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Original article

Audiological Profile in Patients with Tinnitus accompanied with Vitamin B12 Deficiency

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Keywords

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Abstract:

Background: Vitamin B12 is a necessary in the methylation response, which results in the formation of myelin. A lack of vitamin B12 may result in demyelination of nerve cells in the cochlear nerve, resulting in hearing loss and tinnitus. **Aim of this work:** To analyze the effect of Vitamin B12 deficiency on auditory brain stem response and otoacoustic emission in patients suffering from tinnitus. **Patients and Methods:** This was a case-control study with 6 male (20.0%) and 24 female (80.0%) with tinnitus as cases (30 participants) and 7 male (23.3%) and 23 female (76.6%) as controls (30 participants). Pure tone audiometry, Auditory Brain Stem Response, Transient evoked otoacoustic emissions ,Detection of the serum levels of Vitamin B12 and Conventional MRI brain were performed . **Results**: There was a statistically

significant delay at wave III latency in cases than the controls in the right side while in the left side, wave I and III latencies were statistically significant prolonged in cases than the controls**.**.There was no statistically significant correlation between vitamin B12 level and the latency or amplitude of auditory brainstem responses. **Conclusion:**Our findings imply that auditory brain stem response results in patients with tinnitus linked with vitamin B12 deficiency can be impacted.

1. Introduction:

Vitamin B12 is an essential in the methylation reaction, which results in the formation of myelin **[1].** Homocysteine accumulation as a result of vitamin B12 insufficiency can promote inflammation in the vascular system, reduced microvessel flow, and permeability.As a result, decreasing auditory blood supply may cause stria vascularis atrophy. **[2].**

Tinnitus is defined as a phantom auditory experience that arises from an origin or initiate in the cochlea, brainstem, or higher centres and has no identifiable acoustic generator **[3].** Tinnitus impacts not just the elderly but also adolescents, manifesting as hearing loss or normal hearing capacity**[4].**

The precise neuro-pathophysiological explanation of tinnitus is yet unknown. Numerous studies have found a link between tinnitus and vitamin Bl2 deficiency, with a putative link between vitamin Bl2 deficiency and auditory tract impairment **[5].**

Auditory brainstem response (ABR) is a type of early evoked potential response. During ABR, five electrical potentials are extracted from the brainstem's overall activity response to a calibrated sound.ABR abnormalities can emerge as a result of demyelination and axonopathy induced by vitamin B12 deficiency, and a postponed identification of vitamin Bl2 deficiency may end up in an advanced neurological condition[6] **.**

Aim of the work :

To analyze the effect of vitamin B12 deficiency on auditory brain stem response and otoacoustic emission in patients suffering from tinnitus.

2. Material and Methods:

Thirty patients with a mean age of 30.36±6.9 years (18-44 years) participated as the study group.The control group consisted of thirty people whose age ranged from 28 years to 58 years, average was 29.1±5.3 years. The control group consisted of either relatives of the cases or regular clinic attendees. They were chosen to be matched in age and gender to the cases. They were chosen because they had normal bilateral hearing sensitivity and middle ear function, no complaints of audio-vestibular disorders , and no systemic disorders that were known to impair the audio-vestibular system. Patients with tinnitus linked with vitamin B12 insufficiency were recruited from the audiovestibular clinic at Beni-Suef University Hospital's faculty of medicine. The research was conducted from July 2022 to March 2023.

Exclusion criteria:

The patients who had other cause as: any degree of conductive or sensorineural hearing loss, head trauma, neck problems or brain lesion presence are excluded. The

ethical committee of Beni-Suef University's Faculty of Medicine approved the study with approval No:FMBSUREC/05072022/Kamel.All participants provided written informed consent.

All tinnitus patients and controls were subjected to the following:

Taking a thorough medical history: This includes a detailed explanation of the tinnitus complaint.Any relevant symptoms, drugs used, or other disorders were disclosed. (a)pure tone audiometry was carried out, with air and bone conduction thresholds ranging from 250 Hz to 8 kHz for air and 500 Hz to 4 kHz for bone. (b) Speech audiometry was performed using the "AD629 by interacoustics" system, which included the Speech Reception Threshold (SRT) using Arabic spondaic words [7] and the word discrimination score (WDS%) using Arabic phonetically balanced (PD) words [8]. (c) Immittentcemetry with tympanometry (single frequency tympanometry) and auditory reflex threshold were assessed .d-Transient evoked otoacoustic emission (TEOAE) was measured using a (Madsen AccuScreen) analyzer and were determined to be present or missing based on visual inspection.e-Auditory Brain Stem Response "ABR" testing was performed on all patients. Interacoustics EP 25 was used to measure latencies (I, III, V), interpeak latencies (I-III, III-V, I-V), I ,III ,V amplitudes and V/I amplitude ratio. At an intensity of 80 dBHL, clicks were delivered at a rate of 21.1 stimuli per second in rarefaction polarity. Two recordings were collected to ensure that the waveforms could be replicated. f-Detection of Vitamin B12 serum levels using an ELISA kit: A level greater than 221pmo1/L is considered normal, and the likelihood of vitamin B12 deficiency is less than 5%. A conventional MRI brain was done.

Statistical analysis:

IBM running the social science statistics package SPSS 25 were used for the analysis; Mean, standard deviation were used to characterize quantitative variables. Quantitative and qualitative breakdown of the relevant factors.The unpaired t-test was used to compare quantitative variables in parametric data, whereas the chi-squared test was used to analyse categorical variables.The pearson chi squares test was used to determine the relationship between scale factors.The significance level was chosen at P 0.05.

3. Results:

This was a case-control study with 60 participants, including 6 male (20.0%) and 24 female (80.0%) with tinnitus as cases (30 participants) and 7 male (23.3%) and 23

female (76.6%) as controls (30 participants). The study group's age ranged from 18 to 44 years, with an average of 30.36.9 years, whereas the control group's age ranged from 28 to 58 years, with an average of 29.15.3 years. They were age and gender matched.

Table (1): showed that there were 14 cases (47%) with unilateral tinnitus and 16 cases (53%) with bilateral tinnitus.The mean duration of tinnitus was 51.2 weeks with median 38 weeks and ranged from 2 weeks to 192 weeks.

Table (1)Characteristics of tinnitus in cases group:

Tinnitus laterality	Unilateral tinnitus 14(47%)
	Bilateral tinnitus 16 (53%)
Tinnitus duration **Mean±SD (weeks)** **Median (min-max)**	 51.2±50 38(2-192)

Table (2) revealed a statistically significant variation in vitamin B12 levels between patients and controls (P-value0.001).

Table (2) Vitamin B12 level in pmol/L of the studied groups:

Vit B12	**Controls (no=30)**	**Cases (no=30)**	**P-value**
Mean±SD	370.7±153.9	60.3±24.3	**<0.001***

*P-value is significant.

Regarding MRI examination: All cases and controls had normal MRI examination.

Table(3) showed that there were no statistically significant differences between cases and controls regarding the pure tone average (PTA) at 250, 500, 1000, 2000, 4000, and 8000 Hz (P-value>0.05).

Table (3) Hearing thresholds in(dBHL) at different frequencies of the studied groups:

PTA (dB) (mean±SD)	Controls (no=30)	Cases (no=30)	P-value
250 Hz	19.66±2.60	20.00±2.27	0.599
500 Hz	20.50±1.52	20.50±2.40	>0.999
1000 Hz	16.33±2.24	16.50±2.33	0.779
2000 Hz	16.50±2.33	16.16±2.15	0.567
4000 Hz	20.00±1.31	19.83±0.91	0.570
8000 Hz	15.83±1.89	15.66±1.72	0.723

*P-value is significant.

Table(4) revealed that there was a statistically significant delay at wave III in cases compared to controls on the right side, while wave I and III were statistically significant delayed in cases compared to controls on the left side.

Table (4) Comparison of auditory brain stem response (ABR) latency in msec in the studied groups (absolute and interpeak):

Latency	Cases (no=30) (mean±SD)	Control(no=30) (mean±SD)	P-value
Right			
I	1.47±0.13	1.44±0.13	0.32
III	3.69±0.18	3.59±0.16	**0.03***
V	5.51±0.25	5.43±0.17	0.17
I-III	2.21±0.23	2.15±0.20	0.30
I-V	4.02±0.27	3.90±0.48	0.21
III-V	1.81±0.18	1.92±0.47	0.24
Left			
I	1.49±0.12	1.41±0.12	**0.02***
III	3.66±0.15	3.57±0.13	**0.01***
V	5.52±0.23	5.44±0.14	0.12
I-III	2.17±0.20	2.15±0.15	0.64
I-V	3.94±0.51	4.02±0.17	0.41
III-V	1.94±0.46	1.87±0.17	0.44

*P-value is significant

Table (5) demonstrated that the amplitudes of ABR waves in patients and controls on both sides did not differ significantly .The difference in V/I amplitude ratio between patients and controls was also insignificant.

Table (5) Comparison of auditory brain stem response (ABR) amplitude in µV in the studied groups:

Amplitude	Controls (no=30) (mean±SD)	Cases (no=30) (mean±SD)	P-value
Right			
I	0.196±0.011	0.169±0.088	0.011
III	0.314±0.023	0.356±0.141	0.113
V	0.472±0.042	0.519±0.130	0.066
V/I ratio	2.402±0.239	2.149±0.952	0.164
Left			
I	0.205±0.007	0.276±0.122	**0.002***
III	0.333±0.022	0.380±0.147	0.093
V	0.503±0.034	0.542±0.129	0.114
V/I ratio	2.451±0.191	2.2803±1.048	0.384

*P-value is significant.

Table(6) showed that there was a statistically significant difference between cases and controls regarding the TEOAE (P-value<0.05).

Table (6) : Transient evoked otoacoustic emission (TEOAE) of the studied groups (Rt and Lt ears):

TEOAE	Controls (no=30)	Cases (no=30)	P-value
Right			
Pass	30(100.0%)	23(76.7%)	**0.011***
Refer	0(0.0%)	7(23.3%)	
Left			
Pass	30(100.0%)	22(73.3%)	**0.005***
Refer	0(0.0%)	8(26.7%)	

*P-value is significant.

Table (7) showed that there was no statistically significant linear correlation between vitamin B12 level and the ABR latency.

Table (7) Correlation between the vitamin B12 level and latencies of ABR waves:

ABR Latencies			Vitamin B12
Rt	I	Correlation coefficient	.071
		P-value	.708
	III	Correlation coefficient	.066
		P-value	.728
	V	Correlation coefficient	.076
		P-value	.689
	I-III	Correlation coefficient	.005
		P-value	.978
	I-V	Correlation coefficient	-.236
		P-value	.208
	III-V	Correlation coefficient	.257
		P-value	.171
Lt	I	Correlation coefficient	.213
		P-value	.258
	III	Correlation coefficient	-.189
		P-value	.318
	V	Correlation coefficient	-.007
		P-value	.972
	I-III	Correlation coefficient	-.317
		P-value	.088
	I-V	Correlation coefficient	-.157
		P-value	.406
	III-V	Correlation coefficient	.139
		P-value	.463

Table (8) showed that there was no statistically significant linear correlation between vitamin B12 level and the ABR amplitudes .

Table (8) Correlation between the vitamin B12 level and the amplitudes of ABR waves:

ABR amplitudes			Vitamin B12 level
Rt	I	Correlation coefficient	.091
		P-value	.633
	III	Correlation coefficient	-.248
		P-value	.186
	V	Correlation coefficient	-.147
		P-value	.439
	V /I ratio	Correlation coefficient	-.164
		P-value	.386
Lt	I	Correlation coefficient	-.088
		P-value	.643
	III	Correlation coefficient	-.260
		P-value	.166
	V	Correlation coefficient	-.317
		P-value	.088
	V /I ratio	Correlation coefficient	-.138
		P-value	.469

Figures (1 and 2)demonstrated a statistically significant negative correlation between disease duration and wave (I) amplitude in both ears.

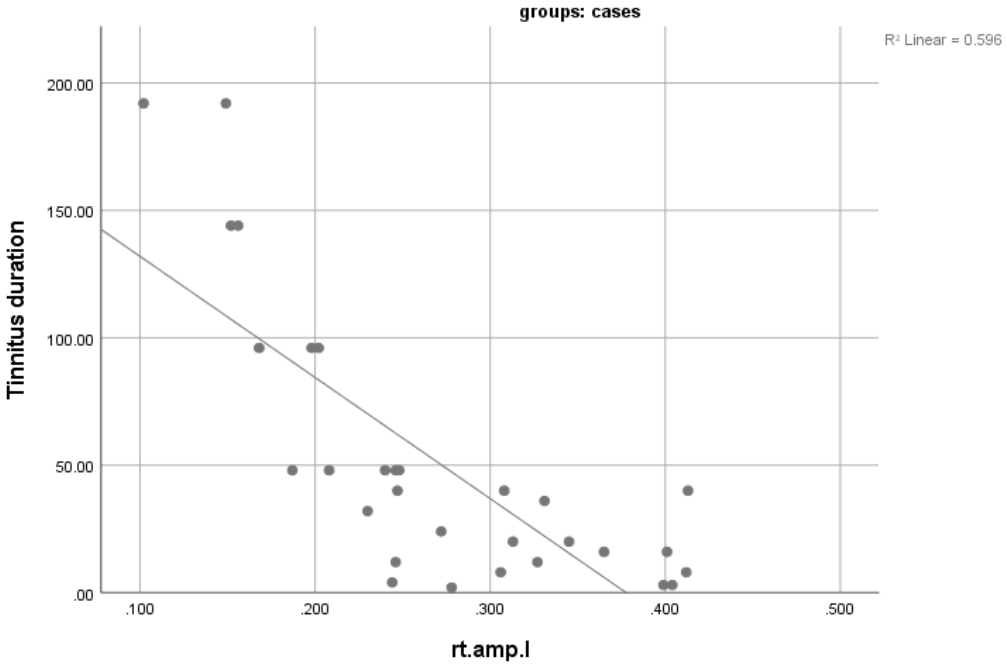

Figure (1) Correlation between tinnitus duration and the right wave I amplitude(amp) in cases

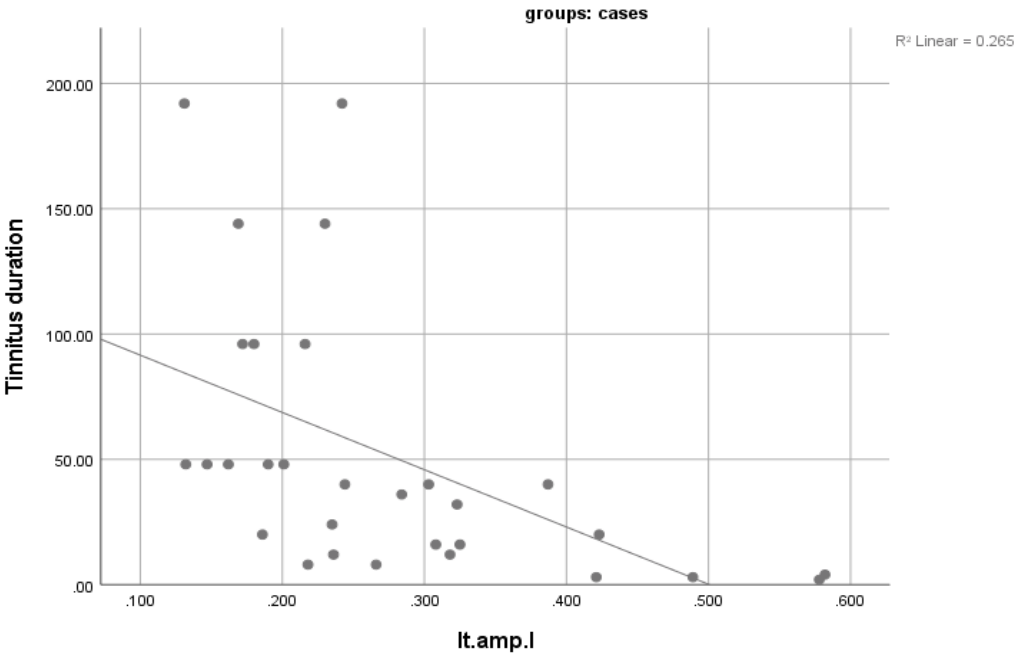

Figure (2) Correlation between tinnitus duration and the left wave I amplitude(amp) in cases

4. Discussion:

Vitamin Bl2 deficiency is widespread and causes significant illness in people of all ages [9]. For cochlear functioning, enough blood supply and healthy nerve tissues are essential. Axonal deterioration, demyelination, and apoptotic death of neurons have all been linked to B12 deficiency. [10].

According to findings from neuroscience, the majority of cases of tinnitus develop by neuroplastic alterations arising in central auditory pathway following impairment of those pathways by destruction to the cochlear transmission mechanism or auditory nerve fibres which express sound information from ribbon synapses on the inner hair cells to brain **[11].**

In the current study, we found that there were 14 cases (47%) with unilateral tinnitus and 16 cases (53%) with bilateral tinnitus (table 1) . Insufficient vitamin Bl2 levels are linked to stria vascularis microvasculature degradation, that may result in diminished endocochlear potential, hearing loss, and tinnitus[12].

In our research, we discovered a statistically significant difference in Vitamin B12 levels between patients and controls (P-value0.001). Tinnitus patients had significantly higher levels of vitamin B12 deficiency (table 2). This could be explained by an inadequate level of vitamin B12, which may result in hearing loss by demyelinating neurons in the auditory nerve. Furthermore, insufficient vitamin B12 and folate intake has been associated to the destruction of the stria vascularis' microvasculature, that may cause hearing loss, tinnitus, and decreased endocochlear potentiality. **[13].**

Regarding ABR findings, we found that there was a statistically significant delay of wave III of ABR in cases than the controls in the right side while in the left side, wave I and III were statistically significant delay in cases than the controls (table 4**)**. Similarly, **Demir et al[14]** discovered that ABR tests findings were abnormal in 7 individuals with serum vitamin B 12 levels of 100 pg/mL. Also,When they compared the patient group to the controls on the basis of ABR I-III, III-V, and I-V interpeak latencies, the patient group had a statistically significant delay. A statistically significant improvement in ABR interpeak latencies was found three months following treatment. Brainstem auditory evoked potential (ABR) abnormalities emerge secondary to demyelination and axonopathy caused by vitamin B12 deficiency, **Demir et al[14]**.

There was no a statistically significant difference in amplitudes of ABR waves in cases and the controls. Also , insignificant difference was detected between cases and

controls regarding V/I amplitude ratio on both sides (table 5).

Turan et al[15] study comprised 30 participants with vitamin B12 deficiency and 30 participants without having a hearing impairment or vitamin B12 deficiency. There was any statistically significant variation in the auditory brain stem response findings regarding wave latencies and amplitudes between the vitamin B12 deficient group and the normal group.

We identified a statistically significant difference in TEOAE between patients and controls in the current study (table 6). Tinnitus appearing as the single symptom in these persons with low plasma vitamin B12 levels suggests that tinnitus may be one of the early symptoms of the many neurological problems related with B12 deficiency. Tinnitus is thought to be produced in this case by auditory nerve dysfunction [16]. This study suggests that a shortage of vitamin B12 has a negative influence on cochlear hearing. Increased methylmalonic acid may lead to neurotoxicity and vasculotoxicity in the inner ear as a result of vitamin B12 deficiency. Homocysteine, which is high in vitamin B12 deficiency, can cause hearing problems in the same way as it is a vasculotoxin and neurotoxic[17].

Thabet et al. [18] used the TEOAE test on 20 patients with normal hearing and unilateral tinnitus complaints. The patients' opposite ear was employed as the control ear in the study. TEOAE responses were abnormal in 85% of the ears with tinnitus complaints, compared to 20% of control ears with abnormal TEOAE responses [18]. TEOAE, on the other hand, did not alter based on the existence or absence of tinnitus in patients with normal hearing [19].

In our study we found that there was no statistically significant linear correlation between vitamin B12 level and the ABR latency (table 7) or amplitude (table 8). While ***Evim et al [20]*** Stated that there was a positive correlation between the degree of vitamin B12 deficiency and the abnormalities of ABR findings.

Figures 1 and 2 show a statistically significant linear negative correlation between disease duration and wave (I) amplitude. An important point in wave I amplitudes was identified in the **(Joo et al,[**21] study, which is consistent with our findings. Non-chronic tinnitus youths had higher wave I amplitudes in tinnitus ears, whereas the majority of chronic tinnitus youths had lower wave I amplitudes.In latent hearing loss, the decreased wave I amplitude is often explained by cochlear synaptopathy, and the matching normal wave V amplitude is experienced as increased central auditory gain [22].

Our findings suggest that ABR and transient otoacoustic emission results could be affected in patients with tinnitus and vitamin B12 deficiency, as evidenced by auditory pathway and cochlea affection in the results of ABR wave I and wave III latencies abnormalities and TEOAE.

5. Conclusion :

There appears to be a link between vitamin B12 deficiency and cochlear function, so the amount of vitamin B12 in the blood should not be overlooked when evaluating auditory function. Although promising, more research on the long-term usefulness of vitamin B12 given orally in an outpatient clinic is required. We expected to collect more important data in cases of long-term B12 deficiency with tinnitus.

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