Seroepidemiology of cytomegalovirus infections in Croatia

Tatjana Vilibic-Cavlek[1,2], Branko Kolaric[3,4], Natasa Beader[2,5], Izabela Vrtar[1], Irena Tabain[1], Gordana Mlinaric-Galinovic[1,2]

[1]Department of Virology, Croatian National Institute of Public Health, Zagreb, Croatia

[2]School of Medicine University of Zagreb, Zagreb, Croatia

[3]Department of Epidemiology, Andrija Stampar Teaching Institute of Public Health, Zagreb Croatia

[4]School of Medicine University of Rijeka, Rijeka, Croatia

[5]Clinical Hospital Centre, Zagreb, Croatia

Author for correspondence:

Tatjana Vilibic-Cavlek, MD, PhD
Department of Virology
Croatian National Institute of Public Health
Rockefellerova 12, 10000 Zagreb, Croatia
e-mail: tatjana.vilibic-cavlek@hzjz.hr

Acknowledgments

This research was supported by the Ministry of Science, Education, and Sports of the Republic of Croatia, Grant No 005-0053443-3447 (to GMG). The authors thank Ljiljana Milasincic, Snjezana Artl, Vesna Cupic, Dubravka Landripet and Ana Pesut for technical assistance. Izabela Vrtar was project associate.

Abstract

Objectives: Cytomegalovirus (CMV) is endemic worldwide, with marked differences in the seroprevalence rates between countries. The aim of this study was to analyze the seroprevalence of CMV infection in Croatia.

Methods: During a three year period (2013-2015), 2438 consecutive serum samples collected from Croatian residents were tested for the presence of CMV IgM and IgG antibodies using enzyme-linked immunoassay. IgM/IgG positive samples were further tested for IgG avidity.

Results: The overall seroprevalence rates for CMV IgG and IgM antibodies were 74.4% and 4.3%, respectively. The IgG seroprevalence differed significantly between population groups: children/adolescents 54.6%, adult general population 77.2%, hemodialysis patients 91.4% ($p<0.001$). CMV seropositivity was strongly age-dependent with prevalence ranging from 53.0% in children less than 10 years to 93.8% in persons above 60 years ($p<0.001$). There was no difference in the prevalence between women with normal pregnancy and women with bad obstetric history. Gender and place of residence was not associated with CMV seropositivity. Using IgG avidity, current/recent primary CMV infection was confirmed by low/borderline avidity index (AI) in 46.7% participants, while in 53.3% high AI indicated CMV reactivation or reinfection. Primary infections were detected mainly in children and adolescents (83.2% and 70.5%), while reactivations/reinfections were common in persons older than 40 (77.0-100%). Reactivations/reinfections were most commonly detected in hemodialysis patients (92.3%). Logistic regression showed that older age and being on hemodialysis were significant predictors of CMV seropositivity.

Conclusions: CMV is widespread in the Croatian population. Older age and being on hemodialysis appeared to be main risk factors for CMV infection.

Key words: cytomegalovirus, seroprevalence, Croatia

Introduction

Cytomegalovirus (CMV) is a ubiquitous virus with high worldwide prevalence ranging from 34%-80% in developed countries to 100% in some parts of Africa [1,2]. Virus is transmitted by close personal contacts through infected body fluids, usually saliva, urine, blood or genital secretions [3]. Primary CMV infections occur mainly in early childhood or adolescence and are usually asymptomatic in otherwise healthy children and adults. Symptomatic CMV infections are typically manifested as a non-specific febrile disease or a mild self-limiting mononucleosis-like syndrome [4]. However, there are many reports of severe or prolonged symptomatic CMV infection in immunocompetent patients [5-7]. After primary infection, CMV establishes a lifelong latent infection that can periodically reactivate [3]. Immunocompromised individuals such as HIV-infected patients, hemodialysis patients and transplant recipients may develop severe CMV disease with a wide spectrum of clinical symptoms including retinitis, hepatitis, colitis, pancreatitis, pneumonitis and encephalitis [8-10]. In addition, pregnant women also represent a risk-group for CMV infection. In seronegative pregnant women, CMV transmission can occur following primary maternal CMV infection. In seropositive women, CMV can cross the placenta during non-primary maternal infection (reactivation of virus or re-infection with a different strain) resulting in congenital CMV infection [11].

In Europe, there is wide range of CMV seroprevalence among countries and different population groups. Prevalence rates are reported to be 41%-92% in children and adolescents [12-15], 45%-94% in adult general population [14, 16-19], 30%-91.5% in pregnant women [20-24] and 68%-99% in hemodialysis patients [25-27].

In Croatia, there are few published studies on the prevalence of CMV infection in selected population groups such as childbearing-aged women and hemodialysis patients [28,29]. The

aim of this study was to analyze the prevalence of CMV infection in the Croatian general population.

Materials and methods

During a three-year period (January 2013-December 2015), a total of 2438 consecutive serum samples were tested for the presence of CMV specific IgM and IgG antibodies. Samples were collected from patients residing all Croatian counties testing at two large medical institutions (Croatian National Institute of Public Health and Clinical Hospital Center Zagreb). There were 1064 males (43.6%) and 1374 females (56.4%) aged one month to 82 years (Figure 1). Patients enrolled in the study were admitted to a routine testing for a preoperative check-up (cardiac surgery, renal transplant program), elevated liver transaminases, lymphatic disorders, neurological disorders, antenatal and postnatal screening, and patients from infertility centers (couples undergoing medically assisted reproduction). Among pregnant women, 238 (76.5%) had a normal pregnancy and 73 (23.5%) had a bad obstetric history (history of intrauterine fetal death, intrauterine growth retardation, stillbirth, and habitual abortions).

Anti-CMV IgM and IgG antibodies were detected using a commercial enzyme-linked immunosorbent assay (ELISA; Vircell, Granada, Spain) and enzyme-linked fluorescent assay (ELFA, Vidas, Biomerieux, Marcy l'Etoile, France). Results were interpreted according to the manufacturer's recommendations: Vircell CMV IgM/IgG, antibody index <9 negative, 9-11 equivocal, >11 positive; Vidas CMV IgM <0.70 negative, 0.70-0.90 equivocal, >0.90 positive, CMV IgG <4 aU/ml negative, 4-6 aU/ml equivocal, >6 aU/ml positive. IgM/IgG positive samples were further tested for IgG avidity to confirm or to rule out primary CMV infection using ELISA (Euroimmun, Lübeck, Germany) or ELFA (Vidas, Biomerieux, Marcy l'Etoile, France).

Statistical analysis

The frequencies are shown with 95% confidence intervals (CI). Difference between groups was assessed using Fischer' exact test. The strength of association between dependent and independent variables was assessed using logistic regression (crude odds ratios; OR, odds ratios adjusted for age and gender; AOR). Due to mother-to-child passive immunity, the youngest age group (<6 months), was excluded from logistic regression models. For statistical analysis, software package STATA/IC ver 11.2 (StataCorp LP, USA) was used. The level of statistical significance was $\alpha = 0.05$.

Results

CMV IgM/IgG seroprevalence according to the characteristics of participant's is presented in Table 1. CMV IgG antibodies were detected in 1815 (74.4%) participants. Women were more often seropositive than men (76.3% *vs*. 72.0%, p=0.015). Of children aged less than 6 months, 84.4% were IgG seropositive indicating transplacentally derived maternal antibodies. A significant progressive increase in IgG seroprevalence with age was observed from 53.0% in children aged 6 months to 9 years to 93.8% in persons older than 60 years (p<0.001). There was no difference in the CMV prevalence among participants residing urban regions (74.4%) and participants residing suburban/rural regions (74.3%, p=0.952). According to population group, seropositivity was lowest in children and adolescents (54.6%) compared to adult general population (77.2%) and hemodialysis patients (91.4%, p<0.001). In pregnant women, there was no difference in the prevalence in women with normal pregnancy and bad obstetric history (78.2% *vs*. 78.1%, p=0.999). Univariate logistic regression showed a steady increase in the strength of association between belonging to an older age group and CMV IgG seropositivity (ORs 2.03-13.3). In addition, adult general population and hemodialysis patients had higher risk for being CMV IgG seropositive compared to children and

adolescents (OR 2.82; 95%CI=2.28-3.48 and 8.83; 95%CI=5.73-13.60, respectively). After standardization for age and gender, being on hemodialysis remained the main predictor of CMV IgG seropositivity (AOR=0.95, 95%CI=1.15-3.41) (Table 2).

CMV IgM antibodies were documented in 105 (4.3%) participants. IgG avidity was low in 38 (36.2%) and borderline in 11 (10.5%) participants indicating current/recent primary CMV infection. In 56 (53.3%) participants, high IgG avidity was found suggesting CMV reactivation or reinfection. Acute infections were most frequently detected in participants aged 6 months-9 years (7.6%) and 20-29 years (6.7%), however they occurred in all age groups (2.4%-4.3%, p=0.005) (table 1). Avidity indices (AI) according to age groups are presented in the Figure 2. Acute primary infections (low AI) were reported mainly in persons younger than 30 years (83.2% aged 6 months-9 years, 75.0% aged 10-19 years, 50.0% aged 20-29 years). In contrast, majority of CMV reactivations/reinfections (high AI) were detected in persons above 40 (76.9%-100%). According to the population group, acute infections were most common in hemodialysis patients (8.6%) compared to 5.0% in children/adolescents and 3.3% in adult general population (p<0.001). Among CMV IgM positive hemodialysis patients, 92.3% showed high AI indicating reactivation or reinfection. In children/adolescents and adult population, prevalence of current/recent primary infection was 80.0%/8.0% and 33.3%/13.0%, respectively (Figure 3).

Discussion

The results of this first large seroprevalence study have demonstrated a high seroprevalence of CMV infection the Croatian general population (74.4%) with significant differences among population groups. Data from European countries showed wide geographical variability. In the general population, seroprevalence in Croatia is comparable to that of Portugal (77%) [14]. Lower prevalence rates were reported in the Netherlands (45.6%) [19], France (49.5%)

[18], Germany (57.25%) [17] and Spain (62.8%) [30], while Hungary, Turkey and Russia showed higher seroprevalence rates (86% and 80.9-94.8%, respectively) [10,13,15,16].

Several European studies have reported a higher CMV seroprevalence in females, although in most instances these differences were small [19,30,31]. Results of this study revealed similar results (76.3% in females *vs*. 72.0% in males). No gender-specific differences were recognized in German adolescents aged 13-16 years [32].

CMV seroprevalence in the Croatian population tends to increase progressively with age from 53.0% in 6 months-9-year-olds to 93.0% in participants older than 60. The only exception to this trend was observed in children less than 6 months who had high prevalence (84.4%) reflecting transient presence of transplacentally derived maternal IgG antibodies. Similar results were found in majority other studies [10,15,18,19,33]. Comparing seroprevalence in the similar age groups, some differences were found in children and adolescents. For example, in Portugal the overall seroprevalence rate (77%) is similar to that of Croatia (74.4%), however, seroprevalence in children/adolescents was higher than in the similar population group in Croatia (64.9%-71.3.5% *vs*. 53.0-55.4%) [14]. Moreover, 82.1% Turkish children were infected with CMV by the age of 6 and 92% by the age of 13 [13].

Several studies published in 1990s-2000s reported higher CMV seroprevalence in hemodialysis patients ranging from 83% to 99.3% [25,26,34]. Croatian hemodialysis patients showed significantly higher seroprevalence rate (91.4%) than adult general population as well (77.2%). In contrast, a Dutch study found the percentage of CMV-seropositive hemodialysis patients within range of the reported prevalence in the general population [27]. Higher prevalence in hemodialysis patients could be explained by the acquisition of CMV through repeated blood transfusions as well as exposure to CMV through contaminated equipment during hemodialysis procedures.

Studies on the prevalence of CMV in childbearing-aged, pregnant and parturient women showed seroprevalence rates of 42.3% in Germany [32], 49% in the United Kingdom [35], 56.3% in Finland [36], 57% in France [22], 62.4% in Poland [37] and 91.5%-97.3% in Turkey [24,38]. Regional differences in CMV seropositivity were observed in Norway (58.5%-72.1%) [23,39] and Belgium (30%-54%) [21,31]. A very low prevalence rate was found in Irish pregnant women (30.4%) [40]. A Russian study reported slightly higher seroprevalence in women with current abortions (81.1%) compared to women with normal pregnancy (78.0%) [20]. There was no difference in CMV seropositivity in Croatian pregnant women with normal pregnancy (78.2%) and pregnant women with bad obstetric history (78.1%).

Place of residence was not found to be a risk factor for CMV seropositivity in Croatia which is consistent with results from Finland [36] and Turkey [13].

In this study, IgM antibodies were detected in 4.3% participants indicating acute CMV infection. Since IgM antibodies could be false positive in some population groups such as hemodialysis patients and pregnant women, serology results should be interpreted with caution. Distribution of acute CMV infections in the Croatian population was bimodal. The highest prevalence of acute infections was reported in children between 6 months and 9 years (7.6%) and young adults between 20 and 29 years (6.7%). A high prevalence documented in young children is probably due to starting attending day-care centers. A study from Belgium demonstrated that probability of CMV seroconversion is significantly associated with the contact with children aged less than 3 years [31]. In addition to contact with young children, a higher prevalence in young adults could be attributable to sexual CMV transmission.

According to population group, acute infections were common in hemodialysis patients (8.6%). Using IgG avidity, recent primary infection (borderline AI) was documented in only 7.7% patients, while in 92.3% high AI indicated CMV reactivation or reinfection.

In conclusion, the results of this study indicate that CMV is widespread in Croatia. More than half of the population (54.6%) is infected by age of 20. Older age and being on hemodialysis appeared to be main risk factors for CMV infection.

Conflict of interests

Authors report no conflict of interests regarding this manuscript.

References

1. Adjei AA, Armah HB, Gbagbo F, Boamah I, Adu-Gyamfi C, Asare I. Seroprevalence of HHV‑8, CMV, and EBV among the general population in Ghana, West Africa. BMC Infect Dis. 2008;8:111.

2. Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. Rev Med Virol. 2010;20:202-13.

3. Hodinka RL. Human cytomegalovirus. In: Versalovic J, Carroll KC, Funke G, Jorgensen JH, Landry ML, Warnick DW, editors. Manual of Clinical Microbiology. 10th ed. Washington, DC: ASM Press; 2011, pp. 1558-74.

4. Lancini D, Faddy HM, Flower R, Hogan C. Cytomegalovirus disease in immunocompetent adults. Med J Aust. 2014; 201:578-80.

5. Karakozis S, Gongora E, Caceres M, Brun E, Cook JW. Life-threatening cytomegalovirus colitis in the immunocompetent patient: report of a case and review of the literature. Dis Colon Rectum. 2001;44:1716-20.

6. Rafailidis PI, Mourtzoukou EG, Varbobitis IC, Falagas ME. Severe cytomegalovirus infection in apparently immunocompetent patients: a systematic review. Virol J. 2008;5:47.

7. Orasch C, Conen A. Severe primary cytomegalovirus infection in the immunocompetent adult patient: a case series. Scand J Infect Dis. 2012;44:987-91.

8. Cavdar C, Celtik A, Saglam F, et al. Cytomegalovirus disease in renal transplant recipients: a single-center experience. Ren Fail. 2008;30:503-6.

9. Beader N, Kalenić S, Labar B. Diagnostic approach and therapy for cytomegalovirus (CMV) infection following allogeneic stem cell transplantation. Lijec Vjesn. 2011;133:389-96.

10. Varga M, Görög D, Kári D, et al. Cytomegalovirus seroprevalence among solid organ donors in Hungary: correlations with age, gender, and blood group. Transplant Proc. 2011;43:1233-5.

11. Wang C, Zhang X, Bialek S, Cannon MJ. Attribution of congenital cytomegalovirus infection to primary versus non-primary maternal infection. Clin Infect Dis. 2011;52:e11-e13.

12. Aarnisalo J, Ilonen J, Vainionpää R, Volanen I, Kaitosaari T, Simell O. Development of antibodies against cytomegalovirus, varicella-zoster virus and herpes simplex virus in Finland during the first eight years of life: a prospective study. Scand J Infect Dis. 2003;35:750-3.

13. Ataman S, Colak D, Günseren F, et al. Investigation of cytomegalovirus seroepidemiology in Antalya with a population-based cross-sectional study and review of related data in Turkey. Mikrobiyol Bul. 2007;41:545-55.

14. Lopo S, Vinagre E, Palminha P, Paixao MT, Nogueira P, Freitas MG. Seroprevalence to cytomegalovirus in the Portuguese population, 2002-2003. Euro Surveill. 2011;16(25).pii: 19896.

15. Zebrun AB, Kuliasheva LB, Ermolenko KD, Zakrevskaia AV. Spread of herpesvirus infections in children and adults in St. Petersburg according to seroepidemiologic study data. Zh Mikrobiol Epidemiol Immunobiol. 2013;6:30-6.

16. Dolgikh TI, Dalmatov VV, Zapariĭ NS, Kadtsyna TV. Cytomegalovirus infection in Omsk region. Zh Mikrobiol Epidemiol Immunobiol. 2008;3:85-7.

17. Lübeck PR, Doerr HW, Rabenau HF. Epidemiology of human cytomegalovirus (HCMV) in an urban region of Germany: what has changed? Med Microbiol Immunol. 2010;199:53-60.

18. Lepage N, Leroyer A, Cherot-Kornobis N, Lartigau I, Miczek S, Sobaszek A. Cytomegalovirus seroprevalence in exposed and unexposed populations of hospital employees. Eur J Clin Microbiol Infect Dis. 2011;30:65-70.

19. Korndewal MJ, Mollema L, Tcherniaeva I, et al. Cytomegalovirus infection in the Netherlands: seroprevalence, risk factors, and implications. J Clin Virol. 2015;63:53-8.

20. Odland JØ, Sergejeva IV, Ivaneev MD, Jensen IP, Stray-Pedersen B. Seropositivity of cytomegalovirus, parvovirus and rubella in pregnant women and recurrent aborters in Leningrad County, Russia. Acta Obstet Gynecol Scand. 2001;80:1025-9.

21. Leuridan E, Ieven M, Hens N, Van Damme P. High susceptibility to cytomegalovirus infection of pregnant women in Flanders, Belgium. Facts Views Vis Obgyn. 2012;4:76-81.

22. N'Diaye DS, Yazdanpanah Y, Krivine A, et al. Predictive factors of cytomegalovirus seropositivity among pregnant women in Paris, France. PLoS One. 2014;9(2):e89857.

23. Odland ML, Strand KM, Nordbø SA, Forsmo S, Austgulen R, Iversen AC. Changing patterns of cytomegalovirus seroprevalence among pregnant women in Norway between 1995 and 2009 examined in the Norwegian Mother and Child Cohort Study and two cohorts from Sor-Trondelag County: a cross-sectional study. BMJ Open. 2013;3(9):e003066.

24. Aynioglu A, Aynioglu O, Altunok ES. Seroprevalence of Toxoplasma gondii, rubella and cytomegalovirus among pregnant females in north-western Turkey. Acta Clin Belg. 2015; doi.org/10.1179/2295333715Y.0000000021

25. Trkulic M, Jovanovic D, Ostojic G, Kovacevic Z, Taseski J. Cytomegalovirus infection in patients with kidney diseases. Vojnosanit Pregl. 2000;57:63-7.

26. Ocak S, Duran N, Eskiocak AF. Seroprevalence of cytomegalovirus antibodies in hemodialysis patients. Turk J Med Sci. 2006;36:155-8.

27. Betjes MG, Litjens NH, Zietse R. Seropositivity for cytomegalovirus in patients with end-stage renal disease is strongly associated with atherosclerotic disease. Nephrol Dial Transplant. 2007;22:3298‑303.

28. Vilibic-Cavlek T, Ljubin-Sternak S, Ban M, Kolaric B, Sviben M, Mlinaric-Galinovic G. Seroprevalence of TORCH infections in women of childbearing age in Croatia. J Maternal Fet Neonatal Med. 2011;24:280-3.

29. Vilibic-Cavlek T, Kolaric B, Ljubin-Sternak S, Kos M, Kaic B, Mlinaric-Galinovic G. Prevalence and dynamics of cytomegalovirus infection among patients undergoing chronic hemodialysis. Indian J Nephrol. 2015;25:95-8.

30. de Ory Manchón F, Sanz Moreno JC, Castañeda López R, Ramírez Fernández R, León Rega P, Pachón del Amo I. Cytomegalovirus seroepidemiology in the community of Madrid. Rev Esp Salud Publica. 2001;75:55-62.

31. Francisse S, Revelard P, De Maertelaer V, Strebelle E, Englert Y, Liesnard C. Human cytomegalovirus seroprevalence and risk of seroconversion in a fertility clinic population. Obstet Gynecol. 2009;114:285-91.

32. Enders G, Daiminger A, Lindemann L, et al. Cytomegalovirus (CMV) seroprevalence in pregnant women, bone marrow donors and adolescents in Germany, 1996-2010. Med Microbiol Immunol. 2012;201:303-9.

33. van Rijckevorsel GG, Bovée LP, Damen M, Sonder GJ, Schim van der Loeff MF, van den Hoek A. Increased seroprevalence of IgG-class antibodies against cytomegalovirus, parvovirus B19, and varicella-zoster virus in women working in child day care. BMC Public Health. 2012;12:475.

34. Sibrowski W, Kühnl P, Kalmar G, Albert S, Böhm BO, Doerr HW. Cytomegalovirus diagnosis in blood donors and risk patients. Beitr Infusionsther. 1990;26:37-9.

35. Pembrey L, Raynor P, Griffiths P, Chaytor S, Wright J, Hall AJ. Seroprevalence of cytomegalovirus, Epstein Barr virus and varicella zoster virus among pregnant women in Bradford: a cohort study. PLoS One. 2013;8(11):e81881.

36. Alanen A, Kahala K, Vahlberg T, Koskela P, Vainionpää R. Seroprevalence, incidence of prenatal infections and reliability of maternal history of varicella zoster virus,cytomegalovirus, herpes simplex virus and parvovirus B19 infection in South-Western Finland. BJOG. 2005;112:50-6.

37. Wujcicka W, Gaj Z, Wilczyński J, Sobala W, Spiewak E, Nowakowska D. Impact of socioeconomic risk factors on the seroprevalence of cytomegalovirus infections in a cohort of pregnant Polish women between 2010 and 2011. Eur J Clin Microbiol Infect Dis. 2014;33:1951-8.

38. Uyar Y, Balci A, Akcali A, Cabar C. Prevalence of rubella and cytomegalovirus antibodies among pregnant women in northern Turkey. New Microbiol. 2008;31:451-5.

39. Barlinn R, Vainio K, Samdal HH, Nordbø SA, Nøkleby H, Dudman SG. Susceptibility to cytomegalovirus, parvovirus B19 and age-dependent differences in levels of rubella antibodies among pregnant women. J Med Virol. 2014; 86:820-6.

40. Knowles SJ, Grundy K, Cahill I, Cafferkey MT, Geary M. Low cytomegalovirus sero-prevalence in Irish pregnant women. Ir Med J. 2005; 98:210-2.

Table 1. Prevalence of CMV antibodies according to the participant's characteristics

Characteristic	Tested	CMV IgM			CMV IgG		
	N (%)	N (%)	95%CI	p	N (%)	95%CI	p
Overall	2438 (100)	105 (4.3)			1815 (74.4)	72.7 - 76.2	
Gender				0.07			0.015
Male	1064 (43.6)	55 (5.2)	3.9 - 6.7		766 (72.0)	69.2 - 74.7	
Female	1374 (56.4)	50 (3.6)	2.7 - 4.8		1049 (76.3)	74.0 - 78.6	
Age				0.005			<0.001
< 6 mo	32 (1.3%)	1 (3.1)	0.1 - 16.2		27 (84.4)	67.2 - 94.7	
6 mo - 9 yrs	249 (10.2)	19 (7.6)	4.7 - 11.7		132 (53.0)	46.4 - 59.3	
10 - 19 yrs	271 (11.1)	7 (2.6)	1.0 - 5.2		150 (55.4)	49.2 - 61.4	
20 - 29 yrs	431 (17.7)	29 (6.7)	4.6 - 9.5		300 (69.6)	65.0 - 73.9	
30 - 39 yrs	584 (24.0)	14 (2.4)	1.3 - 4.0		420 (71.9)	68.1 - 75.5	
40 - 49 yrs	278 (11.4)	12 (4.3)	2.3 - 7.4		237 (85.3)	80.5 - 89.2	
50 - 59 yrs	305 (12.5)	13 (4.3)	2.3 - 7.2		279 (91.5)	87.8 - 94.4	
60+ yrs	288 (11.8)	10 (3.5)	1.7 - 6.3		270 (93.8)	90.3 - 96.3	

Setting				0.604			0.952
Urban	1991 (81.8)	83 (4.2)	3.3 - 5.1		1482 (74.4)	72.5 - 76.3	
Suburban/rural	444 (18.2)	21 (4.7)	3.0 - 7.1		330 (74.3)	70.0 - 78.3	
Population group				<0.001			<0.001
Children/adolescents	496 (20.4)	25 (5.0)	3.3 - 7.4		271 (54.6)	50.1 - 59.1	
Adult general population	1626 (66.7)	53 (3.3)	2.5 - 4.2		1256 (77.2)	75.1 - 79.3	
Hemodialysis patients	314 (12.9)	27 (8.6)	5.7 - 12.3		287 (91.4)	87.7 - 94.2	
Pregnant women				0.999			0.999
Normal pregnancy	238 (76.5)	2 (0.8)	0.1 - 3.0		186 (78.2)	72.4 - 83.2	
Bad obstetric history	73 (23.5)	0 (0)	0 - 4.9		57 (78.1)	66.9 - 86.9	

Table 2. Univariate logistic regression for risk of CMV seropositivity

Characteristic	CMV IgM OR	95%CI OR	CMV IgM AOR*	95%CI AOR	CMV IgG OR	95%CI OR	CMV IgG AOR	95%CI AOR
Male *vs*. female (ref.)	1.44	0.98 - 2.14	NA**	NA	0.80	0.66 - 0.96	NA	NA
Age			NA	NA			NA	NA
6 mo - 9 yrs	1 (ref.)	-			1 (ref.)	-		
10 - 19 yrs	0.32	0.13 - 0.78			1.10	0.78 - 1.55		
20 - 29 yrs	0.87	0.48 - 1.59			2.03	1.47 - 2.80		
30 - 39 yrs	0.30	0.15 - 0.60			2.27	1.67 - 3.09		
40 - 49 yrs	0.55	0.26 - 1.15			5.12	3.38 - 7.76		
50 - 59 yrs	0.54	0.26 - 1.11			9.51	5.93 - 15.26		
60 + yrs	0.44	0.20 - 0.96			13.30	7.76 - 22.77		
Urban *vs*. suburban/rural	0.88	0.54 - 1.43	0.89	0.55 - 1.46	1.01	0.79 - 1.27	0.94	0.73 - 1-20
setting (ref.)								
Population group								
Children/adolescents	1 (ref.)	-	1 (ref.)	-	1 (ref.)	-	1 (ref.)	-

Adult general population	0.63	0.39 - 1.03	1.57	0.81 - 3.06	2.82	2.28 - 3.48	0.94	0.69 - 1.29
Hemodialysis patients	1.77	1.01 - 3.11	6.16	2.57 - 14.75	8.83	5.73 - 13.60	1.98	1.15 - 3.41
Bad obstetric history *vs.* normal pregnancy (ref.)	NA	-	NA	-	1.00	0.53 - 1.88	0.95	0.50 - 1.81

*AOR=adjusted for age and gender; **NA=not applicable

FIGURE LEGENDS:

Figure 1. Distribution of study participants according to age and gender

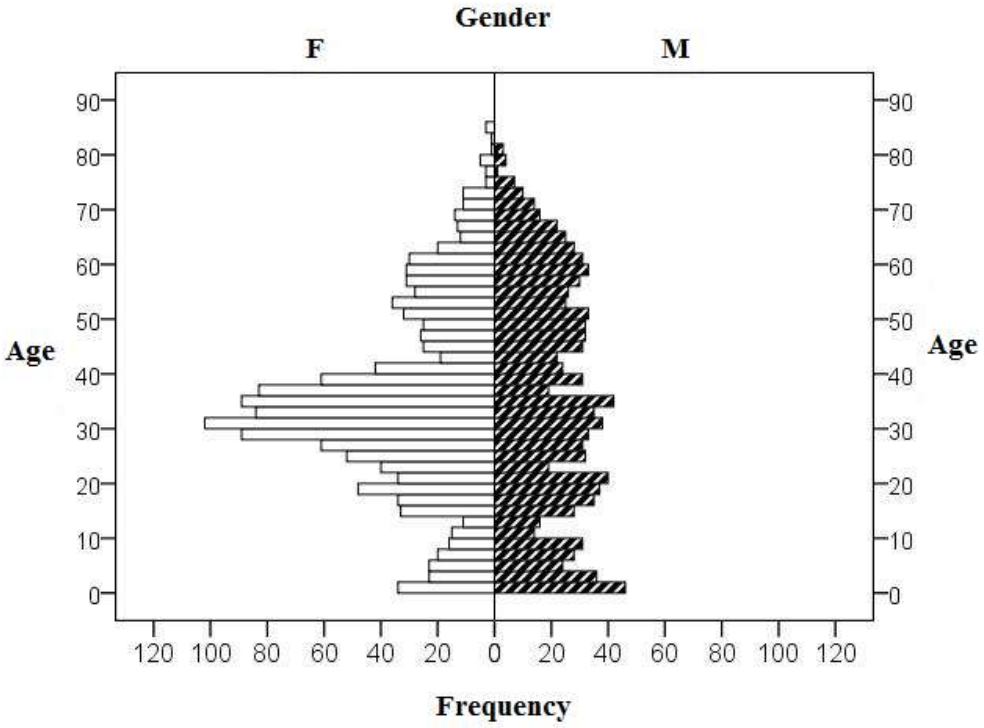

Figure 2. CMV IgG avidity according to participant's age

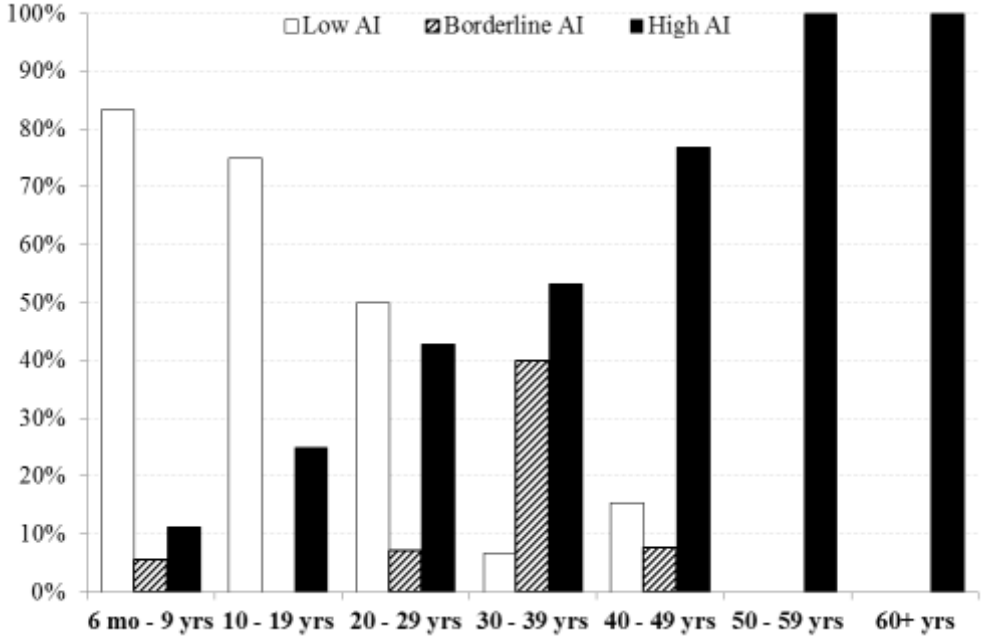

Figure 3. CMV IgG avidity according to population group