ORIGINAL ARTICLE

Identification of serodiscordant couples, their clinical and laboratory characteristics, and vulnerabilities of HIV transmission risk in Northeastern Brazil in the era of pre-exposure prophylaxis (PrEP)

Identificação de casais sorodiscordantes, suas características clínicas, laboratoriais e vulnerabilidades de risco de transmissão do HIV no Nordeste do Brasil na era da profilaxia pré-exposição (PrEP)

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ABSTRACT

Objectives: To evaluate the frequency of HIV serodiscordants couples and their seronegative partners who were candidates for pre-exposure prophylaxis (PrPE), and the knowledge about behavioural measures to reduce virus transmission. **Methods:** The research was performed in Northeastern Brazil, from February 2016 to March 2017. Ninety HIV-positive individuals (Index) and their HIV-serodiscordant partners (n = 17) were submitted for epidemiological, clinical, and laboratory questionnaires, and for rapid laboratory tests for syphilis, hepatitis B and C. **Results:** High frequencies of HIV-syphilis (34.4%) and HIV-HBV (3.3%) coinfection were detected in the HIV-positive individuals. Three new HIV cases were detected in partners. Most participants in both groups (85.6%, Index; 94.1%, Partners) had an excellent degree of knowledge regarding HIV transmission, although nine seronegative HIV partners with a high risk of HIV infection were identified (53%). HIV-positive individuals had a high frequency of HIV-syphilis co-infection and 10% of them did not use antiretroviral by personal option. **Conclusions:** Adoption of PrEP and other preventive measures to prevent HIV transmission in serodiscordants couples should be studied and evaluated.

RESUMO

Objetivo: Avaliar a frequência de casais sorodiscordantes para o HIV candidatos à profilaxia pré-exposição (PrPE) e o conhecimento sobre medidas comportamentais para reduzir a transmissão do vírus. **Métodos:** A pesquisa foi realizada no nordeste do Brasil, de fevereiro de 2016 a março de 2017. Noventa indivíduos HIV positivos (Índice) e seus parceiros HIV negativos (n = 17) foram submetidos a questionários epidemiológicos, clínicos e laboratoriais e a testes laboratoriais rápidos para sífilis, hepatite B e C. **Resultados:** Altas frequências de co-infecção com HIV-sífilis (34,4%) e HIV-HBV (3,3%) foram detectadas nos indivíduos HIV-positivos. Três novos casos de HIV foram detectados em parceiros. A maioria dos participantes dos dois grupos (85,6%, Índice; 94,1%, Parceiros) possuía um excelente conhecimento sobre a transmissão do HIV, embora nove parceiros soronegativos com alto risco de infecção pelo HIV tenham sido identificados (53%). Os indivíduos HIV positivos apresentaram alta frequência de co-infecção por sífilis e 10% deles não usaram antirretroviral por opção pessoal. **Conclusões:** A adoção da PrPE e outras medidas preventivas para prevenir a transmissão do HIV em casais sorodiscordantes devem ser estudadas e avaliadas.

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Introduction

Control of the Human Immunodeficiency Virus (HIV) epidemic depends on the reduction of its transmissibility. It has been observed that up to 60.5% of couples living together for at least one year, in African countries where HIV has a high frequency, are serodiscordant for HIV infection[1]. These couples account for 30.4% of the total number of new cases per year in the general population, in sub-Sahara Africa, and about a third of these are per infection from the partner[2]. Brazilian national health system includes free access to Pre-exposure Prophylaxis (PrEP) to populations at high risk for HIV infection, including men who have sex with men (MSM) and has conducted epidemiological surveillance surveys on adherence, awareness and willingness to use PrEP[3-5].

Early diagnosis contributes to the adoption of behaviors that expose partners to a lower risk of HIV infection. However, many individuals are unaware of their partner's serological status. To increase screening and serologic disclosure, healthcare can be focused on the couple. Couples who perform HIV testing together have a higher chance of revealing their serological results to each other[6]. In San Francisco, CA, a partner service provided a 54% increase in HIV diagnosis in six years of operation[7]. Although effective at testing and diagnosing more people at risk, these partner care programs are not widely implemented in Brazil. According to Jones et al. (2014)[8], 12% of stable heterosexual couples established agreements that allowed for outside partners, and Chemaitelly et al. (2014)[2] found that in about 1% of serodiscordant couples, the negative partner was infected with HIV from sources unrelated to their relationship. Therefore, couple-centered counseling services can provide advice on behavioral measures to reduce virus transmission.

PrEP has been much discussed in Brazil. However, most of the published studies raise the issue about challenges in offering it to persons with the greatest vulnerability, and also their awareness, willingness and adherence to this prophylaxis method[3,5,9]. In the South of Brazil[10], it was identified that new HIV infections were more frequent in serodiscordant couples than in the general population. However, there is no study about this issue in the northeastern region of the country.

Prophylaxis with oral antiretrovirals (tenofovir and emtricitabine), associated with the treatment of the HIV-positive partners, was related to the reduction of the risk of HIV infection in populations of high vulnerability[11]. It is indicated for the HIV-seronegative partner of men who have sex with men (MSM), transgender and heterosexual women whose partner is not treated for HIV or has detectable plasma HIV viral load[12].

In order to obtain new epidemiological and clinical data, this study aimed to evaluate the prevalence of HIV-serodiscordant couples and their knowledge about behavioral measures to reduce virus transmission in northeastern Brazil.

Methods

Design and Study Location

A descriptive, observational, cross-sectional study was performed at the Hospital Alcides Carneiro and at the Specialized Health Centre in Infectious Diseases, from February 2016 to March 2017 in Campina Grande – Paraíba (PB, northeastern Brazil). Both health centres of the Unified Health System (SUS) serve the majority of patients undergoing antiretroviral treatment in Campina Grande and in the surrounding cities.

Recruitment and Study Participants

Between February 2016 and March 2017, 632 people living with HIV/AIDS (PLHA) were recruited, which consisted of all people living with HIV in the two referral centers for antiretroviral treatment. The following inclusion criteria were applied: individuals > 13 years old of any sexual orientation and with a stable partnership (in relationship for at least three months), whose partner(s) HIV serological status was(were) unknown (serodiscordants). Only 90 patients matched those criteria and were named as 'Index' (HIV-positive person from serodiscordant couples). They were interviewed by means of structured questionnaires about sociodemographic and behavioral characteristics at the time of the medical consultation, received a Sexually Transmissible Infection (STI) counseling session, rapid laboratory tests of syphilis, hepatitis B and C, and had their retrospective medical data examined in medical records. Thereafter, the 'Index' was asked to invite their HIV-serodiscordants partners for serological testing (Figure 1), and these were named as 'Partner'. 'Partners' were also evaluated by questionnaires about sociodemographic and behavioral characteristics, submitted to a counseling session on prevention of STIs, and tested for HIV, syphilis, hepatitis B and C. Their interviews were conducted separately from the "index" cases, to ensure privacy.
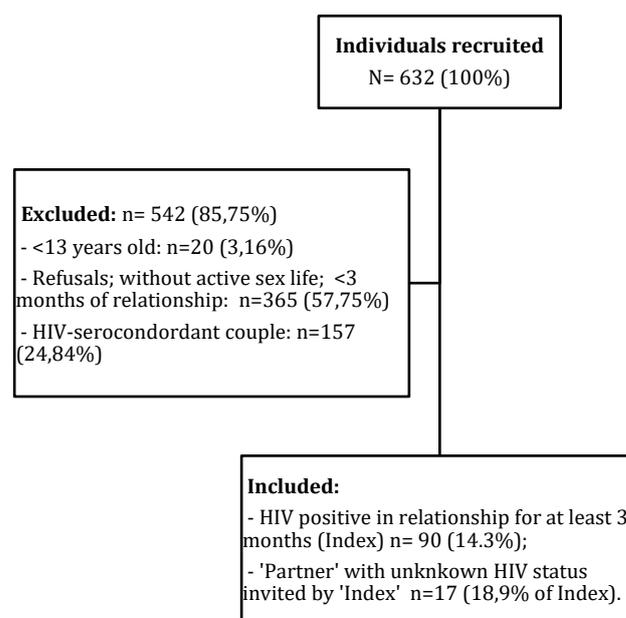

Individuals recruited
N= 632 (100%)

Excluded: n= 542 (85,75%)
- <13 years old: n=20 (3,16%)
- Refusals; without active sex life; <3 months of relationship: n=365 (57,75%)
- HIV-serocondordant couple: n=157 (24,84%)

Included:
- HIV positive in relationship for at least 3 months (Index) n= 90 (14.3%);
- 'Partner' with unknkown HIV status invited by 'Index' n=17 (18,9% of Index).

Figure 1 – Diagram of the screeening, recruitment and exclusion of the serodiscordant couples and their partners that are candidates for PrEP.

Measures and Serological Testing

Data were obtained as described below:

I. 'Index' was interviewed through structured questionnaires elaborated specifically for the study. Questionnaires addressed sociodemographic, epidemiological and clinical data and included the following variables: gender, age, race, level of education, occupation, smoking, alcohol consumption, drug use, time to diagnose HIV infection, use of antiretrovirals drugs (ARV), ART regimen and CD4+ T cell count. Another questionnaire developed and adapted from Kilembe et al.[13] evaluated the knowledge about the risk of HIV transmission (Supplementary material)

II. The 'Index' cases were tested for syphilis (Standard Diagnostic - Korea), HBV (HBsAg, VIKIA Biomérieux - Brazil) and HCV (Standard Diagnostic - Korea). Rapid tests were performed according to the manufacturers' instructions. After the results, counseling sessions regarding STI prevention and treatment, if necessary, were offered.

III. 'Index' was requested to invite their partner(s).

IV. 'Partners' were interviewed by questionnaires, interrogating the existence of previous STI, the knowledge about the risk of HIV transmission, and a scoring system[14] to identify HIV-seronegative partners at greatest risk for HIV acquisition (Supplementary material)

V. 'Partners' were tested for HIV (Standard Diagnostic - Korea), syphilis (Standard Diagnostic - Korea), HBV (Hepatitis B Virus) (HBsAg, VIKIA Biomérieux - Brazil) and HCV (Hepatitis C virus) (Standard Diagnostic - Korea). In case of positive testing, treatment was offered, and the 'Partner' was encouraged to disclose their recent diagnosis to the 'Index'.

Data Analysis

Data were encoded into IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA) for analysis. Descriptive statistics, such as means, frequencies, percentages, interquartile range and minimum and maximum values were used to describe the findings. Pearson's Chi-square or Fisher's exact test, at the level of significance ($\alpha = 0.05$), were applied to evaluate the differences in frequency, for categorical variables. Unpaired Student's t test was used to compare the groups in relation to the numerical variable (age). Verification of the normality and equality of variance hypotheses was performed through the Shapiro-Wilk and Levene F tests.

Ethical approval

The study was approved by the Ethics Committee of the Faculty of Medical Sciences of Campina Grande under number 1.423.871 and it is accordance with Resolution 196/96 of the National Health Council. Informed written consent was obtained from all participants and all identifying information was omitted for confidentiality.

Results

During the study period, 632 PLHAs were recruited, of which 90 (14.3%) met the inclusion criteria and were referred to as 'Index', i.e. HIV-positive individuals with at least three months of relationship. Among the 'Index', 17 (18.9%) agreed to invite their HIV-serodiscordants partner into the survey. The mean age of participants (N = 107, 'Index' and 'Partners') was 39 years old and there was a predominance of males (n = 70, 65.4%). Most patients were economically active (26 – 59 years old) and both groups ('Index' and 'Partners') were heavy consumers of alcohol and marijuana (Table 1).

Table 1 – Sociodemographic and behavioral characteristics of seropositive individuals for HIV (Index) and their HIV-serodiscordants partners (Partners), from February 2016 to March 2017 - Northeastern Brazil (Campina Grande – PB). Values are expressed as n (%) except for overall age.

Characteristics	Index (n = 90)	Partners (n = 17)	p-value
Gender			
Male	62 (68.9)	8 (47.1)	0.083*
Female	28 (31.1)	9 (52.9)	
Age (years)			
Overall (avg ± SD)	39.8 ± 10.4	35.9 ± 14	0.179†
Race			
White	40 (44.4)	5 (29.4)	0.132‡
Black	50 (55.6)	12 (70.6)	
Educational level (years of study)			
< 8	46 (51.1)	10 (58.8)	0.591*
≥ 8	43 (48.9)	07 (41.2)	
Occupation			
Employed	36 (40.0)	7 (41.2)	0.95*
Unemployed	40 (44.4)	8 (47.1)	0.90*
Students	6 (6.7)	-----	
Housewife	8 (8.9)	2 (11.8)	0.73‡
Smoking	29 (32.2)	4 (23.5)	0.477*
Alcohol Consumption	77 (85.6)	14 (82.4)	0.716‡
Marijuana Consumption	33 (36.7)	6 (35.3)	0.914*
Cocaine Consumption	11 (12.2)	1 (5.9)	0.682‡
Crack Consumption	8 (8.9)	1 (5.9)	>0.99‡

*Pearson's Chi-square test; †Student's t-test with equal variances; ‡Fisher's Exact Test. SD, standard deviation.

For 'Index', there was a predominance of heterosexual relationship (n = 56, 62.2%), with the relationships among HIV-positive man/HIV-negative woman and HIV- positive woman/HIV-negative man being equally represented (n = 28, 31% for both). There was a significantly higher proportion of serodiscordant MSM couples (n = 34, 38%; p < 0.0001). The majority of 'Index' (n = 47, 52.2%) declared themselves unmarried, and the remaining confirmed that they were in a stable relationship (n = 27, 30%) or married (n = 16, 17.8%). However, the minority of them (n = 35, 38.9%) reported cohabiting with their partner. A total of 62 participants (68.9%) declared themselves in a monogamous partnership and 43 couples (47.8%) had started the partnership after the 'Index' already knew their HIV serological status. It is important to note that of these 62 participants, 18 (20%) had never disclosed their HIV status to their partner and 19 (21%) did not tell the interviewer if they had already disclosed it to their partner.

Clinical and laboratory evaluation was performed for the 'Index' (Table 2). The mean time to the diagnosis of HIV infection was 6.38 years (standard deviation, SD ± 6.01). Only 11 (12.2%) were diagnosed with HIV infection for less than six months, whereas 55 (61.1%) had been diagnosed for more than three years. More than 87% of the 'Index' were submitted to ART, 48 (60.8%) of which for more than three years. Regarding the laboratory data, 62 'Index' participants (70%) had viral load suppression. The median number of copies/mm^3 was 11,234 (Interquartile range – IQR: 482 - 51,795), in patients with detectable viral load (n = 23, 30%). The median CD4+ T lymphocyte count was 701.5 cells/mm^3 (IQR: 362.5 - 870.25).

Table 2 – Clinical and laboratory characteristics of HIV-positive individuals (Index), from February 2016 to March 2017, Campina Grande – PB (northeastern Brazil) (N = 90).

Variables	n (%)
Time to diagnose HIV infection	
< 6 months	11 (12.2)
6 months to 3 years	24 (26.7)
> 3 years	55 (61.1)
Use of ARV	79 (87.8)
ARV types	
2 INTR* + 1 INNTR †	45 (57.0)
2 INTR + 1 PI‡	31 (39.2)
Others	3 (3.8)
Time of ARV	
< 6 months	7 (8.9)
6 months to 3 years	24 (30.4)
> 3 years	48 (60.8)
CD4+ T Cells (Cells/mm^3)	701.5 (362.5 – 870.25) §
CD4+ T Cells (stratified - Cells/mm^3)	
<200	8 (9.3)
200-500	21 (23.3)
> 500	57 (63.3)
NE	4 (4.4)
Viral load (copies/mm^3)	11,234 (482 – 51,795) $^{\S,//}$

*ITRN: Nucleoside Analog Reverse Transcriptase Inhibitors; †ITRNN: Nucleoside Non-analog Reverse Transcriptase Inhibitors; ‡PI: Protease Inhibitors; §interquartile interval; $^{//}$Calculated only for the 23 'Index' with detectable viral load. NE: not evaluated.

High frequency of HIV-syphilis (n = 31; 34.4%) coinfection was detected in the 'Index' (Table 3). During the serological testing of the partners, three (17.6%) new cases of HIV were detected. Both 'Index' and 'Partner' participants were invited to respond to questionnaires with the objective of assess the degree of knowledge about the risk of transmission or infection with HIV. Most participants in both groups (85.6% - 'Index' and 94.1% - 'Partners') had a degree of knowledge classified as Very Good or Excellent and without statistical differences between the two groups (p = 0.077).

Through the score of Kahle et al.[14], where six or more points indicate a high risk of HIV infection, a total of nine (53%) seronegative HIV 'Partners' with high risk of HIV infection were observed. Of these, two were diagnosed with HIV infection during the survey and were submitted to ART treatment. For the remaining seven, there was an indication of PrEP (Table 4).

Table 3 – HIV-Syphilis, HIV-HBV and HIV-HCV coinfections in HIV-seropositive individuals 'Index' and 'Partner' participants, collected from February 2016 to March 2017, Campina Grande – PB (northeastern Brazil). Values are expressed as n (%).

Infections or coinfections	Index (n = 90)	Partners (n = 17)
Syphilis	31 (34.4)	1 (5.9)
Hepatitis B	2 (2.2)	0 (0)
Hepatitis C	2 (2.2)	0 (0)
HIV	NA	3 (17.6)

Table 4 – HIV testing results among 'Partners' according to the HIV acquisition risk classification (n = 17). One individual did not authorize testing for HIV. Values are expressed as n (%).

Risk of HIV acquisition	Positive	Negative	p-value*
High risk, n = 9 (53)	2 (11.8)	7 (41.2)	0,815
Low risk, n = 7 (41.2)	1 (5.9)	5 (29.4)	
Not evaluated	-	1 (55.9)	

*Fisher Exact test.

Discussion

The frequency of serodiscordant couples for HIV at the Health Centre analyzed was high (14.3%). Given that the prevalence of HIV infection varies across countries, the expected frequency of serodiscordant HIV couples may also vary. In Zambia, which is the country with the seventh highest prevalence of HIV infection - 12.4% of the population between 15-49 years old[15] – the frequency of serodiscordant couples was reported in 10%[16]. In India, the prevalence of infection is only 0.26%[12] and serodiscordance can reach 54.6% of couples with HIV[17]. Brazil has a prevalence of HIV infection of approximately 0.55% for individuals between 15 and 49 years old[12] and only 0.4% in the general population[18]. The frequency of serodiscordant couples reported in this study is close to that observed in China (12.9%)[19], in Tanzania (16.5%)[20] and United States (17%)[21].

The sample was characterized by a predominance of heterosexual couples (62.2%) and the majority of participants had low education. Among the behavioral factors evaluated, the high consumption of alcohol and marijuana was highlighted. The prevalence of heterosexual couples in the present study resembles the 61.7% identified by Rodger et al.[22] in European countries. In most studies, men were the HIV-positive partners (68.9%)[17,19,23-28], while the reverse was observed in South Africa and Kenya, where women were the 'Index' case in 73% of couples[29,30]. Thus, it was verified that, although the MSM couples performed a high frequency of the individuals, they were not the majority, which directs attention to the prevention of viral transmission in populations of lower risk as well.

Among the 'Index' cases that declared stable monogamous relationship (n=62), more than 40% did not reveal their HIV serological status to your partner or did not want to talk about it with the interviewer. Non-disclosure of serological status may have been a determining factor for the low inclusion of HIV-seronegative partners, constituting a limitation of our study. It should be emphasized that the Brazilian model of individualized attention to the 'Index' is endowed with ethical-legal mechanisms that contribute to the inaccessibility of seronegative partners, making it difficult to identify their vulnerabilities by the healthcare teams. However, when couples are counseled and evaluated concomitantly, as in HIV Partner Services, high rates of disclosure (approximately 97%) are achieved[25, 26]. This model of intervention could be more widely adopted in our country.

There was a high consumption of licit drugs in our population. Alcohol consumption was high among 'Index' (85.6%) and 'Partners' (82.4%). These findings are much more significant than those obtained in both Indian and other Brazilian studies, where only 7.2% and 11% of the 'Index', respectively, reported drinking alcohol in the last one to three months[27,31]. The prevalence of illicit drug use, such as marijuana (36.7%), inhaled cocaine (12.2%) and crack (8.9%), was lower than that found in southern Brazil (44%)[31]. It should be noted that the specific use of injectable drugs was not reported by any participant in our study, while relatively high rates (17.3% - 20.7%) were found in other countries[32]. It must be emphasized that the use of licit and/or illicit drugs is associated with the less frequent use of condoms.

Of the 90 PLHA, 79 (87.8%) were undergoing ART. This frequency was higher than that observed in several studies (27% to 74.8%)[22,24,27,32-34]. However, it was below the 92% identified by Wall et al.[26] as well as the target (90%) set by United Nations Programme on HIV/AIDS (UNAIDS)[35]. It is important to note that Brazilian HIV treatment guidelines (www.aids.gov.br/en/professional-health/hiv/protocol-clinical-and-manuals)[36] recommend ART for all individuals, however some individuals refused treatment. Among patients in ART only 70% had an undetectable viral load, which may be indicative of transmission of viral strains with antiretroviral resistance or poor adherence to therapy. Patients with detectable viral load showed a median of 11,234 copies/mm^3 (IQR: 482 - 51,795). The median CD4+ T cells count was high (701.5 cells/mm^3, IQR: 362.5-870.25), which is considerably larger than the median determined by other studies (187 to 436 cells/mm^3)[14, 24, 26, 27, 31, 37, 38].

There was a high HIV-syphilis coinfection rate (34.4%) in the 'Index'. During the testing of seronegative partners, three new cases of HIV infection and a new one of syphilis were identified. The high frequency of syphilis in HIV-positive patients is of concern, due to the increased possibility of viral transmission in the presence of another STI; therefore, it is important to diagnose, treat and raise awareness about methods of prevention of various STIs in order to reduce the chances of HIV transmission from viral carriers.

Although the study was approached in the two largest treatment centers for people living with HIV in the interior of the state of Paraíba (Campina Grande), the sample was of convenience. In addition, another limitation of the study was the low adherence of the partners in the index cases, which hindered a larger and more detailed analysis of the study. This lack of adherence to the study by the partners has several reasons: the index case does not want to reveal its serological status to the partner, the same does not want to perform serological testing and/or interview, the index does not have a steady partner, etc.

Based on our criteria, the risk of HIV infection was high in nine (53%) HIV-negative individuals, and among them, it was possible to identify two new cases of HIV. Among the HIV-positive patients, the high rate of individuals with detectable viral load, high frequency of HIV-syphilis co-infection and a significant proportion (10%) who refused antiretroviral treatment, allied to high frequency of HIV-negative partners which presented high risk of HIV infection demonstrates the importance of establishing PreP in health services in the northeastern regions of Brazil, in addition, it is important to integrate their HIV-negative partners into these services in order to reduce viral transmission, both through educational and biomedical measures.

Conclusions

It was observed at a rate of 14.3% of PLHA that maintained an active sex life for more than three months in the sample. However, among these, a high rate of MSM couples was observed, and a high prevalence of individuals who did not communicate their serological status to the partner and had a high viral load and concomitant syphilitic infection. More than half of HIV negative partners were at high risk of contamination. Thus, the adoptions of prophylactic measures for HIV are urgent in the analyzed population, including with the possibility of greater dissemination of the use of PrEP.

Acknowledgements

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