HIV-2 in West Africa. Epidemiological studies
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Regional differences in HIV trends in The Gambia: results from sentinel surveillance among pregnant women


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Regional differences in HIV trends in The Gambia: results from sentinel surveillance among pregnant women

**ABSTRACT**

**Objective:** To monitor HIV-1 and HIV-2 trends in The Gambia, West Africa

**Methods:** In 1993-5 a nation-wide survey among 29,670 pregnant women attending eight antenatal clinics estimated the seroprevalence of HIV-1 at 0.6%, and of HIV-2 at 1.1%. Five years later sentinel surveillance in pregnant women was established, using unlinked anonymous testing in four clinics. A dried blood spot on filter paper was obtained and tested for HIV antibodies.

**Results:** Between May 2000 and August 2001, 8054 analysable samples were collected at four sites. HIV-1 prevalence rose sharply in one rural area from 0.6% to 3.0% (p < 0.0001), but the rise was small and non-significant in two other rural sites and in the urban site. The HIV-2 prevalence did not change significantly in any of the sites. The overall prevalence of HIV-1 was 1.0% (95% Confidence Interval (CI) 0.8 – 1.3%), and of HIV-2 0.8% (CI 0.6 – 1.0%). Site, nationality and higher age were significantly associated with HIV-1 infection, and higher parity and site with HIV-2 infection.

**Conclusions:** Fifteen years after the first case of HIV-1 was described in The Gambia, the epidemic is still at a low level. There is heterogeneity within the country, with one rural area experiencing a 5-fold rise in 6 years. HIV-2 prevalence in The Gambia is stable.
HIV-2 IN WEST AFRICA

Introduction

In most West African countries the prevalence of HIV-1 is rising, and that of HIV-2 is falling or stable [1-6]. In Senegal HIV-1 prevalence has been remarkably stable, a fact that has been ascribed to that country's effective AIDS control programme [7,8].

Because the epidemiology and clinical impact of the two HIV infections is so different [9,10,11], it is important to distinguish between them in surveillance: a decline in HIV-2 with a concurrent rise in HIV-1 could be interpreted erroneously as a stable HIV prevalence [12].

A sentinel surveillance system has never been in place in The Gambia. The most recent prevalence data are from a nation-wide study among pregnant women attending antenatal clinics in 1993-5 [11]. HIV-1 prevalence was 0.6% (95% Confidence interval (CI) 0.5-0.7%) and HIV-2 prevalence 1.1% (CI 1.0-1.3%).

A national HIV sentinel surveillance among pregnant women was started in 2000. In order to evaluate whether a significant rise of HIV-1 had occurred since the 1993-5 survey, surveillance was done in four of the antenatal clinics used in the previous survey.

Methods

Survey in 1993-5

In a study of mother-to-child transmission of HIV in 1993-5 pregnant women were recruited at eight health centres throughout The Gambia. HIV diagnosis was based on a combination of ELISA's using serum obtained from venous blood samples [11].

Subjects

For the present study, four of the original health facilities were selected as recruitment sites. Serekunda health centre is located in the largest urban area of the country, and is
the busiest clinic. Sibanor health centre is in a rural area on the south bank of the river Gambia, 88 km from the capital. The majority of the people in the area belong to the Jola ethnic group. Farafenni hospital is on the north bank, 194 km inland, where over 50% of people are from the Wollof ethnic group. Basse is a small town in the eastern tip of the country (371 km inland), and there are three major ethnic groups: Fula, Serahuli and Mandinka. These four centres provide antenatal care to over 20% of all pregnant women in The Gambia. Staff from these facilities conduct mobile clinics in villages beyond walking distance of the health facility.

The health worker who completed the routine antenatal card, also filled a study data form. Names or other unique personal identifiers were not recorded.

**Laboratory methods**

A circle of 2 cm diameter on filter paper (Whatman grade BFC 180, Whatman International Ltd, Maidstone, UK) was filled with a few drops of blood. The filter papers with the blood spots were allowed to dry separately overnight in a compartmentalised wooden rack, and collected once every 7 – 14 days.

On reception in the laboratory, a 5.5 mm diameter blood spot was punched out. The spots were eluted in an elution buffer overnight. Eluates were combined in pools of five and screened using ICEHIV 1.0.2 (Murex Diagnostics Ltd, Dartford, UK). If a pool was positive, each individual sample was tested with ICEHIV 1.0.2. Positive samples were then tested for HIV-1 antibodies by Wellcozyme HIV-recombinant-1 (Murex) and for HIV-2 antibodies by ICEHIV-2 (Murex). If the sample was reactive in only one of the ELISA's, it was assigned the corresponding HIV diagnosis. If it was strongly reactive in both it was considered a dual infection with both HIV-1 and HIV-2. These methods were piloted first in the MRC clinic. In the pilot study Wellcozyme-1 (but not ICEHIV-2 or ICEHIV1.0.2) was shown to be slightly less sensitive when testing the eluate than the serum (R Sarge-Njie, manuscript in preparation), so false-negative results for HIV-1 were possible. Therefore, in cases where ICEHIV1.0.2 was positive and both monospecific ELISA's were negative, an HIV-1 particle agglutination test was done (Serodia HIV-1,
Fujirebio Inc, Tokyo, Japan). The results of the Serodia HIV-1 were regarded as final, irrespective of the titre. Most dual serological patterns are due to true dual infections. [13] Therefore women whose samples were dually reactive, were regarded as being infected with both HIV-1 and HIV-2, and analysed both in the HIV-1 group and in the HIV-2 group.

Three types of controls were used: negative, low and high positive DBS filter paper discs (supplied by CDC, Atlanta, US); known HIV-1 and HIV-2 positive sera diluted in freshly drawn HIV negative blood spotted on filter paper and dried; serum controls (provided by test manufacturers).

Statistical methods
In the analysis each health facility was given a weight proportional to the population size of the region that the health facility was regarded to represent. Using the weighted prevalences, risk ratios (RR) comparing the 2000-1 prevalence with that in 1993-5 were calculated.

Ethics
The study employed Unlinked Anonymous Testing [14,15,16]. The women in the study provided a blood sample for other purposes (haemoglobin or syphilis serology) and a few drops, considered to be left-overs, were used for the study. Women were not explicitly told that part of their blood was to be used for HIV surveillance. A parallel system for women to be tested for HIV if they wished so was in place. The study was approved by the Gambia Government / MRC Laboratories Ethics Committee.

Results
Sample were collected between May 2000 and August 2001. In total 8054 samples were available for analysis. HIV infection was found in 170: 94 HIV-1, 61 HIV-2, and 15 HIV-1 and HIV-2 dually positive.
Table 1. HIV-1 and HIV-2 prevalence in 1993-5 and 2000-1 among pregnant women attending four health facilities in The Gambia

<table>
<thead>
<tr>
<th>Site</th>
<th>1993-5</th>
<th>2000-1</th>
<th>p-value</th>
<th>1993-5</th>
<th>2000-1</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>%</td>
<td>n/N</td>
<td>%</td>
<td>risk ratio (95% CI)</td>
<td>n/N</td>
</tr>
<tr>
<td>Serekunda</td>
<td>37/5498</td>
<td>0.7%</td>
<td>30/2998</td>
<td>1.0%</td>
<td>1.5 (0.9-2.4)</td>
<td>0.10</td>
</tr>
<tr>
<td>Sibanor</td>
<td>20/3230</td>
<td>0.6%</td>
<td>49/1627</td>
<td>3.0%</td>
<td>4.9 (2.9-8.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Farafenni</td>
<td>10/3441</td>
<td>0.3%</td>
<td>7/1730</td>
<td>0.4%</td>
<td>1.4 (0.5-3.7)</td>
<td>0.5</td>
</tr>
<tr>
<td>Basse</td>
<td>46/4445</td>
<td>1.0%</td>
<td>23/1699</td>
<td>1.4%</td>
<td>1.3 (0.8-2.2)</td>
<td>0.3</td>
</tr>
<tr>
<td>Overall b</td>
<td>113/16614 (0.5-0.8)</td>
<td>109/8054 (0.8-1.3)</td>
<td>1.5 (1.1-2.1)</td>
<td>0.004</td>
<td>186/16614 (0.9-1.1)</td>
<td>0.8 (0.6-1.0)</td>
</tr>
<tr>
<td></td>
<td>16614</td>
<td></td>
<td>8054</td>
<td></td>
<td></td>
<td>16614</td>
</tr>
</tbody>
</table>

a. Includes HIV-1 and HIV-2 dually infected subjects; b. Weighted prevalence. Weights used: Serekunda 0.30; Sibanor 0.07; Farafenni 0.33; Basse 0.30.; c. The overall prevalence and 95% Confidence Intervals of HIV-1 and HIV-2 in 1993-5 are not exactly the same as that published by O'Donovan [11], as the above prevalences are based on data of only four health facilities, and are weighted according to population size in the areas represented by the health facilities. 95% CI = 95% confidence interval. n/N = number seropositive / total number.
HIV-1

In all four sites the prevalence of HIV-1 rose over the six years, but this rise was small and not significant in three of the sites (Table 1). The only significant and substantial rise occurred in a rural site (Sibanor), from 0.6 to 3.0% (p<0.0001). The risk ratio in Sibanor was 4.9 (CI 2.9-8.2); the risk ratio in each of the other sites was around 1.4. The overall prevalence of HIV-1 rose from 0.7% (CI: 0.6-0.8) in 1993-5 to 1.0 % (0.8-1.3%) in 2000-1 (p=0.004). There was no significant difference in the mean age of participating women between the two studies (p=0.6), but the mean age of HIV-1 infected women was 2.5 years higher in 2000-1 compared to 1993-5 (p=0.0001).

Table 2 shows that the HIV-1 prevalence was lower among pregnant teenagers compared to older women; this phenomenon was restricted to Sibanor (data not shown). HIV-1 infected women were on average 1.4 years older than seronegative women (25.8 vs. 24.4 years; p=0.01). HIV-1 infection was not associated with marital status or parity. The prevalence was higher among Senegalese women compared to other non-Gambians (p=0.016). Significant differences were observed between ethnic groups, the prevalence being highest among the Jola (2.7%), and lowest among the Wolof (0.6%). Among women recruited at Sibanor the HIV-1 prevalence was significantly higher among Senegalese women compared to Gambian women (5.6% vs. 2.5%; p=0.006). This difference was not observed at the other sites.

In a multivariate analysis only site and nationality were significant risk factors. Compared to Basse, the OR for women recruited at Serekunda was 0.7 (CI: 0.4-1.3), at Sibanor 2.2 (CI 1.3-3.9), and at Farafenni 0.3 (CI: 0.1-0.7). The OR for Senegalese nationality was 1.7 (CI 1.0-1.7; p=0.03) and for other non-Gambian nationality (mainly Guinea-Conakry) 0.5 (CI: 0.2-1.7; p=0.3). There was significant interaction (p=0.01) between ethnic group and site: among women recruited in Sibanor, Jola's had a 3.4-fold (CI: 1.0-11) higher odds of having HIV-1 than Mandinka's (baseline group), but in the other sites there was no significant association between Jola ethnicity and HIV-1 infection.

HIV-2

The prevalence of HIV-2 rose in two and decreased in the other two sites (Table 1); all of these changes were small and only one decline was significant (Farafenni; p=0.05). The
<table>
<thead>
<tr>
<th>Age</th>
<th>HIV-1 Sero-prevalence</th>
<th>Odds Ratio</th>
<th>Adjusted OR (95% CI)</th>
<th>HIV-2 Sero-prevalence</th>
<th>Odds Ratio</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>0/33 (0%)</td>
<td>1</td>
<td>1</td>
<td>0/33 (0%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>15-19</td>
<td>12/1551 (0.8%)</td>
<td>1</td>
<td>1</td>
<td>5/1551 (0.3%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>20-24</td>
<td>37/2531 (1.5%)</td>
<td>1.9</td>
<td>2.0 [1.0-4.0]</td>
<td>22/2531 (0.9%)</td>
<td>2.8</td>
<td>1.9 [0.7-5.6]</td>
</tr>
<tr>
<td>25-29</td>
<td>28/2240 (1.3%)</td>
<td>1.7</td>
<td>1.8 [0.9-3.6]</td>
<td>25/2240 (1.1%)</td>
<td>3.6</td>
<td>2.5 [0.8-7.6]</td>
</tr>
<tr>
<td>30-34</td>
<td>20/1074 (1.9%)</td>
<td>2.2</td>
<td>2.3 [1.1-4.6]</td>
<td>14/1074 (1.3%)</td>
<td>4.4</td>
<td>2.6 [0.8-8.7]</td>
</tr>
<tr>
<td>35+</td>
<td>8/518 (1.5%)</td>
<td></td>
<td></td>
<td>9/518 (1.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>6/428 (1.4%)</td>
<td>1</td>
<td>1</td>
<td>1/428 (0.2%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Married</td>
<td>97/7359 (1.3%)</td>
<td>1.0</td>
<td>0.9 [0.4-2.5]</td>
<td>72/7359 (1.0%)</td>
<td>4.4</td>
<td>2.3 [0.3-17]</td>
</tr>
<tr>
<td>Divorced/Widowed</td>
<td>0/10 (0%)</td>
<td>--</td>
<td>--</td>
<td>0/10 (0%)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>21/1692 (1.2%)</td>
<td>1</td>
<td>1</td>
<td>5/1692 (0.3%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>1-2</td>
<td>36/2685 (1.3%)</td>
<td>1.1</td>
<td>0.8 [0.4-1.6]</td>
<td>30/2685 (1.1%)</td>
<td>3.9</td>
<td>3.9 [1.5-10]</td>
</tr>
<tr>
<td>3-4</td>
<td>21/1959 (1.1%)</td>
<td>0.9</td>
<td>0.7 [0.3-1.4]</td>
<td>15/1959 (0.8%)</td>
<td>2.6</td>
<td>2.6 [0.9-7.2]</td>
</tr>
<tr>
<td>&gt;=5</td>
<td>29/1487 (2.0%)</td>
<td>1.5</td>
<td>1.0 [0.4-2.4]</td>
<td>25/1487 (1.7%)</td>
<td>5.4</td>
<td>5.5 [2.1-14]</td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gambian</td>
<td>80/6115 (1.3%)</td>
<td>1</td>
<td>1</td>
<td>62/6115 (1.0%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Senegalese</td>
<td>24/1214 (2.0%)</td>
<td>1.6</td>
<td>1.7 [1.0-2.7]</td>
<td>8/1214 (0.7%)</td>
<td>0.7</td>
<td>0.7 [0.3-1.5]</td>
</tr>
<tr>
<td>Other</td>
<td>3/592 (0.5%)</td>
<td>0.5</td>
<td>0.6 [0.2-1.8]</td>
<td>5/592 (0.8%)</td>
<td>1.0</td>
<td>1.1 [0.4-2.8]</td>
</tr>
<tr>
<td>Ethnic group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandinka</td>
<td>20/2004 (1.0%)</td>
<td>1</td>
<td>1</td>
<td>14/2004 (0.7%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fula</td>
<td>20/1698 (1.2%)</td>
<td>1.1</td>
<td>1.2 [0.6-2.4]</td>
<td>19/1698 (1.1%)</td>
<td>1.5</td>
<td>1.6 [0.8-3.3]</td>
</tr>
<tr>
<td>Wolof</td>
<td>8/1341 (0.6%)</td>
<td>1.1</td>
<td>0.8 [0.3-2.1]</td>
<td>5/1341 (0.4%)</td>
<td>0.9</td>
<td>0.9 [0.3-2.8]</td>
</tr>
<tr>
<td>Jola</td>
<td>42/1562 (2.7%)</td>
<td>1.9</td>
<td>1.6 [0.8-3.0]</td>
<td>26/1562 (1.7%)</td>
<td>2.0</td>
<td>2.1 [1.0-4.5]</td>
</tr>
<tr>
<td>Serer, Manjago, Aku, other</td>
<td>7/606 (1.2%)</td>
<td>1.2</td>
<td>1.1 [0.5-2.8]</td>
<td>5/606 (0.8%)</td>
<td>1.2</td>
<td>1.3 [0.5-3.8]</td>
</tr>
<tr>
<td>Serahuli</td>
<td>9/727 (1.2%)</td>
<td>1.1</td>
<td>0.7 [0.3-1.8]</td>
<td>6/727 (0.8%)</td>
<td>0.9</td>
<td>0.9 [0.3-2.5]</td>
</tr>
</tbody>
</table>

1. No age available of 107 women; 2. No information about marital status of 257 women; 3. No information about parity of 231 women; 4. No information about nationality of 133 women; 5. No information about ethnic group of 116 women; 6. The "crude" Odds Ratio is adjusted for site only; 7. The Odds Ratio for HIV-1 infection in the final model is adjusted for age group, site, and nationality; 8. The Odds Ratio for HIV-2 infection in the final model is adjusted for site and parity. OR = Odds Ratio
overall HIV-2 prevalence decreased from 1.0% (0.85-1.2) in 1993-5 to 0.8% (0.6-1.0) in 2000-1 (p=0.09). The average age of HIV-2 infected women was identical in the two studies (26.5 years).

The prevalence of HIV-2 rose with age (test for trend: p=0.002; Table 2). HIV-2 infected women were on average 2.1 years older than seronegative women (26.5 vs. 24.4 years; p=0.001). There were no significant differences in prevalence by nationality or marital status. Prevalence of HIV-2 increased with parity (test for trend: p=0.001). Significant differences were observed between ethnic groups, the prevalence being highest among the Jola (1.7%), and lowest among the Wolof (0.4%).

In a multivariate analysis age and ethnic group were no longer significant, but higher parity was a significant risk factor, as was site (Table 2). Subjects recruited at Farafenni were less likely, and subjects recruited at Sibanor were more likely to have HIV-2.

Discussion

Compared to 1993-5 the HIV-1 prevalence among pregnant women has significantly risen in one rural area, while the overall prevalence has remained low at 1%. The HIV-2 prevalence showed a non-significant decrease from 1.0% to 0.8%. In a period of 6 years HIV-2 has been overtaken by HIV-1 as the predominant virus.

There were some differences in study design between the 1993-5 and the current study that could have lead to bias. The refusal rate in the first study was high (10%) in Serrekunda but low at the other sites. Thus selection bias may have influenced the risk ratio in Serrekunda. The current study used dried blood spots as opposed to serum and considerable delays occurred before they were eluted and tested, so decay of antibodies could possibly have occurred. We analysed the possible effect that delays before testing might have had on the results (data not shown), and concluded that this was unlikely to have lead to an appreciable underestimate [17].
In 1993-5, HIV-2 prevalence was higher in Sibanor than elsewhere. Although HIV-2 did not rise further, HIV-1 increased 5-fold and was significantly higher among the Jola’s compared to other ethnic groups. Prevalence among Senegalese women attending the Sibanor clinic (less than 10 km from the Senegalese border), most of whom were Jola and living in the Cassamance, the southern province of Senegal, was more than twice as high as that in Gambian women. In this area, where there is an armed conflict, there has been a significant rise in HIV prevalence among female sexworkers [7,12]. The Jola ethnic group in the area around Sibanor celebrates initiation ceremonies, during which marriage bonds are considered temporarily invalid [18]. These ceremonies, which are unique to this area, are popular and attended by Jola’s from far afield; [19] the promiscuity during these ceremonies may be an explanation for the rising HIV-1 prevalence in this area.

Fifteen years after the first case of HIV-1, the prevalence is still low in The Gambia, and the same is true in Senegal. Male circumcision, which was shown to be a protective factor in a recent meta-analysis [20], is nearly universal in The Gambia. The prevalence of herpes simplex virus type 2, an important co-factor for HIV infection [21], is lower in The Gambia [19] than in East Africa [22]. HIV-1 prevalences have been lowest in Muslim countries of North Africa and the Middle East [23], and this is likely to be linked to sexual behaviour. As over 95% of the Gambian population is Muslim [24], the same reasons could underlie the low prevalence in Senegal and The Gambia. Studies on sexual behaviour in The Gambia are needed to further interpret the low prevalence.

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HIV-2 IN WEST AFRICA

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References


