Original Article

Cause-Specific Mortality among HIV-Infected Persons in One Medical Center, Tehran, Iran

Fahimeh Hadavand[1], Payam Tabarsi[1], Fatemeh Abbasi[1*], Latif Gachkar[1], Zahra Arab-Mazar[1,2]

[1] Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Department of Medical Parasitology and Mycology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background: Human immunodeficiency virus (HIV) is one of the major infectious agents, which has important role in the public health challenges, which have affected the world's economic and social situation recent decades. During the last decades, millions of people died due to HIV infection worldwide. However, data remain limited on the causes of death among HIV-infected in Iranian population. The aim of the present study was to assess the cause specific death among HIV positive inpatient persons in Iran.

Materials and Methods: This surveillance was conducted on inpatient HIV positive admissions at Masih Daneshvari Hospital, Tehran, Iran during October 2016 and April 2017.All patient's data were collected via abstraction form, which were ascertained, from medical records and from written logbooks that were kept by the nursing staff on the ward. The data of each admission was recorded from the medical reports at the time of admission and upon discharge. All laboratory data were collected and recorded separately.

Results: Fifty persons were diagnosed as HIV-infected patients, of which 58% of them were classified as AIDS patients. Our findings indicated that the cause of hospitalization were pulmonary 54%, neurological 20%, gastrointestinal 16%, and dermal 10% complications. Overall, 21 patients (42%) were diagnosed with pulmonary tuberculosis, of which one patient died from tuberculosis complications. Four patients died during the study period.

Conclusion: In conclusion, early treatment and/or early use of ART can be improved outcomes. Therefore, early HIV testing and early ART use play important role in mortality reduction among eligible persons.

Keywords: Human immunodeficiency virus (HIV), AIDS, Mortality rate, Opportunistic infections

---

*Corresponding Author: Fatemeh Abbasi, Infectious Disease and Tropical Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran; Email: fatemehabbasi80@yahoo.com

Introduction

Up-to-date and comprehensive data and evidence for levels and trends is critical for informed priority setting for each country. Trends quantify progress against explicit health targets, whether local, national, or global, and help to evaluate where programs are working or not. To identify emerging public health challenges, regular comprehensive updates about causes of death seems to be crucial[1].

According to the health setting reports, morbidity and mortality remain high among HIV-infected patients[3-5]. The mortality rates may differ by the rate of uptake appropriate treatment and by the available level of care at each facility[6]. Since 1996, by using combination, antiretroviral treatment (ART) the prognosis of HIV-

positive patients was consistently improving and the HIV-related morbidity and mortality rates have been decreased worldwide[7-10]. However, it remains limited data evaluating mortality by HIV status among inpatient facilities in Iran. Nevertheless, the case management of HIV-positive patients remains challenging in our country, because there are some problems. In this regard, late diagnosis of HIV infection and late initiation of treatment lead to increasing of AIDS-related morbidity rate among population[8,11-14]. Following the AIDS-related morbidity, tuberculosis (TB) and invasive bacterial diseases are the most frequent disorders in these patients[11,12,15,16]. In other hand, treatment byART regimens may has some adverse effects, and even HIV-positive patients may experience a wider range of co-morbidities, including cancers and cardiovascular diseases[17,18].

It has been reported that, widespread use of highly active antiretroviral therapy (HAART) can lead to changing of causes of death among HIV positive patients dramatically[19-24].Thus, examining the changes in causes of death can inform the clinical management of HIV-infected persons in each geographical situation and also surveying mortality in HIV-infected population is more useful for detecting variation in the availability, utilization, timeliness, or quality of care for this population.

Therefore, the aim of the present study was to assess the cause specific death among HIV positive inpatient persons in Masih Daneshvari Hospital, Tehran, Iran.

Methods

The present study was conducted as a cross sectional surveillance of inpatient HIV positive admissions at Masih Daneshvari hospital, Tehran (capital city of Iran), Iran. All medical admissions from medical wards were recorded over a six-month period between October 2016 and April 2017. Masih Daneshvari hospital with 350 beds is affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran. This hospital selected by the World Health Organization (WHO) as the center for educating students in tuberculosis in the Eastern Mediterranean region (EMRO) at the national level. The Ethics Committee of School of Medicine, Shahid Beheshti University of Medical Sciences approved this study (IR.SBMU.MSP.REC.1395.369). In this study, individual informed consent from the participants were obtained before enrollment.

All patient's data were collected via abstraction form,

Table 1: Laboratory characteristics of HIV-infected patients attended at Masih Daneshvari Hospital, Tehran, Iran, between 2004 and 2014.

Characteristics	Live patients (*n*=46)	Died persons (*n*=4)
Viral load		
>50 copies/ml	17.4% (*n*=8)	50% (*n*=2)
50-499 copies/ml	10.9% (*n*=5)	25% (*n*=1)
500-29999 copies/ml	30.4% (*n*=14)	25% (*n*=1)
≥30000 copies/ml	41.3% (*n*=19)	0% (*n*=0)
CD4 count		
≥500 cells/microL	17.4% (*n*=8)	0% (*n*=0)
200-499 cells/microL	28.3% (*n*=13)	50% (*n*=2)
<200 cells/microL	54.3% (*n*=25)	50% (*n*=2)
HBS-Ag		
Positive	4.3% (*n*=2)	0% (*n*=0)
Negative	95.7% (*n*=44)	100% (*n*=4)
Anti-HCV-antibody		
Positive	32.6% (*n*=15)	0% (*n*=0)
Negative	67.4% (*n*=31)	100% (*n*=4)

which were ascertained, from medical records and from written logbooks that were kept by the nursing staff on the ward. The data of each admission was recorded from the medical reports at the time of admission and upon discharge. All laboratory data were collected and recorded separately. The collected data consist of patient demographics, HIV testing, HIV status, CD4 cell count, ART status and current viral and immunological markers, hematological tests, biochemical tests, microbiological tests, admission diagnosis, and discharge diagnosis. The outcome of each patients was recorded as 'discharged', 'died', or 'transferred to another hospital'.

All data were entered into a SPSS statistical software version 22.0 (IBM Corp., Armonk, USA). Fisher's exact test and Chi Square test were used for assessing the significant correlation between variables. For analyzing the 'died' and 'alive' groups, Mann-Whitney U test was used. For all tests and analysis, the 5% level was considered statistically significant.

Results

In the present study, from 487 persons suspected with HIV infection, 50 were diagnosed as HIV-infected patients, of which 58% (n=29) of them were classified as AIDS patients. The patient's age range was from 20 to 72 years old. The median age of the patients was 34±3 years. A total of 78% (n: 39) of the HIV-infected patients were male and 22% (n: 11) were female, of which 54% were married, 40% (n: 20) were single and 6% (n: 3) were divorce cases. Our analysis indicated that 52% (n: 26) of the patients were unemployment. Four patients died during the study period; in which Tuberculosis, brain abscess, edema and stroke were identified as causes of death. Table/Fig 1 shows the laboratory characteristics and co-infection with hepatitis virus among the HIV-infected patients in this study.

Our results indicated that 42% (n: 21) of the HIV-positive patients were considered as having high-risk perceptions about HIV infection through a self-report questionnaire and met the inclusion criteria. The frequency of these risk factors has been indicated in Table 2. Our findings indicated that the cause of hospitalization were pulmonary 54% (n: 27), neurological 20% (n: 10), gastrointestinal 16% (n: 8),

Table 2: Demographic and HIV-risk history characteristics of HIV- infected patients in attended at Masih Daneshvari Hospital, Tehran, Iran, between 2004 and 2014.

Characteristics	Percentage (*number*)
Marital status	
Married	54% (*n*=27)
Single	40% (*n*=20)
Divorced	6% (*n*=3)
Education	
Illiterate	22% (*n*=11)
Less than high school	48% (*n*=24)
High school diploma	28% (*n*=14)
College education	2% (*n*=1)
Sexual orientation	
Heterosexual (male)	26% (*n*=13)
Heterosexual (female)	16% (*n*=8)
Homosexual or gay	4% (*n*=2)
Unclear	54% (*n*=27)
Intravenous drug user	
Male	32% (*n*=16)
Female	6% (*n*=3)
Cupping history	14% (*n*=7)
Tattoo history	34% (*n*=17)

and dermal 10% (n: 5) complications. Overall, 21 patients (42%) were diagnosed with pulmonary tuberculosis, of which one patient died from tuberculosis complications. Table 3 illustrates the frequency of clinical manifestationsamong the HIV-positive patients.

Discussion

In present study, causes of death of hospitalized HIV-positive patients were studied and were compare with different variables. According to our analysis, age, male gender and low number of CD4 cells (CD4< 200) are associated with increasing the mortality in HIV positive patients (pV< 0.05). Perry et al, were conducted a study in Africa. They showed, among HIV-positive patients who died, a low CD4 cell count (<200) was associated with death and they reported that, patients who died had significantly more neurological and respiratory-related presenting

Table 3: The frequency of different clinical manifestationsamong the HIV-positive patients.

Clinical manifestations	Live patients (*n*=46)	Died persons (*n*=4)
Radiologicalpulmonary manifestation		
Alveolar	4.3% (*n*=2)	0% (*n*=0)
Cavitary	26.1% (*n*=12)	0% (*n*=0)
Interstitial	8.7% (*n*=4)	0% (*n*=0)
Reticular	4.3% (*n*=2)	0% (*n*=0)
Nodular	23.9% (*n*=11)	25% (*n*=1)
Normal	32.6% (*n*=15)	75% (*n*=3)
Cerebral complications		
Mass lesion	6.5% (*n*=3)	75% (*n*=3)
Edema	2.2% (*n*=1)	25% (*n*=1)
Atrophy	4.3% (*n*=2)	0% (*n*=0)
Normal	87% (*n*=40)	0% (*n*=0)
Gastrointestinal complications		
Liver disorder	8.7% (*n*=4)	0% (*n*=0)
Esophageal complication	6.5% (*n*=3)	0% (*n*=0)
Peritoneum complication	2.2% (*n*=1)	0% (*n*=0)
Colon complication	2.2% (*n*=1)	0% (*n*=0)
Normal	80.4% (*n*=37)	100% (*n*=4)
Dermal disorders		
Plaque	6.5% (*n*=3)	0% (*n*=0)
Ulcer	4.3% (*n*=2)	0% (*n*=0)
Abscess	4.3% (*n*=2)	0% (*n*=0)
Normal	87% (*n*=40)	100% (*n*=4)
Tuberculosis	43.5% (*n*=20)	25% (*n*=1)

complaints than patients did who survived[6]. Our study showed, mortality rate among HIV positive inpatients was 8%, which very lower than mortality rate in Africa, which reported 23%[6]. In addition, in present study, Tuberculosis, brain abscess, edema and stroke were identified as causes of death. It has been reported that, mortality rates increased of HIV positive inpatients in Zimbabwe was from 13.3 to 28.6% between 1992 and 2002[24-26]. Although overall mortality in present study was lower than some settings, controlling and preventing to death among the HIV-positive patients is concerning.

Our result showed, 42% of HIV positive patients were infected by *Mycobacterium tuberculosis* (MTB). According to Jam et al study in 2010, 24% of HIV positive patients in Tehran HIV centers were infected by MTB [27]. Later, Khosravi et al during 2012 in Ahvaz province, southwest of Iran, has been reported that, 23% of HIV positive patients suffered by MTB[28]. It seems that, MTB morbidity was increasing among HIV positive persons. Importantly, tuberculosis is endemic in our country, and unfortunately, the rate of resistant strains is increasing[29,30].

According to our analysis, 30% of HIV positive patients were infected by HCV. The importance of HCV/HIV coinfection on overall and cause-specific mortality was discussed[31-33]. However, according to

literature, the role of HCV coinfection in mortality associated with HIV is unclear yet. Some studies have showed HCV infection does not accelerate CD4 decline and AIDS progression[34,35]. Other reports suggested that HCV coinfection is increasing risk for progression to AIDS[36]. It has been reported that[37] eradication of HCV in HIV/HCV positive patients is accompanying with decreases lower risks of both liver and non-liver-related mortality and HIV progression. In present study, the count of CD4 cells in HIV/HCV positive patients was <200 cells/microL.

Conclusion

In conclusion, early treatment and/or early use of ART can be improved outcomes. It proven that lower CD4 cell count is associated with increased mortality, therefore early HIV testing and early ART use play important role in mortality reduction among eligible persons. In addition, bacterial infections were also frequent causes of hospitalization among HIV positive persons. Among these infections, TB is the major cause of hospitalization of HIV-positive persons worldwide. Prophylaxis and controlling programs should be update and new ways, strategies and antibacterial agents should be designed for treatment of drug resistant strains.

Acknowledgment

References

1. Institute for Health Metrics and Evaluation. [accessed Nov 3, 2014] GBD 2013 Protocol: global burden of diseases, injuries, and risk factors. 2013. http://www.healthdata.org/gbd/about/protocol

2. Abubakar II, Tillmann T, Banerjee A. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;385(9963):117-71.

3. Balogou AA, Saka B, Kombate´ D, et al. Causes of mortality associated with HIV/AIDS in health-care facilities in Togo: a six-month prospective study. Trop Doct. 2011;41:215–7.

4. Lewden C, Drabo YJ, Zannou DM, et al. Disease patterns and causes of death of hospitalized HIV positive adults in West Africa: a multicountry survey in the antiretroviral treatment era. J Int AIDS Soc. 2014;17:18797.

5. Kra O, Aba YT, Yao KH, et al. Clinical, biological, therapeutic and evolving profile of patients with HIV infection hospitalized at Infectious and tropical diseases unit in Abidjan (Ivory Coast). Bull SocPatholExot. 2013;106:37–42.

6. Perry ME, Kalenga K, Watkins LF, Mukaya JE, Powis KM, Bennett K, Mmalane M, Makhema J, Shapiro RL. HIV-related mortality at a district hospital in Botswana. International journal of STD & AIDS. 2017;28(3):277-83.

7. Cascade Collaboration. Determinants of survival following HIV-1 seroconversion after the introduction of HAART. The Lancet. 2003;362(9392):1267-74.

8. Braitstein P, Brinkhof MW, Dabis F, Schechter M, Boulle A, Miotti P, Wood R, Laurent C, Sprinz E, Seyler C, Bangsberg DR. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: comparison between low-income and high-income countries. Lancet (London, England). 2006;367(9513):817-24.

9. Laurent C, Diakhate N, Gueye NFN, Toure MA, Sow PS, Faye MA, et al. The Senegalese government's highly active antiretroviral therapy initiative: an 18- month follow-up study. AIDS. 2002;16:1363:70.

10. Seyler C, Messou E, Gabillard D, Inwoley A, Alioum A, Anglaret X. Morbidity before and after HAART initiation in Sub-Saharan African HIV-infected adults: a recurrent event analysis. AIDS Res Hum Retroviruses. 2007;23:1338:47.

11. Moh R, Danel C, Messou E, Ouassa T, Gabillard D, Anzian A, et al. Incidence and determinants of mortality and morbidity following early antiretroviral therapy initiation in HIV-infected adults in West Africa. AIDS. 2007;21:2483:91.

12. Etard JF, Ndiaye I, Thierry-Mieg M, Gueye NF, Gueye PM, Laniece I, et al. Mortality and causes of death in adults receiving highly active antiretroviral therapy in Senegal: a 7-year cohort study. AIDS. 2006;20:11819.

13. Lawn SD, Myer L, Orrell C, Bekker LG, Wood R. Early mortality among adults accessing a community-based antiretroviral service in South Africa: implications for programme design. AIDS. 2005;19:21418.

14. Gabillard D, Lewden C, Ndoye I, Moh R, Segeral O, Tonwe-Gold B, et al. Mortality, AIDS-morbidity and loss to follow-up by current CD4 cell count among HIV-1 infected adults receiving antiretroviral therapy in Africa and Asia: data from the ANRS 12222 collaboration. J Acquir Immune DeficSyndr. 2013;62:555:61.

15. Lawn SD, Badri M, Wood R. Tuberculosis among HIV-infected patients receiving HAART: long term incidence and risk factors in a South African cohort. AIDS. 2005;19:210916.

16. Curtis AJ, Marshall CS, Spelman T, Greig J, Elliot JH, Shanks L, et al. Incidence of WHO stage 3 and 4 conditions following initiation of antiretroviral therapy in resource limited settings. PLoS One. 2012;7:e52019.

17. Boulle A, Orrel C, Kaplan R, Van Cutsem G, McNally M, Hilderbrand K, et al. Substitutions due to antiretroviral toxicity or contraindication in the first 3 years of antiretroviral therapy in a large South African cohort. AntivirTher. 2007;12:75360.

18. Lewden C, May T, Rosenthal E, Burty C, Bonnet F, Costagliola D, et al. Changes in causes of death among adults infected by the Human Immunodeficiency Virus (HIV) between 2000 and 2005. The ''Mortalite´ 2000 & 2005'' surveys (ANRS EN19 and Mortavic). J

Acquir Immune DeficSyndr. 2008;48:5908.

19. Centers for Disease Control and Prevention (CDC). Revised surveillance case definition for HIV infection-United States, 2014. MMWR Recomm Rep. 2014;63(RR-03):1-10.

20. Adih WK, Selik RM, Hu X. Trends in diseases reported on U.S. death certificates that mentioned HIV infection, 1996-2006. J IntAssoc Physicians AIDS Care (Chic). 2011;10(1):5-11.

21. Cohen MH, French AL, Benning L, et al. Causes of death among women with human immunodeficiency virus infection in the era of combination antiretroviral therapy. Am J Med. 2002;113(2): 91-8.

22. Palella FJ Jr, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. J Acquir Immune DeficSyndr. 2006; 43(1):27-34.

23. Buchacz K, Rangel M, Blacher R, Brooks JT. Changes in the clinical epidemiology of HIV infection in the United States: implications for the clinician. Curr Infect Dis Rep. 2009;11(1):75-83.

24. Van der Plas H, Meintjes G, Schutz C, et al. Complications of antiretroviral therapy initiation in hospitalized patients with HIV-associated tuberculosis. PLoS One. 2013;8:e54145.

25. Bardgett H, Dixon M and Beeching N. Increase in hospital mortality from non-communicable disease and HIVrelated conditions in Bulawayo, Zimbabwe, between 1992 and 2000. Trop Doct. 2006;36:129.

26. Pallangyo K, Ha˚ kanson A, Lema L, et al. High HIV seroprevalence and increased HIV-associated mortality among hospitalized patients with deep bacterial infections in Dar es Salaam, Tanzania. AIDS 1992; 6:971–976.

27. Jam S, Sabzvari D, SeyedAlinaghi S, Fattahi F, Jabbari H, Mohraz M. Frequency of Mycobacterium tuberculosis infection among Iranian patients with HIV/AIDS by PPD test. ActaMedicaIranica. 2010;48(1):67.

28. Khosravi AD, Alavi SM, Hashemzade M, Abasi E, Seghatoleslami S. The relative frequency of Mycobacterium tuberculosis and Mycobacterium avium infections in HIV positive patients, Ahvaz, Iran. Asian Pacific Journal of Tropical Medicine. 2012;5(1):71-4.

29. Yamchi JK, Haeili M, Feyisa SG, Kazemian H, Shahraki AH, Zahednamazi F, Fooladi AA, Feizabadi MM. Evaluation of efflux pump gene expression among drug susceptible and drug resistant strains of Mycobacterium tuberculosis from Iran. Infection, Genetics and Evolution. 2015;36:23-6.

30. Kazemian H, Haeili M, Yamchi JK, Rezaei F, Feyisa SG, Zahednamazi F, Mohajeri P, Bostanabd SZ, Shahraki AH, Fooladi AA, Feizabadi MM. Antimycobacterial activity of linezolid against multidrug-resistant and extensively drug-resistant strains of Mycobacterium tuberculosis in Iran. International journal of antimicrobial agents. 2015 Jun 1;45(6):668-70.

31. Hernando V, Perez-Cachafeiro S, Lewden C, et al. All-cause and liverrelated mortality in HIV positive subjects compared to the general population: differences by HCV co-infection. J Hepatol 2012;57: 743–51.

32. Berenguer J, Alejos B, Hernando V, et al. Trends in mortality according to hepatitis C virus serostatus in the era of combination antiretroviral therapy. AIDS 2012;26:2241–6.

33. Hernando V, Alejos B, Monge S, et al. All-cause mortality in the cohorts of the Spanish AIDS Research Network (RIS) compared with the general population: 1997–2010. BMC Infect Dis 2013;13:382.

34. Peters L, Mocroft A, Soriano V, et al. Hepatitis C virus coinfection does not influence the CD4 cell recovery in HIV-1-infected patients with maximum virologic suppression. J Acquir Immune DeficSyndr. 2009;50:457–63.

35. Sulkowski MS, Moore RD, Mehta SH, et al. Hepatitis C and progression of HIV disease. JAMA. 2002;288:199–206.

36. d'Arminio Monforte A, Cozzi-Lepri A, Castagna A, et al. Risk of developing specific AIDS-defining illnesses in patients coinfected with HIV and hepatitis C virus with or without liver cirrhosis. Clin Infect Dis. 2009;49:612–22.

37. Berenguer J, Rodriguez E, Miralles P, et al. Sustained virological response to interferon plus ribavirin reduces non-liver-related mortality in patients coinfected with HIV and Hepatitis C virus. Clin Infect Dis. 2012;55:728–36.