

Seroprevalence of Cytomegalovirus infection and estimate of congenital Cytomegalovirus infection in Isfahan state, Iran: A population based study

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ABSTRACT

Objective: Cytomegalovirus (CMV) is a well-known virus with major consequences in growing fetus, premature infants, and immune deficient individuals. There are few reports in prevalence of CMV infection in Iran, mainly in pregnant women. We conducted an epidemiological study to investigate the age-stratified seroprevalence and epidemiological characteristics of CMV infection in total inhabitants of Isfahan state, central Iran.

Methodology: In a cross sectional study 595 serum samples which were collected randomly from total population of Isfahan state, Iran were used for IgG anti-CMV antibody titration by a commercial enzyme-linked immunosorbent assay (ELISA) kit. Data were analyzed by Statistical Package for Social Sciences for Windows version 15(SPSS). Chi-squared and Fisher exact tests were applied to determine antibody status in different age, gender, education, family member, and residency groups.

Results: The overall prevalence was 98.2 % (586/595). The prevalence in age groups of 6-9, 10-19, 20-29, 30-39, 40-49 and above 49 years were 95.7, 98.6, 97.8, 100, 96.6, and 100 percent respectively. There was no statistical significant association between CMV seroprevalence with age, gender, education, family member, and residency groups ($P < 0.05$).

Conclusions: This study elucidates a very high prevalence of CMV infection in population which acquired it from early childhood. So it is necessary to initiate measures to reduce the burden of CMV disease in fetuses, premature infants, and immune deficient individuals. To treat hearing loss in inapparent congenitally infected infants, repeated auditory exams up to 5 years old has paramount importance.

KEY WORDS: Epidemiology, Cytomegalovirus, Population based study, Immunoassay.

doi: [http://dx.doi.org/10.12669/pjms.291\(Suppl\).3546](http://dx.doi.org/10.12669/pjms.291(Suppl).3546)

How to cite this:

Mostafavi SN, Ataei B, Nokhodian Z, Yaran M, Babak A, Salehi A, et al. Seroprevalence of Cytomegalovirus infection and estimate of congenital Cytomegalovirus infection in Isfahan state, Iran: A population based study. *Pak J Med Sci* 2013;29(1)Suppl:418-422.

doi: [http://dx.doi.org/10.12669/pjms.291\(Suppl\).3546](http://dx.doi.org/10.12669/pjms.291(Suppl).3546)

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INTRODUCTION

Cytomegalovirus (CMV) is the largest member of the Herpesviridae family with several strains and universal distribution.¹ The humans are the only reservoir and transmission occurs by direct or indirect contact with secretions of the infected people. Primary CMV infection is usually asymptomatic, but the virus remains latent in many organs including kidney, lung, gastrointestinal tract, and genitourinary system.¹ After infection, specific T-cells against CMV antigens produced which protects the host from severe primary, secondary,

or reactivated disease. T-cell immunodeficient individuals mainly fetuses, premature infants, transplant recipients, and HIV patients are at high risk for acquiring serious CMV disease involving any organs certainly liver, pancreas, adrenals, lymph nodes, brain, eyes, heart, skin, genitourinary, and gastrointestinal systems.¹ In contrast, humoral immunity has less significant role in protection against CMV infection and mainly lessens severity of the related symptoms and serves as a marker of previous infection.¹

Maternal primary or recurrent infection can cause fetal infection. The rate of fetal transmission in primary maternal infection is 40-50 percent while this parameter in recurrent infection approximates one percent. On the other hand symptoms and sequelae of the infection in maternal primary infection are much more than secondary infection. About 5-15 percent of infants with congenital CMV infection following primary maternal infection shows symptoms of disease at birth mainly as growth retardation, hepatosplenomegaly, thrombocytopenia, pneumonia, microcephaly, cerebral calcification, chorioretinitis, and hearing loss. Another 10-15 percent will show symptoms like hearing loss, visual disorders, and developmental problems later in life.^{1,3} While in fetal infections which occurred following secondary maternal infections few cases were symptomatic at birth⁴ and 5-7% of them would developed hearing loss later.⁵

Seroprevalence of CMV infection mostly is directly related to cultural and socioeconomic status of the population. In developing countries most children acquire the infection before reaching the age of three years and almost all persons have been infected before adulthood. In contrast in developed countries and high socioeconomic people many of the population are sero-negative prior to adolescent ages.¹ This pattern of infection influences the rate and severity of the congenital CMV infections. In developed regions the prevalence of maternal primary infection and symptomatic congenital CMV infection is high, while in developing areas recurrent maternal infection and asymptomatic congenital CMV infection is significant.

At this time CMV disease is a cause of morbidity in immunocompromised conditions including transplant recipient and HIV-infected persons. In addition it is a major cause of mental retardation and sensorineural hearing loss in most regions. Despite these, it is not a noticeable disease in most countries. To understand the transmission dynamics of the disease, seroepidemiological study are necessary.

Most of studies in Iran are about adults; especially volunteer blood donors⁶⁻⁸, female population^{9,10}, students of a university¹¹, or pregnant women¹²⁻¹⁵ who were referred to a medical laboratory, clinic, or hospital.

The purpose of the study was to investigate the age-stratified seroprevalence and epidemiological characteristics of CMV infection in total population of Isfahan state, central Iran.

METHODOLOGY

In a descriptive cross-sectional study 594 serum samples were accidentally selected from among 820 frozen samples. These samples were collected by multistage cluster sampling method from whole inhabitants of Isfahan state, Iran in a seroepidemiological survey on hepatitis A in 2008.¹⁶ All participants agreed and assigned written informed consent to partake in the epidemiological studies on their serums. The research was approved by the regional bioethics committee of the Research Department of Isfahan University of Medical Sciences.

Frozen samples were liquefied in room temperature and examined for IgG anti-CMV antibody with a commercial enzyme-linked immunosorbent assay (ELISA) kit (Dia-Pro, Milan, Italy). In accordance to the protocol of the kit absorbance values less than 9 reported negative, 9-11 equivocal, and more than 11 positive. The serums with borderline absorbance was reexamined and accordingly reported as negative or positive. If the test has borderline result again the serum was omitted from the research.

Ultimately, data analysis was performed with the Statistical Package for Social Sciences SPSS for Windows version 15 (SPSS Inc., Chicago IL.). Chi-square and Fisher exact tests were used to examine seroprevalence in different age, sex, education, family member, marriage state, and residency groups in the studied people. A P-value of less than 0.05 was considered significant.

RESULTS

Out of 595 serum samples examined, results of 585 cases were positive, 9 were negative and one sample was equivocal. On re-examination of this sample, the result was negative. According to these results, the prevalence of the CMV infection in total inhabitants of Isfahan state, Iran was 98.2%. The distribution of age, and residence area in participants was comparable to that of the total inhabitant of Isfahan state in the time of the survey. The seroprevalence of CMV infection in various age groups has been represented in Table-I.

Table-I: The total number of participant and their CMV seroprevalence in accordance to age groups.

Age group (Years)	Total No. of participant	CMV seroprevalence (Percent)
6-9	70	95.7
10-19	73	98.6
20-29	136	97.8
30-39	127	100
40-49	87	96.6
>49	102	100
Total	595	98.2

Statistical analysis revealed that the difference of CMV prevalence between groups of sex (female 98%, male 98.7%), residence (rural 99.1%, urban 98.1%), marital status (single 98.1%, married 98.3%, divorced 100%), education (illiterate 100%, primary school 97.6%, junior high school 95%, high school 99%, diploma and upper 100%), and family number (1-2 person 100%, 3-4 person 97.2%, 5-6 person 99.2%, more than 7 person 100%) is not significant (p-value more than 0.05).

DISCUSSION

The overall CMV seroprevalence in Isfahan state was 98.2%. The seroprevalence was 94% in Orumie city in Iran¹⁷ and varies from 59.2% to 97.3% in reports of other countries: Turkey¹⁸ (97.3%), Jamaica¹⁹ (95%), Portugal²⁰ (77%), Spain²¹ (62.8%), Ghana²² (59.2%), and Australia²³ (57%). The high prevalence of CMV in Iran and other developing countries is due to cultural and socioeconomic status like breast feeding, child rearing practices, and child group activities.

Seroprevalence of CMV infection in age groups of 6-9 and 10-19 were 95.3% and 98.3% respectively. These results were similar to reports from Cameroon²⁴, Brazil²⁵, Turkey¹⁸, and Orumieh of Iran.¹⁷ But they are higher than rates of Taiwan²⁶, Italy²⁷, America²⁸, and Finland.²⁹ The high prevalence in these age groups revealed that congenital, cervico-vaginal, breast feeding and horizontal transfer in kindergartens are the major roots of acquiring infection in the community, and sexual contact has no significant role in transmission of CMV infection in the state. Due to prolonged excretion of CMV after primary infection and also high rate of primary infection in infants and small children, to prevent re-infection of pregnant women with new CMV strain, all pregnant women should be advised to take care of them from exposure to infant's secretions especially urine and saliva.

In another study in Iran¹⁷ the reported CMV prevalence in age groups of less than 1, 1-5, and higher than 5 years old were 73.9%, 73.9%, and 97% respectively. It shows that the role of congenital, perinatal conditions, and breast feeding in transmission of CMV would be more important than children contact in kindergartens.

In current study anti CMV antibody in groups aged 10-19, 20-29 and 30-39 were 98.3%, 97.8%, and 100% respectively. It shows almost all community members after 10 years of age are CMV seropositive. So the chance for finding CMV seronegative donor in organ transplantation or blood transfusion in the community is very low. Therefore after hematopoietic or solid organ transplantation enough searches should be made to diagnose and treat CMV disease appropriately. In addition irradiated blood products should be requested for blood transfusion of premature infants and immunodeficient cases in these areas. Our results were comparable to results from other parts of Iran. Asymptomatic blood donors in Tabriz (82%)⁶, Tehran (89.2%)⁷, and Kashan (97%)⁸ also had high CMV seroprevalence rates. Estimated prevalence in blood donors of India (95%)³⁰ and France (97.1%)³¹ were near to our prevalence.

In our research anti CMV antibody in women aged 10-19, 20-29, and 30-39 in order were 98.3%, 97.8%, and 100%. Similar high rates in child bearing aged and pregnant women were reported from other parts of Iran i.e. Fars⁹, Azerbaijan¹⁰, Kazeroun¹¹, Tehran¹², Kerman¹³, south of Iran¹⁴, Gonabad¹⁵, and also Jordan³², Saudi Arabia³³ and Turkey.³⁴ In contrast CMV seroprevalence in pregnant women of developed countries like Ireland³⁵ (4.4%), Italy³⁶ (30.7%), and Netherland³⁷ (41%) is low to moderate. It shows that most women in Isfahan state and may be other parts of Iran are CMV seropositive before pregnancy and so the chance of symptomatic congenital infection is low. On the other hand approximately 1-1.4 percent of these immune mothers could bear asymptomatic CMV infected child following secondary maternal CMV infection.^{38,39} Unfortunately these infections cannot be diagnosed by screening in pregnancy.⁶ With an estimated 5 percent of permanent auditory loss and neurologic disturbances in this newborns^{6,40}, it seems that 5 to 7 in 10,000 live birth in the province has CMV related complications. Because of so high CMV related sequelae all newborns of the region should be properly examined and offered to perform repeated auditory exam till 5 years old to diagnose and treat this problem in time.

In this study residence, sex, education, family number, and marital status has no significant relation with CMV seroprevalence in the community. Very high CMV seroprevalence in the studied population could mask the effect of various factors. A similar study in Taiwan showed residence and family member have no effect on CMV prevalence.²⁶ While in Italy³⁶, Netherland³⁷, and France⁴¹ the infection was higher in rural areas. In Australia²³ and Jordan³² sex has no role in CMV prevalence.^{13,36} But results of Portugal showed the infection was higher in female gender in ages greater than 10 years. It is associated to frequent relation between mothers and children.²⁰

Limitations of the study: We did not evaluate CMV seroprevalence in age of less than 5 years. So we cannot define the exact effect of congenital, perinatal, breast feeding, and horizontal routs in spread of the infection in the community.

CONCLUSION

This study has revealed a very high prevalence of CMV infection in Isfahan province which acquired during early childhood. Taking care is necessary to prevent secondary infection of the pregnant women, primary infection of the premature infants, and reactivated infection of the immune deficient or organ recipient individuals appropriately. In addition repeated auditory exam in children till 5 years old to diagnosis and treatment of asymptomatic congenitally infected children has paramount importance.

ACKNOWLEDGMENTS

This research has been performed with a grant from Isfahan University of Medical Sciences. The authors are thankful to Mr. Ahmad Reza Pahlevan and Ms. Parisa Shoaee for their valuable assistance in laboratory studies of this project.

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Authors Contributions:

SNA contributed in study design and prepared the first draft of the manuscript. BA, ZN, MY, AS conceived the study design and contribute in data gathering. AB was involved in data analysis and interpretation of the results. All authors have read and approved the content of the manuscript.