 (4.0)	0.349
No	21 (84.0)	24 (96.0)	
Dizziness			
Present	8 (32.0)	1 (4.0)	0.023*
No	17 (68.0)	24 (96.0)	

* statistically significant

Pure tone audiometry results in the 25 cases showed 21 patients (84%) with normal hearing sensitivity, three patients (12%) with mild bilateral high frequency sensorineural hearing loss (SNHL), and one (4%) with severe bilateral SNHL, while among the 25 controls it showed 22 (88%) with normal hearing sensitivity, one (4%) with mild bilateral high frequency SNHL, and two (8%) with mild bilateral conductive hearing loss as shown in Fig. 2.

Regarding vestibular assessment for the study group, all cases and controls underwent videonystagmography (VNG) tests and Romberg and Fukuda tests. Neither cases nor controls showed any abnormalities in Romberg or Fukuda tests.

Positioning nystagmus was not detected in the entire groups, while two patients (8%) and one control (4%) showed positional nystagmus and two patients (8%) and none of controls showed spontaneous nystagmus as shown in Table 4.

During conducting oculography tests, abnormal saccade has been recorded in 20 cases (80%) most of which was long latency and slow velocity and in one control (4%). There was a statistically significant difference between cases and controls as shown in Table 5. On caloric testing, this study revealed 10 cases (40%) with unilateral canal weakness while 15 cases (60%) showed normal caloric test results, and no controls showed any canal weakness, which is also statistically significant.

Figure 3 summed up the comparison between both cases and controls regarding PTA, caloric test, saccade, smooth pursuit, and optokinetic testing.

Moreover, correlation between saccade finding among cases and the risk factors of diabetes like duration, HbA1C level, DKA, and hypoglycemic coma attacks

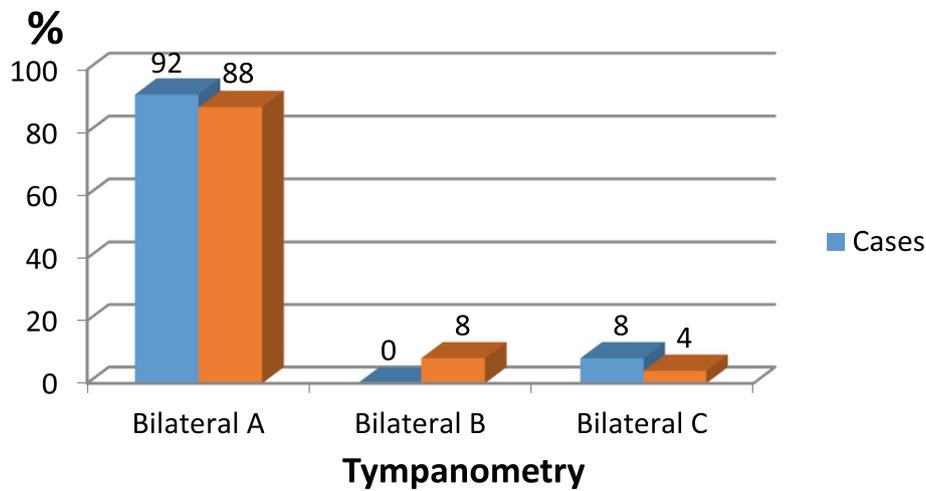


Fig. 1 Tympanometry results

indicated statistically significant positive correlation between increased saccade latency and the level of HbA1C as shown in Table 6.

Discussion

Diabetes mellitus is a real problem that influences the world as a whole and Egypt as well. Regarding Egyptian society, diabetes is widespread in many families, nearly 10.4% of Egyptian population [9]. A study was done to estimate the incidence and prevalence of T1DM in children, and adolescents in three Egyptian governorates (Fayoum, North Sinai, and Suez) showed a prevalence rate of 0.7/1000 and an incidence rate of 4.01/100,000 [9]. Diabetics in Egyptian population may suffer from

many side effects that probably affect badly on their lives as neuropathy, retinopathy, and dermopathy [10].

Regarding symptomatology in the current study, it has been reported that vertigo, tinnitus, and hearing loss in DM patients are likely from inner ear diseases related to glucose metabolism disorders [11].

On the other hand, another study revealed that diabetic patients have significantly higher incidence of sensorineural hearing loss compared to non-diabetic control subjects. However, the role of age of the diabetic patients and glycemic control could not be evaluated in their study [12]. The mechanism underlying auditory pathway abnormality in type 1 diabetes are yet to be confirmed, but reduced conduction efficiency may be a

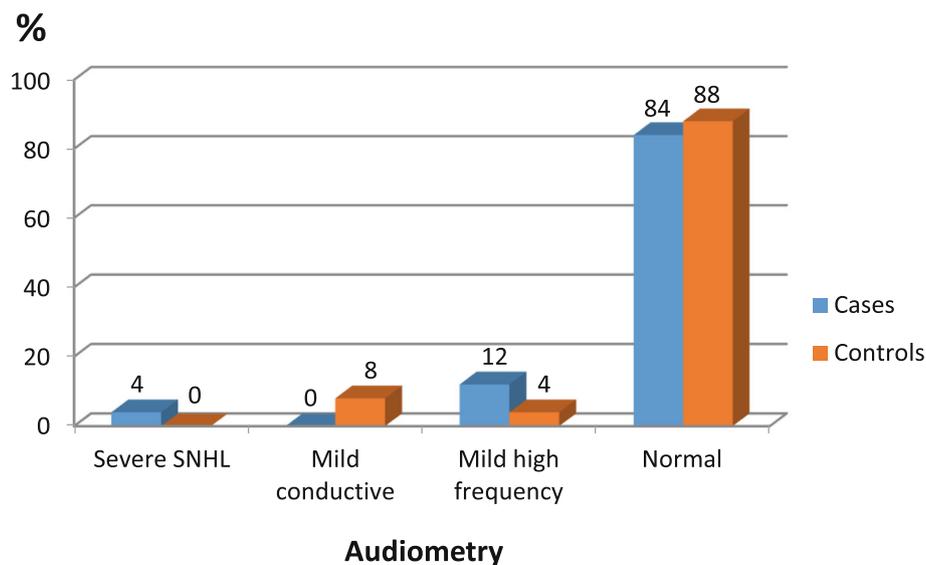


Fig. 2 Audiometry results

Table 4 VNG findings

Variable	Cases (N = 25) N (%)	Controls (N = 25)	P value
Spontaneous nystagmus			
Present	2 (8.0)	0 (0.0)	0.490
No	23 (92.0)	25 (100.0)	
Positional nystagmus			
Present	2 (8.0)	1 (4.0)	1.000
No	23 (92.0)	24 (96.0)	
Positioning nystagmus			
Present	0 (0.0)	0 (0.0)	-----
No	25 (100.0)	25 (100.0)	

consequence of demyelination in the auditory nerves of people with diabetes [13].

Regarding vestibular assessment, oculography revealed that spontaneous nystagmus was detected in only two cases (8%) and not detected in controls, similar to Rafaele et al. [5] who stated that only one individual presented with closed eye spontaneous nystagmus. Eye tracking test results goes in hands with Gawron et al., who stated that in smooth pursuit tests the phase value was of a significantly higher value in diabetic patients than in the control group [6].

According to caloric test results, this study revealed 40% of cases with unilateral canal weakness while 60% showed normal caloric test results, and no controls showed any canal weakness, which is also statistically significant. This agreed with Rafaele et al. [5], who stated that the caloric test was altered in 36.84% ($n = 7$) of the sample; the rest of the sample, 63.15% ($n = 12$), had normal results. On the other hand, this disagreed with Gawron et al., who stated

Table 5 Saccade testing

Variable	Cases (N = 25) N (%)	Controls (N = 25)	P value
Latency			
Long	17 (68.0)	1 (4.0)	< 0.0001 ^a
Normal	8 (32.0)	24 (96.0)	
Velocity			
Slow	6 (24.0)	1 (4.0)	0.042 ^a
Normal	19 (76.0)	24 (96.0)	
Accuracy			
Abnormal	0 (0.0)	0 (0.0)	-----
Normal	25 (100.0)	25 (100.0)	
Overall			
Abnormal	20 (80.0)	1 (4.0)	< 0.0001 ^a
Normal	5 (20.0)	24 (96.0)	

^aSignificant

that peripheral disturbances such as canal paresis occurred only in four (4.22%) cases [6].

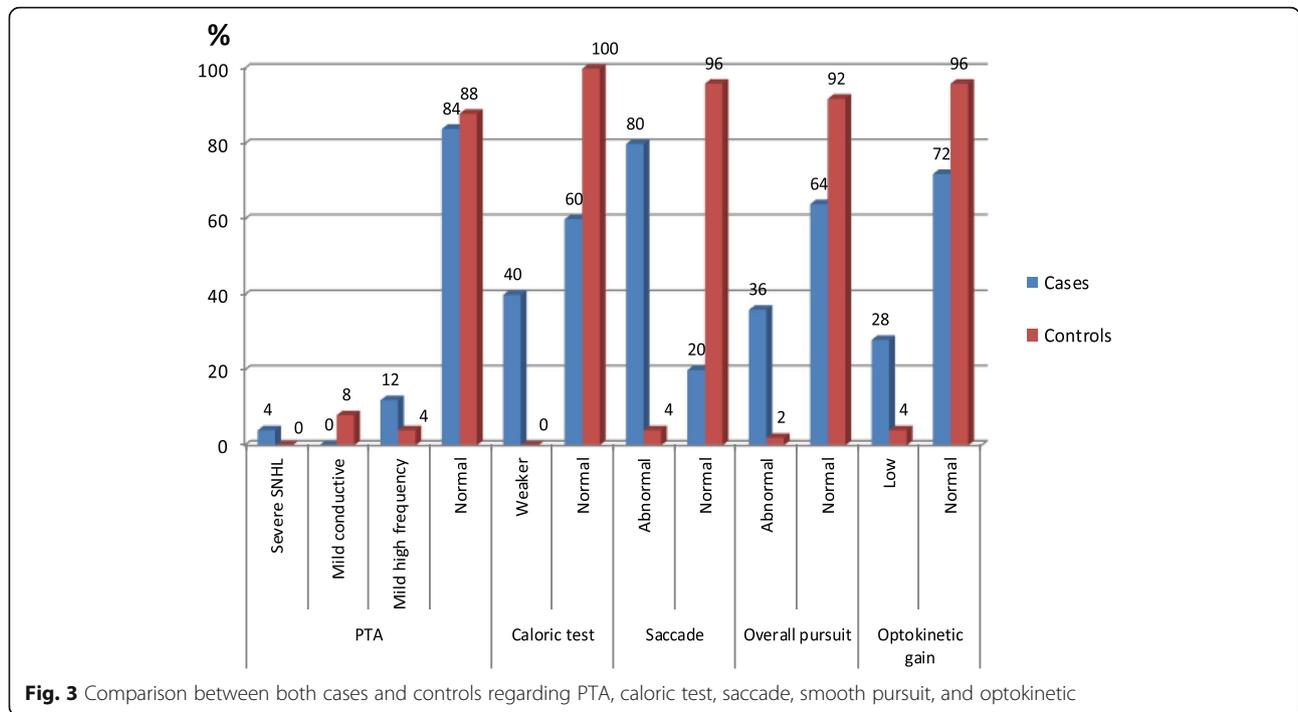
Further analysis was done to identify possible risk factors that could be associated with abnormal saccades in these diabetic children (diabetes duration, HbA1C level, DKA, and hypoglycemic coma attacks). HbA1C was the only statistically significant difference found compared to other factors.

The vestibular organ, and especially its central part, is spread out within different parts of the CNS. Its proper function depends on many individual anatomical and functional compartments that co-operate together. The cerebellum plays a crucial role in the synchronization of saccades with planning and learning in the temporal cortex, as was proved, among others, in investigations with the use of functional nuclear magnetic resonance. So it may be assumed that even small disturbances provoked by diabetes, not detectable in a routine neurological examination, may handicap equilibrium and complex relations present in the vestibular organ [14].

Metabolic disturbances of type 1 diabetes mellitus can also have an effect on different parts of the vestibular organ, but principally the central part. This effect is related to the number and type of hypoglycemic episodes and the duration and control of the disease [14].

So to sum it up, this study suggested that T1DM has an impact on the vestibular function even if asymptomatic; this impact is both central and peripheral but it is most likely central. Gawron et al. [6] concluded that diabetes mellitus type 1 provokes different, probably dispersed disturbances within the vestibular organ; these disturbances within the vestibular organ have a subclinical course. They refer mostly to its central part, despite the lack of any central nervous system impairment in physical neurological examinations [13]. In accordance, Kamali et al. stated that T1DM individuals may suffer from vestibular organ impairment even if there is no otoneurologic symptom [15].

Since saccadic eye movement results from sensory input, central nervous system control, and motor outputs, its impairment might be ascribed to a selective or widespread involvement of the visual pathways, or different central nervous system areas, or of the oculomotor neuromuscular structures. Saccade parameters can be differently influenced by various brain areas: specifically, peak velocity seems to be related to brainstem reticular formation function, while saccade latency seems to depend mainly on higher function [16]. However, an increase of saccade latency may be found in the case of reduced transmission velocity of central neural pathways and also in the presence of impaired visual pathways. In patients with impaired latency, VEMPs revealed impaired function of the visual pathways (increased N75,



P100, N145 latencies, and reduced N75-P100 and P100-N145 amplitudes) in the absence of retinopathy and in the presence of a normal visual acuity. It is known that VEMPs represent a mass response of cortical and possibly subcortical visual areas to visual stimuli [17]. The lack of correlation between the VEMPs impairment and the saccade latency delay suggests that the latter cannot be exclusively ascribed to the dysfunction observed in the visual pathways. This suggests that other neural structures may be involved in the delay of latency in T1DM patients [18].

Consistent with other authors who stated that a quantitative evaluation of saccadic tests can provide important and reliable information on the functional condition of the central part of the vestibular organ and could become one of the helpful additional tools in the estimation of diabetic patients' condition. As a consequence, it could be helpful in treatment planning and treatment result monitoring. Some authors have planned to check the dynamic of otoneurological results in their group of patients in order to see if the disturbances are progressive or reversible. This information could help to work

Table 6 Relation between saccade and characteristics related to diabetes among cases (N = 25)

Variable	Abnormal (N = 20) Mean ± SD, median (range)	Normal (N = 5)	P value
Duration of diabetes (years)	2.87 ± 2.94, 2 (0–9)	2.00 ± 1.00, 2 (1–3)	0.921
HbA1C	9.27 ± 1.90, 9.45 (5–13)	6.54 ± 0.69, 6.10 (6–7.4)	0.006 ^a
Attacks of DKA	1.60 ± 1.58, 1 (1–6)	1.00 ± 0.00, 1 (1–1)	0.909
Bouts of hypoglycemia	1.67 ± 0.52, 2 (1–2)	1.00 ± 0.00, 1 (1–1)	0.571
Variable	N (%)		
DKA			
Yes	12 (60.0)	2 (20.0)	0.160
No	8 (40.0)	4 (80.0)	
Hypoglycemic coma			
Yes	6 (30.0)	1 (20.0)	1.000
No	14 (70.0)	4 (80.0)	

DKA diabetic ketoacidosis, HbA1C glycated hemoglobin which refers to glycemic control

^aSignificant

out the defined set of otoneurological tests that perhaps could reflect diabetic central neuropathy [6]. Accordingly, it would be reasonable to search for selected otoneurological tests that could help monitor neuropathic disturbances in T1DM.

Conclusion

This study proposed that type 1 diabetes mellitus can affect the audiovestibular system of children even in the absence of symptoms. Accordingly, appropriate early rehabilitative management should be planned in an attempt to avoid further complications.

Recommendations

This study suggested the need for a bigger study, including more children, to test the feasibility of implementing a routine audiovestibular assessment protocol for all children suffering from T1DM, and to test how early rehabilitation management can improve the general well-being and quality of life of those children.

Abbreviations

T1DM: Type 1 diabetes mellitus; VNG: Videonystagmography; DKA: Diabetic ketoacidosis; HbA1C: Glycated hemoglobin which refers to glycemic control; SRT: Speech reception threshold; WDS: Word discrimination score; PB: Phonetically balanced words; DM: Diabetes mellitus; AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery Foundation guidelines; SNHL: Sensorineural hearing loss; VEMPs: Vestibular-evoked myogenic potentials

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Authors' contributions

All authors contributed to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript. Dr. RS and Dr. EM were responsible for the audiological and vestibular assessment. Dr. RY was responsible for the pediatric assessment. Prof SG and Prof AR were responsible for analysis of the results and to the writing of the discussion. Also, the manuscript has been read and approved for submission by all authors and has not been submitted or published elsewhere.

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Availability of data and materials

All datasets used are available.

Ethics approval and consent to participate

The study was approved by the local research ethics board of Fayoum University on February 11, 2017 (reference number is not applicable); a written informed consent was obtained from all patients' guardians to participate in this work.

Consent for publication

A written informed consent was obtained from all patients' guardians to publish this work.

Competing interests

None declared.

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