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Late Diagnosis in HIV: Experience of a Portuguese District Hospital between 1998-2022 (Too Late Study)

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Abstract

Background: According to the ECDC's latest report, Portugal has the highest incidence of HIV/AIDS and late diagnosis (lymphocyte TCD4+ count <350 cells/µL) in the European Union. Late diagnosis can significantly impact an individual's health outcomes and the effectiveness of treatment interventions, interfering with overall health outcomes and quality of life.

Objectives: Evaluate evolution of HIV diagnosis between 1998-2022 in a district Hospital comparing demographic, epidemiological, AIDS defining illnesses and mortality data. And evaluating the COVD-19 pandemic years regarding the late diagnosis impact, in this matter comparing 2020, 2021 and 2022 with 2017, 2018 and 2019.

Methods: Retrospective study of HIV patients (pts) with TCD4+ <350 cells/µL at 1st visit between 1998-2018, divided into group A: TCD4+ <200 cells/µL; group B: TCD4+ 200-350 cells/µL. Statistical analysis by Excel® from Microsoft 365®, by using the chi-squared test (χ^2).

Results: From a total of 1175 pts in IDS database, 649 met the criteria but due the lack of data, only 590 were admitted. From these, 63,73% (N=376) in group A and 36,27% (N=214) in B. Demographic and epidemiological characterization revealed (A *vs* B): male predominance of 79,52% *vs* 66.82% (p<0,0001); age at diagnosis<50 years 76,59% vs 84,11% (p<0,0001); transmission by heterosexual contact in 53,45% *vs* 50,93% (p<0,0001). At first health care encounter, 59,84% of group A had an AIDS defining illness-most commonly tuberculosis (33,33%). In a group analysis the percentage of pts in group A raised from 31,4% in 2018 to 32% in 2022. Analysis of mortality showed a death rate of 26,86% in group A *versus* 16,36% in group B (p<0,0001), with a mean duration from HIV diagnosis to death of 2208 days versus 2940 (p<0,0001). On average, time from first Infectious Diseases (ID) consultation to death was 1441 days in group A and 2308 in group B (p<0,0001).

Analyzing before (2017-2019) and during COVID-19 (2020-2022), the prevalence of late presenters (<350 TCD4+/µl) went from 3.90% to 8.81% globally; an increase of 55.77% (23 to 52 pts), maintaining proportion of genders. During COVID-19 an increase in overall mortality was observed 26.86% *vs* 16.36% (group A *vs* B pre-pandemic) to 28.86% *vs* 18.92% (group A *vs* B pandemic) not due COVID infection.

Conclusion: This study highlights the persistent challenge of late HIV diagnosis and its profound impact on patient outcomes. The demographic and epidemiological characterization underscores the need for targeted interventions to address disparities in testing and care access. The observed increase in late presenters and mortality rates during the COVID-19 pandemic underscores the importance of maintaining HIV care services amidst public health crises. Timely diagnosis, early intervention, and comprehensive care remain imperative to improve outcomes and advance towards the goal of ending AIDS as a public health threat by 2030.

Keywords: HIV/AIDS; Late presenters; COVID-19

Introduction

According to a report published in 2022 by the National Institute of Health Doutor Ricardo Jorge (INSA) and the Directorate-General for Health (DGS) [1], between 1983 and 2021, 64257 cases of HIV infection were diagnosed in Portugal, of which 23399 reached the AIDS stage.

According to data collected on 31 October 2022, 1803 cases were reported in which HIV infection was diagnosed in 2020 and 2021, which corresponds to an average diagnosis rate for the biennium of 8.7 cases per 10^5 inhabitants, not adjusted for the delay in notification. Most of the cases corresponded to men (2.5 cases for each case in women), the median age at diagnosis was 39.0 years, and in 27.6% of the new cases the individuals were ≥ 50 years old.

Sexual intercourse was reported in 92.0% of the cases diagnosed in the 2020-2021 biennium, with heterosexual transmission being the most frequent (51.8%). MSM cases accounted for 56.0% of new

diagnoses in men. In the first clinical evaluation, asymptomatic cases predominated, however, in 17.7% there was a concomitant diagnosis of AIDS and 55.4% were late diagnoses according to the new definition, proportions that were higher in the cases of men who reported heterosexual transmission (70.8%). During the years 2020 and 2021, 415 new cases of AIDS were also diagnosed (2.0 cases/10^5 inhabitants).

A total of 298 deaths were also reported in the biennium, 26.8% of which occurred in the five years following the diagnosis of the infection.

It should be noted that, recently presented, a report on the situation of HIV infection in Portugal between 2022 and June 2023 [2], presents data with improvement regarding the incidence of infection although it maintains high rates of diagnosis in late presenters.

Objectives

The purpose of this study is to evaluate the progression of HIV diagnosis through the years, fundamentally between 1998-2022, that is, since the existence of the Infectious Diseases Service (IDS) in a district Hospital serving population 316866 inhabitants by comparing demographic, epidemiological, AIDS defining illnesses and mortality data.

Another important objective is to evaluate the impact of the COVD-19 pandemic years in the late diagnosis, also analyzing demographic, epidemiological, AIDS defining illnesses and mortality data. In this matter, the comparison was based on the 3 years prior to the pandemic (2017-2019) and the years of the pandemic (2020-2022). The year 2022 was included, because, being the end of the pandemic, had a great impact on the return to patient follow-up, as well as the resumption of regular contact with health services by the general population.

Methods

Retrospective study of HIV patients (pts) that presented a lymphocyte TCD4+count <350 cells/μL at 1st visit between 1998-2022, divided into two groups. A group A where patients where consider very late presenters at the time of diagnosis, by having a count of TCD4+ <200 cells/μL and a group B, where pts were considered with late diagnosis if presented TCD4+ count between 200-350 cells/μL. Statistical analysis was done by using Microsoft 365® Excel® and the comparison between populations was done by using the chi-squared ($\chi 2$) test.

Since 1998, the IDS has been using and developing a specific software database for managing patients with HIV. This software, registered and patented by the Portuguese National Data Protection Commission and the National Software Association (Assoft), is built in MS Access® with a Unicode key that allows real-time updates. It integrates patient management, enabling comprehensive follow-up across various parameters, including consultation details, blood analysis results (such as quantitative HIV RNA, peripheral blood immunophenotyping, and TCD4+/TCD8+ ratio), serology for Sexually Transmitted Infections (STIs) and hepatotropic viruses, antiretroviral and prophylactic treatments, prescription history analysis, and treatment resistance or alteration causes. Additionally, it tracks specific pathologies, registers AIDS-defining diseases and other relevant conditions, facilitates chronological analysis, and includes oncological registration and evaluations. The software also supports follow-up through Social Services, Pharmaceutical Services, and Nursing Services.

Besides consultation records, this software allows control and management of hospitalized patients with standard and customized listings and search functionalities. COVID-19 data was obtained using hospital patient records.

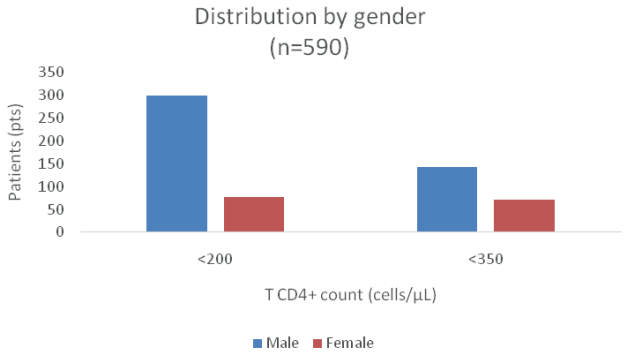
Results

From a total of 1175 pts in IDS database, 649 met the criteria but due the lack or miss data, only 590 were admitted for further analysis. The major data missing, regards pts data like date of birth, nationality, address and in other cases, the risk of HIV transmission lacks specificity, because it's documented as sexual, but cannot characterizes as MSM, heterosexual or another.

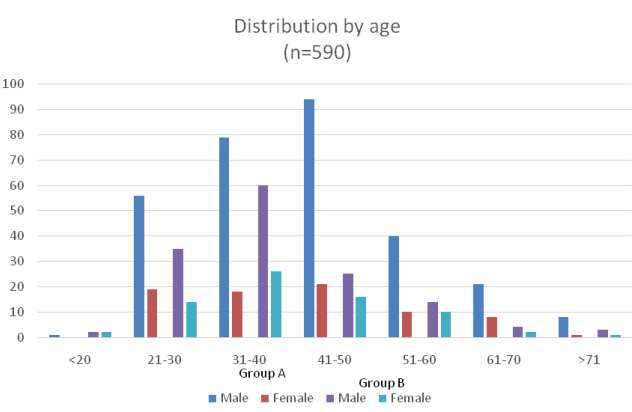
From these [590 pts], 63,73% (N = 376) were, later, divided in group A and 36,27% (N = 214) in group B, considering if they were "*very late presenters*" at the time of diagnosis, by having a count of TCD4+ <200 cells/μL (group A) and a group B, if they were "late presenters" considering TCD4+ count between 200-350 cells/μL at presentation.

When analyzing the demographic and epidemiological characteristics between the two groups in an analysis of A vs B, it was observed that there was a male predominance of 79,52% *vs* 66.82% with statistical significance (Graph 1), and the same was also observed at diagnosis <50 years76,59% *vs* 84,11% (p<0,0001) (Graph 2); the transmission by heterosexual contact observed in the two groups, was 53,45% *vs* 50,93% (p<0,0001) (Graph 3).

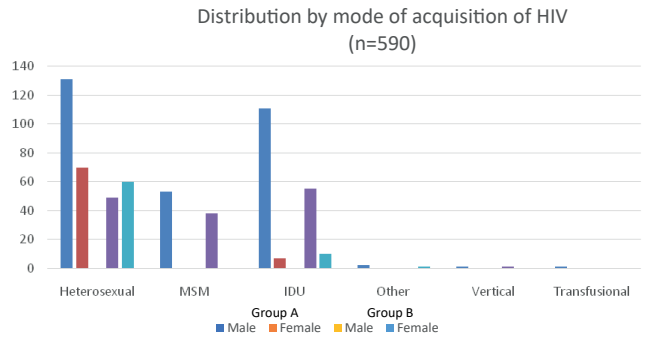
At first health care encounter, 59,84% of group A had an AIDS defining illnesses - most commonly tuberculosis (33,33%). However, other AIDS defining illness were diagnosed as presented in table 1.



Graph 1: Distribution of patients by T CD4+ count, by gender.



Graph 2: Distribution of patients by age, Comparison A and B groups.



Graph 3: Distribution of patients by mode of acquisition of HIV. Comparison A and B groups. Other means -accidental, aggression. Vertical means mother-child transmission.

In a group analysis the percentage of pts in group A raised from 31,41% in 2018 to 32% in 2022. Analysis of mortality showed a death rate of 26,86% in group A *versus* 16,36% in group B (p<0,0001), with a mean duration from HIV diagnosis to death of 2208 days versus 2940 (p<0,0001). On average, time from first Infectious Diseases (ID) consultation to death was 1441 days in group A and 2308 in group B (p<0,0001).

Analyzing before (2017-2019) and during COVID-19 (2020-2022), the prevalence of late presenters (<350 TCD4+/µl) went from 3.90% to 8.81% globally which is statistically significative (p<0,05) with an increase of 55.77% (23 to 52 pts) but maintaining proportion of genders.

During COVID-19 an increase in overall mortality was observed 26.86% *vs* 16.36% (group A *vs* B pre-pandemic) to 28.86% *vs* 18.92% (group A *vs* B pandemic) not due COVID infection, but without statistical significance (p=0.1459).

Discussion

The data demonstrate a concerning increase in late HIV diagnoses during the COVID-19 years, possibly due to healthcare service disruptions and delays in seeking medical care. The high prevalence of heterosexual transmission and male predominance is consistent with other literature on HIV. The higher mortality and shorter lifespan after diagnosis in very late presenters underscore the need for early interventions and improved access to healthcare services.

The demographic and epidemiological data analysis reveals the importance of targeted prevention strategies for subpopulations, such as heterosexual men and individuals over 50, who exhibited a high proportion of late diagnoses.

Conclusions

As conclusion, this study underscores the importance of ongoing and targeted interventions to reduce late diagnoses and improve health outcomes for people living with HIV. The COVID-19 pandemic highlighted vulnerabilities in the healthcare system that needs to be addressed to prevent future increases in HIV-associated mortality.

In this case some recommendations are needed as improved access to testing and treatment expanding access to HIV testing and antiretroviral treatments. The need for awareness campaigns targeting at risk populations and in the strengthening Healthcare Services to ensure the continuity of healthcare services, even in crises such as pandemics.

Continuous monitoring and evaluation are also important, to maintain active epidemiological surveillance and ongoing data analysis to respond quickly to changes in infection trends.

This study, also, provides a detailed view of the evolution of HIV in Portugal and highlights critical areas for future intervention, aiming to reduce the HIV burden and improve the quality of life for those affected.

Table 1: AIDS defining illness by group and gender.

AIDS (Group A)	Male	Female	AIDS (Group B)	Male	Female
Asymptomatic	89	27	Asymptomatic	91	55
Burkitt lymphoma	1	0	Burkitt lymphoma	1	0
Cerebral toxoplasmosis	17	4	Cerebral toxoplasmosis	0	1
Cytomegalovirus infection	5	4	Cytomegalovirus infection	0	1
Colitis	2	0	No focalization	0	1
Esophagitis	2	0	Cryptococcal meningitis	1	0
No focalization	1	3	Esophageal candidiasis	2	1
Retinitis	0	1	HIV encephalitis	2	0
Cryptococcus infection	27	0	Hodgkin's lymphoma	1	0
Disseminated	9	0	Invasive cervical carcinoma	0	2
Meningitis	18	0	Invasive pneumococcal disease	0	3
Esophageal candidiasis	3	1	Non-Hodgkin's lymphoma	5	2
HIV dementia	1	0	Progressive multifocal leukoencephalopathy	1	0
HIV encephalitis	2	1	Mycobacterium avium complex	0	1
Invasive cervical carcinoma	0	2	Pneumocistis jirovecci pneumonia	2	1
Invasive salmonelosis	1	1	Tuberculosis	33	6
Kaposi's sarcoma	9	0	Bone	1	0
Mycobacterium avium complex	4	2	Disseminated	4	0
Non-Hodgkin's lymphoma	11	2	Ganglionar	1	0
Plasmablastic lymphoma	1	0	Meningitis	2	1
Pneumocistis jirovecci pneumonia	33	4	Pleural	2	0
Progressive multifocal leukoencephalopathy	11	0	Pulmonary	23	5
Recurrent pneumonia	1	1			
Thrombocytopenic purpura	0	1			
Tuberculosis	63	12			
Disseminated	15	5			
Ganglionar	3	2			
Intestinal	0	1			
Pleural	3	0			
Pulmonary	42	4			

References

1. Direção-Geral da Saúde, Instituto Nacional de Saúde Doutor Ricardo Jorge (2023) Relatório Infeção por VIH em Portugal – 2022.
2. Direção-Geral da Saúde Instituto Nacional de Saúde Doutor Ricardo Jorge (2023) Infeção VIH e SIDA em Portugal-2023.