

Contents lists available at ScienceDirect

Annals of Medicine and Surgery



journal homepage: www.elsevier.com/locate/amsu

Cross-sectional Study

Prevalence of Ménière's Disease in Syrian Patients with hypothyroidism: Cross-sectional study

Anan Bakdounes^{a,1}, Nawal Akashe^{a,1}, Mhd Obai Alchallah^a, Homam Alolabi^a, Duaa Bakdounes^a, Fatema Mohsen^{a,*}, Louei Darjazini Nahas^b

^a Faculty of Medicine, Syrian Private University, Damascus, Syria

^b Department of Surgery Division of Otorhinolaryngology, Faculty of Medicine, Syrian Private University, Damascus, Syria

ARTICLE INFO

Keywords: Autoimmunity Endolvmph Endocrine disorder Labyrinth War

ABSTRACT

Background: Ménière's Disease, a long-term debilitating disorder has been increasingly found among patients with hypothyroidism. Our study aims to evaluate the prevalence of ménière's disease among hypothyroid patients and assess the interrelationship between patients' symptomology and ménière's disease. Materials and methods: A cross-sectional study was performed at the endocrinology clinics at Damascus Hospital and Syrian Red Crescent Hospital, Damascus, Syria between September 2021 and January 2022. Patients with hypothyroidism were interviewed using a questionnaire. The questionnaire contained questions about sociodemographic information, hypothyroid history, diagnostic criteria of ménière's disease, chief complaint, medical history, and lab test results. Patients, who reported ménière's disease symptoms, were referred to the otorhinolaryngology clinic for confirmation or exclusion of ménière's disease. At the clinic, patients underwent an otoscopy and a pure tone audiometry, probable and definite ménière's disease was diagnosed accordingly. Results: Of 217 hypothyroid patients included in the sample, 17 (7.8%) were diagnosed with definite ménière's disease and 31 (14.3%) were diagnosed with probable ménière's disease. Hypothyroid symptoms reported among patients diagnosed with definite ménière's disease compared to no diagnosis differed by feeling low ($\chi 2$ (1, 217) = 4.014, p = 0.045), and depressive appearance ($\chi 2$ (1, 217) = 8.887, p = 0.003). Patients diagnosed with definite ménière's disease, probable ménière's disease, and both definite and probable ménière's disease were more likely to report that their symptoms affected their lifestyle compared to those that reported no effect $(\chi 2 (3, 217) = 62.565, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), and (\chi 2 (3, 217) = 35.542, p < 0.001), (\chi 2 (3, 217) = 35.542, p < 0.001), (\chi 2 (3, 217) = 35.542, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380, p < 0.001), (\chi 2 (3, 217) = 31.380,$ respectively.

Conclusion: A high number of hypothyroid patients were diagnosed with MD. Clinicians should consider clinically screening for MD among hypothyroid patients presenting to clinics.

1. Introduction

Ménière's disease (MD), a debilitating disorder that affects the membranous labyrinth of the inner ear, was described by Prosper Ménière in 1861 and is diagnosed clinically by recurrent episodes of vertigo along with cochlear symptoms of low or medium frequency sensorineural hearing loss, tinnitus, and/or ear fullness [1]. A previous study revealed that the average annual prevalence of MD was 34.5% and the average annual incidence of MD was 5.0 per 100,000 populations

[2]. The overall incidence of MD was found to be significantly higher in a hypothyroidism cohort 8.65 per 1000 person-years versus a non-hypothyroidism cohort 6.38 per 1000 person-years [3].

MD is classified into two categories: definite MD, and probable MD. The diagnosis of definite MD is based on episodic vertigo associated with low to medium frequency sensorineural hearing loss recorded on pure tone audiometry (PTA) and fluctuating auditory symptoms (tinnitus, and/or fullness) in the affected ear [4]. The duration of vertigo spells ranges from 20 min to 12 h. Probable MD is identified by occasional

https://doi.org/10.1016/j.amsu.2022.104405

Received 7 June 2022; Received in revised form 7 August 2022; Accepted 12 August 2022

Available online 2 September 2022



Abbreviations: MD, Ménière's Disease; PTA, Pure Tone Audiometry; TSH, Thyroid-Stimulating Hormone; ENT, Ear Nose Throat; SD, standard deviations; IRB, Institutional Review Board; DM, Diabetes Mellites; TNFα, Tumor Necrosis Factor α; IL1, Interleukin 1; IL6, Interleukin 6.

Corresponding author. Faculty of Medicine, Syrian Private University, Mazzeh Street, P.O. Box 36822, Damascus, Syrian Arab Republic.

E-mail address: fatemamohsena@gmail.com (F. Mohsen).

¹ Annan Bakdounes and Nawal Akashe are both Dual first authorship.

^{2049-0801/© 2022} The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

vestibular symptoms (vertigo or dizziness) associated with fluctuating aural symptoms lasting between 20 min and 24 h [4]. The aetiology of MD remains unknown; however multiple factors have been blamed including immunologic disease, psychological factors, infections, trauma, genetic predisposition, metabolic disorders, and hormone dysfunction [5].

Thyroid dysfunction is the most common endocrine disorder [6]. Hypothyroidism is the failure of the thyroid gland to adequately secrete thyroid hormones [7]. The clinical presentation of thyroid disease is variable and nonspecific and constitutes a wide spectrum of clinical features [8]. Thyroid failure results in primary hypothyroidism [9]. Hypothyroidism is due to a deficiency in thyroid hormones. Predisposition and pathophysiology are thought to influence the association between autoimmune thyroid disease and many other autoimmune diseases [10,11]. While the prevalence of autoimmune thyroid diseases, is estimated to occur in approximately 1–5% of the general population, Hashimoto's thyroiditis is the most common cause of hypothyroidism and account for 47% [12]. This supports the theory that hypothyroidism contributes to autoimmune disease. Moreover, the abnormal metabolisms of patients with thyroid disease could stimulate the endolymphatic hydrops and MD. [] Hypothyroidism probably changes the composition of endolymphatic fluid through the spread of thyroid autoantibody complexes in the endolymph [13,14]. The measurement of thyroid-stimulating hormone (TSH) is widely used to diagnose hypothyroidism, once diagnosed with hypothyroidism, patients require mandatory lifetime therapy with oral levothyroxine [9].

The Syrian war and the resulting humanitarian crisis have drastically affected the healthcare of civilians. The demand for medicines and medical support has impacted the quality of healthcare Syrians receive. More than 90% of medicines were locally manufactured, before the conflict in Syria. Sadly, the effects of economic sanctions, destruction of pharmaceutical plants and storage facilities for imported medicines, currency crisis, and an increase in operational costs have negatively impacted the production of medicines. As a result, local production of medicines has been reduced to 10%. Therefore, the World Health Organization has evaluated the need for essential medicines, including the need for thyroid hormones, and levothyroxine [15,16]. Currently, there are four thyroxine supplement brands available, the imported brand includes Euthyrox, and nationally manufactured brands include Levothyroxine, Syntroxine asia, and Eltroxin available in dosages: 100 µg, 50 µg, and 25 µg, 100 tablets. Additionally, patients are required to self-fund their lifetime treatment and consultations.

Since both hypothyroidism and MD share a common pathophysiology of autoimmunity, former studies have proved the relationship between hypothyroidism and MD [3,13,17]. Other studies found hearing impairment in patient with Pendred syndrome as well as patients with acquired hypothyroidism [18]. People with hypothyroidism had a hearing loss rate of 43%. Tinnitus was found in 7% of cases and vertigo in 29.1% of cases. The incidence of these symptoms was linearly correlated with the severity of hypothyroidism [19]. Further reports have proved an improvement in patients' MD symptoms when treated appropriately with thyroxine [7,19]. However, none have screened for MD among hypothyroid patients. The aims of this study included: (1) evaluate the prevalence of MD among hypothyroid patients; (2) assess the interrelationship between patients' symptomology and MD; (3) determine the severity of MD on hypothyroid patient's lifestyle.

2. Materials and Methods

2.1. Study design, setting, and participants

A cross-sectional study was performed at the endocrinology clinics at Damascus Hospital and Syrian Red Crescent Hospital, Damascus, Syria between September 2021 and January 2022. All patients diagnosed with hypothyroidism, who agreed to participate, were included in the study. Criteria of exclusion were a history of cerebrovascular accident, panhypopituitarism, brain tumours, or otologic diseases such as otitis media and tympanic membrane perforation. Written informed consent was obtained from patients over the age of 18 years, while informed consent was sought for patients under 18 years of age from the patient and guardian, and the interview was conducted in the presence of the patient's guardian.

2.2. Data collection and procedures

Of 217 patients, who were diagnosed by an endocrinologist with hypothyroidism, attending their regular endocrinology clinic appointment, were interviewed using a questionnaire created by the authors. The questionnaire contained questions about socio-demographic information (such as gender, age, accommodation, work and education status, and smoking), hypothyroid history, diagnostic criteria of MD, chief complaint, medical history, and lab test results. Additionally, questions were included to exclude all differential diagnoses of MD [4].

2.2.1. Diagnosis of ménière disease

The diagnostic criteria of MD include recurrent episodes of vertigo lasting from 20 min to 12 h, tinnitus, low- or mid-frequency sensorineural hearing loss, and ear fullness [4]. Patients, who reported MD symptoms, were referred for a same-day appointment at the otorhinolaryngology clinic. At the clinic, patients underwent an otoscopy to rule out contraindications such as tympanic membrane perforation or ear wax for a pure PTA. Treatment was prescribed for patients who had ear wax and were scheduled for a follow-up appointment with the clinic to monitor treatment and then referred for PTA. Of 48 patients referred to the otorhinolaryngology clinic, 23 patients did not consent to PTA. Depending on the PTA results patients were assessed by an Ear Nose Throat (ENT) specialist and divided into probable MD and definite MD. Definite MD was diagnosed based on the presence of low to mid-frequency sensorineural hearing loss. Probable MD was diagnosed based on symptoms, with or without a normal PTA result.

The work in this study complies with the principles laid down in the Declaration of.

Mathew G and Agha R, for the STROCSS Group. STROCSS 2021: Strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery. International Journal of Surgery 2021; 96:106,165 [20].

2.3. Statistical analysis

Data were displayed as frequencies and percentages for categorical variables, and means with standard deviations (SD) for continuous variables. The Statistical Package for Social Sciences version 25.0 (SPSS Inc., Chicago, IL, United States) was used to analyze the study. The chi-square test was used to compare hypothyroid symptoms against probable MD, definite MD, and both probable and definite MD. Additionally, the chi-square test was performed to examine the relation between MD and its effect on patients' lifestyles. Students' independent *t*-test was used to study the relation between MD and TSH levels. Statistical significance was considered at a p-value <0.05.

Ethical statement

Ethical approval was obtained from the Institutional Review Boards (IRB) of the Faculty of Medicine at the Syrian Private University, Damascus Hospital, and Syrian Red Crescent Hospital. No reference number was given.

2.4. Registration of research studies

- 1. Name of the registry: Prevalence of Ménière's Disease in Syrian Patients with Hypothyroidism.
- 2. Unique Identifying number or registration ID: 8157.

3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

https://www.researchregistry.com/browse-the-registry#home/

3. Results

3.1. Socio-demographic characteristics of patients

Of 217 patients included in the sample, 204 (94%) were females, and 13 (6%) were males, with a mean age of 40.4 (\pm 14.6) years. The ages ranged from 8 to 79 years, and the median age was (40) years. The mean BMI was 27.6 kg/m², and 61 (28.1%) smoke. Unemployed patients represented the majority 128 (59.0%), while non-educated represented the minority 25 (11.0%), respectively (Table 1).

3.2. Clinical characteristics of hypothyroid patients

Common hypothyroid symptoms include tiredness 156 (71.9%), pale skin 144 (66.4%), respiratory distress 141 (65%), lateral hair loss 137 (63.1%), numbness 136 (62.7%), cold intolerance 133 (61.3%), feeling low 129 (59.4%), dry skin 129 (59.4%), dementia 121 (55.8%), head-ache 118 (54.4%), jaundice skin 117 (53.9%), arrhythmias 115 (53.0%), and drowsiness 111 (51.2%). Shockingly, 51 (23.5%) reported non-compliance with levothyroxine therapy, the reasons behind the non-compliance, include neglection, costs, forgetfulness, and unhappiness with the medications directions of use (Table 2)

3.3. Prevalence of MD symptoms

MD symptoms include vertigo 117 (53.9%), tinnitus 87 (40.1%), ear fullness 56 (25.8%), and hearing loss 53 (24.4%) (Table 3). The prevalence of MD was 48 (22.1%), probable MD and definite MD was 31 (14.3%) and 17 (7.8%) respectively (Fig. 1).

3.4. Association between symptoms and MD

3.4.1. Association between hypothyroid symptoms and probable MD Hypothyroid symptoms reported among patients diagnosed with

Table 1

Demographic characteristics of patients.

Group	Categories	N (%)		
Gender	Male	13 (6)		
	Female	204 (94)		
Age	8–13	12 (5.5)		
	14–17	6 (2.8)		
	18-21	4 (1.8)		
	22-42	98 (45.2)		
	43–50	42 (19.4)		
	51-79	55 (25.3)		
Accommodation	City	120 (55.3)		
	Suburb	97 (44.7)		
Work status	Don't work	128 (59.0)		
	Student	22 (10.1)		
	Full time job	40 (19.4)		
	Part time job	18 (8.3)		
	Retired	7 (3.2)		
Education	Non- educated	25 (11.5)		
	Primary	42 (19.4)		
	Elementary	55 (25.3)		
	Senior high	30 (13.8)		
	University/institute	62 (28.1)		
	Postgraduate	4 (1.8)		
Smoking	Cigarette and Water pipe	5 (2.3)		
	Cigarette only	32 (14.7)		
	Water pipe only	24 (11.1)		
	Previous smoker	6 (2.8)		
	Non smoker	150 (69.1)		

Table 2

Clinical characteristics of hypothyroid patients.

Table 2. Clinical characteristics of hypothyroid patients N= 217				
Symptoms	N (%)			
Commitment to the medicine	166 (76.5)			
Weight gain	100 (46.1)			
Loss of appetite	57 (26.3)			
Cold intolerance	133 (61.3)			
Lack of sweating	79 (36.4)			
Drowsiness	111 (51.2)			
Respiratory distress	141 (65.0)			
Chest pain	85 (39.2)			
Tiredness	156 (71.9)			
Headache	118 (54.4)			
Feeling low	129 (59.4)			
Lateral hair loss	137 (63.1)			
Constipation	77 (35.5)			
Menstrual disturbance	70 (32.3)			
Arrhythmias	115 (53.0)			
Numbness	136 (62.7)			
Memory loss	121 (55.8)			
Tongue enlargement	56 (25.8)			
Dry skin	129 (59.4)			
Rough and split hair	101 (46.5)			
Pale skin	144 (66.4)			
Vitiligo	6 (3.8)			
jaundiced skin	117 (53.9)			
Unkept appearance	70 (32.3)			

probable MD compared to no diagnosis were significantly associated with the following: weight gain (χ^2 (1, 217) = 6.828, p = 0.009), cold intolerance (χ^2 (1, 217) = 3.966, p = 0.046), respiratory distress (χ^2 (1, 217) = 5.673, p = 0.017), chest pain (χ^2 (1, 217) = 18.225, p < 0.001), headache (χ^2 (1, 217) = 12.681, p < 0.001), arrhythmia (χ^2 (1, 217) = 6.524, p = 0.011), numbness (χ^2 (1, 217) = 9.222, p = 0.002), and memory loss (χ^2 (1, 217) = 4.982, p = 0.026) (Table 4).

3.4.2. Association between hypothyroid symptoms and definite MD

Hypothyroid symptoms reported among patients diagnosed with definite MD compared to no diagnosis were significantly differed by feeling low (χ 2 (1, 217) = 4.014, p = 0.045), and depressive appearance (χ 2 (1, 217) = 8.887, p = 0.003) (Table 4).

3.4.3. Association between hypothyroid symptoms and the total MD

Hypothyroid symptoms reported among patients diagnosed with both probable and definite MD compared to no were significantly differed by weight gain ($\chi 2$ (1, 217) = 6.686, p = 0.010), cold intolerance ($\chi 2$ (1, 217) = 4.883, p = 0.027), respiratory distress ($\chi 2$ (1, 217) = 9.126, p = .003), chest pain ($\chi 2$ (1, 217) = 14.078, p < 0.001), tiredness ($\chi 2$ (1, 217) = 5.581, p = 0.018), headache ($\chi 2$ (1, 217) = 15.266, p < 0.001), arrythmia ($\chi 2$ (1, 217) = 9.819, p = .002), numbness ($\chi 2$ (1, 217) = 13.628, p < 0.001), and memory loss ($\chi 2$ (1, 217) = 9.248, p = .002) (Table 4).

3.5. Effect of MD on patients' lifestyle

Patients diagnosed with definite MD, probable MD, and both definite and probable MD were more likely to report that their symptoms affected their lifestyle compared to those that reported no effect ($\chi 2$ (3, 217) = 62.565, p < 0.001), ($\chi 2$ (3, 217) = 31.380, p < 0.001), and ($\chi 2$ (3, 217) = 35.542, p < 0.001), respectively (Table 5).

4. Discussion

The literature has repeatedly proven the association between hypothyroidism and MD [3,7,17,21–23]. A retrospective study containing 211 patients with classic MD where 208 patients were tested for hypothyroidism, revealed only one patient with an abnormal test result. They

Table 3

Prevalence of MD symptoms among hypothyroid patients.

Table 2 Table 2	Descelance of MD a		how otherword	notionto N 017
Table 3. Table 3.	. Prevalence of MD s	vmptoms among	nypotnyrola	patients $N = 217$

Symptoms group	N (%)
Vertigo Yes	117
U U	(53.9)
No	100
	(46.1)
Duration of dizziness Seconds	56 (25.8)
Minutes	47 (21.7)
One hour	3 (1.4)
Couple of h	
Day	2 (0.9)
Couple of d	-
Time between vertigo events Hour	6 (2.8)
One day	21 (9.7)
Days	5 (2.3)
Week or m	
Balance Loss of bala Fall down	• •
Tinnitus Yes	7 (3.2) 87 (40.1)
No No	130
no	(59.9)
Frequency of tinnitus High	30 (13.8)
Low	57 (26.3)
Effect of tinnitus on patient Low	65 (30.0)
Moderate	16 (7.4)
Severe	6 (2.8)
Effect of tinnitus on quality of sleep wake from	sleep 10 (4.6)
Don't wake	e from sleep 76 (35.0)
Hearing loss Yes	53 (24.4)
No	164
	(75.6)
Evolution Sudden	14 (6.5)
Gradual Unsteady	35 (16.1) 4 (1.8)
Hearing loss onset During dizz	
Out of dizz	
Not related	
dizziness	
Hearing loss duration Seconds	32 (14.7)
Minutes	16 (7.4)
Hour	2 (0.9)
More	6 (2.8)
Ear fullness Yes	56 (25.8)
No	161
	(74.2)
Eye symptoms Yes	112
	(51.6)
No	105
	(48.4)
Headache Yes	111
	(51.2)
No	106
How does these symptoms affect	(48.8)
How does these symptoms affect your No effect life	143 (65.9)
Low	(65.9) 34 (15.7)
	20 (12 4)
Moderate Severe	29 (13.4) 11 (5.1)

concluded that routine screening of thyroid function was not recommended among MD patients unless a history suggestive of metabolic disorder is present [24].

To the best of our knowledge, this first study tests for MD among patients with hypothyroidism presenting with aural symptoms. After testing for MD among hypothyroid patients presenting with aural symptoms, the prevalence of MD was found to be high (22.1%), probable MD was 14.3% and definite MD was 7.8%. Our findings are higher compared with a study conducted in Taiwan (5%) [3]. We believe that the high prevalence may be due to the lack of awareness among both patients and doctors about the disease and its association with hypothyroidism as well as the inadequate adherence to the medication from the patients.

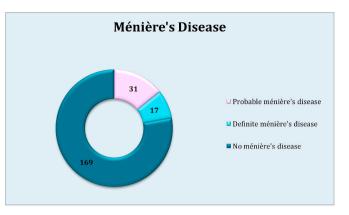


Fig. 1. Distribution of ménière's disease among patients.

MD can be associated with numerous comorbidities including Diabetes Mellitus (DM), hyperlipidaemia, hypertension, and cirrhosis [3,25, 26]. However, the inflammatory or metabolic changes in patients with hypothyroidism may affect the inner ear inflammation and homeostasis of endolymphatic flow [17]. In addition, inflammatory cytokines such as tumor necrosis factor α (IF α) and interleukin 1 and 6 (IL1, IL6) decrease the expressions of sodium/iodine symporter, impeding the iodide uptake in the thyroid gland [27,28]. This inflammatory or degenerative alteration in the inner ear epithelia can also raise the likelihood of MD [17]. Therefore, the disturbance of this composition as a result of the altered metabolism could affect the vestibular functioning.

Definite MD patients were individually related to feeling low (82.4%) and depressive appearance (64.7%). A systematic review found that 50% of MD patients have varying degrees of depression [29]. Therefore, Regular assessment of depressive symptoms among MD patients facilitates early detection of critical cases. This permits a prompt diagnosis and therapy of depression to guarantees a lifelong quality of life for MD patients.

MD is a long-term disabling disease that not only impacts one's psychological wellbeing and physical functioning but also restricts the quality of life through stigmatization [30]. In our study, MD diagnosis was found to affect patients' lifestyles more compared with those who had no diagnosis. Former studies have used scales to assess the quality of well-being among patients with MD; results have shown severely incapacitated patients. Acute episodes of MD are the most debilitating condition endured by people who survive any illness [31]. Currently, there is no cure for MD; however, lifestyle changes can help prevent or reduce attacks [32].

In this study, many patients refused to undergo PTA to confirm their MD diagnosis and were unable to assess vestibular function tests. Thus, the MD endotypes involving degenerated distal endolymphatic sac and hypoplastic endolymphatic sac were indistinguishable. Although associations between MD type and severity may vary, evaluation of clinical otovestibular symptoms in MD is more predictable. Our findings illustrate an association between hypothyroid symptoms and both probable and definite MD. Herein screening for MD in hypothyroid patients is highly recommended, especially if thyroid hormone medication is not already taken. Plan to modify the diagnostic system and follow-up of patients with hypothyroidism and ear complaints to include those at high risk of developing MD. Extend awareness among hypothyroid patients about the importance of committing to hypothyroid medication and their risk of developing untreatable diseases like MD.

5. Limitations

Our study is burdened by several limitations. First, hypothyroidism has numerous etiologies that can be divided into several subgroups and included in the analysis. Second, other thyroid diseases, including hyperthyroidism, goiter, and thyroiditis should be included in future

Table 4

Association between patients' hypothyroidism symptoms and ménière's disease.

Table 4. Association between patients' hypothyroidism symp	ptoms and ménière's disease
------------------------------------------------------------	-----------------------------

Symptoms Probable disease Yes N (%)	Probable ménière's disease		X^2	p- value	Definite ménière's disease		X^2 p-valu	p- value	Ménière's disease		<i>X</i> ²	p- value
		No N (%)			Yes N (%)	No N (%)			Yes N (%)	No N (%)		
Commitment to the medicine	23 (74.2)	143 (76.9)	0.107	0.744	6 (35.3)	160 (80)	17.418	<.001	29 (60.4)	137 (81.1)	8.865	0.003
Weight gain	21 (67.7)	79 (42.5)	6.828	0.009	9 (52.9)	91 (45.5)	0.349	0.555	30 (62.5)	70 (41.4)	6.686	0.010
Loss of appetite	9 (29.0)	48 (25.8)	0.143	0.706	6 (35.3)	51 (25.5)	0.776	0.378	15 (31.3)	42 (24.9)	0.790	0.374
Cold intolerance	24 (77.4)	109 (58.6)	3.966	0.046	12 (70.6)	121 (60.5)	0.672	0.412	36 (75.0)	97 (57.4)	4.883	0.027
Lack of sweating	11 (35.5)	68 (36.6)	0.013	0.908	5 (29.4)	74 (37.0)	0.390	0.532	16 (33.3)	63 (37.3)	0.251	0.616
Drowsiness	18 (58.1)	93 (50.0)	0.164	0.685	11 (64.7)	100 (50.0)	1.356	0.244	29 (60.4)	82 (48.5)	2.117	0.146
Respiratory distress	26(83.9)	115 (61.8)	5.673	0.017	14 (82.4)	127 (63.5)	2.447	0.118	40 (83.3)	101 (59.8)	9.126	0.003
Chest pain	22 (71.0)	63 (33.9)	18.225	<.001	8 (47.1)	77 (38.5)	0.482	0.488	30 (62.5)	55 (32.5)	14.078	<.001
Tiredness	26 (83.9)	130 (69.9)	2.569	0.109	15 (88.2)	141 (70.5)	2.439	0.118	41 (85.4)	115 (68)	5.581	0.018
Headache	26 (83.9)	92 (49.5)	12.681	<.001	12 (70.6)	106 (53)	1.954	0.162	38 (79.2)	80 (47.3)	15.266	<.001
Feeling low	19 (61.3)	110 (59.1)	0.051	0.821	14 (82.4)	115 (57.5)	4.014	0.045	33 (68.8)	96 (56.8)	2.213	0.137
Lateral hair loss	21(67.7)	116 (62.4)	0.330	0.566	11 (64.7)	126 (63.0)	0.020	0.889	32 (66.7)	105 (62.1)	0.331	0.565
Constipation	11 (35.5)	66 (35.5)	0.000	1	9 (52.9)	68 (34.0)	2.455	0.117	20 (41.7)	57 (33.7)	1.029	0.310
Menstrual disturbance	10 (32.3)	60 (32.3)	0.000	1	7 (41.2)	63 (31.5)	0.671	0.413	17 (35.4)	53 (31.4)	0.281	0.596
Arrhythmias	23 (74.2)	92 (49.5)	6.524	0.011	12 (70.6)	103 (51.5)	2.292	0.130	35 (72.9)	80 (47.3)	9.819	0.002
Numbness	27(87.1)	109 (58.6)	9.222	0.002	14 (82.4)	122 (61.0)	3.054	0.081	41 (85.4)	95 (56.2)	13.628	<.001
Memory loss	23 (74.2)	98 (52.7)	4.982	0.026	13 (76.5)	108 (54.0)	3.207	0.073	36 (75.0)	85 (50.3)	9.248	0.002
Tongue enlargement	8 (25.8)	48 (25.8)	0.000	1	4 (23.5)	52 (26.0)	0.050	0.823	12 (25.0)	44 (26.0)	0.021	0.885
Dry skin	22 (71.0)	107 (57.5)	2.485	0.115	11 (64.7)	118 (59.0)	0.212	0.646	33 (68.8)	96 (56.8)	2.213	0.137
Rough and split hair	14 (45.2)	87 (46.8)	0.028	0.868	11 (64.7)	90 (45.0)	2.445	0.118	25 (52.1)	76 (45.0)	0.760	0.383
Pale skin	20 (64.5)	124 (66.7)	0.055	0.815	14 (82.4)	130 (65.0)	2.113	0.146	34 (70.8)	110 (65.1)	0.553	0.457
Vitiligo	0 (0.0)	6 (3.2)	1.187	0.276	1 (5.9)	5 (2.5)	0.667	0.414	1 (2.1)	5 (3.0)	0.107	0.744
jaundiced skin	17	100	0.12	0.911	8 (47.1)	109	0.349	0.555	25	92 (54.4)	0.083	0.773
	(54.8) 7 (22.6)	(53.8) 63 (33.9)	1.550	0.213	11	(54.5) 59 (29.5)	8.887	0.003	(52.1) 18	52 (30.8)	0.775	0.379
Unkept appearance	7 (22.6)	63 (33.9)	1.550	0.213	11 (64.7)	59 (29.5)	8.887	0.003	18 (37.5)	52 (30.8)	0.775	0.3

studies, they may have an impact on the occurrence of MD, due to the metabolic pathological changes and autoimmune nature these diseases have. Third, assessing patients' satisfaction with treatment, quality of life, and the effects of medication compliance and non-compliance warrants further prospective studies to be planned.

6. Conclusions

Many patients with hypothyroidism are diagnosed with MD. Clinicians should consider clinically screening for MD among hypothyroid patients presenting to clinics.

Thyroxine therapy could benefit aural symptoms and may prevent from MD. Further studies are needed to evaluate the efficacy of MD screening programs and thyroxine therapy in hypothyroid patients with MD symptoms.

Availability of data and materials

All data related to this paper's conclusion are available and stored by the authors. All data are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The work in this study complies with the principles laid down in the Declaration of Helsinki (Recommendations guiding physicians in biomedical research involving human subjects. Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964, amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975, the 35th World Medical Assembly, Venice, Italy, October 1983, and the 41st World Medical Assembly, Hong Kong, September 1989). This study was approved by the Institutional Review Board (IRB) at SPU. No reference number was given. Written consent was obtained from all participants. Participation in the study was voluntary and participants were assured

Table 5

Effect of ménière's disease on patient's lifestyle and TSH levels.

		No effect (%)	Mild (%)	Moderate (%)	Severe (%)	X^2	<i>p</i> - value
Ménière's disease	Yes	11 (7.7)	11 (32.4)	18 (62.1)	8 (72.7)	62.565	< .001
	No	132 (92.3)	23 (67.6)	11 (37.9)	3 (27.3)		
Probable ménière's disease	Yes	9 (6.3)	6 (17.6)	13 (44.8)	3 (27.3)	31.380	< .001
	No	134 (93.7)	28 (82.4)	16 (55.2)	8 (72.7)		
Definite ménière's disease	Yes	2 (1.4)	5 (14.7)	5 (17.2)	5 (45.5)	35.542	< .001
	No	141 (98.6)	29 (85.3)	24 (82.8)	6 (54.5)		
Effect of ménière's disease on TS	H levels						
		TSH	t	p- value			
		Mean (\pm SD)					
Meniere disease	Yes	10.2 (19.6)	0.420	0.675			
	No	8.9 (18.9)					
Probable ménière's disease	Yes	11.6 (24.1)	0.757	0.450			
	No	8.8 (18.1)					
Definite ménière's disease	Yes	7.7 (5.9)	0.336	0.737			

that there would be no victimization of anyone who did not want to participate or who decided to withdraw after giving consent.

Funding

This research received no specific grant from the Syrian Private University or any other funding agency in the public, commercial or non-profit sectors.

Author contribution

Anan Bakdounes and Nawal Akashe were responsible for study design, literature search, and write up; Duaa Bakdounes participated in data collection; Mhd Obai Alchallah did the statistical analysis of data and contributed to the written paper; Homam Alolabi participated in the statistical analysis of data; Fatema Mohsen participated in the analysis and interpretation of data and wrote the final draft; Louei Darjazini Nahas participated in the study design and reviewed the final draft. All authors read and approved the final draft.

Registration of research studies

- 1. Name of the registry: Prevalence of Ménière's Disease in Syrian Patients with Hypothyroidism
- 2. Unique Identifying number or registration ID: 10.5281/ zenodo.6616112
- Hyperlink to your specific registration (must be publicly accessible and will be checked): https://zenodo.org/record/6616112#.Yp 9D-KjMI2w

Guarantor

The Guarantors are Anan Bakdounes, Nawal Akashe, Mhd Obai Alchallah MD, Homam Alolabi MD, Duaa Bakdounes, Fatema Mohsen MD, and Louei Darjazini Nahas MD.

Consent

Written consent was obtained from all participants. Participation in the study was voluntary and participants were assured that there would be no victimization of anyone who did not want to participate or who decided to withdraw after giving consent.

Provenance and peer review

Not commissioned, externally peer reviewed.

Financial disclosures/conflicts of interest

This study was received no funds. There are no conflicts of interest, financial, or otherwise.

Declaration of competing interest

None.

Acknowledgments

We are thankful to the management of the Syrian Private University for their support and encouragement in the field of medical training and research. We would like to thank both the endocrine and the otorhinolaryngology team at the Damascus Hospital and the Syrian Red Crescent Hospital. We are thankful to all patients, who participated in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104405.

References

- [1] T. Wright, Menière's Disease, BMJ Clinical Evidence 2015, 2015.
- [2] H. Shojaku, Y. Watanabe, M. Fujisaka, M. Tsubota, K. Kobayashi, S. Yasumura, K. Mizukoshi, Epidemiologic characteristics of definite Ménière's disease in Japan. A long-term survey of Toyama and Niigata prefectures, ORL, journal for oto-rhinolaryngology and its related specialties 67 (5) (2005) 305–309.
- [3] W.L. Lin, C.Y. Chen, T.Y. Hsu, W.K. Chen, C.L. Lin, H.C. Chen, Hypothyroidism is an independent risk factor for Menière's disease: a population-based cohort study, Medicine 98 (15) (2019), e15166.
- [4] J.A. Lopez-Escamez, J. Carey, W.H. Chung, J.A. Goebel, M. Magnusson, M. Mandalà, D.E. Newman-Toker, M. Strupp, M. Suzuki, F. Trabalzini, A. Bisdorff, Diagnostic criteria for Menière's disease, J. Vestib. Res. : equilibrium & orientation 25 (1) (2015) 1–7.
- [5] G. Hwang, R. Saadi, V.A. Patel, J. Liaw, H. Isildak, Thyroid dysfunction in ménière's disease: a comprehensive review, orl, journal for oto-rhino-laryngology and its related specialties 83 (4) (2021) 219–226.
- [6] L. Mehran, A. Amouzegar, F. Azizi, Thyroid disease and the metabolic syndrome 26 (5) (2019) 256–265.
- [7] U.P. Santosh, M.S. Rao, Incidence of hypothyroidism in meniere's disease, J. Clin. Diagn. Res. : J. Clin. Diagn. Res. 10 (5) (2016) Mc01–3.
- [8] P.N. Taylor, D. Albrecht, A. Scholz, G. Gutierrez-Buey, J.H. Lazarus, C.M. Dayan, O. E. Okosieme, Global epidemiology of hyperthyroidism and hypothyroidism, Nat. Rev. Endocrinol. 14 (5) (2018) 301–316.
- [9] M.T. McDermott, Hypothyroidism, Ann. Intern. Med. 173 (1) (2020). Itc1-itc16.[10] R.C. Jenkins, A.P. Weetman, Disease associations with autoimmune thyroid
- disease, Thyroid : Off. J. Am. Thyroid Assoc. 12 (11) (2002) 977–988.
 [11] N. Inoue, M. Watanabe, H. Yamada, K. Takemura, F. Hayashi, N. Yamakawa, M. Akahane, Y. Shimizuishi, Y. Hidaka, Y. Iwatani, Associations between autoimmune thyroid disease prognosis and functional polymorphisms of

A. Bakdounes et al.

susceptibility genes, CTLA4, PTPN22, CD40, FCRL3, and ZFAT, previously revealed in genome-wide association studies, J. Clin. Immunol. 32 (6) (2012) 1243–1252.

- [12] J.J. Díez, Hypothyroidism in patients older than 55 years: an analysis of the etiology and assessment of the effectiveness of therapy, J. gerontology series A Biol. Sci. Med. Sci. 57 (5) (2002) M315–M320.
- [13] G.E. Shambaugh Jr., Endocrine aspects of Meniere's disease, Laryngoscope 69 (1959) 1027–1032.
- [14] W.H. Powers, Metabolic aspects of Meniere's disease, Laryngoscope 82 (9) (1972) 1716–1725.
- W.H. Organization, Syria's Essential Medicine List, 2019. http://www.emro.who. int/syr/publications-other/syrias-essential-medicine-list-2019.html. Accessed 01/ 05/2022 2022.
- [16] W.H. Organization, Shortages in life-saving medicines in Syria of major concern to WHO. http://www.emro.who.int/media/news/shortages-in-life-saving-medicines -syria.html. Accessed 01/05/2022 2022.
- [17] S.Y. Kim, Y.S. Song, J.H. Wee, C. Min, D.M. Yoo, H.G. Choi, Association between Ménière's disease and thyroid diseases: a nested case-control study, Sci. Rep. 10 (1) (2020), 18224.
- [18] F.N. Ritter, The effects of hypothyroidism upon the ear, nose and throat. A clinical and experimental study, Laryngoscope 77 (8) (1967) 1427–1479.
- [19] P.L. Bhatia, O.P. Gupta, M.K. Agrawal, S.K. Mishr, Audiological and vestibular function tests in hypothyroidism, Laryngoscope 87 (12) (1977) 2082–2089.
- [20] G. Mathew, R. Agha, Strocss 2021: Strengthening the reporting of cohort, crosssectional and case-control studies in surgery, Int. J. Surg. 96 (2021), 106165.
- [21] B. Fattori, A. Nacci, A. Dardano, I. Dallan, M. Grosso, C. Traino, V. Mancini, F. Ursino, F. Monzani, Possible association between thyroid autoimmunity and Menière's disease, Clin. Exp. Immunol. 152 (1) (2008) 28–32.

- [22] M. Brenner, D.L. Hoistad, T.C. Hain, Prevalence of thyroid dysfunction in patients with Ménière's disease, Arch. Otolaryngol. Head Neck Surg. 130 (2) (2004) 226–228
- [23] W.H. Powers, Metabolic aspects of Ménière's disease, Laryngoscope 88 (1 Pt 1) (1978) 122–129.
- [24] W.L. Meyerhoff, M.M. Paparella, F.K. Gudbrandsson, Clinical evaluation of Ménière's disease, Laryngoscope 91 (10) (1981) 1663–1668.
- [25] B. Proctor, C. Proctor, Metabolic management in Menière's disease, Ann. Otol. Rhinol. Laryngol. 90 (6 Pt 1) (1981) 615–618.
- [26] J.T. Spencer Jr., Hyperlipoproteinemias in the etiology of inner ear disease, Laryngoscope 83 (5) (1973) 639–678.
- [27] R.A. Ajjan, P.F. Watson, C. Findlay, R.A. Metcalfe, M. Crisp, M. Ludgate, A. P. Weetman, The sodium iodide symporter gene and its regulation by cytokines found in autoimmunity, J. Endocrinol. 158 (3) (1998) 351–358.
- [28] P.M. Schumm-Draeger, Sodium/iodide symporter (NIS) and cytokines, Exp. Clin. Endocrinol. Diabetes : Off. J. Ger. Soc. Endocrinol. Ger. Diabetes Assoc. 109 (1) (2001) 32–34.
- [29] J.J. Patel, D.A. Levy, S.A. Nguyen, H.G. Rizk, T.A. Meyer, Depression in Ménière's disease: a systematic review and meta-analysis, J. Laryngol. Otol. 134 (4) (2020) 293–301.
- [30] K.K. Talewar, E. Cassidy, A. McIntyre, Living with Ménière's disease: an interpretative phenomenological analysis, Disabil. Rehabil. 42 (12) (2020) 1714–1726.
- [31] J.P. Anderson, J.P. Harris, Impact of Ménière's disease on quality of life, Otology & neurotology, Off. Pub. Am. Otol. Soc. Am. Neurotol. Soc. Eur. Acad. otol Neurtol. 22 (6) (2001) 888–894.
- [32] M.J. Pritchard, Understanding Ménière's disease 2: treatment options, Nurs. Times 103 (46) (2007) 30–31.

Annals of Medicine and Surgery 81 (2022) 104405