

Review articles

Association between diabetes and vestibular dysfunction: an integrative review

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ABSTRACT

Purpose: to identify, in the literature, the factors associated with the development of vestibular dysfunctions in individuals with type 2 diabetes mellitus (DM2).

Methods: an integrative review of the literature, whose survey was conducted in the databases ISI, SciELO, LILACS and PubMed, using the following descriptors: “type 2 diabetes mellitus”, “vertigo”, “dizziness”, and “vestibular diseases”. Articles published in the last 10 years that answered the research question (“What factors are associated with the development of vestibular disorders in individuals with DM2?”) were included in the study.

Results: the search returned 426 articles, 10 of which met the eligibility criteria. Most of the participants of the selected studies who had vestibular dysfunctions were women over 40 years old and had more than one comorbidity related to DM2, the main one being the systemic arterial hypertension (SAH). According to the literature, the physiology of the inner ear allows small glucose alterations to influence its normal functioning, which makes diabetic individuals more susceptible to developing vestibular dysfunctions.

Conclusion: according to this study, DM2 can trigger or contribute to the manifestation of vestibular dysfunction, whose main associated factors are advanced age, female gender, and various comorbidities, as dyslipidemia, SAH and metabolic syndrome.

Keywords: Dizziness; Vertigo; Diabetes Mellitus; Labyrinth Diseases

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INTRODUCTION

Diabetes mellitus is one of the most prevalent chronic diseases in the population worldwide, with Brazil as the fourth country most affected by it. According to the International Diabetes Federation, in 2017 approximately 425 million people were diagnosed with diabetes, and it is believed that until 2045 there will be about 629 million diabetics in the world¹.

Type 2 diabetes mellitus (DM2) corresponds to 90% of the cases and occurs more frequently in obese people over 40 years old. It is characterized as a heterogeneous syndrome resulting from the deficiency in insulin secretion or the interference in its function, and its most common clinical manifestation is chronic hyperglycemia². The cause of DM2 has not been fully clarified yet; however, some factors can increase the possibility that an individual will develop the disease, such as environmental, genetic and behavioral factors. It is estimated that 80% of the people with DM2 are overweight and do not practice physical exercise³.

The presence of DM2 has been increasingly significant in the field of otoneurology due to its high prevalence in patients with labyrinth diseases. Among the most recurrent symptoms in these patients, there is dizziness, which has been described as a new complication of diabetes, besides being a potentializing risk factor for falls^{4,5}. Dizziness is characterized as the symptom of disturbed or impaired spatial orientation⁶. Middle-aged and older adults with DM2 who had dysfunctions in other organs and systems, as cardiovascular alterations, peripheral neuropathies, and vestibular symptoms, also present a greater risk of postural imbalance, making them more fragile and vulnerable to falls⁷⁻⁹.

The presence of peripheral neuropathies constitutes an important risk factor for falls in diabetic individuals. Diabetic neuropathy originates in microvascular complications that affect the peripheral sensory and motor nerves, and its prevalence is higher than 50% in patients diagnosed with the disease^{9,10}.

Peripheral vestibular alterations are strongly influenced by insulin and glycemic levels circulating in the blood. The higher these levels, the greater is the patient's susceptibility in developing dysfunction of vestibular origin, as benign paroxysmal positional vertigo (BPPV), endolymphatic hydrops, and Ménière's disease^{8,9}.

The analysis of vestibular dysfunctions must consider all the clinical variables that can be altered, making it necessary to understand the association of

dizziness-triggering alterations in multiple organs and systems, in order to properly approach the diabetic patient. New clarifications about the existing associations between DM2 and vestibular alterations are needed. Such elucidations will contribute to a more effective clinical approach, favoring this population from prevention to intervention. Thus, this study aimed at identifying, in the literature, the factors associated with the development of vestibular dysfunctions in individuals presented with DM2.

METHODS

This is an integrative literature review, conducted in six different stages, namely: identification of the theme; definition of the research question; establishment of the study's inclusion and exclusion criteria; definition of the information to be extracted from the studies selected, and categorization of the studies; evaluation of the studies included in the integrative review; interpretation of the results and presentation of the review/synthesis of knowledge. The survey took place from July to August 2019.

The research was guided by the following question: What factors are associated with the development of vestibular dysfunctions in individuals with DM2? The articles were surveyed in the ISI Web of Science, SciELO, LILACS and PubMed databases, with the following terms: "type 2 diabetes mellitus", "vertigo", "dizziness", and "vestibular diseases", according to the Health Sciences Descriptors (DeCS), in these combinations: "type 2 diabetes mellitus AND vertigo", "type 2 diabetes mellitus AND dizziness", "type 2 diabetes mellitus AND vestibular diseases".

The inclusion criteria adopted for the research were: primary data, cross-sectional articles, published between 2009 and the first semester of 2019, in either English, Portuguese or Spanish. Articles describing type 1 diabetes mellitus or central vestibular dysfunctions, as well as editorials, theoretical reflections, all sorts of reviews, experience reports, dissertations, monographs, theses, and abstracts in annals of events were excluded from the research.

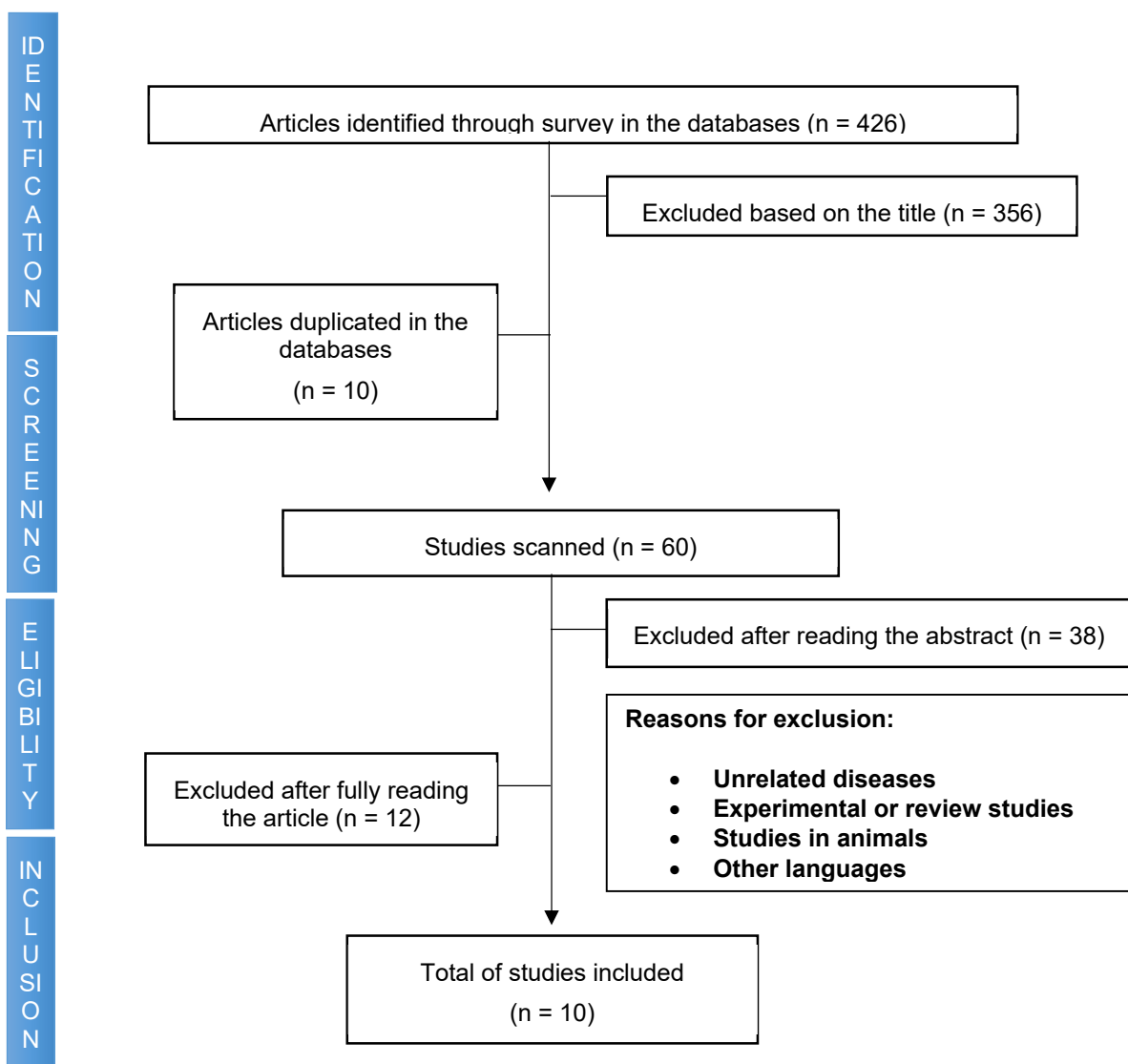
All the papers were analyzed and classified according to the levels of evidence employed by ASHA¹¹ in 2004, adapted from the Scottish Intercollegiate Guideline. The studies were analyzed based on eight scientific study quality indicators, namely: Well-designed meta-analysis of more than one randomized controlled trial (Ia); well-designed randomized controlled study (IIa); well-designed nonrandomized controlled study (Ib);

well-designed quasi-experimental study (IIb); well-designed nonexperimental study (III); report from a specialized committee, consensus conference, clinical experience of respected authorities (IV).

LITERATURE REVIEW

As the databases were surveyed, 426 articles related to the theme were identified (Figure 1). Of these, 356 were excluded based on their title or because they did not answer the research problem in question; 42, after

the abstracts had been read; 7, because they were repeated in the databases; and 12, after the articles had been fully read. The sample was thus composed of 10 articles. The prevailing language was English, followed by Spanish. No studies in Portuguese were identified. The studies included in the research were described in Table 1, by author/year of publication, objectives of the study, number of the sample, and main results. The otoneurological dysfunctions presented in the selected studies and the comorbidities associated with DM2 were described in Table 2.



Source: the author.
Legend: n = number of articles.

Figure 1. Flowchart of the selection of articles in the databases.

Table 1. Listing of the papers analyzed

Authors/Year	Methodological Design	Purpose	Sample	Main Results	Level of Evidence (ASHA, 2004)
Chávez-Delgado et al., 2012 ¹²	Cross-sectional study	To determine the type and degree of cochleovestibular dysfunction in patients with DM2, SAH and dyslipidemia with auditory and/or vestibular symptoms.	385	Age, duration, and extent of polygenic inheritance contribute to the occurrence of cochleovestibular dysfunction.	III
Yamanaka et al., 2013 ¹³	Case-control study	To determine the prevalence of metabolic syndrome and the clinical characteristics associated with metabolic syndrome and vertigo.	333	Metabolic syndrome occurred more frequently in males. Moreover, among the vestibulopathies analyzed, the most recurrent in men was the vertebral-basilar insufficiency. Thus, metabolic syndrome can be associated with the occurrence of vertigo in men.	IIb
D'Silva et al., 2015 ¹⁴	Retrospective study	To examine the relationship between diabetes and BPPV along with known variables, as age, gender, and hypertension.	3933	The study demonstrates that SAH is the mediating factor that contributes to the increase in BPPV prevalence in diabetic individuals.	III
Ward et al., 2015 ¹⁵	Prospective study	To evaluate the degree of association between diabetes and otoconial dysfunctions. To evaluate the association of microvascular complications with the presence of vestibular dysfunction in older adults with diabetes.	50	The adults with DM2 presented worse performances in the vestibular function test regarding the function of the semicircular canals and the otoconia in comparison with the non-diabetic group, causing various vestibular complications.	IIb
Albernaz, 2016 ¹⁶	Retrospective study	To describe the symptoms of the inner ear metabolic disorders, as well as the examinations necessary to establish diagnoses.	376	Due to the physiology of the inner ear, the auditory and vestibular symptoms usually occur before other manifestations of metabolic alterations, potentially favoring an early diagnosis of hyperinsulinemia, intestinal sugar malabsorption, or diabetes.	III
D'Silva et al., 2017 ¹⁷	Cross-sectional study	To analyze the otolith function in people with diabetes and concomitant BPPV; and, examine the relationships between the VEMP variables and the diabetes-related variables.	77	Both individuals with BPPV and those with diabetes presented otolith dysfunction, indicating that BPPV and DM can independently affect the utricular function.	III
Jáuregui-Renaud et al., 2017 ¹⁸	Cross-sectional study	To evaluate the function of the utricle and horizontal semicircular canals in patients with DM2, with/without a history of falls, who received primary care.	101	Patients with DM2 that did not seek care due to sensorial or balance decline presented impaired utricular function, even in the absence of semicircular canal dysfunction or history of falls. In addition, the occurrence of falls may not be independently related to the vestibular function.	III
D'Silva et al., 2017 ¹⁹	Case-control study	To examine postural oscillation in people with DM2 who present untreated symptomatic BPPV.	52	Individuals with BPPV, with and without DM2, presented greater postural oscillation when standing with eyes closed and standing in comparison with people with DM and healthy people. The presence of peripheral neuropathy was also described as contributing to postural instability.	IIb
Bepari et al., 2018 ²⁰	Case-control study	To compare the prevalence and the association of metabolic disorders in cases of vertigo with a control group.	110	The individuals with vertigo presented high thyroid and circulating lipids levels. Such factors indicate the importance of dietary control and hormonal therapy in vertiginous patients.	IIb
Naik e Tilloo, 2019 ²¹	Cross-sectional study	To evaluate and find the proportion of patients with DM2 with sensorineural hearing loss and vestibular dysfunction, as well as the association with glycemic control.	100	There is a significant association between DM2, auditory sensorial loss, and vestibular dysfunction, especially with the aggravation of the glycemic control. Controlling diabetes would avoid the complications associated with the vestibular system, ensuring these patients a better lifestyle.	IIb

Source: the author.

Legend: DM2 (type 2 diabetes mellitus); BPPV (benign paroxysmal positional vertigo)

Table 2. Description of the otoneurological dysfunctions presented in the studies selected and the comorbidities associated with DM2.

Authors/Year	Vestibular Dysfunction	Comorbidities
Chávez-Delgado et al., 2012 ¹²	Cochleovestibular dysfunction	SAH, dyslipidemia, overweight, sedentarism, smoking
Yamanaka et al., 2013 ¹³	Ménière's disease, BPPV, and vertebral-basilar insufficiency	MS
D'Silva et al., 2015 ¹⁴	BPPV and Ménière's disease	SAH
Ward et al., 2015 ¹⁵	Utricular dysfunction	Neuropathy and retinopathy
Albernaz, 2016 ¹⁶	Vestibular and cochlear dysfunctions	Hypoglycemia and hyperglycemia
D'Silva et al., 2017 ¹⁷	BPPV	SAH and peripheral neuropathy
Jáuregui-Renaud et al., 2017 ¹⁸	Dizziness and vertigo	peripheral neuropathy, retinopathy, and SAH
D'Silva et al., 2017 ¹⁹	BPPV	Obesity and peripheral neuropathy
Bepari et al., 2018 ²⁰	Dizziness	High LDL and thyroid-stimulating hormone levels associated with MS
Naik e Tiloo, 2019 ²¹	BPPV and unilateral vestibular dysfunction	Sensorineural hearing loss and uncontrolled hyperglycemia

Source: the author.

Legend: DM2 (type 2 diabetes mellitus); BPPV (benign paroxysmal positional vertigo); SAH (systemic arterial hypertension), LDL (low-density lipids); MS (metabolic syndrome)

All the articles included in the study presented a mean age of over 40 years. Such a result agrees with the literature, which describes the prevalence of DM2 after 40 years old². The females were prevalent in nine of the ten articles included. The high prevalence of females can be attributed both to hormonal cycle variations and women seeking health services more often. Moreover, individuals with DM2 presenting vestibular dysfunctions had more than one clinical alteration associated with it, of which the main ones are systemic arterial hypertension (SAH), metabolic syndrome (MS), retinopathy, and peripheral neuropathy^{12,14,15,19}. In two studies analyzed^{13,19}, the levels of dizziness and the number of clinical alterations were directly proportional to age.

Four other studies^{12,14,15,18} identified SAH as one of the risk factors for the development of vestibular dysfunction associated with DM2, of which BPPV is the main one. The vascular effects of SAH and diabetes can lead to tissue hypoxia and cochleovestibular degeneration, causing increased stiffness of the arterial walls. Increased arterial pressure compromises capillary blood flow and, consequently, the transportation of oxygen. Thus, nutrients are not sufficiently furnished to the inner ear structures^{15,22,23}.

The influence of the MS on the vestibular system as a factor associated with irreversible cochleovestibular deterioration was investigated in three studies^{12,13,20}. The term MS refers to a set of risk factors that increase

the possibility of a person developing cerebrovascular diseases and diabetes. Diabetes is associated with microvascular modifications, leading to alterations in inner ear blood flow, with symptoms of disturbance of body balance. The occurrence of hyperglycemia generates an increase in inflammatory mediators and protein glycation, causing these to be functionally inactive, in addition to auto-oxidation of glucose particles, leading to the formation of free radicals; these cause the destruction and dysfunction of cells, as the pancreatic β -cells, which produce insulin. This connection between the inflammation and physiopathology of the inner ear vessels interfere with the local blood flow. Due to the lack of collateral circulation, any type of local arterial occlusion can cause an ischemic event, which brings about vestibular dysfunctions in the patient^{13,24}.

Bepari et al.²⁰, when evaluating the hemograms of a group of diabetic patients, identified high values of thyroid-stimulating hormone (T3, T4 and TG), besides the increase in low-density lipids (LDL). The increase in serum cholesterol is one of the risk factors for the development of atherosclerosis, which also has a role in the vestibulocochlear vessels, especially in individuals over 40 years old. Hence, the importance of multidisciplinary clinical follow-up is highlighted, including hormonal and dietary therapy²⁰.

Six articles report on the influence of hyperglycemia on the functioning of the vestibular system^{13,15-18,21}.

Endolymphatic hydrops was prevalent in 45% of the individuals with MS associated with dyslipidemia. The inner ears are very sensitive organs and are often the first ones to present signs of disorder in metabolism. Since glucose is one of the most efficient substrates for the maintenance of the endolymphatic potential, its excess generates a hydro-electrolytic imbalance that directly affects the transportation of sodium and potassium ions. Ionic imbalance displaces potassium from the endolymph to the perilymph, and sodium in the opposite direction, causing an accumulation of water in the internal compartments. Such alteration leads to what is called endolymphatic hydrops^{16,25}. Hypoglycemia can also be associated with dizziness, as described in a study¹⁶. The inner ear physiology requires sharp metabolic activity. Glucose unavailability, as occurs in hypoglycemia, causes functional modifications in the inner ear, resulting in symptoms of vestibular disturbance.

The individuals with diabetes are prone to developing complications, as peripheral neuropathy and retinopathy, which are associated with increased risk of falls²⁶⁻²⁸. This fact can be explained by the excessive production of free radicals in the neural cells and structures resulting from the high levels of circulating glycemia, which brings about diminished fibrinolytic activity and membrane repolarization. These alterations cause irreversible damage to the protein constitution of the myelin sheath, responsible for the demyelination of the peripheral nerves, leading to the development of neuropathies and retinopathies. Since the static and dynamic balance results from the harmonic interaction between the visual, somatosensorial, musculoskeletal and vestibular systems, the microvascular complications in these systems interfere with the adjustments necessary to maintain body balance. Falls stand out among the main concerns related to imbalance, due to their great influence on the affected individual's general health^{9,28,29}.

BPPV was the most recurrent vestibular dysfunction in the studies analyzed^{13,14,17,19} and it has been more frequently described in diabetic individuals. These results support the hypothesis of a vascular role in the etiopathogenesis and recurrence of BPPV^{14,17}, which results from an abnormal stimulus of the cupula of any semicircular canal when the head position is changed. The movement of the otoconia in the macula inside the semicircular canals abnormally stimulates the cupula, generating nervous impulses^{30,31}. DM2 is associated with the vascular damages in the inner ear, possible

labyrinthine ischemia, favoring otoconial detachment, leading to the occurrence of BPPV. The affection of other vascular diseases, as SAH and hyperlipidemia, causes a further reduction or total interruption of local blood flow^{12,30}.

Five of the articles selected in this study were classified as level of evidence III, and five, as level of evidence IIb, according to ASHA¹¹. The design of the papers found was considered of medium and low scientific evidence, although it should be considered that nonexperimental studies also have great relevance to better understand a specific theme. In most of the studies included, the participants presented other diseases associated with DM2, which makes it even more difficult to outline the repercussions of diabetes on the vestibular system, as different metabolic and vascular disorders, either associated or not, are causal agents. Medications, hormonal dysfunctions, inadequate eating habits, life habits, sedentarism and stress can equally aggravate or trigger labyrinthopathies^{31,32}. Further long-term follow-up studies of individuals with DM2 presenting vestibular repercussions are made necessary in order to better outline the complications resulting from diabetes mellitus. Furthermore, it is of utmost importance that each patient be periodically and multidisciplinary followed up, for their general health and quality of life to be improved.

CONCLUSION

This study shows that DM2 can trigger a vestibular dysfunction or contribute to its manifestation. In the literature, advanced age, female gender, and comorbidities such as dyslipidemia, systemic arterial hypertension, and metabolic syndrome were identified as the main factors associated with the development of vestibulopathies in type 2 diabetic patients.

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