INFLUENCE OF AUDITORY-VESTIBULAR FUNCTION IN TYPE 1 DIABETES MELLITUS: A SYSTEMATIC REVIEW

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This Dissertation is submitted as part of fulfilment for the Degree of

Master of Science in Audiology

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August, 2022

CERTIFICATE

This is to certify that this dissertation entitled **"Influence of Auditory-Vestibular Function in Type 1 Diabetes Mellitus: A Systematic Review"** is the bonafide work submitted as part of fulfilment for the Degree of Master of Science in Audiology of the student with Registration No. 20AUD006. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other Universities for the award of any other diploma or degree.

Mysuru

August, 2022

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Mysuru

August, 2022

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DECLARATION

This dissertation entitled **"Influence of Auditory-Vestibular Function in Type 1 Diabetes Mellitus: A Systematic Review"** is the result of my own study under the guidance of Dr. Prawin Kumar, Associate Professor, Department of Audiology, All India Institute of Speech and Hearing, Mysore-06 and has not been submitted earlier to any other Universities for the award of any other diploma or degree.

Mysuru

August, 2022

Register Number: 20AUD006

This Dissertation is dedicated to my Mummy.

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"I am exactly where I meant to Be"

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ABBREVIATIONS

T1DM	Type I Diabetes Mellitus
IDF	International Diabetes Federation
C-VEMP	Cervical Vestibular Evoked Myogenic Potential
SCC	Semicircular Canal
EGFR	Estimated glomerular filtration rate
UAE	Urinary albumin excretion
V-HIT	Video Head Impulse Test
HRQoL	Health Related Quality of Life
WHO	World Health Organization
APHAB	Abbreviated Profile of Hearing Aid Benefit
SSQ	Speech, Spatial and Qualities of Hearing Scale questionnaire
RALP	Right anterior and left posterior planes
LARP	Left anterior and right posterior planes
HbA1c	Glycated hemoglobin

ABSTRACT

Diabetes mellitus (DM) is one of the metabolic disorders which is manifested by hyperglycemia brought on by abnormalities in insulin secretion, insulin action, or both. Type 1 DM occurs due to beta cell loss and absolute or relative insulin insufficiency, which result in hyperglycemia and hypoinsulinemia. Individuals with type 1 DM do experience dizziness, tinnitus, and hearing loss. The vestibular-cochlear abnormalities seen in these individuals have been linked to angiopathy and neuropathy due to diabetes mellitus. The present study aimed to systematically review the findings of published literature in terms of influence on audio-vestibular system due to type 1 diabetes mellitus. There are different databases (PubMed, Google Scholar, Scopus, & Web of Science) which were searched and identified 16,201 articles based on Booleans used. Out of 16,201 articles, there are 27 articles selected based on the inclusion and exclusion criteria for the study. Out of 27 full-length articles, 20 articles were related to auditory system and 7 articles were related to vestibular system. Overall, studies related to the assessment of auditory system based on both conventional and advanced audiological assessment (pure tone audiometry, high frequency audiometry, immittance, otoacoustic emission, click evoked ABR and frequency following response, and auditory late latency response) reported mixed finding in individuals with T1 DM. Studies reported with or without sensorineural hearing loss including involvement of peripheral and central auditory system. Similarly, vestibular assessment (behavioral vestibular tests, cVEMP, ENG, & vHIT) reported peripheral and central vestibular impairment due to T1 DM. the hyper or hypo-function of the vestibular system are reported in the individuals with type 1 DM. Studies also reported temporal processing deficit in individuals with type 1 DM apart from impaired quality of life. The primary reason for these changes if any reported in the studies are possibly due to

reduced conduction efficiency result from demyelination, and/or neural dys-synchrony. Further, the subtle auditory processing deficit could also be one of the reason for the abnormalities noticed in the type 1 DM. Moreover, despite clinically normal audiometric thresholds, neural deficits are reported in the individuals with type 1 DM. Hence, present review suggests regular follow-up for audio-vestibular assessment of those individuals having type 1 DM for early identification and effective management of the deficits if any.

Key Words:

Diabetes Mellitus, ABR, cVEMP, VNG, Vestibular test, DPOAEs

Chapter 1

Introduction

The human ear is most complex and well protected inside the temporal bone. The auditory systems are divided into peripheral and central components. The peripheral auditory system includes external, middle, inner ear including cochlea. Whereas the central auditory system consisted of auditory nerve and above structure which help in decoding the information at the auditory cortex. The inner ear consists of the sensory organs for hearing and balance which include the cochlea and vestibular end-organs. These organs are innervated by the eighth cranial nerve from which inferior and superior vestibular nerve divide and supply to vestibular-end organs. There are several factors which can damages to the audio-vestibular structure over the years in day-to-day life such as noise exposure, ototoxicity, presbycusis, diabetes, and auto-immune disorders.

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (American Diabetes Association, 2009). Diabetes mellitus is classified according to the aetiology of the disorder (American Diabetes Association, 2017). The two major types of DM are type 1 DM and type 2 DM. Type 1 DM is characterized by the loss of beta cells with total or relative insulin deficiency causing hyperglycemia and hypoinsulinemia (Jauregui-Renaud, 2016; Rigon et al., 2007). In individuals with type 1 DM, the pancreas produces either very little or no insulin. Insulin resistance, which results in a reduced level of response from the target tissue to the insulin produced by the pancreas, is a defining feature of type 2 diabetes (Kamali et al., 2013). Long-term effect of the DM are dysfunction, and failure of various organs, including the eyes, kidneys, nerves, heart, and blood vessels, which is linked to the chronic hyperglycemia

of diabetes (Begic et al., 2016). Hearing loss has been linked to type I and type II diabetes mellitus, with proposed causes including micro-vascular illness, acoustic neuropathy, and oxidative stress. Patients with diabetes mellitus frequently experience dizziness, tinnitus, and hearing loss. The vestibular-cochlear abnormalities seen in these patients have been linked to angiopathy and neuropathy produced by diabetes mellitus (Maia & De Campos, 2005). Diabetes mellitus is a condition where blood glucose levels are persistently elevated above the normal range. It happens either because there is insufficient insulin or because there are substances present that interfere with insulin's ability to work (Adriano & Sylvia, 2006). In individuals with diabetes, glycemic level increase beyond physiological levels which generates glucose and it build up within fluids and its large osmotic potential alters the functioning of all the systems including auditory and vestibular system (Adriano & Sylvia, 2006). Overall, studies reported damages of the audio-vestibular system in long-term due to DM.

Aim of the Study

The present study aimed to review the impact on audio-vestibular function due to Diabetes Mellitus type I.

Objectives of the Study

- Influence of Diabetes Mellitus type I on auditory functioning (peripheral and Central).
- Influence of Diabetes Mellitus type I on vestibular functioning (peripheral and Central).

Chapter 2

Review of literature

Diabetes mellitus is a world-wide life style disease that can lead to public health and socio-economic problems. Individuals that live in developing countries and disadvantaged communities are at a greater risk for these problems (Mbanya, Motala, Sobngwi, Assah, & Enoru, 2010). Type 2 DM is the most common type of diabetes, accounting for more than 90% of all cases (Amod et al., 2012), while type 1 DM accounts for 10- 15% of all cases (Rance et al., 2014). The intricate association between diabetes and its influence on auditory and vestibular system functioning is reported under different sub-heading.

2.1. Diabetes mellitus and Blood supply

Diabetes mellitus interferes with the metabolism of glucose and causes chronic hyperglycaemia commonly known as high blood sugar. Hyperglycaemia is a typical complication associated with type 1 and type 2 DM. It is said to be the main causal factor for the incidence and development of angiopathy (Jauregui-Renaud, 2016). Angiopathy refers to a disease of the blood vessels, characterised by the abnormal development of new blood vessels (Xu, Kanasaki, Kitada, & Koya, 2012). Diabetic angiopathy causes micro- and macro-vascular complications. Micro-vascular complications can be described as complications that permanently affect the small blood vessels in the body (Fowler, 2008). The narrowing of small blood vessels leads to damage and failure of various organs and tissues of the body causing diabetic nephropathy, neuropathy and retinopathy (Fowler, 2008; Kamali et al., 2013). Macro-vascular complications affect the larger blood vessels in the peripheral or coronary vascular system. Macro-vascular complications include the process of atherosclerosis which causes narrowing of the arterial walls in the body (Fowler, 2008). This leads to coronary artery disease, peripheral arterial disease and stroke.

The primary cause of morbidity and mortality in DM is the direct and indirect effects of hyperglycemia on the human vascular tree (Fowler, 2008). In addition to the above mentioned complications, abnormal glucose metabolism, which causes hyperglycaemia, can effect proper functioning of the inner ear structures (Rigon et al., 2007).

2.2 Diabetes mellitus and inner ear

The cochlea and vestibular end-organs are among the sensory organs for hearing and balance found in the inner ear. The eighth cranial nerve innervates and supplies blood to both of these organs (Stach, 2010). Due to the common nerve and blood supply, DM can harm the vestibular end-organs in addition to the auditory system (Ward et al., 2015). The effective functioning of the inner ear depends on the stability of the internal environment as created by microcirculation (Xipeng et al., 2013). Oxygen and nutrient rich blood are delivered to body tissues including the inner ear through small blood vessels. Sensory hair cells in the inner ear are vulnerable to ischemia therefore microcirculation is necessary to maintain the ion and fluid balance in the inner ear (Shi, 2011). Abnormalities in microcirculation can cause end-organ damage (Struijker-boudier.,2007). Angiopathy negatively affects this microcirculation, by it reducing the transport and flow of blood to the inner ear (David et al., 2015). Complications in cochlear blood supply can lead to cochlear dysfunction (Xipeng et al., 2013). The vestibular end-organ also depends on a constant supply of oxygen and glucose which is impeded by angiopathy (David et al., 2015).

Another cause to consider related to vestibulocochlear manifestations in DM is neuropathy. Neuropathy can be described as the progressive degeneration of nerve fiber's axons (David et al., 2015). Diabetic neuropathy is characterised by a decrease in motor and sensory activity of the peripheral nerves, as well as demyelination of nerves

which in turn cause a decrease in the conduction velocity. This in turn can lead to labyrinth dysfunction (David et al., 2015).

2.3 Diabetes mellitus and hearing loss

The relationship between DM and hearing loss has been studied by various researchers (Dąbrowski, Mielnik-niedzielska, & Nowakowski, 2011; Gawron, Pospiech, Orendorz-Fraczkowska, & Noczynska, 2002; Hou, Xiao, Ren, Wang, & Zhao, 2015; Jauregui-Renaud, 2016; Teng et al., 2017). However, the relationship between DM and hearing loss still remains controversial (Ciorba, Aimoni, & Bovo, 2012). Previous research (Kalkan, Bayram, Gökay, Cura, & Mutlu, 2018; Özel, ÖzkiriŞ, Gencer, & Saydam, 2013; Pandey, Pandit, & Pandey, 2016; Prakash & Sumathi, 2013; Herrera-Rangel et al., 2015; Razzak, Bagust, Docherty, Hussein, & Al-Otaibi, 2015; Sahu & Sinha, 2015; Ward et al., 2015) focused primarily on the auditory and vestibular function of individuals with type 2 DM due to its higher incidence, but it is still unclear if the same alterations occur in those with type 1 DM. The limited studies that reported on type 1 DM found a close link between hearing loss and diabetes (Austin et al., 2009; Dąbrowski et al., 2011; David et al., 2015; Hou et al., 2015; Malucelli et al., 2012; Rance et al., 2014; Teng et al., 2017; Xipeng et al., 2013). Individuals with any type of DM can experience symptoms such as tinnitus and aural fullness (David et al., 2015). The hearing loss proved to be mild or subclinical, bilateral, progressive, sensorineural and predominantly in the high frequencies (Dąbrowski et al., 2011).

Click evoked auditory brainstem responses (ABR) were also affected. The wave V latency and wave I-V inter-amplitude latency is longer compared to that of the healthy participants. A study by Malucelli and colleagues (2012) found type 1 DM individuals are having higher (poorer) mean hearing threshold at any frequency. A total of 23/30

(76.7%) diabetic individuals had hearing loss compared to only 12/30 (40%) non-diabetic participants. Hou and colleagues (2015) found significantly elevated audiometric thresholds at 250Hz, 1000Hz, 2000Hz, 4000Hz, and 8000Hz in the right ear and in the left ear at 250Hz, 500Hz, 1000Hz, 4000Hz and 8000Hz in the type 1 diabetic participants, compared to non-diabetic participants. Nevertheless, in total 24/50 (48%) individuals with DM presented with hearing loss. The pure tone average (PTA) and thresholds for frequencies at 250Hz-4000Hz in the left ear and at 250Hz-8000Hz in the right ear were significantly different between the diabetes and non-diabetic groups (Andriëtte et al.,2018).

Dabrowski et al. (2011) reported that the mean hearing threshold for type 1 DM participants was worse in the higher frequencies (3000Hz-12000Hz) when compared to that of healthy participants. A total of 6/31 (19.35%) type 1 DM participants had hearing loss compared to only 3/26 (11.54%) healthy participants. The mean transient evoked otoacoustic emissions (TEOAE) amplitude for the type 1 DM participants were smaller. Auditory brainstem responses (ABR) were also affected.

Auditory dysfunction proves to be related to disease duration, high density lipoprotein (HDL) cholesterol level, systemic blood pressure, microalbuminuria, glycosylated haemoglobin (GHbA1c), triglyceride and age of the patient (Hou et al., 2015). The study by Hou and colleagues (2015) indicated that a prolonged disease duration, a lower HDL cholesterol level and a higher systolic blood pressure level may increase type 1 diabetics 'risk of hearing loss. Another study concluded that poorly controlled and complicated diabetic individuals are at an even higher risk of developing hearing loss (Sunkum & Pingile, 2013).

2.4 Diabetes Mellitus and Vestibular Dysfunction

Vestibular dysfunction is still a newly identified secondary manifestation among diabetic patients (Schubert et al., 2010). The central and peripheral vestibular system are affected by microangiopathy (Prakash & Sumathi., 2013). Most often studies reported bilateral, progressive, sensorineural hearing loss and predominantly affecting high frequencies (Dąbrowski et al., 2011). Microangiopathy causes ischemia of the vestibular apparatus and alters the inner ear fluid metabolism leading to labyrinthine dysfunction (Kalkan et al., 2018). Particularly in those with type 1 diabetes, the extent of vestibular end-organ impairment appears to be primarily influenced by the frequency and kind of hypoglycemic events (Gawron et al., 2002). Furthermore, type 1 DM vestibular end-organ dysfunction may be influenced by the length of the disease and, to some extent, blood glucose levels (Gawron et al., 2002). To date only a few studies reported vestibular dysfunction in individuals with type 1 DM (Gawron et al., 2002; Kamali et al., 2013; Kamali, Hajiabolhassan, Fatahi, & Nasliesfahani, 2013; Klagenberg et al., 2007; Prakash & Sumathi, 2013; Rigon et al., 2007; Scherer & Lobo, 2002; Tavakoli et al., 2014).

Klagenberg and colleagues (2007) performed video electronystagmography tests (VENG) including spontaneous nystagmus test, positional nystagmus test, pendular tracking test, optokinetic nystagmus test, pre-and post-rotary nystagmus with the pendular swing rotary test, and pre- and post-caloric nystagmus test. All the above test results were within normal limits except caloric test. A total of 18/30 (60%) of the individuals with type 1 DM included in their study had vestibular dysfunction. Of these individuals, 13/30 (43%) did not report feelings of dizziness. In another study, 19 participants were considered for VENG tests, including semi-spontaneous nystagmus test, directional/fixating nystagmus test, optokinetic nystagmus test, pendular tracking

test, and caloric test (Rigon et al., 2007). In this study also only the caloric test results were abnormal in 7/19 (36.84%) type 1 DM individuals (Rigon et al., 2007).

Scherer and Lobo (2002) performed an electronystagmography (ENG) evaluation including spontaneous nystagmus test, semi-spontaneous nystagmus test, pendular tracking, optokinetic nystagmus test and pre- and post-caloric nystagmus. Peripheral vestibular dysfunction was found in 8/12 (66.7%) individuals with type 1 DM as indicated by altered caloric test results though 62.5% of the individuals did not report any dizziness symptoms. Therefore, the vestibular end organ can be affected in individuals with type 1 DM, even when such individuals do not have any symptoms or complaints (Rigon et al., 2007; Scherer & Lobo, 2002).

Interestingly, Gawron et al. (2002) reported that the metabolic disturbances found in type 1 DM cause impairment in the peripheral vestibular structures, but mostly in the central structures as shown by impaired optokinetic responses observed in 36/95 (37.89%) diabetic participants, spontaneous nystagmus in 10/95 (10.53%) individuals and the presence of positional nystagmus in 21/95 (22.11%) individuals. When comparing cervical vestibular evoked myogenic potential (cVEMP) results of participants with type 1 DM with healthy controls, the cVEMP responses of individuals with type 1 DM were more affected than healthy participants (Kamali et al., 2013). The latencies of P1 and N1 were significantly longer in individuals with type 1 DM. No correlation was found between VEMP responses and GHbA1c levels and the average blood glucose concentration over three months. Additionally, there were no differences in the absolute and relative amplitudes of the VEMP responses between the experimental and control group (Kamali et al., 2013). Another study compared the cVEMP responses of 15 individuals with type 1 DM, 15 individuals with type 2 DM and 10 healthy participants. The researchers concluded that only the cVEMP

amplitudes were statistically different between type 1 DM participants and non-diabetic participants (Tavakoli et al., 2014).

Individuals with type 1 DM and complications such as neuropathy are at an even higher risk for vestibular dysfunction compared to 20 individuals without neuropathy (Kamali et al., 2013). Mean peak latencies of P1 and N1 for individuals with DM and neuropathy were longer compared to individuals with DM without neuropathy and healthy participants. However, the exact number of participants with abnormal test results was not reported (Kamali et al., 2013). Overall, review of literature highlights several factors which directly or indirectly influence the functioning of audio-vestibular system due to T1 DM.

Chapter-3

Methods

The current study focused on systematically reviewing the articles that assessed the auditory and vestibular functioning in Individual with Type 1 Diabetes Mellitus (T1DM). According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) declaration, a formal study protocol was created. This chapter focuses on the procedures used in the study.

3.1 Internet Search Engines

Studies were chosen from PubMed, Google Scholar, Scopus, and Web of Science, among other databases. A search was conducted using acceptable keywords to identify publications connected to the current research topic. The keywords used for the search are Immittance and Diabetes Mellitus (Type I), Pure tone audiometry (PTA) and Diabetes Mellitus (Type I), OAEs and Diabetes Mellitus (Type I), ABR and Diabetes Mellitus (Type I), C-VEMP or O-VEMP and Diabetes Mellitus (Type I), V-HIT and Diabetes Mellitus (Type I), Caloric test and Diabetes mellitus (Type I), other Behavior test of vestibular system and Diabetes Mellitus (Type I), Hearing loss, blood sugar level and insulin level along with their derivatives and the necessary Boolean operators. Duplicates in the primary sample were discovered and eliminated. Further, the articles title and abstract were screened. All the selected manuscript was published in peer-reviewed journals. The articles meeting the inclusion criteria as mentioned in section 3.3 were selected for further review. The articles failing to meet the inclusion criteria were excluded from the study.

3.2 Data Extraction (Selection and Coding)

A pre-piloted form was used for the extraction of data from the included studies. The extracted information included the study population, methodology, participants demographic related to T1DM, Insulin level, data included relating auditory-vestibular tests and the severity of the problem due to type I diabetes mellitus.

3.3 Criteria for Inclusion and Exclusion

Experimental research tapping on the effect of auditory and vestibular function secondary to T1DM was acknowledged. Controlled trial data on glycated hemoglobin (HbA1c), the fasting blood sugar test (FBS), and the post-prandial glucose test (PPBS) that demonstrate the presence of T1DM were included. The full length articles available in English only were considered. Those studies related to type 2 diabetes (T2DM), different regional language, review article and case study were excluded.

3.4 Data Synthesis and Analysis

The investigations used a variety of clinical and methodological approaches. As a result, qualitative evaluations of the responses of the individual studies to associated research topics were done utilizing various T1DM metrics. A systematic review was carried out in accordance with the review article's methodological approach.

Chapter 4

Results

The current systematic review aimed to describe audio-vestibular function in individuals with type 1 DM and determine the disease's impact on their lifestyle. The relevant articles were considered based on the inclusion criteria and with the help of the search engine. The selected articles were considered based on detailed audio-vestibular evaluations such as pure tone audiometry, immittance audiometry, otoacoustic emission, auditory brainstem response, auditory late latency response and vestibular tests (cVEMP, VNG & vHIT) performed on type 1 DM and compared with non-diabetic healthy individuals.

4.1 Extraction of the Study

A total of 16,201 articles were identified using a database search engine, among which 1,446 were excluded due to duplication (Table 1). The title and abstract screening were carried out for the remaining 14,755 articles for further consideration. Out of 14,755 articles, 451 were considered due to the availability of a full-length manuscript accessed by the researcher. Out of 451 articles, only 27 full-length articles fulfilled all the inclusion criteria considered for further study. Among 27 full-length articles, 20 were related to the effect of Type I DM on the auditory system, and the remaining 7 were related to the effect of Type I DM on the vestibular system. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram is used for the present systematic review while selecting the articles (Figure 4.1).

Figure 4.1

PRISMA flowchart of the literature review process

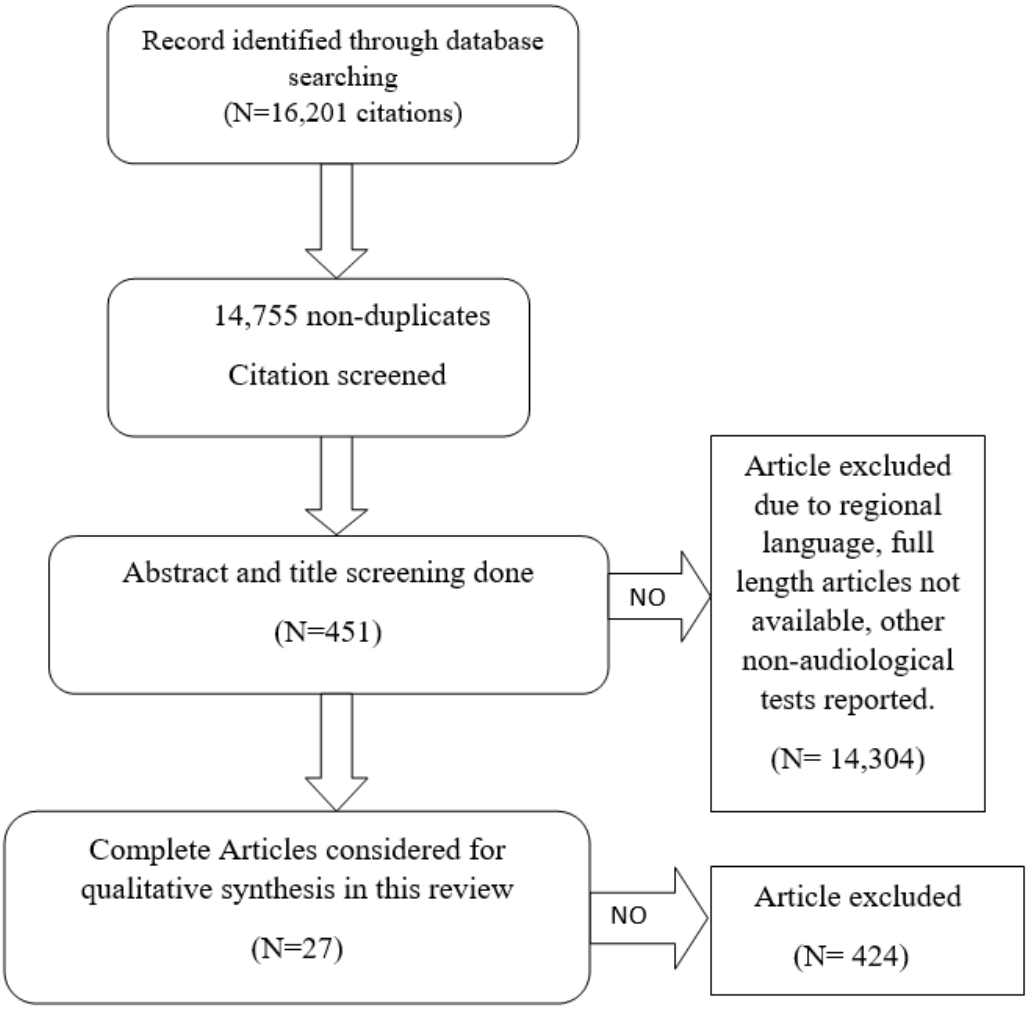

Table 1:

Number of articles related to audio-vestibular system in T1DM through different search engine

Database	Auditory related articles (n)	Vestibular related articles (n)	Total
PubMed	1860	676	2536
Google Scholar	4680	960	5640
Scopus	3125	900	4025
Web of Science	4130	670	4800

4.2 Quality Analysis

A critical appraisal skills programme (CASP) checklist was used to analyze the selected studies (Figure 4.2). The checklist contains 12 questions to analyze each article. While analyzing the results, most studies lack identifying the confounding factors that might have deviated from the results and the accounting for the same. Also, some studies considered confounding factors like duration and glycemic control of diabetes. However, improvement or differences might have been possible if the subjects had been followed up for longer. All the studies had shown acceptable results and good implications for practice and are in line with the earlier published studies.

Figure 4.2

Quality Assessment of Articles selected for Systematic Review.

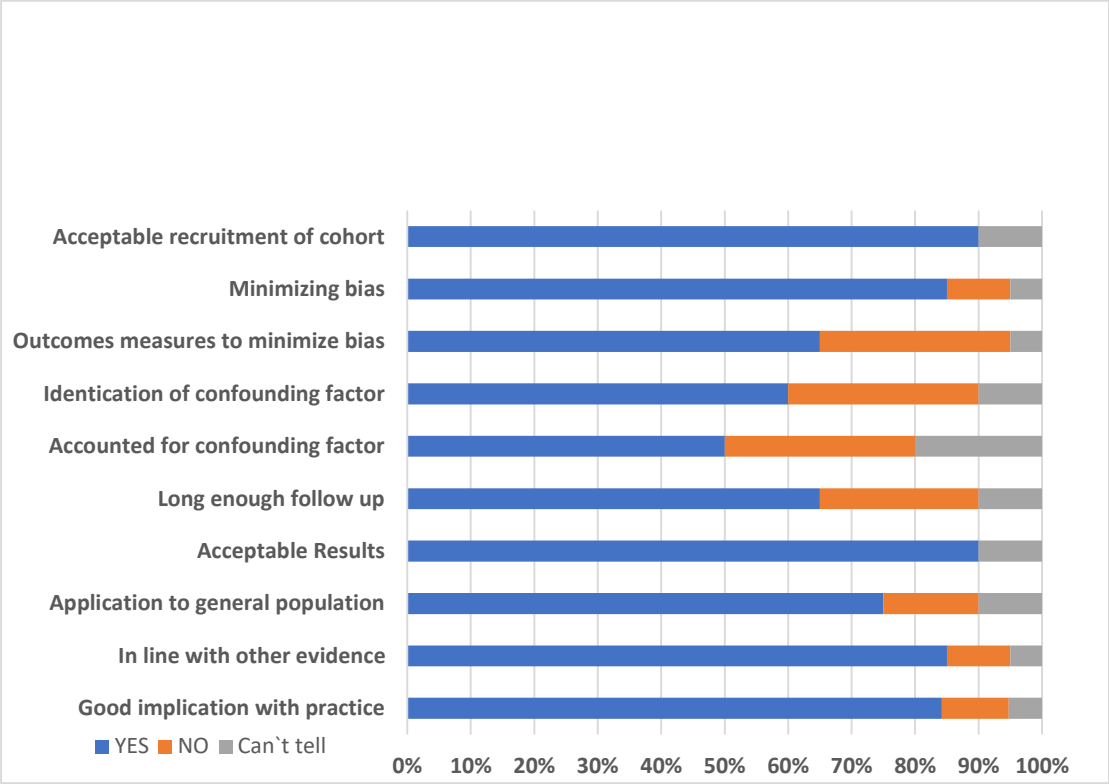

Table 2:

Summary of audiological tests and their findings regarding type-1 diabetes mellitus.

Sl. No.	**Author/Year**	**Patients Demographics**	**Audiological Test performed**	**Outcomes (++/- -/NS)**
1	Braite et al., 2019	EG: 50 children CG: 51 children Age range: 7-18 years	PTA, Immittance, OAEs and contralateral suppression of OAEs.	PTA: NS OAE: significant reduction of contralateral OAEs(++)
2.	Malucelli et al., 2012	EG: 30 children Mean age: 25.9 ± 10.4 years CG: 51 children Mean age: 26.56 ± 9.6 year Age range:18-55 years	Conventional and High frequency PTA	HF PTA: More accurate than conventional PTA (++)
3	Celik et al., 1996	EG: 75 Subjects CG: 45 Subjects Mean age: 45.3 years	PTA	PTA: Statically significant difference found between two groups (++)
4	Dąbrowski et al., 2018	EG:31 Subjects Mean age: 29.1 ± 7.1 years CG: 26 Subjects Mean age: 30.3 ± 7.8 years	PTA, TEOAEs and ABR.	PTA: the threshold is poorer at high frequency (++), TEOAEs: amplitude reduced (++) & ABR: latency were delayed inT1DM(++)

5	Pessin et al., 2008	EG: 40 Subjects Age Range:6 to 36 years (mean: 15.83 years) CG: 20 Subjects Age Range:8 to 31 years (mean: 19.6 years)	PTA, Immittance and ABR.	PTA: NS Immittance: NS ABR: delay of interpeak latency I-III
6	Radwan et al., 2017	EG: 30 children CG: 20 children Age Range: 6 to 17 years (mean: 12.78 years)	PTA, Immittance, ABR and ALLR	PTA: NS Immittance: NS ABR& ALLR: delayed absolute latencies (++)
7.	Felício et al., 2018	Total: 37 Subjects, Age range: Below 8 years	DPOAEs	DPOAEs: Abnormal DPOAEs response in high-frequency bands in T1DM (++)
8	Lasagni et al., 2016	EG: 31 Subjects CG: 10 Subjects Mean age: 33 ± 2.3 years	PTA, DPOAEs and ABR.	PTA: NS (--) DPOAEs: amplitude is reduced (++) ABR: absolute and interpeak latency were delayed(++)

9	Elbarbary et al., 2012	EG: 75 Subjects CG: 33 Subjects Mean age: 14.7 ± 2.6 years	OAEs, Contralateral OAEs and TEN test	OAE: NS TEN test:(++) Contralateral TEOAEs: significantly higher amplitude with noise suppression in T1DM (++)
10.	Schade et al., 2018	EG: 1,150 Subjects CG: 288 Subjects Mean age: 55.4 ± 6.9 years	PTA and high frequency PTA.	HF audiometry: (++)
11.	Rance et al., 2016	EG: 19 children CG: 19 children Mean age: 13.4 years	PTA, DPOAEs, ABR, SRT and APHAB questionnaire	PTA: NS (--) DPOAE: significant lower amplitude in EG (++) ABR: Wave V was significantly delayed (++) SRT: significantly higher (poorer) for T1DM children APHAB: more difficulty in everyday listening and communication than controls (++)

12.	Lisowska et al., 2001	EG: 42 Subjects Mean age: 33 ± 7.7 years CG: 33 Subjects Mean age: 31.7yrs	PTA, Immittance, DPOAEs and ABR.	PTA: NS Immittance: NS ABR: Delayed in interpeak latency of ABR (++) DPOAEs: Reduced mean amplitude in DPOAEs(++)
13	Pudar et al., 2009	EG: 50 subjects Range: 5 to 58 years Mean age: 28.1 years CG: 30 subjects Mean age: 28.9 years	PTA and ABR.	PTA: higher frequency SNHL (++) ABR: delayed in absolute latency and interwave latency (++)
14.	Spankovich et al., 2019	EG: 40 adults CG: 20 adults Age range: 18 to 28 years	PTA and OAEs (TEOAEs, DPOAEs and DPOAE fine structure)	PTA and OAEs: NS (--) DPOAE fine structure: Reduced number of fine structure peaks and components amplitudes in T1DM. (++)

15.	Botelho et al., 2014	EG: 40 adolescents CG: 40 adolescents Age range: 10 to 19 years	PTA and OAEs (TEOAEs and DPOAEs)	PTA and TEOAEs: NS; DPOAEs: The statically significant difference found between two groups DPOAE than other tests (++)
16.	ALDajani et al., 2015	EG: 70 Children CG: 30 Children Age range: 4 to 14 years	PTA, OAEs and ABR.	PTA, OAEs and ABR: NS Except for subclinical involvement of the apical
17.	Barbara Hmar et al. 2020	1,441 participants. Range: 13 to 39 years.	PTA and self-administered hearing questionnaire	PTA: (++) high-frequency SNHL
18.	Spankovich et al.,2017	EG: 20 Subjects CG: 20 Subjects Age range: 18 to 28 years (Mean: 27.25 ± 2.7 years)	OAEs (TEOAEs & DPOAEs), ABR	OAEs & ABR: NS

19	Aljasser et al., 2020	EG: 30 subjects CG: 30 subjects Age range:19 to 35 years (mean: 26.8 years)	ABR,FFR, speech in noise test and SSQ questionnaire.	FFR: significantly reduced in T1DM (++) SIN: worse performance for T1DM (++) SSQ: worse score in T1DM(++)
20.	Dąbrowski et.al.,2011	EG: 31 Subjects Mean age: 29.1 ± 7.1 years CG: 26 Subjects Mean age: 30.3 ± 7.8 years	PTA, TEOAEs and ABR.	PTA: significantly higher at high frequencies (++), TEOAEs: mean amplitude of TEOAE was lower(++), ABR: delayed latency of peak V and interpeak latency (++).

Note: *ABR- auditory brainstem response; ALLR- auditory late-latency response; CLS - contralateral suppression; CG- control group; EG- experimental group; DPOAE-distortion-product otoacoustic emission; TEOAE-transient evoked otoacoustic emission, PTA-pure-tone audiometry; SDS-speech discrimination score; SRS-speech recognition score; Notes: (++), significant effect of type-1 diabetes mellitus; (–-), no significant effect of type-1 diabetes mellitus.*

Table 3:

Summary of vestibular tests and their findings regarding type-1 diabetes mellitus

No	Author/Year	Patients Demographics	Vestibular Test performed	Outcomes (++/- -/NS)
1.	Kamali et.al.,2013	EG: 24 Subjects CG: 24 Subjects Age range:15-40 years	C-VEMP at 500Hz	C-VEMP: mean peak latency of P13 and N23 was statistically significant difference between groups (++)
2.	Gawron et.al., 2002	EG: 95 children Age range: 6 to 28 years. (mean age 15.5 years; CG: 44 children Age range: 6 to 28 years.	PTA, Tympanometry, ABR and Electronystagmography(ENG)	PTA: Reduced threshold in T1DM (++). Tympanometry: A type ABR: prolonged latency of wave I & V (++) ENG: metabolic disturbances present in Type I diabetes (++)
3.	Rance et.al.,2014	EG: 20 subjects CG: 10 subjects	PTA, OAEs , ABR, temporal processing, speech perception measures and VOR gain.	PTA: NS (--) OAEs: NS (--) ABR: Significant delayed latency (++), Temporal processing: delayed in T1DM (++), Speech perception: Lower phoneme discrimination score in T1DM VOR gain: NS (--)

4.	Ribeiro et.al., 2020	EG: 35 Subjects Range: 18 to 71 years Mean Age: 35.37 ± 10.98year CG: 100 Subject	Video Head Impulse Test (v-HIT)	v-HIT; Statically difference gain found in posterior and left anterior canal found between two group(++)
5	Klagenberg et.al.,2007	Total: 30 Subjects Age range: 7-56 years	PTA, Immittance and VNG	PTA: (++) Immittance: NS (--) VNG: (++)
6	Rigon et.al., 2007	EG: 19 Subjects CG: 19 Subjects Age range: 8-25 years	ENG evaluation.	ENG: showed impairment in 47.36% T1DM (++)
7	Mohammad et.al.,2018	EG: 65 children Mean age: 10.3 ± 1.7 years CG: 130 children Mean age: 9.8 ± 1.5 years	PTA, DPOAEs, ABR, Bedside HIT, dynamic visual acuity test.	PTA: poorer AC threshold (++) ABR: prolonged peak latency of wave V (++), DPOAEs: significant difference in T1DM (++), Vestibular tests: NS (--).

Note: *Amp, amplitude; AR, asymmetry ratio; c-VEMP, Cervical vestibular-evoked myogenic potential; o-VEMP, ocular vestibular-evoked myogenic potential; CG, control group; EG, experimental group; VEMP, vestibular-evoked myogenic potential; vHIT, video head impulse test, ENG-Electronystagmography test. Notes: (++), significant effect of type-1 diabetes mellitus; (–), no significant effect of type-1 diabetes mellitus.*

4.3 Audiological Evaluation in Type-1 Diabetes Mellitus

The present literature review reported 27 studies that explored the audio-vestibular system's involvement in individuals with T1DM. Tables 2 and 3 summarised the studies that dealt with audio-vestibular assessment and its finding. The audiological assessment includes pure tone audiometry, Immittance evaluation, otoacoustic emission (TEOAEs & DPOAEs), auditory brainstem response (ABR), and auditory late latency response (ALLR), and frequency following response(FFR).

4.3.1 Behavioural test and self-reported questionnaire used in type 1 Diabetes mellitus

A study by Schade and his colleague reported high frequency SNHL among T1 DM compared to non-diabetic individuals. The correlation analysis showed a 10% increase in the time-weighted mean HbA1c, whereas a 32% and 19% increase in speech and high-frequency hearing impairment (Schade et al., 2018). Most of the studies reported the similar finding using pure tone audiometry in T1 DM (Barbara Hmar et al., 2020; Celik et al., 1996; Dąbrowski et al., 2011; Gawron et al.; 2002; Klagenberg et al., 2007; Malucelli et al., 2012; Mohammad et al. 2018; Pudar et al., 2009). A study reported using the Abbreviated Profile of Hearing Aid Benefit (APHAB) and Speech, Spatial and Qualities of Hearing Scale (SSQ) questionnaire, which assesses the patient's ability in different listening situations. To ascertain whether the hypothesised effects of type 1 DM on auditory function appear in real-world listening conditions, type 1 DM individuals' subjective experiences of hearing disability was evaluated using a self-report auditory disability test. According to Rance et al. (2016), school-age children with T1DM reported much more difficulty than age- and sex-matched controls, particularly in noisy or reverberant situations like classrooms and playgrounds.

Additionally, they discovered that T1 DM children had much greater (poorer) speech reception thresholds. A study by Aljasser et.al (2020) reported a significant difference in spatial subscales and overall scores on SSQ in type 1 DM compared to non-diabetic individuals.

4.3.2 Otoacoustic Emissions (TEOAE/DPOAE) in type 1 Diabetes Mellitus

A study by Dabrowski et al. (2011) reported a reduction in the mean TEOAE amplitude in type 1 DM compared to non-diabetic individuals. Another study in T1DM by using DPOAEs fine structure revealed that reduced number of fine structure peaks and component amplitudes with the primary difference in the reflection component. The above finding suggests early cochlear pathology identification in T1 DM (Aljasser et al., 2020; Spankovich et al., 2017). Elbarbary et al., 2012, through Contralateral suppression, OAEs showed significantly higher amplitude with noise suppression which probably indicates poor functioning of the efferent pathway in T1 DM. Another study found reduced mean amplitude in DPOAEs in T1 DM (Lisowska et al., 2001). Braite and colleagues reported significant differences in the activation of the MOC reflex between the groups with and without T1 DM. Their findings probably suggested the presence of early auditory dysfunction of the efferent pathway in patients with T1DM (Braite et al.,2019).

4.3.3 Auditory brainstem responses (ABR) & frequency following response (FFR) in Diabetes Mellitus

A study by Dabrowski and his colleagues (2011) reported that wave V latency and wave I-V inter-amplitude latency were longer compared to healthy participants. Another study related to ABR in children with type I DM children reported delay in ABR wave latencies in comparison to the typically developing children which probably

indicates an abnormality in the neural conduction in patients (Radwan et al., 2017). Aljasser and his colleague's study on despite the absence of an increase in the audiometric threshold, FFR in T1DM found a connection with worse neural temporal coding in the brainstem. They stated that before any anomalies can be found using conventional clinical diagnostics, FFR may offer an early sign of brain damage in T1DM (Aljasser et al., 2020). Study done by Lasagni et al (2016) reported similar finding. In another study done by Rance et al (2014), in which they performed the test i.e. temporal processing and speech perception measures to identify the temporal processing deficit in T1DM and reported abnormal rapid amplitude modulation and difficult to be perceived by the clinical group. While there was no significant difference between the groups for detection thresholds for low-rate stimuli (10 Hz), the TIDM group had significantly higher (worse) thresholds for high-rate stimuli (150 Hz)). This pattern suggests a problem in encoding rapid signal changes and suggests a temporal processing impairment in T1 DM. A Study done by Aljaser and his colleagues performed tests of speech perception in noisy environments and behavioural tests of temporal coding (inter-aural phase difference discrimination and the frequency difference limen) revealed that the T1DM group had considerably lower FFRs to both temporal envelope and temporal fine structure.

4.4 Vestibular Evaluation in type I Diabetes Mellitus

Parts or all of the vestibular structures may be involved in the process by which DM impairs vestibular function. The microangiopathic consequences, which include ischemia of the vestibular structures, changes in the metabolism of the inner ear fluid, and loss of Type-I hair cells in the saccule, are the main causes of vestibular dysfunction in T1DM. Table 3 summarizes the T1DM studies that deal with vestibular evaluations.

4.4.1 Vestibular-evoked myogenic Potential (VEMP) in type I Diabetes Mellitus

Hearing loss has been linked to type I diabetes mellitus, with proposed causes including micro-vascular illness, auditory neuropathy, and oxidative stress. Patients with diabetes mellitus frequently experience dizziness, tinnitus, and hearing loss. In a study by Kamali et al reported that the c-VEMP mean latency of P13 and N23 is statistically significant between the groups i.e. T1 DM and Control group. Another study done on VEMP by Gawron and his colleague (2013) reported that the metabolic disturbances found in type 1 DM cause disturbances in the peripheral vestibular structures, but mainly in the central structures, as shown by impaired optokinetic responses observed in 36/95 (37.89%) diabetic participants, spontaneous nystagmus in 10/95 (10.53%) individuals and the presence of positional nystagmus in 21/95 (22.11%) individuals. When comparing cVEMP results of participants with type 1 DM with healthy controls, the cVEMP responses of individuals with type 1 DM were more affected than healthy participants (Kamali et al., 2013). No correlation was found between cVEMP responses and GHbA1c levels and the average blood glucose concentration over three months. Additionally, there were no differences in the absolute and relative amplitudes of the VEMP responses between the experimental and control group (Kamali et al., 2013).

4.4.2 Video head impulse test (vHIT) in type I Diabetes Mellitus

Following a review of the literature on vHIT, which includes evaluating each semi-circular canal (RALP, LARP & Lateral planes) in different planes to assess 100 healthy children with normal peripheral hearing, and a control group, which consisted of 35 children with type I DM. They concluded that individuals with type 1 diabetes mellitus had lower gains in the left anterior canal and posterior semi-circular canals compared to non-diabetics. In the group with DM, velocity displayed a significant

difference in the left lateral, anterior right, and left posterior canals; however, velocity was unrelated to the gain in the semi-circular canals (Ribeiro, Morganti, & Mancini, 2019).

4.4.3 Videonystagmography (VNG) in type I Diabetes Mellitus

There are studies related to VNG, which assess and record eye movement, which helps in the nystagmus direction & its intensity. Klagenberg and colleagues (2007) performed video electronystagmography tests (VNG), including spontaneous nystagmus test, positional nystagmus test, pendular tracking test, optokinetic test nystagmus test, pre-and post-rotary nystagmus with the pendular swing rotary test, and investigation of pre- and post-caloric nystagmus. All the test results were within normal limits except for the caloric result of these individuals, 13/30 (43%) who did not report feelings of dizziness. Another study on 95 children who performed a VNG test found that the metabolic disturbances in T1 DM showed disturbance in different parts of the vestibular organ but mostly in its central parts than the peripheral (Gawron et al., 2002). A Study was done on 96 adolescents and a test was performed on VNG, and they found that the vestibular system showed impairment in VNG in 47.36% of individuals with diabetes mellitus type 1 (Rigon et al., 2007). Another study by Gawron et al (2002) performed VNG test and found the metabolic disturbance present in Type I diabetes causes disturbance in the central part of the auditory nervous system.

Chapter 5

Discussion

The present systematic review aimed to study the effect of type 1 Diabetes mellitus on auditory-vestibular function and determine their quality of life. The findings showed that compared to non-diabetics, T1DM does have impact on both qualities of life and auditory-vestibular functioning. This chapter will mention the possible reason as explained in literature.

5.1 Effect of Type-1 Diabetes Mellitus on auditory function

Study reported mixed finding in terms of association between type 1 DM and hearing impairment. The prevalence of hearing loss is reported to be higher in T1 DM. These higher percentages of hearing impairment in T1 DM were reported based on the finding of pure tone audiometry, extended high frequency audiometry, otoacoustic emissions, auditory brainstem responses, and auditory late latency responses. Few studies do report no noticeable difference between T1DM and the control group when using conventional pure tone audiometry (Abd El Dayem et al., 2014; Osterhammel & Christau, 2009). Whereas high frequency audiometry showed poorer (reduced) thresholds in high frequency in T1 DM individuals (Abd El Dayem et al., 2014; Ferrer et al., 1991; Kurien et al., 1989). The difference in conventional and extended high-frequency audiometry results reflects early indication of the damage of the outer hair cells in high frequency region (basal turn of the cochlea) in T1 DM individuals and same could be traceable through HF audiometry. The basal turn is tuned for the coding of HF sounds.

Otoacoustic emission which is one of the non-invasive procedure help in assessing the functioning of the outer hair cells and reported to be affected in the

individuals with T1 DM. The TEOAE amplitude, fine structure of DPOAE peaks and amplitude is reported to be poorer (reduced) in individuals with T1DM. The possible reason for lower (poorer) TEOAE amplitude could be because of cochlear microvasculature damage in T1 DM individuals and leads to outer hair cell malfunction or loss (Ottaviani et al., 2002). The considerable variation in fine structure of DPOAE amplitude and peak could be due to lower linear reflection in T1 DM because the degree of linear reflection affects the fine structural peaks (Spankovich et al., 2019). They also reported reduced amplitude of fine structure of DPOAE at lower stimulus levels while maintaining the better amplitude at higher stimulus levels which indicated the possible loss of cochlear non-linearity among individuals with type 1 Diabetes mellitus. Further, type 1 DM might cause a metabolic disruption in the cochlea, perhaps due to cochlear micro-angiopathy, decreasing the driving force and gain of the cochlear amplifier could be another possible reason for reduced stimulus frequency OAEs, low-level TEOAE, and low-level DPOAE fine structure. Study reported absence of contralateral suppression of TEOAE among T1DM which reflects poor functioning of the efferent pathway in individuals with T1DM. They also reported MOC reflex abnormalities at high frequencies. It could be because of variations in the location of auditory nerve fibres, which demonstrate that the activation of the MOC fibers differ between the apical and basal areas, changes in the basal region where the high frequencies are located (Braite et al., 2019; Jr. et al., 2005). Another possible reason reported in the literature is vascularization, which is severely harmed by insufficient insulin distribution and first gets manifest in the basal area (Braite et al., 2019).

Auditory brainstem responses help in assessing the functioning of the auditory nerve and study reported in general prolonged (poor) latencies among individuals with T1DM. The latencies provide information on the velocity at which electrical sound

impulses travel through different sections of the auditory brainstem. The prolongation of these latencies would indicate that diabetes causes a delay in the conduction of auditory impulses in the brainstem. The other possible reason could the neuronal involvement among diabetic individuals (Pessin et al., 2008). Therefore, it is not surprising that the diabetes condition would cause significant alterations in the neural functioning at the level of the brainstem. Early research indicated that the vasa nervorum of the seventh and eighth cranial nerves showed change in the T1 DM individuals. Further, hyperglycemia resulted in significant neuronal injury and microglial activation in the frontal cortex and hippocampus among diabetic individuals. The further consequence of the same leads to the central nervous system impairment, demyelination of ganglion cells, numerous infarctions in neural tissue, thickening of the vasa nervosa of the acoustic nerve, and deterioration of the myelin sheath's electro-conductive qualities (auditory neuropathy) among diabetic individuals (Rance et al., 2016). Therefore, it is well supported from the studies the micro-structural changes due to T1 DM (hyperglycemia) in the functioning of the auditory nerve at the level of brainstem.

The pathophysiology among diabetic individuals and diabetic neuropathy is also explained by oxidative stress (Giacco et.al;2010). High glucose levels cause the mitochondria's inner membrane to malfunction, which results in the production of free radicals. It ultimately causes an excess generation of reactive oxygen species, which causes the death of neuronal cells. Therefore, this can also be one of the reasons for reduced (poor) ABR responses. These findings are well supported by other studies (Shatdal et al.,2018 and Ranee et al.2013). However, few studies are not in concensus with the above finding (Takkar et al.,2005; Fedele et al.,2012; Di Leo et al.2007; and Klagenberg et al., 2007). They reported alike performance between healthy individuals

and T1DM using auditory brainstem responses (Rasdwaan et al., 2016). The auditory pathway at the higher centres are more complex and challenging which showed differences only when there are demanding task/tokens instead of simple task. This may be further explaining significance of assessing higher centres in individuals with T1DM instead only dependent on basic and simple audiological evaluation. Similar explanation also holds good for the finding of the auditory late latency responses i.e. demyelization and degeneration of ganglion cells, and nerve fibres have reached the brainstem and cerebrum. Several authors reported that microangiopathy of the vasa nervosum, which results in demyelination of the neural trunk causes damage to the neural tissue in T1DM individuals. Diabetic neuropathy results from alteration in the electrophysiological properties of myelin sheath due to various metabolic disturbances also induced among diabetic individuals. The pathological changes in the myelin sheath, whether quantitative or qualitative or both, induce the alteration in normal and synchronic neural conduction processes, which results in the slowing of conduction velocity along with affected nerves that leads of delayed latencies of cortical potential. Hence, overall study showed evidences and deleterious effect of type 1 Diabetes mellitus in children and adults on the auditory system functioning.

5.2 Effect of type 1 Diabetes Mellitus on Vestibular functioning

Vestibular functioning is assessed using several behavioral and electrophysiological measures and reported to be affected among individuals with T1 DM. The vestibular assessment showed effect of T1DM on both central and peripheral vestibular systems. One of the study reported the possible cause of the peripheral vestibular disorders due to micro-angiopathy, which changes the metabolism of inner ear fluid and results in labyrinthine dysfunction by causing ischemia of the vestibular system (Kalkan et al., 2018). Specifically, in those with type 1 diabetes mellitus, the

extent of vestibular end-organ damage appears to be influenced mainly by the frequency and kind of hypoglycemia events (Gawron et al., 2002). Another factor which can also influence the damage to the vestibular system are the duration of the disease and blood glucose controls may also contribute to type 1 DM's vestibular end-organ dysfunction (Gawron et al., 2002). The production of cellular ATP and the proper operation of the potassium and sodium pumps depend on glucose. As a result, metabolic alterations that influence glucose metabolism may result in less energy production. Due to this, the ion concentration in the supply endolymph and perilymph is altered, resulting in a modification of the altered electric potentials that cause vertigo. The reduced glucose production will also have influence on the functioning of Stria vascularis and since Stria vascularis has a very high metabolic rate, requiring continual expenditure to keep potassium and sodium concentrations in the endolymph at their ideal levels, any alteration in this ionic imbalances leads to alter the functioning of the vestibular system. The production of cellular ATP and the correct operation of the potassium and sodium pumps depend on glucose. As a result, metabolic alterations that impact glucose metabolism can lower energy levels, and changing electric potentials might cause dizziness. The reason for vestibular damage in the central system is that T1DM is a chronic metabolic condition that exposes people to risk for vascular disease. Chronic hyperglycemia damages tissue using advanced glycation end products and oxidative stress mechanisms. Additionally, the toxic damage to connective tissue causes demyelination of the nerves, thickening of the arterial walls, and macro- and microangiopathies. Study by Kocdor et al (2016) found selective reduction in type I vestibular hair cells (sensory epithelia) among diabetic individuals. In one of the animal based study, Myers and colleagues reported large disrupted portions of myelin sheath lamellae of the vestibular and auditory nerves in induced diabetic rats. They also found

thinning of the myelin sheath and smaller axonal fibers' diameters, indicating oxidative stress injury and altered inner ear fluid metabolism. Hence, overall most of the studies reported the effect of type 1 Diabetes mellitus on the delicate vestibular structure. Therefore, early identification and prevention can help preserving the functioning of the audio-vestibular system and protect for the damage due to Type 1 Diabetes mellitus.

Chapter 6

Summary and Conclusion

The present study aimed to review the impact due to type I diabetes mellitus and its influence on audio-vestibular functioning. The present study also aimed to highlight the possible reason for damage to the auditory and vestibular function secondary to type I diabetes mellitus. The audio-vestibular tests which include PTA, OAE, ABR, ALLR, FFR, VNG, V-HIT and VEMP test most often help the professionals in assessing the functioning of the auditory and vestibular systems in individuals with type I DM.

Due to the mixed finding reported in the literature, there is still debate and deliberation over the location of the lesion in T1DM-related auditory and vestibular impairment. Several studies have reported subtle and functional audio-vestibular impairment due to type 1 DM. They have proposed causes such as interference with nutrient transportation due to thickening in the basilar membrane vessels, oxidative stress, that is, the excessive production of reactive oxygen species from electron leakage in the mitochondria caused by the hyperglycemic state which results in neuronal cell death atrophy of spiral ganglion neurons, demyelination of the AN, and the loss of outgrowth of neurons. Through various measurements of the audio-vestibular test as mentioned above, they concluded that there is some alteration in the auditory and vestibular system function that leads to the change in the structural and functional ability of the inner ear, as reflected in the different test results. It may be possible to detect temporal processing impairments in T1DM patients using a more complex stimulus to test the auditory brainstem response such as complex ABR instead of the click-evoked ABR. Despite the fact that these results suggest that the FFR may have significant potential as a diagnostic test to identify auditory nerve functioning and brainstem neural impairment in individuals with T1 DM. Similarly, various vestibular tests such as VNG, vHIT, and

cVEMP have shown vestibular impairment due to type 1 DM. Therefore, based on the present systematic review, it is recommended to implement audio-vestibular assessment among individuals with type 1 DM.

Implication of the study

- Present systematic review throw light on awareness about impact of type 1 DM on audio-vestibular system.
- present review also helps in understanding the possible options for the prevention of the influence of diabetes mellitus type I on auditory-vestibular function.

Future Direction

- Type I diabetes mellitus can affect the audio-vestibular system of children and adults without evident sign and symptoms related to audio-vestibular system and hence regular follow-up is recommended.
- There are several factors (duration of diabetes, type of diabetes, blood sugar level, & cognition ability) which is directly or indirectly influencing the effect on audio-vestibular system due to type 1 DM can be explored.

Chapter 7

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