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Editorial

Why should boys and men receive HPV vaccine?

INTRODUCTION

Human papillomavirus (HPV) is one of the most common sexually transmitted infections and a major cause of various types of cancers, as well as of anogenital warts and oral lesions in both the genders. In women, HPV is strongly related to cervical, vaginal, vulvar, and anal cancers, and is also considered the agent responsible for precursor lesions[1]. HPV infection in men is a major concern owing to its infectivity potential. It may occur in anal and urethral area, on the penis, oral cavity, and larynx[2]. Currently, the clinical manifestations caused by HPV are considered vaccine-preventable diseases.

The scientific community and the medical societies question the ethics of HPV immunization strategies directed exclusively to women. Historically, vaccinations based on risk or gender were not successful in reducing the disease[3]. Although vaccination in women can substantially reduce the incidence of diseases related to HPV in women (and, to some extent, in men, as known as "herd protection" effect), vaccination programs based on gender and with low coverage have slowed the impact of the diseases. The women vaccination has been leading to a limited effect of the "herd protection," so that the true potential of the HPV vaccine is not fully achieved. Therefore, the gender-neutral vaccination (for female and male) in adolescents would be the adequate manner to achieve the actual herd protection against HPV infection[4,5].

Vaccines are considered to be one of most effective measures of public health. Some diseases are controlled, and others were eradicated owing to vaccination. From the individual perspective, vaccination can determine the difference between health and sickness, life and death.

PAPILLOMAVIRUS AND MAN

Sexually transmitted diseases (STDs) are among the most common public health issues around the world[6,7]. According to the World Health Organization (WHO), the estimated number of curable STDs worldwide oscillates around 498.9 million new cases per year[8]. HPV is the most common sexually transmitted infection among the STDs, of which approximately 25% are easily disseminated by direct skin contact during sexual intercourse (vaginal, oral, and anal), although this is not the only route of transmission[9].

Estimates suggest that there are approximately 20 million people infected with HPV in the United States of America, and approximately 5.5 million new cases occur in the country every year. Over 7% of adolescents reported sexual initiation under 13 years of age. In Brazil, studies show that more than 30% of women and approximately 50% of men become sexually active before 14 years of age. What concerns us the most is the fact the age group more often affected by STIs, including HPV is adolescents aged up to 19 years[10,11].

HPV infections in men are most often asymptomatic, and prevalence rates are poorly understood, but some studies are available.

Man presents a lower immune response to natural infection with low levels, or often null, antibodies; subsequently, there is poor protection against infections. This is corroborated by frequent relapses and persistence of the lesions in men. Moreover, a man plays a role of reservoir and transmitting agent of this STD, indicating that the penis and urethra are the most frequent sites. It is believed that male infection contributes significantly to the infection and subsequent cervix uteri disease in women, and it is estimated that over 70% of partners of women with cervical HPV infection are carriers of the virus DNA.

Worldwide, approximately 1.9 million people have genital condylomata acuminata. It is estimated that 1% of sexually active adults have had some visible genital warts, whereas 15% had a subclinical infection. Overall, a probable share of 75% of the sexually active population is estimated to have been exposed to the virus at some point.

Condyloma, or genital warts, is the most common disease found in the anogenital region. These lesions are not evenly distributed over the genitalia, and the most frequently affected locations in men are the frenulum, the balanopreputial sulcus, the glans, and the foreskin – areas which are often difficult to handle and to adhere to treatment. Warts are generally caused by HPV types 6 and 11, and rarely have oncogenic potential[2,12,13]. However, psychosocial issues are significant sources of morbidity among men and women. Patients report feeling ashamed after diagnosis and with a high level of anxiety, which impacts their sexuality and their social relationships[14-16].

In the head and neck, injuries can also appear as recurrent respiratory papillomatosis (RRP), which affects adults and children. RRP is a benign tumor that is characterized by the presence of epithelial lesions of verrucous aspect, which can be pedunculated, isolated, or multiple, depending on their evolution. Such lesions may trigger severe manifestations, such as respiratory insufficiency owing to the obstruction mechanism of the upper, and sometimes lower, airways, which also may cause death. It is considered one of the most difficult diseases to control owing to its high recurrence[14,17,18]. Injuries can affect the mouth, nose, pharynx, esophagus, and the whole tracheobronchial tree. The laryngeal location (most frequent, with 50% of cases) is the state of the glottis. However, the subglottic location has the worst prognosis as it may cause dyspnea and sometimes requires an emergency tracheotomy, which may be tracheobronchial, and even lung, extension factor. About the rinopharyngo-esophageal location, warts may appear on the uvula, the tonsils, the soft palate, the base of the tongue, hypopharynx, and esophagus[19,20].

Data show that 5.2% of all cancers worldwide are caused by HPV, and types 16 and 18 are primarily responsible for a substantial number of alterations. In addition to cervical cancer, other

regions may be involved, such as anal cancer in 90%, vulvar and vaginal cancer in 40%, penile cancer in 30–50%, and oropharyngeal cancer in 33–72%[2,20] (**Chart 1**).

The annual load of penile cancer was estimated at 22,000 cases worldwide (correlating strongly with cervical cancer rates). This disease is a public health problem; however, studies on the association of HPV with penile carcinomas are still rare, because this type of cancer is rare in developed countries. However, in developing countries, this statistic changes significantly as it represents up to 10% of male cancers in some parts of Africa, South America, and Asia[26]. In Brazil, incidence rates vary from 5.5 to 16%, being higher in the north and northeast regions in 1% and the south and southeast regions in 4%, primarily affecting men in the fifth and sixth decades of life (**Table 1**).

Men who have sex with men (MSM) and individuals living with HIV represent the population at greatest risk for persistent infection, and there is a greater chance of developing anal cancer[31]. Since 2005, a prospective multicenter study (Brazil, Mexico, USA) is being conducted with men to assess the prevalence of HPV infection in men aged 18–70 years. The prevalence of infection with the types of high and low risk of multiple infections was not different in the three countries. The prevalence of HPV infection in Brazil was 72.3%; in the United States of America it was 61.3%, and in Mexico, the prevalence was 61.9%.

The prevalence of HPV in the anal canal is not restricted to the group of MSM: the researchers found that among men who have sex with women (MSW) the prevalence was 12.2%, and among MSM it was 47.2%. It is worth noting that the prevalence of HPV 16 was twice as common among MSM with relation to MSW group (the potential high risk of the HPV 16 was identical in the anal area when compared to the cervix). The infection by various types of HPV was also ten times more frequent in MSM compared to MSW group[32].

Chart 1 – Impact of type-specific HPV disease.

Types	Female	Male
6 and 11	>90% of genital warts[22,26] ~25% of low-grade cervical lesions[23,26] RRP intrauterine transmission from mother to child and/or at the birth canal[24,25]	>90% of genital warts[22,26] Transmission to women[21] RRP vertical transmission[24,25]
16 and 18	~25% of low-grade cervical lesions[23,26] ~50% of high-grade cervical lesions[26,27] ~70% of cervical cancers[26-28] ~70% of high-grade vulvar/vaginal lesions[26,29] ~40% of vaginal and vulva cancers[21,26,30]	~90% of anal cancers[21,26] ~30% of penile cancers[21,26,30] ~33–72% of oropharyngeal cancers[21,26,30] Transmission to women[21]

Table 1 – Crude incidence rates of HPV-associated cancers (Brazil).

	Men	Women
Cervical cancer	-	18.4
Anal cancer	0.3–1.0	0.8–1.4
Vulvar cancer	-	0.3–1.8
Vaginal cancer	-	0.4–1.2
Penile cancer	0.7–2.3	-
Oropharyngeal cancer (excluding nasopharynx)	4.7	0.9

VACCINATION AGAINST HPV – STRATEGIES, GENDER, AND RISKS

The HPV vaccines have been licensed since 2006 in more than 129 countries for women aged 09–26 years after consistent results were demonstrated in clinical studies, according to which the vaccine is effective in preventing HPV infections (depending on the producer and clinical outcome analyzed). They are also prevented by virus-like particles (VLPs) included in vaccines: genital warts (VLP 6 and 11) and intraepithelial lesions of the cervix, vagina, and vulva (VLP 16 and 18), according to **Figure 1**.

Approximately 60 countries included HPV vaccine in their national immunization programs[33]. The strategies of the global implementations of HPV vaccination are based on gender and risk (women, reduction of cervical cancer). That was the right and proper way precisely because it is a new prevention tool, which until then was driven by several hypothetical mathematical analyses of gains in quality of life and cost-effectiveness.

In June 2016, Garland et al.[34] published a systematic review on the impact and effectiveness of quadrivalent HPV vaccine (6,11,16, and 18) in the period of 10 years, showing the real world experience. The authors evaluated the use of the HPV quadrivalent vaccine in immunization programs nationwide, as well as its effectiveness and safety in nine countries: Australia, Germany, Belgium,

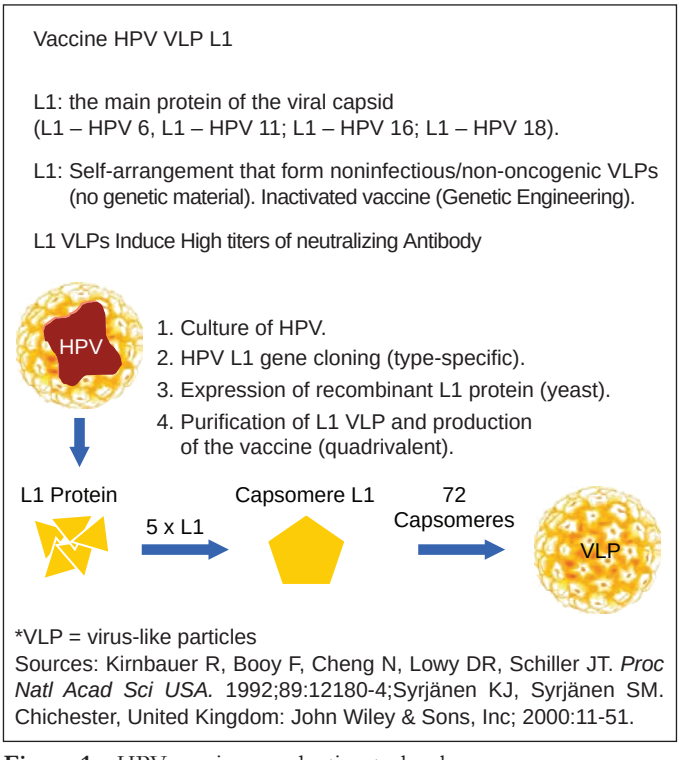

Figure 1 – HPV vaccine: production technology.

Canada, Denmark, USA, France, New Zealand, and Sweden in the period from 2007 to 2016.

In a short period, the first impact observed in all nine countries was genital warts decrease. Three to five years after the introduction of the vaccine, and when the vaccinated girls were in the age to start undergoing routine screening tests, a significant decrease in the prevalence of infections induced by HPV (6, 11, 16, and 18) in the regions of the cervix and vagina was observed. The incidence rates of genital warts, abnormal cytology, high-grade lesions, and AIS *(adenocarcinoma in situ*) have also declined.

The real world has shown robust results of effectiveness and safety in girls and young women. However, although there is the possibility of "herd protection," the infection and disease rates in men still prevail. Moreover, the group of MSM would not benefit from such programs and would also cease to receive this protection.

In April 2007, the Australian government was the first and most successful country to implement a national vaccination program against HPV (Immunise). The program was gradually launched in the second quarter of 2007, focusing on girls aged 12–18 years; from the third quarter of the same year until the end of 2009, the program covered (catch-up*)* young women aged 18–26 years. In 2010, after the phases of catch-up (12–18 years) of women, the vaccination program started to be extended to girls aged 12–13 years. The coverage has averaged 72.5% for the group of girls aged 12–17 years. However, when young women aged 18–26 years were assessed, the coverage in the group was between 38 and 53%. The study revealed that immunization coverage registered an important decline owing to the removal of the vaccination program from the schools.

The infection by HPV 6 and 11 decreased from approximately 75 to 88% in women aged 25 years or less, with a reduction of up to 92.6 % in cases of genital warts diagnosed among women aged less than 21 years after four years of implementation of the vaccination program. The percentage of new cases per year of genital warts in men, according to age in the preceding period (04 years) of the implementation of the vaccination program, was 13.7%. After four years of program implementation, the percentage was 6.3%, showing a reduction of 54%. A significant reduction of 72.3% in heterosexual men aged less than 21 years and no reduction for heterosexual men aged over 21 years or MSM was observed.

Despite the high vaccination coverage and evidence of "herd protection," in 2013 the vaccination program included boys in the first year of high school (aged 12–13 years). In 2013 and 2014, the program intended to cover boys between 14 and 15 years of age[35]. The overall results in women, and preliminary results in men are not yet available.

Several reasons were raised by the group responsible for the program to continue with the vaccination program:

- Evidence of clinical efficacy of HPV vaccine from the vaccination program in women was an important factor to extend it to men.
- Gender-neutral vaccination strategy ensures greater equity in the prevention of diseases related to HPV.
- Men should have the opportunity to reduce the individual risk of HPV disease through vaccination. n.

Vaccination of men, in addition to preventing the HPV-induced alterations, will bring the benefit of reducing the male virus reservoir, which will lead indirectly to a reduction in the risk of cervical cancer in women, breaking the chain of contamination.

CONCLUSION

Considering all the aspects mentioned in this editorial, we must return to the main question:

Why should boys and men receive a vaccine against HPV?

- HPV is worrying various agencies committed to sexual and reproductive health worldwide and in our country. In this context, man has been presented as a vector and reservoir of infection by HPV.
- There is no risk group for HPV.
- The main target groups for vaccination against HPV should be adolescent boys and girls.
- Preteens should receive full scheme before the onset of sexual activity; thus, they would be immunized if in contact with the viruses included in the vaccine, which would prevent being infected by HPV.
- Boys showed a better immunological response (that is, produced more antibodies to fight infection) when receiving the vaccine, compared to young adults. When we do an evaluation of natural infection and immune response induced by the vaccine, it is observed that boys had a better immune response. In other words, they developed more antibodies than girls and women.
- Men do not respond adequately to natural HPV infection and often do not generate immunological memory (B) and may be susceptible to other types of infection and the same type of virus of the previous infection.
- Men who have sex with unvaccinated women will not be protected.
- MSM are completely unprotected owing to vaccination programs exclusive for women.
- Vaccination of adolescents is a challenge in public health. However, the availability of vaccination campaigns in schools was effective and the most efficient way to achieve high vaccination coverage.
- Discussions on the ethics of immunization strategies against HPV targeted exclusively to women.
- Men should have the opportunity to reduce the risk of individual HPV diseases through vaccination, ensuring greater equity in the prevention of diseases related to HPV. Examples are seen in the past, such as immunization against rubella performed only in the female population, did not lead to the disease reduction. Many of these strategies were later replaced by universal vaccination of young people, regardless of gender (gender neutral), to achieve high levels of protection and indeed reduce the congenital rubella syndrome.
- With HPV vaccination available for boys in the public health network, we will enable a discussion (health education) for this

segment of the population. Men very often are disconnected from the actions on sexual and reproductive health education, such as consistent condom use, family planning, testing for syphilis, HIV, and hepatitis B (including vaccination), among many other actions. Prevention methods may be complementary and not mutually exclusive.

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Early impact in reducing cervical abnormalities in Campos dos Goytacazes, RJ, Brazil, after introduction of the quadrivalent HPV vaccine for girls 11–15: is it time to think about HPV vaccine in boys?

Impacto precoce na redução de anormalidades cervicais em Campos dos Goytacazes, RJ, Brasil, depois da introdução de vacina quadrivalente de HPV em meninas de 11 a 15 anos: é hora de pensar em vacinas HPV para rapazes?

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ABSTRACT

Introduction: Human papillomavirus (HPV) is a huge concern in public and private health. The prevention of this condition is the combination of the use of Papanicolaou smear test, condoms and HPV vaccines. Campos dos Goytacazes, RJ, is the first Brazilian municipality to implement in September 2010 the quadrivalent HPV vaccine (Gardasil®) for girls in the age group of 11–15 years, in a hybrid strategy of vaccination (schools and health centers). In 2014, the vaccination was started also for boys, at the same time that the Ministry of Health introduced it for girls. **Objective:** The aim of the study was to analyze the trends in reduction of low-grade cervical abnormalities five years after the introduction of the quadrivalent HPV vaccine in this municipality (primary outcome). Furthermore, this study evaluated the relative risk (RR) of each of the groups studied, in order to explain the protective effect of the vaccine (secondary outcome). **Methods**: The ecological analysis evaluated the impact of HPV vaccination as a protective factor against low risk of HPV abnormalities. Results of the Pap smear test obtained from the Brazilian Ministry of Health's Sistema de Informação do Câncer do Colo do Útero (SISCOLO) were categorized in low-grade abnormalities (LGA) and high-grade abnormalities (HGA). This preliminary study focused in LGA rates, which were estimated for a 1-month period and then stratified by four age groups (<20; 20–24; 25–30; >30 years) from 2007 to 2014. A quantitative comparison of LGA temporal trends before and after vaccination was done with Quasi-Poisson regression analysis. The protective effect of the vaccine over time was evaluated by calculating the RR in each age group. **Results:** The study showed significant decrease of more than 60% in LGA in women <20 years old, and less, almost 50% for the other groups. HPV vaccine was a protective factor, because the RR result was <0.0001 in all age groups. **Conclusions:** Although the studies show that the pre-HPV neoplastic lesions may be reversible spontaneously, it is undeniable that the vaccine contributes greatly to the high reduction rates, associated with high vaccination coverage. These results are the first in Brazil and in future may address the necessity to discuss the vaccination for boys in the context of the same results obtained in Australia.

Keywords: Papillomaviridae; human papillomavirus recombinant vaccine quadrivalent, types 6, 11, 16, 18; Papanicolaou test; immunization coverage; uterine cervical neoplasms.

RESUMO

Introdução: O papilomavírus humano (HPV) é uma grande preocupação na saúde pública e privada. A prevenção dessa condição é a combinação do uso do exame de Papanicolaou, de preservativos e de vacinas contra o HPV. Campos dos Goytacazes é o primeiro município brasileiro a implementar em setembro de 2010 a vacina quadrivalente contra o HPV (Gardasil®) para meninas de 11 a 15 anos de idade em uma estratégia híbrida de vacinação (escolas e centros de saúde). Em 2014, a vacinação começou para os meninos na mesma época em que o Ministério da Saúde introduziu a vacina para as meninas. **Objetivo:** O objetivo do estudo foi analisar as tendências na redução de anormalidades cervicais de baixo grau cinco anos depois da introdução da vacina quadrivalente de HPV na cidade (resultado primário). Além disso, esta investigação avaliou o risco relativo de cada grupo analisado, de maneira a explicar o efeito protetor da vacina (resultado secundário). **Métodos:** A análise ecológica avaliou o impacto da vacinação contra o HPV como um fator protetor contra o baixo risco de anormalidades pelo HPV. Os resultados do teste de Papanicolaou, obtidos por meio do Sistema de Informação do Câncer do Colo do Útero (Siscolo) do Ministério da Saúde, foram categorizados em anormalidades de baixo grau (LGA) e anormalidades de alto grau (HGA). Este estudo preliminar foi centrado nas taxas de LGA, as quais foram estimadas para o período de um mês e estratificadas por quatro grupos etários (<20; 20-24; 25-30; >30 anos) de 2007 a 2014. A comparação quantitativa das tendências temporais de LGA antes e depois da vacinação foi feita com análise de regressão de Quase-Poisson. O efeito protetor da vacina ao longo do tempo foi avaliado por cálculo do risco relativo em cada grupo de idade. **Resultados:** O estudo mostrou diminuição significativa de mais de 60% em LGA em mulheres de <20 anos de idade e de pelo menos cerca de 50% para os outros grupos. A vacina contra o HPV foi um fator de proteção, por causa do resultado do risco relativo de <0,0001 em todas as idades. **Conclusões:** Embora os estudos mostrem que as lesões pré-neoplásicas do HPV possam ser reversíveis espontaneamente, é inegável que a vacina contribuiu grandemente para as taxas elevadas de redução, associadas com a alta cobertura vacinal. Esses resultados são os primeiros no Brasil e podem dirigir no futuro a necessidade de discutir a vacinação dos meninos no contexto dos mesmos resultados obtidos na Austrália.

Palavras-chave: Papillomaviridae; vacina quadrivalente recombinante contra HPV tipos 6, 11, 16, 18; teste de Papanicolaou; cobertura vacinal; neoplasias de colo de útero.

INTRODUCTION

The human papillomavirus (HPV) is the most common infection of the genital tract. It is a sexually transmitted virus with a high outcome of morbidity and mortality, accounting for about 270,000 deaths of cervical cancer annually in women worldwide, 85% of them in low- and middle-income countries[1].

According to the World Health Organization (WHO), more than 819 million men and women (11.7% of the world population) are infected with this virus[2]. In Brazil, it is estimated that there are approximately 10 million infected with HPV and that 700,000 cases occur each year, and it is considered therefore an epidemy[3]. The risk of acquiring HPV infection during their lifetime for sexually active men and women is at least 50%. At age 50, at least 80% of women will have acquired genital HPV infection[4].

HPV is non-enveloped viruses with an icosahedral capsid, presenting circular double-stranded DNA encoding growth proteins. It belongs to a heterogeneous family of more than 100 different genotypes. Among these genotypes, 40 of them can infect the anogenital region[5]. They are classified as high-risk and low-risk HPV.

In molecular epidemiology, the most important HPV types are 16 and 18 (high risk), responsible for 70% of cases of cervical cancer, and types 6 and 11 (low risk), which account for 90% of cases of genital warts[6-8]. This virus can be also associated with other types of cancer, in addition to affecting the anogenital tract, such as the cancer on the laryngeal, respiratory, and digestive tracts[9,10].

The portfolio for the protection against HPV considers the combination of Papanicolaou smear (preventive) associated with the use of condoms and vaccination as state of the art in preventing the HPV infection. Currently, the Ministry of Health provides the vaccine freely for the entire country since 2014, only for girls. Alternatively, the municipality of Campos dos Goytacazes, in the state of Rio de Janeiro, Brazil, began in September 2010 free vaccination for all girls between 11 and 15 years old, living in the city, and expanded this statement to the boys in 2014[11]. Interestingly, Campos dos Goytacazes followed the national program protocol immunization against HPV in Australia.

OBJECTIVE

The aim of the study was to analyze the trends in the reduction of low-grade cervical abnormalities five years after the introduction of the quadrivalent HPV vaccine in this municipality (primary outcome). Furthermore, this investigation evaluated the relative risks (RR) of each of the groups studied in order to explain the protective effects of the vaccine (secondary outcome).

METHODS

Characteristics of the city

Campos dos Goytacazes is the municipality with the largest jurisdiction in the state of Rio de Janeiro, comprising 4,026 km^2 of territorial distribution, with an estimated population of 483.970 individuals according to the latest demographic census[12] (**Figure 1**). The economic activity is mainly supported by petroleum extract, which represents 80% of the Brazilian production.

Study description

An historical cohort was formed to evaluate the impact of HPV vaccination as a protective factor against low-risk HPV abnormalities. The results of the Pap smear test obtained from the Brazilian Ministry of Health database (SISCOLO system), were categorized in low-grade abnormalities (LGA) and high-grade abnormalities (HGA). This preliminary study focused in LGA rates, which were estimated for 1-month period and stratified by four age groups (<20; 20–24; 25–30; >30 years) from 2008 to 2014.

Place and duration of the study

The study was conducted at the Hospital Escola Álvaro Alvim (HEAA), the only hospital of the municipality responsible for conducting cervical smear tests by the Unified Health System (SUS). It is known for its total number of scans each year. An active research was carried out within each test in these eight years. In the case of presence of a positive test for low- or high-grade lesions, we categorized it according to the year of realization, age and degree of this lesion.

Ethical consideration

The study was conducted in compliance with the ethical principles originating in, or derived from, the Declaration of Helsinki, and in compliance with all Good Clinical Practices. The study was approved by the Ethical Committee of the Faculdade de Medicina de Campos (Protocol No. 33063214.4.0000.5244).

This is the first Brazilian ecological analysis of reduction of low-grade abnormalities related to HPV vaccination in the first city in Brazil that introduced the quadrivalent vaccine against HPV.

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Calculation of vaccination coverage

The coverage calculation was performed using a method described by Moraes et al.[13], which gives a relationship between the number of vaccinated and the total number of individuals of the same age. The female population used in the denominator was calculated for the years 2010, 2011, and 2012, according to Brazilian Institute of Geography and Statistics (IBGE). They were entered in the numerator of immunization data for the first and third doses (full course).

Calculation of the Pap smear coverage

According to the protocol of the Ministry of Health[14], every woman who has or has had sexual life must undergo the preventive periodic review, especially those between 25 and 64 years old. Initially, the test should be done annually. After two consecutive tests (with an interval of one year) with normal results, preventive tests can now be done every three years. Thus, considering the city's population of 119,000 women, it has to be about 4,000 who will be examined in this age group of 25 and 26 years (4,000 per age group). Considering two standard tests and performance after three years, we have a total denominator of 47,000 Pap smears per year to be held in the city to achieve 100% coverage screening.

Study design and data analysis

Data of Pap smears were collected from the HEAA database. The variables analyzed were age and the type of abnormalities grade. Data of Pap smears were collected from the HEAA database. The study included the first Pap smear of the patient in the timeline. The variables analyzed were age and the type of cervical abnormalities. Inclusion criteria were to be a resident of the municipality and a Pap smear with cervical abnormalities classified in low and high; exclusion criteria were indeterminate cervical abnormalities and sequential Pap smear after any cervical intervention.

Statistical analysis included a quantitative comparison of LGA temporal trends before and after vaccination, which was done with Quasi-Poisson regression analysis by using R archive network software®.

The same statistical analysis had calculated the protective effect of the vaccine on the timeline and was assessed by calculating the RR in each age group, and the aim of estimating the protection of the vaccine.

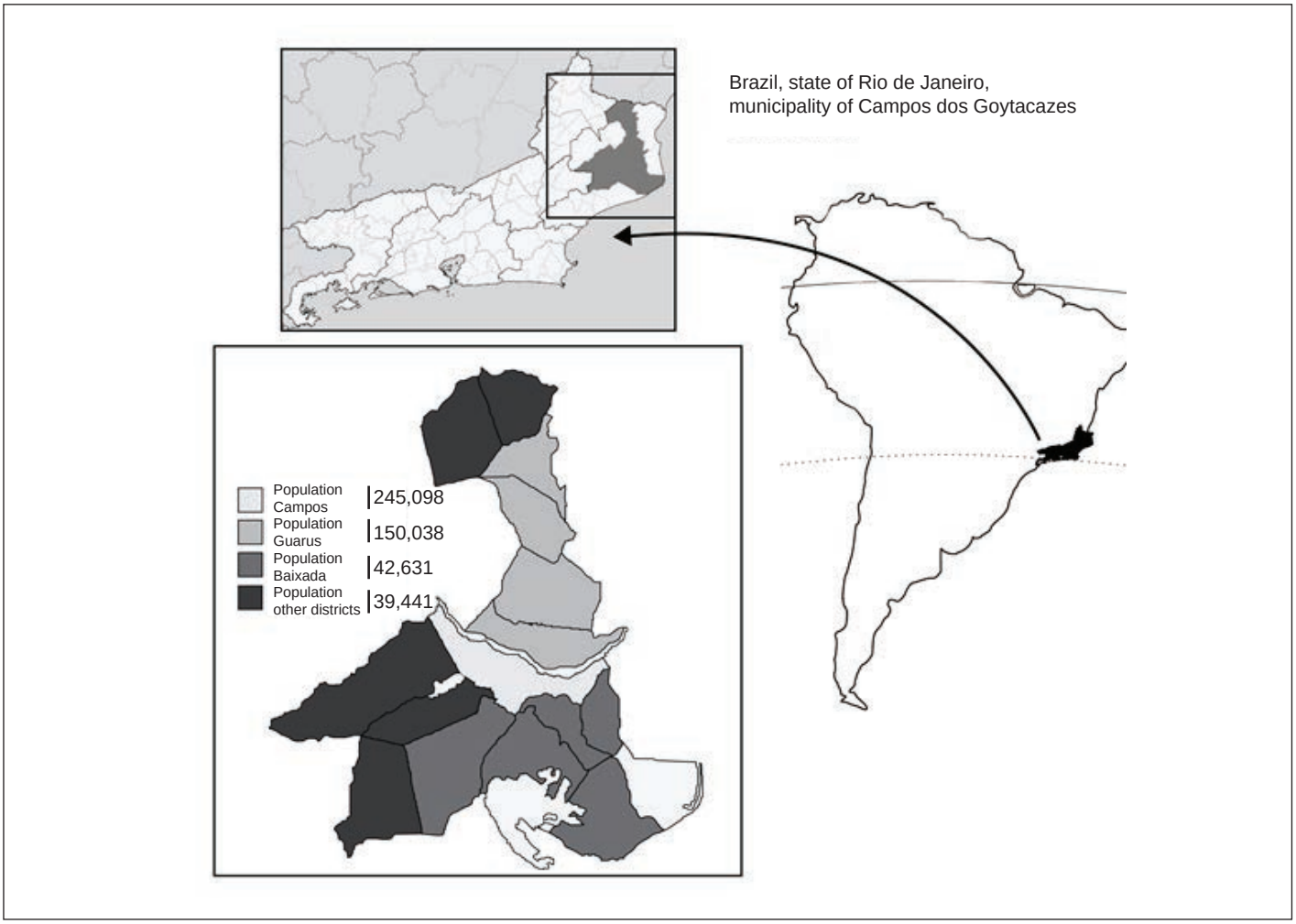


Figure 1 – Map of the municipality of Campos dos Goytacazes, state of Rio de Janeiro, Brazil.

RESULTS

Vaccination coverage

Table 1 summarizes the number of vaccines administered in 2010–2014. In this period, they were applied in about 103,326 doses, vaccination coverage variables. It should be noted that in 2010 the third dose of the vaccine had not been administered because of the beginning of the implementation of the vaccine in September 2010.

Another important comment appears about the period including the end of 2013 and beginning of 2014, with the implementation of the HPV vaccine by the Ministry of Health. Conversely, the federal government HPV vaccine schedule consisted of the alternative scheme of three doses in the time frame of zero, six and 60 months.

Table 2 shows the Pap smear coverage for each year, before and after the vaccination intervention. It should be noted that the Pap smear coverage of the city of Campos dos Goytacazes always had a level below the Brazilian average, which according to Brazilian surveys is about 65%[15].

Table 1 – Quadrivalent HPV vaccine coverage among adolescents by dose and year of vaccination, Campos dos Goytacazes, Brazil.

	11 years (vg/pop=vc)	12 years	13 years	14 years	15 years	AVC (%)
2010						
1st dose	1,583/4,083=38.7%	1,695/3,923=43.2%	2,321/3,969=58.4%	1,930/4,031=47.8%	3,219/4,280=75.2%	52.9%
3st dose	0	0	0	0	0	0.0%
2011						
1st dose	3,756/4,122=91.1%	3,121/3,960=78.8%	3,948/4,007=98.5%	3,210/4,069=78.8%	4,231/4,321=97.9%	89.02%
3st dose	2,650/4,122=64.2%	2,054/3,960=51.8%	3,218/4,007=80.3%	2,430/4,069=59.7%	2,980/4,321=68.9%	65.1%
2012						
1st dose	3,680/4,159=88.4%	3,223/3,996=80.6%	3,890/4,042=96.2%	3,460/4,105=84.2%	4,087/4,359=93.7%	87.9%
3st dose	2,423/4,159=58.2%	3,112/3,996=77.8%	2,980/4,042=73.70%	2,646/4,105=64.4%	2,530/4,359=58%	66.2%
2013						
1st dose	3,025/4,052=74.6%	3,834/4,161=92.1%	2,737/4,177=65.5%	1,995/4,133=48.3%	1,754/4,385=40%	64.1%
3st dose	1,209/4,159=29.8%	1,209/4,161=24.5%	1,366/4,177=32.7%	802/4,133=19.4%	987/4,385=22.5%	25.78%
2014						
1st dose	3,428/4,052=84.6%	3,054/3,996=76.4%	3,525/4,177=84.3%	425/4,133=10.2%	335/4,385=7.6%	52.62%
3st dose	424/4,052=10.2%	3,110/3,996=77.8%	343/4,177=8.2%	120/4,133=2.9%	104/4,359=2.3%	20.28%
Total doses	**22.178**	**22.358**	**21.646**	**16.917**	**20.227**	**103.326 doses**

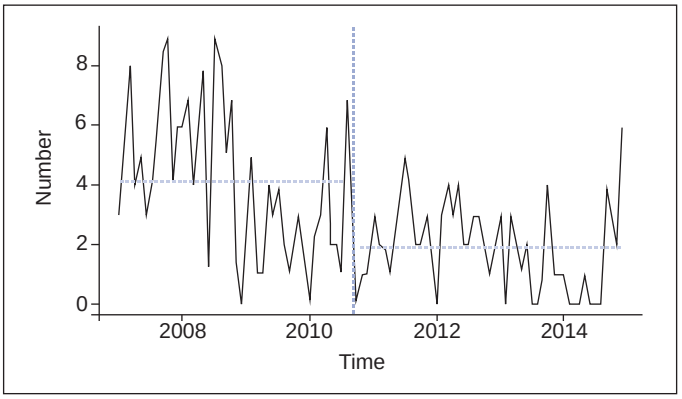
Vg: vaccines given; pop: adolescent population in the years 2010, 2011, 2012, 2013 and 2014; vc: vaccination coverage; AVC: average vaccination coverage.

Table 2 – Pap smear coverage and absolute number of low-grade and high-grade abnormalities, Campos dos Goytacazes, 2010–2014.

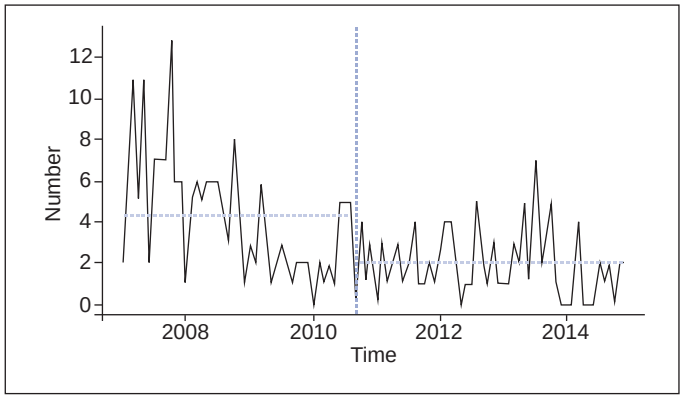
	Years	Pap test	Pap smear coverage (%)	LGA	HGA	LGA + HGA
2008	Total	21,120	44,90	346	78	424
	Up to 20	1,668		71	6	77
	21–30	4,118		117	17	134
	>30	15,334		158	55	213
2009	Total	22,108	47	205	65	270
	Up to 20	1,923		29	7	36
	21–30	3,647		76	13	89
	>30	16,538		100	45	145
2010	Total	24,438	51,90	197	112	315
	Up to 20	2,370		39	7	44
	21–30	4,276		52	24	82
	>30	17,792		106	81	187
2011	Total	27,780	59,10	210	123	334
	Up to 20	2,111		34	6	40
	21–30	4,500		59	29	88
	>30	21,169		117	88	205
2012	Total	18,931	42,40	171	67	238
	Up to 20	1,684		34	5	39
	21–30	3,407		53	10	63
	>30	13,840		84	52	136
2013	Total	27,485	58,40	143	41	184
	Up to 20	2,033		21	1	22
	21–30	4,919		58	2	60
	>30	20,533		64	38	102
2014	Total	24,337	51,70	92	70	160
	Up to 20	2,263		18	2	20
	21–30	4,234		26	7	33
	>30	17,840		48	61	107

LGA: low-grade abnormalities; HGA: high-grade abnormalities.

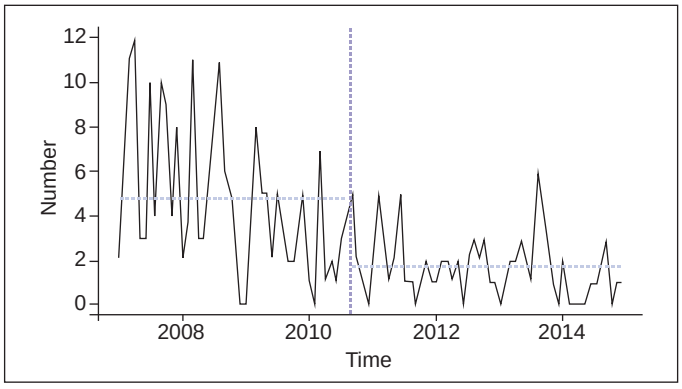
We recorded a significant decrease of 54.2%, considering all ages, in the incidence of LGA, by just comparing three years before and three years after the implementation of the quadrivalent vaccine (**Graphics 1, 2, 3 and 4**). However, the most important reduction was observed in the age group between 21 and 30 years (55.2%), followed by the age group above 30 years (53.2%), and at last the age group comprising the girls until 19 years old.



Graphic 1 – Low-grade abnormalities reduction in women aged up to 19 years old.



Graphic 2 – Low-grade abnormalities reduction in women aged 20–24 years old.



Graphic 3 – Low-grade abnormalities reduction in women aged 25–29 years old.

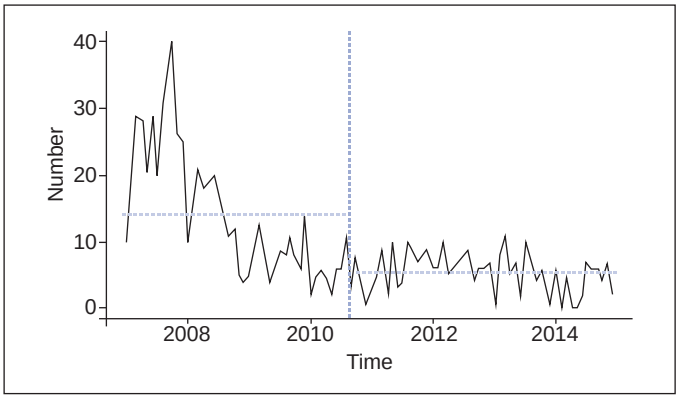
The next analysis comprised the RR evaluation, which can be observed in **Graphic 5**. In that analysis, it is undeniable that the vaccination played an important role in the reduction of the cervical preneoplastic abnormalities, with RR <0.0001 in all age groups. Again, it is not a surprise that the vaccination is a protective intervention mainly in the group with the women between 25 and 29 years old.

DISCUSSION

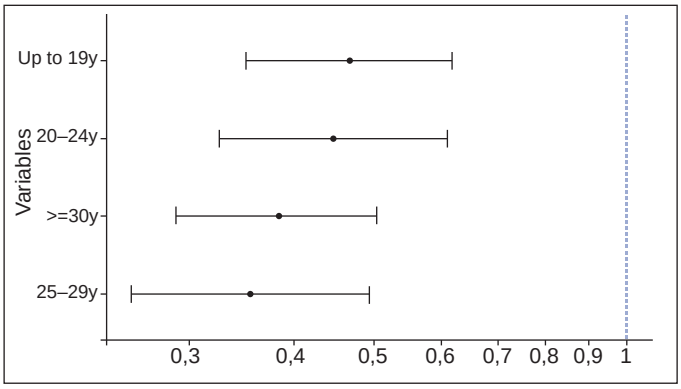
In this study, we sought to determine the possible effect of the HPV vaccine by reducing LGA in a middle city of the countryside of Brazil. So far, Campos dos Goytacazes was the first city in Brazil that implemented HPV vaccine until March 2014 with its own resources when the Ministry of Health introduced the vaccine for girls. In the same time the municipality introduced the vaccine for boys.

From 2010 to 2014, more than 100,000 doses of Gardasil® were administered and the technicians of the public health overcame some challenges, like the "hybrid" strategy of vaccination by using schools and public sites; the prejudice that the parents and relatives had associated with the vaccination, like sexual issues, among others. This strategy showed the reduction in genital warts, but the reduction in LGA was being conducted[16].

Once again, the implementation of this vaccine was challenging, but we tried to overcome it by reducing the LGA in at least 50% for all age groups. These findings are close to the preliminary study in Victoria, Australia, which showed some findings that allowed



Graphic 4 – Low-grade abnormalities reduction in women aged 30 years old and above.



Graphic 5 – Relative risk in purchasing low-grade abnormalities in women by age group.

reduction from 40,80 to 47,49% in some age groups. The same article showed the protective role of the HPV vaccine by the reduced RR[17].

After that, other studies showed similar results. In the United States of America, Hariri et al.[18] evaluated the effectiveness of Gardasil® in women who received more than one dose of vaccination. This interesting study showed the reduction in prevalence of the cervical abnormalities from 53.6% to 28.4% in women who were vaccinated at least 24 months before the trigger test.

A recent study from Sweden showed more important results in women aged 13–29 years old who were vaccinated for HPV and were followed for a HPV screening. In this investigation, the effectiveness of the vaccine was about 75% for those girls initiating vaccination before 17 years old[19].

There are several limitations in this study. First, there are some publications that address the role of the natural immunity in the regression of LGA. According to Schiffman and colleagues[20], the immune response to HPV naturally leads to virus destruction in three years; it is expected that there may be influence of chance in the improvement of the cases and this factor must be carefully excluded from the study. Another factor that should be carefully analyzed is the vaccination coverage, important to the achievement of successful strategies against HPV unfavorable outcomes. Finally, we must infer the role played by the coverage of the Pap smear test, we should monitor this indicator carefully to properly assess the impact of vaccination in improving the incidence of LGA and HGA.

CONCLUSION

Although the studies showed that the cervical LGA and HGA lesions might be reversible spontaneously, it is undeniable that the vaccine contributed greatly to the high reduction rates, associated with high vaccination coverage. These results are the first in Brazil and may address in the future the necessity to discuss the vaccination of boys in the context of the same results obtained in Australia.

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Conflict of interests

The authors reported no conflict of interests.

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Clinical-nutritional profile of HIV patients in a referral hospital in the northeast of Brazil

Perfil clínico-nutricional de portadores do vírus HIV atendidos em um hospital de referência do Nordeste brasileiro

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ABSTRACT

Introduction: The acquired immunodeficiency syndrome is a chronic, progressive, and degenerative disease. Since the introduction of antiretroviral therapy (ART), a significant reduction in mortality and morbidity rates has been recorded. However, patients may present cardiometabolic changes throughout the treatment. **Objective:** To assess the clinical and nutritional profile of HIV patients treated in a referral hospital in northeast Brazil. **Methods:** Descriptive cross-sectional study performed in inpatient and outpatient units for infectious and parasitic diseases at the Hospital of the Universidade Federal de Pernambuco Nutritional and clinical variables were assessed. The sample was a non-probabilistic convenience sample. The data were entered into Excel for Windows® and analyzed using SPSS® software (version 13.0), with a 5% level of significance set for the rejection of the null hypothesis. **Results:** In total, 110 patients were assessed (54.5% in infirmary). The mean age was 39±11 years, with15.4% of the individuals aged 50 years or more. Of the total, 64.5% were male. Among the patients in the ward, 52.5% had metabolic complications; 1.6% had lipodystrophy, and 15% had wasting syndrome, while ambulatory patients showed values of 76%, 4%, and 4%, respectively. Time of diagnosis, indication, time, and adherence to ART showed no differences between the groups. **Conclusion**: The metabolic changes related to cardiovascular risk factors and the preservation of nutritional status prevailed in ambulatory patients, while the clinical-nutritional profile of hospitalized patients showed energy-protein malnutrition as the most common complication, with greater involvement of the immune system and increased frequency of opportunistic infections and gastrointestinal symptoms. The use of licit and/or illicit drugs, the lack of knowledge about the importance of medication, and the negligence in care were the main reasons for the irregular use of ART.

Keywords: wasting syndrome; lipodystrophy syndrome associated with HIV; acquired immunodeficiency syndrome.

RESUMO

Introdução: A AIDS caracteriza-se como doença degenerativa, crônica e progressiva. Após a introdução da terapia antirretroviral (TARV), observou-se uma importante redução na morbimortalidade. No entanto, ao longo do tratamento, os indivíduos podem apresentar alterações cardiometabólicas. **Objetivo:** Avaliar o perfil clínico-nutricional de portadores de HIV atendidos em um hospital de referência do Nordeste brasileiro. **Métodos:** Estudo do tipo descritivo transversal realizado no ambulatório e na unidade de internação de Doenças Infecto-Parasitárias (DIP) do Hospital das Clínicas da Universidade Federal de Pernambuco. Foram avaliadas variáveis nutricionais e clínicas. A amostra foi não probabilística por conveniência. Os dados foram digitados no programa Excel para Windows® e as análises realizadas no Programa SPSS® versão 13.0, com nível de significância de 5% para rejeição de hipótese de nulidade. **Resultados:** Foram avaliados 110 pacientes (54,5% em enfermaria). A média de idade foi 39±11 anos, e 15,4% possuíam 50 anos ou mais. Do total, 64,5% eram do sexo masculino. Entre os pacientes de enfermaria, 52,5% apresentaram complicações metabólicas; 1,6%, lipodistrofia e 15%, síndrome consumptiva, enquanto os pacientes ambulatoriais apresentaram valores de 76%, 4% e 4%, respectivamente. Tempo de diagnóstico, indicação, tempo e adesão à TARV não mostraram diferenças entre os grupos. **Conclusão**: As alterações metabólicas relacionadas a risco cardiovascular e à preservação do estado nutricional prevaleceram nos pacientes ambulatoriais, enquanto o perfil clínico-nutricional dos internados mostrou a desnutrição energético-proteica como a complicação mais frequente, com maior comprometimento do sistema imunológico e maior frequência de infecções oportunistas e sintomas gastrointestinais. O uso de drogas lícitas e/ou ilícitas, a falta de conhecimento sobre a importância da medicação e a negligência no autocuidado foram os principais motivos para o uso irregular da TARV.

Palavras-chave: síndrome de emaciação; síndrome de lipodistrofia associada ao HIV; síndrome da imunodeficiência adquirida.

INTRODUCTION

The identification of the acquired immunodeficiency syndrome (AIDS) has become a milestone in the history of humanity, highlighting it as one of the emerging infectious diseases by the great magnitude and extent of the damage caused to the population. AIDS behaves like a degenerative, chronic, and progressive disease, which is accompanied, during its evolution, by weight loss, and malnutrition of multifactorial origin[1].

In Brazil, the policy of universal and free distribution of antiretroviral drugs to infected people with the human immunodeficiency virus (HIV), stands out as an effective strategy to combat AIDS, which led to the introduction of antiretroviral therapy (ART). ART is the combination of three or more drugs that can significantly reduce morbidity and mortality rates and the prevalence of malnutrition among people living with AIDS, making it present characteristics of a chronic disease and require their carriers to maintain proper antiretroviral therapy[2].

One of the challenges has been to seek patients' adherence to established protocols, since non-compliance undermines both the effectiveness of the treatment and the spread of an epidemic by certain types of multidrug resistant viruses, with clinical and nutritional repercussions. It must be said that non-adherence has become a major issue in debates in the area, given the high number of patients who

The study was conducted at the Hospital of the Universidade Federal de Pernambuco (HC-UFPE) – Recife (PE), Brazil.
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do not properly use the scheme of medications prescribed or completely abandon their use[3].

ART is changing the nutritional status of patients with HIV. Before the advent of ART, the deficits of vitamins and minerals and energy-protein malnutrition were associated as the greatest nutritional problems of the time, with malnutrition accounting for 80% of the mortality of AIDS patients[4].

Today, with advances in ART, people living with HIV commonly present a variety of adverse metabolic events throughout the infection, characterized by dyslipidemia changes in body fat distribution, insulin resistance, glucose intolerance (GI), and high blood pressure. Even in the era of ART, weight loss, and depletion of body cell mass are still observed in this population. The incidence of alterations in nutritional status, both obesity induced by changes in body composition and malnutrition caused mainly by non-adherence to ART, tends to increase, and the monitoring of nutritional status of asymptomatic, symptomatic, or patients with changes in body weight is essential[5].

A detailed assessment of nutritional status, carried out considering the energy needs, exacerbated catabolism, metabolic changes, and understanding of peculiarities that this population is exposed, not only allows the tracking of malnourished patients with metabolic disorders, as well as possible interventions for recovery of nutritional status and consequent better survival[5].

METHODS

This is a descriptive, cross-sectional study. The data were collected in direct interview with patients and caregivers and through other information transcribed from medical records.

The research was conducted with patients of both genders with HIV, admitted in the ward of Infectious and Parasitic Diseases (IPD), and in the outpatient clinic of IPD at the Hospital of the Universidade Federal de Pernambuco (HC-UFPE) during the period ranging from June to November 2014. The sample was non-probabilistic for convenience, composed of all patients treated in the clinic and hospitalized in the general ward of HC-UFPE who were eligible and agreed to participate in the research during that time frame. Exclusion criteria were patients who were in use of corticosteroids and anabolic steroids; had undergone liposuction or liposculpture in the previous six months; who had fluid retention (ascites and edema); pregnant women; patients in palliative care; with impossibility of locomotion; and patients who had cognitive changes that hindered the obtaining of relevant information.

The research was conducted after approval from the Research Ethics Committee of the Universidade Federal de Pernambuco (Opinion No: 624.987/CAAE: 27561214.9.0000.5208), in obedience to resolution No. 466/12 of the National Health Council on "Research Involving Human Subjects". Patients were informed by the researcher on the procedures, risks, and benefits of the research, and their voluntary participation by signing the free and informed consent.

Participants were weighed using a digital electronic scale, platform type, by Filizola®, with a maximum capacity of 150 kg and accuracy of 100 g, and height was measured by stadiometer attached to the scale platform with a capacity of 1.90 m ± 1 mm. With weight and height measurements, the body mass index (BMI) was calculated, which has been classified in accordance with the values indicated by the World Health Organization (1998)[6] for adults. For the elderly (>60 years), the reference was Lipschitz (1994)[7]. The percentage of weight loss was assessed in the period prior to the hospitalization or treatment in the outpatient clinic. It was obtained using the following formula: weight loss (%) = (usual weight – current weight) × 100 ÷ usual weight. The classification followed the parameters of Blackburnet and Thornton[8]. Usual weight was based on the usual weight of the patient when he was healthy, and normally performing their routine activities.

Measurement of waist circumference (WC) was made from the midpoint between the costal margin and the iliac crest, using a non-extendible metric fiber tape with divisions in centimeters, accurate to millimeters. The cutoff points for increased risk of the International Diabetes Federation (2005) were used[9].

The measurement of arm circumference (AC) was performed according to the technique proposed by Kamimura (2006)[10]. The triceps skinfold thickness (TSF) was obtained with a Lange adipometer®, according to recommendations of Lee and Nieman (1995)[11]. To obtain the arm muscle circumference (AMC), the formula by Gurney and Jellife (1973)[12] was used, which utilizes the AC and TSF variables. The classification of the TSF, AC, and AMC was compared to the standard of reference: up to 74.9 years[13].

The measurements were performed in duplicate, and it was assumed a variation of 0.5 cm for the measures of height, AC, WC, and 100 g for measurements of weight. If the values obtained differed from the previously prescribed margin of error, a third measurement was carried out, adopting the average of the two values closest to each other.

We evaluated the serum by their respective methods: hematocrit, hemoglobin, mean corpuscular volume (MCV), leukocytes (Pentra 120), albumin (Beckman Coulter Automation), fasting blood glucose (God – DBP DiaSys/Beckman Coulter Automation), total cholesterol and fractions, triglycerides (God – DBP DiaSys/Beckman Coulter Automation), review of total lymphocyte count, and CD4 T lymphocytes (flow cytometry/Facsalibur-Multitesta).

For the identification of opportunistic infections (OIs) and diseases associated with HIV, the clinical diagnosis made by the medical team and recorded in the patient record was consulted.

Patients were asked about the regular use or not of ART. When patients reported irregular use, they were questioned about the possible factors responsible for irregularities.

Presence of wasting syndrome was considered when the individual was involuntarily losing weight greater than 10%, associated or not with fever documented for more than 30 days, weakness, and diarrhea (>2 bowel movements per day for more than 30 days). Presence of lipodystrophy was characterized when WC >102 cm for men and >88 cm for women and/or had fat accumulation in the neck, upper back, or chest. Diagnosis was given by patient self-report and by means of the observation of abnormal deposits of body fat.

Assessments of changes mentioned above were made by consulting records, direct questions to patients about changes in physical condition over the years, anthropometric assessment, physical examination, fasting blood glucose, and lipid profile.

For the diagnosis of diabetes and GI, the cutoff points of the Brazilian Society of Diabetes were used, 2013–2014[14], and for the identification of dyslipidemia, the cutoff points of the Brazilian Society of Cardiology[15].

Data were entered into Excel for Windows®, and the analysis conducted in SPSS®, version 13.0. Continuous variables were tested for normality of distribution using the Kolmogorov–Smirnov test. The variables with normal distribution were described as mean and standard deviation, while those with non-normal distribution were presented as medians and their interquartile ranges.

In statistical inference tests, the proportions were compared using the χ^2 test of Pearson. The means of the variables with normal distribution were compared by Student's *t* test (two variables), and the Mann–Whitney test (two variables), and the Kruskal–Wallis test (more than two variables) when the criterion of normality and/or homoscedasticity had not been met. A significance level of 5% for the rejection of the null hypothesis was used.

RESULTS

We evaluated 110 patients, and of these, 54.5% were from the ward and 45.5% from the clinic. The mean age was 39±11 years, being 23.7% between 18 and 29 years, 30.9% between 30 and 39 years, 30.0% between 40 and 50 years, and 15.4% with age greater than 50 years. In total, 65.5% were male. **Table 1** shows the clinical characteristics of the study population.

The following reasons were cited for the irregular use of ART: use of legal drugs and/or illicit drugs (17.3%), lack of knowledge about the importance of medicine, negligence in care (11.7%), forgetfulness (9.9%), depressive disorders and/or denial of the disease (6.3%), and others (54.8%).

The most common reasons that led to the hospitalization were bacterial infections (32.47%), diseases caused by protozoans (16.80%), diseases caused by viruses (12.20%), neoplasms (8.80%) and causes that were not directly linked to HIV infection (29.74%). In the clinic, most frequent co-infection related to HIV was the Herpes Zoster, with a percentage of 3.5%. Patients with no apparent pathologies were 62.5%.

The presence of gastrointestinal symptoms in the week prior to participation in the study was also analyzed. In the ward, 79% of patients reported some related clinical manifestation: diarrhea (15.8%), nausea (15.8%), appetite loss (11.6%), and vomiting (11.6%) were the most reported. In the clinic, these events were reported by 50% (n = 25), being abdominal pain (10%), heartburn (44%), nausea, and bloating (6.95%) the most prevalent.

Some metabolic abnormalities were identified: diabetes mellitus, dyslipidemia, and hypertension accounted for 5%, 37.5%, and 5% in the ward and the 6%, 52%, and 8% in the clinic, respectively. Among patients in the clinic, 10% showed GI. Wasting syndrome was found in 15% of the patients in the ward and in 4% in the clinic, while lipodystrophy was found in 1.6% and 4%, respectively, in the two study sites.

Tables 2 and **3** show the anthropometric variables and the nutritional status of the population studied, respectively. **Table 4** describes the surveyed biochemical variables.

Stratifying the levels of T-CD4 (cells/mm3): in the ward, 82.8% patients obtained values of T-CD4 < 350 and 17.4% > 350; at the clinic 66% of patients obtained T-CD4 > 350 and 34% < 350. The value of 350 cells/mm^3 was used as a cutoff point as it is used in notifications of illness and orientation to the beginning of ART.

DISCUSSION

In the population studied, the majority were male (64.5%), with an average age of 39±11 years, being the most affected age group between 30 and 39 years. This profile is similar to that found in studies by Castro et al. (2013)[16] e Schuelter-Trevisol et al. (2013)[17], in which the majority of the population was composed of young adults and males. The data were also in accordance with recent data from the Epidemiological Bulletin of 2014[18], which showed 65% of the cases in men and in the predominant age range from 25 to 39 years, which may be justified by the correspondence to the period of greater sexual activity.

Table 1 – Clinical variables of patients with HIV from ward and clinic of the HC-UFPE Recife, in the year 2014.

	Site		p value
	Ward	Clinic	
Time for diagnosis (years)*	Median (IQ) 2 (0.20–8.70)	Median (IQ) 2 (1.12–9.25)	0.070
Indication of ART**	n (%) 56 (93.30)	n (%) 44 (88.00)	0.507
Time of ART (years)*	Median (IQ) 0.8 (0.30-7.00)	Median (IQ) 2 (1.00-8.00)	0.100
Regular use of ART**	n (%) 30 (50.00)	n (%) 29 (56.00)	0.246
Current scheme	n (%)	n (%)	
2NRTI+NNRTI	34(60.71)	21 (47.80)	
2NRTI+IP/r	23 (23.20)	11 (25.00)	0.130
2NRTI+IP	4 (7.14)	2 (4.54)	
Others	5 (9.00)	10 (22.72)	

ART: Antiretroviral therapy; IQ: Interquartile Range; NRTI: Nucleoside Reverse-Transcriptase Inhibitors; NNRTI: Non-Nucleoside Reverse-Transcriptase Inhibitors; IP: Protease Inhibitor; r: Ritonavir.
*Student's *t* test (mean and standard deviation); **Fisher's exact test.

Table 2 – Anthropometric variables of patients with HIV from ward or clinic of the HC-UFPE Recife, in the year 2014.

	Site		p value
	Ward	Clinic	
Usual Weight (kg)*	63.86±13.96	66.06±13.66	0.419
Current Weight (kg)*	55.57±14.14	67.81±11.17	<0.001
Body mass index (kg/m^2)*	20.00±3.90	25.21±4.55	<0.001
Arm Circumference (cm)*	24.16±4.16	28.83±4.07	<0.001
Triceps skinfold thickness (mm)**	9.0 (6.00–13.90)	15.5 (7.00–26.00)	0.001
Arm muscle circumference (cm)	20.81±3.54	23.44±3.40	<0.001
Waist circumference (cm)	–	90.38±9.96	–

*Student *t* test (mean and standard deviation); **Mann-Whitney test (median and interquartile range).

Table 3 – Classification of nutritional status of patients with HIV from ward or clinic of the HC-UFPE Recife, in the year 2014.

Variables	Site		p value
	Ward n (%)	Clinic n (%)	
Body Mass Index*			
Malnutrition	24 (41.40)	2 (4.10)	
Eutrophia	27 (46.60)	23 (46.90)	<0.001
Overweight	7 (12.10)	24 (49.00)	
Arm Circumference*			
Malnutrition	51 (85.00)	24 (68.20)	
Eutrophia	9 (15.00)	17 (34.00)	<0.001
Overweight	0 (0.00)	9 (18.00)	
Triceps Skinfold Thickness*			
Malnutrition	44 (73.30)	25 (50.00)	0.030
Eutrophia	5 (8.30)	5 (10.00)	0.030
Overweight	11 (18.30)	20 (40.00)	0.030
Arm Muscle Circumference**			
Malnutrition	49 (81.70)	22 (65.10)	<0.001
Eutrophia	11 (18.30)	27 (55.10)	
Waist circumference*			
High Risk	–	27 (54.00)	–
%Weight Loss*	14.56±8.70	7.02±4.97	0.021

*χ^2 Pearson test; **Yates Correction.

Table 4 – Biochemical variables of HIV patients from ward or clinic of HC-UFPE - Recife, in 2014.

	Site		p value
	Ward	Clinic	
Hematocrit (%)*	31.20±6.74	40.53±4.66	<0.001
Hemoglobin (g/dL)*	10.41±2.29	13.61±1.58	<0.001
MCV (fl)*	88.88±12.30	95.80±10.47	0.002
Leukocytes (/mm^3)*	5,064.08±2,808.02	6,359.18±2,002.41	0.008
Typical lymphocytes (%)*	22.82±11.27	31.17±9.50	<0.001
Albumin (g/dL)	2.81±0.84	–	–
Total cholesterol (mg/dL)*	151.24±66.10	176.35 ±41.06	0.043
HDL cholesterol (mg/dL)*	36.96±17.17	46.98±12.87	0.005
LDL cholesterol (mg/dL)*	87.72±49.44	94.26±24.80	0.531
Triglycerides (mg/dL)*	138.23±72.23	145.30±78.36	0.689
CD4+ (/mm^3)*	185.66±224.50	519.53±317.70	<0.001

MCV: Mean Corpuscular Volume; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; CD4+: CD4 T lymphocytes (immune cells); *Student *t* test (mean and standard deviation).

Ideally, the diagnosis of HIV infection is done early, soon after infection. However, the low specificity of the seroconversion of the virus, the long asymptomatic period or the presence of symptoms similar to typical viruses infections, such as avian flu, make this diagnostic process difficult. The definition of delayed diagnosis widely accepted is a CD4 cell count in patients below 350 cells/ml or symptoms compatible with AIDS[19]. In this study, the time of diagnosis showed a significant difference between patients from the ward and the outpatient clinic. This fact can be explained by the non-investigation of diagnosis as early or late.

The indication of ART showed no significant difference between patients of both origins (93.3% in ward and 88% in the clinic). Studies that compare both these two environments are scarce in the literature. In a study that examined 476 medical charts and schedules of compulsory notification (outpatients), 64.1% had indication and made use of the anti-retroviral medication[17]; in a study that assessed only patients admitted (n=50), 68% had indication and made use of the aforementioned medication[16]. Among those admitted to the ward, factors for no indication of ART were related to admissions to treat conditions unrelated to HIV and good individual immune performance. Those from the clinic may have a reduced indication of ART due to recent diagnosis and good immune performance. Regarding the regularity in the use of ART, it was expected that the deficiency was more pronounced in the ward than in the clinic, because the main reasons for hospitalization were related to the onset of pathologies related to AIDS. Although there is no difference in the use, a significant portion of the population admitted was observed to have been diagnosed very recently or during hospitalization, already with an indication of ART, and these were advised and supervised daily by health professionals, which guaranteed the proper use of medication. Another important aspect is that over half of the patients, in both places, were not properly using the medication prescribed, as evidenced by Seild et al. (2007)[20]. In another study conducted at the Specialized State Center in Diagnosis, Care and Research (CEDAP), reference unit for care in HIV/AIDS in the city of Salvador, among the 216 patients

followed up for one year, 25% did not use correctly and regularly the antiretroviral drugs[21].

The medical literature refers the difficulties of adherence to treatment are derived, in part, to the complexity of ART, to the extent that some medicines need to be ingested with food, other fasting, or in temporal sequences in combination with other medicines, which requires organization and commitment of the patient in relation to its treatment, in addition to effects caused by the drug combination. In addition to these factors, studies have demonstrated a negative association between moderate consumption/abuse of alcohol and other drugs and adherence.[22].

The presence of gastrointestinal clinical manifestations was common in a significant proportion of the patients, both in the ward (79%) as in the clinic (50%). In the literature, we found the main causes for such disorders, those being the influence of HIV in intestinal cells, the presence of OIs, the high incidence of parasitic diseases, including the intestines, and the side effects of ART[23].

The presence of OI or defining pathologies of AIDS (diseases that are associated to the biochemical tests and assist in the diagnosis of the syndrome) were more frequent in patients hospitalized. These conditions can bring serious clinical, nutritional, and physiological repercussions, requiring more discerning treatment and monitoring that, many times, can only be carried out with the patient hospitalized. In the clinic, individuals present a better immune status, being less prone to OIs and, on the other hand, more susceptible to diseases that are not related to HIV and cardiovascular diseases, results similar to those of Da Silva et al.[24].

The percentages of metabolic complications were 52.5% in the ward and 76% for patients in the outpatient clinic. Similar values were found in other studies, in which the authors suggest that such complications may be related both to ART, since different regimes of therapy and time of use have promoted different changes in metabolism, just as presence of the infection itself. Metabolic complications linked to HIV can improve after changes in lifestyle, since proper nutrition and regular physical activity can promote the control of these changes[25].

Lipodystrophy found in HIV infection is considered an adverse effect to the use of ART, characterized by the redistribution of body fat with fat reduction in peripheral region and an increase in the abdominal region. This adverse effect was found in 1.6% of patients in the ward, and 4% of the clinic, although such percentages are considered low compared to other studies such as Diehl et al.[26], which found 55% of lipodystrophy. However, when analyzing the BMI and WC of outpatients, high values of these parameters were found. In contrast, the values of AC and TSF revealed a high percentage of malnutrition, which may suggest a redistribution of body fat.

When assessing the anthropometric variables (BMI, AC, AMC, TSF) and its nutritional classifications, it was found that the outpatients had higher values of these parameters, corroborating the literature, in which patients who had a better disease control and better immune status were more likely to be eutrophic or overweight. In contrast, in those whose infection was advanced, with the presence of OIs and depletion of the immune system, were more prone to malnutrition and wasting syndrome[27].

As for the biochemical variables, hospitalized patients had lower hemoglobin, hematocrit, MCV, leucocytes, and lymphocytes in relation to patients in the clinic. It is known that many factors can contribute to changes in these values, among them the very marrow suppression caused by HIV, OIs, malnutrition, and others, leading to anemia or even pancytopenia, which are hematological changes more frequent in these patients[28].

Diehl et al. (2008)[26] studying patients who lived with HIV treated in the outpatient clinic, found values of CD4 (431.4 ± 254.5) similar to those of the outpatients in this study (519.53 ± 317.7), and higher than those of the ward (185.66 ± 224.5). The values of total lymphocytes and CD4 show improved immune performance in clinic patients. This aspect may have directly influenced on the differences in nutritional profile, and found a higher number of cases of malnutrition in patients in the ward, and eutrophication or excess weight among those who attended the outpatient clinic. The latter often were carriers of the virus, but had not developed the syndrome (AIDS) and, consequently, had no depletion of nutritional status.

It is important to emphasize the importance of nutritional monitoring, through which it is possible to educate and provide proper nutrition to maintain or improve the nutritional status of patients with HIV.

CONCLUSION

Despite the diagnosis, time of use, and regularity of ART showing no significant difference between inpatients and outpatients, the metabolic changes related to cardiovascular risk and preservation of nutritional status prevailed in outpatients, whereas the clinical and nutritional profile of admitted patients showed the protein-energy malnutrition as the most common complication, with greater involvement of the immune system and increased frequency of OIs and gastrointestinal symptoms. The use of licit and/or illicit drugs, the lack of knowledge about the importance of medication, and the negligence in self-care were the main reasons for the irregular use of ART.

In the face of the findings, it is important to emphasize that every patient infected with HIV should be directed to the dietician soon after diagnosis, to assess their nutritional profile and to determine necessary diet-therapeutic interventions individually, to treat possible nutritional deficiencies and to maintain or restore the nutritional status, promoting a better quality of life.

Conflict of interests

The authors reported no conflict of interests.

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Analysis of the sexual exposure trends to human immunodeficiency virus - HIV in Teresina, Piauí state

Análise das tendências de exposição sexual ao vírus da imunodeficiência humana - HIV em Teresina, Piauí

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ABSTRACT

Introduction: In Brazil, approximately 60% of cases of acquired immunodeficiency syndrome (AIDS) are associated with some form of sexual contact, of which almost half are due to unprotected sex between men who have sex with men. However, this profile has been changing, focusing particularly among avowedly heterosexual people living in peripheral areas of large cities and in the interior of the states. **Objective:** To analyze the epidemiological trend of sexual exposure to human immunodeficiency virus (HIV) in the city of Teresina, Piauí State. **Methods:** A time series, descriptive, retrospective, longitudinal, study with a quantitative approach was carried out based on the analysis of cases reported by the National System Diseases Notifications (SINAN). **Results:** Between 1987 and 2013, Piauí presented a total of 3.574 AIDS cases; Teresina city is following the national trends of HIV transmission, especially in relation to the heterosexual tendency, which represents more than 50% of reported cases. Notifications among men were preponderant: 71.9% of cases, which accumulated an average of 92.4 notifications. The proposed linear trend model is explained in about 85% of the reported data and shows a rise in cases among men. **Conclusion:** The proposed objective was achieved, demonstrating that there is a heterosexualization trend of the transmission of HIV/AIDS in Piauí. Teresina follows the configuration of the AIDS epidemic that occurs throughout Piauí. There is a trend of heterosexual transmission of the disease, especially among men.

Keywords: HIV; health vulnerability; men's health.

RESUMO

Introdução: No Brasil, a epidemia da síndrome da imunodeficiência adquirida (AIDS) tem aproximadamente 60% dos casos associados à transmissão sexual, sendo quase metade decorrente de relações desprotegidas entre homens que fazem sexo com homens (HSH). No entanto, esse perfil vem mudando, incidindo, principalmente, sobre pessoas declaradamente heterossexuais, residentes em regiões periféricas das grandes cidades e no interior dos estados. **Objetivo:** Analisar a tendência epidemiológica de exposição sexual ao vírus da imunodeficiência humana (HIV) em Teresina, Piauí. **Métodos:** Realizou-se um estudo descritivo, retrospectivo, longitudinal, censitário, de série temporal, com abordagem quantitativa, a partir da análise dos casos notificados pelo Sistema Nacional de Agravos de Notificações (SINAN). **Resultados:** No período de 1987 a 2013, o Piauí registrou 3.574 casos de AIDS; Teresina está seguindo as tendências nacionais de transmissão do HIV, principalmente no que se refere à tendência heterossexual, que representa mais de 50% dos casos notificados. Predominam as notificações entre homens: 71,9% dos casos, com média de 92,4 notificações. O modelo de tendência linear proposto é explicado em cerca de 85% dos dados notificados e mostra uma ascensão dos casos entre homens. **Conclusão:** O objetivo proposto foi alcançado, demonstrando que no Piauí ocorre a tendência de heterossexualização da transmissão do HIV/AIDS. Teresina segue a configuração da epidemia da AIDS que ocorre em todo o Piauí. Há uma tendência de heterossexualização da transmissão da doença, especialmente entre os homens.

Palavras-chave: HIV; vulnerabilidade em saúde; saúde do homem.

INTRODUCTION

The human immunodeficiency virus (HIV) is a lentivirus that causes the acquired immunodeficiency syndrome (AIDS), which brings about the progressive failure of the immune system, facilitating opportunistic infections and cancers. The invasion of the body may occur by hematogenous, sexual, and/or vertical routes. Thus, contact with body fluids, blood, semen, vaginal content, pre-ejaculatory fluid, breast milk, as well as unprotected sex, sharing contaminated needles or syringes, and perinatal transmission are characterized as the main forms of dissemination of the virus[1].

The first report on the AIDS epidemic happened in the US when a high number of cases in male adults, especially those who adopted homosexual practices, were identified. The increasing number of new cases, especially in poorer countries, led to the conclusion that it was a new disease, probably of infectious and contagious etiology[2].

In Brazil, approximately 60% of reported cases are associated with some form of sexual contact, and almost half are due to unprotected sex among men who have sex with men (MSM). At the beginning of the epidemic, this population group concentrated the most cases; then, AIDS spread among injecting drug users, hemophiliacs and people receiving blood transfusions or blood products. From the mid-1990s of the 20th century, the epidemic has spread among heterosexuals, which is currently the sexual exposure subcategory with the highest number of reported cases of the disease[2].

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According to the Brazilian Epidemiological Bulletin[3] of 2011, there were 241,469 deaths from AIDS in the country from 1980 to 2010. These data reflect the importance of studies on the population at risk and on that affected by HIV. Brazil has shown significant changes in the epidemiological situation of AIDS: there has been a considerable increase in heterosexual transmission and in the number of affected women, thus creating a new profile of people living with HIV/AIDS, which characterizes the trends of heterosexualization and feminization of this epidemic, according to Passos et al.[1] and Felix and Ceolim[2].

It has been observed that people with lower education and income have been affected, which was termed as the "pauperization process," as well as the increase in cases among individuals in the extreme age groups (young and old). In a broad social and geographical perspective, it has also been observed what has been termed as the "infection interiorization," which is the spread of the epidemic to a growing number of remote municipalities of the major metropolitan areas, intensely affecting those who live in communities less assisted by the government[4].

In this context, the following questions have arisen: how have the trends of sexual exposure to HIV been occurring in Teresina, the state capital of Piauí? Has the epidemiological profile of AIDS in Teresina followed the national and global trends?

OBJECTIVE

To analyze, exclusively and individually, the epidemiological trend of sexual exposure to HIV in Teresina, state capital of Piauí.

METHODS

This is a descriptive, retrospective, longitudinal time series census study with a quantitative approach, carried out from the analysis of data reported by the National Diseases Notifications System (SINAN).

Both the population and the sample are composed of all cases of HIV/AIDS reported through SINAN in Piauí between 1987 and July 2013. Data collection took place between September and November 2014 through the SINAN page, using mobile internet in the library of Campus Amilcar Ferreira Sobral at Universidade Federal do Piauí (CAFS/UFPI).

The collected data were exposed for analysis in spreadsheets created using Microsoft Excel, version 2013, filled by double entry (typing) in order to avoid failures in the database. They were analyzed with descriptive and inferential statistics, stating data proportions and means, the incidence of cases year by year and the behavioral analysis of the time series, or historical data, using statistical tests with a significance level of 0.05.

The regression equation of the linear model was estimated from the number of AIDS cases in the state capital for the analysis of trends in heterosexuals, and the percentages of occurrence and their means were calculated. The coefficient of determination (R^2) of the estimated lines was also verified.

Due to the use of secondary and public data, this study is exempt from the approval of an Ethics Committee. However, the guidelines from Resolution No. 466/2012, corresponding to confidentiality and reliability of information, were followed[5].

RESULTS

According to the Brazilian Institute of Geography and Statistics (IBGE), Piauí had an estimated population of 3.195 million people by July 2014. The capital Teresina concentrated 26.3% of the total (840,600), being the most populous city in the state.

Over 7,000 people contract the virus daily, and one person dies every 20 seconds of an AIDS-related disease throughout the world[6]. The region of sub-Saharan Africa remains the most affected, with 60% of people living with HIV – of which 58% are women, as shown in **Figure 1**.

According to SINAN, there were 3,574 cases of AIDS in Piauí between 1987 and 2013. Teresina presented 2,192 such notifications, which represents 61% of the total cases in the state. The records corroborate the heterosexualization profile, as shown in **Figure 2**. Of the total cases registered in Teresina (2,192), 52.9% occurred among avowedly heterosexual individuals.

It may be noted that the number of AIDS cases is higher among men (average of 92.4 cases) every year. However, the cases reported in women have increased significantly, as shown in **Figure 3**. The straight linear trend (y=7.9072; x=18.2560) allows the inference that there is an upward trend (positive angular coefficient), year by year, in cases affecting men. Furthermore, about 85% (R^2=0.8521) of the record variability can be explained by the estimated line.

Teresina has the highest population density of the state, as well as social and economic conditions that make it unique. Such conditions would entail huge imbalance between the reality experienced

Figure 1 – World map of the areas with the highest estimated number of people living with HIV in 2013. Source: UNAIDS[7].

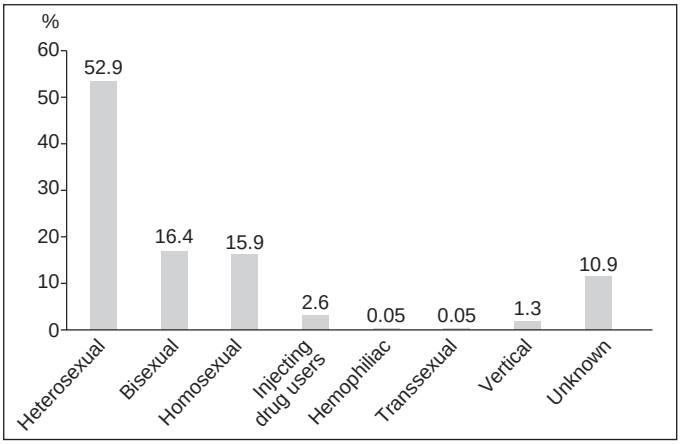

Figure 2 – Total number of AIDS cases in Teresina, by exposure category.

in Teresina and in other cities in the state, due to which the capital greatly influences the high number of cases in Piauí.

In Piauí, as well as in Brazil and the world, the increase in cases in people who claim to be heterosexual constitutes the main trend of HIV infection, as shown in **Figure 4**. Such an event can be explained by the large increase in cases among women and by the association with the statistics of violence against them.

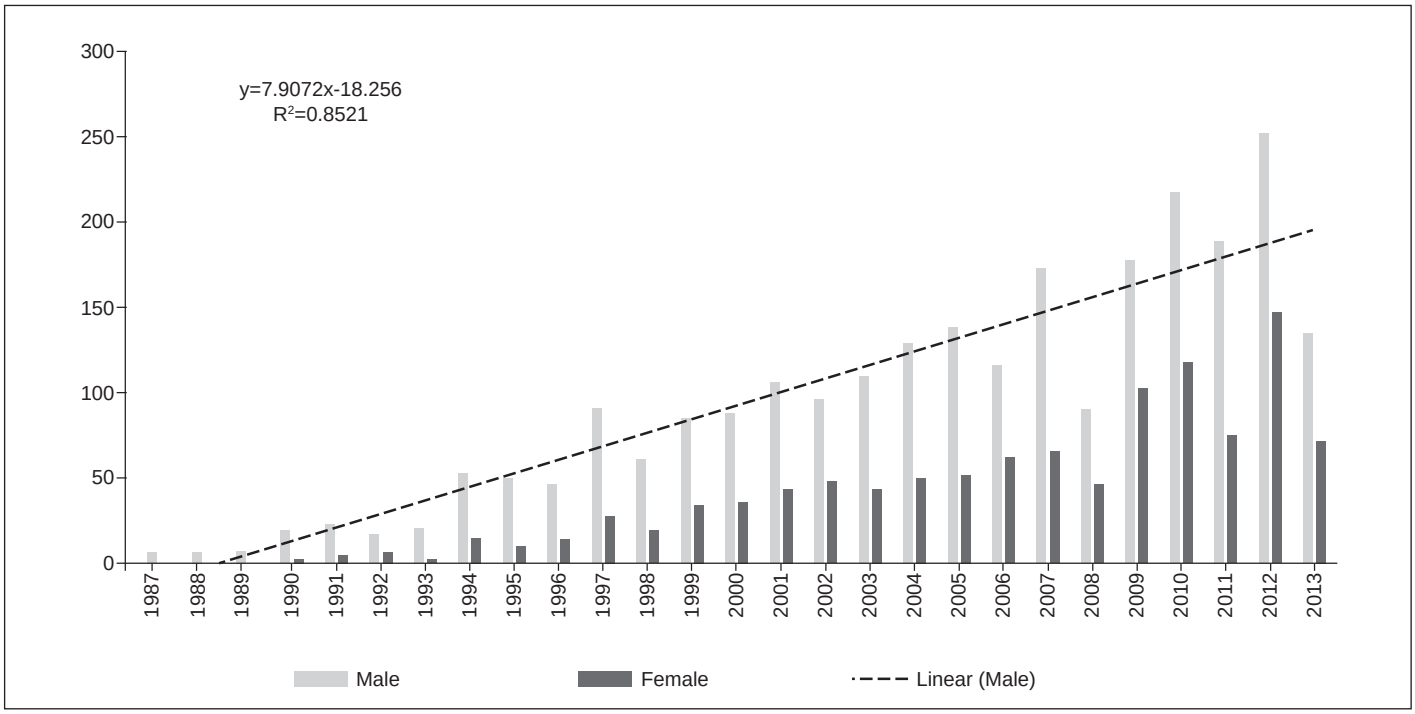

Figure 3 – Absolute frequency distribution of AIDS cases in the state of Piauí, by gender, between 1987 and 2013.

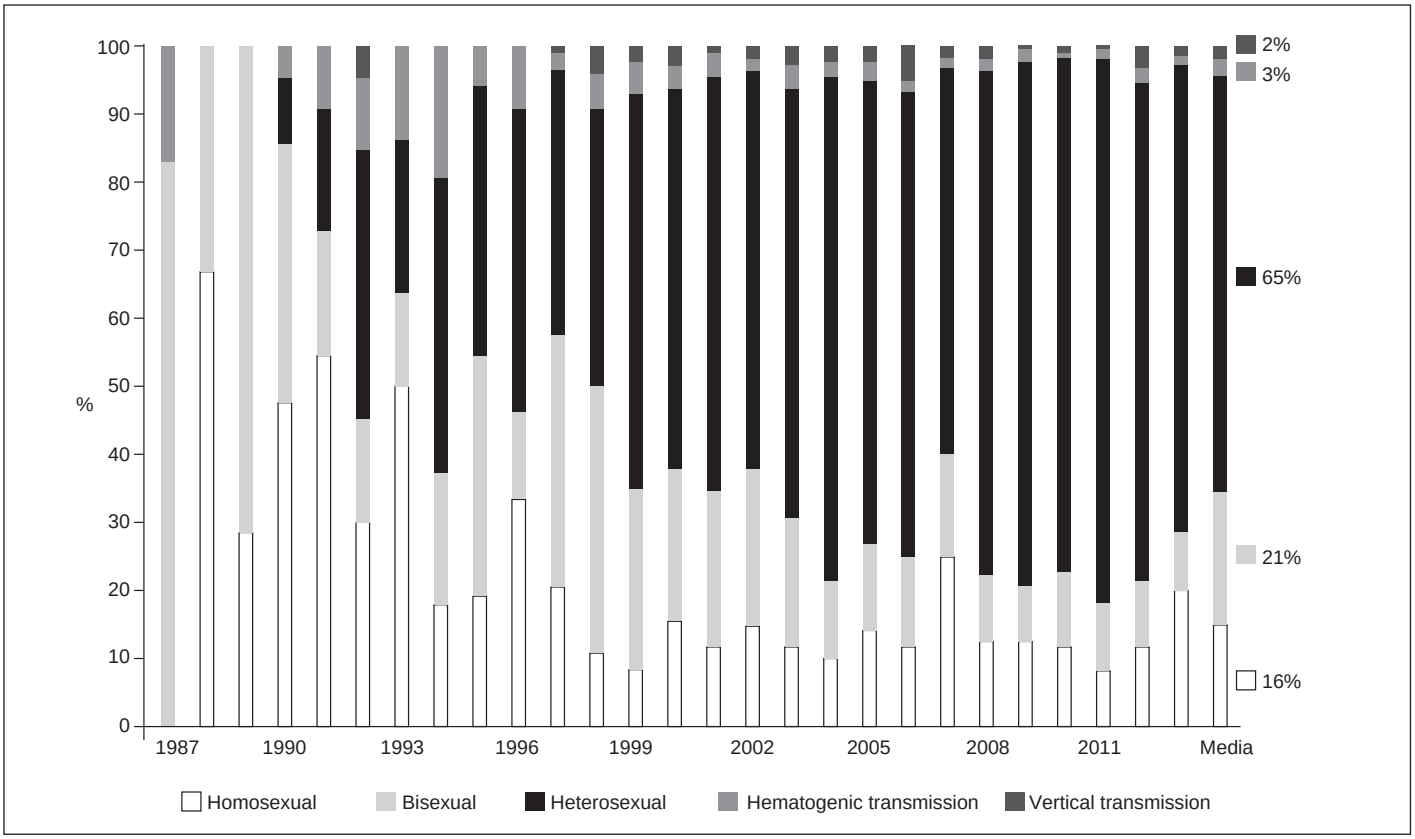

Figure 4 – Percentage distribution of AIDS cases in Teresina, year by year, according to the exposure category.

A downward trend can be observed in the records among the self-declared gay and bisexual people, and an upward trend among heterosexuals. Since the epidemic began in the city, and therefore the state, the reported cases of hematogenic and vertical infection have remained stable.

It was found that Teresina is following national trends, especially with regard to the heterosexual trend, which represents over 50% of all reported cases. The remaining of the most prevalent HIV exposure categories were bisexual and homosexual, which verified the prevalence of sexual transmission of the virus in that area.

DISCUSSION

The number of cases of the disease among men is higher than the number of cases in women, but this difference has been decreasing over the past years. In 2011, were registered 1.7 cases in men for each 1.0 case in women[8].

Despite the predominance of cases among men in the reality of Teresina (71.9% of cases), the occurrence among women has also increased. For Taquete and Meireles[9], a determinant of the vulnerability of women to HIV is the search for a personal identity and sexual-affective curiosity, since, in order to reaffirm themselves as women, some adolescents are exposed to sexual practices earlier, on most occasions with older men, in which their negotiating power is limited. There is still inequality between the genders, in which the incorporation of gender expression puts women at a low level of dignity, increasing their vulnerability to HIV and sexually transmitted diseases in general.

The HIV epidemic in the world continues to have profound effects on women, men and transgenders. Overall, female sex workers are 13.5 times more likely to live with HIV than other women. A study carried out with sex workers in eight Brazilian cities showed higher prevalence rates in Rio Grande do Sul (17.9–19.5%) and lower (1.2–2.4%) in Sergipe[6].

Martins et al.[6] point out that although the interiorization is a current trend of the HIV epidemic, AIDS cases are still concentrated in the most populated municipalities. Between 1987 and 2013, AIDS in Piauí was focused on capital; however, there is a visible increase in the number of inner cities that register cases over the years. Moreover, the dynamics of the virus in Piauí are different from the rest of Brazil and the world, with a prevalence of cases among avowedly heterosexual men.

The significant number of cases of the disease can be explained by factors such as the subservience of women, the dismissal of condom use in relationships considered stable and gender representations, very stigmatized by the marginalized, provincial, and socially vulnerable population[10].

The large cities of Piauí and throughout Brazil are full of people who do not have access to education, health services, and prevention/protection measures against diseases, thus facing significantly higher health risks. Under such social conditions, many diseases, especially HIV, spread more quickly[7].

It is important to note that, in Teresina, when self-reporting as heterosexual, the person stands between those more likely to get the AIDS virus, either by engaging in multiple partnerships, due to lack of awareness about the dangers of unprotected sex, the insufficient public policies, the lack of interest in seeking health services – seeing as some homosexuals self-declare as heterosexuals – or the influence of the increasing number of cases among women[11,12].

Gender-based violence is so culturally naturalized that many men adopt it, but ignore it. In addition, many women do not see themselves as victims of any violence. This behavior is one of the causal factors of the increased vulnerability of women to HIV. Unequal relations between men and women observed in many affective-sexual relationships hinder the safe exercise of sexuality and violate sexual and reproductive rights[9].

As fundamental human rights, sexual and reproductive rights have two distinct and complementary aspects. One points to the individual dimension of these rights and affirms freedom, privacy, intimacy, and autonomy, which presupposes no state intervention in the regulation of sexuality or reproduction. The other aspect is focused on the development of specific public policies to ensure the rights necessary for the free exercise of sexual and reproductive rights of individuals[9].

Thus, state action is necessary to guarantee such rights, among which are access to affordable, safe, and appropriate information; health services and sexual and reproductive education, as well as policies to promote gender equality, not allowing the submission of women and girls; and eliminating any gender discrimination.

The government has a duty to guarantee the rights of the population and, therefore, must formulate and implement actions related to sexual and reproductive health. With regard to adolescents and young people, the challenge is greater, because it is necessary to meet their specific characteristics and respond to their demands, generated by different life situations.[13].

CONCLUSION

The purpose of the study was achieved and, based on the hypotheses raised, it is possible to predict the number of AIDS cases in Teresina with a degree of efficiency of 85%. It has demonstrated the trend of heterosexualization of the transmission of HIV/AIDS in Piauí, which supports the existing literature, indicating the analogy of a predominant epidemiological trend that characterizes the current profile in the country.

Teresina follows the configuration of the epidemic occurring throughout the state of Piauí. There is a trend of heterosexual transmission of HIV/AIDS. However, the infection tends to spread among men.

Throughout the research, some obstacles were present. Among them, the outdated information system, the limited financial resources, and the possibility of information bias due to the reliability of the data, which do not always faithfully portray the reality of the municipalities and the capital, locus of the research.

It is important to stress the need for vigilance on the part of higher authorities of the reliability of public data and the commitment of those responsible for data input in the notifications systems, in order to ensure they are up-to-date and that they correspond to reality.

It is expected that this study base further investigations and assist the redirection of public policies related to the transmission and control of HIV.

Conflict of interests

The authors reported no conflict of interests.

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THE RISK OF GENITAL INFECTIONS IN WOMEN USING INTRAUTERINE DEVICE

O RISCO DE INFECÇÕES GENITAIS EM MULHERES USUÁRIAS DE DISPOSITIVO INTRAUTERINO

Gustavo Gomes Martins[1], José Eleutério Junior[2], Tiago Tomaz[1], Caio Lucio de Andrade[1], Warner Campos[1]

ABSTRACT

Introduction: Intrauterine devices (IUDs) are widely used contraceptive methods that have a possible association with lower genital tract infections. **Objective:** To assess whether IUD is associated with genital tract infection and which pathogens cause it. **Methods:** Systematic review of studies in PubMed database, Highwire-Stanford, and Google Scholar using the following keywords: "cytology IUD," OR "IUD AND cytology" OR "cytology" OR "cytological techniques," OR "cytological AND techniques," OR "cell biology," OR "cell" and "biology". **Results:** Sixteen out of the 2,817 initial articles were selected using the inclusion criteria. On the basis of these studies, the microorganisms that can colonize the IUD, the main acute pelvic inflammatory disease occasioner is *Actinomyces spp*. There is a risk 14 times greater of the presence of *Actinomyces spp*. in IUD users than in non-users. However, there would be a higher apparent depuration of human papillomavirus (HPV) infection among copper T users. **Conclusion:** There is an association between the use of IUD and some genital infections such as bacterial vaginosis; however, more evidently associated with *Actinomyces spp*. There is a possible higher depuration of infection by HPV among copper T users.

Keywords: intrauterine devices; /cytology; reproductive tract infections.

RESUMO

Introduçao: Dispositivos intra-uterinos (DIU) são amplamente usados como método contraceptivo e têm uma possível associação com infecções do trato genital inferior. **Objetivo:** Avaliar se o uso de DIU está associado com infecções do trato genital e por quais patógenos. **Métodos:** Revisão sistemática de estudos dos bancos de dados PubMed, Highwire-Stanford e Google Scholar usando as seguintes palavras-chave: "*cytology* IUD" OR "IUD AND *cytology*" OR "*cytology*" OR "*cytological techniques*" OR "*cytological* AND *techniques*" OR "*cell biology*" OR "*cell* AND *biology*". **Resultados:** Foram encontrados inicialmente 2817 artigos e selecionados 16, que obedeciam os critérios de inclusão. Com base nestes estudos, o microorganismo associado ao uso de DIU e principal causa de doença inflamatória pélvica é o *Actinomyces spp*. Há risco 14 vezes maior de presença do *Actinomyces spp.* em usuárias de DIU em relação a não usuárias. No entanto, parece haver uma maior depuração aparente de infecção por Papilomavírus humano (HPV) entre usuárias de DIU de cobre. **Conclusão:** Há uma associação entre o uso de DIU e algumas infecções genitais, tal como vaginose bacteriana; no entanto, o agente mais evidentemente associado é o *Actinomyces spp*. Há uma possível maior depuração de infecção por HPV entre usuárias de DIU de cobre.

Palavras-chave: dispositivos intrauterinos; /citologia; infecções do sistema genital.

INTRODUCTION

Intrauterine devices (IUDs) are long-term contraceptive methods with high effectiveness. It is estimated that more than 80 million women are using them for contraception in the world[1,2]. There is no reliable statistical data in Brazil.

Surprisingly, there is a reference with a lower incidence of cervical cancer in women using IUDs, although human papillomavirus (HPV) infection is not decreased in relation to the general population[3].

However, the use of IUD seems to be associated with the increase in the risk of infection caused by other microorganisms, which might occur in the first 20 days after its insertion[1], or over time, especially in case of prolonged use[4-6]. The most frequent pathogens observed in the method's users are *Actinomyces ssp.*, *Prevotella spp*., and *Mycoplasma hominis*[2].

The characteristic of these microorganisms is the ability to colonize these devices forming biofilms, which consists of layers of bacteria joining the epithelial cells hosts in an organized manner, thereby creating an environment of microbiome imbalance which might reach the upper genital tract[2]. The prolonged use of IUD can also cause the imbalance in the vaginal bacterial flora, enabling the proliferation of anaerobic microorganisms as *Gardnerella vaginalis*, predisposing to the emergence of bacterial vaginosis[7,8].

OBJECTIVE

Evaluate the reports published in recent years on the association of the use of IUD with genital infections through a systematic review.

METHODS

A systematic review of studies was carried out in PubMed database, Highwire-Stanford and Google Scholar using the following keywords: "cytology IUD," or "IUD" and "cytology" or "cytology," or "cytological techniques," or "cytological" and "techniques," or "cell biology," or "cell" and "biology".

Only those reports in English, Spanish, and Portuguese which had summaries, and considered infections associated with the use of the IUD published between 2002 and 2015, were taken into account. After selection, the works evaluated were those found to present a greater relevance considering the level of recommendation and strength of evidence suggested by the publication of the Brazilian Medical Association.

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RESULTS

Sixteen out of the 2,817 initial articles were selected, thus meeting the inclusion criteria for reading. In general, the presence of microorganisms in the female genital tract can cause pelvic inflammatory disease (PID). Among the microorganisms that can colonize the IUD, the main cause of acute PID is the *Actinomyces spp*.[9], and the predominant species found is the *Actinomyces israelii*[6,10].

DISCUSSION

Actinomyces are Gram-positive anaerobic non-spore-forming bacteria that can be pathogenic or commensal. In the oropharynx and in the gastrointestinal tract, bacteria are commonly commensal; however, a pathogenicity occurs when they are present in the genital tract[5].The favorable environment to anaerobes can be established inside the vagina, facilitating the growth of *Actinomyce ssp*.[11]. Moreover, IUDs are associated with infections because they significantly change the components of glycosaminoglycans of the cervical mucus, which protects the female genital tract from infections[12].

To colonize the IUD, bacteria can form biofilms, which consist of layers of host cells and bacteria soaked in a matrix consisting of a layer of exopoly saccharide responsible for the infection characterization[2]. Biofilm bacteria are usually resistant to antimicrobials, which makes the treatment of infected women more difficult, especially if the removal of the IUD is not carried out[2]. In addition, the removal of the device should be recommended, although the frequency of pelvic action mycosis is extremely low, and if it occurs, can be fatal[11]. Thus, it is important that the clinician has notion that beyond the use of antibiotics is important for the removal of the IUD for effective treatment.

In the genital tract, these bacteria promote pelvic action mycosis, granulomatouschronic infection characterized by the presence of dense fibrous connective tissue and pus. The infection can expand through anatomical structures and lead to fistulas and abscesses. Ramos et al.[10] indicate one or more of the symptoms: dyspareunia, dysmenorrhoea, itching, bleeding in coitus, menorrhagia, menstrual flow with blood in IUD users which detected the presence of *Actinomyces spp*. Matsuda et al.[13] reported that the detection rate of *Actinomyces* in cervical and endometrial cytologies in actinomycotic pelvic abscesses was of 77.7%.

A study indicates a 14 times higher risk of the presence of *Actinomyces* in IUD users than in non-users[5]. The prevalence of these microorganisms also seems to be associated with the time of use of the IUD. Lucas et al.[6] shows that in 56.5% of positive cases studied, *Actynomyces* consisted of users of IUD for more than 5 years. On the other hand, Pál et al.[2] studied 51 users of IUD for over 10 years and observed that 29 of them had *Actinomyces spp*. in the genital tract. While Discacciati et al.[9] observed an *Actinomyces* rate of 7% in IUD users and 0% in non users.

While Kim et al.[14] showed that of the 52 patients positive for *Actinomyces*, 42 were users of IUD, of which 65.8% used the device for more than 60 months. This study showed that the pathogen incidence was much lower in Mirena users compared with copper IUD. The copper IUD and the levonorgestrol IUD are equally associated with the development of atypical squamous cells of undetermined significance (ASCUS) after the insertion of the device in patients who have had a normal cervical cytology. However, the copper IUD was associated with a higher rate of depuration of HPV infection when compared with Mirena[15].

According to Silva et al.[8] the users of IUDs showed significantly more benign epithelial changes (p=0.0002) than non-users. In addition, they presented a significantly higher frequency (p=0.0009) of bacterial vaginosis in cytological studies. Findik et al.[11] showed a higher frequency of bacterial vaginosis, *Candida spp*., and *Actinomyces spp*. (p>0.001), when compared to women who used oral contraceptive. Baris et al.[16] showed a statistically significant report (p=0.03) between bacterial vaginosis and the use of birth control, including IUDs (12% of patients with IUD presented vaginosis). However, Discacciati et al.[9] did not identify significant differences in detecting inflammatory and cytopathological changes in cervical smears in the 104 IUD users, as compared to a group of 104 women who used another type of contraceptive method, not establishing a relationship between the use of IUDs and the increased risk for the development of dysplasia. There was no significant difference in the detection of *Candida spp*. or *Trichomonas vaginalis* between the two groups.

CONCLUSION

Although some studies have associated the use of IUD with some genital infections, such as bacterial vaginosis[14,16], the most common association was related with *Actinnomyces spp*.[5,9,11]. Such cases should be evaluated very carefully because of the risk of complications such as PID. In addition, the possible greater depuration of infection with HPV requires more extensive studies.

Conflict of interests

The authors reported no conflict of interests.

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STIGMA OF HIV POSITIVE EXPRESSED THROUGH VEILED PREJUDICE

ESTIGMA DO HIV POSITIVO EXPRESSO POR MEIO DO PRECONCEITO VELADO

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ABSTRACT

Introduction: The term *stigma* was coined by the ancient Greeks to refer to signs made in the body meaning something bad on the morale of those who had them. **Objective:** To verify the presence of discriminatory attitudes of users of Unified Health System regarding HIV-positive individuals, as well as the perception about the possibility of acquiring some kind of disease during dental treatment. **Methods:** The data collection instrument consists of a semi-structured questionnaire. This study included interviews asking the following questions: individuals agree to be treated by a HIV-positive dentist, after the treatment of a HIV-positive patient or an inmate; the perception of the possibility of acquiring illnesses in a dental office; concern regarding sterilization of materials used and the manner of sterilization. **Results:** Two hundred individuals were interviewed, 142 would accept to be treated after a HIV-positive patient and 160 after an inmate. Moreover, 162 would be available for treatment by a HIV-positive dentist. However, when questioned about the preference, 93 would prefer to be treated before a HIV-positive patient and 60 before an inmate. **Conclusion:** Patients showed discriminatory attitudes toward seropositive people, expressed sometimes in a veiled manner, and the perception about the possibility of getting some kind of infection during dental treatment.

Keywords: prejudice; HIV seropositivity; acquired immunodeficiency syndrome; health personnel; sexually transmitted diseases.

RESUMO

Introdução: O termo estigma foi criado pelos gregos da Antiguidade para referirem sinais feitos no corpo que evidenciavam algo ruim sobre a moral de quem os apresentava. **Objetivo:** Objetivou-se verificar a presença de atitudes discriminatórias de usuários do sistema público de saúde em relação a indivíduos HIV positivo, além da percepção dos mesmos sobre a possibilidade de contraírem algum tipo de doença durante o tratamento odontológico. **Métodos:** O instrumento de coleta de dados consistiu de um questionário semiestruturado. Realizaram-se entrevistas com perguntas relacionadas à concordância do indivíduo ao atendimento por um cirurgião-dentista HIV positivo, após o atendimento de um paciente soropositivo, ou um presidiário; a percepção da possibilidade de se contrair alguma doença no consultório odontológico; preocupação com relação à esterilização dos materiais utilizados e conhecimento sobre a forma de esterilização. **Resultados:** Foram entrevistados 200 indivíduos, sendo que 142 afirmaram que aceitariam ser atendidos após um paciente HIV positivo e 160 após um presidiário. Ainda, 162 se disporiam ser tratados por um cirurgião-dentista HIV positivo. Entretanto, quando questionados em relação à preferência, 93 prefeririam o atendimento antes de um indivíduo soropositivo e 60 antes de um presidiário. **Conclusão:** Conclui-se que os pacientes apresentam atitudes discriminatórias em relação a pessoas soropositivas, expressa às vezes de maneira velada e a percepção sobre a possibilidade de contrair algum tipo de infecção durante o tratamento odontológico.

Palavras-chave: preconceito; soropositividade para HIV; síndrome da imunodeficiência adquirida; pessoal de saúde; doenças sexualmente transmissíveis.

INTRODUCTION

The term *stigma* was created by the ancient Greeks to refer to signs in the body that meant something bad about the morale of those who presented them. People who had particular requirements, approved by the society, were called by Goffman[1] as "normal." On the other hand, attitudes that the "normal" showed, many times without thinking, with people with a stigma, were discriminatory. An ideology to explain the danger they represent, using specific stigma terms, as retarded[1] or crippled, and nowadays "aidético" for individuals with acquired immune deficiency syndrome.

Prejudice is a way of thinking in which the person comes to a conclusion that prejudges, and the term "veiled" relates to what is hidden, obscure or concealed. Thus, we can understand the concept of veiled prejudice as the one that people know, but deny having it[2]. Currently, in Brazil, there are laws that punish discrimination and prejudice against HIV-positive individuals[3], and probably many people hide their true feelings for fear of punishments that they might have to suffer.

Few works have sought to observe the patient's perception regarding the subject addressed.

OBJECTIVE

To observe the discriminatory attitudes of the Unified Health System (SUS) users concerning the dentists and other seropositive individuals, as well as their perception of the possibility of being infected with some kind of disease during odontological treatment.

METHODS

The research was approved by the Human Research Ethics Committee within the standards required by Resolution 466/12, under the case number FOA-02411/2011.

The study is a descriptive, transversal character research, with a quantitative approach. Initially, the Secretary of Health of the municipality was contacted to be informed about the purpose of the study, and the subsequent use of the data collected to obtain their support

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for the research. Subsequently, the adjustment of the questionnaire was accomplished by a pilot study to a different Health Centers (HC) of the municipality.

The study population was composed of the users of the public system of oral health in the city of Araçatuba, São Paulo, Brazil, which was informed of the goals as well as the confidentiality of the information. Individuals who have agreed to participate signed a free consent term.

The map of the city was split in five sectors, one central and four peripherals, with the purpose to obtain a sample of HC patients with different socioeconomic characteristics.

The interviews were conducted by a trained researcher so that the questions had no influence on the answers.

A period of two months for data collection was stipulated, occurring between January and February 2014. The interview was conducted in a private room, inside the HC, in the day scheduled for the patient, every day of the week, causing no interferences in the normal local activities.

The instrument of data collection consisted of a semi-structured questionnaire, composed of open and closed issues, with questions on demographic factors such as gender, age, and education; the perception of the risk of acquiring some type of illness during the dental treatment; concern with the cleaning and sterilization of the material; personal protective equipment used by dental surgeon; perception of a disease whose transmissibility is biggest (AIDS or hepatitis); acceptance and preference of care after a patient with AIDS or a convict; and agreement to be treated by a dentist with AIDS.

A group of inmates were included due to the existence of prisons in the neighboring towns and because these individuals receive dental treatment in the Public Health System. Studies show that there is a high rate of inmates that show sexually transmitted diseases; among them, positive serology for HIV and syphilis, in addition to injectable drug use and blood transfusion history[4,5], encouraging discriminatory attitudes toward those groups of individuals.

The collected data were tabulated by the Epi Info™ 7, statistically analyzed by BioStat 5.0[6] software, through the test for comparing two proportions with a significance level of 5% and presented in absolute frequencies and percentages.

RESULTS

The research universe was composed of 254 individuals, and 54 (21,3%) of them did not accept to participate in the survey, even after they were informed of the confidentiality of the data obtained, which denotes the taboo involving the subject under study. Of those individuals surveyed, 143 (71.5%) were women. Concerning the individual acceptance or non-acceptance to be treated after a patient with AIDS or a convict, 142 (71%) said that they accept the treatment after a HIV- positive patient and 160 (80%) after a convict. However, when questioned about the preference for treatment before or after an HIV-positive patient or a convict, 93 (46.5%) preferred the treatment before an HIV-positive individual, and 60 (30%) before an inmate.

Among the individuals interviewed, 162 (81%) informed that they accepted to be treated by a HIV positive dentist.

Regarding the possibility of acquiring some type of infection in the dental office, 171 (85.5%) believed that it could occur, and 166 (83%) were concerned whether dental material was autoclaved; however, 147 (73.5%) did not know how it was performed.

There was a significant statistical difference between individuals who initially accepted treatment after a HIV-positive patient or a convict, and those who claimed to prefer to be treated before them.

DISCUSSION

The different forms of stigma and discrimination in relation to HIV/AIDS occur due to the characteristics of the disease that manifest themselves causing large impacts in the lives of the carriers[7], resulting in the self-stigmatization, where individuals tend to accept the society's negative beliefs and isolate themselves from social contact, which is considered the most difficult stigma to overcome[8].

Usually, we can observe the prejudice through the declination of the treatment by the dental surgeon to the immunodeficiency carrier patient, with the most absurd motives, such as: "I'll take a vacation for an indefinite period" or "I have a problem with my equipment." Regarding other health professionals, the bad service to the virus carrier is justified by the possibility that the professional might acquire the disease[9]. The difficulty to obtain service in the health area for HIV carriers is 11.7 times greater. Despite the professionals in this area are much more informed about the disease, they are unprepared to deal with this situation[9].

Our research showed that some of the interviewers prefer the treatment before a convict, and this occurs due to the stigma that revolves around this population. It is estimated that 20% of the Brazilian convicts are HIV carriers, which is the result of overcrowded, precarious, and unhealthy jails, which make prisons a favorable environment for the spread of epidemics and infection, especially due to the occurrence of homosexuality and sexual violence practiced among the inmates as well as the use of injectable drugs[11].

Sometimes prejudice is not shown in a clear way. A research carried out with adolescents asked about their way of discrimination, and one of the answers was the following: "I don't do anything, I don't exclude nor treat bad, but I'm always distrustful," demonstrating that prejudice is not evident, but it is expressed in a veiled way[12], which probably occurs due to the punishment that the individual may suffer, as the Brazilian law 12,984 prohibits all forms of discrimination[13]. According to this law, discrimination against carriers of human immunodeficiency virus and AIDS patients is a crime punishable by up to four years in prison and fine[3].

The prevention of cross-transmission of the AIDS virus and hepatitis is a crucial aspect in odontology, where preventive measures must be used during treatment[14]. A survey carried out with students of odontology showed that it is the main danger to the patient, as they confessed to failing in the cleaning and the decontamination of material and equipments used during the procedures[15]; this highlights a failure in the training of future professionals.

There is a real risk, though minimal, of health professionals transmitting AIDS virus to their patients. This is an extremely delicate issue, because on one side there is the concern of the patient whether he is at a minimal risk of acquiring the disease from the dentist, and on the other side there is the right of the professional to preserve his serology, protecting himself from personal, professional, and social discrimination[16].

As for the possibility of contracting some type of infection in the dental office, most of the interviewers believed that it could occur, in corroboration with another study[16], and many individuals showed concern as to whether the dental materials were sterilized, as many of them did not even know how the sterilization was performed. This interest derives from the concern about HIV transmission in the dental office, by the social representation that the disease presents and that is linked to behaviors not accepted by the society, hatching the misconception of "risk groups"[17]. It is important to point out that regarding accidents this risk is small, and depends on the type of accident and the patient's viral load. The risk of HIV infection is much smaller than the risk of hepatitis virus infection, with estimates 0.3% for HIV, 1% to 10% for hepatitis C and 40% for hepatitis B[10].

Despite the consistent efforts of the Ministry of Health to disseminate the guidelines regarding the disease through the national program for STD/AIDS[18], lack of access to information and knowledge concerning HIV contamination and transmissibility causes the attitudes of the population to stay attached to myths, beliefs, emotions, and discussions of everyday life, not taking into consideration the scientific knowledge, which provides information of the true ways of transmission and prevention of the disease.

Further studies need to be carried out involving larger populations, so that the existence of different forms of prejudice to users of the Public Health System in relation to HIV-positive individuals can be confirmed. The implementation of educational strategies should be proposed to eradicate any form of discrimination.

CONCLUSION

Although the result of the research cannot represent the opinion of all the users of the Public Health System, the study suggests that there is prejudice and discrimination in relation to HIV carriers, often expressed in a veiled manner and also the perception of the possibility of acquiring some kind of infection during odontological treatment.

Conflict of interests

The authors reported no conflict of interests.

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