The "AMA-Brazil" cooperative project: a nation-wide assessment of the clinical and epidemiological profile of AIDS-related deaths in Brazil in the antiretroviral treatment era

Projeto cooperativo AMA-Brasil: um estudo nacional do perfil clinico e epidemiológico dos óbitos relacionados à AIDS na era da terapia antirretroviral

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Abstract

The objective of this study was to assess the profile of AIDS-related deaths in the post antiretroviral therapy (ART) scale up period in Brazil. A casecontrol study was conducted including a nationally probabilistic sample of AIDS deaths and living controls. Data were abstracted from medical records and nation-wide databases of AIDS cases, mortality, ART care, and laboratory testing. Interrupted (adjusted odds ratio - AOR 4.35, 95%CI: 3.15-6.00) or no use of ART (AOR 2.39, 95%CI: 1.57-3.65) was the strongest predictor of death, followed by late diagnosis (AOR 3.95, 95%CI: 2.68-5.82). Criterion other than CD4 < 350 had a higher likelihood of death (AOR 1.65, 95%CI: 1.14-2.40). Not receiving recommended vaccines (AOR, 1.76, 95%CI: 1.21-2.56), presenting AIDS-related diseases (AOR 2.19, 95%CI: 1.22-3.93) and tuberculosis (AOR 1.50, 95%CI: 1.14-1.97) had higher odds of death. Being an injecting drug user (IDU) had a borderline association with higher odds of death, while homo/bisexual exposure showed a protective effect. Despite remarkable successes, Brazilians continue to die of AIDS in the post-ART scale up period. Many factors contributing to continued mortality are preventable

HIV infections; Anti-Retroviral Agents; Mortality; Health Services Accessibility

Introduction

Brazil's governmental policy to provide free and universal access to antiretroviral therapy (ART) to all its citizens in need was initially viewed with skepticism inside and outside the country, with doubts raised as to whether such a lofty goal could be achieved. Nevertheless, Brazil passed Federal Law nº. 9.313/96 1 in 1996 guaranteeing the right to receive ART within the Unified National Health System (SUS) and launched an ambitious, nation-wide initiative to deliver ART through a comprehensive network of accredited public health units. Concerns that soon followed included the sustainability of the initiative given the high costs and complexity of the therapeutic regimens (now less complex with simplified fixed-dose combinations) 2; the necessity to procure, monitor, and dispense different drugs on a continuous basis over a large and heterogeneous country; and the need to permanently monitor treatment, manage side effects, and optimize adherence. Available data to date document that ART adherence in Brazil is comparable to the best standards in high-income countries 3 and that the survival of people living with AIDS increased dramatically after the introduction of ART 4,5. Moreover, the much feared massive emergence and dissemination of HIV resistant to antiretroviral drugs has not materialized 6.

Despite these major achievements, AIDS remains a major cause of mortality in Brazil.

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Trends in mortality show an initial rapid reduction in AIDS-related deaths after 1996, slowing after 2000, and with disparities between the different regions of the country 7. AIDS mortality increased from the early 1980s through the mid-1990s, and started to decline before the wider availability of ART, initially among men but not among women 8. In 1996, the national AIDS mortality rate was 9.6 per 100,000 inhabitants, declining to 7.6 in 1997. Mortality declined most markedly in the Southeast (the most industrialized and richest region and home to approximately 60% of reported AIDS cases), from 15.3 per 100,000 in 1996 to 6.5 in 2007. In contrast, in the North and Northeast regions (the least industrialized and poorest) mortality increased from 2.7 per 100,000 to 4.7 in the North and from 3.0 to 3.5 in the Northeast over the same period 9. Recent studies have shown substantial delays in receiving ART among persons eligible according to Brazilian Ministry of Health guidelines 10,11, compromising the potential benefits of therapy to individuals and accentuating disparities within society. Such delays appear to have a disproportionate impact on disenfranchised populations, such as injecting drug users (IDU), jeopardizing the broad principles of the program in terms of equity, comprehensiveness, and involvement of the affected populations 12.

The clinical and epidemiological characterization of "who", "why", and "how" people continue to die of AIDS in the era of ART in the country with the earliest and most comprehensive scale up is vital to maximizing the benefits of care and treatment programs worldwide. Cohort studies are considered the gold standard for assessing factors leading to death; however, such studies are rare in low- and middle-income countries due to their high cost, complexity, and need for long-term follow-up. The latter requirement is especially challenging given the long survival time with AIDS in the ART era. Other epidemiological designs, particularly the case-control study, may offer cheaper and simpler alternatives that can be carried out in low-income contexts while improving generalizibility to municipalities, states, or countries. The present study analyzes the clinical and epidemiological profile of a probabilistic sample of AIDS deaths in Brazil compared to comparable controls during the post-ART scale up period, with the aims of assessing risk factors for death, population level differences in mortality, and associations with prevailing practices in different care facilities and localities.

Methods

Overall study design

The study had two components, one descriptive of persons living and dying of AIDS, and a second using a case-control design to characterize factors associated with death due to AIDS in Brazil in 2003. We selected the year 2003 as marking a point in time when ART had achieved ample and consistent coverage in Brazil and in which mortality data would be complete.

Study population, sampling methods, and sources of data

Cases were persons dying of AIDS obtained from a probabilistic sample of all AIDS deaths reported to the Mortality Information System (SIM) in 2003. Controls were selected from a random sample of persons living with AIDS registered as cases in the National AIDS Cases Database (SINAN-AIDS) in 2003 matched to the same municipalities from which the cases were randomly selected. Potential controls were excluded if the patient was found to have died during the period under analysis (i.e., up to December 31, 2003).

Selection of subjects and collection of data were based on a combination of medical record abstraction and use of national level databases. In Brazil, AIDS cases are mandatorily reported to SINAN-AIDS using standard data collection forms with a minimum number of required data elements ¹³. Additional information was obtained from other nationwide databases, including mortality (SIM), the database recording ART initiation and dispensing (SICLOM), and the National Laboratory Database (SISCEL) recording CD4+ cell counts and HIV viral loads performed for individual patients by each laboratory.

A random, one-stage cluster sampling strategy was used to produce a study population proportional to the national AIDS mortality burden. Using SIM, a roster was created that included all municipalities where at least 30 AIDS deaths occurred in 2003, stratified by Brazil's five macroregions (South, Southeast, Central, North, and Northeast). Using a start determined from a random numbers table, a 1 in 3 sampling fraction from the roster of municipalities was chosen, creating a random one-third sample of all eligible municipalities in Brazil. The final sample included (municipality followed by respective state) Porto Velho (Rondônia) in the North; João Pessoa (Paraíba), Maceió (Alagoas), Recife (Pernambuco), and Salvador (Bahia) in the Northeast; Goiânia (Goiás) in the Central; São Gonçalo (Rio de Janeiro), Uberaba (Minas Gerais), Guarulhos,

Santo André, Jacareí, Barretos, Cruzeiro, Guarujá, Franca, Catanduva, Presidente Prudente, and Marília (São Paulo) in the Southeast; and São José, Itajaí (Santa Catarina), Rio Grande, and São Leopoldo (Rio Grande do Sul) in the South. In each of these randomly selected municipalities, data were collected on all persons dying of AIDS and an equal number of persons with AIDS alive through 31 December, 2003 through a simple random sample. We increased the total number of randomly selected controls by 20% to account for some controls being discovered as deceased before 31 December 2003 upon data collection and to account for missing data.

To ensure that all persons dying of AIDS in the municipalities were included, the research team further investigated deaths not initially registered as due to AIDS but ascribed to unknown causes, as well as all deaths due to diseases associated with AIDS, and deaths among people aged 20-49 years old using a list of ICD-10 (International Classification of Diseases, 10th Review) codes for diseases and conditions associated with AIDS. This list was originally produced by the Programa de Aprimoramento de Informação sobre Mortalidade - Pro-AIM, from São Paulo City, which has been investigating deaths putatively associated with AIDS since 1990 14. Also in the selected municipalities, original medical records were reviewed to confirm AIDS diagnoses and cause of death in the suspected cases. When such a death was found to be associated with AIDS, the person was included as a "case".

Data collection procedures comprised both the abstraction of information from medical records and downloading from the above-mentioned databases. Data were transcribed into a standardized case report form devised for the study. The form included age, sex, place of residence, time elapsed since first HIV diagnosis, stage of the disease at the time HIV infection was diagnosed, therapeutic regimens used up to the last appointment or death, disease stage at ART initiation, adherence to ART as recorded in the medical record, prophylaxis for opportunistic infections, vaccines administered to the patients since HIV diagnosis, and all co-infections and/ or opportunistic infections/diseases. Additional information included the type of clinic where the cases and controls received follow-up care (e.g., public, private, affiliated with universities, etc.) and whether they were general institutions treating different medical conditions or HIV specialized services. Data were abstracted by trained health professionals with previous experience in surveillance under the supervision of a senior researcher in each of the selected municipalities. A supervisor was in charge of reviewing each case report form and double-checking for missing and contradictory information. Case report forms were reviewed a second time by the investigators, with remaining inconsistencies and missing information summarized and sent back to local supervisors for reconciliation or further abstraction.

Statistical analysis

Data were analyzed following standard methods for non-paired case-control studies. Variables were first assessed for their association with case status (i.e. death) in a bivariate analysis. A final multivariable model was selected using stepwise forward logistic regression, with candidate variables being those associated with death at the level of p < 0.05 in bivariate analyses. To account for the study design, regions were defined as strata, municipalities were defined as clusters, and estimates were weighted for the relative frequency of AIDS deaths reported for each macroregion. The multivariable model was fitted using the Wald test, considering a statistical significance of 0.05 for retention in the final model. The final model also took into consideration the plausibility of associations based on previous studies carried out in Brazil and elsewhere. Analyses were carried out using SPSS version 17 (SPSS Inc., Chicago, USA).

Ethical considerations

The risks associated with this study were minimized due to the fact all information was abstracted from existing secondary sources. No individual patients or their families were contacted by the study team and abstracted data had all identifying elements removed. The study protocol was reviewed and approved by the institutional review boards (IRBs) of Santa Casa de São Paulo, the Centro de Referência e Treinamento DST/AIDS in São Paulo, and several of the selected municipalities, where required.

Results

From the 64 Brazilian municipalities with 30 or more AIDS deaths registered in 2003, we randomly selected 22 municipalities stratified on macroregion of Brazil. Within this sample, 1,214 deaths were recorded; records could be found for 1,004 (97.2%). Of the randomly selected 1,439 controls, records were found for 1,115 (92.1%). With statistical adjustment for clustering by location and the proportion of AIDS burden, the sample is approximately representative of the nation.

The largest portion of the sample (43.5%) were from the Southeast region, followed by the Northeast (28%), the South (19.1%), Central (6.7%), and North (2.7%). Most patients (72.3%) received free care in public services, with the remainder using services at private hospitals, university hospitals, or other organizations with varying forms of payment or benefits.

The majority of patients were male and under the age of 40. Nearly half (49.3%) had not completed basic or elementary education. Characteristics of the study population are shown in Table 1.

Cases significantly differed from controls in being more likely to be in the lowest education level (odds ratio - OR = 1.74, 95% confidence interval - 95%CI:1.07-2.84), and less likely to be in the homosexual transmission category (OR = 0.65, 95%CI 0.50-0.84), and to have been diagnosed according to criteria other than CD4 < 350 (OR = 2.97, 95%CI: 1.96-4.51) (Table 2). The factor most strongly associated with death was never having received ART (OR = 6.8, 95%CI: 4.28-8.92); interrupted ART was also significantly associated with death (OR = 3.58, 95%CI: 2.65-4.85). Other care related variables associated with death included not receiving prophylaxis for opportunistic infections (OR = 1.4, 95%CI: 1.03-1.89) and not receiving vaccines recommended for HIV-positive patients (OR = 3.74, 95%CI: 2.74-5.10). Cases were also more likely to have any disease associated with AIDS (OR = 2.44, 95%CI: 1.34-4.45) and tuberculosis in particular (OR = 1.65, 95%CI: 1.27-2.13). Time since the first HIV-positive test result being less than one year (OR = 4.39, 95%CI: 3.25-5.93) and time from AIDS diagnosis to death (OR = 5.84, 95%CI: 4.47-7.65) which are markers of late diagnosis, were both found to be associated with increased mortality.

In the multivariate analysis (Table 3), interrupted (adjusted odds ratio – AOR = 4.35, 95%CI: 3.15-6.00) or no use of ART (AOR = 2.39, 95%CI: 1.57-3.65) was the strongest predictor of death, followed by late diagnosis (i.e., less than one year since diagnosis, AOR = 3.95, 95%CI: 2.68-5.82). Even after controlling for time with AIDS, persons diagnosed by a criterion other than CD4 < 350 had a higher likelihood of death (AOR = 1.65, 95%CI: 1.14-2.40). Patients not receiving recommended vaccines (AOR = 1.76, 95%CI: 1.21-2.56), patients presenting diseases associated with AIDS (AOR = 2.19, 95%CI: 1.22-3.93), and patients diagnosed with tuberculosis (AOR = 1.50, 95%CI: 1.14-1.97) had higher odds of death. Being in the IDU exposure category maintained a borderline association with higher odds of death, while homo/bisexual exposure showed a protective effect.

Discussion

Brazil is widely recognized for its leadership in guaranteeing free and ample access to ART for all its citizens. The period of most rapid scale up in Brazil occurred from 1996 to 2003, whereas for much of the rest of the world the wide availability of ART began after 2003. The experiences of Brazil can serve as a sentinel of what may happen in the post-ART scale up world internationally.

The first lesson learned from our study is that vital statistics, surveillance data, and monitoring and evaluation systems continue to detect significant rates of AIDS-related mortality. We found that not receiving ART was an independent predictor of death among AIDS patients in Brazil. While not surprising in itself, this finding serves as a poignant reminder that there are remaining disparities in access to, delivery, and uptake of ART in the post scale-up period 15 and that AIDS continues to be a significant cause of death and suffering. In addition to the heterogeneity of services and their quality, stigma and discrimination can also hamper the benefits of ART 16 as the groups with the lowest uptake of ART are those who are most severely marginalized. Further efforts are needed to achieve maximal ART coverage at a level of high quality, especially among the stigmatized or hidden populations, who are often at highest risk of infection.

We also found that late diagnosis was an independent predictor of mortality, as indicated by the significant association of death with shorter intervals of time from diagnosis when the criteria for AIDS diagnosis were conditions associated with more severe immune-suppression. This finding was independent of ART initiation, indicating that the full benefits of treatment are not realized when patients are not identified earlier in the course of infection. The finding speaks to the need for enhanced campaigns to make Brazilians more aware of the risks of HIV infection, to seek HIV testing and, when positive, to be brought into care earlier. The results of our study reinforce the wider benefit of earlier initiation of ART. The likelihood of survival was greater for persons whose eligibility criterion was CD4 count < 350, compared to those whose criterion was CD4 < 200 or having an opportunistic infection, even after controlling for initiating ART. These findings, evident in our data from 1996 to 2003, are in agreement with the most recent treatment guidelines issued several years later 17.

We are encouraged that our analysis confirms that earlier initiation of ART adopted by Brazil leads to a significant lengthening of survival. Other findings point to the possibility of further reducing disparities in AIDS mortality. For

Table 1

Characteristics of study participants.

Characteristics	Control		Case		p-value
	n	%	n	%	
Sex					
Male	420	38.5	343	33.7	
Female	670	61.5	675	66.3	0.122
Total	1,090		1,018		
Age group (years)					
15-29	167	15.4	187	18.4	
30-39	482	44.3	430	42.2	0.315
40-49	329	30.2	289	28.4	
50+	111	10.2	113	11.1	
Total	1,089		1,019		
Education					
Incomplete elementary	452	45.8	452	57.7	
Elementary	185	18.7	143	18.2	0.001
High School	291	29.5	155	19.8	
College group	59	5.9	34	4.3	
Total	987	0.7	784		
AIDS case definition	, , ,		, , ,		
Caracas	301	27.7	223	22.2	
CDC	200	18.4	346	34.5	< 0.001
CD4	586	53.9	283	28.2	(0.00)
Death	300	33.7	150	15.1	
Total	1,087		1,002	13.1	
Criterion CD4	1,007		1,002		
Yes	586	53.9	283	28.3	
No	501	46.1	718	71.7	< 0.00
Total	1,087	40.1	1,001	71.7	< 0.00
Exposure criteria	1,007		1,001		
Blood/IDU	210	19.4	204	24.9	
Blood/Transfusion	24	2.2	204	2.6	0.003
Sexual homo/bisexual	226	20.9	113	13.8	0.003
Sexual heterosexual	622	57.5	480	58.7	
Total	1,082	37.3	818	36.7	
Time from the 1st positive HIV test result (years)	1,002		010		
[n = 2,005]					
0	195	18.2	470	50.3	
1-4					< 0.00
	479	44.7	246	26.3	< 0.00
5-20	397	37.1	219	23.4	
Total	1,071		935		
Time from AIDS diagnosis to death or to the last visit					
to the clinic (years)	2/2	24.2	//0	/ - /	
0	262	24.2	660 210	65.6	- 0.00
1-4	530	48.9	219	21.8	< 0.00
5-20	292	26.9	126	12.5	
Total	1,084		1,005		
Diseases	0.10	0.4.4	010	04.0	
Yes	942	86.4	912	94.0	
No	148	13.6	59	6.0	0.005
Total	1,090		971		

(continues)

Table 1 (continued)

Characteristics	Control		Case		p-value
	n	%	n	%	
Tuberculosis					
No	867	79.5	716	70.3	
Yes	223	20.5	302	29.7	0.001
Total	1,090		1,018		
CD4					
0-199	526	51.2	377	64.0	
200-350	310	30.2	103	17.4	< 0.001
351+	191	18.6	110	18.6	
Total	1,027		590		
Hepatitis B					
Yes	54	5.6	56	8.1	
No	902	94.4	634	91.9	0.12
Total	956		690		
Hepatitis C					
Yes	135	14.3	144	21.3	
No	805	85.7	532	78.7	0.001
Total	940		676		
Antiretroviral treatment					
None	84	8.4	269	30.9	
Past use	96	9.6	178	20.4	< 0.001
Current use	816	82.0	423	48.7	
Total	996		870		
Prophylaxis for opportunistic diseases (at least one)					
Yes	691	67.4	536	59.7	
No	334	32.6	361	40.3	0.034
Total	1,025		897		
Recommended vaccines (at least one given)					
Yes	214	19.6	63	6.1	
No	876	80.4	956	93.9	< 0.001
Total	1,090		1,019		

CDC: Centers for Disease Control and Prevention; IDU: injecting drug users.

example, vaccination, prevention of tuberculosis, and prevention of other AIDS associated illnesses can be addressed in routine, comprehensive treatment of HIV-infected persons. The higher mortality among largely impoverished IDU points to potentially preventable co-morbidities and causes of death in these populations. It is possible that in the face of the impressive impact of ART, care providers may neglect to include prophylaxes and vaccines in the routine care, in spite of existing guidelines and specialized services. As survival of AIDS patients lengthens, their longer term health care needs, including dealing with ART side-effects, non-AIDS related treatment, and prevention will increasingly need to be considered.

We recognize limitations in our study. Primarily, we were constrained to using data recorded in electronic databases or retrievable from local medical records, with the quality and completeness of the data varying by location and type of services. It is therefore likely that other factors associated with mortality may have gone undetected in our study. Second, there may be underreporting of AIDS-specific mortality, also varying by region. There may also be regional variations in causes of death among AIDS patients that were not detected due to small samples for some of the regions. The retrospective nature of the design also limits the interpretation of causality.

Despite the limitations, our approach illustrates the benefits of routinely examining

^{*} Excluding AIDS at death as criterion.

Table 2

Selected risk factors for deaths among AIDS patients in a multivariate (logistic) regression model.

Characteristics	OR (unadjusted)	95%CI
Sex [n = 2,110]		
Male	1.23	0.94-1.6
Female	1.00	
Age group (years) [n = 2,109]		
9-29	1.11	0.70-1.7
30-39	0.88	0.60-1.29
40-49	0.87	0.60-1.25
50+	1.00	
Education $[n = 1,771]$		
Incomplete elementary	1.74	1.07-2.8
Elementary	1.35	0.98-1.8
High School	0.93	0.62-1.39
College group	1.00	
Exposure criteria [n = 1,900]		
Blood/IDU	1.26	0.95-1.67
Blood/Transfusion	1.14	0.53-2.42
Sexual homo/bisexual	0.65	0.50-0.8
Sexual heterosexual	1.00	
Criterion CD4 < 350 [n = 2,089]		
No	2.97	1.96-4.5
Yes	1.00	
ARV Treatment [n = 1,865]		
None	6.18	4.28-8.92
Past use	3.58	2.65-4.8
Current use	1.00	
Prophylaxis for opportunistic diseases (at least one) [n = 1,921]		
No	1.40	1.03-1.89
Yes	1.00	
Recommended vaccines (at least one given) [n = 2,110]	0.74	0.74.5.44
No	3.74	2.74-5.10
Yes	1.00	
Diseases [n = 2,062]	0.44	4 2 4 4 4
Yes	2.44	1.34-4.4
No Tuborculosis (n = 2.110)	1.00	
Tuberculosis [n = 2,110]	1.65	1 27 2 1
Yes No	1.00	1.27-2.13
NO CD4 level (first)	1.00	
0-199	1 25	0 27 1 0
200-350	1.25 0.58	0.87-1.80 0.42-0.8°
351+	1.00	0.42-0.0
Time from the 1st positive HIV test result (years) [n = 2,005]	1.00	
0	4.39	3.25-5.9
1-4	0.93	0.73-1.19
5-20	1.00	5.75-1.1
Time from AIDS diagnosis to death or to the last visit to the clinic (years) $[n = 2,090]$		
0	5.84	4.47-7.6
1-4	0.96	0.79-1.10
5-20	1.00	0., ,-1.10

95%CI: 95% confidence interval; ARV: antiretroviral; IDU: injecting drug users; OR: odds ratio.

Table 3

Adjusted model for multivariate analysis of AIDS deaths among participants (n = 1,648). AMA Brazil Project, 2003.

Characteristic	Adjusted OR	95%CI
Exposure group		
Blood/IDU	1.26	0.92-1.73
Homo/bisexual	0.75	0.59-0.95
Heterosexual	1.00	
Criterion CD4 < 350		
No	1.65	1.14-2.40
Yes	1.00	
Vaccination		
No	1.76	1.21-2.56
Yes	1.00	
Time with AIDS (years)		
< 1	3.95	2.68-5.82
1-4	1.14	0.99-1.45
5-20	1.00	
Diseases		
Yes	2.19	1.22-3.93
No	1.00	
Tuberculosis		
Yes	1.50	1.14-1.97
No	1.00	
ARVT		
None	2.39	1.57-3.65
Past use	4.35	3.15-6.00
Current use	1.00	

95%CI: 95% confidence interval; ART: antiretroviral therapy; IDU: injecting drug users; OR: odds ratio.

data available in Brazil on the national level, enhanced by data retrievable at the municipal and facility level. While cohort studies remain the gold standard for assessing predictors of mortality, the long period of time entailed in assessing mortality precludes the use of cohort studies in many areas. Our methods provide a basis for assessing the progress of the national response to the HIV epidemic using a concrete and verifiable endpoint (i.e. mortality). Ultimately, the aims of extending life and reducing disparities in mortality need to be assessed with death as the outcome. The experience of Brazil with ART scale up may differ from the experience of other nations, regions, and locations 17; nevertheless, our approach is one that could be widely adopted as an efficient, low cost method for assessing what has been achieved and what remains to be done in the response to HIV around the world.

Brazil has made significant strides in providing universal ART access to people living with HIV/AIDS since 1997. Data presented in this study highlight additional areas where improvements can be made: HIV testing and counseling and treatment should be a priority both to favor earlier entrance into treatment and to decrease costs associated with the management of patients with advanced immunodeficiency.

Case management strategies should target IDU including interventions tailored to the special needs of IDU.

Key points highlighted by this study included the need to implement vaccinations as stated by the national and international guidelines and to offer comprehensive management of HIV and tuberculosis.

Resumo

Analisou-se o perfil clínico e epidemiológico dos óbitos relacionados à AIDS no período posterior à implementação da terapia antirretroviral (TARV) no Brasil, em um estudo caso-controle, com amostra representativa de óbitos por AIDS e de pessoas vivendo com AIDS, utilizando dados secundários. Abandono (odds ratio ajustada – AOR = 4,35, IC95%: 3,15-6,00) ou não uso da TARV (AOR = 2,39, IC95%: 1,57-3,65) foi o mais forte preditor de morte, seguido de diagnóstico tardio (AOR = 3,95, IC95%: 2,68-5,82). Critério de definição de AIDS que não o "CD4 < 350" esteve associado a uma maior probabilidade de morte (AOR = 1,65, IC95%: 1,14-2,40). Pacientes que não receberam vacinas recomendadas (AOR = 1,76, 95%CI: 1,21-2,56), apresentando doenças associadas à AIDS (AOR = 2,19, IC95%: 1,22-3,93) e com tuberculose (AOR = 1,50, IC95%: 1,14-1,97), tiveram maior risco de morte. A categoria de exposição UDI apresentou maior chance de óbito. Apesar do sucesso com as introduções precoces da TARV, brasileiros continuaram a morrer de AIDS no período posterior à implementação da terapia, e muitas das causas subjacentes a essa mortalidade são preveníveis.

Infecções por HIV; Anti-Retrovirais; Mortalidade; Acesso aos Serviços de Saúde

Contributors

M. A. S. M. Veras was responsible for the study conception and design, coordinating data collection, analysis and interpretation, writing up the article and approving the final version. M. C. A. Ribeiro participated in the design, data analysis, write-up and approval of the final version. L. F. Jamal participated in the design, collection and analysis of data, write up and approval of the final version. W. McFarland contributed towards the design, data analysis, write-up and approval of the final version. F. I. Bastos participated in the data analysis, write-up and approval of the final version, K. B. Ribeiro collaborated in the design, data analysis, write-up and approval of the final version. R. B. Barata contributed towards the design, analysis, write-up and approval of the final version. J. C. Moraes participated in the design, creation of the data base and approval of the final version of the article. A. L. Reingold participated in the design, writeup and approval of the final version.

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References

- Brasil. Lei nº. 9.313, de 13 de novembro de 1996. Dispõe sobre a distribuição gratuita de medicamentos aos portadores de HIV e doentes de AIDS. Diário Oficial da União 1996; 14 nov.
- Boyd MA. Improvements in antiretroviral therapy outcomes over calendar time. Curr Opin HIV AIDS 2009: 4:194-9.
- Nemes MI, Carvalho HB, Souza MF. Antiretroviral therapy adherence in Brazil. AIDS 2004; 18 Suppl 3:S15-20.
- Marins JR, Jamal LF, Chen SY, Barros MB, Hudes ES, Barbosa AA, et al. Dramatic improvement in survival of Brazilian AIDS patients. AIDS 2003; 17:1675-82.
- Guibu IA, Barros MBA, Cordeiro MRD, Tayra A, Alves MCGP, Pereira GFM. Estudo de sobrevida de pacientes de AIDS no Brasil, 1998 a 1999 fase I regiões Sul e Sudeste. Boletim Epidemiológico AIDST 2008; V:51-3.
- Baggaley RF, Petersen ML, Soares MA, Boily M-C, Bastos FI. Human Immunodeficiency Virus: resistance to antiretroviral drugs in developing countries. In: Sosa AJ, Byarugaba DK, Amábile-Cuevas CF, Hsueh P-R, Kariuki S, Okeke IN, editors. Antimicrobial resistance in developing countries (Emerging infectious diseases of the 21st century). New York: Springer; 2009. p. 75-94.
- Hacker MA, Petersen ML, Enriquez M, Bastos FI. Highly active antiretroviral therapy in Brazil: the challenge of universal access in a context of social inequality. Rev Panam Salud Pública 2004; 16: 78-83.
- Lowndes CM, Bastos FI, Giffin KM, Vaz dos Reis AC, d'Orsi E, Alary M. Differential trends in mortality from AIDS in men and women in Brazil (1984-1995). AIDS 2000; 14:1269-73.
- Ministério da Saúde. Boletim Epidemiológico AIDST 2008; Ano V, nº. 1.
- Ministério da Saúde. UNGASS resposta brasileira 2005-2007: relatório de progresso do país. http://www.aids.gov.br/data/documents/stored Documents/%7BB8EF5DAF-23AE-4891-AD36-1903553A3174%7D/%7B99A24D99-A80D-4E04-B7C2-786F24B5B689%7D/ungas2008%20portug06-final.pdf (accessed on 09/Sep/2009).

- Souza Jr. PRB, Szwarcwald CL, Castilho EA. Atraso na introdução de terapia antiretroviral em pacientes infectados pelo HIV no Brasil, 2003-2006. Clinics 2007; 62:579-84.
- Malta M, Bastos FI, Silva CM, Pereira GF, Lucena FF, Fonseca MG, et al. Differential survival benefit of universal HAART access in Brazil: a nation-wide comparison of injecting drug users versus men who have sex with men. J Acquir Immune Defic Syndr 2009; 52:629-35.
- Revisão da definição nacional de caso de AIDS em indivíduos com 13 anos de idade ou mais, para fins de vigilância epidemiológica. http://www.aids.gov. br/udtv/link203.htm (accessed on 15/Oct/2009).
- 14. Veras MASM, Drumond Jr. M, Lira MTA. A importância da AIDS como causa de morte no município de São Paulo. In: Secretaria Municipal da Saúde, organizador. Coletâneas de Textos do Pro-AIM. São Paulo: Secretaria Municipal da Saúde; 2003. p. 30-1.
- Nemes MI, Melchior R, Basso CR, Castanheira ER, Britto-Alves MT, Conway S. The variability and predictors of quality of AIDS care services in Brazil. BMC Health Serv Res 2009; 9:51.
- 16. Oliveira IB. Acesso universal? Obstáculos ao acesso, continuidade do uso e gênero em um serviço especializado em HIV/AIDS em Salvador, Bahia, Brasil. Cad Saúde Pública 2009; 25 Suppl 2:S259-68.
- Consenso terapêutico. http://www.aids.gov.br/as sistencia/conso2.htm (accessed on 16/Dec/2009).
- 18. Grinsztejn B, Veloso VG, Friedman RK, Moreira RI, Luz PM, Campos DP, et al. Early mortality and cause of deaths in patients using HAART in Brazil and the United States. AIDS 2009; 23:2107.

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