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HIV/AIDS Mortality in Brazil, 2000–2015: Are there reasons for concern?

Mortalidade por HIV/Aids no Brasil, 2000-2015: motivos para preocupação?

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ABSTRACT: ***Introduction and objective:*** Mortality studies are essential for the monitoring of the HIV/AIDS epidemic. Quality and completeness of data from the mortality information system (SIM) require complementary approaches. ***Methods:*** Two sources of data were used to assess mortality trends due to HIV/AIDS in Brazil from 2000 and 2014/15: a) data from the SIM published by the Department of STDs, AIDS, and viral hepatitis, and b) Global Burden of Disease 2015 (GBD 2015) studies. Descriptive analyses were carried out and trends in relative reduction of age-adjusted mortality rates per 100,000 inhabitants were compared according to the two methods. ***Results:*** Overall, the magnitude of the mortality rates estimated by the GBD method, for Brazil and its Federative Units (FU), was greater than those obtained from the SIM. The relative reduction was higher for SIM data and there were shifts in the ranking according to the FUs. Between 2000 and 2014/15 there was an increase in the mortality rates for most of the FUs (78 and 88% according to the SIM and GBD, respectively). ***Conclusion:*** Data regarding mortality due to HIV/AIDS in Brazil should be of concern, regardless of the method used. Differences in magnitude, relative reductions, and ranking can be attributed to methodological differences, but the GBD is broader, with a higher capacity to capture incorrectly classified data and causes of death not registered or not coded as being due to HIV/AIDS. Alternative and complementary data sources can provide important information for HIV/AIDS public policies in Brazil.

Keywords: AIDS. Mortality. Brazil. Descriptive epidemiology.

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RESUMO: ***Introdução e objetivo:*** Estudos de mortalidade são fundamentais no monitoramento da epidemia de HIV/Aids. Qualidade e completude dos dados do sistema de informação de mortalidade (SIM) requerem abordagens complementares. ***Métodos:*** Foram utilizadas duas fontes de dados para avaliação das tendências de mortalidade por HIV/Aids no Brasil entre 2000 e 2014/15: a) dados do SIM publicados pelo Departamento de DST, Aids e Hepatites Virais; e b) estudos de carga de doença 2015 (GBD 2015). Foi conduzida a análise descritiva e realizada uma comparação das tendências de redução relativa dos coeficientes de mortalidade por 100 mil, padronizados por idade. ***Resultados:*** A magnitude dos coeficientes de mortalidade estimados pelo GBD para o Brasil e estados foi maior do que a daqueles obtidos pelo SIM. A redução relativa foi maior para os dados gerados pelo SIM e houve mudança de ranking de acordo com os estados. Entre 2000 e 2014/15, houve aumento nos coeficientes de mortalidade para a maioria dos estados (78 e 88%, segundo o SIM e o GBD, respetivamente). ***Conclusões:*** São preocupantes os dados sobre mortalidade por HIV/Aids no Brasil, independentemente do método utilizado. As diferenças de magnitude, redução relativa e ranking podem ser atribuídas a diferenças metodológicas, sendo o GBD mais abrangente e com maior capacidade de captar dados classificados incorretamente, não registrados ou não codificados como causa de óbito devido ao HIV/Aids. O estudo de fontes complementares e metodologias alternativas podem fornecer importantes subsídios para as políticas públicas de HIV/Aids no Brasil.

Palavras-chave: Aids. Mortalidade. Brasil. Epidemiologia descritiva.

INTRODUCTION

The global HIV/AIDS epidemic continues to be a relevant public health issue, despite numerous advances in recent years[1]. Among these is antiretroviral therapy (ART), which was introduced in the 1990s and improved in the first ten years of the 21st century. In recent years, important advancements in ART have been obtained, including a simplification in the proposed design, the introduction of new combinations of medication with distinct action mechanisms, the reduction of side effects, etc.

In addition, the indication for ART has been changed over the years, initially demonstrating effectiveness in increased survival, in maternal–infant transmission, in the prevention of infection after accidental puncture wounds, for example, post-exposure prophylaxis (PEP), and, subsequently, in the reduction in the rate of progression to AIDS among those infected by HIV. Among the cited consequences are a drastic reduction in mortality due to HIV/AIDS, a reduction in the incidence of opportunistic infections, and an improvement in the quality of life among those living with HIV/AIDS. More recently, the effectiveness of ART has been verified in the prevention of HIV infection among those who are not infected and find themselves at potential risk, especially through sexual exposure, known as pre-exposure prophylaxis (PrEP)[2].

Following these advances, the recommendation to initiate ART has been modified over the years. In the 1990s, ART was indicated only when people showed signs related to AIDS or when their levels of $CD4^+$ T lymphocytes were below 200/mm^3, and now ART is indicated for anyone who is infected by HIV, regardless of their symptomatology or degree of immunosuppression.

For this reason, the HIV/AIDS epidemic now has the potential to be controlled in the near future, even though the perspective of a cure or complete elimination of HIV is limited.

Regarding the mortality due to HIV/AIDS, an important global reduction has been observed (45% from 2005 to 2015). From 2010 to 2015, there was also a reduction in various regions: 38% in Eastern and Southern Africa; 24% in Asia and the Pacific; 24% in Western Europe and North American; 18% in Latin America and the Caribbean, 10% in Western and Central Africa. However, in Central Asia, Eastern Europe, Northern Africa and the Middle East, there was an increase of 22%[3].

In Brazil, since the mid-1990s, free access to HIV/AIDS diagnosis and treatment has been established through the Brazilian Unified Health System (acronym in Portuguese – SUS), with relevant impact in public policies for the treatment of the disease[4]. Since then, the country has followed the worldwide trend of testing for HIV/AIDS and treating it as early as possible.

The surveillance and monitoring of the evolution of the HIV epidemic are conducted by the Department of STDs/AIDS and Viral Hepatitis from the Ministry of Health (acronym in Portuguese – DDAHV/MS) and are centered on three aspects: virus infection, evolution into AIDS, and deaths[5]. Data on mortality, which is one of the main indicators used, are periodically published by DDAHV/MS and provide important subsidies for the public policies for the prevention and control of the disease in this country. In general, global data are published for the entire country, stratified according to Federative Units (FU) and grouped by regions. The data on deaths, which is the object of this study, were obtained from the Mortality Information System (acronym in Portuguese – SIM), without specifically considering potential sources of errors, such as incorrect classification of underlying cause, underreporting of deaths, or utilization of complementary systems and information regarding deaths due to HIV/AIDS. Global Burden of Disease (GBD) Studies are among the strategies to better assess trends for the cause of death in various countries, including Brazil[6]. The analytical strategies of GBD go beyond obtaining data from formal systems such as the SIM. Various sources of data are utilized for reporting aggravated conditions and for theoretical statistical models, which enable the reclassification of the basic causes of death and, potentially, a wider view of the mortality conditions in certain regions or countries and, thus, contribute with additional subsidies to public policies for awareness and prevention. In this study, we intend to compare mortality coefficients for HIV/AIDS on basis of monitoring conducted by the DDAHV/MS with those observed in the GBD studies between 2000 and 2014/15.

METHODS

Descriptive and trend analyses were conducted for death due to HIV/AIDS, between 2000 and 2015, for Brazil and the FUs. Two sources of data were utilized for the comparisons: a) data published by the DDAHV/MS[5,7] and b) data estimated by the GBD 2015 study[6]. First, a linear trend analysis was utilized, with the FUs being grouped by region according to the DDAHV/MS data. Second, the mortality coefficients were compared according to the sources of information, estimating the percentage of change.

The data published by the DDAHV/MS were based on the SIM, from which deaths whose underlying cause was HIV/AIDS (ICD10: B20 to B24) from 2000 to 2014 were selected. The data were expressed in coefficients per 100,000 inhabitants, and adjusted by age[5].

For the second source of information, the estimates were based on the GBD 2015, which included multiple assessments of the burden of the disease from 1999 to 2015. Detailed descriptions of the methodology and the approach of the GBD have been published[3]. The mortality estimates for HIV/AIDS from the GBD 2015 and the methods employed were described in detail in recent publications[3,6]. The estimates presented in this study were obtained from the Institute for Health Metrics and Evaluation, GBD 2015[8].

Similar to the DDAHV/MS, the GBD 2015 utilizes the vital statistics from the SIM as its main data source for analyses on vital mortality statistics. The causes of death are classified according to a hierarchical list of 249 causes of death, organized into four levels. The first level includes

1. transmissible, maternal, neonatal, and nutritional conditions;
2. non-communicable diseases (NCD); and
3. external causes.

On a second level, the following are included: the 20 main causes of death in the country; mortality due to HIV/AIDS and tuberculosis, a part of the group of transmissible, maternal, neonatal, and nutritional conditions, is classified at this level (A.1 – HIV/AIDS and tuberculosis). The third level separates the two causes of death, tuberculosis (A.1.1) or HIV/AIDS (A.1.2). The fourth level subdivides and classifies mortality due to HIV/AIDS as a result of the deaths registered as the underlying cause being tuberculosis (A.1.2.1) and those resulting from deaths due to other diseases (A.1.2.2) (GBD 2016).

In this study, researchers analyzed HIV/AIDS-related mortality in the third level, which also includes data contained in the fourth level. Changes relative to the mortality coefficients due to HIV/AIDS were also descriptively assessed in relation to the remaining levels defined by the GBD 2015, comparing 2000 to 2015.

For the HIV/AIDS estimates, the GBD 2015 improved the natural history epidemiological models developed by UNAIDS to estimate the weight of HIV/AIDS at the national and global levels[3]. The mortality estimates with HIV being the underlying cause considered the following:

- the mortality estimates obtained using the Spectrum software;
- the excess of mortality due to HIV/AIDS in the process for mortality estimates due to all causes[9]; and
- estimates from the Gaussian-smoothed space-time regression process.

The data were obtained in the vital records systems and were adjusted according to the under recording of total deaths and the incorrect classification of the underlying causes of death. The methods were adapted to produce final mortality estimates, depending on the age group and the availability and quality of mortality data due to HIV/AIDS from each country.

In this analysis, the results are presented for Brazil and for each of Brazilian FUs. The mortality coefficients per 100,000 inhabitants, adjusted by age, and the percentages relative to the changes between 2000 and 2014/15 are presented. The data published by the DDAHV were compared

with the estimates from the GBD 2015 regarding the relative change in the coefficients. For the DDAHV data, the comparison was between 2000 and 2014; for the GBD, 2000 to 2015 was considered. Considering that these are general analyses, this difference does not interfere in the central objectives proposed. The percentage of change by FU was classified into three groups:

1. reduction in mortality (negative percentage);
2. no reduction or a 50% increase in mortality; and
3. increase above 50%.

Next, the ranking was compared indicating the change in the position of the FU in relation to each source of information.

RESULTS

The trend analysis, according to the DDAHV data, indicates a small reduction in mortality (b = -0.0618) due to HIV/AIDS, from 2000 to 2014, for Brazil as a whole (Figure 1). However, there are important regional differences in terms. Whereas in the southeastern region of Brazil there is evidence of a downward trend (b = -0.2354), in the northeastern and northern regions there is an indication of an increase in mortality (b = 0.1179 and b = 0.2889, respectively). The southern and central western regions were found to be stable, with a discreet reduction (b = -0.0146 and b = -0.0029, respectively).

According to DDAHV/MS data, the largest coefficients were found in Rio de Janeiro, in 2000 (11.4/100,000), and in Rio Grande do Sul (10.6/100,000), in 2014. A similar finding

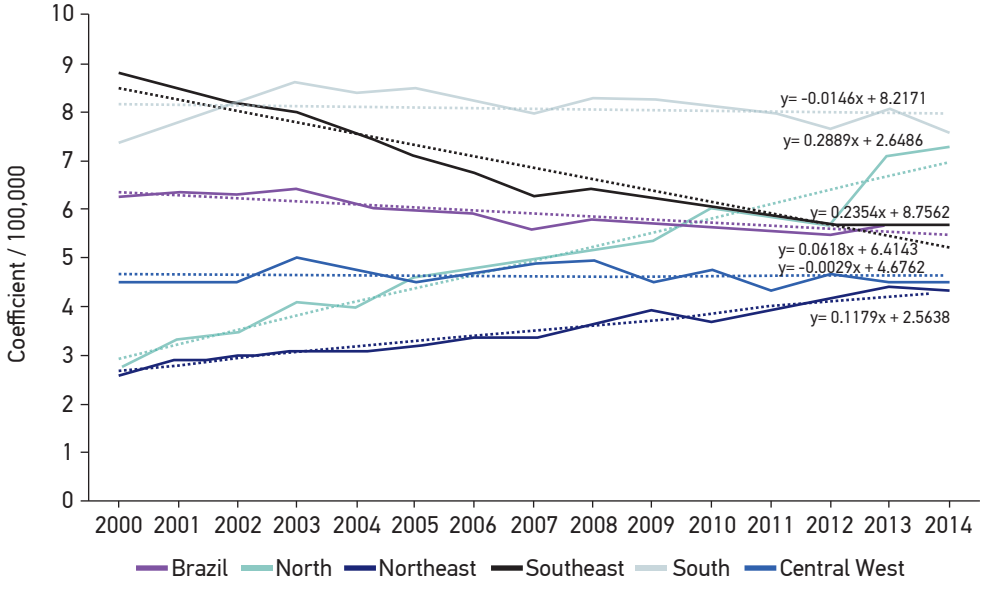

Figure 1. HIV/AIDS-related mortality coefficients per 100,000 inhabitants, adjusted by age, Brazil and Regions, from 2000 to 2014, according to the DDAHV.

was obtained in GBD 2015, but with larger magnitudes in terms of rates (15.7/100,000 for Rio de Janeiro in 2000 and 17.7/100,000 for Rio Grande do Sul in 2015).

In general, there was a reduction in the mortality coefficient due to HIV/AIDS on a national level, compared to the two sources between 2000 and 2014/15. From 6.3 in 2000 to 5.7 in 2014, per 100,000 inhabitants according to the DDAHV; and from 9.6 in 2000 to 9.5 in 2015, per 100,000 inhabitants according to the GBD 2015. It is worth noting that there is a larger magnitude (52 and 66% larger for 2000 and 2014/15, respectively) of the coefficients according to the GBD 2015, but with a lower relative reduction (-9.5 and 0.9%, respectively) (Table 1).

As for the relative changes, important differences were observed. According to the DDAHV data, of the 27 FUs, merely 6 (22.2%) had a reduction in the coefficients (mean reduction = -20.4%), with the largest reduction found in São Paulo (-54%) and the lowest reduction in Goiás (-5.4%). Nine FUs (33.3%) showed an increase of 50% or no reduction (mean = 19.9%). Pernambuco presented the largest increase in this group (48.8%). Finally, a worrisome portion of FUs (44%) presented an increase of over 50% of mortality due to HIV/AIDS during the period, varying from 52.0% in Bahia to 875% in Amapá (mean = 217.9%).

Just as worrisome is the situation presented by the GBD data. The main differences occurred in the magnitude of the coefficients (larger in all of the FUs when compared to the DDAHV data), in the relative changes (lower in all of the FUs), and in the changes in the ranking of the FUs. Whereas a smaller number of FUs presented a reduction in the coefficient (11.1%), most of them (85.2%) had an increase of up to 50% (mean = 25.9%) and 1 FU (Amazonas) presented an increase of 50% in the mortality coefficients due to HIV/AIDS. As for the relative change ranking, there is a dynamic that should be better appreciated: according to the GBD 2015, 3 FUs maintained their respective rankings, when compared to the DDAHV data (São Paulo and the Federal District with reductions and Paraná with relative increase); 13 FUs went up in their ranking, in other words, improved their position; and, finally, 11 FUs had a lower ranking.

DISCUSSION

Despite the differences in magnitude and trends, the situation revealed by the two analyses is worrisome. Both indicate that, unlike what was expected, the mortality coefficients for HIV/AIDS in Brazil are heterogeneous and present an important increase over the years analyzed. Few FUs had a reduction, and São Paulo had the largest impact according to both sources. It is worth noting the high mortality coefficients for Rio de Janeiro and Rio Grande do Sul, which were revealed by both analyses. However, the largest relative increase in mortality coefficients is in the northern and northeastern regions, with a similar result in both approaches.

There are potential explanations for this situation that needs to be further investigated. In a system with free and universal access to care with well-established ART distribution, better mortality indicators are expected. It is known, however, that various factors can interfere in this process. One of the most important factors is the low rates of HIV testing in general and, specifically, among the key populations that characterize an HIV epidemic in Brazil, mainly men who have sex with men (MSM). During a multicenter study concerning 10 Brazilian cities, less

Table 1. HIV/AIDS-related mortality coefficients per 100,000 inhabitants, adjusted by age, Brazil and Regions, from 2000 to 2014/15.

Data according to the DDAHV/MS					Data according to the GBD 2015				
Ranking		2000	2014	Relative Change 2000-2014 (%)		2000	2015	Relative Change 2000-2015 (%)	Ranking
	Brasil	6.3	5.7	-9.5	Brasil	9.6	9.5	-0.9	
1	São Paulo	11.3	5.2	-54.0	São Paulo	15.5	11.3	-27.0	1
2	Distrito Federal	6.1	4.2	-31.1	Distrito Federal	7.1	6.1	-13.4	2
3	Santa Catarina	8.6	6.9	-19.8	Rio de Janeiro	15.7	15.2	-3.3	3
4	Rio de Janeiro	11.4	9.5	-16.7	Minas Gerais	6.5	6.8	4.1	4
5	Minas Gerais	4.4	3.7	-15.9	Rio Grande do Norte	3.0	3.5	14.3	5
6	Goiás	3.7	3.5	-5.4	Mato Grosso do Sul	7.2	8.5	17.4	6
7	Acre	2.7	2.7	0.0	Roraima	10.3	12.2	17.7	7
8	Mato Grosso do Sul	5.6	5.6	0.0	Santa Catarina	9.7	11.6	19.2	8
9	Rio Grande do Sul	10.4	10.6	1.9	Goiás	5.1	6.1	20.4	9
10	Paraná	4.6	5.1	10.9	Paraná	5.9	7.1	20.6	10
11	Roraima	6.2	7.3	17.7	Paraíba	4.3	5.2	21.1	11
12	Espírito Santo	5.1	6.2	21.6	Ceará	4.7	5.7	21.1	12
13	Mato Grosso	4.6	6	30.4	Bahia	5.1	6.2	21.9	13
14	Ceará	2.3	3.4	47.8	Mato Grosso	6.6	8.1	22.5	14
15	Pernambuco	4.3	6.4	48.8	Amapá	6.2	7.6	23.2	15
16	Bahia	2.5	3.8	52.0	Espírito Santo	6.5	8.1	25.1	16
17	Rondônia	2.9	4.7	62.1	Acre	4.5	5.6	25.4	17
18	Sergipe	2.4	4.2	75.0	Rondônia	4.7	6.0	27.7	18
19	Rio Grande do Norte	1.4	2.5	78.6	Pernambuco	6.9	8.9	27.7	19
20	Paraíba	1.5	3.4	126.7	Piauí	4.5	5.9	31.6	20
21	Piauí	1.5	3.6	140.0	Sergipe	3.7	5.0	32.7	21
22	Alagoas	1.5	4.7	213.3	Tocantins	3.6	5.0	36.2	22
23	Tocantins	1.3	4.2	223.1	Rio Grande do Sul	12.9	17.7	37.0	23
24	Pará	2.5	8.1	224.0	Maranhão	6.9	9.7	39.4	24
25	Maranhão	1.6	5.6	250.0	Alagoas	4.1	5.8	40.6	25
26	Amazonas	2.2	8.7	295.5	Pará	6.4	9.5	48.0	26
27	Amapá	0.8	7.8	875.0	Amazonas	6.9	10.8	56.5	27

than 50% of the MSM reported having been tested for HIV before in their life[10]. Lack of early testing leads to unknown positive status and, consequently, not seeking treatment. The late diagnosis of HIV in Brazil has been revelatory. Between 2003 and 2006, 58.6% of AIDS diagnoses were conducted when the CD4 $^{+}$ T lymphocytes count was below 350/mm^3, with 12.5% conducted after death[11]. Factors such as low perception of risk, barriers for taking care of one's health, low availability of tests, stigma, and prejudice corroborate the worsening of this situation. Another factor of great importance that potentially contributes to the mortality is that low use of ART among those being cared for in renowned centers. The rate of non-use of ART in the first months of treatment is high (30–44%)[12] and the irregular use of it can reach up to 66% according to recent studies[13]. Brazil is a long way from the UNAIDS goal which includes 90% of infections having been diagnosed, 90% of these tied to ART services, and 90% of these with virologic control (90-90-90) with the ambitious proposal of eliminating HIV by 2030[14]. According to the continuous care model (cascade care), the DDAHV/MS estimates that Brazil should have reached 83% of its infections having been diagnosed, 56% receiving treatment and only 46% with an undetectable viral load[5,7]. The data from the GBD 2015 can indicate that these estimates are probably overestimated and need to be reviewed. In addition to the higher mortality, the low adherence causes resistance to one or another therapeutic plan, leading to uncontrolled viral load and consequently primary transmission of resistant strains. During a national study with MSM, a primary resistance was estimated to be 21.4% among those who had never been treated and 35.8% among those receiving treatment[15].

Despite the two analyses indicate similar trends, studies with distinct methodologies should be viewed with caution. It is possible that the broader identification of causes due to HIV/AIDS according to the GBD 2015 is the result of a larger comprehensiveness and capacity of reclassifying the causes due to HIV/AIDS, including reallocating garbage codes and misclassifications. Whereas the GBD generates estimates, data according to the DDAHV/MS can be considered more "raw" and, therefore, susceptible to more sources of mistakes due to the low reliability on the filling out of declarations of death as a whole. In addition, the data quality obtained from the SIM varies between FUs, and, consequently, the downward and upward trends in mortality according to FU can be a consequence of data quality and not necessarily an actual trend, at least in part. This becomes evident considering the heterogeneous percentages of change observed in the two methodologies. In addition, analyses of mortality due to HIV/AIDS in countries facing HIV epidemic which is concentrated in key populations, such as Brazil, should be stratified by sex, age, and, especially, by population subgroups for which the incidence of HIV infection is potentially higher, including in men who have sex with men and people who inject drugs.

CONCLUSION

The GBD 2015 can be an important instrument for complementing information based solely on the SIM, but not necessarily is an isolated alternative. There is an urgent need to assess the HIV/AIDS situation in Brazil, as a whole, including the increase of HIV and

syphilis among young adults, the low perception of risk, the low testing rates, and the late access to treatment. The increase in mortality is a strong indicator of the inefficiency of public policies in the prevention and awareness of HIV in the country.

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