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HIV-Related Healthcare Needs and Access Barriers for Brazilian Transgender and Gender Diverse People

Angelo Brandelli Costa[1] · Anna Martha Vaitses Fontanari[2] · Ramiro Figueiredo Catelan[3] · Karine Schwarz[2] · Juliana Ledur Stucky[1] · Heitor Tome da Rosa Filho[2] · Paola Fagundes Pase[1] · Daniel Augusto Mori Gagliotti[4] · Alexandre Saadeh[4] · Maria Inês Rodrigues Lobato[2] · Henrique Caetano Nardi[3] · Silvia Helena Koller[5,6]

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Abstract

The aim of this study is to investigate HIV-related healthcare needs and access barriers for Brazilian transgender and gender diverse people. Data were collected from gender identity clinics and the questionnaire was also made available on the Internet. Out of the 543 participants—62.1% ($n = 337$) transgender women, 28.7 ($n = 156$) transgender men and 9.2% ($n = 50$) gender diverse people, 63.7% had been tested at least once in their lives. The prevalence of self-reported HIV-positive status among transgender women was 16.5%, of which 92.0% reported having a physician with whom they regularly consulted about HIV, whereas none of the transgender men or gender diverse people reported HIV-positive status. In addition, 8.2% of transgender men and 12.5% of gender diverse people did not know their serological status. Finally, 71.0% of the participants were unfamiliar with post-exposure prophylaxis. The study discusses the need for adequate behavior-oriented HIV health policies and training of healthcare professionals regarding the needs of Brazilian transgender and gender diverse people.

Keywords Transgender people · HIV testing · HIV treatment · Brazil · Post-exposure prophylaxis

Introduction

Burden of HIV Among Transgender and Gender Diverse People

Data from a recent meta-analysis show that transgender women (TW) are highly vulnerable to HIV infection. In a sample of 11,006 TW, the estimated prevalence of HIV was 19.1%; compared to the general population, TW are 48.8 times more likely to contract HIV [1]. Another meta-analysis revealed an even greater risk among TW sex workers [2]. The study suggests that TSW face unique structural, interpersonal, and individual vulnerabilities that contribute to their high risk of HIV infection. In Brazil, the scenario is similar [3]. Grinsztejn et al. [4] recruited 345 TW from Rio de Janeiro, Brazil, using respondent-driven sampling and found that 31.2% presented HIV diagnosis, indicating that TW bear the largest burden of HIV among any at-risk population in Brazil.

HIV prevalence is low among transgender men (TM), varying between 0 and 4.3% [5–7]. Regarding specifically gender diverse people (GDP), or those who identified with a gender outside the gender binary, there is even less data

✉ Angelo Brandelli Costa
angelo.costa@pucrs.br; brandelli.costa@ufrgs.br

1 Department of Psychology, Pontifícia Universidade Católica do Rio Grande do Sul, Avenida Ipiranga 6681, Prédio 11, Sala 933, Porto Alegre, RS, Brazil

2 Gender Identity Program (PROTIG), Hospital de Clinicas de Porto Alegre (HCPA), Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil

3 Department of Social Psychology, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil

4 Transdisciplinary Gender Identity and Sexual Orientation Service (AMTIGOSNUFOR), Hospital de Clinicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), Universidade de São Paulo (USP), São Paulo, SP, Brazil

5 Department of Psychology, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil

6 Optentia Research Focus Area, North-West University, Vanderbijlpark, South Africa

available [8]. Data collection in lower- and middle-income countries such as Brazil is still scarce regarding these populations [7].

Stigma and Healthcare Access

Stigma and prejudice increase the vulnerability of transgender and gender diverse (TGD) people, whether through direct violence and discrimination or by hampering access to healthcare and preventing inclusion in the labor market. In Brazil, the high degree of prejudice against lesbian, gay, bisexual, and transgender populations is well known [9]. Stigma and prejudice are especially evident towards TGD individuals, whose gender expressions differ from hegemonic beliefs [10]. According to the Trans Murder Monitoring Project, Brazil has one of the highest TGD-related homicide rates in the world [11]. In addition to explicit violence, TGD individuals still encounter barriers, motivated by direct or indirect discrimination, in accessing public services, particularly healthcare [12].

HIV Testing for Transgender and Gender Diverse People

Recent studies evaluated HIV testing among TGD in low- and middle-income nations, using qualitative research with in-depth interviews and focus groups and quantitative research with online and in person surveys. Briefly these studies revealed barriers to HIV testing, such as homeless [13], mental health (daily/weekly alcohol use and post-traumatic stress symptoms) [14], unawareness [15], cost [15–17], healthcare provider mistreatment [18, 19], confidentiality breaches [16, 18–20], HIV-related stigma [13, 15, 16, 18–20] and internalized homonegativity [13]. Furthermore, it was highlighted that HIV testing frequently did not included counseling [20] and that lack of support was an important barrier for HIV testing [17]. HIV testing was the main focus of those studies, with one exception that evaluated associations between HIV prevention and human rights for sexual minorities. Therefore, there is a lack of studies considering other forms of HIV prevention, such as post-exposure prophylaxis (PEP), and access to health care after HIV diagnosis. Moreover, recent studies included men who have sex with men (MSM) in tandem with transgender women (TW) in their sample, which could be a confusing for two main reasons. First, considering transgender women among MSM is by itself a form of discrimination, since most transgender women are not, and do not want to be recognized as, men. Second, none of the studies acknowledged gender diverse people, focusing predominantly on sexual behavior and, therefore, neglecting the impact of gender identity on increasing sexually transmitted infection (STI) prevalence; gender identity can affect social and contextual factors that can increase vulnerability and risk on proximate factors, like sexual behavior [2, 21–23].

The UNAIDS fast-track commitments to end AIDS by 2030 prioritize successfully integrating people living with HIV into healthcare to suppress their viral load, improve their health, and reduce their risk of transmitting HIV. To that end, people living with HIV must fully embrace the HIV care continuum, learning about their HIV-status, and adhering to antiretroviral therapy as soon as possible. Understanding the context in which TGD access HIV-testing and HIV-related healthcare is an important step within the new strategy.

The objective of this study is to report HIV-related healthcare needs and access barriers for TGD people in Brazil. Trans-related discrimination in HIV-oriented healthcare context was also investigated. This is the first study to thoroughly analyze the barriers that TW face in accessing free universal healthcare and the difficulties that TM and GDP have when accessing HIV-related healthcare.

Methods

The Trans Health Research Project is a hospital and web-based cross-sectional survey, based on input from the medical and TGD communities, aimed at assessing the healthcare needs and access barriers of TGD residents in two Brazilian states. It is an evidence-informed, policy-making initiative. The methods are described in detail in another study derived from this research [12].

This study was approved by the institutional review board and Human Ethics Committee of Hospital de Clínicas de Porto Alegre (HCPA) and Universidade Federal do Rio Grande do Sul (UFRGS) as well as by the Universidade de São Paulo (USP) and its institutional review board. Written informed consent was obtained from all the study participants.

Participants

Data were collected in two Brazilian states: Rio Grande do Sul and São Paulo. Both states have gender identity programs that provide gender-affirming surgery at university hospitals. Since the Brazilian National Health System provides georeferenced care, patients seeking gender affirmation must undergo these procedures in the states in which they live. Before and after group and individual meetings, patients from the two programs were invited, though convenience sampling, by the researchers to voluntarily answer an electronic version of the survey. The questionnaire was also available on the Internet through an online Facebook announcement targeting TGD during two time periods: July–October 2014 and January–March 2015. The

participants have not receive neither payment incentive nor any direct benefit for joining the research.

Instruments

The survey was modeled after the TransPULSE project [24], one of the first large-scale studies to address the health needs and vulnerabilities of TGD individuals and barriers to healthcare access. For this study, it was adapted to Portuguese for use in the Brazilian population by a group of health practitioners who work in gender and sexual diversity fields and assessed by members of the Brazilian TGD community.

Gender identity was evaluated using the two-question method, and subjects were considered eligible to participate if they reported a gender different from that assigned to them at birth [25]. Organized social movements in Brazil prefer the terms *travesti*, transsexual and trans person (man or woman) to the Anglophone umbrella term transgender [26]. *Travesti* is a culturally specific gender identity term used in Brazil [27]. Based on their self-reported gender identity, participants were re-categorized as transgender women (TW), transgender men (TM) or gender diverse people (GDP). TW were those who were designated male at birth, but identified as women, trans women or *travestis*. TM were those designated as female at birth, but identified as men or trans men, while GDP were those who identified with a gender outside the gender binary.

Race/skin color/ethnicity was attributed using the census categories of the Brazilian Institute of Geography and Statistics: white, black, yellow (mostly East Asians), and indigene. The category *pardo* was also used, which commonly refers to Brazilians of mixed-race, typically a mixture of white, Afro- and native Brazilian. With respect to HIV-related healthcare access and barriers, participants answered questions on reasons for avoiding testing, reasons for testing, and discrimination in the HIV treatment context. The possible answers to these questions were modeled on the experiences of TGD community members and health professionals who work with them.

Participants also answered questions related to HIV testing frequency, self-reported serological status, use of antiretroviral therapy, and knowledge and use of PEP.

Data Analysis

Central tendency and frequency statistics were calculated and the relationships between HIV-testing and sociodemographic factors were determined using χ^2 tests and the Mann–Whitney U-test (continuous measures). The strength of the association between each correlate and HIV testing was expressed as an odds ratio, with a 95% confidence interval, via logistic regression. Although age was collected as a continuous variable it was analyzed, along with the rest of the variables, as ordinal. Indigenes from the race/skin color/ethnicity category and widow(er)s were excluded from this analysis due to the low sample size.

Results

Seven hundred and one volunteers answered the survey. However, considering the complete questionnaire used in the present article, the total sample consisted of 543 TGD people—62.1% ($n = 337$) TW, 28.7 ($n = 156$) TM and 9.2% ($n = 50$) GDP. Of these, 84.5% ($n = 459$) responded to the survey online and 15.5% ($n = 84$) in the two hospitals. The average age of the participants was 26.8 years (95% CI [26.1, 27.5], SD 8.8, Mdn 24), ranging from 18 to 65 years old. Most of the sample (53.2%) was of emerging adults (ages between 18 and 24 years). More sociodemographic data can be found in Table 1.

Regardless of whether they had been previously tested for HIV infection, participants were asked if they had avoided testing for any of the reasons reported in Table 2.

With regards to HIV testing in particular, 63.7% ($n = 346$, N = 543) of participants had already been tested at least once in their lifetime. Regarding gender identity, 72.7% ($n = 245$) of TW, 50.6% ($n = 77$) of TM and 52% ($n = 26$) of GDP had been tested. Determinants for testing are shown in Table 3.

Most respondents (46.7%, $n = 158$, N = 338) had been tested in the last 6 months. Specifically, 23.1% ($n = 78$) had been tested in the past 3 months, 23.7% ($n = 80$) from 3 to 6 months previously, 17.8% ($n = 60$) from 6 months to 1 year, 16.9% ($n = 57$) between 1 and 2 years ago, and 18.6% ($n = 63$) more than 2 years previously. No statistically significant difference was found for testing frequency according to gender identity (X^2 (8.338) = 3.06, $p = 0.930$).

According to the logistic regression (Table 3) age, marital status, race/color/ethnicity and religiosity were associated to HIV-testing.

Table 4 summarizes reasons why participants sought HIV testing. Most were tested as part of a routine medical check-up, for hospitalization or surgical procedure.

Considering the total tested sample, including TW, TM and GDP, self-reported HIV prevalence was as follows: 11.8% ($n = 40$, N = 339) of participants reported being HIV positive; 79.1% ($n = 268$), HIV negative; 7.1% ($n = 24$) did not know; and 2.1% ($n = 7$) preferred not to reveal their HIV status. With regards to gender identity, 16.5% ($n = 40$, N = 242) of TW reported being HIV positive; whereas none of the TM or GDP reported HIV-positive status. However, 8.2% ($n = 6$, N = 73) of TM and 12.5% ($n = 3$, N = 24) of GDP did not know their serological status, comparing to 9.1% of TW ($n = 31$, N = 339).

Table 1 Demographic characteristics

	Transgender women (N = 337) N (%)	Transgender men (N = 156) N (%)	Gender diverse people (N = 50) N (%)
Age groups			
18–24	154 (45.7)	100 (64.1)	35 (70.0)
25–34	111 (32.9)	36 (23.1)	11 (22.0)
35–44	50 (14.8)	15 (9.6)	2 (4.0)
45–54	17 (5.1)	5 (3.2)	–
55–64	5 (1.5)	–	2 (4.0)
Race/color/ethnicity			
White	243 (72.1)	120 (72.1)	36 (72.0)
Pardo	68 (20.2)	23 (20.2)	4 (8.0)
Black	18 (5.3)	10 (5.3)	5 (10.0)
Yellow	7 (2.1)	3 (2.1)	5 (8.0)
Indigene	1 (0.3)	1 (0.3)	–
Education			
None	7 (2.1)	2 (1.3)	1 (2.0)
Elementary education	32 (9.5)	19 (12.2)	–
High school education	214 (63.5)	99 (63.5)	31 (62.0)
Higher education	62 (18.4)	31 (19.9)	14 (28.0)
Graduate studies	22 (6.5)	5 (3.2)	4 (8.0)
Population of city of residence			
5000–50,000 inh.	69 (20.5)	38 (24.4)	9 (18.0)
50,000–100,000 inh.	43 (12.8)	10 (6.4)	5 (10.0)
100,000–500,000 inh.	84 (24.9)	48 (30.8)	6 (12.0)
More than 500,000 inh.	141 (41.8)	60 (38.5)	30 (60.0)
Marital status			
Single	253 (75.1)	111 (71.2)	39 (78.0)
Common-law marriage	45 (13.4)	32 (20.5)	1 (14.0)
Married	31 (9.2)	12 (7.7)	3 (6.0)
Divorced	7 (2.1)	1 (0.6)	
Widow(er)	1 (0.3)	–	1 (2.0)
Religious beliefs			
Have a religion	270 (80.1)	112 (71.2)	33 (66.0)
No religion or atheist	67 (19.9)	45 (28.9)	17 (34.0)

Of the HIV-positive people (all TW), only 7.7% ($n = 3$, N = 39) reported not having a physician with whom they regularly consult about HIV. Of HIV positive people, 18.0% ($n = 7$, N = 39) stated they were not using medication to treat HIV.

Table 5 presents a list of discrimination scenarios related to HIV treatment. It considers exclusively HIV-positive TW. Almost half of the HIV-positive participants (48.7%, $n = 19$) reported some type of discrimination in the healthcare context. For more details, a recent publication contains data concerning discrimination in general healthcare including HIV-related [12].

Finally, access to information on PEP was investigated (N = 544). Of the respondents, 71% ($n = 386$) did not know what it was; 26.5% ($n = 144$) were familiar with it, but had never used it; and only 2.6% ($n = 14$) had already used it. In an assessment based on gender identity, 69.4% ($n = 234$, N = 337) of TW, 74.5% ($n = 117$, N = 157) of TM and 70.0% ($n = 35$, N = 50) of GDP were unfamiliar with PEP. In addition, only 3.0% ($n = 10$, N = 337) of TW, 1.3% ($n = 2$, N = 157) of TM and 4.0% ($n = 2$, N = 50) of GDP had used PEP.

Discussion

To date, this is the first study to thoroughly analyze the barriers that TGD individuals face in accessing free universal healthcare policies and the difficulties they encounter in obtaining HIV-related healthcare.

Table 2 Reasons to avoid HIV-testing by gender identity (multiple answers)

Have you ever AVOIDED HIV testing for any of these reasons?	Transgender women (N = 337) N (%)	Transgender men (N = 156) N (%)	Gender diverse people (N = 50) N (%)
I always had safe sex, so I didn't believe I needed to get tested	84 (24.9)	15 (9.6)	11 (22.0)
I was afraid I might be HIV positive	59 (17.5)	5 (3.2)	11 (22.0)
I don't believe I'm at risk	59 (17.5)	52 (33.3)	16 (32.0)
It was not important to me to get tested	48 (14.2)	29 (18.6)	16 (32.0)
I always used clean needles so I didn't believe I needed to get tested	43 (12.8)	36 (23.1)	13 (26.0)
I felt healthy, so I didn't believe I needed to get tested	42 (12.5)	19 (12.2)	4 (8.0)
I hadn't had sex recently, so I didn't believe I needed to get tested	37 (11.0)	11 (7.1)	8 (16.0)
I didn't know where to get anonymous testing	23 (6.8)	7 (4.5)	5 (10.0)
The HIV testing staff are/have been hostile or insensitive to me	22 (6.5)	6 (3.9)	3 (6.0)
Other reasons	22 (6.5)	21 (13.5)	6 (12.0)
I didn't want other people to know I got tested	20 (5.9)	2 (1.3)	4 (8.0)
I didn't want my partner to know I got tested	8 (2.4)	1 (0.6)	–

Avoidance of HIV Testing: Lack of Anonymity and Fear of Harassment

In addition to general healthcare scenarios [10, 12, 28], trans-related discrimination is also reported with regard to HIV related-care. With respect to HIV testing, Table 2 highlights avoidance due to concerns over anonymity and expected prejudice: 6.8% of participants did not know where to get tested anonymously and 5.9% would not want others to know about their testing. Previous data already demonstrated that resistance to testing in trans women is related to uncertainty regarding the confidentiality of results [29]. Additionally, 6.5% of the respondents believed health professionals would harass them. Table 5 contains discrimination experiences related to health professionals providing HIV-related care.

Nevertheless, more than 70.0% of our sample had already been tested for HIV at least once and 68.9% had done so in the previous 6 months. This is almost twice as high as the national average; considering data from the Ministry of Health's 2008 Awareness research, attitudes and practices related to STI and AIDS in the Brazilian population, 36.5% of participants reported having been tested for HIV at least once in their lifetime and 38.4% stated they had been tested in the past 12 months [30]. In agreement with our results, 84.4% of *travestis* of another research in the north of Brazil reported they had been tested for HIV at some point in their lives 47.30% in the previous 12 months [31]. Likewise, 69.0% of *travestis* in a research conducted in a northwester Brazilian state had been tested for HIV [32]. Contrasting with Brazilian data, a recent study in Canada, using the same methodology, reported that only 54.0% of participants (including TM) had been tested for HIV infection [5].

The majority of our sample cited routine or non-HIV-associated care as reasons for testing. Despite the high frequency of testing, avoidance due to stigma and prejudice may prompt lower treatment adherence and can, therefore, be addressed by public policies.

Care Continuum: Where Do You Go After Testing?

In regard to the care continuum, most participants stated adherence to treatment and the use of medication. According to the Brazilian Epidemiological AIDS and STI Report [7, 33] 3% of people diagnosed with HIV adhere to treatment and 48.0% take medication. Our study showed better results: 92.3% linked to care and 82.1% using antiretroviral therapy. Paradoxically, our sample exhibited a high prevalence of HIV infection, suggesting some exhaustion of current prevention strategies. According to international guidelines [34], PEP is an option to avoid HIV infection. PEP has been a policy for sexual exposure to HIV in Brazil since 2010. It is available for cases of sexual violence, unprotected sexual intercourse and occupational accidents. Nevertheless, 71.0% of participants were unfamiliar with PEP, highlighting the need to promote new prevention strategies for those groups.

HIV Across Healthcare, Accentuating the Medicalization and Stigmatization of TGD

Studies evaluating the impact of health policies on TGD health have highlighted that the emphasis on HIV has prompted the medicalization and stigmatization of this population. Despite the focus on HIV, in Brazil, for example there are still limitations in terms of accessing prevention policies and treatment alternatives by this groups [35]. Therefore, inasmuch as TGD individuals are

Table 3 HIV-testing by sociodemographics

	n (%)	Wald	Odds ratio	95% CI
Age groups				
18–24	132 (45.7)	41.83**	0.18	0.10–0.30
25–34	134 (84.8)	5.22**	0.40	0.18–0.88
35–44	58 (86.6)	0.10	0.83	0.26–2.62
45–54	17 (77.3)	1.39	3.07	0.48–19.65
55–64	5 (71.4)	55.32	Ref.	Ref.
Race/color/ethnicity[a]				
White	248 (62.3)	4.05*	0.51	0.27 – 0.98
Pardo	69 (72.6)	0.01	1.08	0.27 -4.35
Black	18 (54.6)	0.03	0.92	0.41 – 2.09
Yellow	10 (66.7)	5.05	Ref.	Ref.
Indigene	1 (50.0)	–	–	–
Education				
None	7 (70.0)	0.27	1.56	0.30 – 8.15
Elementary education	29 (56.9)	0.02	0.94	0.39 – 2.24
High school education	204 (59.3)	0.80	0.70	0.32 – 1.52
Higher education	83 (77.6)	0.06	1.14	0.40 - 3.26
Graduate studies	23 (74.2)	2.151	Ref	Ref
Population of city of residence				
5000–50,000 inh.	63 (54.3)	0.80	0.71	0.34 -1.50
50,000–100,000 inh.	38 (65.5)	0.01	1.02	0.60 – 1.73
100,000–500,000 inh.	81 (58.7)	3.58	0.66	0.48 - 1.01
More than 500,000 inh.	164 (71.0)	5.28	Ref.	Ref.
Marital status[b]				
Single	247 (61.3)	0.03	1.05	0.61 - 1.80
Common-law marriage	52 (62.0)	4.64	0.35	0.13 – 0.91
Married	40 (87.0)	0.45*	1.88	0.29 - 11.97
Divorced	6 (75.0)	4.85	Ref.	Ref.
Widow(er)	1 (50.0)		–	–
Religion				
Have a religion	278 (67.2)	4.81*	1.70	1.06-2.69
No religion or atheist	68 (52.7)	–	Ref.	Ref.

$^{**}p < 0.05$, $^{***}p < 0.01$

[a]Excluding indigene

[b]Excluding widow(er)s

targeted as a priority in terms of HIV policies, healthcare professionals are not trained in regard to the needs of this population, making them more vulnerable to HIV infection.

Data from Argentina shows that a high proportion of TW avoid health services due to stigma, discrimination, and exposure to violence [28]. This demonstrates the importance of providing formal training for health professionals on issues related to gender and sexuality. Furthermore, the specific needs of the TGD population must be addressed, providing better quality services that respect cultural differences and therefore minimize barriers to healthcare access.

Limitations

The sample used in this research was not representative of all Brazilian states; as such, estimates based on these data could be biased. Furthermore, the level of education of the sample is higher than the Brazilian average and less educated TGD probably face additional barriers due to education and knowledge about the characteristics of, and need for, health care and treatment [36]. It adequate accessibility to a physician once diagnosed with HIV infection could also indicate a sample bias, since a small part of the sample was collected from the two gender identity programs, located in hospitals, where medical assistance and referrals are easier.

Table 4 Reasons for HIV-testing by gender identity (multiple answers)

	Transgender women (N = 242) N (%)	Transgender men (N = 76) N (%)	Gender diverse people (N = 24) N (%)
Part of a routine medical check-up, for hospitalization or a surgical procedure	84 (34.7)	38 (50.0)	9 (37.5)
I just wanted to find out if I was infected or not	79 (32.6)	8 (10.5)	10 (41.7)
I felt I had unsafe sex	65 (26.9)	3 (4.0)	5 (20.8)
No particular reason	50 (20.7)	22 (28.95)	7 (29.2)
Someone suggested I should be tested	38 (15.7)	10 (13.2)	3 (12.5)
I was concerned I could give HIV to someone	21 (8.7)	2 (2.6)	5 (20.8)
I had sex with someone I knew was HIV positive	7 (2.9)	–	–
I was feeling sick	14 (5.8)	–	–
I thought I might have been exposed at work	9 (3.7)	1 (1.3)	1 (4.2)
I had been sexually assaulted	9 (3.7)	–	–
I had sex with someone who I suspected was HIV positive	16 (6.6)	1 (1.3)	–
I shared needles or drug-using equipment	2 (0.8)	–	–
I had to get tested for life insurance coverage	–	1 (1.3)	–
I do not know	2 (0.8)	1 (1.3)	–
Other	9 (3.7)	5 (6.6)	3 (12.5)

Table 5 Discrimination in HIV-related healthcare contexts faced by transgender women living with HIV infection (multiple answers)

Because you are a TGD individual, has a healthcare provider ever…	Transgender women (n = 39) N (%)
None of the above	20 (51.3)
Not used the name you indicated that you wanted to be called	9 (23.1)
Told you that you were not really TGD	4 (10.3)
Used hurtful or insulting language about TGD identity or experiences	3 (7.7)
Told you they do not know enough about TGD-related care to provide it	3 (7.7)
Belittled or ridiculed you for being TGD	3 (7.7)
Refused to see you or ended your care because you were TGD	3 (7.7)
Refused to examine parts of your body because you are TGD	3 (7.7)
Thought the gender listed on your ID or forms was incorrect	2 (5.1)
Discouraged you from exploring your gender	1 (2.6)
Refused to discuss or address TGD-related health concerns	1 (2.6)

Is important to note that the worst health care access and greatest discrimination may be experienced by TGD with no access to the Internet or tertiary care.

An important limitation is the fact that all measures used were self-reported. There are a number of well documented biases in the use of HIV and sexual behavior related self-report measures [37]. However, a recent study done in Brazil with MSMs found that self-report of HIV infection was a reliable indicator among that group; agreement between self-report and the test was very good (kappa = 0.88) [38]. Although populations have distinct characteristics, TGD and MSM, taking into account inherent biases, the data of the present research can be considered reliable.

An additional limitation was the low statistical power in regression analysis on HIV-testing. For the variable marital status, the χ^2-test revealed significant associations with the dependent variable ($p < 0.01$). By contrast, the corresponding odds ratios for these relationships exhibited 95% confidence intervals including 1, falling just short of statistical significance.

Despite these limitations, the results indicate that HIV-related health policies for TGD populations need to foster initiatives aimed to control HIV infection, such as prevention. Additionally, continuous training of health practitioners is needed to mitigate potentially prejudiced attitudes in HIV-related healthcare contexts. This study also demonstrates the

urgent need for adequate behavior-oriented HIV healthcare policies and training of professionals regarding the needs of TGD.

Authors Contribution All the authors contributed significantly and are in agreement regarding the contents of this manuscript. AC designed the study, wrote the protocol, was responsible for analysis, and participated in data interpretation, draft of the article and final approval of this version. AF, JS and RC participated in data analysis and interpretation, draft of the article and final approval of this version. HF, DG, KS and PP participated in the study design and final approval of the article. AS, HN, ML and SK were responsible for the study design and data interpretation, as well as draft of the article and its final approval.

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Compliance with Ethical Standards

Conflicts of interest The authors declare that there are no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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