Effect of a healthcare gender gap on progression of HIV/AIDS defined by clinical-biological criteria among adults from Cordoba City (Argentina) from 1995 to 2005

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ARTICLE INFO

Article history:
Received 10 December 2008
Accepted 22 September 2009
Available online 1 de marzo de 2010

Keywords:
AIDS
HIV
Gender
Clinical course

ABSTRACT

Objective: To establish the influence of clinical status at diagnosis and of gender on progression of HIV/AIDS determined by clinical-biological factors in patients from Cordoba City (Argentina) from 1995 to 2005.

Methods: Gender and clinical and laboratory data were evaluated by descriptive statistics, non-parametric survival analysis, and generalized linear models at the beginning of the study (diagnosis) and at the end (hospital records, n=209).

Results: At diagnosis, women (n=28, 13.4%) had a higher probability of being asymptomatic than men (n=181, 86.6%). High viremia was associated with advanced clinical stages, but was inversely related to CD4 count. Truncated Kaplan-Meier curves were similar for both sexes. The probability of not having AIDS criteria at the end of the study was higher in patients without these criteria at diagnosis. Women had a higher probability of having AIDS at the end of the follow-up than men. In contrast, men had a higher prevalence of venereal diseases (n=38, 21%), dysmetabolic profile (n=14, 7.7%) and positive serology for opportunists (n=31, 17.1%). Marker diseases were mainly represented by internal mycosis and waste syndrome, although less specific findings (anemia, oral lesions) were also associated with progression.

Conclusions: Using an integrative approach, high viremia was critically linked to clinical and lymphocyte impairment. Early diagnosis was a major determinant of clinical course, with women having a worse prognosis. However, men were diagnosed in clinically advanced stages and with other non-HIV-related entities, which could affect progression. These findings should be integrated into the planning of preventive strategies.

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Condicionamiento de la evolución del VIH/sida definida por criterios clinicobiológicos en adultos de la ciudad de Córdoba (Argentina), de 1995 a 2005, por la brecha sanitaria existente entre ambos sexos

RESUMEN


Métodos: El sexo, los datos clínicos y los de laboratorio fueron evaluados por estadística descriptiva, análisis de supervivencia no paramétrico y modelos lineales generalizados al inicio (diagnóstico) y al final del estudio (registro hospitalario, 209 casos).

Resultados: Las mujeres (n=28, 13,4%) tienen mayor probabilidad de estar asintomáticas que los hombres (n=181, 86,6%) en el momento del diagnóstico. La viremia alta está asociada con estudios clínicos avanzados, pero está inversamente relacionada con el de CD4. Las curvas truncadas de Kaplan-Meier son similares para ambos sexos. La probabilidad de no tener criterios de sida al final del estudio está incrementada para los pacientes diagnosticados sin ellos. Además, las mujeres tienen mayor probabilidad de presentar sida que los hombres al finalizar el seguimiento recuento. No obstante, ellos mostraron una elevada prevalencia de enfermedades venéreas (n=38, 21%), perfil dismetabolico (n=14, 7,7%) y serología para oportunistas (n=31, 17,1%). Las enfermedades marcadoras fueron principalmente micosis internas y síndrome consumivo, aunque hallazgos menos específicos (anemia, lesiones orales) también se asociaban a la progresión.

Conclusiones: Utilizando un enfoque integrador, la viremia estuvo muy ligada al empeoramiento clínico y linfocitario, siendo el diagnóstico temprano un determinante mayor de evolución, con las mujeres teniendo peor pronóstico. Sin embargo, los hombres fueron diagnosticados avanzados clínicamente, con otros problemas no asociados al VIH que podrían afectar su evolución. Estos resultados deberían ser integrados en el planeamiento sanitario de prevención.

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Furthermore, the integration of different
Asymptomatic people were tested in regard to
In the construction of the interaction
Subsequently, this study uses an integral trend
UNAIDS has estimated that at least 40 million people live with
HIV/AIDS, with 3 million deaths and 5 million new cases every
The number of HIV/AIDS cases notified in Argentina since
1, when the obligatory notification began, was 34,803 with
A prevalence. The majority of people living with this infection
reside in Capital Federal (30%), Buenos Aires (30%), Cordoba (6%)
and Santa Fe (4%). In the year 2005, Argentina exhibited rates of
12.9 HIV cases and of 4.3 AIDS cases per 100,000 persons, which
have tended to decrease since the year 1997, when HAART was
introduced. Regarding Cordoba, the rate of HIV cases per 100,000
persons was 11.6 in 2005. The most relevant transmission way
was sexual (82% of women and 73% of men, of which 31%
corresponded to homosexual practice). Also, 4.6% of women and
14.5% of men used injected drugs. The 4.3% of the cases were due
to vertical transmission.2
The epidemiological characterization of the infection is
difficult due to its varying spread patterns in different regions
worldwide.3 Consequently, infection behaviour should be ana-
yzed thoroughly in each population in the context of the general
pandemic reality.4 Furthermore, the integration of different
statistical methods is necessary, so that reliable tools may be
obtained for medical decision mechanisms. Patient surveys
should be realized by medical institutions in order to improve
engagement and retention in care, and to achieve an organiza-
tional self-assessment to effect operational changes that minimize
barriers to care.5 Subsequently, this study uses an integral trend
of HIV/AIDS in an Argentinean city, and its purpose is to establish
the role of the diagnostic condition and the gender influence in
this infection by establishing the close relationship between
medical status at diagnosis and during evolution, by means of
analysis of the clinical and biological markers of the HIV infection.

Methods

Subjects and setting

Data were collected from hospital records (Hospital Nacional
de Clinicas, Universidad Nacional de Cordoba) anonymously in
agreement with ethical concerns for 209 adult patients from the
Cordoba City (Argentina) in the period 1995–2005. Non experi-
mental procedures were performed for this prospecting work
made in retrospect, with a sample under current medical control
being described.

Patients were classified according to the Control Disease
Center criteria, regarding the peripheral blood CD4 count (1:
> 500, 2: 200–499, 3: < 200 CD4 cells/μL), plasmatic viral load
(< or > 100 000 copies/mL-VL-) and clinical categories (A: health
or non-related diseases; B: related diseases; C: marker diseases,
opportunism).6 Asymptomatic people were tested in regard to
antecedents of risk behaviours. Patients who exhibited < 200-
CD4, > 10^5-VL and/or opportunistic pathologies were obligatorily
treated with antiretroviral drugs. Individuals who presented
AIDS criteria (clinical category C and/or level 3 of CD4) at the
diagnostic instance were considered lately-diagnosed patients.
The transmission ways were in accordance with governmental data.2

Laboratory

CD4 and VL were assayed by flow cytometry and RT-PCR,
respectively.7 Other biochemical probes had been performed
using standard commercial kits, provided by Wiener Lab (Argen-
tina).

Statistical analysis

Results are expressed as mean (SD). Clinical-biological records
were studied during diagnosis and progression, with the descrip-
tive analyses examining the prevalence of clinical and biochem-
ical parameters. Data recorded at the time of serological
confirmation were analyzed by two different approaches. First,
the clinical stage was considered as the response variable, and a
proportional odds model was fitted,8 with gender and VL factors
as covariates in the linear predictor. Then, the association
between CD4, gender and VL was assessed using a log-linear
model for ordinal data.9 In the construction of the interaction
terms, this association model considers scores for the three
ordered CD4 categories.

The incidence rate of opportunism was calculated for each
gender, assuming that individual times could vary (IR=new cases
of opportunism/Σ individual times free of opportunism).10
Also, using the appearance of marker diseases (opportunism)
as the clinical evolution indicator, the cumulative probability
was estimated for time free of these by the Kaplan-Meier
method.12 with gender differences being investigated by the
log-rank test.13

Finally, the association between the initial and final medical
status, i.e. at the diagnosis and at the end of the study, was
analyzed by log-linear models,10 with patients being classified
according to sex and presence/absence of AIDS criteria, at each
instance. This categorization of initial and final stages avoids
treatment being a confounding factor, since treatment was strictly
given to every patient diagnosed with AIDS. Newly diagnosed
patients (< 1 evolution year) were excluded, since they did not
have enough time to change the category.

The significance level used was α=0.05. Data were analyzed
using InfoStat2007e.1 (InfoStat Group, http://www.infostat.co-
m.ar) and R version 2.0.1 (R Development Core Team, http://

Results

181 men (86.6%) were of mean age 35.2 ± 8.7 (range=18–66),
and 28 women (13.4%) were 38.1 ± 10.4 (range=20–61). This
included 15% men and 25% women who had been recently
diagnosed (< 1 year from the diagnosis). Patients were enrolled at
27.11 ± 1.84 (men) and 4.78 ± 2.34 (women) individuals per year,
including mainly the 24–42 year-old range at different clinical
stages (table 1).

Diagnosis

71.8% men presented stage A. Nonetheless, 37.6% had other
negative medical conditions (not specifically related to AIDS),
including abnormal laboratory tests. These laboratory findings
were: sustained high IgG in mononucleosis-like syndromes
(Toxoplasma spp., cytomegalovirus, Epstein-Barr virus) (n=31),
dyslipemia (n=14), altered asymptomatic hepatogram (n=8), sustained high IgG for other pathogens (Trypanosoma cruzi, hepatitis B and A viruses) (n=4), among others (n=5). Other sexually transmitted diseases were present in 21% of patients (early syphilis: 18, chronic hepatitis: 13, papilloma virus: 5, genital herpes simplex: 2, molluscum contagiosum: 1). There were 7 cases of acute retroviral syndrome, with stage B being principally represented by polymyositis, oral candidiasis, herpes zoster, leucopenia and thrombocytopenia. Anaemia was also a common finding in progressing patients (n=2, B1; n=1, C2; n=10, C3). Oral lesions were found in 16 persons, 13 with AIDS, corresponding to oropharynx candidiasis and oral hairy leukoplakia. When CD4 decreased, seborrheic dermatitis, acute respiratory infections, Kaposi’s sarcoma and wasting syndrome emerged. Pulmonary pneumocystosis (n=11), oesophageal candidiasis (n=4), disseminated histoplasmosis (n=2), progressive multifocal leukoencephalopathy (n=2) and retinitis by cytomegalovirus (n=1) formed the marker illnesses. Other advanced clinical events were chronic diarrhoea, fever of an unknown origin, severe thrombocytopenia, peripheral neuropathy and persistent generalized pruritus, all without a clear etiological diagnosis. Pulmonary tuberculosis complicated with meningitis was also found.

85.7% women were diagnosed as being asymptomatic, with 14.3% being detected during routine serological control in obstetric patients. Also, oropharynx candidiasis was identified in a B2 case. The rest were considered as AIDS cases, presenting consumption with anaemia and oral hairy leukoplakia, herpes zoster, pulmonary pneumocystosis, cerebral toxoplasmosis, meningocœphalitis by Cryptococcus, persistent polyadenopathy and neutropenia.

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The proportional odds model (deviance=4.958, df=5, p=0.292) showed that women have higher odds (4.13 times) of presenting a better clinical condition than men (p=0.023), for a fixed VL. The odds of having an advanced clinical stage are higher (12.41 times) for VL > 100,000 copies/ml (p < 0.001) for a given gender. Furthermore, the association log-linear model was suitable for

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Table 1
Clinical-epidemiological profile of the studied sample

<table>
<thead>
<tr>
<th>A. Demographic compositiona</th>
<th>Men (n=181)</th>
<th>Women (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ranges</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[18;24)</td>
<td>9 (5.0%)</td>
<td>2 (7.1%)</td>
</tr>
<tr>
<td>[24;30)</td>
<td>37 (20.4%)</td>
<td>3 (10.7%)</td>
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<tr>
<td>[30;36)</td>
<td>60 (33.1%)</td>
<td>8 (28.6%)</td>
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<tr>
<td>[36;42)</td>
<td>44 (24.3%)</td>
<td>5 (17.9%)</td>
</tr>
<tr>
<td>[42;48)</td>
<td>13 (7.2%)</td>
<td>4 (14.3%)</td>
</tr>
<tr>
<td>[48;54)</td>
<td>9 (5.0%)</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>[54;60)</td>
<td>5 (2.8%)</td>
<td>1 (3.6%)</td>
</tr>
<tr>
<td>[60;66)</td>
<td>4 (2.2%)</td>
<td>1 (3.6%)</td>
</tr>
</tbody>
</table>

| B. Diagnostic medical status according to the viral load (copies/ml) |
|-----------------------------|------------|-------------|
| CDC stagesb                 | Men (n=181) | Women (n=28) |
| A1                          |            |             |
| < 10^5 (n=136)              | 72 (53.0%) | 6 (33.3%)   |
| > 10^5 (n=45)               | 9 (20.0%)  | 2 (20.0%)   |
| A2                          |            |             |
| < 10^5 (n=18)               | 40 (29.4%) | 10 (55.6%)  |
| > 10^5 (n=10)               | 6 (11.1%)  | 2 (20.0%)   |
| A3                          |            |             |
| B1                          |            |             |
| < 10^5 (n=1)                | 2 (1.5%)   | 2 (1.1%)    |
| > 10^5 (n=5)                | 2 (4.5%)   | 0 (0.0%)    |
| B2                          |            |             |
| < 10^5 (n=1)                | 10 (7.4%)  | 0 (0.0%)    |
| > 10^5 (n=5)                | 4 (8.9%)   | 0 (0.0%)    |
| B3                          |            |             |
| < 10^5 (n=1)                | 3 (2.2%)   | 0 (0.0%)    |
| > 10^5 (n=5)                | 4 (8.9%)   | 0 (0.0%)    |
| C1                          |            |             |
| < 10^5 (n=1)                | 1 (0.7%)   | 0 (0.0%)    |
| > 10^5 (n=5)                | 1 (2.2%)   | 0 (0.0%)    |
| C2                          |            |             |
| < 10^5 (n=1)                | 1 (0.7%)   | 0 (0.0%)    |
| > 10^5 (n=5)                | 1 (2.2%)   | 0 (0.0%)    |
| C3                          |            |             |
| < 10^5 (n=1)                | 6 (4.4%)   | 0 (0.0%)    |
| > 10^5 (n=10)               | 20 (44.4%) | 0 (0.0%)    |

a Clinical records from the Hospital Nacional de Clinicas of Cordoba, Argentina (year 2005).

b Classification from Control Disease Centers (CDC), USA.

![Fig. 1. Kaplan-Meier curves for clinical evolution of HIV infection](https://example.com/figure.png)
per person taking place during their evolution. The curves of Kaplan-Meier, depicted in figure 1, did not show any differences between genders ($X^2=0.163$, df=1, $p=0.686$). Data from 31 men and 2 women (17% vs. 7%) were considered as truncated, since they were diagnosed already ill.

Regarding medical re-stratification (deviance=0.005, df=2, $p=1$) described in the Table 2, the odds of not having AIDS criteria when the follow-up finishes are higher for patients (8.76 times) being diagnosed without AIDS ($p<0.001$), for a given gender. Also, women have higher odds (4.65 times) of presenting AIDS at the end of the study than men ($p=0.003$), given an initial condition.

### Discussion

The HIV/AIDS management involves early detection and close evaluative monitoring, with epidemiological studies in developing countries being imperative to support sanitary strategies. In the present work, although many patients were at stage A, a several advanced cases were still found. Moreover, the deleterious effect of VL on CD4 and the clinical condition could be seen from the point of diagnosis. Despite the fact that gender did not affect the CD4, men had a greater possibility than women of being clinically impaired at the time of diagnosis. Consequently, early detection should be strongly encouraged to improve prognosis and infection control, especially in male individuals, considering that prevention messages are not being performed appropriately. Among initial findings, the common occurrence of venereal diseases in the males accounted for both behavioural and pathological indicators, which could be preliminary motives for consulting. The clinical and laboratory prevalence for opportunistic infections and/or debilitating conditions justified that their screening included the asymptomatic patients. Chagas disease deserves special attention, although it is not distributed worldwide, but it depends on the immune status, with geographic variations of tropical endemic infections being often not considered. During successive medical appointments, hemogram alterations were commonly found, especially anaemia, whose frequency increased as infection progressed. Oral lesions exhibited the same behaviour with regard to progression, as also did seborrhoea, respiratory infections and Kaposi sarcoma, with these being related to decreasing levels of CD4. Due to the relevance of oral lesions, often sub-diagnosed and/or inadequately treated, buccal evaluation is encouraged. Another problem linked to low CD4 was the waste syndrome (principal marker disease together with pneumocystosis), followed by other disseminated mycoses and neurological affections. Nonetheless, it is necessary to bear in mind that opportunistic diseases are not reciprocally excluding, and that other problems with an unclear etiopathology can also appear.

Different statistical models were applied, since the incidence measures only give summary information. The Kaplan-Meier method allowed evolution to be studied, by taking marker diseases as the progression criteria, although no differences between genders were found. However, initially ill people were not considered, thus causing a different data truncation for each one. Indeed, the initial clinical status is relevant for gender comparisons and infection management. For categorical data, generalized linear models give a complete description about associations, with increased power for detecting them.

In the analysis of medical re-stratification, it was confirmed that an early diagnosis was important in patient prognosis, since individuals without initial AIDS criteria tended to stay in this situation at the end of the study. Regarding gender, under the mentioned methodological conditions (analyzing the HIV/AIDS evolution in an alive population under sanitary control), female evolution exhibits a worse prognosis than men, which will imply further studies in order to develop complementary medical actions to modulate their pathological progression. There is an ongoing debate concerning a potential gender effect. Several factors may be involved in this response, although a previous work established that no differences between sexes existed respect to antiretroviral therapy. In the same research, low patient adherence and presence of pharmacological toxicity (evaluated in a specific subgroup under treatment) were the main determinants of therapeutic failure. However, in another work, women benefited less from care, even though they were admitted at earlier stages and offered standardized therapies with unclear reasons, requiring further studies. In addition, the CD4 predicting value for specific sociodemographic groups is discussed, with VL having higher prognostic strength.

Concerning the promotion of norms regarding risk reduction, the peer education and gender-specific HIV prevention interventions may be useful. In this sense, interventions seeking to promote gender equity and to reduce HIV/STI may be more effective when the socioeconomic context of gender ideologies is assessed and addressed. HIV prevention programs should be designed to increase knowledge about HIV transmission, treatment, prevention and personal risk of contraction as well as correct misconceptions about individuals with HIV or AIDS and promote sex communication among partners. Since gender-related behaviours have been proposed as risk determinants, the measures of relational attitudes and experiences become relevant to characterize sexual risk, especially among men.

The proper evaluation of HIV urban behaviour should be focused for different populations, since it allows developing accurate health policies. Also, the integration of analytical tests may enhance the outcomes’ value. Overall, an integrative assessment, which studies of clinical-biological factors by different methodologies, allows the close relationship between diagnostic stages and progression to be accomplished, in the polymorphic long-term HIV infection.

### References