Inner ear dysfunction in patients with Behcet’s disease
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Background
Behcet’s disease (BD) is a rare immune-mediated small-vessel systemic vasculitis that often presents with mucous membrane ulceration and ocular problems. Alajouanine and colleagues first described inner ear involvement in BD in 1961. The cochlea is more frequently involved than the vestibular labyrinth or the central vestibular tracts. Hearing is commonly impaired in BD and rates vary between 24 and 62%.

Objective
The current study investigated the incidence, relationship, and characteristics of audiovestibular disturbances in patients with BD compared with age and sex-matched healthy individuals.

Patients and methods
The participants of this prospective study classified into two groups. The study group consisted of 15 patients (six men and nine women) with BD and the control group consisted of 15 healthy volunteers (five men and 10 women) without otological symptoms. A wide range of tests were conducted; all patients were evaluated by conventional pure-tone audiometry (0.25–8.0 kHz), high-frequency audiometry (8.0–16.0 kHz), and vestibular test battery in terms of bithermal caloric test and computerized dynamic posturography testing.

Results
There was no significant differences between the two groups in terms of sex and age. Abnormalities of the pure-tone audiometry showed that 34% of patients demonstrated variable degrees of sensorineural hearing loss, while 60% of patients demonstrated abnormal audiograms at the high-frequency audiometry. In terms of vestibular assessment, 34% of patients demonstrated abnormalities at the caloric test, while 47% demonstrated abnormalities at the computerized dynamic posturography testing.

Conclusion
The outcome of this study confirms the association between the inner ear dysfunction and the BD. Inner ear dysfunction in BD could be attributed to the presence of vasculitis or neuropathy that could happen on top of chronic inflammation process associated with BD. Therefore, patients with BD should be regularly subjected to otolaryngological evaluation to diagnose and for follow up of any audiovestibular involvement.

Keywords:
Behcet’s disease, caloric test, dizziness, hearing loss, inner ear

Introduction
Behcet’s disease (BD) is a chronic systemic autoimmune disease characterized by a triple-symptom complex of recurrent oral aphthous ulcers, genital ulcers, and uveitis [1]. This disease was first described by Dr Behçet in 1937 as a clinical triad of aphthous ulceration, genital ulceration, and iridocyclitis [2]. The prevalence of BD is highest in countries of the Eastern Mediterranean, the Middle East and the Eastern Asian rim [3]. The International Study Group of Physicians for BD (1992) has established a set of guidelines to aid in the proper diagnosis of Behcet’s patients [4]. They established the International Study Group's Diagnostic Criteria for Behçet Disease (ISGBD), which suggested the following criteria for the diagnosis: recurrent oral ulcerations (aphthous or herpetiform) at least three times in 1 year, additionally, patients must present any two of the following: (a) recurrent genital ulcerations; (b) eye lesions (uveitis or retinal vasculitis) observed by an ophthalmologist; (c) skin lesions (erythema nodosum, pseudofolliculitis, papulopustular lesions, acneiform nodules); or (d) positive ‘pathergy test’ read by a physician within 24–48 h of testing.

Cho et al. [5] reported that BD affects men and women to an equal extent. It may involve the pulmonary, gastrointestinal, central nervous system, and

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cardiovascular systems. The disease can lead to numerous signs and symptoms that may seem unrelated at first. They may include mouth sores, eye inflammation, skin rashes, and genital sores. The effects of BD vary from person to person and may clear up by itself. Treatment involves medications to reduce the symptoms and signs of BD and to prevent serious complications, such as blindness [5]. Inner ear involvement in BD was first described by Alajuannine et al. [6]. They reported that the cochlea is more frequently involved than the vestibular labyrinth or the central vestibular tracts. Hearing is commonly impaired in BD and rates vary between 24 and 62% [7–12].

According to Kulahli et al. [11], the type of hearing loss is usually high-frequency sensorineural hearing loss and the auditory brainstem response testing is generally not abnormal. The literature also supports findings of frequent vestibular problems [13–16]. On the other hand, Kulahli et al. [11] did not find a high prevalence of vestibular involvement at BD. Sugasawa and Ishikawa [17] suggested that there was high vestibular ocular reflex gain with vestibular testing. In the literature, there were many reports of audiovestibular disturbances in BD, but in most of the studies, patients were not compared with healthy controls, and many studies did not include monitoring of inner ear involvement via measurements of vestibular function. The current study investigated the incidence, relationship, characteristics of audiovestibular disturbances in patients with BD compared with age-matched and sex-matched healthy individuals.

**Patients and methods**

The participants of this prospective study were classified into two groups. The study group consisted of 15 patients (six men and nine women) with BD and the control group consisted of 15 healthy volunteers (five men and 10 women) without otological symptoms. The diagnosis of BD was based on criteria described by the ISGBD. These diagnostic criteria require the presence of oral ulceration in addition to any two of the following: genital ulceration, skin lesions, eye lesions, or a positive pathergy test.

All patients underwent otolaryngological and dermatological evaluation; all patients fulfilled the criteria of the ISGBD. Through questionnaires, a detailed information was obtained regarding the patient’s past medical, audiovestibular, and neurological histories. Study participants with any metabolic, autoimmune, or connective tissue disorders that might be associated with audiovestibular symptoms were excluded from this study.

None of the patients in the study and control groups had any past history of hearing loss, ear infection, ear trauma, acoustic trauma, usage of otoxic drugs. Written informed consent was obtained from the patients and the local ethics committee approved the study protocol.

A wide range of tests were conducted; all patients were evaluated by conventional pure-tone audiometry (CP-PTA) at the frequency range of 0.25–8.0 kHz, high-frequency audiometry (HFA) at 8.0–16.0 kHz using an AC-40 Interacoustics Clinical Audiometer (Interacoustics, Assens, Denmark), in addition to the vestibular test battery which consisted of bithermal caloric test and the computerized dynamic posturography (CDP) testing. Caloric testing was performed using an infrared video-oculographic system (Micromedical Technologies, Chatham, Illinois, USA) and a Brookler–Grams open-loop irrigation unit with standard bithermal irrigations of 30°C and 44°C for 45 s. Based on the Jongkee’s index formula, canal paresis more than 25% was considered abnormal; total eye speed less than 20 was considered abnormal; directional preponderance more than 30% was considered abnormal. The CDP was performed using Equitest System (Version 4.0; NeuroCom, Clackamas, Oregon, USA); three basic tests were performed: the sensory organization test, the motor control test, and the adaptation test.

**Statistical analysis**

Statistical analysis was performed using the statistical package for the social sciences software for Windows (v. 13; SPSS Inc., Chicago, Illinois, USA). Baseline demographic characteristics were expressed as means with a SD. The independent samples t-test was used to compare the parametric conditions of two groups and χ² for comparison of categorical variables. Mann–Whitney U-test was carried out for nonparametric conditions. A P-value of less than 0.05 was considered significant for all comparisons.

**Results**

Table 1 is demonstrating the demographic features of the study group versus the control group. The study group consisted of 15 patients (six men and nine women) with BD. The control group consisted of 15 individuals (five men and 10 women); mean ages of patients with BD and healthy volunteers were 40.25±8.95 (range 25–56) years and 39.47±9.91 (range 23–58) years, respectively. There was no significant difference between the two groups in terms of sex and age. Table 2 shows the descriptive and clinical features of the study group; the duration of BD ranged from 3 to 25 years (mean 10.7±6.4 years).
Table 1 Demographic criteria of the study group versus the control group

<table>
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<th>Demographic variable</th>
<th>Study group</th>
<th>Control group</th>
<th>P-value</th>
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<td><strong>Age (years)</strong></td>
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<tr>
<td>Range</td>
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<tr>
<td>Mean±SD</td>
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<td>39.47±9.91</td>
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<tr>
<td><strong>Sex</strong></td>
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</tr>
<tr>
<td>Men</td>
<td>6</td>
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</tr>
<tr>
<td>Women</td>
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<tr>
<td><strong>Total number</strong></td>
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</table>

Table 2 and Fig. 1 summarizes the different clinical presentations at the study group; a 100% of patients reported a history of oral ulcers, while 80% of patients reported genital ulcers and positive pathergy test; 54% of patients reported a history of dizziness and imbalance; 40% of patients reported a history of eye symptoms; 34% of patients reported skin lesions at some time during the course of the disease; and finally auditory symptoms were reported in a minority of patients (27%) in terms of hearing loss and difficulty in speech discrimination. Table 3 demonstrates the differences at the audiometric test results between the study and the control groups, which was statistically significant at all the tested frequencies (0.25–16 kHz).

Abnormalities of the PTA including the C-PTA and HFA were defined as hearing thresholds of more than 25 dB in at least two frequencies. As shown in Fig. 2, 34% of patients demonstrated variable degrees of sensorineural hearing loss ranging from mild to severe at the C-PTA, while 60% of patients demonstrated abnormal audiograms at the HFA; most of the patients at this series demonstrated mild to moderate high-frequency sensorineural hearing loss, while only three (20%) patients demonstrated moderately severe to severe sensorineural hearing loss with variable configuration. In terms of vestibular assessment, 34% demonstrated abnormalities at the caloric test, while 47% demonstrated abnormalities at the CDP testing. Overall, 47% of the study group demonstrated combined audiological and vestibular abnormalities.

Discussion

BD is a rare immune-mediated small-vessel systemic vasculitis that often presents with mucous membrane ulceration and ocular problems. It affects blood vessels of nearly all sizes and types, ranging from small arteries to large ones, and involving veins too. Because of the diversity of blood vessels it affects, manifestation of BD is heterogeneous and may occur at many sites throughout the body. However, the disease has a predilection for certain organs and tissues. Audiovestibular involvement is...
On the basis of findings of the present study (Table 2), neither age of patients nor duration of the disease had any correlation with audiovestibular involvement. Other studies demonstrated a controversy about this correlation as Brama and Fainaru [7] reported that the incidence of audiovestibular manifestation occurred more often in older patients with a longer duration of the disease. On the other hand, Soylu et al. [18] did not report any relation between the hearing loss and other systemic manifestation in Behcet’s patients. Moreover, Gemignani et al. [9] did not find any correlation between audiovestibular involvement and the age or the disease duration.

Audiovestibular involvement in BD was first described by Alajouanine et al. [6], which demonstrated the presence of hearing loss and gaze nystagmus in a patient with BD complicated by meningoencephalitis. Since then, a number of studies concerned with the autoimmune involvement of the inner ear in autoimmune diseases have been published. One common finding in all these studies is that hearing impairment exists in autoimmune diseases, usually at high frequencies. Gemignani et al. [9] reported that rates of hearing loss among patients with BD have ranged from 15 to 80%. The current study confirmed the involvement of the audiovestibular system in BD as 34% of the study group demonstrated sensorineural hearing loss at the C-PTA testing, while 60% demonstrated hearing loss at high frequencies. Caloric test was abnormal in 34% of patients, while the CDP testing was abnormal in 47% of patients.

Several studies have been conducted in an attempt to determine the precise anatomic location of audiovestibular involvement in BD. The overall outcome of those studies demonstrated cochlear involvement in 64% of cases, retrocochlear involvement in 4%, vestibular involvement in 28%, and external and middle ear involvement in 4% of patients with BD [15]. It is interesting that most of the study group did not express any complaint regarding their hearing as most of the study group had mild to moderate high-frequency sensorineural hearing loss that did not cause

<table>
<thead>
<tr>
<th>Frequency (kHz)</th>
<th>Study group</th>
<th>Control group</th>
<th>P-value</th>
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</thead>
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<tr>
<td></td>
<td>dB (mean±SD)</td>
<td>Minimum</td>
<td>Maximum</td>
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<tr>
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<td>24.66±21.41</td>
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<tr>
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<td>44.33±27.95</td>
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<tr>
<td>14</td>
<td>47±27.17</td>
<td>25</td>
<td>110</td>
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<tr>
<td>16</td>
<td>51.66±25.95</td>
<td>25</td>
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*P<0.05, significant.
any communication problems in their daily life. The configuration and degree of hearing loss was not consistent among the study group, so typical type of audiogram was not observed among this series of patients, but we believe that the degree of hearing loss may be related to the severity of BD as there were two patients with bilateral severe sensorineural hearing loss who were detected among patients who showed severe full symptoms according to the ISGBD criteria (patient number 4 and 13 in Table 1).

Choung et al. [14] reported that if the vasculitis affecting the common cochlear artery aggravates over time, hearing impairment could occur suddenly or progressively. Gemignani et al. [9] reported that sudden hearing loss may be the first sign of cochlear involvement, and the HLA–B51 antigen is associated with ear involvement. Soylu et al. [18] reported that 27% of patients demonstrated some degree of sensorineural hearing loss on PTA testing and 50% of them demonstrated higher frequencies hearing loss. Furthermore, Erdinli et al. [19] reported also high frequencies (6 and 8 kHz) involvement in comparison with speech frequencies. Pollak et al. [20] study demonstrated that hearing impairment was found in 54% of patients and the bilateral cochlear involvement was the most common inner ear affection finding.

In the context of dizziness and vestibular assessment, this study demonstrated that dizziness was the fourth most frequent presentation among the different clinical presentations of the study group (Fig. 1). Evereklioglu et al. [15] reported that dizziness and vertigo was the fifth most frequent finding, but it was not clear whether this imbalance was due to peripheral or central vestibular involvement. Furthermore, this series of patients demonstrated that 54% of patients complained of dizziness and vertigo, but vestibular disturbances were detected only in 34% in the calor ic test and 47% in the CDP testing. These findings are similar to the results of Pollak et al. [10], which demonstrated vestibular involvement in 38.5%. It is interesting that vestibular disturbances appeared to be unrelated to the severity of BD like the auditory disturbances.

Furthermore, the current study demonstrated that the incidence of vestibular involvement in terms of dizziness is more common than the cochlear involvement in terms of hearing loss. This could be attributed to diverse causes of dizziness including peripheral and central causes of dizziness in BD. On the other hand, the lack of correlation between the audiovestibular involvement and the other organs involvement could be attributed to the multifocal nature of the disease process. Moreover, the lack of correlation between the auditory and vestibular manifestations in BD could be explained by understanding the anatomical vascular supply of the inner ear as the saccule, cochlea, and posterior semicircular canal are supplied by the common cochlear artery, while the anterior and horizontal semicircular canals in addition to the utricle are supplied by the anterior vestibular artery. The anterior vestibular artery and the common cochlear artery are the main branches of the labyrinthine artery, but they could be selectively involved by immunologically mediated inflammation, which could explain this lack of correlation [14].

**Conclusion**

The outcome of the current study confirms the association between inner ear dysfunction and BD. Inner ear dysfunction in BD could be attributed to the presence of vasculitis or neuropathy that could happen on top of the chronic inflammation process associated with BD. Therefore, patients with BD should be regularly subjected to otolaryngological evaluation to diagnose and for follow up of any audiovestibular involvement. The positive findings in audiovestibular assessment will be helpful in the proper diagnosis and management of patients with BD.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**


