Factors associated with immunovirological discordances, immunological and virological failures in patients living with HIV-1 and followed up at the Bobo-Dioulasso day hospital in 2019.

Facteurs associés aux discordances immunovirologiques, aux échecs immunologiques et virologiques chez les patients vivant avec le VIH-1 et suivis à l'hôpital de jour de Bobo-Dioulasso en 2019.

Damolga M[1], Zougmoré WMJA[1,5], Ouattara AK[3,4,9], Sombié HK[1,3,4], Sawadogo Y[1,2], Samba JJC[1], Ouattara CA[1,6,10], Poda A[1,7,8], Ouédraogo AS[1,2,8].

[1]Emerging and Re-emerging Pathogens Laboratory, Sourô SANOU University Hospital, Bobo-Dioulasso, Burkina Faso;
[2]Bacteriology-Virology Department, Sourô SANOU University Hospital, Bobo-Dioulasso, Burkina Faso;
[3]Laboratory of Molecular Biology and Genetics (LABIOGENE), Joseph KI ZERBO University, Ouagadougou 03, Burkina Faso;
[4]Pietro Annigoni Biomolecular Research Center (CERBA), Ouagadougou 01, Burkina Faso;
[5]Laboratory Department, Banfora Regional Hospital, Burkina Faso;
[6]Nazi Boni University, Higher Institute of Health Sciences, Department of Public Health, Bobo-Dioulasso 01, Burkina Faso;
[7]Infectious Diseases Department, Sourô SANOU University Hospital, Bobo-Dioulasso 01, Burkina Faso;
[8]Faculty of Medicine and Pharmacy, Institute of Health Sciences, Nazi BONI University, Bobo-Dioulasso 01, Burkina Faso;
[9]Center Manga University, Norbert ZONGO University, Manga, Burkina Faso,
[10]Souro Sanou University Hospital Center, Department of Public Health, Bobo-Dioulasso, Burkina Faso.

Corresponding author: Maxime DAMOLGA; Emerging and Re-emerging Pathogens Laboratory, Bobo-Dioulasso, Burkina Faso (LaPathER). Email: maximedamolga@gmail.com

Abstract

Objective: To determine the prevalence of immunovirological discordance, immunological and virological failures and factors associated in patients living with HIV-1 and followed at the day hospital in Bobo-Dioulasso.
Methods: This descriptive cross-sectional study was conducted from January to December 2019, including HIV-1 human immunodeficiency virus positive patients followed at the adult day hospital in Bobo-Dioulasso and, having received two consecutive measurements of viral load and CD4 T cell count during the year. Data extracted from the evaluation and operational monitoring of ESTHER programs database were analyzed using STATA and SPSS V.20.0.
Results: A total of 261 patients were included in this study. The median age of the study population was 46 ± 10.64 years, with a predominance of the female (70.50%). We noted that 8 patients were in immunological failure (3.06%) with a predominance of married people and subjects aged between 50-59 years. 115 patients had virological failure (44.06%) with a majority of women. The prevalence of immunovirological discordance was (1.92%) with a male predominance (60%). Among the patients with immunovirological discordance, 60 % were between 40-49 years of age and 60 % were married.
Conclusion: The prevalence of virological failures was 44.06% in our study population, those of immunovirological discordance and immunological failures was low, or 1.92% and 3.06% respectively. The main groups encountered in immunovirological discordance and immunological and virological failures in our study population were 40-59 age group, housekeeper, married and not in school.
Key words: HIV-1, immunovirological discordance, associated factors.

Résumé

Objectif: Déterminer la prévalence des discordances immunovirologiques, des échecs immunologiques et virologiques et les facteurs associés chez les patients vivant avec le VIH-1 et suivis à l'hôpital de jour de Bobo-Dioulasso.
Méthodes: Cette étude transversale descriptive a été menée de janvier à décembre 2019, incluant les patients séropositifs pour le virus de l'immunodéficience humaine VIH-1 suivis à l'hôpital de jour pour adultes de Bobo-Dioulasso et, ayant bénéficié de deux mesures consécutives de la charge virale et du taux de lymphocytes T CD4 au cours de l'année. Les données extraites de la base de données d'évaluation et de suivi opérationnel des programmes ESTHER ont été analysées à l'aide de STATA et SPSS V.20.0.

Résultats : Un total de 261 patients a été inclus dans cette étude. L'âge médian de la population étudiée était de 46 ± 10,64 ans, avec une prédominance féminine (70,50%). Nous avons noté que 8 patients étaient en échec immunologique (3,06%) avec une prédominance des personnes mariées et des sujets âgés de 50-59 ans. 115 patients étaient en échec virologique (44,06%) avec une majorité de femmes. La prévalence de la discordance immunovirologique était de (1,92%) avec une prédominance masculine (60%). Parmi les patients présentant une discordance immunovirologique, 60 % étaient âgés de 40 à 49 ans et 60 % étaient mariés.
Conclusion : La prévalence des échecs virologiques était de 44,06% dans notre population étudiée, celles des discordances immunovirologiques et des échecs immunologiques étaient faibles, soit respectivement 1,92% et 3,06%. Les principaux groupes rencontrés dans les discordances immunovirologiques et les échecs immunologiques et virologiques dans notre population d'étude étaient la tranche d'âge 40-59 ans, les femmes de ménage, les personnes mariées et non scolarisées.
Mots clés : VIH-1, discordance immunovirologique, facteurs associés.

Introduction

Since the end of the 1990s, human immunodeficiency virus (HIV) infection has become a persistent chronic disease thanks to antiretroviral molecules that make it possible to control viral replication (1). Despite the strong involvement of health systems, it remains a major public health problem with 34 million people infected (2, 3). Antiretroviral (ARVs) effectively inhibit viral replication and aim to reduce plasma viral load (< 50 copies/ml) and restore immunity (2, 4). Studies have shown that after 6 months of treatment, the viral load becomes undetectable with a remarkable increase in the CD4+ T cell count. However, there are patients who show a partial immune response to treatment with a CD4+ T cell count < 200/mm^3 despite an undetectable plasma viral load and vice versa (2). This partial response to ARV treatment is called immunovirological discordance. The risk of mortality has been estimated to be between 3% and 23% in patients with immunovirological discordance compared to 1% to 7% in patients with a good immunovirological response (5). The prevalence of immunovirological discordance after six months of antiretroviral therapy was estimated at 19.07% in resource-limited countries in Africa, Asia and Latin America (6). However, a 29% prevalence of immunovirological discordance was reported in Rwanda in 2016 (7). In France, a prevalence of immunovirological discordance of 10-27% was reported by Borsa in 2009, in patients on treatment (8). In Burkina Faso, a 14% prevalence of immunovirological discordance was reported in 2012 in the general population while it was estimated at 23.8% by Bazie *et al.* in 123 HIV-positive female sex workers on ARV treatment (9, 10). However, Ouédraogo *et al.* reported 4% of immunovirological discordance in their study conducted at the Bobo-Dioulasso Day Hospital in 2015 in Burkina Faso (11).Daye Kà *et al.* showed in their study in Dakar that factors such as a history of TB, advanced age at initiation of ARV treatment, initial CD4 count < 100 cells/mm^3 and male sex were significantly associated with immunovirological discordance (2). However, none of these factors provide a complete explanation for the lack of immune reconstitution in HIV-positive patients on ART. Immunovirological discordance is an obstacle to achieving the World Health Organization (WHO) 95-95-95 targets set for 2030 and the associated factors are poorly documented in some African countries, notably Burkina Faso where HIV prevalence is estimated at 1% (1). To fill this gap, we proposed to determine the prevalence of immunovirological discordance, immunological and virological failures as well as the prevalence of associated factors in patients treated and followed up at the Bobo-Dioulasso Day Hospital.

Materials and methods

Study design

This was a descriptive cross-sectional study from January to December 2019. It focused on HIV-1 infected patients followed up at the adult day hospital of the Sourô Sanou University Hospital Center of Bobo-Dioulasso. We included in the study all patients who initiated their antiretroviral treatment at the Bobo-Dioulasso Day Hospital, who had two measurements of viral load and CD4+ T lymphocytes after 6 months of ARV treatment and who came during the study period. The study obtained the approval of the Director General of the Souro Sanou University Hospital Center. All participants gave their free and informed consent. Confidentiality and anonymity with respect to information collected on study subjects were respected during and after the study. Only the Evaluation and Operational Monitoring of ESTHER Programs (ESOPE) number of the patients was mentioned.

Data collection: Sociodemographic and biological data for each selected patient were collected using the ESOPE (Evaluation and Operational Monitoring of ESTHER Programs) software. Virological failure was defined as a detectable HIV-1 plasma viral load between two consecutive measurements at least 6 months after initiation of antiretroviral therapy. Immunological failure was defined as a loss of CD4+ T cells between two measurements at least 6 months after initiation of antiretroviral therapy. Immunovirological discordance was defined as the observation of CD4+ T-cell loss after at least 6 months of antiretroviral therapy despite virological success (undetectable viral load) and vice versa (2).

Statistical analysis: The data collected were analyzed using STATA software version 14 and SPSS V.20. Quantitative variables were presented as mean ± standard deviation and qualitative variables as number and percentage (%).

Results

Socio-demographic characteristics: Table I shows the general characteristics of our study population. A total of two hundred and sixty-one patients were included, one hundred and eighty-three of whom were female, giving a sex ratio (M/F) of 0.41. The median age was 46 ± 10.64 years with extremes between 20 and 75 years. The most common age groups were 40-49 years (39.10%) and 50-59 years (24.10%). The majority of patients was not educated (44.40%) and married (49.80%).

Table I : General characteristics of the study population

Parameters	Numbers	Percentage (%)	CI (95%)
Gender			
Male	78	29.90	24.90-35.60
Female*	183	70.10	64.40-75.10
Age groups			
[20-29]	12	4.60	2.30-7.30
[30-39]	50	19.20	14.60-24.10
[40-49]*	102	39.10	33.00-45.20
[50-59]	63	24.10	19.20-29.90
[60-69]	32	12.30	8.40-16.10
[70-79]	2	0.80	0.00-1.90
School level			
Not in school*	116	44.40	38.70-50.60
Primary	76	29.10	23.40-34.90
Secondary	62	23.80	19.20-29.90
Superior	7	2.70	0.80-4.60
Marital status			
Married*	130	49.80	43.70-55.90
Single	60	23.00	18.40-28.00
Widow (er)	60	23.00	18.00-28.00
Divorced	11	4.20	1.90-6.90

**: Predominant group, CI: confident interval*

Biological characteristics

Table II shows the frequencies of immunovirological discordance, immunological and virological failure and factors associated. Patients with immunological failure represented 3.06% of our study population with a male-female parity. The age group most affected was 50-59 years, representing 37.50% of immunological failures. In addition, among the patients with immunological failure, those whose function was not specified, those who were not in school and those who were married predominated with respectively 50.00%, 62.50% and 62.50%. There were a hundred and fifteen patients with virological failure, or 44.06% of our study population. In this group, we observed a predominance of women, or 70.43%. The distribution according to age group and profession showed that the 40-49 age group and housekeeper were more represented with 33.04% and 55.65% respectively. In addition, married and uneducated patients were also predominant with 41.74% and 44.35% respectively.Concerning immunovirological discordance, only 1.92% of the patients included in the present study were affected with a female majority (60%). The age group of 40-49 years presented the most cases of immunovirological discordance. In addition, there was an equal distribution of IVD among housekeeper and those, whose activity was not specified, as well as those with no schooling and those with primary education, or 40.00% for each group. Married people were in the majority of immunovirological discordance cases with a prevalence of 80.00%.

Table II: Factors associated with immunovirological discordance, immunological and virological failure

	Parameters	Immunological failure, *n* (%)		Virological failure, *n* (%)		Immunovirological discordance, *n* (%)	
		presence 8 (3.06)	*absence 253 (96.94)*	*presence 115 (44.06)*	*absence 146 (55.94)*	*presence 5 (1.92)*	*absence 256 (98.08)*
Gender	Female	4 (50.00)	180 (71.15)	*81 (70.43)	103 (70.55)	2 (40.00)	181 (70.70)
	Male	4 (50.00)	73 (28.85)	34 (29.57)	43 (29.45)	*3 (60.00)	75 (29.30)
Age group (years)	20-29	1 (12.50)	11 (4.35)	6 (5.22)	6 (4.11)	0 (0.00)	12 (4.69)
	30-39	2 (25.00)	48 (18.97)	25 (21.74)	25 (17.12)	1 (20.00)	49 (19.14)
	40-49	2 (25.00)	100 (39.53)	*38 (33.04)	64 (43.84)	*3 (60.00)	100 (39.06)
	50-59	*3 (37.50)	60 (23.72)	30 (26.09)	33 (22.60)	1 (20.00)	61 (23.83)
	≥ 60	0 (0.00)	34 (5.14)	16 (13.91)	18 (12.33)	0 (0.00)	34 (13.28)
Occupation	Other	4 (50.00)	44 (17.39)	24 (20.87)	24 (16.44)	*2 (40.00)	47 (18.36)
	Farmer	0 (0.00)	13 (5.14)	4 (3.48)	9 (6.16)	0 (0.00)	13 (5.08)
	Trader	1 (12.50)	33 (13.04)	17 (14.78)	17 (11.64)	1 (20.00)	32 (12.50)
	Civil servant	0 (0.00)	30 (11.86)	6 (5.22)	24 (16.44)	0 (0.00)	30 (11.72)
	Housekeeper	*3 (37.50)	133 (52.57)	*64 (55.65)	72 (49.32)	*2 (40.00)	134 (52.34)
Marital status	Married	*5 (62.50)	120 (47.43)	*48 (41.74)	77 (52.74)	*4 (80.00)	121 (47.27)
	Single	2 (25.00)	63 (24.90)	29 (25.22)	36 (24.66)	1 (20.00)	64 (25.00)
	Widow(er)	1 (12.50)	59 (23.32)	33 (28.70)	27 (18.49)	0 (0.00)	60 (23.44)
	Divorced	0 (0.00)	11 (4.35)	5 (4.35)	6 (4.11)	0 (0.00)	11 (4.30)
School level	Not in school	*5 (62.50)	111 (43.87)	*51 (44.35)	65 (44.52)	*2 (40.00)	114 (44.43)
	Primary	3 (37.50)	73 (28.85)	37 (32.17)	39 (26.71)	*2 (40.00)	75 (29.30)
	Secondary	0 (0.00)	62 (24.51)	26 (22.61)	36 (24.66)	1 (20.00)	60 (23.44)
	Superior	0 (0.00)	7 (2.77)	1 (0.87)	6 (4.11)	0 (0.00)	7 (2.73)

*Variables are expressed as numbers (percentages), *: predominant factors in immunovirological failures and discordance.*

Discussion

The objective of this study was to determine the prevalence of immunovirological discordance, immunological and virological failures and factors associated in patients living with HIV-1 and followed at the Bobo-Dioulasso day hospital. We showed that patients with immunological failures represented 3.06% of our study population. This result is lower than those found by Ouédraogo *et al.* in Burkina Faso in 2015 and Anude *et al.* in Nigeria in 2013 who reported 11.9% and 22.6% in their study population respectively (11, 12). The occurrence of immunological failures could be partly due to insufficient plasma concentration of the antiretroviral molecules administered as a result of lack of adherence (forgetfulness, discontinuation, travel...) to ARV treatment (11). There are also deleterious drug interactions between antiretroviral molecules. Indeed, the insufficient plasma concentration of antiretroviral molecules will cause the viruses to escape and thus replicate (2). As a result, the number of CD4 T lymphocytes will decrease despite ARV treatment.In our study, the age group 50-59 years presented the most cases of immunological failure, i.e. 37.50%. Indeed, this age group is more vulnerable to opportunistic infections that can lead to a weakening of the immune system, resulting in a loss of CD4 T lymphocytes (12). Married and not in school groups had the highest immunological failure rate (62.50%). This high rate of immunological failure among the uneducated could be explained by non-compliance with ARV treatment (under-information...) following the level of education.Our study revealed that 44.06% of our patients were in virological failure. This result is higher than those of Van Vaerenberg *et al.* in Europe, Ouédraogo *et al.* in Burkina Faso in 2015, Ahoua *et al.* in Uganda in 2009 and Fibriani *et al.* in Indonesia in 2013, who reported 28%, 6.5%, 10.9% and 9.1% respectively in their study population (11, 13-15). The high rate in our study could be due to the presence of comorbidity in some patients. Also, that could be explained by the fact that we defined virological failure as any detectable plasma viral load between two consecutive measurements after at least 6 months of antiretroviral treatment. The female gender had the highest virological failure rate in our study, 71.15%. Our results are different from those of Ojha *et al.* in 2016 and Karade *et al.* in 2016 who found that the male gender predominated with 10.9% and 13.3% respectively (16, 17). This difference could be explained by the fact that our study population was mainly female. The age group 40-49 years presented the most cases of virological failure with 39.53% of cases. Ndahimana *et al.* in 2016 reported a high rate of virological failures in age group ≤ 24 years (18). This difference could be explained by non-compliance with ARV treatment among adults due to their different occupations and also by the fact that this age group was also the most represented in our study population. Virological failures were more common among housekeeper (55.65% of cases) and not in school group (44.35% of cases). This rate could be explained by the fact that both housekeeper and people without schooling generally lack information about HIV, which may lead them to engage in risky behavior. The rate of virological failure was also high among married people (41.74% of cases). Our results are different from those of Ndahimana *et al.* in 2016 who found that single people were in the majority with 15.6% of the general population (18). In our study, patients with immunovirological discordance represented 1.92%. These are patients who have a loss of CD4 count and paradoxically an undetectable viral load and vice versa (2). This result is lower than that found by Ouédraogo *et al.* who reported a 4% rate of immunovirological discordance at the Bobo-Dioulasso Day Hospital in 2015 (11). This difference is probably due to sample size and viral load detectability thresholds. Our threshold of 20 copies of detectability being lower than those of other authors.

Immunovirological discordance was most frequently encountered in male patients (60% of cases). Kà *et al.* in 2017 also reported a predominance of male gender in immunovirological discordance (2). Indeed, male gender is often associated with a poor immune response. According to Kelly *et al.* in 2016 and Bazié *et al.* in 2022, this can be explained by the fact that thymic production, which is closely linked to CD4+ T cell production, is higher in females (5, 10).The age group with the highest number of immunovirological discordance was 40-49 years, or 60% of cases. Ouédraogo *et al.* and Kà *et al.* both reported a higher prevalence of immunovirological discordance in the age group above 35 years (2, 11). Older age is often associated with a poor immune response and is due to decreased thymic production due to involution of the thymus and therefore decreased CD4+ T cell secretion (11).

Conclusion

Our study found a prevalence of immunovirological discordance, immunological and virological failures of respectively 1.92%, 3.06% and 44.06% in patients living with HIV-1 and followed at the Bobo-Dioulasso day hospital. The main groups encountered in immunovirological discordance and immunological and virological failures in our study population were 40-59 age group, housekeeper, married and not in school. Although the prevalence of immunovirological discordance and immunological failures is not high in our study, further research is needed to assess the impact of this partial immunological response on the occurrence of opportunistic infections.

Competing interests
All authors declare that they have no conflict of interest in this manuscript.
Financing:
This study was not funded.
Authors' contributions
WAMJZ, YS and ASO participated in the design of the study. YS, WAMJZ, MD collected and analyzed the samples. MD, JJCS, YS, HKS analyzed and interpreted the data. JJCS, YS, WAMJZ, HKS, AKO, CAO contributed to the writing of the manuscript. AP, ASO reviewed and approved the manuscript.
Acknowledgements
We are grateful to all who participated in this study. We would particularly like to thank the clinical team and the Virology laboratory of the Bobo-Dioulasso day hospital.

Reference

1. Adam T, Margaret TM, Jorg-Janne V, Niels O, M John G, et al. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. The lancet HIV. 2017;4(8):e349-e56.
2. Kà D, Manga NM, Ngom-Guéye NF, Ndiaga D, Diop M, Cisse-Diallo VMP, et al. [Factors associated with immunovirologic dissociation in HIV-1-infected patients under highly active antiretroviral therapy in the Ambulatory Treatment Center (ATC) in Dakar]. The Pan African medical journal. 2017;27:16.
3. Yang H-Y, Beymer MR, Suen S-c. Chronic Disease Onset Among People Living with HIV and AIDS in a Large Private Insurance Claims Dataset. Scientific Reports. 2019;9(1):18514.
4. Arts EJ, Hazuda DJ. HIV-1 antiretroviral drug therapy. Cold Spring Harbor perspectives in medicine. 2012;2(4):a007161.
5. Kelly C, Gaskell KM, Richardson M, Klein N, Garner P, MacPherson P. Discordant Immune Response with Antiretroviral Therapy in HIV-1: A Systematic Review of Clinical Outcomes. PloS one. 2016;11(6):e0156099.
6. Tuboi SH, Brinkhof MW, Egger M, Stone RA, Braitstein P, Nash D, et al. Discordant responses to potent antiretroviral treatment in previously naive HIV-1-infected adults initiating treatment in resource-constrained countries: the antiretroviral therapy in low-income countries (ART-LINC) collaboration. Journal of acquired immune deficiency syndromes (1999). 2007;45(1):52-9.
7. Kayigamba FR, Franke MF, Bakker MI, Rodriguez CA, Bagiruwigize E, Wit FW, et al. Discordant Treatment Responses to Combination Antiretroviral Therapy in Rwanda: A Prospective Cohort Study. PloS one. 2016;11(7):e0159446.
8. Borsa L. échec de la restauration immunitaire: prise en charge et perspectives. in Colloque inter COREVIH Nord/Nord-Ouest. 2009.
9. Tiba F, Nauwelaers F, Traoré S, Coulibaly B, Ouedraogo T, Compaoré A, et al. Immune Reconstitution During the First Year of Antiretroviral Therapy of HIV-1-Infected Adults in Rural Burkina Faso. The open AIDS journal. 2012;6:16-25.
10. Bazié WW, Somé DY, Traoré IT, Sanon A, Konaté I, Tassembedo S, et al. Immunovirological discordance among female sex workers who start antiretroviral therapy in Burkina Faso. BMC infectious diseases. 2022;22(1):117.
11. M OS, J Z, A SK, G KC, S K, A H, et al. Dissociation immuno-virologique chez les patients infectes par le VIH-1 sous traitement antiretroviral a l'hopital de Jour de Bobo-Dioulasso de 2008 a 2012 (Burkina Faso). Le Mali médical. 2015;4:58-64.
12. Anude CJ, Eze E, Onyegbutulem HC, Charurat M, Etiebet MA, Ajayi S, et al. Immuno-virologic outcomes and immuno-virologic discordance among adults alive and on anti-retroviral therapy at 12 months in Nigeria. BMC infectious diseases. 2013;13:113.
13. Van Vaerenbergh K, Harrer T, Schmit JC, Carbonez A, Fontaine E, Kurowski M, et al. Initiation of HAART in drug-naive HIV type 1 patients prevents viral breakthrough for a median period of 35.5 months in 60% of the patients. AIDS research and human retroviruses. 2002;18(6):419-26.
14. Ahoua L, Guenther G, Pinoges L, Anguzu P, Chaix ML, Le Tiec C, et al. Risk factors for virological failure and subtherapeutic antiretroviral drug concentrations in HIV-positive adults treated in rural northwestern Uganda. BMC infectious diseases. 2009;9:81.
15. Fibriani A, Wisaksana R, Indrati A, Hartantri Y, van de Vijver D, Schutten M, et al. Virological failure and drug resistance during first line anti-retroviral treatment in Indonesia. Journal of medical virology. 2013;85(8):1394-401.
16. Ojha CR, Shakya G, Dumre SP. Virological and Immunological Status of the People Living with HIV/AIDS Undergoing ART Treatment in Nepal. BioMed research international. 2016;2016:6817325.
17. Karade SK, Ghate MV, Chaturbhuj DN, Kadam DB, Shankar S, Gaikwad N, et al. Cross-sectional study of virological failure and multinucleoside reverse transcriptase inhibitor resistance at 12 months of antiretroviral therapy in Western India. Medicine. 2016;95(37):e4886.
18. Ndahimana J, Riedel DJ, Mwumvaneza M, Sebuhoro D, Uwimbabazi JC, Kubwimana M, et al. Drug resistance mutations after the first 12 months on antiretroviral therapy and determinants of virological failure in Rwanda. Tropical medicine & international health : TM & IH. 2016;21(7):928-35