Seroprevalence of IgG Antibodies to Herpes Simplex Virus Type-1 in Nigerian Children

Shaibu AM, Aminu M, Musa BOP and Bugaje MA
Department of Microbiology, Faculty of Science, Ahmadu Bello University, Zaria
Department of Immunology, Ahmadu Bello University Teaching Hospital Zaria
Department of Paediatrics, Ahmadu Bello University Teaching Hospital Zaria

ABSTRACT

Background: Herpes simplex virus type-1 (HSV-1) can cause chronic ulcerative infection in immuno-suppressed children leading to latency with subsequent reactivate in the conjunctiva resulting in scarring, thickening of the cornea and blindness. They are also common cause of fatal sporadic encephalitis in 70% of paediatric patients. This cross sectional study determined the prevalence of HSV-1 in children in Kaduna State, Nigeria.

Method: A total of 377 blood samples were collected from children less than five years old attending some selected hospitals in Kaduna State and analyzed for HSV-1 IgG antibodies employing Enzyme immune assay technique by using commercially available ELISA Kits.

Results: Sero-prevalence rate of 57.8 % (218 /377) was obtained. The highest prevalence of HSV-1 infection was obtained in children in age group 49-60 months (85.2%) and lowest in children in age group 13-24 months (44.8%). Further analysis of the result of children less than one year old showed that children 9-16 weeks old were more susceptible to HSV-1 infection. HSV-1 infection was significantly associated with age ($\chi^2=37.92$, df =4, $p = 0.001$). Though a higher prevalence was obtained in female children (61.5%) than male children (54.5%), the difference observed in the prevalence was not statistically significant ($\chi^2=1.84$, df =1, $P =0.105$). HSV-1 infection was significantly associated with children who were in school ($\chi^2=15.28$, df =1, $P =0.001$) with a higher prevalence of 74.3%.

Conclusion: Over half of the children sampled were protected from HSV-1 infection while 42.2% were susceptible to the infection and were at risk of developing severe HSV-1 manifestation which includes keratitis, encephalitis and Keratoconjunctivitis.

Keywords: Seroprevalence, Herpes Simplex Virus Type-1, Children, ELIZA, Kaduna State, Nigeria

INTRODUCTION

Herpes Simplex Virus (HSV) belongs to the family Herpesviridae and is a large enveloped DNA virus of icosahedral symmetry divided into two types, HSV1 and HSV 2 (1-3). The virus is an ever-present pathogen that usually causes either asymptomatic infection or skin and mucosal diseases (4). Herpes Simplex Virus type-1 (HSV-1) is the most common cause of sporadic fetal encephalitis in paediatric children (3,5,6) and accounts for 23% of serious neurological disease in children (7). Neonatal herpes is a potentially devastating consequence of perinatal transmission of HSV, with significant morbidity and mortality (3, 8).

Prevalence of HSV infection varies throughout the world, poor hygiene, overcrowding, low socio-economic status, birth in developing country have been identified as some of the risk factors associated with the virus (2, 9). Herpes Simplex Virus type-1 is acquired through direct contact with infected lesions and body fluids. The prevalence of HSV-1 infection increases progressively from childhood to adulthood, the seroprevalence being inversely proportional to socioeconomic background (9). The virus may reactivate in the conjunctiva and reoccurrences of HSV-1 results in scarring, thickening of the cornea and blindness (3, 10). In the United States, HSV-1 infections are second only to trauma as cause of corneal blindness (3). There is however no published data on the relationship between corneal...
blindness and HSV-1 in Nigeria where we have many blind individuals. Herpes Simplex Viruses have become a world health problem because of its devastating clinical manifestations amongst HIV/AIDS children (2, 9). The virus is not a reportable disease in Nigeria and there is a dearth of information on its seroprevalence in neonates and children. The study was therefore conducted to determine the seroprevalence of HSV-1 infection in children 0-5 years attending some selected hospitals in Kaduna state, Nigeria.

Materials and Methods

Study Area
The study was conducted in Kaduna State, Nigeria. Kaduna state occupies part of the north central region of Nigeria. The Global location of Kaduna state is between 06° and 113° north of the equator and occupies an area of approximately 48,732.2 square kilometers.

Study Population
A total of 377 blood samples were randomly collected from male and female children 0-5 years old in three selected health care facilities from January 2011 to August 2011. The health care facilities include Barau Dikko Specialist Hospital (BDSH) Kaduna, Ahmadu Bello University Teaching Hospital (ABUTH) Zaria and Institute for Child Health (ICH) Banzazzau, Zaria.

Ethical Approval
Approval for the study was obtained from the ethical committee of the hospitals and consent for the participation of the children in the study were obtained from parents or care givers. Prior to the sample collection, demographic and clinical information of the children were obtained using structured questionnaires administered to parents or caregivers who consented to the study.

Sample Collection and Processing
Using a sterilized disposable syringe, 3ml of venous blood was collected aseptically by a clinician and dispensed into a plain sterile sample bottles and transported safely to the laboratory. The blood samples were centrifuged at 2,500 rpm and serum collected into clean, sterilized plain sample bottles using a clean dry Pasteur pipette. The sera were stored at -20°C until needed for analysis (11).

Analysis of Sera by Enzyme-Linked Immunosorbent Assay
The sera were tested for the presence of HVS-1 IgG antibodies using a commercially available IgG enzyme-linked Immunosorbent assay (ELISA) Kit manufactured by DIAGNOSTIC AUTOMATION, INC. USA. The ELISA uses HSV-1 antigens for the detection of anti-HSV-1 IgG antibodies in serum. The absorbance was read at 450 nm using an ELISA micro titer plate reader (Sigma Diagnostic). The presence or absence of anti-HSV-1-specific IgG antibodies in the test samples was calculated according to the manufacturer’s instructions. Results were obtained by comparing the antibody titers with the cut off values of the positive and negative controls.

Statistical Analysis
Data obtained were analyzed using SPSS statistical package version 17. Pearson Chi-square test of association was used to determine association between variables and seropositivity to HSV-1 infection in the children at 0.05 significant levels.

RESULTS

Of the 377 serum samples obtained from children aged 0-5 years, 218 were seropositive to HSV-1, giving a prevalence of 57.8% (Table 1). Analysis of the results by gender showed seroprevalence of 54.5% (108/198) and 61.5% (110/179) to HSV-1 for male and female children respectively (Figure 1). Although, the prevalence was higher among girls compared to boys, the difference was not statistically significant ($\chi^2 = 1.84, df = 1, P = 0.105$). The prevalence of HSV-1 according to age group is shown in Figure 2. The highest prevalence (85.2%: 46/54) was recorded among children in age group 49-60 months while the lowest (44.8%: 47/105) was recorded in age group 13-24 months. There was a statistically significant association between HSV-1 and age ($\chi^2 = 37.92, df = 4, P = 0.001$). Further analysis of the result of children in the age group 0-12 months showed a significant association between HSV-1 and age ($\chi^2 = 20.808, df = 5, P = 0.001$). The highest prevalence was recorded in children within 9-16 weeks of age (84.6%), followed
by children within 0-8 weeks (64.3%), 17-24 weeks (62.5%), 25-32 weeks (52.6%), 33-40 weeks (26.3%) and the lowest prevalence was observed in children within 41-48 weeks (23.5%).

The seroprevalence rate was significantly \( (\chi^2 = 15.28, df=1, P=0.001) \) higher among children in school (74.3% 75/101) compared to children who were not in school (51.8% 143/276) as shown in Table 2. Children who were in school were more likely to be infected with HSV-1 infection than those who were not in school (OR=1.43, 95%CI = 0.5851-0.7898).

The results obtained were analyzed according to the mode of delivery of the children enrolled in the study (Table 3). There was a higher preponderance in children delivered by spontaneous vaginal delivery (58.7% 205/349) as compared to those delivered by caesarian section (46.4% 13/28) though the difference was not statistically significant \( (\chi^2 =1.61, df=1, p=0.142) \).

The prevalence of HSV-1 infection was 54.1% (109/196) in children with 1-3 siblings while children with more than 9 siblings had the highest prevalence (76.9% 10/13) (Figure 3). The association between number of children per family to the infection was however not statistically significant \( (\chi^2 =6.45, df=3, p=0.092) \).

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**Figure 1:** Percentage distribution of IgG antibody to HSV-1 in relation to gender in children 0-5 years in Kaduna State, Nigeria.

**Figure 2:** Percentage distribution of IgG antibody to HSV-1 among different age groups in children (0-5) years in children in Kaduna State, Nigeria.

**Figure 3:** Percentage distribution IgG antibody to HSV-1 in children 0-5 years old in relation to number of children per family in children in Kaduna State, Nigeria.

**Table 1:** Seroprevalence of IgG antibody to HSV-1 in children (0-5) years attending some selected hospitals in Kaduna State.

<table>
<thead>
<tr>
<th>Hospitals</th>
<th>No. of Samples Tested</th>
<th>Number Positive</th>
<th>Percentage Positive</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BISH</td>
<td>126</td>
<td>62</td>
<td>49.2</td>
<td>40.63-57.83</td>
</tr>
<tr>
<td>ABUTH</td>
<td>125</td>
<td>80</td>
<td>64.0</td>
<td>55.28-71.88</td>
</tr>
<tr>
<td>ICH</td>
<td>126</td>
<td>76</td>
<td>60.3</td>
<td>51.59-68.47</td>
</tr>
<tr>
<td>TOTAL</td>
<td>377</td>
<td>218</td>
<td>57.8</td>
<td>52.79-62.71</td>
</tr>
</tbody>
</table>

\( (\chi^2 =6.41, df=2, P=0.047) \)

**Key**

BISH-Benue State Hospital
ABUTH-Abia State University Teaching Hospital
ICH-Institute for Child Health
A seroprevalence of 57.8% was obtained in this study which was relatively high and this could in part be attributed to the mode of transmission of HSV-1 which includes direct contact with lesions and through saliva. The result implies that 42.2% of the children in the study were susceptible to HSV-1 infection and were not immunized against the virus. These pockets of susceptible children are at risk of developing severe HSV-1 manifestation which includes gingivitis, Keratoconjunctivitis and fetal encephalitis. If these children are immunocompromised and their cellular immunity is impaired, infection may spread and involve respiratory tract, esophagus and intestinal mucosa as has been shown in children with AIDS and patients under immunosuppressive treatment like bone marrow, renal and cardiac transplant recipients; In addition, if any of these susceptible children is malnourished, he or she will be prone to fatal disseminated HSV infection (3, 5).

The result is similar to the prevalence of 59% obtained in children in Eritrea (12), 59% in New Mexico (13) and 55% in Syria (14) but higher than those reported in Germany, Israel and England where a prevalence of 31%, 38% and 20% were obtained respectively (15-17). The prevalence rate in this study was however lower than that of 99.7% obtained among older children in Kaduna state (18) and 69% among adults in Plateau state (19). The lower prevalence obtained in this study may be as a result of age difference in the study population. Earlier studies have found the prevalence of HSV-1 to increase with age progressively (9, 20-22). The published studies in Nigeria sampled older children and adults while the present study sampled younger children 0-5 years old.

Seropositivity of HSV-1 IgG antibody in relation to the selected hospitals showed the lowest and highest prevalence amongst children attending BDSH and ABUTH respectively. The lower prevalences seen in BDSH could be due to a number of factors. It could be due to higher number of neonates and younger children who may not have had contact with the virus seen in the unit; or due to increased personal hygiene among the patients as the clinic is situated in Kaduna which is an urban centre; in addition, the clinic is a primary health care centre. The higher prevalence recorded for ABUTH may be due to increased number of patients attending the tertiary health care centre where patients with clinical disease are more likely to be referred.

There was a highly statistically significant association between age group and infection with HSV-1. The rise in seroprevalence rate with age is similar to the findings in Tanzania, Germany and Israel where HSV-1 seroprevalence was found to increase with increasing age (16, 17, 21). The prevalence obtained for children in age group 0-12 months and 13-24 months were similar. The prevalence of 44.8% in age group 0-12 months in this study is similar to the prevalence (49%) obtained in newborns in England and Wales (20). However, prevalence obtained in this age group could reflect in part maternal antibody (IgG) status, since the antibodies can cross the placenta. The decrease in prevalence (44.8%) in age group 13-24 months could be due to waning of maternal antibody. Studies have also revealed that
early childhood stress can also elevate antibody levels in these children (25). The highest prevalence of the infection in age group 49-60 months could be associated with increased level of interaction among children.

A high prevalence rate of 74.3% was obtained in children who were in school in this study compared to children who were not in school. Earlier studies have not made such comparison. The increased prevalence in children who attended formal education may be associated with the higher degree of interaction amongst children with their peer from variable cultures.

There was no statistically significant association between the mode of delivery of children and seropositivity to HSV-1 infection, although a higher prevalence was observed in children delivered via normal delivery (spontaneous vaginal delivery) than in children delivered via caesarian section. The higher prevalence seen in children born via normal delivery may be as a result of contact with infected secretion from the mucosa lining of female genital tract during labour. Caesarian section on the other hand has been shown to reduce the risk of transmission from mother to child during delivery (26, 27).

The high seroprevalence of HSV-1 among children with high number of siblings seen in this study could be associated to the closer interaction amongst the siblings and overcrowding as also postulated by Brinzli et al (28).

**CONCLUSION**

Herpes simplex virus type-1 seroprevalence of 57.8% was obtained in children in this study, indicating that over half of the children sampled were protected from HSV-1 infection. However, 42.2% of the children were susceptible to the infection and were at risk of developing keratitis, encephalitis and Keratoconjunctivitis. Younger age and school attendance were risk factors associated with HSV-1 infection among children in the study.

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