Journal of Fundamental and Applied Sciences

ISSN 1112-9867

Available online at http://www.jfas.info

Research Article

FREQUENCY AND COMPARISON OF SEROEPIDEMIOLOGY HSV AND CMV IN WOMEN WITH NATURAL CHILDBIRTH AND ABORTION IN SHAHID BEHESHTI HOSPITAL, ABADAN, IRAN

N. Jomehzadeh[1,2], F. Shahi[2], S. Kooti[1], Z. Gorjian[1], H. Abdollahi Lorestani[1], A. Tamimi[1]
A. Sobhani[1], S. Khoshnood[2*]

[1]Abadan School of Medical Sciences, Abadan, Iran
[2]Department of Microbiology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Published online: 01 September 2017

ABSTRACT

Background: Cytomegalovirus and Herpes simplexvirus are one of the most common causes of congenital infections.

Objectives: The purpose of this study was to determine the seroprevalence of herpes simplex virus type 1 (HSV-1), type 2 (HSV-2) and CMV antibody in pregnant women admitting to antenatal care clinic of Shahid Beheshti Hospital in Abadan, Iran. Serum samples were collected during the study.

Methods: The enzyme-linked immunosorbent assay was used to detect anti-HSV-1, anti-HSV-2 type and anti- CMV. Socio-demographic and obstetric characteristics were used for further study.

Results: Between January and December 2016, we have studied 325 pregnant women referred to Shahid Beheshti Hospital. The mean of women's age was 27.66 ± 5.96 years old (range 16 to 43 years). Of the 325 participants in this study, 40 (12.3 %) were HSV-1 seropositive, 78 (24%) were HSV-2 seropositive and 36 (11%) were CMV seropositive. A combined analysis was performed for HSV-1 and HSV-2: the percentages of individuals testing regarding both HSV-1 and HSV-2 negative, both HSV-1 and HSV-2 positive, were 207 (63.7%) and 4 (1.2%) respectively.

Author Correspondence, e-mail: Saeed.khoshnood22@gmail.com

doi: http://dx.doi.org/10.4314/jfas.v9i3.32

Conclusion: In summary, this study showed a relatively low proportion of pregnant women in our region since they were exposed more to HSV and CMV infection than another part of Iran. CMV and HSV screening of pregnant women and their neonates can play a role in decreasing congenital infection and its severe consequences.

Keywords: Herpes simplex virus type 1 and type 2, Cytomegalovirus, Pregnancy, Neonatal herpes.

1. BACKGROUND

Herpes simplex virus (HSV) and Human Cytomegalovirus (CMV) are the member of the herpes family that are known to have an intrauterine transmission with noticeable morbidity and mortality (1,2). Herpes simplex virus type 2 (HSV-2) is the major cause of genital herpes that almost always sexually transmitted but HSV-1 is usually transmitted via non-sexual contacts. However, in some developed countries, HSV-1 has become a major cause of genital herpes (3).

HSV infection also results from contact between the newborn and either HSV-1 or HSV-2 that is present in the birth canal of an asymptomatic mother during delivery (4). In recent decades, the incidence of HSV infection has been increasing; and concerns about this infection are growing among women of reproductive age (5) because of the primary HSV infection in first half of pregnancy is related with high incidence of spontaneous abortions, congenital malformations and still births (4). CMV is the major cause of congenital infection with about a range of 0.2–2.5 percent of birth prevalence (6,7).The clinical symptoms of CMV in pregnant women range from asymptomatic forms in 90% of cases to severe fetal damage and death due to abortion (8). In utero, transmission of the virus to the fetus can occur during primary infection, reactivation or reinfection of seropositive mothers (9) but rarely reactivated maternal infections result in fatal damage (2). Congenital CMV infection also causes similar birth defects: mental retardation, retinochoroiditis and hearing loss. Approximately 30% of infected newborn babies die due to congenital CMV (10).

Although Cytomegalovirus and Herpes simplexvirus are one of the most common causes of congenital infections; however, the rate of these infection among women with natural childbirth and abortion are yet undetermined in Iran and this might worsen the outcome of the disease (4).Their diagnosis is usually determined by the presence of specific antibody or by the seroconversion in paired sera. Thus the detection of the immunologlobulins against HSV and CMV is the best procedure for the identification of the infection in asymptomatic or

apparent cases (2). Enzyme-linked immunosorbent assay (ELISA) is a reliable and sensitive test for determining the seroprevalence to assess the relation of these infections in cases of natural childbirth and abortion (4).

Since previous studies have suggested that HSV and CMV infection during pregnancy are associated with spontaneous abortion, congenital malformations and preterm childbirth may be seen (11-13). Therefore, we used ELISA methods to study the seroprevalence and associated possible risk factors for CMV, HSV-1 and HSV-2 infections among women with natural childbirth and abortion.

2. METHODS

2.1.Study Population and Design

This was a cross sectional study which was conducted at Shahid Beheshti Hospital in Abadan, Iran. Between January and December 2016, 325 pregnant women who were admitted the antenatal care clinic were enrolled. After endorsing a consent form, related medical, socio-demographic and obstetric characteristics were collected using pre-tested questionnaires under standardized conditions. The study examined and approved by the ethics review committee on human research of the Abadan school of medical sciences. Blood specimens were collected by venipuncture and serum samples stored in cryovials at -20°C until testing.

2.2.Laboratory methods

A commercially in vitro ELISA kit (Radim, Rome, Italy) was used for detection IgG & IgM human antibodies against the HSV- 1 and HSV-2 specific glycoprotein G2 according to the manufacturer's instruction (14-15). Previous studies have shown that this method has an acceptable sensitivity and specificity for identifying herpes simplex virus (16). All of the samples which were collected from pregnant women were also screened for CMV IgG and IgM by using a commercial ELISA kit (Radim, Rome, Italy). The last available serum sample of IgM & IgG negative women was also evaluated for IgM & IgG to detect seroconversion. In the interpretation of IgG and IgM test, the optical density (OD) of each negative control and cut-off calibrator (10 RU/ml) were considered. Statistical analyses were done by software SPSS 16.0. We used Fisher’s exact test when appropriate and the Chi-square test to compare proportions. The P value and confidence intervals were ≤ 0.05 and 95%, respectively (17).

3. RESULTS

Between January and December 2016, we studied 325 pregnant women referred to Shahid Beheshti Hospital in Abadan, Iran. The mean of women's age was 27.66 ± 5.96 years old (range 16 to 43 years). Majority 50.2 % (n=163) of the study, individuals were aged between 26 to 35 years. The educational level of the enrolled subjects was 10.2% (n=33), 51% (n=166) and 38.8% (n=126) for illiterate, high school or less and more than high school, respectively. Fifty two percent of the sample surveyed were living in urban and 48% were living in rural areas. The median gestation week of the individuals was 33 weeks and ranged from 4 to 41 weeks (33.51± 9.88), regarding the majority of study subjects. Among the participants, the majority 51% (n=166) had less than three children and 17.8% (n=58) had a history of abortion. Moreover, 52.3 % (n=170) of the participants had a history of Sexually Transmitted Infection (STI). Serum specimens were collected and screened for HSV-1, HSV-2 and CMV specific IgM antibodies. The association of HSV and CMV infections and other variables were shown in Table 1.

Table 1. Subject characteristics and seroprevalence of HSV-1, HSV-2 and CMV according to various factors

Variable	No (%)	Percentage positive for HSV- 2	Percentage positive for HSV- 1	Percentage positive for CMV
		P = 0.4	P = 0.2	P = 0.6
Educational level				
Illiterate	33 (10.2)	6/33	5/33	2/33
High school or less	166 (51)	39/166	23/166	17/166
More than high School	126 (38.8)	33/126	12/126	17/126
Age groups		P = 0.2	P = 0.7	P = 0.9
15-25	121 (37.2)	22/121	14/121	13/121
26-35	163 (50.2)	37/163	19/163	18/163
36-45	41 (12.6)	9/41	7/41	5/41
Address		P = 0.4	P = 0.2	P = 0.2
City	169 (52)	39/169	26/169	22/169
Village	156 (48)	39/156	14/156	14/156
Abortion				
Yes	58 (17.8)	17/78	34/40	11/58
No	267 (82.2)	61/78	6/40	25/267
		P = 0.8	P = 0.9	P = 0.6

Number of pregnancy	261(80.3)			
3p≥Numberof pregnancycy		61/261	31/2	30/261
	64(19.7)			
4p ≤Number of pregnancy		17/64	9/64	6/64
Number of children		P = 0.5	P = 0.8	P = 0.5
2C≥Number of Child	264(81.2)	64/264	33/264	30/264
3C ≤ Number of Children	61(18.8)	14/61	7/61	6/61

3.1.HSV and CMV Seroprevalence

Among participants of this study, 40 (12.3 %) were HSV-1 seropositive, 78 (24%) were HSV-2 seropositive and 36 (11%) were CMV seropositive. A combined analysis was performed for HSV-1 and HSV-2: the percentages of individuals testing regarding both HSV-1 and HSV-2 negative, both HSV-1 and HSV-2 positive, were 207 (63.7%) and 4 (1.2%) respectively.

4. DISCUSSION

In recent years, the incidence of herpes simplex infection is growing as the major causes of morbidity and mortality especially in during pregnancy (18). Seroprevalence studies of herpes simplex infection such as HSV-1, HSV-2 and CMV are important for a better understanding of the public health importance of disease concerned with these viruses. Furthermore, genital herpes is one of the most prevalent sexually transmitted diseases and it is also accounted the major risk factor for neonatal herpes (6,19,20). Therefore, in this study, we describe the serological epidemiology of infection and possible risk factors related to CMV, HSV-1 and HSV-2 infections among the women with natural childbirth and abortion in a teaching hospital in Abadan, South of Iran.

According to our the results, 40 (12.3 %) of the patients were seropositive for HSV-1, which was low as compared to studies conducted in a similar study population in Switzerland (79.4%), USA (63%) (19, 21). While, in compared to other studies, the seropositive rates of HSV-2 was slightly higher than that reported previously in Iran (18, 22). Overall, the seroprevalence rates of HSV-1 and HSV-2 was reported in the different population groups from various studies of the Iran ranging from 2% to 90.7% and zero to 43.7%, respectively (23, 24). Our finding showed, the considerable rate of herpes virus infection among pregnant

women was related to the increase of age and had a history of Sexually Transmitted Infection (STI), but this result was not significant statistically.

Moreover, our results suggest that the women who had a history of abortion are not exposed to infection, this shows HSV-infection is not accounted as a main risk factor for abortion in our population studies. The overall prevalence of CMV antibodies among pregnant women in our regions was 11% (36/325). This is a lower prevalence than observed by Arbabpour and colleagues in 2011 the region of Kazeroon– Fars where 97.69% of the women had antibodies against CMV infection (25). In a study conducted by Beiranvand and *et al*, 2011, 90.6% of cases were positive for CMV antibodies (26).

Contrary to the previous study conducted in East of Iran, the high (72.1%) seroprevalence of CMV antibodies at the third trimester among pregnant women (27). However, the low prevalence rates of CMV in this study compared to the rest of the studies in Iran and other parts of the world may be due to social variations, such as differences in a population study, population behavior, identification methods, and local infection control police (22).

Among the 11% (36/325) CMV-positive women, 11 (30.5%) had a history of abortion and the majority of women were with an age range between 15 to 35 years old. This may be due to increased frequency of exposure to sexual intercourse. In general, several risk factors were assessed in this study. Based on our results, there was not a significant relationship between the positive rate of the HSV and CMV-infection and age, abortion history and number, education level and the stage of pregnancy.

In summary, this study showed a relatively low proportion of pregnant women in our region who were exposed to HSV and CMV infection than another part of Iran. Moreover, we identified young women to be at the highest risk of acquiring HSV and CMV infection. Thus, molecular testing methods should be required in medical diagnostic laboratories since they can differentiate acute and chronic infection and help to control and prevention of infections. Both diagnostic laboratory and clinical evaluations are essential in establishing the diagnosis of CMV and HSV infections. CMV and HSV screening of pregnant women and their neonates can play a role in decreasing congenital infection and its severe consequences.

5. ACKNOWLEDGMENT

The authors of this study would like to acknowledge the nursing and medical personnel of infants and childeren ward in Shahid Beheshti Hospital in Abadan, for their cooperation to collect the clinical samples.

6. FOOTNOTES

Authors' Contribution: All the authors cooperated in conducting the isolation, performing the experimental work, as well as in writing the manuscript.

Funding: This study was supported by a fund provided by Abadan School of Medical Sciences (Grant number: 92 U-012) (Code of ethics:IR.ABADANUMS.REC.1394.19)

7. REFERENCES

1. Umeh EU, Onoja TO, Aguoru CU, Umeh JC. Seroprevalence of Cytomegalovirus Antibodies in Pregnant Women, Benue State, Nigeria. *J Infect Dis Ther*. 2015. doi: 10.4172/2332-0877.1000242.

2. Shrivastava G, Bhatambare G, Patel K. Seroprevalance of toxoplasma, rubella, CMV and HSV infection in pregnant women in central India. *Int J Health Syst Disaster Manage*. 2014;**2**(3):166. doi: 10.4103/2347-9019.142202.

3. Anzivino E, Fioriti D, Mischitelli M, Bellizzi A, Barucca V, Chiarini F, Pietropaolo V. Herpes simplex virus infection in pregnancy and in neonate: status of art of epidemiology, diagnosis, therapy and prevention. *Virol J*. 2009;**6**(1):40. doi: 10.1186/1743-422X-6-40. [PubMed: 19348670].

4. Tiwari S, Arora BS, Diwan R. TORCH IgM seroprevalence in women with abortions as adverse reproductive outcome in current pregnancy. *Int J Med Sci*. 2016;**4**(3):784-8. doi: 10.18203/2320-6012.ijrms20160518.

5. Aljumaili ZKM, Alsamarai AM, Najem WS. Seroprevalence of Herpes Simplex Virus Type 2 (HSV 2) in women with bad obstetric history. *Am J Dermatol Venerol*. 2013;**2**(3):31-8. doi: 10.5923/j.ajdv.20130203.04.

6. Maingi Z, Nyamache AK. Seroprevalence of Cytomegalo Virus (CMV) among pregnant women in Thika, Kenya. *BMC Res Notes*. 2014;**7**(1):794. doi: 10.1186/1756-0500-7-794. [PubMed: 25392013]

7. Mamuye Y, Nigatu B, Bekele D, Getahun M. Maternal and Congenital cytomegalovirus infection and zero rubella IgM prevalence in newborns in St. Paul's Hospital Millennium Medical College. *BMC Res Notes*. 2016;**9**(1):476. doi: 10.1186/s13104-016-2274-1.

8. Aljumaili ZKM, Alsamarai AM, Najem WS. Cytomegalovirus seroprevalence in women with bad obstetric history in Kirkuk, Iraq. *J Infect Public Health*. 2014;**7**(4):277-88. doi: 10.1016/j.jiph.2013.08.006. [PubMed: 24629348]

9. Munro SC, Hall B, Whybin LR, Leader L, Robertson P, Maine GT, Rawlinson WD. Diagnosis of and screening for cytomegalovirus infection in pregnant women. *J Clin Microbiol*. 2005;43(9):4713-8. doi: 10.1128/JCM.43.9.4713-4718.2005.

10. Ali S, Khan FA, Mian AA, Afzal MS. Seroprevalence of cytomegalovirus, herpes simplex virus and rubella virus among pregnant women in KPK province of Pakistan. *J Infect Dev Ctries*. 2014;**8**(03):389-90. doi: 10.3855/jidc.3854. [PubMed: 24619273]

11. Kost BP, Mylonas I, Kästner R, Rack B, Gingelmaier A, Friese K. Congenital cytomegalovirus infection in pregnancy: a case report of fetal death in a CMV-infected woman. *Arch Gynecol Obstet*. 2007;**276**(3):265-8. doi: 10.1007/s00404-007-0327-3. [PubMed: 17333226]

12. Iwasenko JM, Howard J, Arbuckle S, Graf N, Hall B, Craig ME, Rawlinson WD. Human cytomegalovirus infection is detected frequently in stillbirths and is associated with fetal thrombotic vasculopathy. *J Infect Dis*. 2011;**203**(11):1526-33. doi: 10.1093/infdis/jir121. [PubMed: 21592980]

13. Straface G, Selmin A, Zanardo V, De Santis M, Ercoli A, Scambia G. Herpes simplex virus infection in pregnancy. *Infect Dis Obstet Gynecol*. 2012. doi: 10.1155/2012/385697.

14. Ashley Morrow R, Nollkamper J, Robinson NJ, Bishop N, Smith J. Performance of Focus ELISA tests for herpes simplex virus type 1 (HSV-1) and HSV-2 antibodies among women in ten diverse geographical locations. *Clin Microbiol Infect*. 2004;**10**(6):530-6. doi: 10.1111/j.1469-0691.2004.00836.x. [PubMed: 15191381]

15. Shen JH, Huang KY, Chao-Yu C, Chen CJ, Lin TY, Huang YC. Seroprevalence of Herpes Simplex Virus Type 1 and 2 in Taiwan and Risk Factor Analysis, 2007. *PloS one*. 2015;**10**(8):e0134178. doi: 10.1371/journal.pone.0134178. [PubMed: 26252011]

16. Liermann K, Schäfler A, Henke A, Sauerbrei A. Evaluation of commercial herpes simplex virus IgG and IgM enzyme immunoassays. *J Virol Methods*. 2014;199:29-34. doi: 10.1016/j.jviromet.2014.01.001. [PubMed: 24418499]

17. Khoshnood S, Eslami G, Hashemi A, Bahramian A, Heidary M, Yousefi N, Mohammdi F, Gholami M. Distribution of Aminoglycoside Resistance Genes Among Acinetobacter baumannii Strains Isolated From Burn Patients in Tehran, Iran. *Arch Pediatr Infect Dis*. 2017;**5**(3). doi: 10.5812/pedinfect.57263.

18. Asgari S, Chamani-Tabriz L, Asadi S, Fatemi F, Zeraati H, Akhondi MM, Shahnazi A. HSV-2 seroepidemiology and risk factors among Iranian women: a time to new thinking. *Iran Red Crescent Med J*. 2011;**13**(11):818.

19. Xu F, Markowitz LE, Gottlieb SL, Berman SM. Seroprevalence of herpes simplex virus types 1 and 2 in pregnant women in the United States. *Am J Obstet Gynecol*. 2007;**196**(1):43-e1. doi: 10.1016/j.ajog.2006.07.051. [PubMed: 17240228].

20. Munjoma MW, Kurewa EN, Mapingure MP, Mashavave GV, Chirenje MZ, Rusakaniko S, Hussain A, Stray-Pedersen B. The prevalence, incidence and risk factors of herpes simplex virus type 2 infection among pregnant Zimbabwean women followed up nine months after childbirth. *BMC Womens Health*. 2010;**10**(1):2. doi: 10.1186/1472-6874-10-2.

21. Kucera P, Gerber S, Marques-Vidal P, Meylan PR. Seroepidemiology of herpes simplex virus type 1 and 2 in pregnant women in Switzerland: an obstetric clinic based study. *Eur J Obstet Gynecol Reprod Biol*. 2012;**160**(1):13-7. doi: 10.1016/j.ejogrb.2011.09.030. [PubMed: 21982938]

22. Tavakoli A, Monavari SH, Bokharaei-Salim F, Mollaei H, Abedi-Kiasari B, Fallah FH, Mortazavi HS. Asymptomatic Herpes Simplex Virus Infection in Iranian Mothers and Their Newborns. *Fetal Pediatr Pathol*. 2017;**36**(1):27-32. doi:10.1080/15513815.2016.1229368. [PubMed: 27762667]

23. Alsamarai AM, Khalil Z, Aljumaili M. Seroepidemiology of Toxoplasma, Rubella, Cytomegalovirus and Herpes Simplex Virus-2 in women with bad obstetric history. PART I: Toxoplasma and Rubella infections. *Our Dermatol Online*. 2013;4:522-35. doi: 10.7241/ourd.20134.135

24. Malary M, Abedi G, Hamzehgardeshi Z, Afshari M, Moosazadeh M. The prevalence of herpes simplex virus type 1 and 2 infection in Iran: A meta-analysis. *Int J Reprod Biomed*. 2016;14(10):615-624.

25. Arabpour M, Kaviyanee K, Jankhah A, Yaghobi R. Human cytomegalovirus infection in women of childbearing age throughout Fars Province-Iran: a population-based cohort study. *Malays J Microbiol*. 2007;**3**(2):23-8. doi: /10.21161/mjm.01107.

26. Delfan-Beiranvand M, Sheikhian A, Birjandi M, Fazeli M. Seroprevalence of Cytomegalovirus Infection in Pregnant Women Referred to Health Care Center of Khorramabad. *Iran J Virol*. 2011;5(4):11-6.

27. Bagheri L, Mokhtarian H, Sarshar N, Ghahramani M. Seroprevalence of cytomegalovirus infection among pregnant women in Eastern Iran. *Braz J Infect Dis*. 2012;16(4):402-3. doi: 10.1016/j.bjid.2012.01.002

How to cite this article:
Jomehzadeh N, Shahi F, Kooti S, Gorjian Z, Abdollahi Lorestani H, Tamimi A, Sobhani A, Khoshnood S.Frequency and comparison of seroepidemiology HSV and CMV in women with natural childbirth and abortion in Shahid Beheshti hospital, Abadan, Iran. J. Fundam. Appl. Sci., 2017, *9(3), 17481757.*