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AIDS epidemic trends after the introduction of antiretroviral therapy in Brazil

ABSTRACT

OBJECTIVE: Universal access to antiretroviral therapy starting from 1996 has changed HIV/AIDS epidemic profile in Brazil. The objective of this study was to review the epidemiology of HIV/AIDS epidemic in Brazil.

METHODS: Indicators of temporal trends were developed for Brazilian regions from 1990 to 2003 using the Ministry of Health's databases. Exponential regression models adjusted to the 1990-1996 trends were used to estimate expected values for the entire period.

RESULTS: The proportion of AIDS hospitalizations has not changed over the study period but there was a decrease in hospitalizations among those using therapy. There was a 2.7 growth in those receiving Highly Active Anti-Retroviral Therapy (HAART) from 1997 to 2003. HIV/AIDS incidence and mortality rates rose up to 1995 in all regions. From 1996, there has been a gradual reduction in mortality rates while incidence rates have increased. In all regions, except in the Northern region, expected incidence rates have been greater than the observed ones in the last years but these differences were statistically significant only in the Southeastern and Midwestern regions.

CONCLUSIONS: The observed trend can be explained by universal access to ARV therapy in Brazil, which had a significant impact on HIV/AIDS mortality. But other factors, such as years of epidemic, prevention actions, knowledge on HIV/AIDS, years of schooling, need to be considered as well.

KEYWORDS: Acquired immunodeficiency syndrome, prevention & control. Acquired immunodeficiency syndrome, trends. Highly Active Anti-Retroviral Therapy (HAART). Brazil.

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Figure 1 - AIDS hospital admission rates in the SUS, Brazil, 1998-2003.

INTRODUCTION

The introduction of Highly Active Anti-Retroviral Therapy (HAART) allied to prevention and control actions against the acquired immunodeficiency virus (HIV) and other sexually transmitted diseases have changed the HIV/AIDS epidemic profile.

While reverse transcriptase inhibitors have been used in AIDS treatment since 1987, significant advances in HAART have been only possible through studies elucidating HIV infection immunopathogenesis.^{3,4,7} Declining trends in HIV/AIDS morbimortality have been seen in development countries even before HAART introduction attributed to prophylaxis and better clinical management of opportunistic infections. However, the advent of protease inhibitors has reinforced this trend.¹⁴

Brazil was one of the first developing countries to ensure universal free access to ARV drugs through the Brazilian Unified Health System (SUS) available since 1996. A major strategy of the ARV Access Program created by the National Program for STD/AIDS (PN-DST/AIDS) was establishing consensual technical recommendations for antiretroviral therapy by consulting committees (Law 9.313/96). The health care program for those living with HIV/AIDS also includes other actions aiming at reducing hospital admissions by providing specialized outpatient care, day hospital, and home care.

All these strategies to halt the epidemic advance have been built on the involvement of the organized society and federal and state authorities as well as increasing involvement of local authorities.¹

In the case of Brazil the question to be raised is whether, given the gaps between and within different country regions, the aforementioned initiatives have had a similar impact to that seen in developed countries with respect to reducing HIV/AIDS cases

and mortality, opportunistic infections, and hospital admissions. To better describe changes in the HIV/AIDS epidemic profile in Brazil taking into consideration regional differences data review is required. This review intends to contribute to the evaluation of HIV/AIDS prevention and control actions and the direction of new interventions in Brazil.

The present study had the purpose of evaluating the epidemiology of HIV/AIDS epidemic in Brazil. An analysis of time progress, trends, and disease distribution was carried out by country regions, gender, and exposure category based on data available from the Brazilian Ministry of Health. HAART impact on HIV/AIDS morbimortality was also assessed for the period between 1990 and 2003.

METHODS

The study was conducted based on the analysis of secondary information on HIV/AIDS epidemic in Brazil from the following government databases: DATASUS, National Disease Surveillance Data System (SINAN), Mortality Information System (SIM), AIDS Epidemiological Bulletin, and National Program for STD/AIDS monitoring system (MONITORAIDS).²⁰

The temporal trend analysis of AIDS cases for the years between 1990 and 2002, and deaths occurring two years after disease diagnosis included estimates of incidence and mortality rates for all Brazilian regions and by gender.

Exponential regression models adjusted to the 1990-1996 time series, a time period before universal access to HAART, allowed to estimate expected rates for the entire time series and, more importantly, to compare expected and observed rates for the period between 1997 and 2003. That is to say, what would have happened in the time series if prevention and control actions would have been the same as in the years before 1997 throughout the entire epidemic.

RESULTS AND DISCUSSION

Review of AIDS epidemiology in Brazil

Among Latin American countries, Brazil is the most affected by AIDS epidemic in absolute numbers. It is estimated 1.8 million people living with HIV/AIDS in the region, and a third lives in Brazil. Higher HIV prevalences are seen in smaller countries such as

Guatemala, Honduras, and Belize.* There were reported 371,827 AIDS cases in Brazil from 1980 up to June 30, 2004, and an incidence rate of 17.2 cases per 100,000 inhabitants⁹ in 2004. National estimates of the number of HIV infected people range around 600,000 for the years 1998,¹⁸ 2000,¹⁹ and 2002.¹⁵

Approximately 60% of cases reported in Brazil are related to any category of sexual contact, and almost half (42.9%) of them are due to men having unprotected sex with men. This group accounted for the majority of cases in the first years of the epidemic. Then AIDS has disseminated among intravenous drug users and those receiving blood transfusions and/or blood products. From mid 1990's of the 20th century, the epidemic has spread among heterosexuals, which now comprise the sexual exposure subcategory with higher number of reported disease cases. Consequently, HIV/AIDS incidence has rapidly increased among women and men: women ratio has been reduced

from 18.9:1 in 1984 to 1.5:1 in 2004, reaching 0.9:1 in the 13-19 years age group (adolescents) in 2006. It is estimated 16,410 (0.4%) infected pregnant women aging between 15 and 34 years.²⁰ Mother-to-infant transmission has been decreasing nationwide: from 16% in 1997²¹ to 7.8% in 2001 and 3.7% in 2002 but showing regional differences.**

Increasing incidence rates have been seen among those population segments with lower schooling and lower socioeconomic condition. The same has been observed among those living in urban areas with less than 50,000 inhabitants.^{5,6,15} The epidemic behavior seems to be evidencing social and gender inequalities in Brazil.

In regard to mortality, the cumulative deaths for the period 1980-2004 were 171,923. Mortality rates among men were higher in 1995 (15.1 per 100,000 inhabitants) and then they decreased to lower rates of

Figure 2 - AIDS incidence and mortality rates (cases per 100,000 inhabitants; deaths per 100,000 inhabitants) by regions. Brazil, 1990-2002.

*Joint United Nations Programme on HIV/AIDS - UNAIDS. Disponível em <http://www.unaids.org> [acesso em 24 abr 2006]

**Succi RCM. Transmissão Vertical do HIV no Brasil: resultado preliminar de um estudo colaborativo multicêntrico. In: XIV Congresso Brasileiro de Infectologia Pediátrica e III Jornada Paranaense de Infectologia Pediátrica, 2005, Foz do Iguaçu. *Jornal Paranaense de Pediatria - Edição Especial*, Curitiba: Sociedade Paranaense de Pediatria 2005;6:13.

around 8.8 per 100,000. Mortality rates among women have remained steady, around 4.0 per 100,000 throughout the time series. The highest rates were seen in 1996, 4.8 per 100,000.¹¹

Antiretroviral Therapy Program covered 160,000 people in 2004. The estimated coverage was 170,000 people in 2005, including all HIV/AIDS cases requiring drug therapy, those at risk of HIV exposure due to occupational injuries, and newborns of HIV-infected mothers.¹²

It was possible to indirectly measure the impact of antiretroviral therapy use on the epidemic using indicators such as hospital admission rates, outpatient care, and emergency room and day hospital visits.⁸ Interestingly, the proportion of AIDS hospital admissions in SUS remained the same over time. However, lower admission rates have been reported among HAART patients in healthcare services. Parallel to that, between 1997 and 2003, there was a 2.7 increase in those receiving HAART (Figure 1).

AIDS epidemic trends in five Brazilian regions

Some studies^{2,20} have pointed out temporal changes in AIDS epidemic in Brazil showing a trend toward the stabilization of incidence rates, starting mostly

from 1997 after the introduction of universal HAART. However, the epidemic slowdown has not been consistent all over Brazil. Brito et al² assessed regional patterns of AIDS progress and verified a trend toward stabilization and slowdown mostly in São Paulo (Southeastern region), whereas increasing rates were still seen in the Northeastern region.

The study of time progress of AIDS cases in the period between 1990 and 2002 and deaths occurring two years after disease diagnosis was possible through comparative analysis of incidence and mortality rates. HIV/AIDS incidence and mortality rates have increased steadily and consistently in different Brazilian regions up to mid 1990's. However, there has been gradual decrease in mortality since 1996, and increasing incidence rates have no more been associated with increasing deaths. Moreover, in the Southeastern region, incidence rates seem to have decreased as well since 1998 to a lower level than mortality with a slight breakout again in 2002 (Figure 2).

The temporal trend analysis of HIV/AIDS incidence and mortality by gender for the same period showed different trends. Incidence rates among men have slowed down since 1999 with slight growth in 2002, while among women there has not been clear evidence of slowing down. A case series analysis by regions subsequently to 2002 could better indicate these trends. Mortality rates by gender have showed a more significant reduction among men since 1997 but this trend has been toward stabilization in both men and women in the following years (Figure 3).

A comparison between observed and expected cases for the period 1990-2003 found expected incidence rates higher than those observed in all regions, except in the Northern region, in the last years of this time series. But differences between means (case incidence) of observed and expected rates were only statistically significant in the Southeastern and Midwestern regions. These differences have been evidenced in these regions as early as 1999, while they have become evident – though much less evident – in the Northern region only since 2000. These differences have also become noticeable in the Northeastern region since 2000 and in the Southern region since 2001 (Figure 4).

HIV surveillance in Brazil

A report of the Joint United Nations Program on HIV/AIDS (UNAIDS)¹³ called "Second

Figure 3 - AIDS incidence and mortality rates (cases per 100,000 inhabitants; deaths per 100,000 inhabitants) by gender. Brazil, 1990-2002.

generation HIV surveillance: the next decade” proposes that national and subnational systems of epidemiological surveillance (ES) for HIV/AIDS mainly focus on recovering the view of ES as a valuable source of information for health actions.

This document presents the would-be principles of these new “second generation surveillance systems” for HIV/AIDS.¹⁰ The first two principles recommend that ES systems should be adjusted to the epidemic trend to be able to monitor changes in the HIV infection dynamics. The third and fourth principles refer to the need of ES to focus on both HIV risk behaviors and HIV infection, targeting those populations at higher risk of getting infected, developing the disease or dying from any HIV-related opportunistic disease. The goal is to detect HIV infection at earlier stages using behavioral studies to better understand the HIV/AIDS epidemiology. The fifth principle of the “Second Generation Surveillance” report suggests the potential use of data from other information sources.

Following the fifth principle, a ES is expected to be

able to track observed changes focused on HIV risk behaviors and HIV infection, targeting the most vulnerable populations. This “second generation surveillance” can be accomplished in Brazil by properly and consistently gathering together several information sources. This could be made through the assessment and link of national databases, such as SINAN, SIM, Drug Logistics Management System (SICLOM), and Laboratory Testing Control System (SISCEL). Besides, periodical population-based surveys and sentinel surveillance (surveillance of sentinel groups and events through sentinel network) could provide additional data on HIV/AIDS epidemiology.

HIV/AIDS surveillance in Brazil now consists of universal reporting of AIDS cases, surveillance of sentinel populations (STD outpatient clinics and pregnant women in labor), HIV serological status and/or behavioral studies targeting specific populations and surveillance in testing and counseling centers (CTA).

Over the first 20 years of epidemic (1980-2000) the main ES strategy was universal compulsory AIDS case

Table - HIV prevalence estimates in those aged 15-49 years. Brazil, 1998, 2000, and 2004.

Year	Gender		Total (%)
	Male (%)	Female (%)	
1998	0.82	0.41	0.61
2000	0.84	0.47	0.65
2004	0.80	0.42	0.61

Source: National Program for STD/AIDS. MONITORAIDS, 2005

reporting. AIDS was included in the listing of compulsory case reporting in December 22, 1986 (Ministry of Health's Administrative Decree n. 542) and universal compulsory reporting of HIV-positive pregnant women and HIV exposed children is established by the Ministry of Health's Administrative Rule n. 993/2000.¹¹

Since 1992, the Brazilian Ministry of Health has been carrying out surveillance of sentinel groups and repeated behavioral and cross-sectional studies of HIV infection prevalence among target populations such as pregnant women attending prenatal care and STD clinics, Army draftees, and SUS pregnant women in labor.

Some studies, like the 1998 sentinel study on pregnant women in labor modified from 2000 to comprise a representative sample of pregnant women,¹⁵ have allowed estimating HIV prevalence at different time points of the epidemic (Table). It can be noted very similar estimates around 0.6% for cross-section studies conducted in 1998,¹⁸ 2000¹⁹ and 2004,¹⁵ which suggests likely stabilization of the epidemic.

A study comprising 8,002 pregnant women attending prenatal care in CTAs of 27 municipalities in Southern Brazil, based on data from CTA Information System (SI-CTA), estimated 0.5% HIV prevalence and 0.3%-0.6% 95% confidence interval in this population. The study database comprised 25% minimum coverage of pregnant women for 2003. The variable associated to higher prevalence rates was lower schooling.*

A major study commissioned by the PN-DST/AIDS, opening up the dichotomy between HIV surveillance and sexual behavior information, was carried out among Brazilian Army draftees in 1998. HIV prevalences of 0.19%, 0.12% and 0.08% were estimated for Northern/Midwestern and Southern regions and the states of Rio de Janeiro and São Paulo, respectively. Lower schooling was also found to be associated to higher risk sexual behavior. The Northern and Midwestern regions showed the lowest socioeconomic indicators among draftees.¹⁷

Also concerning behavioral surveillance, a 2003 study conducted by the Ministry of Health** in a representative sample of Brazilian population aged 14 years and over who were sexually active in the previous six months found that 28% had been HIV tested at least once before. The testing proportion varied by age groups: 22.5% in those aged 15-24 years, 36.4% in 25-39 years, and 21.3% in 40-54 years. Socioeconomic condition was once more associated to HIV status awareness. According to social strata used in the study, lower testing rates were seen among both men (13.7%) and women (28.35) in D/E strata. In A/B strata, 36.1% men and 43.4% women had been tested. HIV testing rates among pregnant women were 51.5% in 2002 and 57.4% in 2003.

Understanding the observed trends has been complicated by the different stages and profiles of AIDS epidemic in Brazil. When analyzed by regions, the epidemic showed a mixed trend: increasing incidence rates in most regions but declining rates in the Southeastern region. Mortality rates have generally decreased but this decrease is only statistically significant in the Southeastern region. Women mortality rates have significantly increased in the Northern, Northeastern, and Southern regions. There are several assumptions to explain these scenarios in Brazil and there is a need for further studies specifically focusing on socioeconomic, demographic, and behavioral aspects, as well as at biological markers for circulating HIV viruses.

Evidence gathered must be examined comparatively taking into consideration their incompleteness and other limitations of information sources. At the time of data analysis (November 2005), the AIDS database available showed information inconsistencies from 2003. In an attempt to address case underreporting, the PN-DST/AIDS joined together different databases, which allowed to recovering hundreds of new cases by state. However, as the unified database has not yet been properly checked there are duplicated cases for the year 2004. This has impaired the analysis of major variables such as schooling, which significantly lost consistency after databases were joined together.

Increasing AIDS cases in several Brazilian regions can be partially explained by services response. There are still AIDS cases that have late access to health services and have limited chances of benefiting from adequate therapy. A study by Brito et al² carried out in a Northeastern state showed that about half of

*Cardoso AJC, Griep RH, de Carvalho HB, Barros A, da Silva SB, Remien RH. Sexual behavior and HIV-infection among pregnant women receiving prenatal care: an information system for HIV epidemiological surveillance in Brazil 2005 (no prelo).

**Ministério da Saúde. Programa Nacional de DST e Aids. Pesquisa com a população sexualmente ativa, 2003. Disponível em <http://www.aids.gov.br> [acesso em 30 abr 2006]

HAART users only got to know their HIV status at the time they are hospitalized due to clinical manifestations of immunodeficiency. In addition, those who did not know their HIV status were 50% more likely to present symptoms at their first visit to a specialized service compared to those who did it.

Key elements for understanding differences in the epidemic trends by regions are the following: epidemic course, coverage of prevention actions, people's knowledge on HIV/AIDS, level of schooling and other socioeconomic factors.

Universal access to antiretroviral therapy, which impact on mortality and survival rates has been well documented, would not be enough to explain declining rates over time. Indicators of behavior changes, such as considerable increase (178%) of condom sales in the period 1995-2004, may not have yet exerted an impact on the number of AIDS cases as they are usually a late manifestation of the infection.

Stabilization of infection prevalence can be explained by other factors, such as increased mortality and/or reduced survival. To monitor HIV prevalence, studies should be conducted to further the analyses and better understand HIV trends and survival and AIDS

mortality taking into account the observed gaps between different regions.

There is also a need to carefully review HIV surveillance in Brazil. Data is still scarce to assess whether initiatives such as awareness campaigns like "*Fique sabendo*" (You showed know), and the implementation of 329 CTAs and quick HIV testing in the Northern region among others, have effectively expanded access to HIV testing to most vulnerable populations in different regions of Brazil.

It is proposed that second generation HIV surveillance be implemented linking HIV serological diagnosis, AIDS surveillance, and risk behavior data. Also, sentinel surveillance studies should be designed to allow estimating HIV infection by region and in particular cases of greater vulnerability such as border areas and large population concentration areas.

Although trend curves stratified by schooling were not presented here, there is well documented evidence of the so-called "epidemic pauperization".^{5,6} A national program for HIV/AIDS management should develop specific actions targeting population segments living in poverty and reflect the different epidemics in the different regions requiring specific individual responses.

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