Prevalence of Herpes Simplex Virus Types 1 and 2 and Associated Sociodemographic Variables in Pregnant Women Attending King Fahd Hospital of the University

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Objectives: The risk factors associated with herpes simplex virus (HSV) seropositivity in pregnant women in Saudi Arabia are not known. This study was aimed at identifying the sociodemographic variables associated with seroprevalence of HSV-1 and HSV-2 in pregnant women in a Saudi hospital.

Materials and Methods: This is a hospital-based cross-sectional study that included all pregnant mothers who delivered at King Fahd Hospital of the University (KFHU) over a period of two years (November 2002 to October 2004). Anti-HSV-1 and anti-HSV-2 IgG and IgM antibodies were determined using type-specific ELISA. Each subject completed a structured questionnaire. Relevant sociodemographic variables were analyzed.

Results: A higher prevalence of HSV-1 IgG antibodies (93.2%) was found in those mothers who were not educated (illiterate or read and write only) in comparison with pregnant women with formal school education (p = 0.021). This was confirmed by using multiple regression analysis (p = 0.027). The prevalence of HSV-2 IgG was higher among civil servants and teachers (40.0% and 14.7% respectively) than in unskilled labourers, professionals, or housewives (p = 0.0001). Using multiple regression analysis, the prevalence of HSV-2 IgG was found to increase in older mothers (p = 0.037). No statistically significant association was found between HSV seroprevalence and other socio demographic variables.

Conclusions: Identifying the sociodemographic factors associated with HSV infection will help in understanding the epidemiology of HSV infection in Saudi women and may help in designing preventive measures.

Key Words: HSV-1, HSV-2, pregnant women, IgG, IgM, sociodemographic variables.

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INTRODUCTION
Herpes simplex virus (HSV)-1 and HSV-2 are common human pathogens, infecting approximately 90% and 22% of the population in the USA respectively. Infection with either virus results in lifelong latent infection. Recurrences may lead to clinical lesions or asymptomatic shedding. HSV-1 typically initiates infection upon contact with oral mucosae. Although HSV-2 has a predilection for the genital mucosae, genital herpes can be caused by either HSV-1 or 2. Primary genital HSV-1 or HSV-2 infection in pregnant women can result in abortion, premature labor and congenital and neonatal herpes. HSV-2 infections in the newborn are particularly severe and frequently involve the CNS.

Worldwide, the incidence and prevalence of HSV-1 and 2 infections are increasing yearly (silent epidemic). In the USA, there is more than 45 million people currently infected with HSV, with <1 million cases diagnosed yearly. HSV-2 seroprevalence increased by almost one third from 16.4% to 21.8% from 1976 to 1994 in people over 12 years old. Among healthy adult populations, HSV-2 seroprevalence is higher in the USA than in Europe. Prevalence of HSV-2 infections in the general population in developing Asian countries and the Middle East appears to be lower. As in the developed world, HSV-2 seropositivity is uniformly higher in women than in men and increases with age.

In general, HSV-2 seroprevalence is high in populations whose behavior leads to a high risk of acquiring other sexually transmitted infections (STIs), such as STI clinic attendees and sex workers (SWs). HSV infection is regarded as the most common STI in the world. Genital herpes is a cause of morbidity and increases the risk of HIV acquisition, resulting from disruption of mucosal membranes. There is a scanty data on the seroprevalence of HSV-1 and HSV-2 antibody in the Saudi population. Hossain investigated the seroepidemiology of infection resulting from HSV-1 by indirect immunofluorescence and various techniques in children, healthy adults, pregnant women and male patients with recurring genital ulcerations. The overall prevalence of HSV detection varied between 16.6% and 90%. However, the authors did not assess antibodies to HSV-1 or HSV-2 and no comparison was made between HSV-1 and HSV-2 in this population. Ghazi et al estimated the overall IgG antibodies to HSV-1 and HSV-2 in healthy individuals and in pregnant women. HSV-specific IgM antibodies were not measured. Alzahrani et al described the serotyping of HSV (HSV-1 and HSV-2) IgG and IgM antibodies in pregnant Saudi women and their neonates in King Fahd Hospital of the University in Kebbar, Saudi Arabia. The results showed that 84.1% of the pregnant women had detectable levels of HSV-1 IgG antibodies, 6.8% had detectable levels of HSV-2 IgG antibodies, 4.9% had detectable levels of HSV-1 IgM antibodies and 0.5% had detectable level of HSV-2 IgM antibodies. Only three cord blood samples had detectable levels of HSV-1 IgM antibodies, and none had detectable HSV-2 IgM antibodies.

Little is known about the risk factors associated with HSV seropositivity in pregnant Saudi women. Identification of the risk factors may help to improve the control measures of HSV infection.

The aim of this study was to identify socio-demographic variables associated with seroprevalence of HSV-1 and HSV-2 in pregnant Saudi women.

Patients, Materials and Methods
This was a hospital-based cross-sectional study conducted at King Fahd Hospital of the University (KFHU) in Al Khobar city, in the Eastern Province of Saudi Arabia. The study population consisted of all pregnant mothers who delivered in the third trimester. The period of the study was two years (from November 2002 to October 2004). Techniques used for data collection included:

a. Interviews of pregnant mothers
With informed consent, each mother was questioned during an antenatal visit or in the delivery room. A trained female physician with two trained nurses performed face-to-face interviews at the hospital using a structured questionnaire under standardized conditions. The questionnaire was designed to collect detailed information on (a) socio-demographic characteristics (b) lifestyle and habits (c) medical history. The socio-demographic and lifestyle variables considered to be of importance included: age, nationality, consanguinity, education level, education level of husband, monthly family income, occupation, number of family members, number of children below five years and past history of sexually transmitted infections. The interviewers were blind to the HSV serological status of the subjects and
were unaware of the study hypotheses. They were trained to treat all subjects the same way.

**b. Blood samples and statistical analysis**

Blood samples were collected from the subjects by venepuncture, and serum samples were analyzed for HSV-1 and HSV-2 IgG and IgM antibodies using a type-specific ELISA that eliminated the problem of cross-reactivity between HSV-1 and 2 (Gull, USA). The techniques used conformed to the manufacturer’s recommendations. All samples were negative for HIV and syphilis. Data were entered into a d-Base file (MS Excel). Bivariate analysis between the dependent and the independent variables were performed using Chi-square, t-test and paired t-test as appropriate. Analysis of variance ANOVA was used to test difference in means for qualitative variables. The level of significance was set at <0.05 throughout the study. For multiple logistic regression analysis, a backward stepwise analysis was used. Ten variables considered important were entered into the model. These were: age, nationality, consanguinity, education level, education level of husband, family income per month, occupation, number of family members, number of children below 5 years, and past history of sexually transmitted infections. All analyses were performed with SPSS statistical software. Reliability testing for socio-demographic variables was performed using the split-half method and was 0.66 i.e. ranging from fair to good agreement.

**RESULTS**

### 1. Association of HSV–1 IgG with Sociodemographic Variables (N =459)

Of the 459 pregnant Saudi women who were included in the study, 386 (84.1%) were found to be seropositive for HSV-1 IgG antibodies. The serological status of the pregnant women was compared with sociodemographic and life-style variables.

The educational level of the subject was statistically significantly associated with HSV-1 IgG (p = 0.021). A higher prevalence (93.2%) was found in those women who were not educated (illiterate or could read and write only) in comparison with those women with formal school education (Table 1). No statistically significant difference between HSV-1 IgG prevalence and other socio demographic variables could be demonstrated.

The HSV-1 IgG serological status of the pregnant mothers and their sociodemographic variables were further analyzed using multiple regression analysis. Backward stepwise methods were used. As shown in Table 2, the only variable found to be significantly associated with prevalence of HSV-1 IgG was the education level of the mother. Mothers who were not educated and those with a low level of education were 2-9 times more likely to have HSV-1 IgG than mothers with a higher level of education. This result confirms the finding in the bi–variable analysis.

### 2. Association of HSV–2 IgG with Sociodemographic Variables (N =459)

Of the 459 pregnant Saudi women who were included in the study, 31 (6.8%) were found to be seropositive for HSV-2 IgG antibodies. HSV–2 IgG prevalence was statistically significantly associated with the occupation of the mother (p = 0.0001). Although the numbers that were positive were small, the prevalence of HSV-2 IgG was higher among civil servants and teachers (40.0 % and 14.7 % respectively) than in unskilled labourers, professionals, or housewives.

No statistically significant difference between HSV-2 IgG prevalence and other socio demographic variables were found. Further analysis of the HSV-2 IgG serological status and the sociodemographic variables was performed using multiple regression analysis. Backward stepwise methods were used. As shown in Table 3, the prevalence of HSV-2 IgG was statistically significantly associated with the age of the mother while controlling for other confounding variables. Prevalence of HSV-2 IgG was more likely to increase with age.

### 3. Association of HSV–1 IgM with Sociodemographic Variables (N =459)

Of the 459 pregnant Saudi women who were included in the study, 27 (5.9%) were found to be seropositive for HSV-1 IgM antibodies. The serological status of the pregnant women was compared with sociodemographic and lifestyle variables considered important. There was no statistically significant difference between HSV-1 IgM prevalence and sociodemographic variables.

Although a higher prevalence was found among Non-Saudis, among women who were first and second degree relatives of their husbands, and among women who were not educated, and those
Table 1: Association of HSV-1 IgG with Sociodemographic Variables (N=459)

| Socio-demographic variable                  | HSV-1 IgG | Total No. | p-value |
|--------------------------------------------|-----------|-----------|---------|
|                                            | Positive No. (%) | Negative No. (%) |         |
| Nationality:                               |            |           |         |
| Saudis                                     | 199 (85)   | 35 (15)   | 234     |
| Non-Saudis                                 | 187 (83.1)| 38 (16.9) | 225     |
| Age (17-49 years, mean 28.7 years)         |            |           |         |
| Education level of mother:                 |            |           | >0.05   |
| Not educated (illiterate + read and write) | 68 (93.2)  | 5 (6.8)   | 73      |
| Educated (had formal schooling)             | 318 (82.4)| 68 (17.6) | 386     |
| Occupation of mother:                      |            |           | >0.05   |
| Housewife full-time                        | 331 (84.7)| 60 (15.3) | 391     |
| Civil service                              | 9 (90.0)   | 1 (100)   | 10      |
| Teacher (primary to secondary school)       | 26 (76.5)  | 8 (23.5)  | 34      |
| Profession (doctor, university teacher, nurse)| 13 (81.3)| 3 (18.8)  | 16      |
| Unskilled laborer                          | 7 (87.5)   | 1 (12.5)  | 8       |
| Monthly income of family/month in Saudi Riyals |            |           |         |
| <4000                                      | 318 (82.4)| 68 (17.6) | 386     |
| 4000-<6000                                 | 103 (79.8)| 26 (20.2) | 129     |
| ≥ 6000                                    | 75 (86.8)  | 12 (13.8) | 87      |

*significant

Table 2: Multiple logistic regression analysis showing variables associated with HSV-1 IgG

| Variable                  | B   | S.E. of B | Significance level (p-value) | OR   | 95% CI of OR |
|---------------------------|-----|-----------|------------------------------|------|--------------|
| Educational level of mother | 1.067 | 0.482 | 0.027 | 2.908 | 1.130-7.481 |
| Constant                  | 2.610 | 0.463 | 0.000 | -     | -            |

Table 3: Multiple logistic regression analysis showing variables associated with HSV-2 IgG

| Variable | B   | S.E. of B | Significance level (p-value) | OR   | 95% CI of OR |
|----------|-----|-----------|------------------------------|------|--------------|
| Age of the mother | 0.065 | 0.031 | 0.037 | 1.067 | 1.004-1.134 |
| Constant | 3.528 | 1.325 | 0.008 | -     | -            |

who were, these differences did not reach statistical significance. All samples were negative for HSV-2 IgM antibodies.

DISCUSSION

Herpes simplex virus (HSV) is a common sexually transmitted infection (STI), and the prevalence of this infection has increased significantly over the last two decades in many developed and developing countries. Known co-factors for HSV transmission include age, gender, race, serological status, lack of condom use, history of STI, HIV infection, socioeconomic status, the frequency of sexual contacts, duration of HSV in the source partner and duration of relationship.1

In our study, the education level of the mother was statistically significantly associated with HSV-1 IgG. A higher seroprevalence (93.2%) was found in those women who were not educated (illiterate, and read and write only) compared with pregnant women with formal school education. This might be explained by the fact that a lower level of education was an indicator of low socioeconomic status which was a risk factor for HSV infection.

Using bi-variate analysis, HSV-2 IgG prevalence was statistically significantly associated with the occupation of the mother. Although the numbers that were positive were small, the prevalence of HSV-2 IgG was higher among civil service employees and teachers (40.0 % and 14.7 % respectively). This may well be due to an infection acquired from the husband while traveling abroad. When both husband and wife were employed, the socioeconomic status the family is likely to be high and the family would tend to spend their annual vacation abroad.

Using multiple regression analysis, prevalence of HSV-2 IgG was statistically significantly associated with the age of the mother while controlling for other confounding variables. The prevalence of HSV-2 IgG is more likely to increase with increasing age. Possible explanation for this finding is the increase in sexual activity with the increase in age. This is in agreement with published
data. HSV-2 seropositivity is known to increase with age.

The association between HSV-1 seropositivity and education was confirmed by multiple regression analysis (see results). The objective of educational interventions is to limit HSV transmission. There are few data on the effectiveness of such interventions but much of the published data, from the UK and the USA, suggest that they may be beneficial. In the USA, project RESPECT demonstrated that counseling those at risk might reduce HSV acquisition, a conclusion supported by data from candidate HSV vaccine trials and educational initiatives for other STIs. Patients should be educated on the natural history of genital HSV infection, variability in recurrence and strategies of limiting transmission risk. Healthcare providers should give consistent, relevant information and sources where patients can access further information. Serological testing may allow an opportunity to counsel patients about genital herpes. A significant barrier to effective implementation of educational interventions is the general public's low level of accurate knowledge on genital herpes, especially about asymptomatic shedding, transmission, risk reduction strategies and therapeutic options. Often, there does not seem to be any association between knowledge and behavior, rendering success largely dependent on the character of the patients. Due to the lack of knowledge, mass education campaigns may be required, although targeted campaigns may provide a more cost-effective solution. These campaigns should target young adults who have the highest rate of HSV acquisition. Pregnant women should be educated about this, particularly since they are likely to have the strongest motivation for avoiding infection from partners because of the possibility of neonatal herpes.

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