ORIGINAL ARTICLE

Eastern Journal of Medicine

East J Med 30(4): 596-601, 2025
DOI:10.55052/ejm.2025.76429

Prevalence of Cytomegalovirus İnfection in Pregnant Women in Van, Turkey

Latif Hacıoğlu[1*], Gürcan Türkyilmaz[2], Ersin Onat[1], Cagri Ates[1], Onur Karaaslan[1], Erbil Karaman[1], Hanım Güler Şahin[1]

[1]Van Yuzuncu Yil University, Faculty of Medicine, Department of Obstetrics and Gynaecology, Van, Turkey
[2]Lokman Hekim University, Faculty of Medicine, Department of Obstetrics and Gynaecology, Ankara, Turkey

ABSTRACT

This study aimed to investigate the seropositive rates of pregnant women against CMV infection and compare seroprevalence in different age groups in Van. This study aimed to investigate the seropositive rates of pregnant women against CMV infection and compare seroprevalence in different age groups in Van.

The CMV serology results of 1665 women screened in the first trimester of pregnancy were evaluated between January 2022 and January 2024. The cohort's pregnant women were divided into three groups based on maternal age to make a comparison. Group 1 consisted of pregnant women aged 18-24, group 2 of pregnant women aged 25-35, group 3 of pregnant women over 35 years old. Categorical values were analysed by the chi-square test. A p-value <0.05 was considered statically significant.

The mean maternal age was 29.2±5.9 (range 18-43) years. CMV IgM was positive in 1.6%, 1.3% and 1.2% of women in group 1, group 2 and group 3 respectively. There was no significant difference in CMV IgM positive rates between age groups (p: 0.87). CMV IgG-positive women composed 95.8%, 96.3% and 97.8% of the population and it was similar among groups (p: 0.71). In our cohort 3.5% of women were seronegative and 96.5% were seropositive in CMV serology screening. CMV IgM, IgG were positive in 24 (1.4%) pregnant women CMV IgG avidity was high in 18, low in 4 and intermediate in 2 women.

Our results demonstrate that CMV seropositive rate is very high in our region and seroprevalence is similar between young and older women.

Keywords: Cytomegalovirus, pregnancy, screening, seroprevalence

Introduction

Cytomegalovirus (CMV) is a member of the highly species-specific Herpesviridiae family. Humans are its only host. CMV infects monocytes, macrophages, and endothelial cells, but it can reproduce in most cell types. When acquired during pregnancy, CMV infection is asymptomatic in about 90% of women or represented with flu-like symptoms in the remaining cases.

CMV is the most prevalent cause of congenital infection, the primary nongenetic cause of sensorineural hearing loss (SNHL), the primary infection-related cause of congenital malformations, and a significant cause of neurologic disability. It is responsible for 8–21% of all congenital SNHL at birth and up to 10% of all cases of cerebral palsy (2, 3). 1 kaynak yok 2 ve 3. Kaynağa geçilmiş revise edilmelidir

CMV can present as a primary infection (PI) or a non-primary infection (NPI) when a later reactivation or reinfection occurs. Since around 90% of pregnant women exhibit asymptomatic PI, clinical observations rarely detect it, making serological tests the primary diagnostic method. Seroconversion indicates the PI. When seroconversion remains unproven, a combination of IgG, IgM, and IgG avidity patterns aids the diagnosis. On the other hand, serological tests in NPI can be wrong because IgM can last for a long time or IgM reacts with CMV serological kits. Typically, the serological diagnosis of recurrent infection relies on an increasing IgG titer and a high IgG avidity index; however, serological testing may fail to diagnose NPI due to the detection of other serological patterns (4). Therefore, amniocentesis and a CMV-PCR test in amniotic fluid are the only conclusive tests for fetal infection following maternal NPI.

***Corresponding Author:** Latif Hacıoğlu, Faculty of Medicine, Department of Obstetrics and Gynecology, Van Yuzuncu Yıl University, Van, Turkey
E-mail: latifhacioglu@yyu.edu.tr, Phone Number: +90 (507) 472 53 53, Fax: +90 432 225 17 47
ORCID ID: Latif Hacıoğlu: 0000-0001-5843-3237, **Gürcan Türkyilmaz:** 0000-0002-5514-0233, **Ersin Onat:** 0000-0002-6153-241X, **Cagri Ates:** 0000-0001-5341-4950, **Onur Karaaslan:** 0000-0002-4599-1173, **Erbil Karaman:** 0000-0003-1058-2748, **Hanım Güler Şahin:** 0000-0002-8596-0734
Received: 06.03.2025, **Accepted:** 05.09.2025

Both maternal and neonatal universal screening programs are not routinely available worldwide. The prevalence of neonatal infection correlates with maternal seroprevalence ranging from 0.4 to 1% in countries with low, intermediate, and high seroprevalence, respectively. NPI are responsible for the majority of congenital CMV infections in countries with high seroprevalence (5). Since serology does not aid in the diagnosis of NPI, conducting serology screening tests in regions with high seroprevalence is not a rational decision.

We aimed to investigate the seroprevalence of CMV IgM and IgG antibodies in pregnant women in our province of Van, Turkey, between 2022 and 2024 and to determine the effectiveness of serology screening in the first trimester of pregnancy in various age groups.

Material and Methods

In our study, the CMV serology results of 1665 women screened in the first trimester of pregnancy were evaluated between January 2022 and January 2024. The data of serology results were obtained from the laboratory automation system. The local ethics committee permitted the clinical study, and patients submitted signed informed consent. Relevant clinical data was obtained from patients' electronic medical records.

The cohort's pregnant women were divided into three groups based on maternal age to make a comparison. Group 1 consisted of pregnant women aged 18-24, group 2 of pregnant women aged 25-35, and group 3 of pregnant women over 35 years old.

The serum samples were studied with the Cobas e 602 (Roche Diagnostics, Switzerland) system using the electrochemiluminescence immunoassay ECLIA method. The results were evaluated as negative and positive values based on the kit manufacturer's cut-off values. A value <0.85 COI was negative and a value >0.9 COI was considered as the positive index value for CMV IgM, while a value of <0.5 U/ml was considered negative and >1.0 U/ml positive for CMV IgG. When CMV IgM was positive and IgG was negative the serology test was performed three weeks later and if the CMV IgM negative and IgG positive detected it was assumed as seroconversion and PI was verified. In women with both positive CMV IgM and IgG, a CMV IgG avidity test was conducted to determine whether acute or chronic infection. A CMV Ig G avidity index greater than 65% was considered high avidity which indicates infection passed before more than 12 weeks however less than 40% was considered low avidity and used as a potential marker for acute infection. Values ranging from 40 to 65% were considered intermediate, and further investigations were carried out.

In women with high avidity, no further evaluation was performed and routine obstetric care was carried out. For patients with low avidity amniocentesis was performed in 20 weeks of gestation and CMV PCR analysis was performed in amniotic fluid. For women who did not accept invasive procedures detailed counselling about perinatal CMV infection was provided and serial detailed fetal sonography and fetal neurosonography were performed. In neonates suspected of perinatal CMV infection, CMV PCR tests were conducted in saliva or urine within 3 weeks of life.

All data analyses were performed using SPSS (Statistical Packages for the Social Sciences) software, version 22.0 (SPSS Inc., Chicago, USA). Numbers and percentages were used as descriptive statistical methods to evaluate the data. Categorical values were analysed by the chi-square test. A p-value <0.05 was considered statically significant.

Results

We recruited 1665 women for analysis in our study. The mean maternal age was 29.2±5.9 (range 18-43) years. CMV IgM was positive in 1.6%, 1.3% and 1.2% of women in group 1, group 2 and group 3 respectively. There was no significant difference in CMV IgM positive rates between age groups (p: 0.87). 98.5% of all the women were CMV IgM negative and there was no significant difference in the groups (p: 0.75). CMV IgG negative women distribution were 4.2%, 3.6% and 2.1% in groups and it was similar between age groups (p: 0.56). CMV IgG-positive women composed 95.8%, 96.3% and 97.8% of the population and there was no significant difference between age groups (p: 0.71). In our cohort 3.5% of women were seronegative and 96.5% were seropositive in CMV serology screening (Table 1 and Graphic-1).

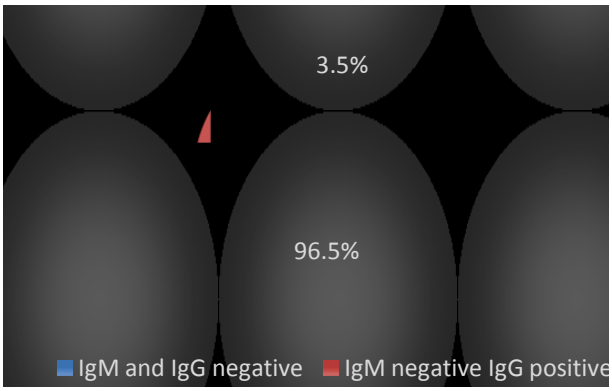
CMV IgM and IgG were positive in 24 (1.4%) pregnant women and a CMV IgG avidity test was conducted to determine whether acute or chronic infection. Low CMV IgG avidity was detected in 2 women in both group 1 and group 2 and there was no low avidity patient in group 3. In addition, 6, 9 and 3 women had high avidity in group 1, group 2 and group 3 respectively. A total of 18 women

Table 1: CMV IgM and IgG Serology Results According To Patients' Age Groups In Two Years (N:1665)

CMV serology	Group 1 n(%)	Group 2 n(%)	Group 3 n(%)	Total n(%)	p-value
CMV IgM positive	8 (1.6)	13 (1.3)	3 (1.2)	24 (1.4)	0.87
CMV IgM negative	488 (98.3)	918 (98.6)	235 (98.8)	1641 (98.5)	0.75
CMV IgG positive	475 (95.8)	897 (96.3)	233 (97.8)	1605 (96.3)	0.71
CMV IgG negative	21 (4.2)	34 (3.6)	5 (2.1)	60 (3.6)	0.56

Table 2: CMV IgG Avidity Results in CMV IgM and CMV IgG-Positive Patients

CMV IgG avidity	Group 1 n(%)	Group 2 n(%)	Group 3 n(%)	Total n(%)
High avidity	6 (75)	9 (69.2)	3 (100)	18 (75)
Low avidity	2 (25)	2 (15.3)	0	4 (16.6)
Intermediate avidity	0	2 (15.3)	0	2 (8.3)



Graphic 1: Distribution of CMV seronegative and seropositive pregnant women in total cohort

with high avidity, 4 women with low avidity and the remaining 2 women with intermediate avidity were detected. Due to low patient numbers statistical analysis was not performed among the three age groups with both CMV IgM and IgG positive (Table-2).

Among women with low avidity, only 1 case accepted amniocentesis and the CMV PCR result was negative in amniotic fluid. The remaining 3 cases were counselled comprehensively about perinatal CMV infection and serial detailed ultrasound and fetal neurosonography were performed. In 2 fetuses detailed fetal anatomic scan and fetal neurosonography were normal otherwise in 1 fetus multiple hyperechogenic punctuations in the liver and hyperechogenic intestines were revealed. Fetal neurosonography and fetal brain MRI were normal. After birth, all three cases were analysed for perinatal CMV infection. In two cases who had normal sonographic features antenatally were negative for CMV infection and the postnatal course was uneventful. In the last case with multiple hyperechogenic punctuations in the liver and hyperechogenic intestines in the perinatal period, postnatal CMV infection was revealed via urine CMV PCR. Postnatal valacyclovir therapy was initiated.

Discussion

Our data demonstrate that CMV seroprevalence is very high in our region on the eastern side of Turkey. We collected data from 1665 women in the first trimester of pregnancy and showed that the seropositive rate of CMV infection was 96.5%. Furthermore, we showed that seroconversion rates were similar in different age groups. It is well known that maternal seroconversion reflects socioeconomic conditions. The prevalence is higher in individuals with low socioeconomic and low educational status. Also, crowded families are a great risk factor for CMV transmission (6). According to national statistics, the eastern side of Turkey has the lowest income and education level. Our cohort's socioeconomic features may explain our region's high CMV seroconversionon.

Although CMV is the most common perinatal infection and represents a public health concern, neither national nor international organisations recommend maternal or neonatal screening (7). Nonetheless, various obstacles impede effective and simple screening strategies. The first issue to

address is that in countries with low seroprevalence, PI is primarily responsible for prenatal CMV infection, however, this may not be true in countries with high seroprevalence, where NPI is the primary cause of perinatal CMV infection. Maternal serology does not allow the diagnosis of NPI. The second important issue is a lack of effective prevention and treatment actions. Although perinatal valacyclovir therapy demonstrates promising results, more well-designed researches are needed before it is routinely used in clinical practice (8).

The global CMV seroprevalence in women of reproductive age is estimated to be around 86%, with significant differences observed between high- and low-income locations.

The highest rates were reported in the Eastern Mediterranean region, Western Pacific region and African region with over 90%. The lowest rates were shown in the European region about 70% (9, 10).

Seroprevalence significantly influences the prevalence of congenital cytomegalovirus infection and the fraction of congenital CMV infection following either PI or NPI. Numerous studies have shown that in high seroprevalence regions, the rate of congenital CMV infection increases, with most cases occurring after NPI. For example, in France, CMV seroprevalence in pregnant women was reported to be 60%. The prevalence of congenital CMV infection was 0.37%. 52% of cases occurred following PI, whereas 48% occurred after NPI (11). In contrast, in Brazil, CMV seroprevalence was identified at 98%, with a 0.5% prevalence of congenital CMV infection. Furthermore, 90% of congenital CMV cases were caused by NPI, with just 10% occurring after PI (12).

The prevalence of CMV seropositivity in pregnant women was evaluated in various publications in different regions of our country. Koçak and Kan assessed the CMV seropositive rate in the middle of Anatolia between 2016 and 2018 among 3363 pregnancies. They showed that CMV IgG and CMV IgM seropositive rates were 96.4% and 1.7% respectively (13). Inci et al. analysed 1043 pregnant women in the East side of the Black Sea region and revealed that CMV IgM and CMV IgG positive rates were 1.6% and 98.6% respectively (14). Yılmaz and Ucar et al. assessed the CMV serology results of 6798 pregnant women in Erzurum and calculated that the CMV seropositive rate was 99.2% (15). Peker et al. evaluated 3062 pregnant women in İzmir and demonstrated that CMV seroprevalence was 94.2% and there was no significant difference between maternal age groups (16). Altunal et al. compared seropositive rates among Turkish and Syrian refugee pregnant women and found that the CMV IgG positive rate was 99.5% in Turkish and 100% in Syrian refugee women and there was no significant difference (17). We have calculated CMV seropositive and seronegative women as 96.5% and 3.5% respectively. Our results were similar to those of other publications from our country.

The prevalence of neonatal CMV infection is higher in countries where women have a high seropositive rate compared to those with low seroprevalence rates. Moreover, most neonatal CMV infections occur after NPI which is very hard or even impossible to make a diagnosis with serology. In this instance, amniocentesis is the sole diagnostic technique for fetuses exhibiting ultrasound abnormalities associated with CMV. Consequently, precise identification of CMV-related ultrasonography abnormalities is crucial for diagnosing NPI-associated infected fetuses. Prenatal ultrasonographic findings can be gross or subtle and consist of cranial, and extracranial features. Maternal viremia is associated with placental invasion which may result in placentomagaly. After placental invasion, the most frequent extracerebral findings are hyperechogenic bowel and fetal growth restriction. The most common cerebral abnormalities are ventriculomegaly, microcephaly, and cerebral calcifications, usually associated with a first-trimester PI. Other ultrasound signs are more subtle, such as periventricular echogenic halo or intracranial calcifications (18). Although the whole image of a seriously damaged infant with obvious growth restriction, microcephaly, and hydrocephalus is unlikely to go unnoticed, prenatal ultrasonography of newborns with symptomatic congenital CMV infection seldom detects any problem. In foetuses with unknown infectious status, ultrasonography alone has poor accuracy, indicating congenital CMV infection in just one-third of cases and having a positive predictive value of 35% (19). In our cohort, only one fetus with low avidity presented with ultrasound features which showed hyperechogenic bowel and liver punctuations. Unfortunately, we could not perform amniocentesis for fetal diagnosis due to lack of family consent, and congenital CMV infection diagnosis achieved in the neonatal period.

Due to several challenges with prenatal diagnosis, newborn screening may be able to identify cases

not identified during the prenatal period and provide early treatment. Currently, universal neonatal screening is not recommended in any country. Neonatal diagnosis is suggested when maternal PI is documented, compatible neonatal symptoms exist, and newborns fail to pass the universal hearing test. However, neonatal hearing screening will identify only 20-60% of congenital CMV-related sensorineural hearing loss, hence overlooking late-onset cases (20, 21).

There are some limitations of our study. First and foremost, our study's retrospective design and lack of a huge patient cohort are issues. Another issue is that we could not provide information about the socioeconomic status and education level of patients. Also, we can not determine the prevalence of neonatal CMV infection due to the lack of a neonatal screening program.

Our findings showed that CMV seroprevalence is very high in our region and it is compatible with other studies conducted in other regions of our county. Furthermore, there was no significant difference between younger and older women. This table reveals that NPI will be accountable for the majority of neonatal CMV cases in our region. Routine CMV serology screening does not seem logical since NPI is not possible to diagnose with serology. Understanding CMV ultrasonography findings and carefully examining them in each fetus, as well as performing amniocentesis when appropriate, may improve the diagnostic rate of NPI-related CMV infections.

References

1. Smithers-Sheedy H, Raynes-Greenow C, Badawi N, Fernandez MA, Kesson A, McIntyre S, Leung KC, Jones CA. Congenital Cytomegalovirus among Children with Cerebral Palsy. J Pediatr 2017; 181: 267-271.e1.
2. Goderis J, De Leenheer E, Smets K, Van Hoecke H, Keymeulen A, Dhooge I. Hearing loss and congenital CMV infection: a systematic review. Pediatrics 2014; 134: 972-82.
3. Nance WE, Lim BG, Dodson KM. Importance of congenital cytomegalovirus infections as a cause for pre-lingual hearing loss. J Clin Virol 2006; 35: 221-225.
4. Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. Rev Med Virol 2010; 20: 202-213.
5. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol 2007; 17: 253-276.
6. Navti OB, Al-Belushi M, Konje JC; FRCOG. Cytomegalovirus infection in pregnancy - An update. Eur J Obstet Gynecol Reprod Biol 2021; 258: 216-222.
7. Ssentongo P, Hehnly C, Birungi P, Roach MA, Spady J, Fronterre C, Wang M, Murray-Kolb LE, Al-Shaar L, Chinchilli VM, Broach JR, Ericson JE, Schiff SJ. Congenital Cytomegalovirus Infection Burden and Epidemiologic Risk Factors in Countries With Universal Screening: A Systematic Review and Meta-analysis. JAMA Netw Open 2021; 4: e2120736.
8. Fowler K, Mucha J, Neumann M, Lewandowski W, Kaczanowska M, Grys M, Schmidt E, Natenshon A, Talarico C, Buck PO, Diaz-Decaro J. A systematic literature review of the global seroprevalence of cytomegalovirus: possible implications for treatment, screening, and vaccine development. BMC Public Health 2022; 22: 1659.
9. Maltezou PG, Kourlaba G, Kourkouni E, Luck S, Blázquez-Gamero D, Ville Y, Lilleri D, Dimopoulou D, Karalexi M, Papaevangelou V. Maternal type of CMV infection and sequelae in infants with congenital CMV: Systematic review and meta-analysis. J Clin Virol 2020; 129: 104518.
10. Balegamire SJ, McClymont E, Croteau A, Dodin P, Gantt S, Besharati AA, Renaud C, Mâsse B, Boucoiran I. Prevalence, incidence, and risk factors associated with cytomegalovirus infection in healthcare and childcare worker: a systematic review and meta-analysis. Syst Rev 2022; 11: 131.
11. Leruez-Ville M, Magny JF, Couderc S, Pichon C, Parodi M, Bussières L, Guilleminot T, Ghout I, Ville Y. Risk Factors for Congenital Cytomegalovirus Infection Following Primary and Nonprimary Maternal Infection: A Prospective Neonatal Screening Study Using Polymerase Chain Reaction in Saliva. Clin Infect Dis 2017; 65: 398-404.
12. Mussi-Pinhata MM, Yamamoto AY, Aragon DC, Duarte G, Fowler KB, Boppana S, Britt WJ. Seroconversion for Cytomegalovirus Infection During Pregnancy and Fetal Infection in a Highly Seropositive Population: "The BraCHS Study". J Infect Dis 2018; 218: 1200-1204.
13. Kan Ö, Koçak Ö. Cytomegalovirus (CMV) screening results in pregnant women admitted to a tertiary center in the middle Anatolia. Turk Hij Den Biyol Derg 2019; 76: 423-430
14. Inci A, Yener C, Guven D. The investigation of toxoplasma, rubella and cytomegalovirus seroprevalancies in pregnant women in a state hospital. Pam Tıp Derg 2014; 7: 143-146
15. Yilmaz, A., and M. Ucar. Prevalence of Toxoplazma, Cytomegalovirus and Rubella in Pregnant Women in Erzurum, Turkey. Annals of Medical Research 2021; 6: 1123-7.
16. Peker BO, Müderris T, Yurtsever SG, Kaya S. İzmir ilinde gebelerde sitomegalovirüs (CMV) IgG ve IgM antikorlarının seroprevalansı: CMV IgG

avidite testlerinin analizi. Turk Mikrobiyol Cemiy Derg 2022; 52: 56-62.
17. Altunal LN. Seroprevalance of Toxoplasma gondii, Rubella and Cytomegalovirus among pregnant refugees and Turkish women: a retrospective comparative study. South Clin Ist Euras 2018; 29: 235-239.
18. Mappa I, De Vito M, Flacco ME, di Mascio D, D'Antonio F, Rizzo G. Prenatal predictors of adverse perinatal outcome in congenital cytomegalovirus infection: a retrospective multicenter study. J Perinat Med 2022; 51: 102-110.
19. Buca D, Di Mascio D, Rizzo G, Giancotti A, D'Amico A, Leombroni M, Makatsarya A, Familiari A, Liberati M, Nappi L, Flacco ME, Manzoli L, Salomon LJ, Scambia G, D'Antonio F. Outcome of fetuses with congenital cytomegalovirus infection and normal ultrasound at diagnosis: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2021; 57: 551-559.
20. Fowler KB, McCollister FP, Sabo DL, Shoup AG, Owen KE, Woodruff JL, Cox E, Mohamed LS, Choo DI, Boppana SB; CHIMES Study. A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening. Pediatrics 2017; 139: e20162128
21. Boppana SB, Ross SA, Shimamura M, Palmer AL, Ahmed A, Michaels MG, Sánchez PJ, Bernstein DI, Tolan RW Jr, Novak Z, Chowdhury N, Britt WJ, Fowler KB; National Institute on Deafness and Other Communication Disorders CHIMES Study. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. N Engl J Med 2011; 364: 2111-2118.