



REVIEW ARTICLE

SURVIVAL STUDIES IN PATIENTS WITH AIDS THROUGHOUT HISTORY

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ABSTRACT

Survival and evolution of clinical and laboratory diagnosis of AIDS patients have improved considerably after the start of the availability of HAART since 1996. In addition, there is a reduction in the number of hospitalizations of people living with HIV / AIDS, a decrease in opportunistic infections and an increase in chronic diseases, among them hepatic, cardiovascular, renal, among others. The studies of survival of people with AIDS are one way of assessing the epidemic situation, the parameters of the evolution of the disease, the patients' living conditions, and particularly the impact of intervention measures and policies.

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INTRODUCTION

The Acquired Immunodeficiency Syndrome (AIDS) was identified in the late 1970s, with the earliest cases being detected in the United States, Haiti, and Central Africa. The first investigations identified the following characteristics of the patients, the known 5H - Homosexuals, Hemophiliacs, Haitians, Heroinomanes (users of injectable heroin) and Hookers (sex workers in English), since the new disease was concentrated in these groups at the beginning of the pandemic (Goedert *et al.*, 1986; Turner *et al.*, 1987; Marques, 2002). In the beginning, the involvement was mainly in males, appearing soon after the first cases in women related to sexual practice or exposure to blood (Vermelho *et al.*, 1999). Deaths occurred in young adults, caused by infections such as *Pneumocystis jiroveci* pneumonia, previously known as *Pneumocystis carinii*, candidiasis, toxoplasmosis, and neoplasias such as Kaposi's sarcoma, diseases of rare incidence in the adult population. Such events, characterized by the unusual behavior of these pathologies, indicated the emergence of a "new" disease, which entered the list of concerns of public health authorities in the United States of America (USA) (Neto and Baldy, 1991; Veronesi, 1991). In 1983, the Pasteur Institute in Paris, the

researcher Luc Montagnier isolated the first time a retrovirus, known as LAV (Lymphadenopathy Associated Virus) associated with the "new" disease. In contrast, in 1984, the US government announced that Dr. Robert Gallo of the National Cancer Institute isolated a retrovirus that causes AIDS, called HTLV-III (Human T Cell Lymphotropic Viruses). Following the creation by the World Health Organization of the Special Program on AIDS in 1986, an international committee evaluated and stated that LAV and HTLV-III are the same virus. A new name was given: HIV (Human Immunodeficiency Virus) (Galvão, 2002). The serological diagnosis for HIV is performed using methods that detect the presence of antigens and or antibodies specific for HIV1 (Peçanha *et al.*, 2002). Since the availability of the test in 1985 in the USA (Galvão, 2002) HIV tests combined with detection of antigens and antibodies have gradually improved in both sensitivity and specificity (Peçanha *et al.*, 2002). It was only in 1986 that clinical improvement was observed when administering the drug Zidovudine-AZT to patients with Kaposi's sarcoma (Schaurich *et al.*, 2006).

The number of AIDS cases has grown at an alarming rate in the following years with almost synchronic record in countries in Africa, Central America - Caribbean, South America and Europe conforming rapidly as a global public health problem making it possible to understand that all people were susceptible to HIV infection (Mann *et al.*, 1993). Several understandings about the disease have been outlining in

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society. Between the biological and social risk, stood the realization that for the transmission of the virus was the influence of specific behaviors, in addition to biological susceptibility. Differentiate through life experiences and are influenced by the community, for others, cultural and social entities (Rocha and Samudio, 2014; Garcia and Souza, 2010). With the intention of grouping several fields of knowledge, health scientists highlighted the concept of "vulnerability" in the early 1990s, seeking strategies to confront AIDS (Garcia and Souza, 2010). The concept of vulnerability was expressed as a "set of individual and collective aspects related to the degree and mode of exposure to a given situation and, in an inseparable way, to greater or lesser access to adequate resources to protect itself from the undesirable consequences of that situation" (Ayres *et al.*, 2003). Soon after the identification of AIDS and the causative agent, the efforts of the scientific community focused on identifying the persons who were directly affected by the epidemic (group of concepts and risk behavior), and the means of transmission and prevention methods of new cases (Schaurich *et al.*, 2006; Lima *et al.*, 1996). Survival and evolution of clinical and laboratory diagnosis of AIDS patients have improved considerably after the start of the availability of HAART since 1996. In addition, there is a reduction in the number of hospitalizations of people living with HIV / AIDS, a decrease in opportunistic infections and an increase in chronic diseases, among them hepatic, cardiovascular, renal, among others (Guibu *et al.*, 2011; Menesia *et al.*, 2001; Chequer *et al.*, 1992; Padoin *et al.*, 2013; Pereira *et al.*, 2013; Marins *et al.*, 2003; Sterne *et al.*, 2005; Lima *et al.*, 2007; Sandoval and Caceres, 2013). Despite the positive impact on patient survival, the lack of access to medication, health services - especially those with specialized assistance - and the difficulties related to adherence to treatment, still have negative repercussions on the survival of these patients, being factors consistently influenced by the socioeconomic situation (Menesia *et al.*, 2001; Padoin *et al.*, 2013; Pereira *et al.*, 2013).

Besides sociodemographic variables and access to medication, the occurrence of opportunistic infections and comorbidities have also been associated with the prognosis of AIDS. The survival time of people with AIDS is related to social, individual and medical-assistance factors. Higher survival also depends on age and is higher in younger age groups, but the importance of sex in this association remains controversial, since the occurrence in men was significantly higher at the beginning of the epidemic, decreasing this association in later decades (Menesia *et al.*, 2001). The use of markers of socioeconomic conditions such as schooling, occupation, family income in epidemiological studies is presented in studies that verified the mortality and survival of patients with AIDS (Farias and Cardoso, 2002; Rapiti *et al.*, 2000). Most studies have a worse prognosis and lower survival rates among low-income and school-age patients. Ethnic and racial factors have been pointed out as predictors of the poor evolution of the disease in the USA (Rapiti *et al.*, 2000; Barbosa and Sawyer, 2003; Beer *et al.*, 2014; Castro *et al.*, 2013; Lima and Freitas, 2013; Singh *et al.*, 2013; Westergaard *et al.*, 2014). The studies of survival of people with AIDS are one way of assessing the epidemic situation, the parameters of the evolution of the disease, the patients' living conditions, and particularly the impact of intervention measures and policies (Guibu *et al.*, 2011). One of the first studies looked at the length of survival of patients with Acquired Immunodeficiency Syndrome in the United Kingdom and the relationship of the disease with

opportunistic infections showed that those with Kaposi's sarcoma had only a better prognosis (Marasca and McEvoy, 1986). A study of survival analysis of AIDS cases associated with hemophilia in the USA found that patients diagnosed in 1986 survived more than those with a previous diagnosis with a median survival time of 11.7 months (Stehr-Green *et al.*, 1989).

Survival analysis methodology was recommended among the groups of patients with clinical follow-up (Quesenberry *et al.*, 1989) and was widely used in studies that began to verify the pharmacological action of antiretroviral Zidovudine used at the beginning of the epidemic (Mulder *et al.*, 1990; Jacobson *et al.*, 1991; Moore *et al.*, 1991) as well as the studies of hospital records of hospitalization and outpatient follow-up (Seage *et al.*, 1990). In 1991, a large study (Piette *et al.*, 1991) examined the survival patterns of people with AIDS from the Centers for Disease Control (CDC) in the United States, using 23,271 cases diagnosed between January 1984 and December 1986, identifying the clinical and demographic factors, temporal trends and the use of covariates that indicated the geographic region of the cases using the Cox regression model. Major regional differences and implications for health service planning were observed. The era of studies that verified the possible differences in the survival time of patients with AIDS began, defining the clinical, demographic and behavioral variables that could influence the survival. Taking into account the diversity of races and ethnicities, ages, risk behaviors, men and women, increased survival was strongly associated with such variables and the early diagnosis for clinical care within comparable settings (Hanson *et al.*, 1993; Lemp *et al.*, 1992; Lemp *et al.*, 1990; Friedland *et al.*, 1991; Reeves and Overton, 1988). In 1993 one of the first papers was published discussing a summary of the literature on the survival time of people with AIDS and their race / color, summarizing the evidence on the association of the black and white race with the infection. From this study it was suggested that the race / color could also function as an important marker for socioeconomic factors and access to health care, which results in a shorter survival time for these people (Seage *et al.*, 1993). The strong relationship of opportunistic co-infections and decreased patient survival after diagnosis of AIDS has become the subject of approaches that sought to identify predictors of improved survival. Early diagnosis and improved patient care guaranteed more satisfactory results for the effects of lead-time bias and better treatment after diagnosis (Kimmel *et al.*, 1993). For the HIV - infected patients who used continuous ambulatory peritoneal dialysis and with terminal renal failure the median survival was 13 months compared to 38 months for the uninfected population between February 1984 and April 1992 (Curtis and Patrick, 1993).

The CD4 lymphocyte count was then used to estimate the likelihood of remaining AIDS-free after HIV infection through a cohort study of individuals who created a linear regression model by extrapolating the CD4 count to predict disease development after 1993. Such a study may suggest that even with the treatment available at the time, up to a quarter of patients with HIV infection would survive for 20 years after seroconversion without developing AIDS (Phillips *et al.*, 1994). In Europe, to examine the pattern of survival and factors associated with disease outcome in patients with AIDS, researchers conducted a cohort study with data collected retrospectively from the records of 6,578 adults diagnosed between January 1979 and December 1989 in order to Survival after the time of diagnosis (Iatrakis *et al.*, 1994). This type of

methodological approach has been used to understand the dynamics of the disease in past times, to plan new health actions to guarantee a better living condition and to compare with published studies the survival experiences already observed in infected people in different countries (Iatrakis *et al.*, 1994; Poznansky *et al.*, 1995; Low *et al.*, 1996). Prospective studies developed to estimate survival medians and also the changes related to infection since the diagnosis of AIDS provided a differential view to the data that were previously collected in medical records and became part of a powerful tool to evaluate the living conditions of the people who lived with the disease, their life expectancies, the development and relation of coinfections, and the value of the provision of health services for HIV (Mocroft *et al.*, 1997; Hillman *et al.*, 1997).

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