

Infection with herpes simplex virus type 2 (HSV-2) in pregnant women

Israa Hashim Saadoon, *Ph.D*; Sumaya T. Saihood, *F.I.C.O.G.*

Date Submitted: 17/9/2015

Date Accepted: 12/11/2015

Address for Correspondence:

Dr. Sumaya T. Saihood
Department of Obstetrics &
Gynecology, College of Medicine,
Tikrit University, Iraq.

Abstract

Background: During pregnancy, certain infections in the mother can be more severe than usual like hepatitis or latent viruses such as herpes simplex virus (HSV) and cytomegalovirus (CMV) can reactivate and infect the fetus. Disseminated herpes simplex (HSV) virus infection during pregnancy is rare, but important to recognize, as disseminated disease can have a serious outcome for both the mother and neonate. **Aim of the study:** The aim of this study was to identify seroprevalence of HSV-2 in pregnant women in Tikrit city and its relation with abortion.

Methods: The current study included 135 pregnant women who attended to Tikrit Teaching Hospital for the period from beginning of October/2013 to the end of April/2014. Blood samples were collected from each woman for laboratory diagnosis of HSV-2 IgG and HSV-2 IgM antibodies.

Results: The research revealed that HSV-2 IgG and HSV-2 IgM antibodies were found in 37 (27.4%) and 13 (9.62%) respectively out of 135 pregnant women. There was significant correlation between HSV-2 IgG seropositive and age of pregnant women, while no such relation was found between HSV-2 IgM and age. There is no-significant relation between both HSV-2 IgG and HSV-2 IgM antibodies with gestational time of pregnancy. Antibodies of HSV-2/ IgG and IgM were detected in 40.54% and 53.85% respectively of pregnant women with history of abortion and the result was significant at $P < 0.05$. There was non-significant relation between HSV-2 IgG antibodies and HSV-2 IgM antibodies and No. of abortions.

Conclusions: Herpes simplex virus type 2 (HSV-2) infection is one of the important infections in pregnant women. The current study revealed a significant role of HSV-2 in abortion and since the first time infection of the mother associate with risk of transmission of infection to the fetus or newborn and its sequelae it is necessary to screen all pregnant women for HSV-2 infection for proper management.

Key words: HSV-2, pregnant women, abortion.

INTRODUCTION

The HSV-2 virus is classified in the alphaherpes subfamily of the family *Herpesviridae*. All herpesviruses are morphologically similar, with an overall size of 180 to 200 nm.^[1, 2]

In the infected person, there is an active and latent phase. After an incubation period of about a week, the active phase begins. During the active phase, the virus multiplies explosively between 50,000 and 200,000 new virions are produced from each infected cell. The

primary infection and reactivation can occur without any symptoms and apparently healthy people can transmit HSV-2 to their sexual partners or their newborns.^[3] The chance of acquiring infection increases with age.^[4]

Herpes Simplex Virus Type 2 is usually acquired as a sexually transmitted disease, so antibodies to this virus are seldom found before puberty. Surveys using type-specific glycoprotein antigens recently determined that 17% of adults in the United States possess HSV-2

antibodies, with seroprevalence higher among women than men, higher among blacks than whites, and age related.^[2]

Babies exposed to the initial genital herpes lesions as they pass through the birth canal can be infected. Herpesviruses can permanently disable or kill these young patients. Recurrent lesions, however, are not as harmful to newborns, presumably because maternal antibodies provide protection. Patients shedding herpesviruses from bursting blisters can infect their own or another person's esophagus, eyes, or skin. An estimated 4 billion people worldwide are infected with herpesviruses, and about 86 million have genital herpes lesions.^[5] Seroprevalence of HSV-2 in developing Asian countries is comparable (10–30%) to that observed in North America and Northern Europe.^[6]

Because of the high morbidity and mortality rates of neonatal infection, special attention must be paid to preventing transmission during delivery. Where active HSV lesions are present on maternal tissues, Cesarean section delivery may be used to minimize contact of the infant with infected maternal genital secretions, but Cesarean delivery may not be effective if rupture of the membranes precedes delivery by more than several hours. Avoiding the birth canal is particularly important if the mother has a primary HSV infection late during pregnancy.^[7] The aim of this study was to identify seroprevalence of HSV-2 in pregnant women in Tikrit city and its relation with abortion.

PATIENTS AND METHODS

The current research included 135 pregnant women (aged from 17-49 years) who attended to Tikrit Teaching Hospital for the period from beginning of October/2013 to the end of April/2014. Pregnant women with HBV and/or HCV infection and those with other chronic diseases were excluded from this study.

Five ml of blood was collected from each woman by vein puncture using disposable syringes. The blood was placed in plastic disposable tubes; it was left to stand at room temperature (20- 25°C) to allow it to clot, then the sera were separated by centrifugation at 3000 rpm for 10 minutes and stored at -20°C until the time of test.

Serological investigation included detection of HSV-2/ IgG antibodies and HSV-2/ IgM antibodies by using enzyme-linked immunosorbent assay (ELISA); from Biocheck, CA, USA.

Statistical Analysis

The statistical analysis was performed using chi-square test. P values less than 0.05 were considered statistically significant.

RESULT

The current study revealed that out of 135 pregnant women, HSV-2 IgG and HSV-2 IgM antibodies were detected in 37 (27.4%) and 13(9.62%) respectively... Table 1.

Table 1. Frequency of HSV-2/ IgG and IgM Antibodies in Pregnant Women.

No. of Women	HSV-2/ IgG		HSV-2/ IgM	
	No.	%	No.	%
135	37	27.4	13	9.62

The current study revealed significant correlation between HSV-2 IgG seropositive and age of pregnant women, while the relation between HSV-2 IgM and age was non-significant... Table 2.

Table 2. Frequency of HSV-2/ IgG and IgM Antibodies According to Age Groups.

Age Group (yr.)	No. of women	HSV-2/ IgG		HSV-2/ IgM	
		No.	%	No.	%
≤ 29	76	14	37.84	9	69.23
30-39	38	12	32.43	3	23.08
40-49	21	11	29.73	1	7.69
Total	135	37	100	13	100
X ²		10.0001		1.1307	
P		< 0.05		> 0.05	

The current research showed that the highest rate of HSV-2 IgG antibodies was found in women within the 3rd trimester of pregnancy, while the highest rate of HSV-2 IgM was found in women within the 1st trimester of pregnancy. However, the result was non-significant... Table 3.

Table 3. Frequency of HSV-2/ IgG and IgM Antibodies According to Gestational Age.

Gestational Age	No. of Women	HSV-2/ IgG		HSV-2/ IgM	
		No.	%	No.	%
1 st trimester	43	9	24.32	7	53.85
2 nd trimester	55	13	35.14	4	30.77
3 rd trimester	37	15	40.54	2	15.38
Total	135	37	100	13	100
X ²		4.5074		3.2945	
P		> 0.05		> 0.05	

The present study revealed that 40.54% and 53.85 % of pregnant women with HSV-2/ IgG and IgM respectively had history of abortion. The result was significant at P< 0.05... Table 4.

Table 4. Association between HSV-2/ IgG and IgM Antibodies and History of Abortion.

History of Abortion	No. of Women	HSV-2/ IgG		HSV-2/ IgM	
		No.	%	No.	%
+ ve	38	15	40.54	7	53.85
- ve	97	22	59.46	6	46.15
Total	135	37	100	13	100
X ²		3.8702		4.6971	
P		< 0.05		< 0.05	

The present study showed that the highest rate of seropositive for HSV-2/ IgG was found in women with 2 abortions followed by those with three abortions or more. The relation was non- significant at $P < 0.05$. The highest rate of HSV-2/ IgM was recorded in women with 1 abortion followed by those with 2 and those with three abortions or more (the same rate for each group). The result was non- significant... Table 5.

Table 5. Association between HSV-2/ IgG and IgM Antibodies and No. of Abortions.

No. of Abortions	No. of Women	HSV-2/ IgG		HSV-2/ IgM	
		No.	%	No.	%
1	17	4	26.67	3	42.86
2	13	6	40	2	28.57
≥ 3	8	5	33.33	2	28.57
Total	38	15	100	7	100
X ²		3.827		0.317	
P		> 0.05		> 0.05	

DISCUSSION

Antibodies to HSV-2 rise during the age of adolescence and sexual activity. During primary infections, IgM antibodies appear transiently and are followed by IgG and IgA antibodies that persist for long periods. Antibodies appear in 4–7 days after infection and reach a peak in 2–4 weeks. They persist with minor fluctuations for the life of the host. Detection methods available include neutralization, immunofluorescence, and enzyme-linked immunosorbent assay.^[2] Data obtained by the present research revealed that HSV-2 IgG and HSV-2 IgM antibodies were found in 27.4% and 9.62% of pregnant women. Another study concerning pregnant women in Babylon province reported that 28.9% and 22.2% of cases were positive for HSV-2 depending on IgM and IgG respectively.^[8]

Concerning pregnant mothers visiting the antenatal clinic and delivery room in King Fahd Hospital of the University (KFHU) in Al-Khobar, Saudi Arabia...6.5% had detectable level of HSV-2 IgG antibodies, and 0.5% had detectable level of HSV-2 IgM antibodies.^[9] In Turkey, high levels of HSV-2 (42%) were found

amongst pregnant women in the city of Erzurum in Eastern Anatolia Region, Turkey.^[10] In Istanbul however, lower HSV-2 seroprevalence was observed. Only 5% of pregnant women were infected with HSV-2.^[11]

Comparing the developing countries, substantially higher rates of HSV-2 have been observed in sub-Saharan Africa, where prevalence in adults ranges from 30% to 80% in women.^[12] In fact the strongest association with HSV-2 infection appears related to the number of sexual partners.

The present work revealed that the highest rate of HSV-2 IgG antibodies was found in women within the age group ≤ 29 years, followed by those within the age group 30-39 years. The result was significant ($P < 0.05$). Regarding HSV-2 IgM antibodies, the highest rate was detected in women who aged less than or equal to 29 years, followed by those within the age group 30-39 years. However, the result was non-significant ($P > 0.05$)... Table 2. Data obtained by the present work are in agreement with published data. In Babylon province, the distribution of age with type of infection according IgM antibodies to herpes showed that the main age of infection was from (25-40 years).^[8] In Saudi Arabia, prevalence of HSV-2 IgG was statistically significantly associated with the age of the mother. Possible explanation for this finding is the increase in sexual activity with the increase in age.^[9] In each country of Europe, HSV-2 seropositivity becomes more common from adolescence onwards and increases in the population with age, with a decline in the older age groups in some countries.^[13]

The present work revealed that HSV-2 IgG seropositive was found at highest rate in of women within the 3rd trimester of pregnancy(40.54%), followed by those within the 2nd trimester (35.14%) and those within the 1st trimester of pregnancy (24.32%). Concerning HSV-2 IgM, the highest rate was found in women within the 1st trimester of pregnancy (53.85%) followed by those within the 2nd trimester and those within the 3rd trimester (30.77% and 15.38% respectively). However, the result was non-significant... Table 3.

Al- Marzoqi *et al* ^[8] reported that the highest rate of IgM antibodies to HSV-2 was detected in women within the 2nd trimester (63.5%) followed by those within the 3rd trimester and 1st trimester of pregnancy (19.2% and 17.3% respectively). On the other hand, HSV-2 IgG was detected in 27.1% of serum samples obtained during the first trimester of pregnancy from Saudi women attending Maternity and Children's Hospital in Makkah.^[14]

Some maternal infections, especially during the early gestation, can result in fetal loss or malformations because the ability of the fetus to resist infectious organisms is limited and the fetal immune system is unable to prevent the dissemination of infectious organisms to various tissues.^[15] The danger of intrauterine HSV transmission is highest during the first 20 weeks of gestation because it can lead to abortion, stillbirth and congenital anomalies.^[16]

Recent findings revealed that first-time infection of the mother is the most important factor for the transmission of genital herpes from mother to foetus/newborn. In fact, the pregnant woman who acquires genital herpes as a primary infection in the latter half of pregnancy, rather than prior to pregnancy, is at greatest risk of transmitting these viruses to her newborn.^[17] When primary HSV infection occurs during late pregnancy, there is not adequate time for antibodies to develop and suppress viral replication before labor.^[18]

The current research revealed significant relation between HSV-2 IgG antibodies and HSV-2 IgM and history of abortion....Table 4. Non-significant relation was found between both HSV-2 IgG antibodies and HSV-2 IgM antibodies and No. of abortions....Table 5. Previous study concerning herpes simplex infections with incidence of abortion in pregnant women in Babylon province revealed that abortion according to herpes was 5.8%, first trimester was the highest ratio of infection than other two trimesters.^[8] However, another study in Egypt confirmed a significant increase of HSV in patients with recurrent abortions compared with pregnant patients without recurrent abortions, which denotes that HSV may predispose to this condition.^[19] For unknown reasons, the HSV-2 virus is associated with a higher-than-normal rate of cervical cancer and miscarriages.^[3] Herpesvirus reactivation frequently occurs during the first months of pregnancy because of the progesterone-linked immunodepression.^[20]

Kapranos and Kotronios^[21] reported on the significant role of HSV in the first trimester pregnancy loss and its detection by sensitive and accurate nested PCR, which would permit prompt antiviral therapy for a successful future pregnancy: HSV was detected in 43.2% of early pregnancy loss and in 16.7% cases of elective pregnancy termination.

Herpes can be spread to an infant during vaginal delivery, leading to congenital (neonatal) herpes. Congenital herpes is one of the most life-threatening of all infections in newborns, affecting approximately 1,500 to 2,200 babies per year in the United States. It can result in neurological involvement as well as blindness. As a result any female who has had genital

herpes should have a caesarean section instead of delivering vaginally.^[3]

REFERENCES

1. Levinson W. Review of Medical Microbiology and Immunology. 13th ed. McGraw-Hill companies. Inc. United States of America. 2014
2. Brooks GF, Carroll KC, Butel JS, Morse SA, Mietzner TA. Jawetz, Melnick and Adelberg's Medical Microbiology. 26th ed. McGraw-Hill companies. Inc. United States of America. 2013: 467-91.
3. Willy JM, Serwood LM, Woolverton CJ. Prescott, Harley and Klein's Microbiology. 7th ed. McGraw-Hill companies. Inc. United States of America. 2008: 933.
4. Fatahzadeh M, Schwartz RA. Human herpes simplex virus infections: epidemiology, pathogenesis, symptomatology, diagnosis, and management. J Am Acad Dermatol 2007; 57 (5): 737-63.
5. Acheson NH. Fundamentals of Molecular Virology. 2nd ed. John Wiley & Sons, Inc. 2011; 285- 301.
6. Weiss H. Epidemiology of herpes simplex virus type 2 infection in the developing world. Herpes 2004. 11 Suppl 1: 24A-35A.
7. Ryan KJ, Ray CG. Sherris Medical Microbiology. 6th ed. McGraw-Hill companies. Inc. United States of America. 2014; 245-69.
8. Al-Marzoqi AHM, Kadhim RA, Al-Janabi DKF, Hussein J, Hussein HJ, Al Taei ZM. Seroprevalence study of IgG and IgM antibodies to toxoplasma, rubella, cytomegalovirus, *Chlamydia trachomatis* and herpes simplex II in pregnancy women in Babylon province. Journal of Biology, Agriculture and Healthcare 2012; 2 (10):159-64.
9. Obeid O E. Prevalence of herpes simplex virus types 1 and 2 and associated sociodemographic variables in pregnant women attending King Fahd Hospital of the University. J Family Community Med. 2007 Jan-Apr; 14(1): 3-7.
10. Smith JS, Robinson NJ. Age-specific prevalence of infection with herpes simplex virus types 2 and 1: a global review. J Infect Dis 2002; 186 Suppl 1: S3-28.
11. Dolar N, Serdaroglu S, Yilmaz G, Ergin S. Seroprevalence of herpes simplex virus type 1 and type 2 in Turkey. J Eur Acad Dermatol Venereol 2006; 20 (10): 1232-6.
12. Weiss H. Epidemiology of herpes simplex virus type 2 infection in the developing world. Herpes 2004; 11:24A-35A.
13. Pebody RG, Andrews N, Brown D, et al. The seroepidemiology of herpes simplex virus type 1 and 2 in Europe. Sex Transm Infect 2004; 80 (3): 185-91.
14. Ghazi HO, Telmesani AM, Mahomed MF. TORCH agents in pregnant Saudi women. Med Principles Pract 2002; 11:180-2
15. Levett, PN. Seroprevalence of HSV-1 and HSV-2 in Barbados. Medical Microbiology and Immunology 2005; 194: 105-7.
16. Sauerbrei A, Wutzler P. Herpes simplex and varicella-zoster virus infections during pregnancy: current concepts of prevention, diagnosis and therapy, Part 1:

herpes simplex virus infections. *Med Microbiol Immunol* 2007; 196(2): 89-94.

18. Anzivino E , Daniela Fioriti D, Mischitelli M, et *al.* Herpes simplex virus infection in pregnancy and in neonate: status of art of epidemiology, diagnosis, therapy and prevention. *Virology Journal* 2009, 6:40-51.
19. Enright AM, Prober CG. Neonatal herpes infection: Diagnosis, treatment and prevention. *Semin Neonatol* 2002; 7:283-91.
20. Zaki M E, Goda H. Relevance of parvovirus B19, herpes simplex virus 2, and cytomegalovirus virologic markers in maternal serum for diagnosis of unexplained recurrent abortions. *Arch Pathol Lab Med* 2007; 131:956–60.
21. Burlingham WJ. A lesson in tolerance – maternal instruction to fetal cells. *N Engl J Med* 2009; 360:1355–7.
22. Kapranos NC, Kotronias DC. Detection of herpes simplex virus in first trimester pregnancy loss using molecular techniques. *In Vivo* 2009; 23:839- 42.