

# Viral Seroprevalence in Tinnitus

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Cite this article as: Özgüler M, Susaman N. Viral Seroprevalence in Tinnitus. *Cyprus J Med Sci* 2019; 4(3): 251-6.

## BACKGROUND/AIMS

Tinnitus is a common medical problem that disrupts patient comfort. The majority of the reasons accused in the etiology of tinnitus are unknown. The aim of the present study was to determine the serology of the viruses, especially antibodies, related to Herpes Simplex Virus (HSV), Varicella Zoster Virus (VZV), Cytomegalovirus (CMV), Epstein Barr Virus (EBV), measles, mumps, rubella, toxoplasma, and parvovirus B19 in patients with tinnitus. We think that viral infections may be an important factor in tinnitus.

## MATERIAL and METHODS

Enzyme linked immunosorbent assay (ELISA) tests were done for both immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies. For statistical evaluation, the SPSS 15 program was used.

## RESULTS

We found HSV-1 IgM/IgG and anti-VZV IgM/IgG seropositivity as 0% and 80% and 0% and 90%, respectively. Anti-CMV IgM and CMV IgG antibodies were detected as 0% and 100%, respectively, and Epstein Barr Virus Viral Capsid Antigen (EBV VCA) IgM, EBV VCA IgG, Epstein Barr Virus Nuclear Antigen (EBNA) IgM, and EBNA IgG seropositivity as 0%, 90%, 0%, and 95%, respectively. Anti-rubella IgM and IgG antibodies were detected as 0% and 90%, respectively. We found anti-measles IgM/IgG and anti-mumps IgM/IgG seropositivity as 2.5% and 80% and 2.5% and 87.5%, respectively. We determined anti-toxoplasma IgM/IgG antibodies as 0% and 40%, respectively, and parvovirus B19 IgM/IgG seropositivity as 5% and 95%, respectively.

## CONCLUSION

Infections may be a cause for tinnitus. When our results were compared with both international and national studies for parvovirus serology, higher rates for parvovirus B19 seropositivity have been observed in patients with tinnitus in our study. More comprehensive and more patients included in the studies may contribute to the literature.

**Keywords:** Parvovirus B19, seroprevalence, tinnitus, viral infections

## INTRODUCTION

Tinnitus is a common medical problem that disrupts patient comfort. It is described as a perception of sound in the absence of an external source. In recent studies, the prevalence of tinnitus is estimated to be 10%–15%. Mild to moderate complaints have been reported in 60% of patients, while severe complaints have been seen in 40% of patients (1).

The majority of the reasons accused in the etiology of tinnitus are unknown. Generally, tinnitus can be categorized as continuous, intermittent, or temporary clinically. Continuous tinnitus and intermittent tinnitus are described as chronic tinnitus, whereas temporary tinnitus is considered as an acute episode and does not have a potential for recurrence (2).

The known etiology of tinnitus are peripheral auditory lesions, sudden sensorineural hearing loss, noise exposure or noise-induced hearing loss (most common cause), head or neck trauma, chronic neck or jaw problems, systemic ototoxic therapies, acute or chronic otologic infection, or iatrogenic (surgery) causes. Alternatively, damage or compression of the auditory nerve (e.g., microvascular compression from skull base mass and vestibular schwannoma) can also lead to tinnitus perception. It is emphasized that the face and neck can directly influence the central auditory neural pathways (3).

In addition, temporomandibular joint disorders; cervical spine disorders including arthritis, cervical spine joint, and intervertebral disk degeneration; fibromyalgia; and whiplash injuries have been linked with tinnitus perception. The accused neural mechanisms include the specific trigeminal nerve and cervical inputs (3).

The majority of infectious agents can cause head and neck inflammation, and some of the viruses cause nerve-related latent infections. The herpesvirus family all cause latent infections in humans. Latency with all herpesviruses in humans is probably associated with frequent subclinical reactivation, which may lead to neuronal inflammation (4-6).

Latency is described as infectious agents, especially viruses, that cause chronic persistent infections by escaping a cell-mediated immune response. A reactivated virus may spread and initiate an epidemic among susceptible contacts, such as Varicella Zoster Virus (VZV). Viral latency can also be seen in the development of several chronic diseases dependent on the immunological response. Examples of latent infection include rubella, cytomegalovirus (CMV), ebstein barr Virus (EBV), hepatitis B virus (HBV), human immunodeficiency virus (HIV), latent Herpes simplex virus (HSV), VZV, adenovirus, and progressive rubella panencephalitis. Latent viral infections affect the incidence and pathogenesis of acute viral disease in several ways (4).

In the present study, we aimed to determine the serology of the viruses, especially viruses that have latency potential, such as HSV, VZV, CMV, and EBV. Furthermore, anti-measles, anti-mumps, anti-rubella, anti-toxoplasma, and parvovirus B19 antibodies were detected in patients with tinnitus. We think that latent viral infections may cause intermittent reactivation and cause neural inflammation and recently tinnitus.

## MATERIAL and METHODS

### Patients

The study was conducted between December 2018 and April 2019. Firat University ethical approval [2019/10 (03); Date 13.06.2019; Approval No: 10 (03)] and informed consent were obtained. Inclusion criteria were as follows:

- No complaints about infectious diseases,
- No chronic metabolic diseases (e.g., malignancies, diabetes, and hypertension),
- No drug use,
- Without defined allergic disorder.

Five cc blood samples were collected, sera were obtained, and ELISA tests (Architect-Abbott, USA) were done for hepatitis B virus surface antigen (HBsAg), hepatitis B virus surface Antibody (anti-HBs), hepatitis C virus antibody (anti-HCV), human immunodeficiency virus antibody (anti-HIV), HSV immunoglobulin (Ig)M, HSV IgG, CMV IgM, CMV IgG, VZV IgM, VZV IgG, ebstein barr virus viral capsid antigen (EBV VCA) IgM, EBV VCA IgG, ebstein barr virus Nuclear Antigen (EBNA- IgM), EBNA IgG, ebstein barr virus early antigen (EBV EA) IgM, EBV EA IgG, anti-rubella IgM, anti-rubella IgG, anti-measles IgM, anti-measles IgG, anti-mumps IgM, anti-mumps IgG, parvovirus

B19 IgM, parvovirus IgG, toxoplasma IgM, and toxoplasma IgG immediately.

### Statistical Analysis

The Statistical Package for the Social Sciences 15 program (SPSS Inc.; Chicago, IL, USA) was used for statistical evaluation.

## RESULTS

A total of 40 (28 male and 12 female) patients were included in the study. The mean age of the patients was 51±11 years. The demographic characteristics and results of the patients are presented in Table 1.

We found HSV-I IgM/IgG and anti-VZV IgM/IgG seropositivity as 0% and 80% and 0% and 90%, respectively. Anti-CMV IgM and CMV IgG antibodies were detected as 0% and 100%, and EBV VCA IgM, EBV VCA IgG, EBNA IgM, and EBNA IgG seropositivity as 0%, 90%, 0%, and 95%, respectively. Anti-rubella IgM and IgG antibodies were detected as 0% and 90%, respectively. We found anti-measles IgM/IgG and anti-mumps IgM/IgG seropositivity as 2.5% and 80% and 2.5% and 87.5%, respectively. We determined anti-toxoplasma IgM/IgG antibodies as 0% and 40%, respectively, and parvovirus B19 IgM/IgG seropositivity as 5% and 95%, respectively. The mean antigen/antibody titers of the positive groups are presented in Table 2.

## DISCUSSION

In present study, we evaluated Toxoplasma- Other- Rubella-Cytomegalovirus-Herpes (TORCH), mumps, parvovirus, EBV, and CMV antibodies in patients who have complaints of tinnitus. In our study, we found HSV-I IgM and IgG seropositivity as 0% and 80%, respectively. In the international literature, HSV-I mean seroprevalence has been presented as 88.4%–99.2% in those adults (7, 8). In Turkey, there is limited study about HSV serology. In a study from Turkey, anti-herpes simplex IgG and IgM antibodies have been detected as 73.8%–80.0% and 28.6%, respectively (9, 10). Our results were found to be lower than foreign national studies but similar as studies from Turkey. Our lower rates can be related to socioeconomic differences and also to different age groups. In our study, the mean age of the patients was 51 years.

In the present study, we found VZV IgM and IgG seropositivity as 0% and 90%, respectively. In a previous study, varicella seroprevalence has been found to be 97.8% (11). In different ethnic groups, VZV seroprevalence has been reported as 95% among women born in the United Kingdom (UK) and 90% among South Asian women born in Asia (12). In a study from Turkey by Kayın et al. (13), 3570 samples have been tested, and VZV IgM seropositivity and seronegativity have been reported as 7.6% and 89%, respectively. The number of VZV IgG seropositivity and seronegativity has been reported as 72.2% and 23.2%, respectively. In another study, VZV seropositivity rate has been reported as 99.7% in healthcare workers (14). Our results are similar as other foreign literature's results and Ciliz's study (14). However, our results are higher than Kayın et al.'s study. The reason can be related to differences in age groups.

We found CMV seropositivity rates for CMV IgM and CMV IgG antibodies as 0% and 100%, respectively. In international stud-

**TABLE 1.** Demographic characteristics and test results

<b>A. Demographic characteristics</b>	
• Male/female, n (%)	28/12 (70/30)
• Mean age (year)	51±11
<b>B. Test values</b>	
	<b>Results, n (%)</b>
• HBsAg positivity	4 (10)
• Anti-HBs positivity	22 (55)
• Anti-HCV positivity	2 (5)
• Anti-HAV IgG positivity	40 (100)
• Anti-HIV positivity	0 (0)
• HSV IgM positivity	0 (0)
• HSV IgG positivity	32 (80)
• CMV IgM positivity	0 (0)
• CMV IgG positivity	40 (100)
• VZV IgM positivity	0 (0)
• VZV IgG positivity	36 (90)
• EBV VCA IgM positivity	0 (0)
• EBV VCA IgG positivity	36 (90)
• EBNA IgM positivity	0 (0)
• EBNA IgG positivity	38 (95)
• Anti-rubella IgM positivity	0 (0)
• Anti-rubella IgG positivity	36 (90)
• Anti-measles IgM positivity	1 (2.5)
• Anti-measles IgG positivity	32 (80)
• Anti-mumps IgM positivity	1 (2.5)
• Anti-mumps IgG positivity	35 (87.5)
• Parvovirus B19 IgM positivity	1 (2.5)
• Parvovirus B19 IgG positivity	38 (95)
• Toxoplasma IgM positivity	0 (0)
• Toxoplasma IgG positivity	16 (40)
• VDRL	0 (0)
• TPHA	0 (0)

HBsAg: Hepatitis B Surface antigen; Anti-HBs: Hepatitis B Surface Antibody; Anti-HCV: Hepatitis C virus Antibody; Anti-HAV IgG: Hepatitis A virus Antibody Immunoglobulin G; Anti-HIV positivity: Human Immunodeficiency Virus Antibody; HSV IgM: Herpes Simpleks Virus Immunoglobulin M; HSV IgG: Herpes Simpleks Virus Immunoglobulin G; CMV IgM: Cytomegalovirus Immunoglobulin M; CMV IgG: Cytomegalovirus Immunoglobulin G; VZV IgM: Varisella zoster virus Immunoglobulin M; VZV IgG: Varisella zoster virus Immunoglobulin G; EBV VCA IgM: Epstein Barr virus Immunoglobulin M; EBV VCA IgG: Epstein Barr virus Immunoglobulin G; EBNA IgM: Epstein Barr Virus Nuclear Antigen Immunoglobulin M; EBNA IgG: Epstein Barr Virus Nuclear Antigen Immunoglobulin G; VDRL: Venereal Diseases Research Laboratory, TPHA: Treponema Pallidum Hemagglutination Assay

ies, CMV seroprevalence was 49% among White British women, 89% among South Asian UK born women, and 98% among South Asian women born in South Asia (12). In studies from Turkey, anti-cytomegalovirus antibodies were detected as 80.0% in the study group (9). Seropositivity rates of CMV IgM and IgG antibodies were 0.1% and 99.8%, respectively (15). These differences remained after adjusting for socio-demographic factors, vaccination history, and ages.

**TABLE 2.** Cut-off values, mean antigen/antibody titers, 95% confidence intervals, and minimum–maximum ranges

<b>Antigen/antibody</b>	<b>Test cut-off value for positivity</b>	<b>Mean positive titers</b>	<b>95% CI</b>	<b>(Min–max) Range</b>
HBsAg	>0.99	1825		(0.06–3297)
Anti-HBs	>999	274		(0–1000)
Anti-HCV	>0.99	1.63		(0–1.63)
Anti-HAV IgG	>0.99	95		(0–12.05)
HSV IgM	>1	0.30	0.17–0.43	(0.16–0.62)
HSV IgG	>5	45.5	1.3–52.4	(0.34–100)
CMV IgM	>0.85	0.23	0.8–0.38	(0.06–0.56)
CMV IgG	>6	212.7	191–234	(93–250)
VZV IgM	>9	1.6	1.1–2.2	(0.69–2.7)
VZV IgG	>9	16	9.6–23.5	(5.5–940)
EBV VCA IgM	>0.9	0.26	0.4–0.47	(0.07–0.84)
EBV VCA IgG	>1.1	4.35	3.3–5.3	(2.6–5.7)
EBNA IgM	>1	0.21	0.11–0.33	(0.10–0.39)
EBNA IgG	>1	2.04	1.4–2.6	(1.5–3.5)
Anti-rubella IgM	>1	0.16	0.006–0.32	(0.0–0.52)
Anti-rubella IgG	>5	86.2	7.5–165	(1.70–476.4)
Anti-measles IgM	>9	3.08	1.7–4.3	(0.25–11.90)
Anti-measles IgG	>9	21.5	14–29	(2.80–34.9)
Anti-mumps IgM	>9	2.7	1.7–3.6	(0.48–19.70)
Anti-mumps IgG	>9	20.8	13.3–28.2	(4.9–34.7)
Parvovirus B19 IgM	>0.9	0.25	0.18–0.33	(0.20–0.47)
Parvovirus B19 IgG	>2	27	14.5–39.7	(5–43)
Anti-toxoplasma IgM	>1	0.14	0.07–0.22	(0.08–0.34)
Anti-toxoplasma IgG	>1.6	14.8	1.1–3.2	(0.03–24.9)

CI: confidence interval; HBsAg: Hepatitis B Surface antigen; Anti-HBs: Hepatitis B Surface Antibody; Anti-HCV: Hepatitis C virus Antibody; Anti-HAV IgG: Hepatitis A virus Antibody Immunoglobulin G; HSV IgM: Herpes Simpleks Virus Immunoglobulin M; HSV IgG: Herpes Simpleks Virus Immunoglobulin G; CMV IgM: Cytomegalovirus Immunoglobulin M; CMV IgG: Cytomegalovirus Immunoglobulin G; VZV IgM: Varisella zoster virus Immunoglobulin M; VZV IgG: Varisella zoster virus Immunoglobulin G; EBV VCA IgM: Epstein Barr virus Immunoglobulin M; EBV VCA IgG: Epstein Barr virus Immunoglobulin G; EBNA IgM: Epstein Barr Virus Nuclear Antigen Immunoglobulin M; EBNA IgG: Epstein Barr Virus Nuclear Antigen Immunoglobulin G

We evaluated EBV VCA IgM, EBV VCA IgG, EBNA IgM, and EBNA IgG as 0%, 90%, 0%, and 95%, respectively. EBV seroprevalence has been reported as 94% in a previous literature (12). In a previous study, EBV VCA IgG has been reported as 90% seroprevalence after the age of 26 years (16). In another study, mean EBV seropositivity has been found to be 96.4%–97.9% (11, 17). Our results are similar with the literature.

Anti-rubella IgM and IgG antibodies were detected in our study group and their seropositivity rates were found to be 0% and 90%, respectively. In the international literature, rubella seroprevalence has been reported as 87.6%–90.4% (11, 18). In Turkey, the seropositivity rate of rubella IgG has been found to be 94%–98.8% (9, 15, 18). In a study from our country, 613 pregnant women have been evaluated for rubella antibodies, and rubella IgG seroprevalence

has been found to be 99.5% and IgM antibodies have been found to be 0.3% (19). Our results are similar with the literature.

In our study, we found anti-measles IgM and IgG seropositivity as 2.5% and 80%, respectively. Measles susceptibility was found to be 20% in our patients. In a previous study, the seroprevalence rates of measles-specific IgG antibodies have been found to be 94.1%, 94.2%, and 96.6% in Rwandan patients, Swedish patients, and Swedish students, respectively (20). In previous studies, the seroprevalence rate of measles-specific IgG antibodies has been reported as 88%–95% (11, 21). In a study conducted in all healthcare workers, measles immunity has been detected as 88.1%. In a comprehensive report, measles immunity has been evaluated in age groups and found to be 72% in ages 18–25 years, 88.8% in ages 26–35 years, 95.2% in ages 36–45 years, and 91.8% in ages >45 years, respectively (22).

In a literature from Turkey, a total of 803 sera have been tested for anti-measles antibodies. Seropositivity rate has been reported as 90.4% for measles IgG (23). The percentage of susceptibility to measles has been found to be 0.24% (24). Our results appear to be lower than the literature. It can be related to vaccination history of the patients.

In our study, we found anti-mumps IgM and IgG as 2.5% and 87.5%, respectively. In a previous study, mumps seropositivity has been tested among measles seropositives, and the rate has been detected as 87.0% (18). In a study from Turkey, mumps seroprevalence has been reported as 90.4% (23). Our results are similar with the literature.

In our present study, we determined anti-toxoplasma IgM and IgG antibodies as 0% and 40%, respectively. The sensibility to toxoplasma was found to be 60%. In a previous study, anti-toxoplasma IgG has been found to be 29.9% among the participants, and anti-toxoplasma IgM has been detected as 0.37%. In another study, toxoplasma seroprevalence has been studied in pregnant women, and the seroprevalence in the first, second, and third trimesters has been reported as 30.4%, 30.6%, and 26.1%, respectively (25). In a meta-analysis, Malary et al. (26) investigated 43 studies with a total sample size of 22,644 for toxoplasma seroprevalence. The pooled seroprevalence of anti-toxoplasma IgG and IgM antibodies has been reported as 41.3% and 4.0%, respectively. In another meta-analysis, Mizani et al. (27) reported *Toxoplasma gondii* seroprevalence in Iranian women and found to be 43% in pregnant women and 33% in girls and the childbearing age groups. Our results are similar with Malary's and Mizani's meta-analysis.

In a literature from Turkey, anti-toxoplasma antibodies have been presented as 31.7% (9). In addition, in a previous study, 804 serum samples have been collected from pregnant women, and toxoplasma IgM and IgG seropositivity rates have been found to be 0.2% and 36.9%, respectively (15). In another study, toxoplasma serologies have been evaluated in pregnant women, and toxoplasma IgG seropositivity has been found to be 36.0% and toxoplasma IgM seropositivity has been found to be 0.3% (19). In a different study, anti-*T. gondii* IgG seropositivity and anti-*T. gondii* IgM seropositivity have been calculated as 41.1% and 4.3% in pregnant women, respectively (28). In addition, 3340 pregnant women were evaluated for toxoplasma IgM and IgG

antibodies. IgM and IgG seropositivity rates have been found to be 3.6% and 57%, respectively (29). Our results are in the range of reported rates in Turkish studies.

In the present study, we found parvovirus B19 IgM seropositivity and seronegativity as 5% and 95%, respectively. In addition, parvovirus B19 IgG was found to be 95%. Dual positivity was not seen in the group. In a previous study, 6583 sera have been collected from adults, and 649 sera have been collected from healthy Thuringian children and adolescents. The overall parvovirus B19 seroprevalence has been found to be 72.1% in adults, 66.9% in adolescents (18–19 years), and 79.1% in the elderly. In another study, parvovirus seroprevalence has been detected as 75% in those aged >45 years (30). Similar rates have been reported in the European population when Belgian (74%), Italian (79%), and German (77%) blood donors were tested (31–33). In another study, a total of 1633 samples have been evaluated for parvovirus B19 IgM, and 540 samples have been detected for both parvovirus B19 IgM and IgG antibodies. Parvovirus B19 IgM antibodies have been found to be 7.53%, and seroprevalence of IgG antibodies has been found to be 27.96%. Dual positivity (IgG and IgM) has been found to be 2.40% (34).

In a study from Turkey, a total of 156 pregnant women have been analyzed for parvovirus B19. While parvovirus B19 IgG has been found to be 64.7%, parvovirus B19 IgM positivity alone has been detected in any women. Both parvovirus B19 IgG and IgM have been found to be 1.9% (35). In studies conducted in different patient and age groups, parvovirus seroprevalence has been reported as 16%–64% (36–41). When both international and national studies for parvovirus serology were compared, it appeared that parvovirus B19 seropositivity was detected to be higher in patients with tinnitus.

In conclusion, infections may be a cause for tinnitus. There are many rates about viral seroprevalence in the literature. However, to the best of our knowledge, this is the first study conducted in patients with tinnitus. When both international and national studies for parvovirus serology were compared in different patient groups, higher rates for parvovirus B19 seropositivity have been observed in patients with tinnitus in the present study. More comprehensive and more patients included in the study may contribute to the literature.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Firat University Ethical Committee [2019/10 (03); Date 13.06.2019; Approval No: 10 (03)].

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – M.Ö., N.S.; Design – M.Ö., N.S.; Supervision – M.Ö., N.S.; Materials – M.Ö., N.S.; Data Collection and/or Processing – M.Ö., N.S.; Analysis and/or Interpretation – M.Ö.; Literature Search – M.Ö.; Writing Manuscript – M.Ö., N.S.; Critical Review – M.Ö., N.S.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.



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