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Av. Roberto Silveira, 123 - Niterói - RJ - Brazil
CEP: 24230-150 - Tel.: + 55 (21) 2710-1549
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Outeiro de S. João Batista, s/nº
Campus do Valonguinho - Centro
Niterói - RJ - 24210-150 - Brasil
Tel.: +55 (21) 2629-2495 - 2629-2494
Fax: +55 (21) 2629-2507

E-mail: dst@dst.uff.br
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Editorial

Interaction of HPV with vaginal ecosystem in vaginal and cervical carcinogenesis

In 1951, Henrietta Lacks died at the Johns Hopkins Hospital (Baltimore, USA) due to cervical cancer, and then a more comprehensive study on this tumor was born and put immortal cells to the scientific world: the cells of Henrietta Lacks, HeLa cells[1].

Only in the 1970s and 1980s the various studies on virology and epidemiology associated with clinical evidence concluded that infection by one or more high-risk human papillomavirus (HPV) type is the leading cause of anogenital cancer[2]. In the end of the 20th and beginning of 21st century, epidemiological studies reported the concept of high-risk HPV repeatedly and its establishment as a main risk factor for cervical cancer. HPV 16 and 18 are responsible for 70% of all cervical cancer cases, and probably other squamous cell carcinomas[3].

The discrepancy between the high frequency of HPV infections among young women, including the oncogenic types, and cervical cancer clearly shows that the infection itself is not all it takes to the development of a neoplasm, even in cases of persistent infection.

HPV has a characteristic tropism — in cutaneotropic or mucosotropic forms —, in its different preferred locations of the human body. The most common clinical presentations of viral infection are condylomas and cervical cancer.

Viruses, especially HPVs, are essentially intracellular parasites with a genetic and structural complexity that requires a complex response by the host. They bind to cells through specific receptors, which shows their tropism (epitheliotropic viruses). Likewise, they require a specific biochemical and metabolic structure of the host cell in order to replicate. They get into defensive stratagems, to avoid being recognized by the host cell, through toll like receptors (TLR) and attempt to break the immune system. Immune response to HPVs is quite different than that to other viruses, once it is accompanied by low levels of antibodies in the blood (acquired immunity). By adopting the mimetic behavior of the host cellular immunity, it will cause cytopathic effects in some specific tissues[4].

HPV infection is exclusively intraepithelial, with its replication depending on the viral cycle, on the cell differentiation, as well as persistence to epithelial cells level. Once they reach the basal layer of keratinocytes, they can remain in the episomal form, or latency, or take advantage of this differentiation to perform viral integration (linear form) or replication.

HPV replication needs the cell differentiation so that its proteins can be expressed. On the other hand, immune response is far, so there is no recognition by Langerhans cells or antigen-presenting cells (APC). This virus has no cytolytic activity, so its infection is not accompanied by inflammation (neutrophils, monocytes, macrophages, *natural killer-cells* – NK, dendritic cells and APC, B and T lymphocytes, cytokines, acute phase proteins, complement proteins, and lysozymes), but it performs viral replication, a phenomena that can explain the decrease or block in effective immune response of the innate and acquired immunities[4]. These infections may become chronic and lesions can persist and establish for months or years.

Many studies based on the agent characteristics suggest that, in women presenting pathological cytology, the determination of viral load and the detection of overexpression of E6/E7 *RNAm* may be important indicators of prognosis, which may avoid overtreatment and lead to a more customized assistance.

So cervical carcinogenesis is influenced by — besides the agent characteristic (genotype, variants, viral load per cell unit, presence of multiple genotypes, expression and integration to the host's genoma) — environmental factors (such as alcohol consumption, smoking habit) and by the host's features (vaginal microbiome, immune tolerance) that can determine the risk of malignancy.

Therefore, beyond the aforementioned agent's characteristics (HPV), we must emphasize the importance of external factors, such as smoking and alcoholic habits, long-term use of sex steroids (oral contraceptives and hormone replacement therapy), gynecological infections (Herpes simplex virus – HSV, Cytomegalovirus – CMV, *Chlamydia trachomatis* and other sexual transmitted viruses), and some other unspecific inflammations that may lead to changes in the immune system and to an unbalance in vaginal microbiome. Some recently published studies have suggested the possibility of association between cervical cancer and changes in the vaginal ecosystem through the modification of microbiome[5,6]. Thus, all these agent and host characteristics may contribute with cervical immunosuppression and favor carcinogenesis. This information may help in primary and secondary prevention in order to identify risk groups.

As to the host, we give importance to genetic and immunologic factors, as well as nutritional features and sexual behavior (number of sexual partners and their characteristics, age of sex initiation), and to some endogenous factors that could cause genotoxicity, mutagenicity, irreversible cell transformation and proliferation.

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The female genitalia is widely affected when it comes to HPV, namely the cervix. This led scientists to perform exhaustive research on the physiology of lesions in this spot. The cervix is part of a reproductive organ (uterus) that plays an important role during fecundation and gestation, being subjected to hormonal influences (endogenous and exogenous), traumatic, infectious factors by the host that facilitates HPV infection.

Currently, the changes in sexual behavior of the population (especially in developed countries) have increased the incidence of HPV infection in other regions of the body, including oro-pharyngeal and anal tissues, among others. As a consequence, there was a diversification in scientific studies and publications on HPV.

Markers of cervical carcinogenesis prognosis are based on the natural history of HPV lesions (agent and host). Therefore, biomarkers of all biological levels (genotype and phenotype) may help understand the complex mechanism of carcinogenesis; especially the interaction between different cofactors and acquired (environmental) and genetic (individual) susceptibility. Consequently, these mechanisms may contribute with the clarification of cervical cancer etiology and pathogenesis in the different phases of a woman's life.

Advances in molecular biology techniques (research on types of viruses, virus load, overexpression of RNAm, specific biomarkers p16 and Ki-67) and their application in clinical trials, namely epidemiological studies, allowed the characterization and estimative of HPV infection in different populations, specific localizations, after migrations, and the etiology between infection and certain types of genotypes.

To sum up, we suggest a customized clinical/therapeutic management to avoid unnecessary treatments, based on the patient's past medical history (age of sex initiation, number of sexual partners, anovulatory cycles, parity, nutrition, alcohol and smoking habits, genetics, immunity etc.), on gynecologic infections, on the assessment of the vaginal ecosystem (pH, lactobacillus), on cytopathologic diagnosis (atypical pavimentous cells of undetermined significance; low grade squamous intraepithelial lesions – LSIL; high grade squamous intraepithelial lesions – HSIL, Atypical glandular cells – AGC; Cervical Intraepithelial Neoplasia I – CINI; and Cervical Intraepithelial Neoplasia I and II – CINII/III), on molecular diagnosis (HPV, viral load, HSV, CMV, *Chlamydia trachomatis, Mycoplasma*, *Ureaplasma*, *Neisseria gonorrhoeae*) and on the Immunohistochemical study (p16 e Ki-67) of dysplasia components[7-9].

MARIA CLARA BICHO
Gynecologic oncologists at British Hospital
Head of Gynecology and Obstetrics at Hospital de Santiago
Researcher of the Dermatology & Venereology Unit, Institute of Molecular Medicine, Medical School of Universidade de Lisboa
E-mail: mclara.bicho@gmail.com

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Association of sanitary pads and clothing with vulvovaginitis

Associação de absorventes higiênicos íntimos e vestimentas com vulvovaginites

Marcela Grigol Bardin[1], Paulo César Giraldo[2], Cristina Laguna Benetti Pinto[3], Virgínia Pianissoni Piassaroli[1], Rose Luce Gomes do Amaral[3], Nádia Polpeta[1]

ABSTRACT

Introduction: Vulvar occlusion and moisture buildup resulting from the use of sanitary pads, synthetic underwear and/or tight pants are considered risk factors for the development of vulvovaginitis (VV). However, this association is still poorly elucidated. **Objective:** To associate the use of sanitary pads and clothing with the presence of bacterial vaginitis (BV) and vaginal candidiasis (VC). **Methods**: Cross-sectional study aimed at analyzing the use of sanitary pads and clothing in 307 volunteers from 18 to 45 years old, with and without BV and/or VC. A questionnaire comprehending six domains was applied individually to the volunteers, in an outpatient gynecology clinic at a university hospital (University of Campinas, Brazil). This study analyzed three of six domains. Vaginal material was collected for microbiologic diagnosis of BV (Nugent criteria) and VC (Gram stain and culture of the fungus in Saboureaud). Exclusion criteria were: use of antibiotics within 15 days, history of cancer, positive HIV and/or syphilis and immunosuppressive disease. Statistical analysis were made with Fischer and chi-square tests, using the software EPI INFO 0.5. Significance level was set at $p<0.05$. **Results:** In total, 141 (46%) women were diagnosed with VV. The mean age was 32 (±6.8) years and most women were Caucasian (52%), had a steady partner (83%) and were using hormonal contraceptives (64.5%). Women with presence of VV used more panties made of synthetic fabric (10.6% x zero), had more menstrual cycles (72.3 x 55.4%) than those without VV ($p<0.005$ and $p<0.0001$) and showed patterns of sanitary pads similar to those without VV. **Conclusion:** Habits of usage of sanitary pads is not associated with the presence of VV. Presence of menstrual cycle and use of synthetic underwear have been related with greater frequency of VV.

Keywords: vaginitis; bacterial; candidiasis; vulvovaginal; hygiene; absorbent pads; clothing; type of underwear.

RESUMO

Introdução: A oclusão vulvar e o acúmulo de umidade em decorrência do uso de absorventes higiênicos, roupas íntimas sintéticas e/ou calças justas são considerados fatores de risco para o desenvolvimento de vulvovaginites (VV). Contudo, esta associação ainda está mal esclarecida. **Objetivo:** Associar a prática do uso de absorventes higiênicos e vestimentas à presença de vaginose bacteriana (VB) e/ou candidíase vaginal (CV). **Métodos:** Estudo de corte transversal analisou o uso de absorventes higiênicos e vestimentas de 307 voluntárias de 18 a 45 anos, com e sem VB e/ou CV. Um questionário com seis domínios foi aplicado individualmente às voluntárias, nos ambulatórios de ginecologia de um hospital universitário (Unicamp, BR). Este estudo analisou três dos seis domínios. Coletou-se material vaginal para diagnóstico microbiológico de VB (critérios de Nugent) e CV (bacterioscopia corada por Gram e cultura em meio Saboureaud). Critérios de exclusão: uso de antibiótico nos últimos 15 dias, histórico de câncer, HIV+, sífilis e doença imunossupressora. A análise estatística utilizou teste exato de Fischer e qui-quadrado, pelo EPI INF 0.5. O nível de significância considerada foi $p<0,05$. **Resultados:** Do total, 141 (46%) das mulheres foram diagnosticadas com VV. A média de idade foi de 33 (±6,8) anos e a maior parte das mulheres era caucasiana (52%), tinha um parceiro fixo (83%) e utilizava métodos hormonais contraceptivos (64,5%). As mulheres com VV utilizaram mais calcinhas de tecido sintético (10,6% x zero), apresentaram mais ciclos menstruais (72,3 x 55,4%) que aquelas sem VV ($p<0,005$ e $p<0,0001$) e apresentaram hábitos de uso de absorventes semelhantes. **Conclusão:** Os hábitos de uso de absorventes higiênicos não estão associados à presença de VV. Já a presença de ciclos menstruais e uso de calcinhas de tecido sintético se relacionou a maior frequência de VV.

Palavras-chave: vaginose bacteriana; candidíase vulvovaginal; higiene; absorventes higiênicos; vestuário; tipo de calcinhas.

INTRODUCTION

Vulvar epithelial tissue differs from other regions of the human body because of its structure, occlusion, hydration and susceptibility to friction, but as well as other epithelial tissues, its function is to protect the organism from harmful agents through defense cells[1]. However excessive occlusion and humidity in the area of vulva caused by synthetic underwear, tight pants, menstruation and the use of sanitary pads may have a negative influence on the skin barrier and cause changes in temperature and pH of the region, making the vulva susceptible to vulvovaginal diseases[2-4]. The most common types of vulvovaginitis in the reproductive age of women are bacterial vaginitis (BV) and vulvovaginal candidiasis (VC), and they usually manifest as vaginal discharge accompanied by bad odour and itching, respectively[5].

Vaginal discharge — either physiological or caused by vulvovaginitis — is usually disturbing for women, and one of the main reasons of this population's seeking for gynecological care[6]. This is also one of the main factors that lead women to use sanitary pads outside of the menstrual period, the so-called panty liners[7]. Currently, panty liners are widely used by women, regardless of their social group. Around 50% of North-American and North-European females use them in their reproductive age[8]. In Brazil, although these data are only disseminated by non-scientific publications, they reach similar values[7]. Medical-scientific literature, on the other hand, raises a series of questions about the potential risks of long-term use of sanitary pads to women's health[3,9,10].

The most common concern among women is the sanitary pad, which in contact with the vulva increases the local temperature,

[1]Post-graduate student at Department of Obstetrics and Gynecology, Faculdade de Ciências Médicas, Universidade Estadual de Campinas (Unicamp) – Campinas (SP), Brazil.
[2]Full professor at Department of Obstetrics and Gynecology, Faculdade de Ciências Médicas, Unicamp – Campinas (SP), Brazil.
[3]PhD; Professor at Department of Obstetrics and Gynecology, Centro de Atenção Integrada à Saúde da Mulher, Unicamp – Campinas (SP), Brazil.

maintain the natural humidity of the area in contact with the skin, and change vulvar or vaginal pH, causing physiological changes that could favor fungus and bacteria growth; therefore, vaginal infections such as vulvovaginal candidiasis (VC) could install much more easier[3]. Runeman et al.[5] performed a study with 58 women used to wear non breathable sanitary pads, with a plastic layer, for three menstrual cycles in between flow days (panty liners). Vulvar temperature, pH and humidity increased significantly compared to women not using them or using breathable types. In another study, the same authors[9] found a large number of aerobic microorganisms in the vulva of women who had used non breathable pads compared to women who had used breathable types or did not use the product.

Just like the sanitary pads, clothing may also cause changes in the genital microbial flora due to humidity and changes in temperature, thus causing alterations in the genital ecosystem and irritations, allergies or discharge[3]. The traditional skirts and dresses have been replaced by jeans, and cotton by synthetic panties, which impairs the ventilation to external genitalia, and it can be worsened by the use of files stocking[11]. Elegbe and Botu[12] reported that women using loose pants had less episodes of VV by *Candida albicans*. Another study made an association of swelling and other morbidities in the female urethral region with the use of tight clothing[13]. Reed[14] concluded that very little is known about the influence of tight clothing on the recurrence of vaginal candidiasis.

Other studies[3,15] have assessed changes in vulvovaginal ecosystem by clothing and sanitary pads and, although results suggest that breathable pads are safe for females' health, the relation between the use of pads and types of clothes with the occurrence of genital infections has not been completely elucidated. The present study was aimed at assessing and comparing the habit of using sanitary pads and certain types of clothes in women with bacterial vaginitis and/or vulvovaginal candidiasis.

METHODS

This is a cross-sectional cohort study performed in a University Hospital (Universidade Estadual de Campinas, Brazil) conducted with 314 women aging 18-45 from March to November, 2013. Women who had used antibiotics in the previous 15 days, who were pregnant, had chronic and degenerative diseases (cancer, diabetes, immunosuppression), diagnosed with syphilis, HIV or hepatitis were excluded from the sample.

A questionnaire about daily habits and intimate care, with 60 questions (I – genital washing; II – use of sanitary pads; III – underwear; IV – genital waxing; V – genital ornaments (piercings and tattoos), and IV – sexual activity) was applied confidentially and individually to women, always by the same researcher. This study analyzed domains I and II. The tool was specifically drawn up for this research, because literature had no other available that was scientifically validated.

After the interview, females were submitted to gynecological examination, with performance of vaginal swab for microbiological assessment. The swab was prepared in a glass slide, stained by the Gram method, and analyzed by optical microscopy. Fungi culture in Agar-Sabouraud growth media was made to identify fungal infections, as well as the Whiff test, and pH measurement using a colorimetric reaction scale (Merck®-Germany) ranging from 0 to 14.

In order to diagnose BV, the criteria by Nugent et al.[16] were applied. To diagnose VC, we considered the presence of white discharge with mycelium or blastopore growing at swab. To assess these data, two main groups were created: women with vulvovaginitis (BV, VC, BV + VC) and women without it. Therefore, females previously undiagnosed and without inflammation at the swab (more than four leukocytes per field boost) composed the control group. Eighteen women refused to participate, and seven were excluded from the sample due to suspicion of endocervicitis (n=3) and desquamative inflammatory vaginitis (n=4).

This study was approved by the Ethics Committee of the Medical Sciences School of UNICAMP (protocol 3816/2013), and all participants signed the informed consent form. Statistical analysis considered frequency, percentage, mean and standard deviation (SD), and the χ^2 and Fischer Exact tests were used to established associations between domains of the questionnaire and vulvovaginitis (BV, VC and both). Significance level was set at $p<0.05$.

RESULTS

Among 307 participants, 166 (54.07%) women were not diagnosed with vulvovaginitis and 141 (45.93%) were: 61 had VC, 72 had BV and 8 had both (VC + BV). Patients' mean age was 33 (±7), mean body mass index (BMI) was 27.1 (±5.5), with mean time of study of 10.2 (±3.3) years. Most females (83%) were married or had a fix partner, used hormonal contraceptive methods (63.5%), and did not smoke (89.3%). Almost half of the sample was composed of white (52.8%) and catholic (51.5%) patients. No statistically significant differences were found between groups as to these variables. Women with vulvovaginitis, total and isolated (VC, BV and both), had more menstrual cycles than the group without it (p=0.0002).

The number of sanitary pads used in the heavier days of the menstrual cycle, use of tampons, use of panty liners, type of pads used in between cycles, vulvar sensitivity according to the patients' referral, and vulvar irritation caused by the sanitary pads were identical in both groups (**Table 1**). Irritations mentioned were: hyperemia, swelling, epithelial desquamation, fissuring and itching (**Table 1**).

Most of the women investigated were used to wearing cotton panties (VC=59%, BV=47.2%, VC + BV=62.5%, without VV=64.5%). However, women presenting vulvovaginitis (10.6%), especially BV (15.3%), were more likely to wear synthetic panties ($p<0.0001$) than those without it (0%). The variables design of the underwear, patient' perception of allergic reactions to synthetic tissues, sensation of genital compression by the clothes, use of tight pants and the number of tissue layers in contact with the vulva at bedtime were similar between groups (**Table 2**).

DISCUSSION

In our study, women with VV had more periods than women without it. Menstrual flow makes women wear more sanitary pads, which may favor the onset of infections. Nevertheless, many other

Table 1 – Gynecological features and the use of sanitary pads in women with and without vulvovaginitis.

Variables	Without VV	With VV	p-value	Types of VV			p-value
	Total (166) n (%)	Total (141) n (%)		VC (61) n (%)	BV (72) n (%)	VC+BV (8) n (%)	a = without VV x VC b = without VV x BV c = without VV x VC+BV
Amenorrhea							
No	92 (55.4)	102 (72.3)	0.002	45 (73.8)	52 (72.2)	5 (62.5)	<0.05 (a.b.c)*
Yes	74 (44.6)	39 (27.7)		16 (26.2)	20 (27.8)	3 (37.5)	
Time spent away from home							
≤5h	61 (36.8)	48 (34)	ns	23 (37.7)	22 (30.6)	3 (37.5)	ns*
6h to 9h	55 (33.1)	52 (36.9)		23 (37.7)	27 (37.5)	2 (25)	
≥10h	50 (30.1)	41 (29.1)		15 (24.6)	23 (31.9)	3 (37.5)	
Number of SP in the heaviest day of flow							
≤3	60 (65.2)	69 (67.6)	ns	29 (64.4)	36 (69.2)	4 (80)	ns*
>3	32 (34.8)	33 (32.4)		16 (35.6)	16 (30.8)	1 (20)	
Use of tampons							
No	84 (91.3)	84 (82.4)	ns	40 (88.9)	40 (76.9)	4 (80)	ns*
Yes	8 (8.7)	18 (17.6)		5 (11.1)	12 (23.1)	1 (20)	
Use of panty liners							
Never	100 (60.2)	86 (61)	ns	41 (67.2)	41 (56.9)	4 (50)	ns*
Sometimes	30 (18.1)	23 (16.3)		10 (16.4)	11 (15.3)	2 (25)	
Always	36 (21.7)	32 (22.7)		10 (16.4)	20 (27.8)	2 (25)	
Type panty liners used							
With plastic layer	30 (18.1)	22 (15.6)	ns	8 (13.1)	13 (18.1)	1 (12.5)	ns*
Without plastic layer	27 (16.3)	20 (14.2)		10 (16.4)	8 (11.1)	2 (25)	
Does not know	9 (5.4)	13 (9.2)		2 (3.3)	10 (13.9)	1 (12.5)	
Sensitivity of vulva							
Normal	80 (48.2)	80 (56.7)	ns	28 (45.9)	47 (65.3)	5 (62.5)	ns*
Sensitive	69 (41.6)	47 (33.3)		27 (44.3)	18 (25)	2 (25)	
Hypersensitive	17 (10.2)	14 (9.9)		6 (9.8)	7 (9.7)	1 (12.5)	
Reaction of vulva to SP							
No	61 (46.6)	51 (42.9)	ns	22 (43.1)	24 (40)	5 (62.5)	ns*
Yes	70 (53.4)	68 (57.1)		29 (56.9)	36 (60)	3 (37.5)	

p-value calculated using χ^2 and Fischer Exact tests*; VV: vulvovaginitis; VC: vaginal candidiasis; BV: bacterial vaginitis; ns: non significant; SP: sanitary pads.

factors change in this situation (hygiene frequency, hormones, less sexual relations) and can also cause changes in the vaginal flora reported in literature[4,17,18]. Sanitary pads are used during period, panty liners are used between them, and these are products widely available and accessible nowadays, including to the poorest sectors of society[3]. The need for comfort (feeling dry and clean) during and after the menstrual cycle is probably the most relevant factor leading 50% of North-American and North-European women to wear sanitary pads. Some other reasons (early discharge, blood leakage even with a tampon in use, urinary incontinence, vaginal flow) also have been reported[8,9]. Also, many women often complain about the excess of humidity and even physiological discharge[6,19].

The literature points menstrual cycles as phases where women get more susceptible to vulvovaginal infections[4,17,18]. Eschenbach et al.[4] performed a study on the mucosa, discharge and vaginal microbiota in three phases of the menstrual cycle of asymptomatic women, and described that the rate of Lactobacillus growth increased between the cycles and, on the contrary, the concentration of different species (other than Lactobacillus) was higher during menstrual flow, which demonstrates that the vaginal microbiota goes through microbiological changes in this phase.

More than half of the women who use sanitary pads, daily or only during flow, reported any type of reaction of the vulva to them. The main complaints were itching, fissuring, swelling and/or hyperemia. The literature holds some questionings about the potential risks of long-term use of sanitary pads to women's health, once there is increase in the temperature of the area, change in vulvar or vaginal pH, and maintenance of humidity, which can favor bacterial and fungus growth, and, therefore, vulvovaginal infections[3,5,8-10,19]. But we found no differences as to this aspect. Maybe it applies to women with recurrent VV, not to those presenting acute episodes, and this requires deep further investigation.

Runeman et al.[19] performed a study with 58 women who used neutral non breathable panty liners (with plastic layer) between three menstrual cycles, and reported that vulvar temperature, pH and humidity increased significantly compared to women who did not use it or used breathable types. Another study by the same authors[9] showed a high rate of aerobic microorganisms in the vulva of women using non breathable panty liners compared to those not using them. Jancovic et al.[18] found a higher incidence of VC in women who were used to wear underwear with cotton lining between menstrual cycles in comparison to those no wearing them (p=0.0001). However, Giraldo et al.[20] did not find significant difference as to the presence of candidiasis or bacterial vaginitis in women using breathable sanitary pads for 75 consecutive days in comparison to the Control Group, composed of women using only cotton underwear in the same period, which suggests that breathable sanitary pads are safe to women's health.

Table 2 – Information about use of underwear by women with and without vaginitis.

Variabless	Without VV	With VV	p-value	Types of VV			p-value
	Total (166) n (%)	Total (141) n (%)		VC (61) n (%)	BV (72) n (%)	VC+BV (8) n (%)	a = without VV x VC b = without VV x BV c = without VV x VC+BV
Fabrics of underwear							
Cotton	107 (64.5)	75 (53.2)	<0.0001	36 (59)	34 (47.2)	5 (62.5)	
Synthetic	0 (0)	15 (10.6)		4 (6.6)	11 (15.3)	0 (0)	<0.0001* (b)
Synthetic with cotton lining	59 (35.5)	51 (36.2)		21 (34.4)	27 (37.5)	3 (37.5)	
Underwear pattern							
Bikini or thong	105 (63.3)	93 (66)		44 (72.1)	45 (62.5)	4 (50)	
Thong	24 (14.5)	21 (14.9)	ns	6 (9.8)	12 (16.7)	3 (37.5)	ns
String	21 (12.7)	14 (9.9)		6 (9.8)	8 (11.1)	0 (0)	
Boxer	16 (9.6)	13 (9.2)		5 (8.2)	7 (9.7)	1 (12.5)	
Allergic reaction to synthetic underwear			ns				ns*
No	101 (63.9)	87 (64.4)		38 (63.3)	45 (64.3)	4 (80)	
Yes	57 (36.1)	48 (35.6)		22 (36.7)	25 (35.7)	1 (20)	
Does the underwear compress the genitalia?			ns				ns
No	147 (88.6)	122 (86.5)		54 (88.5)	62 (86.1)	6 (75)	
Yes	19 (11.5)	19 (13.5)		7 (11.5)	10 (13.9)	2 (25)	
Tight pants							
No	67 (40.4)	46 (32.6)	ns	21 (34.4)	23 (31.9)	2 (25)	ns
Yes	99 (59.6)	95 (67.4)		40 (65.6)	49 (68.1)	6 (75)	
To sleep, they wear							
0 layer	27 (16.3)	23 (16.3)	ns	12 (19.7)	11 (15.3)	0 (0)	ns*
1 layer	75 (45.2)	65 (46.1)		22 (36.1)	40 (55.6)	3 (37.5)	
2 layers	64 (38.6)	53 (37.6)		27 (44.3)	21 (29.2)	5 (62.5)	

p-value calculated using χ^2 and Fischer Exact tests*; VV: vulvovaginitis; VC: vaginal candidiasis; BV: bacterial vaginitis.

It is noteworthy that 59.3% of women chose to wear cotton underwear daily. However, 63.2% wear tight pants very frequently, which could even zero the benefits related to ventilation of cotton underwear[3,13,15]. Cotton underwear is strongly recommended by gynecologists who support that this type of fabrics favors ventilation compared to synthetic ones, and this could contribute positively with the maintenance of the vulvar microbiota[15]. Conversely, these properties are said to be zeroed by the use of tight pants, especially jeans, which prevents ventilation and compress the region, causing local occlusion, friction and ischemia. This type of clothing can potentially change the temperature, humidity and pH of the region[3,13,15].

Data from our study suggests that women with vulvovaginal infections wear more synthetic underwear ($p<0.0001$), in particular those with bacterial vaginitis ($p<0.0001$), and that over 60% of the sample wore tight pants routinely. This was not observed among the cases of candidiasis, which confronts general remarks. This is still a controversial matter in the literature, and, although most studies have not found differences between women of the control group and with candidiasis as to tight clothing and synthetic underwear[13,15], our findings agree with those by Guaschino et al.[21], who found an association of Candida sp. and bacterial vaginitis with the frequent wearing of synthetic underwear and tight pants, among other female habits.

The authors say that the lack of ventilation, obstruction of transpiration, warm environments, vaginal discharge full of bacteria, and the microtraumas caused by the clothes' rubbing on the skin favor microorganism multiplication. This result was not expected though, once synthetic underwear with cotton lining has not been related to changes. We believe that the presence of cotton lining does not change the occlusion caused by synthetic materials. Moreover, we found no significant differences in the number of layers of nightclothing between groups. This non relation between types of nightclothing and vulvovaginitis has been pointed by Heidrich et al.[13].

One can say that the habits of use of sanitary pads are currently related to women lifestyle, for they spend more hours away from home and in environments that do not allow hygiene with running water. Thus, our study suggests that this habit may not be associated with the onset of vaginal candidiasis or bacterial vaginitis in women without other trigger factors. The natural changes that come with period, and the use of non breathable clothing are also associated with acute episodes of vaginal candidiasis, and specially bacterial vaginitis.

The limitations of this study were related to the nature of the sample (free demand on a University Hospital). However, the high rate of women who accepted to take part in the study may actually have balanced this aspect. The tendency to misleading responses in an attempt to give the "right answer" must be considered in the interviews performed in the study. Inaccuracies may have occurred when it came to the number of sanitary pads used in their period's heaviest flow day, type of sanitary pad used (facing uncertainty of their knowledge about the plastic layers of panty liners). However, as the researcher who made the interviews was the same during the entire study, she tried to avoid it.

CONCLUSION

The habit of using sanitary pads is related to the presence of VV. Menstrual cycles, on its turn, and use of synthetic underwear is more frequently related to vulvovaginitis.

Conflict of interests

The authors report no conflict of interests.

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Address for correspondence:
PAULO CÉSAR GIRALDO
Rua Alexander Fleming, 101 – Cidade Universitária "Zeferino Vaz"
Campinas (SP), Brazil
CEP: 13083-881
Tel: +55 (19) 3788-9306
E-mail: giraldo@unicamp.br

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Epidemiological aspects mortality of acquired immunodeficiency syndrome in the city of Florianópolis, Brazil (1986–2006)

Aspectos epidemiológicos da mortalidade por síndrome da imunodeficiência adquirida em Florianópolis, Brasil (1986–2006)

Janelice Bastiani[1], Maria Itayra Padilha[2]

ABSTRACT

Introduction: The acquired immunodeficiency syndrome (AIDS) affects young adults of working age and commits sectors of society. **Objective:** To describe epidemiological aspects of AIDS deaths, people aged 13 and older living in Florianópolis (SC) from 1986 to 2006. **Methods:** descriptive, retrospective study of secondary data from the National Information System for Notifiable Diseases (Sinan), Information System (SIM) and the Brazilian Institute of Statistics and Geography and Statistics (IBGE). **Results:** There were 1,285 deaths, with 954 men and 331 women. Among them: men aged between 20 and 39, ignored skin color, complete high school and exposure categories for drugs and/or heterosexuality; women aged between 20 and 39, complete high school, ignored skin color, exposure categories and heterosexual heterosexual/drugs. **Conclusion:** The main epidemiological characteristics were age between 20-39 years old, male, skin color ignored, the average level of schooling. In males, the exposure category, emphasis is given to drugs, heterosexual/drugs, heterosexual and homosexual, the female standouts are the categories heterosexual, heterosexual/drugs and drugs. The ratio of deaths was higher among men than among women. Deaths due to AIDS in Florianópolis, show a decline from 1996 with improved survival for patients with AIDS.
Keywords: acquired immunodeficiency syndrome; mortality; epidemiology.

RESUMO

Introdução: A síndrome da imunodeficiência adquirida (AIDS) afeta os adultos jovens em idade produtiva e compromete setores da sociedade. **Objetivo:** Descrever aspectos epidemiológicos dos óbitos por AIDS de pessoas com 13 anos e mais residentes em Florianópolis (SC) entre 1986 e 2006. **Métodos:** Estudo descritivo, retrospectivo, de dados secundários do Sistema de Informação Nacional de Agravos de Notificação (Sinan), do Sistema de Informações sobre Mortalidade (SIM) e do Instituto Brasileiro de Geografia e Estatística (IBGE). **Resultados:** Ocorreram 1.285 óbitos, sendo 954 de homens e 331 de mulheres. Destacam-se: os homens com idade entre 20 e 39 anos, cor da pele ignorada, ensino médio completo e categorias de exposição drogas e/ou heterossexualidade; as mulheres com idade entre 20 e 39 anos, ensino médio completo, cor da pele ignorada, categorias de exposição heterossexual e heterossexual/drogas. **Conclusão:** As principais características epidemiológicas foram idade entre 20 e 39 anos, sexo masculino, cor da pele ignorada, escolaridade entre o nível médio. No sexo masculino, quanto à categoria de exposição, há destaque para drogas, heterossexual/drogas, heterossexual e homossexual; no sexo feminino, os destaques são as categorias heterossexual, heterossexual/drogas e drogas. A razão dos óbitos foi maior entre os homens do que entre as mulheres. Os óbitos por AIDS em Florianópolis apresentaram declínio a partir de 1996, com aumento de sobrevida para portadores de AIDS.
Palavras-chave: síndrome da imunodeficiência adquirida; mortalidade; epidemiologia.

INTRODUCTION

The acquired immunodeficiency syndrome (AIDS) has become a cruel disease for humanity. Researchers believe that the human immunodeficiency virus (HIV) started being disseminated beyond Africa, affecting men, women and children in the 1970s — 1971 precisely. It affects working young adults, thus impairing some sectors of the society, causing social and economic problems in the workforce or in the number of orphans due to the disease across the world[1,2].

The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that in 2010 there were 34 million people with HIV in the world, 6.65 million with AIDS under treatment, 70 million pregnant women protected and under retroviral treatment, 20 million homosexuals, 7 million sex workers, 10 million injecting drug users (IDUs) being assisted at HIV/AIDS prevention services, and 7 million orphans due to the disease[3].

Forecasts for the next two years were 2.6 million new cases of AIDS, 1.3 million avoidable deaths due to opportunistic illnesses, increasing up to 50% of the disease incidence. Statistics indicate a reduction in AIDs incidence; however, sex workers, homosexuals and IDUs are still disproportionally affected by the epidemics. Fifty percent of people eligible for AIDS treatment worldwide do not have access to antiretroviral, children affected have less access to treatment compared to adults, and many people are unaware of their serologic status[3].

In Brazil, AIDS follows the same path as in other countries. Researchers have been studying trends and determinant factors of the disease, defining the epidemics behavior in social nuclei (federal States and regions), and helping structure and organize public policies of the Sexually Transmitted Diseases-AIDS National Program[4,5].

Between 1980 and 2011, 608,230 new cases of AIDS were registered in Brazil, in increasing order by region: 323,069 in the

[1]Nurse. MD in Nursing by Universidade Federal de Santa Catarina (UFSC). Member of Grupo de Estudos da História e Conhecimento da Enfermagem e Saúde − São José (SC), Brazil.
[2]Nurse. PhD in Nursing by Escola Anna Nery da Universidade Federal do Rio de Janeiro (UFRJ). Post-octorate degree at Lawrence Bloomberg Faculty of Nursing at University of Toronto − Canada. Coordinator of Grupo de Estudos da História da Enfermagem e Saúde da UFSC. Researcher at National Council for Scientific and Technological Development (CNPq) − Florianópolis (SC), Brazil.

Southeast, 104,671 in the South, 64,706 in the Northeast, 31,011 in the Central-west, and 21.389 in the North[6].

Between 1980 and 2010, 241,469 deaths by AIDS as basic cause have been reported. In the last ten years, there was a reduction by 11.1% in mortality by AIDS in the country, but an increase in North, Northeast and South regions. Nevertheless, obits dropped in Southeast region and stabilized in the Central-West region[6].

In 2010, the State of Santa Catarina was in the 3rd place in the ranking of cases of AIDS in Brazilian federal states and in the 4th place in the ranking of incidence (30.2/100,000 inhabitants) and mortality rate (9.4/100,000 inhabitants), which is above the national average. Since 1998, Florianópolis, capital of Santa Catarina, have been placed among the cities with the highest rates of incidence and mortality in Brazil[6].

The questioning of this paper, based on the literature, is: what is the trajectory of AIDS in adults (notified and investigated) living in Florianópolis between 1986 and 2006?

The choice of this period is justifiable by the notification of the first case of AIDS in Florianopolis in 1986, and by the breakup of the prevention, assistance and care services for HIV/AIDS into the island and mainland territories of the city in 2006.

OBJECTIVE

To describe epidemiological aspects of deaths by AIDS among people aging 13 or more and living in Florianópolis between 1986 and 2006.

METHODS

This is a descriptive and retrospective study. The study population was composed of adults with AIDS living in Florianópolis, registered between 1986 and 2006 in the National Disease Notification System – AIDS (SINAN-AIDS) and in the Mortality Information System (SIM), and who died due to AIDS between 1986 and April 2010.

The orientation for cases were AIDS notification and investigation sheets for patients aging 13 or more[7], and death certificates (DC) as a source of notification (suspected or confirmed); therefore, all deaths due to AIDS as a primary/basic or contributing/secondary cause registered in SINAN-AIDS and SIM.

As the validated cases, after final diagnosis, with the SINAN-AIDS sheets properly filled in by the deadline and sent, after investigations, to the municipal, state and federal scopes[8]. Inclusion criteria was: people aging 13 years or more[7], notified for AIDS between 1986 and 2006, both genders, living in Florianopolis, searched for in SINAN-AIDS and/or SIM for death due to AIDS until April 2010, as well as cases meeting criteria by the AIDS epidemiological surveillance, based on the norms by the Center for Disease Control (CDC), in the USA: modified CDC criteria, Rio de Janeiro/Caracas criteria, exceptional CDC criteria, exceptional criteria for deaths and/or exceptional ARC criteria (AIDS-Related Complex) + death[8].

Exclusion criteria were cases in persons under 13 years of age, cases not meeting the criteria by the AIDS epidemiological surveillance, obits not related to AIDS (as primary/basic or contributing/secondary cause) and duplicity of cases in SINAN-AIDS and SIM.

We requested authorization for data collection, in March and April 2010, from SINAN-AIDS and SIM, at the epidemiological surveillance sector of the Municipal Department of Health in Florianópolis. Demographic data were collected from the website of Brazilian Institute of Geography and Statistics (IBGE), made available in March 2010[9].

The variables collected from SINAN-AIDS and SIM were: gender (male, female, ignored), age group (<20 years, 20–29, 30–39, 40–49, 50–59, 60 and more), akin color (white, other, ignored), education level (none, elementary school, high school, higher education, ignored), exposure category (work-related accident, bisexuality, bisexuality/drugs, drugs, hemophilia, hemophilia/drugs, heterosexuality, heterosexuality with risk partners, heterosexuality/drugs, heterosexuality/hemophilia, homosexuality, homosexuality/drugs, ignored), and population data of men and women living in Florianópolis between 1986 and 2006.

The software Epi Info 3.5.1 of the DCD was used to organize and analyze data. Results are presented in absolute numbers and frequencies, mortality coefficient and graphs.

The study was approved by the Ethics Committee of Universidade Federal de Santa Catarina (UFSC) in November 5, 2009, process 331, title page 290589, registration number 3813.0.000.242-09.

RESULTS

Between 1986 and 2006, SINAN-AIDS registered 3,209 cases of AIDS in adults from Florianópolis, aging 13–60 years or more. Of these cases, 1,285 adults (40%) died due to AIDS in Florianópolis from 1987 to January 2010, being 954 (74.2%) males and 331 (25.8%) females. The ratio between males and females was (M/F) 3:1.

Results show that deaths in adults aging 20–29 years of both genders are prevalent (71.7% males and 70.4% females) (**Table 1**).

There are significant differences between the variables sex and schooling; however, most adults had finished high school (83.1% males and 84.8% females) (**Table 1**).

As to the variables gender and skin color, the larger number of obits in males and females was in the ignored category (63.4% males and 59.5% females). We must emphasize that the variable "skin color" was not properly filled in, which resulted in a large number of ignored cases (**Table 1**).

Regarding sex and exposure category, men were more related to drugs, heterosexuality/drugs, heterosexuality and homosexuality, totaling 77.7%. Women, on the other hand, were mostly associated with heterosexuality, heterosexuality/drugs and drugs, with prevalence of 84.3% (**Table 2**).

Mortality rates were stable in ascending order between 1987 and 1996, with a drop in deaths after this period and consequent increase in survival rates among adults living with AIDS (**Table 3**).

About the survival and mortality by AIDS between 1986 to 2006, it was observed that between 1995-1997 the number of deaths decreases significantly, confirming the increased survival of carriers from that period (**Graph 1**).

Table 1 – Distribution of deaths due to AIDS in adults according to gender and age group, schooling and skin color, Florianópolis, Santa Catarina, Brazil (1986-2006).

Gender	Males 954		Females 331	
Variables	**f**	**%**	**f**	**%**
Age Group				
<20 years	16	1.6	15	4.6
20–29 years	276	28.9	105	31.7
30–39 years	408	42.8	128	38.7
40–49 years	173	18.1	54	16.3
50–59 years	55	5.8	18	5.4
60 and +	26	2.8	11	3.3
Schooling				
None	47	5.0	19	5.8
Elementary	200	21.0	67	20.2
High	593	62.1	214	64.6
Higher	82	8.6	18	5.4
Ignored	32	3.3	13	4.0
Skin color				
White	290	30.4	99	30.0
Others	59	6.2	35	10.5
Ignored	605	63.4	197	59.5

f: frequency.
Source: National Disease Notification System (SINAN), Mortality Information System (SIM) (March and April 2010).

Table 2 – Distribution of deaths due to AIDS in adults according to gender and exposure category, Florianópolis, Santa Catarina, Brazil (1986–2006).

Gender	Males 954		Females 331	
Exposure category	**f**	**%**	**f**	**%**
Work–related accident	1	0.1	–	–
Bisexual	45	4.7	–	–
Bisexual/drugs	23	2.4	–	–
Drugs	237	24.8	37	11.2
Drugs/hemophilic	1	0.1	–	–
Hemophilic	1	0.1	–	–
Heterosexual	172	18.0	179	54.1
Heterosexual/drugs	221	23.1	63	19.0
Heterosexual/hemophilic	1	0.1	–	–
Heterosexual with risk partner	44	4.6	34	10.3
Homosexual	113	11.8	–	–
Homosexual/drugs	35	3.6	–	–
Ignored	64	6.6	18	5.4

f: frequency.
Source: National Disease Notification System (SINAN), Mortality Information System (SIM) (March and April 2010).

Table 3 – Coefficient of mortality by acquired immunodeficiency syndrome per 10,000 inhabitants by sex. Florianópolis, Santa Catarina, Brazil (1986-2006).

Year	Gender		Year	Gender	
	Males	**Females**		**Males**	**Females**
1987	0.1	0.1	1997	5.6	1.5
1988	0.7	0.4	1998	4.9	1.0
1989	0.9	–	1999	4.6	1.0
1990	2.2	0.1	2000	4.3	1.1
1991	1.7	0.6	2001	4.4	1.6
1992	3.3	1.1	2002	4.7	1.4
1993	4.9	1.7	2003	4.4	1.7
1994	7.7	2.0	2004	4.3	0.9
1995	7.0	2.4	2005	4.5	1.8
1996	7.2	2.3	2006	4.1	1.2

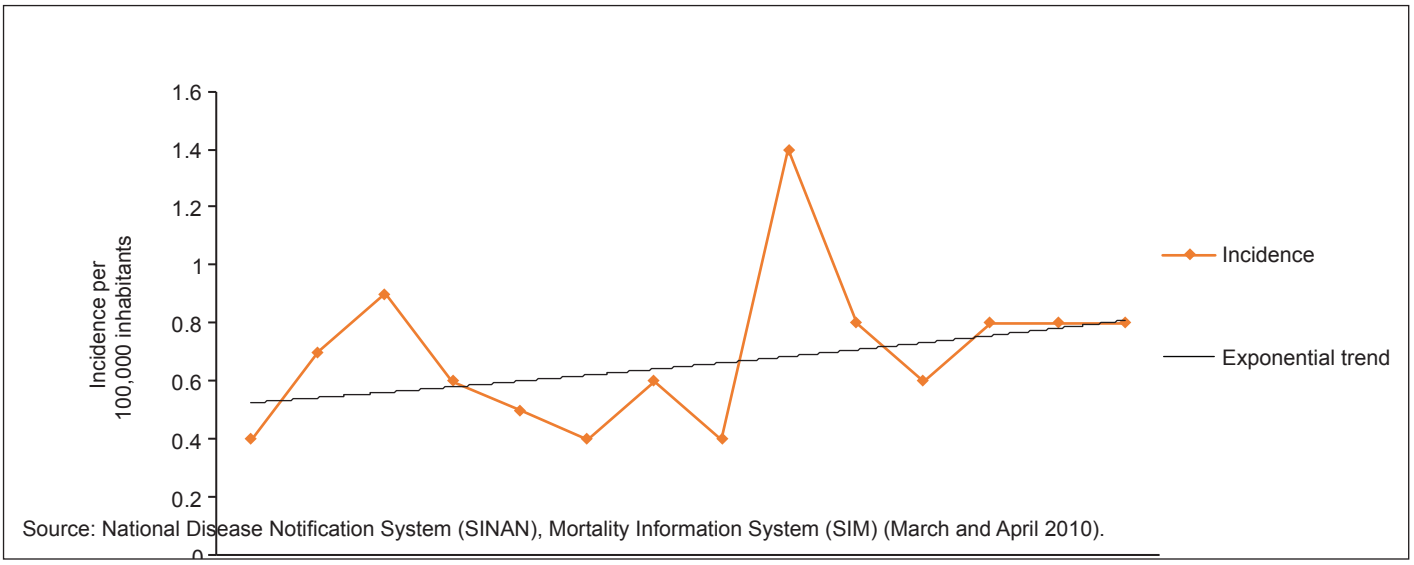
Source: National Disease Notification System (SINAN), Mortality Information System (SIM) and SUS Database (DATASUS) (March and April 2010).

DISCUSSION

In 2002, the Special Session of the United Nations General Assembly (UNGASS) was devoted to listing the monitoring and assessment of AIDS central indicators: contextual indicators, indicators related to the Brazilian Program for DST/AIDS, and impact indicators (morbimortality)[10]. In 2005, the UNGASS updated these indicators to commitment and social actions, behavior and knowledge, and impact (population at higher risk of HIV infection). The new indicators cover the monitoring of population subgroups (15–24 years old) in countries presenting concentrated epidemics, including Brazil. The risk of neglecting a population group to the detriment of exposed subgroups represents a fragility of the monitoring proposal: to renege on HIV/AIDS among young adults[10].

The literature tell us that, in the historical series from 1980 to 2011 in Santa Catarina, 30,284 cases of AIDS and 8,806 deaths by AIDS were reported[6]. In 2009, the Epidemiological Report by the Health Ministry showed that, among the 15 municipalities with the larger number of AIDS cases reported in Santa Catarina in the 1980s and 1990s, 51.1% were related to Florianópolis municipalities: Joinville and Itajaí[11].

Research show that the population who sought to find out their serologic status for HIV in Centers for Testing and Counseling (CTA) of Santa Catarina between 1984 and 2005 was composed of men and women who had been exposed to the HIV by sexual and blood routes, aging 20–29 years and followed by 30–39 year-olds[10,11]. Age groups with higher prevalence of deaths by AIDS in Florianópolis are those who seek the CTAs, that is, adults.



Graph 1 – Historical series of adults with AIDS according to year of diagnosis and current status (alive or dead), Florianópolis, , Santa Catarina, Brazil (1986–2006).

The analysis of the results unfolds deaths among adults aging 20–39 years; however, young adults and elderly (extremes of age groups) are vulnerable and exposed to the disease and to death. Studies on this condition indicate that late diagnosis, delayed treatment and the decrease in immune response also decrease survival of patients with AIDS, thus increasing the number of deaths[12].

Results show that adults who died due to AIDS compose a significant portion of the working and reproductive population, so they are more likely to infect their sexual partners. Advances in AIDS diagnosis and treatment emphasize that deaths interfere with family and social structures, investments in prevention actions and health promotion, which makes the follow-up with Family Health Teams, in the implementation of Adolescents, Men and Women Health Policies, really important for a new perspective of the disease involution[12,13].

The social level of adults who died by AIDS is a good parameter for the access to health services and care[10]. Lacking information about adults' income, we analyzed schooling. In Florianópolis, 62.1% of men and 64.6% of women had fulfilled elementary and high schools. In the analysis by age group, low educational levels among men increase deaths; among females, high educational levels increases deaths. There may be tendency among males with low schooling of not using protection in heterosexual/bisexual relations and when using injecting drugs, sharing needles or syringes without thinking about possible risks for their partners' health[4].

Among females, the risk of death increases along with the educational level. Many women find out AIDS when performing HIV tests, in antenatal care or after the death of their sexual partners. Women tend to accept unprotected sexual relations either by a request by their partners or by the belief that the person would not infect them. These situations imply the responsibility of health professionals in the approach to changes in sexual behavior[13-16]. Skin color is a gap in data collection, as the study shows. Historically, it leads our society to social and economic inequality, hampering an equal access to assistance and treatment in some parts of the country[17].

Predominantly Azorean ascendancy in Florianópolis, mixed with the immigration of Italians, Germans and other European people, and with people from neighboring States and from the Southeast region suggest predominance of white skin among the deaths by AIDS[18]. Information found in AIDS and Obit Declaration (OD) investigation sheets may be related to the cultural aspect of feeling part of an ethnical group, and the association between skin color and social status[17]. The depreciation of health professionals in the form filling by patients is also an important factor.

Studies performed in Brazil show that, in the 1980s, cases of AIDS were restricted to men, hemophilic patients, bisexual men, women with IDUs as partners and female sex workers[19,20]. In Florianópolis, the number of obits by AIDS, since the epidemics started, supports the finding in studies regarding exposure categories among males (IDU, heterosexual/IDU and heterosexual) and females (heterosexual, heterosexual/IDU and IDU).

Untill the 1990s, issues with drug trafficking and consumption, especially cocaine, showed the exposure of IDUs to AIDS in the South region, with epidemics spotted in coastal municipalities of Santa Catarina and Rio Grande do Sul[15,17,21]. These facts represent the process of heterosexualization, feminization, interiorization and impoverishment of the disease in the 20th century.

Women had been exposed to HIV, a risky situation that favors infection. AIDS, a disease that is insidious and asymptomatic for years; the economic dependency on their sexual partner; informal or low-paid employability; cultural social and religious patterns; sexual and domestic violence; and the lack or inefficiency of public policies aimed at females contribute to their exposure and vulnerability. Women aging 30–39 years (47.5%) reported not using condoms and women above 40 years old (64.3%) reported never having used it in sexual relations, which makes clear their total exposure to the virus[17,22].

The drop in mortality starting from 1996 is related to the introduction of antiretroviral treatment, increasing survival (with quality of life)

from 10 to 15 years, even though the disease is not curable. Late diagnosis, resistance of patients to antiretroviral drugs, gaps in assistance, difficulties in adhesion and improper treatment of co-infections such as hepatitis and tuberculosis still contribute to lethality among adults living with AIDS. The access to prevention resources, to health services and to early treatment, on the other hand, favor survival among these patients[17,21].

Stabilization and reduction in obits are related to the treatment with antiretroviral drugs, especially in the South and Southeast regions, where the epidemics is established for longer, with the control of drugs entrance and consumption, the change in the pattern of injecting drugs use to oral or inhalation routes (ecstasy, crack rocks, crystal, among others), and the reduction of cases among homosexual/bisexuals, and IDUs[5].

There is an approximation in the curve for the year of diagnosis and the year of death until 1995, but from 1996 on, the values were dissociated, as there was a reduction in the number of deaths and an increase in AIDS notifications.

These counterpoints of the population in the 1980s and beginning of 1990s are a characteristic of morbimortality by AIDS. When the subject is prevention, Brazil has invested in public policies to promote access to health, education and social features for the population in general[10,11,13,21].

Epidemiological surveillance of Florianópolis, paying attention to AIDS and to the perspective of treatment with antiretroviral drugs, invested in a decentralization of assistance to AIDS patients and created, starting in 2006: two Specialized Centers (SAEs) located in the center and in the mainland, two Assistance and Advising Centers (CTAs) in the central area (inland) and in the mainland, and the Program for Damage Reduction (PRD), aiming at avoiding HIV transmission among IDUs. The distribution of antiretroviral drugs in the municipality is performed in the pharmacy-school, which acts in conjunction with UFSC[23].

Knowing and analyzing epidemiological data allow the advance in knowledge about epidemiological trajectories of diseases, and help in the planning of strategies to confront illnesses. Therefore, we suggest that advances in studies about AIDs mortality (and other diseases) be made.

Household surveys on deaths by AIDS require large samples of people/families and have high cost, which makes it unfeasible to monitor mortality by AIDS. A strategy used in social micro-environments is the search in secondary databases, with data collection and analysis of variables associated with time, space and the person.

CONCLUSION

People aging 13 years or more who died due to AIDS in Florianópolis between 1986 and 2006 had some epidemiological characteristics in common: age between 20–39 years, male sex, ignored skin color, educational level until high school. Among men, some exposure categories emphasized are drugs, heterosexuality/drugs, heterosexuality and homosexuality; among women, the most common categories were heterosexuality, heterosexuality/drugs and drugs. Death ratio was higher among men than among women.

Deaths by AIDS in Florianópolis decreased from 1996 on, causing an increase in AIDS survival rates. However, despite the easier access to antiretroviral drugs, which improve survival, there is a need for AIDS monitoring in all population groups.

Conflict of interests

The authors report no conflict of interests.

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Address for correspondence:
JANELICE BASTIANI
Rua Adhemar da Silva, 1.158, fundos − Kobrasol
São José (SC), Brazil
CEP: 88101-090
Tel: +55 (48) 9903-0224/3259-5825
E-mail: bastiani@ibest.com.br

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Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome prevention and transmission liability

A prevenção contra vírus da Imunodeficiência Humana/Síndrome da Imunodeficiência Adquirida e responsabilidade da transmissão

Monica Paraguassu[1]

ABSTRACT

Introduction: A study on the relationship between the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) transmission and the need for preventive education and information measures. **Objective**: To research the references on social reality to guide a preventive-repressive criminal policy aimed at the HIV/AIDS transmission, but able to strengthen the importance of prevention through information and education measures. **Methods**: A retrospective and prospective interdisciplinary theoretical study, in the field of public health policy and legal-international-criminal-environmental terms, concerning the execution of the perspective of universal human rights considering cultural relativism, the hypothesis of the right to the difference and the peculiarities of the matter of affective-sexual relationships and HIV/AIDS transmission. **Results**: The importance of preventive measures against the HIV/AIDS transmission through the universalization of health. **Conclusion**: The need for public policies emphasizing information and educational actions about the disease and its mode of transmission, that is, emphasizing the need of condoms in sexual relations, the co-liability of the person being infected, and the window period in order to avoid criminalization as a solution.

Keywords: human rights; health public policy; disease prevention; crime; HIV.

RESUMO

Introdução: Estudo sobre a relação entre a transmissão do vírus da imunodeficiência humana (HIV)/síndrome da imunodeficiência adquirida (AIDS) e a necessidade de medidas preventivas de informação. **Objetivo:** Buscar referências na realidade social para nortear uma política criminal preventivo-repressiva dirigida à transmissão do HIV/AIDS, mas que seja capaz de relevar a importância da prevenção por meio de medidas de informação e educação. **Métodos**: Estudo teórico prospectivo e retrospectivo, e interdisciplinar, entre o campo da política de saúde coletiva e os termos jurídico-internacional-ambiental-penais, no que concerne à efetivação da perspectiva da universalização dos direitos humanos, considerando o relativismo cultural, a hipótese do direito à diferença e as particularidades inerentes ao binômio da questão relações afetivo-sexuais e transmissão do HIV/AIDS. **Resultados**: A importância de medidas preventivas contra a transmissão do HIV/AIDS por meio da universalização da saúde. **Conclusão**: A necessidade de políticas públicas de ênfase na informação e na educação sobre a doença e o modo de transmissão, portanto da "janela imunológica", da necessidade do uso de preservativo e da corresponsabilidade da vítima, de modo a evitar a criminalização e o uso da lei penal como solução.

Palavras-chave: direitos humanos; políticas públicas de saúde; prevenção de doenças; crime; HIV.

INTRODUCTION

This paper is dedicated to the relation between the criminal policy for Human Immunodeficiency Virus (HIV) transmission, whose infection results in the Acquired Immunodeficiency Syndrome (AIDS), and the lack of measures to inform the population about this disease's prevention. The basic argument of this study is "the right to love", used to understand one's omission of their seropositivity to their affective-sexual partner, supported by the principle of *habeas corpus* (HC), number 98,712, from November 5th, 2010, decided by the Supreme Federal Court (STF). Originally, this appeal has been related to cases of individuals contaminating their partners with HIV by not wearing condoms deemed attempted murder. The STF changed the imputation of crime of attempted murder to risk of serious infection, article 131 of the Penal Code.

The position of STF is based on the Technical Paper (NT) on the criminalization of HIV sexual transmission, NT 350/2009, November 27, 2009, by the Department of Sexually Transmitted Diseases, AIDS, and Viral Hepatitis of the Health Surveillance Secretariat of the Ministry of Health (SVS/MS).

Such a legal instrument supports the perspective of confronting HIV and AIDS outside the scope of criminalization of transmission and criticizes penalization as a means of prevention. It also draws attention to the need of universalization of preventive health public policies, and so emphasizes the lack of measures to disseminate information about the many factors favoring HIV/AIDS epidemics. On the authorities side, there is a lack of information on the pool of HIV-positive people; on the individuals side, there is a lack of knowledge about: their serologic status; the high transmissibility of the virus during the "window period"; the need of preventive measures such as use of condoms; the success of antiretroviral therapy (ART); the "cocktail" highly active antiretroviral therapy (HAART); and the understanding that AIDS is no death sentence, but a treatable disease.

This study explored the issues of HIV/AIDS transmission and the current matters requiring a universal preventive understanding of human rights, with a view to the progression of the disease beyond the social groups — drug users and homosexuals, for instance — that have been stigmatized in the 1980s, for nowadays the picture of the epidemics is feminized and heterosexualized,

[1]PhD from Université de Paris I; Scholarship from Coordenação de Aperfeiçoamento de Pessoal de Ensino Superior (CAPES); Professor of the Postgraduate Course in Constitutional Law at Universidade Federal Fluminense (UFF) – Niterói (RJ), Brazil.

especially due to deficient information, as above-mentioned. As alternative to this issue, we emphasize the thesis of objective imputation, presenting the victim's self-endangering and consent as penal response coherent to this relation, once it shows the understanding of the current risk society that supports the status of "victims" in penalization, considering their role of protagonists of their own lives, not of mere spectators, and therefore sharing the liability of transmission with the person who infected them.

OBJECTIVE

To seek references in social reality to guide a criminal, preventive, repressive policy aimed at HIV/AIDS transmission that is also able to give importance to prevention with educational measures of information dissemination.

METHODS

The methodology used in this study should be identified as juridical, theoretical, retrospective and prospective, and interdisciplinary.

This is a retrospective theoretical reflection that takes HC 98.712/2009 as example, but also provides elements for a prospective analysis once it uses the theory of objective imputation, within the strands of victim self-endangering and consent as a response to the need of HIV/AIDS transmission liability, without promoting stigmas by criminalizing the virus carrier, thus reshaping the status of the victim in penalization.

This is a multidisciplinary study, once it involves Law and Medicine. In the legal field, we make reference to Human Rights and Environmental Law, to the model of liberal State-Society criminal justice policies, and to the notion of universal respect for human rights. In the medical-scientific field, we present orientations by the Health Ministry in NT 350/2009.

In the Law Field, environmental human rights are present in the dyad affective-sexual relations and HIV/AIDS transmission when it comes to the right to quality of life and healthy environment:

> The notion of quality of life goes through a polysemic semantic field: it is related to life ways, conditions and style, but also comprehends sustainable development and human ecology. It is also related to democracy, development and human and social rights. As to health, the notions unite and result in the collective building of standards of comfort and tolerance that a society will use as parameter (p. 10)[1].

The above-mentioned dyad is also studied under the perspective of the Liberal State-Social criminal policy, whose basic premises are protection of individual legal goods and social peace[2] in the face of individual guaranties, rights and freedoms guaranteed by the democratic state of rights. The context of polemics, beliefs and prejudice involving HIV/AIDs transmission was taken into consideration, so as to allow reflections on which legal goods are protected, whether this protection may contribute with social peace or not, and how the arguments of universal respect for human rights — where such objectives are based on — considers particularities, and behavioral and cultural differences. That is why the notion of universalization of human rights is still addressed in Law, and it means that humans are subjected to rights, but this expression has been misunderstood and treated as an imposition of absolute truths and values; if this were true, particularities would have been banished in History of Men, which obviously implies erasing differences in all dimensions. The human right to information is fundamental so that there can be prevention of HIV/AIDS. Interdisciplinarity is also present in references of the Medical field. The binomial Medicine-Law is also essential for the total understanding of this issue. The society cannot fail in considering that positions and decisions are not to be inflexible. Legal responses are weak, fragile, and temporary given uncertainties and constant changes in Medicine; therefore, in view of this complexity, the understanding of Law principles must not be lost sight of, especially reasonableness, within the framework of the contemporary society. NT 350/2009 is reference object in this study because it meets the binomial Medicine-Law by pointing the biases of the public health policy, which must be the basis of the public criminal law policy in order to assist the society.

In these terms, we attempted to exit the dichotomist frame of common sense: on one hand, collective health issues against the matter of epidemics, requiring a preventive-repressive character to AIDS transmission; on the other hand, moral-repressive reasons related to moralists — religious or not — that link the disease to socially stigmatized groups, denying the possibility of dissemination to people from all social strata, as underlined by NT 350/2009:

> Despite scientific advances and the widening of access to information, prevention, diagnosis and treatment, and despite all sexually active people being potentially exposed to HIV regardless of gender, ethnicity, sexual orientation or profession, the stigma and prejudice concerning people living with HIV is a serious obstacle to the confrontation of the epidemics (Item 11).

As a result, these perspectives do not reinforce the need for more and clearer information, and, instead of protecting people, they make them vulnerable and punished by the lack of information, education, and public policies aimed at preventive educational actions.

RESULTS

Criminal Law is used as response in our society — even being a risk society — to address the matter of HIV/AIDS transmission, as the emblematic case brought to STF, HC 98,712, decision dating from October 5th, 2010. Originally, a case of an individual who infected his partner by not wearing condom was treated as attempted murder, and therefore judged by Jury Trial. Nevertheless, the STF changed the imputation of this crime to serious risk of infection, so the process was sent to one of the common criminal divisions of the State of Sao Paulo. The decision says:

> Severe disease — HIV transmission — intentional crime against human life versus transmitting serious illnesses. Facing prediction

expressed as to the criminal approach, it is not appropriate to fit the case of risk of serious infection as intentional crime against human life (HC 98,712).

Considering that the society is protected because an individual marginalized in various dimensions (i.e. the standard of prison profile, because they are "mannerless and misinformed" when excluded from the formal educational system and stigmatized as homosexual, drug user, and so on) has been arrested for not using condom by ignorance or negligence verges on surrealism, for the right to punish by the State is no absolute duty, but an essentially subsidiary measure to be used as *ultima ratio*[3]. This expression, meaning the last refuge guaranteed by Human Rights, is a subsidiary public policy to be used when all other means have been exhausted or ineffective.

Crime is the result of impunity, or the belief in institutions that restrain criminality. Therefore, effective preventive public policies should constitute the basis of the solution for this problem, considering: current context of the risk society, implementation of preventive measures, and the liability of victim in penalization. Everything according to the theory of objective imputation and the theory of risk, mischaracterizing criminal features of the approach or considering it in regard to the defendant using the argument of "right to love" to exclude illegality in the state of necessity, or culpability in the state of unenforceability of divergent conduct, to the extent of consensual affective-sexual relations. In order for that to occur, information must be fully accessible by all the society.

The line of reasoning presented here is oriented by NT 350/2009. This technical paper addresses the need to establish a public policy of prevention universalization, underlying the lack of measures for dissemination of information about many factors contributing with the HIV/AIDS epidemics by the authorities and the people.

The item 1, 2, 12 and 13 of this NT alert to the need to avoid criminalization of transmission and the use of penalization to do justice and prevent it[4], in the name of human rights and the principles of secrecy and confidentiality, in order to impede that such measures be borne by people based on their serologic status; item 3 emphasizes universal access to prevention, to treatment, to care and support for HIV patients; item 4 underlies widening of access to diagnosis in view of unawareness of serologic status; item 5 draws attention to the "window period", the time period between infection and detection of HIV antibodies in the blood that can last over 30 days and is of great risk of transmission; item 6 reinforces the status of the disease, which goes from death sentence to treatable illness upon early diagnosis and proper treatment; item 7 addresses the reduction of transmission risk by a subject under treatment; items 8 and 9 point out the use of condoms as preventive measure within a policy of assistance and prevention; items 10 and 11 bring about preventive measures in the fields of information and transmission co-liability.

Nowadays, the Brazilian society cannot be seen as totally intolerant to particularities and differences; maybe disguised. When this disease is understood as transmissible only to groups that are already excluded, a road to wider contamination is opened, once there is no general, common or frequent knowledge, nor a concerning about the vulnerability of all to infection, as feminization and heterosexualization of the disease is currently seen:

> The behavioral feature should be understood according to standards of the relationships people maintain, where the risk is a consequence of their behaviors and depend on the other and on the social context they are both inserted (p. 38)[5].

The level of misinformation remains, even though some changes can be seen, once the civil society takes two stances — especially shown by the Media. On one side, little emphasis is given to the risk of contamination as a means of avoiding generalized and directed discrimination to stigmatized groups; on the other side, silence results in an open road to transmission, especially between the young, and therefore lack of information about the exact number of infected people, the effects of antiretroviral therapy — which improves quality of life, but is not able to cure — the use of condom as prevention measure, and the "window period", where transmissibility is very high.

DISCUSSION

The definition of a preventive-repressive public policy should be based on spreading more information and education, as mentioned in items 1, 2 and 11 of NT 350/2009, moving away from the idea that criminal law may be the solution of the problem by criminalizing the transmission of a disease. This view is comprehended by the following perspective:

> Environmental health appears as social priority in health promotion, as institutionalization, by the Health Ministry, of the National Environmental Management System, whose main objective is to know and stimulate interaction between health, environment, and development, aiming at strengthening the people's participation in health promotion and quality of life (decree 3.450, May 10, 2000) (p. 147)[6].

Therefore, the confrontation of the problem of HIV/AIDS transmission seems to be through interdisciplinary understanding, beyond criminal law, firstly being recognized the fact that all live in a risk society. One of the perspectives is the search for ethics in the modern industrial society, considering the references of Environmental Law such as the "principle of responsibility", the "precautionary principle", the "principle of common but differentiated responsibilities".

The "principle of responsibility"[7] focuses on the reflection about the so-called Ethics of Respect, once the technology in modernity has become a threat, and understands that society is living inside a bubble of values and that the guide to survival goes beyond physical living, predicting danger. Human affairs are indissolubly linked, and one cannot avoid their acting to affect the other's acts and destiny; therefore, when an individual puts their goods to risk, they are also putting to risk something over which they have no right, belonging to the other. This is the reflection of the instruments of

International Environment and Quality of Life Law, presented at the Stockholm Convention, in 1972, when addressing the "precautionary principle", the "principle of common but differentiated responsibilities", or the sustainability paradigm criticized since Eco-92, which defends "meeting the present needs, without compromising the needs of future generations".

The reasons of the risk society are not external to it; its ailments and threats are inherent to post-industrial society, whose problems are related to shortage and wealth, the fear of risks other than historical ones, once current risks are global and cross-border, i.e. radioactivity, pollution, research on transgenics[8]. This society also produces other "immunossuppressed" factors that favor the development of diseases, i.e. unemployment, social inequalities, individualism, visible and invisible risks of many dimensions such as drugs, medication, irradiations, pollution, stress, and hunger[9].

Created by society itself, risks and damages must be faced with a notion of social contract, modernization of political, state, social and familial life. Going beyond on these issues, public policies must prevent disease causes ahead of the matter of virus, reaching the modern society behavior in various dimensions, as stated by Fleck:

> The WHOQOL was developed from the principle of quality of life as a comprehensive matter that may be applied to many diseases and non-medical situations […]. The first module of WHOQOL developed was HIV/AIDS in view of its medical relevance, impact on quality of life, social stigma and the specificities of contagion. First, experts from eight nationalities gathered (including countries with high rate of cases such Brazil, United States, Zambia, Zimbabwe and India). Specific issues relating to peculiarities of HIV/AIDs patients were raised, comprising their assessment of quality of life. For example, social rejection, social assistance system overload, reasons for this overload, impact on sexuality, fear of infecting other people and many other aspects were addressed (p. 37)[10].

The choices in criminal Law are guided by political-scientific rules, according to the reality and influences of social bodies in relation to criminal phenomenon. Punitive logic is preferred in certain social sectors and, therefore legislative inflation never goes out of fashion, especially because the population is not well educated or informed. Notwithstanding, the explanatory statement of the general part of the new Criminal Procedure Code, Law 7.209 from July 11th, 1984, item 23, about criminal imputability, points that the readjustment of the process of character formation must be imputed to education, not to law.

Unfortunately, HIV/AIDS transmission is not out of this trouble. To exit this situation, population should be educated about quality of life in a healthy environment as prevention premise, a kind of "ecopedagogy", the knowledge of the individual as protagonist in his context, underlying that any person may transmit the virus and any person can be infected (item 11, NT 350/2009), also considering that the main transmission route is sexual intercourse or affective-sexual relations, as HIV may be present in the blood, semen, vaginal discharge, and also in breast milk.

Ironically, the true demonstration of universalization and socialization of human rights has been the idea that, being sexual relation the leading transmission route, among others, it is a condition in which all individuals may find themselves.

Recognizing the HIV/AIDS epidemics must be the starting point of public health policies. Therefore, we must not disseminate the perspective of pointing a scapegoat nor the perverse logic of choosing criminal law as the main response to it, especially considering the reaching of media. By nature, this is a flawed, violent, contradictory instrument, once it is related to the past suffering of the weak. Criminal law is not a preventive or educational solution, neither a tool for social peace, as the current guarantee penal theories support that there must be the *ultima ratio,* which means the criminal law is an instrument of public policy to be used in limit situations, thus in conjunction to public health policies.

There is a covering up of the epidemics in the absence of information, being lost the access to prevention universalization, indicated in NT 350/2009, item 3. The lack of information is seen in many aspects of the problem. Dissemination of knowledge is essential in the following situations:

a) Antiretroviral therapy along with early diagnosis and adequate treatment has made AIDS a treatable chronic disease, not a death sentence anymore; however, once in treatment, the individual has the wrong idea of wellness in very little time, facing the success of medication. Having a good perception of well-being, this individual maintains his/her affective-sexual relations. This is a serious problem; caution must be taken not to transmit HIV, but also to avoid other STD infections, as reinfection increases viral load and the risk of acquiring other viral illnesses, thus hindering the efficacy of treatment. Important to note that studies reported that "individuals started presenting metabolic changes such as dyslipidemia, insulin resistance, glycemic changes and others, as well as HIV lipodistrophy" (p. 233)[11].
b) The need to inform the population about the window period, according to NT 350/2009, item 5, the time period between the infection with HIV until the body produces enough HIV antibodies to be detected in the blood, lasting even more than 30 days, with high risk of transmission.
c) The need to inform the population about the disease aiming at changing the picture of individuals aware of their serologic status, and the need to use condoms, considering research and items 4, 7, 8, 9 and 10 of NT 350/2009, pointing out the increase of AIDS in certain regions, among the young, and the feminine and heterosexual character of the epidemics. Recent studies have brought this information and the following (report of increasing rates in the North and Northeast of the country):

   > Incidence among the homosexual youth and young females is increasing; the raise in new cases among women aging 15 – 24 years caused an intervention aiming at male ratio, as the number of women diagnosed in this age group exceeds the number of men in the same age (p. 227)[12].

Nevertheless, similar data were found in a research performed in 2006:

> In the first half of the 1980s, identification of new cases was restricted to the States of São Paulo and Rio de Janeiro, large urban centers. The epidemiological profile of patients was: males, high socioeconomic status, homosexuals or bisexuals. At the end of the decade, the disease reached other regions of the country, so there was a progressive change in this profile to increasingly heterosexual: females, low income, medium and small cities (p. 2369)[13].

Sadala and Marques completed the picture: "the change in prevalence per gender is an example of this transformation: 25 men for each woman in 1991 to 2 men for each women in 2000" (p. 2369)[13]. Maliska *et al.* point another aspect of the disease related to the disease "impoverishment":

> Many issues have been raised in Brazil concerning AIDS epidemics: it has been characterized by microregional sources with different increasing rates; progressive increase in cases among women by heterosexual transmission; drop in mortality rates due to the implementation of retroviral therapy in 1996; progressive impoverishment of the disease, reaching areas that are distant from large urban areas, smaller and poorer; proportional increase among people with low educational levels and precarious labor market position (p. 86)[14].

d) Therefore, HIV/AIDS is not actually an object of information dissemination for clarification not because society is tolerant, but ignorant by fear, not understanding; people have fear towards the other, not for the other[15]. Society is caring in fear. Society itself helps misinformation by the worship of beauty, esthetics, body health, and youth in an attempt to avoid discrimination, lacking relevant knowledge about real facts and conditions.

Some considerations emphasize one's liability over their own health (p. 2575)[16]:

> Although the literature on the relation men-health care tries to highlight the non-liability of individuals over their health (constant references of female mediators in male health care is a clear example), the transposition of this cultural dimension of care to assistance and health professionals' work must consider the cultural dimension, but not reinforce it, in order to develop subjects' autonomy in health. The focus of individual liability to reduce risks of diseases must not forget structural factors, including social and economic status, ethnicity and sexual orientation, which directly impacts health.

Along with the individual's valuing of their own health, the thesis on penal liability must go through changes when it comes to the victim. Issues of self-endangering and consensual risk taken would be considered, as stated by the theory of objective imputation[17], situations where the victims are responsible for their own behavior, including not using condoms, that is, having unprotected sexual relations[18], sharing of needles and syringes, not being able to chose partners or women's overtrusting their partners and therefore exposing to the virus[19]. In such a case, criminal law may consider the following:

a) self-endangering can only be used for individual legal goods and only in cases where the victim is older than 18 years and with preserved mental faculties;
b) in order for that to occur, the victim must have acted voluntarily and been aware of the risks to which is being exposed;
c) in self-endangering, free and conscious behavior of the victim is determinant for a harmful result that was not wanted by any of the parties at first (p. 166)[20].

The potential victim must therefore understand the importance of education and information to population, once they are victim of themselves, of their free will, being responsible for their own acts and for their importance in society. Liberalism is the theoretical basis of human rights that praises free choice and free will; therefore the person is free to practice not only their rights and freedoms, but also their duties and wills. Once "desire is not an order", according to Gikovate (2010), "The desire is part of the human voluntary domain, while the need is obligatory." (p. 27). "[…] free is the man who can say yes and also no to an erotic situation". […] "In order for us to think in freedom, we must long for an active reason interfering and deciding more than biology, and not blindly respecting rules and beliefs of the culture we live in, what we usually do by fear of rejection or lack of courage to make mistakes, choosing the same mistakes made by most people" (p. 202-3). […] "being free is not being like this or that; it corresponds to the intimate joy resulting from coherence, when we are capable of acting the same way we think" (p. 203)[21].

So, the principles of liability, prevention and precaution should be part of the pedagogical public policy, once HIV/AIDS transmission brings a complex social response with it, as the defendant in the criminal procedure is also a victim of the disease.

These arguments are the merits of the contingent of HIV/AIDs infected homosexuals, who claim the "right to love" and, finding themselves fragile by this condition, need understanding to turn the situation around, also stating that they need to hid the information from their affective-sexual partners. This has also been pointed out in this research[22]. The right to love is a legal interpretation used to exclude illegality in the state of need or to exclude the guilt in the state of unenforceablilty of diverse conduct when it comes to consensual affective-sexual relations.

The matter of silence, that is, when one does not warn their sexual partner about their condition with HIV/AIDS is the current reason for non using condoms, for the person understands that by not using it, their partner will not identify them as virus carrier, which would in turn prevent them from the "right to love". It not only shows the affectionate needs of this person that should be assisted with psychological care, but also the lack of information about the risks of reinfection due to increase in viral load and of being affected by other viral diseases, which can hinder the efficacy of antiretroviral therapy.

Not to mention that, although people have defined behaviors when facing risk situations, it is not possible to identify them as virus carriers, showing the real problem and the need to disseminate information to the entire population. There is also the risk of "window period"— the time period between the infection with HIV until the body produces enough HIV antibodies to be detected in the blood, and which can last more than 30 days, with high risk of transmission.

Notwithstanding, sexual relations without the use of condoms without direct intention, for the aforementioned reasons, must not presume volition to endanger one's life (chapter III of the Penal Code) or to body injury (chapter II of the Penal Code); therefore, it's no presumption of blame, but object of interpretation for the right to exercise intimacy, that must be related to the perspective of victim liability. This is the notion of intimacy:

> Intimacy is related to the exclusivity people reserve to themselves, without any social repercussion, not even their private life that, even being isolated, is lived with others (family, work colleagues, leisure) (p. 77)[23].

Besides the right to intimacy, to honor, to privacy and to image, fundamental, inviolable rights according to the Federal Constitution in item 5th X, "rights relating to personality of the social being"[24], facing public interests, the principle of reasonability is also considered. One of the dimensions of the right to intimacy complies with jurisprudential decision RO 623003520065070012, which states the following: according to the World Health Organization (WHO) and the International Labor Organization (ILO), in the scope of employment, general professions are not risky to HIV transmission; seropositive and asymptomatic people must be treated as any other employee; people presenting symptoms or illnesses must be treated as ill employee, and the employer does not bear the right to demand the worker to participate in investigative procedures or to inform the employer about their condition, aiming at non-discrimination[25].

CONCLUSION

The privileged path for the confrontation of HIV/AIDS transmission should not be criminal law, but must go through demystification of the disease, surpassing the idea of looking for the guilty for its transmission, a measure that benefits manufacturers of chemical reagents, appliances and drugs. We must privilege the undermined, malnourished organisms that have been affected by many infections, transforming the immunosuppressed into "immunoefficient" people, so that they do not be prone to tumors and infections.

This problem must then be faced with a universally preventive Medicine that can be accessed in a non-discriminatory way and with other public policies aimed at adequate nutrition, healthy environment and well-being, prophylaxis for healthy people against any viruses through vaccination campaigns, thus making "immunoefficient" subjects and especially eliminating hunger, unemployment, diseases, poverty, waste, and disrupted families.

To sum up, references made by NT 350/2009 must be considered, for it constitutes an instruction containing research results underlying the importance of preventive measures for health universalization, chiefly the wide use of information about the disease and behaviors that may lead to it, including condom use, alerts about the "window period", and the liability of the victim in HIV/AIDS transmission in order to avoid criminalization of HIV transmission by the indiscriminate use of criminal law.

Conflict of interests

The author report no conflict of interests.

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Address for correspondence:
MONICA PARAGUASSU
Faculdade de Direito da Universidade Federal Fluminense
Rua Presidente Pedreira, 62 – Ingá
Niterói (RJ), Brasil
CEP: 24210-470
Tel.: + 55 (21) 98866-2842
E-mail: monica.paraguassu.uff@gmail.com

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Delta hepatitis in Rondônia: epidemiological analysis from 1999 to 2012

Hepatite delta em Rondônia: análise epidemiológica de 1999 a 2012

Gabriel de Deus Vieira[1], Henrique Schroeder Affonso Coelho[1], Rodrigo Barbosa Passos[1], Eloisa Barbosa Brum[1], Raquel Mascarenhas Pereira[1], Paula de Carvalho Magalhães[1], Camila Maciel de Sousa[1]

ABSTRACT

Introduction: Hepatitis Delta virus (HDV) is considered an important cause of severe liver disease. **Objective:** This study aimed at an epidemiological analysis of cases diagnosed in Rondônia. **Methods:** A retrospective study from 1999 to 2012 was done through data provided by the State Agency of Health Surveillance of Rondônia (AGEVISA-RO). The variables analyzed were: year of diagnosis, gender, age, contact with patients known to have hepatitis B virus (HBV), ethnicity, vaccination, exposure to risk factors, mechanism of infection and clinical manifestation. **Results:** 149 cases have been reported, with an average incidence of 0.7 cases per 100,000 inhabitants/year; 62.4% of these were males and 5.3%, females. The most common age group was between 20 and 39 years. About hepatitis B vaccination, the majority took no vaccine dose. The most common route of transmission was sexual (71.8%), and most patients were in the chronic phase of the disease (95.9%). **Conclusion:** The population affected by the virus is mainly composed of men in the sexually active age group, with sexual intercourse as the main mode of transmission. Low adherence to vaccination by the population affected was observed; thereby, measures of education and public awareness are needed.

Keywords: epidemiology; hepatitis D; Hepacivirus.

RESUMO

Introdução: O vírus da hepatite Delta (VHD) é considerado um importante causador de doença hepática grave. **Objetivo:** Este estudo objetivou realizar uma análise epidemiológica dos casos diagnosticados em Rondônia. **Métodos:** Foi feito um estudo retrospectivo de 1999 a 2012, por meio de dados cedidos pela Agência Estadual de Vigilância em Saúde de Rondônia (AGEVISA-RO). As variáveis analisadas foram: ano de diagnóstico, gênero, faixa etária, contato com paciente sabidamente portador do vírus da hepatite B (VHB), cor, vacinação, exposição aos fatores de risco, mecanismo de infecção e forma clínica. **Resultados:** Foram notificados 149 casos da doença, tendo uma incidência média de 0,7 casos/100.000 habitantes/ano; destes, 62,4% são do gênero masculino e 5,3% são gestantes. A faixa etária mais comum foi entre 20 e 39 anos. Sobre a vacinação da hepatite B, a maioria não tomou nenhuma dose da vacina. A forma mais comum de aquisição do vírus foi a sexual (71,8%), estando a grande maioria dos pacientes na fase crônica de doença (95,9%). **Conclusão:** A população acometida pelo vírus constitui-se, principalmente, de homens na faixa etária sexualmente ativa, tendo como principal meio de transmissão a relação sexual. Observou-se baixa aderência da população acometida à vacinação; com isso, medidas de educação e conscientização da população se fazem necessárias.

Palavras-chave: epidemiologia; hepatite D; Hepacivírus.

INTRODUCTION

Hepatitis D virus or Delta hepatitis (HDV), from the *Deltaviridae* family, requires the concomitant presence of hepatitis B virus (HBV)[1] in a human body in order to infect it, and constitutes an important public health problem, once it may cause acute or chronic liver disease[2]. It is estimated that about 18 million people around the world are infected by HBV[3,4].

In Brazil, the prevalence of infection varies according to the region: in South and Southeast, endemicity is low; in the Central West and Northeast, it is medium; and in the Amazonic region, endemicity is high[5].

Infection by HDV is worrisome in areas of increased transmission of HBV. In most cases, HDV causes an asymptomatic infection that evolves to chronic disease or origins acute liver insufficiency that may progress to cirrhosis[6].

The Amazonic region has the highest prevalence of HBV in the world and, consequently, the highest rates of HDV superinfection[7]. In the Brazilian Amazonia, Delta hepatitis affects many individuals of river-side and indigenous populations, being associated with severe forms of acute jaundice[8].

OBJECTIVE

To perform an epidemiological analysis on Delta hepatitis, in Rondônia.

METHODS

This is a retrospective, descriptive epidemiological study about cases of Delta hepatitis diagnosed in the State of Rondônia from 1999 to 2012. Data and statistics by the Surveillance agency of the State (*Agência Estadual de Vigilância em Saúde de Rondônia* – AGEVISA-RO) were used through *Sistema de Informação de Agravo de Notificação* (Sinan) NET and Sinan W, aiming at a better analysis of the information about the disease.

Variables studied were: year of diagnosis, gender, age group, contact with patients known to have HBV, ethnicity, vaccine, exposure to risk factors, route of infection and clinical presentation. The software used in statistical analysis were *Microsoft Excel 2010 and* e *BioEstat 5.3*.

[1]Department of Medicine at Faculdade São Lucas (FSL) − Porto Velho (RO), Brazil.

RESULTS

In the period assessed, 149 cases of Delta hepatitis were reported, with average prevalence of 10.6 cases/year (**Table 1**) and average annual incidence of 0.7 cases/100,000 inhabitants (**Figure 1**). In 2007, the prevalence of cases was the highest, with atypical pattern compared to other years (**Figure 2**). Out of these cases, 93 (62.4%) were in males and 56 (37.6%) in females, and 8 of them (5.3%) were pregnant.

Fourteen individuals (9.3%) had had contact with a patient diagnosed with hepatitis B. As to age groups, the one with larger number of cases was 20–39 years (51%). The most common ethnicity was Parda (61.1%), and 84% of subjects in the sample had not taken HBV vaccine. As to exposure to risk factors, 41 (27.5%) patients had been exposed to dental treatment and 31 (20.8%) to surgical procedures. The main route of transmission was sexual intercourse (51 subjects, 71.8%). When it comes to clinical presentation of the disease, 4.1% were in the acute phase and 95.9% in the chronic phase (Table 2).

Table 1 – Prevalence, population, relative frequency and sample proportion of patients with Delta hepatitis in the State of Rondônia (1999–2012).

Year	Variables		
	n	Population	fr
1999	5	1,296,832	0.033
2000	10	1,379,787	0.067
2001	12	1,407,878	0.008
2002	9	1,431,776	0.060
2003	8	1,455,914	0.053
2004	6	1,479,940	0.040
2005	9	1,534,584	0.060
2006	7	1,562,406	0.046
2007	23	1,590,027	0.154
2008	12	1,493,566	0.080
2009	10	1,503,911	0.067
2010	12	1,562,409	0.080
2011	13	1,576,455	0.087
2012	13	1,590,011	0.087
Total	**149**	–	–

fr: relative frequency.
Source: Sistema de Informação de Agravo de Notificação (Sinan) NET and Sinan W.

DISCUSSION

In Brazil, from 1999 to 2011, 2,197 cases of Delta hepatitis were reported, being these, 1,679 (76.4%) in the North region[9], which shows the high prevalence in this portion of the country. Observing the box plot for the prevalence of cases in Rondônia, one notes an atypical number in 2007; according to AGEVISA, this is due to a change in the information centre during that year, going from Sinan W to Sinan NET.

According to Fonseca et al.[10], most patients with hepatitis are males because they are also widely affected by HBV. In a study about hepatitis markers in a hospital of Pará, Amaral et al.[11] found a higher prevalence among males (83.3%) and noticed that the mostly affected age group is that between 31 and 45 years and that Pardos were more prone to the disease. According to Alboleda et al.[12], in the Amazonic region, due to early infection by HBV, a large number of cases is reported in individuals under the age of 15. In other regions of the world, the disease affects older people, being a lot more common in the 3rd and 4th decades of life[13]. In our study, we also found a high prevalence among males, Pardos and people aging 20–39 years.

We found a rate of 6.8% of indigenous subjects infected. Many Brazilian studies have shown high endemicity in this population[14,15]. Braga et al.[16] performed a study in 7 indigenous villages and found a prevalence of 13.4% for HDV in people infected by HBV. HDV

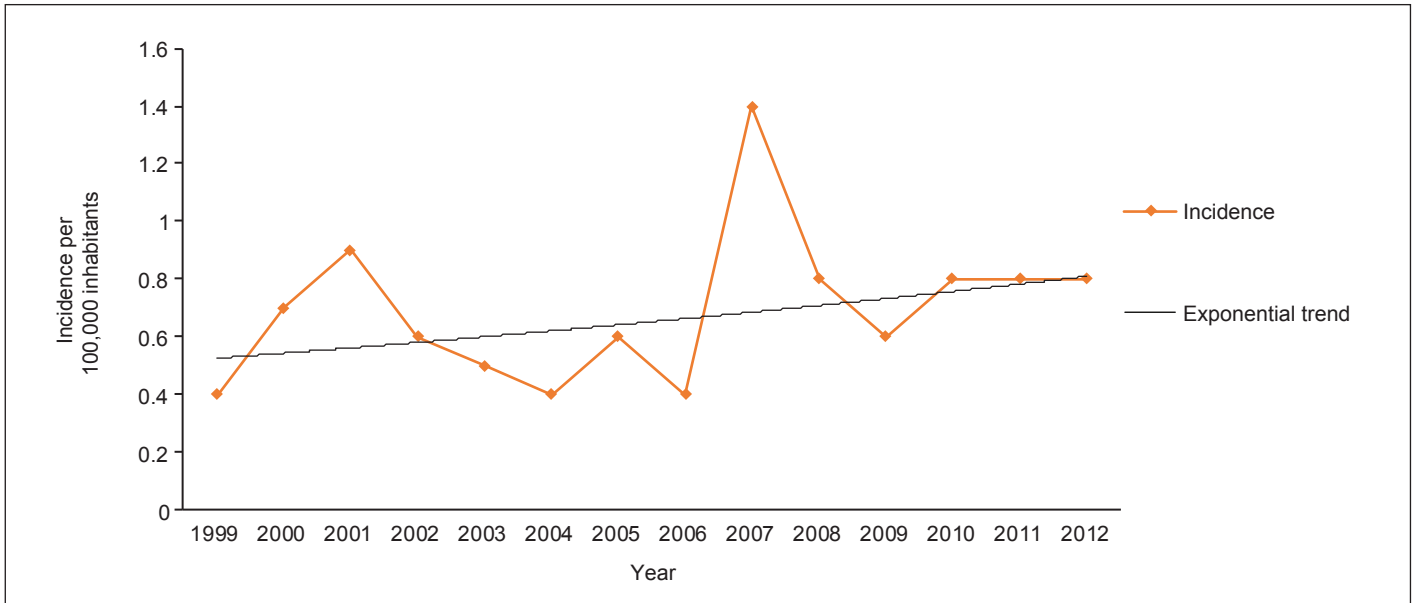

Figure 1 – Incidence and exponential trend of cases of Delta hepatitis diagnosed in the State of Rondônia (1999–2012).

Figure 2 – Box plot of the prevalence of Delta hepatitis in Rondônia (1999–2012).

transmission happens mostly among 5 to 12 years-old and young adults by familial contact or sexual intercourse. Some factors favor transmission among indigenous, including their habits, genetics and contact with other indigenous groups[17].

HBV vaccine is an important prophylactic measure against HDV, and became mandatory in Brazil in 2000. In our study, 84% of patients infected had not taken any dose of the vaccine. There are some reasons that lead people not to take vaccines such as: fear of side effects, lack of information and time unavailability[18].

The main routes of transmission were sexual intercourse and parenteral. We also found, in this study, sexual intercourse as the most common means of infection and, among risk factors, patients had been more frequently exposed to dental and surgical treatments.

In general, 5.3% of women infected were pregnant. In a study about Delta hepatitis markers in Lábrea, Amazonas, Braga *et al*[16] reported high prevalence among 6 to 12 years-old, and found that infection took place mostly by vertical means or by familial contact. Vertical transmission may be related to the high infectivity of the virus during pregnancy, with serological signs and viral replication favoring vertical transmission of HBV and concomitantly of HDV[19].

In this study, most individuals were in the chronic phase of the disease, being strong candidates to hepatic cirrhosis and hepatocellular carcinoma.

The North region of the country held most cases of Delta hepatitis, where it is still endemic. Rondônia has an average prevalence of 10.6 cases/year, but this number could be even larger due to under-reporting among river-side and countryside populations.

CONCLUSION

The population affected by the virus is mainly composed of men in the sexually active age group, where the main route of transmission is sexual intercourse. Low adherence to vaccination was observed, even though this is an effective prophylactic method. Therefore, the public health authorities should give more attention to the whole picture involving the disease, creating awareness policies and giving information about routes of transmission and prevention.

Table 2 – Social and clinical data of patients with Delta hepatitis in Rondônia (1999–2012).

Variables	n	%	Ignored data*
Age group			0
0−9	2	1.3	
10−19	9	6	
20−39	76	51	
40−59	57	38.2	
>60	5	3.3	
Ethnicity			32
Pardo	72	61.1	
Caucasian	22	18.8	
Black	11	9.4	
Indigenous	8	6.8	
Asian	4	3.4	
HBV vaccine			0
Complete	13	8.7	
Incomplete	11	7.3	
Not taken	125	84	
Exposure to risk factors			0
Dental treatment	41	27.5	
Surgical procedure	31	20.8	
Three or more partners	22	14.7	
Tattoo/*piercing*	9	6.1	
Blood transfusion	5	3.3	
Work-related accident	2	1.2	
Hemodialysis	2	1.2	
Inhalable illicit drugs	1	0.6	
Acupuncture	1	0.6	
Main route of transmission			78
Sexual	51	71.8	
Hemodialysis	9	12.7	
Surgical procedure	8	11.3	
Intimate contact	1	1.4	
Vertical	1	1.4	
Blood transfusion	1	1.4	
Work-related accident	0	0	
Use of injectable drug	0	0	
Clinical presentation			27
Acute	5	4.1	
Chronic	**117**	**95.9**	

HBV: hepatitis B virus.
*Data unavailable in the system because the notification form was not filled.
Source: Sistema de Informação de Agravo de Notificação (Sinan) NET and Sinan W.

Conflict of interests

The authors report no conflict of interests.

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Address for correspondence:
GABRIEL DE DEUS VIEIRA
Departamento de Medicina da Faculdade São Lucas
Rua Alexandre Guimarães, 1.927 − Areal
Porto Velho (RO), Brazil
CEP: 76804-373
Tel: +55 (69) 3211-8046
E-mail: gabrielvieira.mg@hotmail.com

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Is screening for anal squamous intraepithelial lesions in women with genital human papillomavirus intraepithelial lesions necessary?

Há necessidade de rastreio para lesão intraepitelial anal em mulheres com lesões intraepiteliais genitais por papilomavírus humano?

Francisco Eugênio de Vasconcelos Filho[1], José Eleutério Júnior[2], Bruno Hállan Meneses Dias[1], Angélica Maria Holanda Pascoal da Silva[1], Ana Carolina Rodrigues de Andrade[1]

ABSTRACT

Introduction: There seems to be a fairly close relationship between genital and anal lesions associated with human papillomavirus (HPV) and with the pathogenesis of malignancies in such sites. **Objective**: This review seeks to analyze published papers that suggest the necessity for anal intraepithelial lesions screening in women with HPV genital intraepithelial lesions. **Methods**: A systematic review of original research published between 2001 and 2014 was performed in the databases PubMed, HighWire, Cochrane Library and Google Scholar. The keywords for the search were: "screening" or "early detection of cancer" and "anus" or "anus diseases" or "neoplasms anus" and "woman" or "women" and "HPV" or "DNA probes, HPV". **Results**: 1,203 articles were selected in the first search. After the reviewers applied exclusion and inclusion criteria and analyzed the papers, 15 were selected to compose this review. Most of them showed higher rates of anal intraepithelial lesions in women with genital intraepithelial lesions than in regular women. We also found a correlation between genital neoplasms and anal infection by oncogenic HPV types and the role of the virus in the pathogenesis of anal cancer. **Conclusion**: Screening for anal lesions in women with HPV genital lesions should be indicated, and further studies are required to determine the best methods.

Keywords: early detection of cancer; anus; neoplasm; women; papillomavirus infections.

RESUMO

Introdução: Parece haver uma relação bastante estreita entre lesões genitais e anais associadas ao papilomavírus humano (HPV), bem como sua relação com a patogênese de neoplasias nesses sítios. **Objetivo**: Avaliar a existência de dados publicados que sugiram a necessidade de rastreio para lesão intraepitelial anal entre mulheres com lesões genitais associadas ao HPV. **Métodos**: Foi realizada uma revisão sistemática de pesquisas originais publicadas entre 2001 e 2014 nos bancos de dados: PubMed, HighWire, Biblioteca Cochrane e Google Acadêmico. As palavras-chave para busca foram: "rastreio" ou "detecção precoce de câncer" e "*anus*" ou "*anus diseases*" ou "*anus neoplasms*" e "*woman*" ou "*women*" e "HPV" ou "*DNA probes, HPV*". **Resultados**: A busca inicial retornou 1.203 artigos. Após a aplicação dos critérios de exclusão e inclusão e da análise dos revisores, restaram 15 trabalhos, que foram empregados para compor a presente revisão. Grande parte dos estudos apontou que mulheres com lesões genitais pelo HPV apresentavam maior risco de lesões anais, em comparação com mulheres normais. Verificou-se também a relação entre neoplasia genital e infecção anal por tipos oncogênicos do HPV e o papel do vírus no desenvolvimento de câncer anal. **Conclusão**: O rastreio de lesões anais em mulheres com lesões genitais por HPV deve ser indicado. O método mais adequado para tal ainda deve ser mais bem estudado.

Palavras-chave: detecção precoce de câncer; ânus; neoplasmas; mulheres; infecções por papilomavírus.

INTRODUCTION

Infection by human papillomavirus (HPV) is related to the pathogenesis of numerous types of cancer, including cervical, anal, vulvar, penis and even head and neck cancer. The closest relation is found with cervical cancer, where research indicates 99.7% of cases associated with HPV infection[1], followed by anal cancer with a 90% rate of correlation. Although this is a rare neoplasm (incidence of 1:100,000), the number of cases has grown in the last years among both women and men[1].

Screening programs have been used aimed at early detection of cervical lesions, whose incidence is of 500,000 new cases per year worldwide. However, anal cancer — with 30,000 new cases per years — has not been screened routinely[2]. For some risk groups, especially men with human immunodeficiency virus (HIV) and who have sex with other men, current protocols cover annual anal cytology screening[2]. On the other hand, there is no program for women, even those who present HPV lesions in the lower genitourinary tract.

Comparative studies on anal and cervical cytology sampling have shown that HPV infection in one of these sites increases the risk of lesions in the adjacent region. This may indicate that a cervical lesion could be a source for anal infection[3]. Another hypothesis raised is that the anal mucosa could function as a vat for the virus[4]. Therefore, there seems to be a close relation between genital and anal lesions, as well as with the pathogenesis of neoplasms in these sites[3,4]. Although this association is well

Study carried out at the Medical School of Universidade Federal do Ceará (UFC) – Fortaleza (CE), Brazil.
[1]Students of Faculty of Medicine of UFC – Fortaleza (CE), Brazil.
[2]Professor of Motherhood and child department at UFC – Fortaleza (CE), Brazil.

known, there is no consensus about the use of a method that can identify anal intraepithelial lesions in women presenting genital intraepithelial lesions.

OBJECTIVE

To look for data suggesting the need for screening of anal intraepithelial lesions among women presenting genital lesions related to HPV.

METHODS

In order to perform the systematic review, we carried out a search on medical literature databases between January 2001 and January 2014. The websites chosen were PubMed, HighWire, Cochrane Library and Google Scholar. Keywords used were "screening" or "early cancer detection" and "anus" or "anus disease" or "anus neoplasms" and "woman" or "women" and "HPV" or "DNA probes, HPV".

Studies carried out only with men, with immunocompromised patients and those on subjects other than intra-anal lesions were excluded from the review; papers published over than 12 years earlier, review articles and case reports were not selected either. Finally, only studies written in English, Portuguese and Spanish were picked.

Three reviewers participated in the article selection, in compliance with recommendations by the Brazilian Medical Society (AMB)[5]. At first, studies were chosen based on their headings. Then, the abstracts were analyzed in order to restrict the selection to papers that were really on the theme proposed and that met the inclusion criteria. Papers approved were then included in the research. If the reviewers disagreed on any of the studies, this would be assessed by a fourth one to define if it would be excluded or included. Finally, the articles selected composed the sample of our work.

RESULTS

The search on databases returned 1,203 results, but after the application of inclusion criteria, 125 articles were selected in the first phase. Then, the qualitative analysis excluded 110 more articles, totaling 15 studies included (**Figure 1**) and (**Table 1**).

In a case-control study by Dailing et al.[3], HPV was identified by polymerase chain reaction (PCR), among 187 women diagnosed with anal cancer, in 89% of them (149 women), and HPV type 16 was found in 74% of cases[3].

Blomberg et al.[4], in a cohort study carried out in 1978-2008 with 32,933 Danish women presenting genital warts, found that the presence of these lesions is strongly related to the emergence of anal, vulvar, vaginal, cervical, penis, and even head and neck cancers. Relative risk estimates for anal and vulvar cancer were higher between the first and fourth years of follow-up after genital warts diagnosis and, although the risk decreases over the years, it remained significantly increased for more than 10 years. In a cross-sectional study conducted with 102 women presenting high-grade neoplasm or cancer in the lower genitourinary tract who were submitted to anal cytology and HPV search by PCR, Park et al.[6] reported that women with genital neoplasms were at higher risk of anal infection by oncogenic HPV types, regardless of the site of the neoplasia (cervical, vaginal, vulvar or more than one site).

Valari et al.[2] conducted a study with 235 women with suspicion or confirmation of HPV-related pathologies in cervical, vaginal or vulvar regions, where HPV, high-risk HPV and (messenger ribonucleic acid) mRNA were researched in anal and cervical material, with positive results in 45%, 31% and 8%, respectively, for anus and 56%, 39% and 25%, respectively, for vagina; positive results for mRNA was significantly lower for the anal compared to the cervical region. Absolute or partial agreement between HPV types in both sites was 74%. According to these authors, presence of genetic material in the cervix was a risk factor for its presence in the anal regions, and in HPV tests, having had more than three sexual partners was also a risk factor.

In a prospective study conducted with 185 women from 5 different places in the USA, using anal and cervical cytology (liquid-base cytology, ThinPrep™) with HPV DNA detection by PCR in both sites, Hessol et al.[7] found 9% of abnormal anal cytology and histology, being atypical (2%), condylomas (2%), anal intraepithelial neoplasm (AIN-I) (3%) and AIN-3 (1%), and 19% of abnormal cervical cytology and histology, being atypical (11%), condylomas (3%), cervical intraepithelial neoplasms (CIN-I) (3%), CIN-II (1%) and CIN-III (1%).

Regarding HPV infection in different spots, 50% of the women had anal infection and 15% had cervical infection, and in 8% of the cases both sites were infected. As to the type of HPV in anal infection, 12% had only oncogenic types and 33% had only non-oncogenic types, as both types were found in 5% of the sample. In cervical infection, 6% had only oncogenic types and 7% only non-oncogenic types, with both types being identified in 2% of the women. In this group, the proportion of women reporting practice of anal sex was 46%.

Palefsky et al.[8] conducted a cohort study with 68 women with risk factors for HIV infection to investigate the presence of HPV in the anus by PCR and hybrid capture, and PCR detected HPV in 24 (42%) of the 57 women in the sample. HPV was detected by hybrid

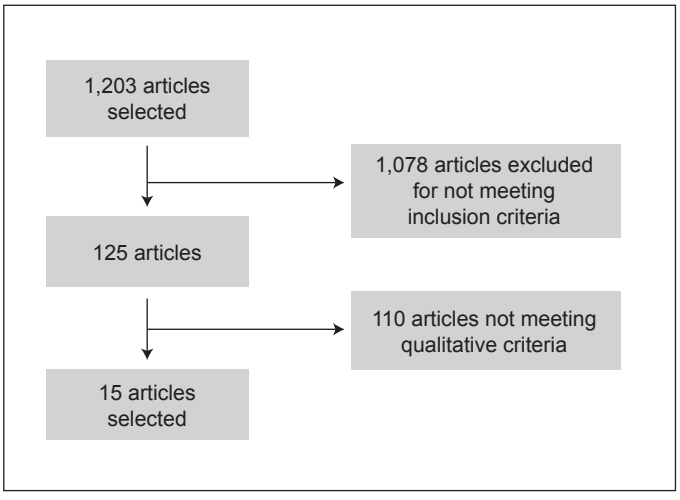

Figure 1 – Selection of studies.

Table 1 – Studies analyzed in the systematic review on the need for screening for anal intraepithelial lesions in women presenting genital intraepithelial lesions caused by human papillomavirus.

Study	Year of publication	Study design	Women (n)	Method of analysis	Results
Blomberg *et al.*	2012	Retrospective cohort study	32,933	Statistical analysis	Presence of genital warts increases the risk of cervical and anal cancer.
Crawford *et al.*	2011	Cross-sectional study	100	Anal histology Oropharyngeal histology	HPV detected in anal samples of 100% of women presenting low-degree GSIL and 82.7% of those with high-degree GSIL.
Hessol *et al.*	2011	Prospective cohort study	185	Anal cytology Cervical cytology PCR	
Jacyntho *et al.*	2011	Cross-sectional study	260	Perianoscopy Vulvoscopy Colposcopy High-resolution anoscopy	Incidence of ASIL in women with GSIL was significantly higher than among non-affected women.
Nielsen *et al.*	2011	Retrospective cohort study	1,434 (anal cancer) 388 (anal intraepithelial neoplasia)	Statistical analysis	Incidence of anal cancer doubled in Denmark because of the increase in HPV neoplasm.
Valari *et al.*	2011	Cross-sectional study	235	Cytology PCR Flow cytometry Statistical analysis	Cervical HPV infection is the leading predictor factor for anal affection.
Calore *et al.*	2010	Cross-sectional study	49	Cervical cytology Anal cytology	Patients with cervical HSIL are at higher risk of presenting abnormal anal cytology results.
Goodman *et al.*	2010	Prospective cohort study	897	PCR	The chance of women with cervical HPV lesion presenting anal lesions with the same etiology is higher than among normal women and vice-versa.
Giraldo *et al.*	2009	Cross-sectional study	260	Anoscopy	Women with GSIL have ASIL more frequently than normal patients.
Park *et al.*	2009	Cross-sectional study	102	Anal cytology PCR	Women with genital neoplasm are at higher risk of anal involvement by high-risk HPV types.
Véo *et al.*	2008	Cross-sectional study	80	Genital hybrid capture Anal hybrid capture	Incidence of HPV in the anal region of women presenting cervical lesions was higher than in women of the control group.
Edgren *et al.*	2007	Retrospective cohort study	3,747,698	Statistical analysis	The risk of anal cancer is 4.68 times higher among women with CIN-III compared to normal women.
Hernandez *et al.*	2005	Prospective cohort study	1,363	PCR	Women with cervical HPV are 3.3 times more likely to present anal involvement compared to normal women.
Dailing *et al.*	2004	Case-control study	187	PCR	89% of anal tumors in women were positive for HPV.
Palefsky *et al.*	2001	Prospective cohort study	68	PCR Hybrid capture	Patients at risk for HIV infection presented high rates of HPV infection.

HPV: human papillomavirus; GSIL: genital squamous intraepithelial lesions; PCR: polymerase chain reaction; ASIL: anal squamous intraepithelial lesions; HSIL: high-grade cervical intraepithelial lesions; CIN: intraepithelial cervical neoplasia; HIV: human immunodeficiency virus.

capture in 20 (30%) out of 67 samples. The same group of authors reported that, among patients submitted to anal and cervical HPV detection, 43% had anal infection and 24% had cervical infection. Hessol et al.[7] found that 50% of their sample had anal infection and 15% had cervical involvement, while Valari et al.[2] reported high positivity rates (45%) for HPV DNA at anal smears, similarly to cervical smears (56%).

Calore et al.[9] assessed 49 women with abnormal cervical cytology and reported that among women with low-grade squamous intraepithelial lesions (SIL), 50% also had abnormal anal cytology, while 61.5% of those with high-grade SIL had abnormal anal results. These findings would suggest that patients with cervical high-grade SIL are more prone to presenting abnormal anal cytology.

A cohort study[10] with 897 Hawaiian women carried out in 1998-2008 aimed to compare the risk of infection in the cervix or secondary infection n the anus to a previous adjacent infection. The authors reported that the risk of women with cervical HPV infection developing anal infection is higher among women without precedent infections. In turn, a cross-sectional study with 260 Brazilian women (184 with GSIL and 76 without it)[11] showed that history of more than 4 anal sexual relations per year and presence of genital herpes were risk factors for the emergence of ASIL. The study also showed that the prevalence of ASIL in women with GSIL was significantly higher than in women without the lesions (17.4% against 2.6%). Finally, women with GSIL in 3 or more sites (cervix, vagina, vulva or perianal region) have 13.1 times higher risk of ASIL compared to control group.

Another cross-sectional study with 100 women presenting cervical lesions, where histology sampling of the anal and oropharingeal regions were collected, HPV was detected in anal cells of 100% of low-grade genital lesions and in 82.7% of high-grade genital lesions[1].

In a cross-sectional study using anoscopy in 260 patients of the Brazilian public health service, where 184 has genital squamous intraepithelial lesions (GSIL) and 76 were normal (control group), Giraldo et al.[12] showed that low and high-grade anal lesions (ASIL) were more common in patients with GSIL. Besides that, they found out that women with high-grade GSIL had 5.2 times more ASIL than those without genital lesions, and women with low-grade GSIL had 7.66 times more ASIL than those of the control group.

In accordance with these findings, Véo et al.[13] used hybrid capture to search for low and high-risk HPV in the anal and genital regions of 80 women and found out that, in a group of women with CIN-II or III in the genital region, incidence of HPV in the anus was 35%, against 10% in control group. Furthermore, high-risk HPV was detected in 22.5% of the women in study group against 5% in control group. In a cohort study starting in 1999, in Hawai, with 1,363 women who had anal and cervical samplings submitted to PCR for HPV detection, Hernandez et al.[14] showed that women with cervical infection had a 3.3 times higher risk of presenting anal infection compared to healthy women.

Edgren et al.[15], in a cohort study with 3,747,698 Swedish women aging 18–50 years, found out that the risk for anal cancer emergence was 4.68 times higher, on average, among women presenting CIN-III lesions compared to those with no lesion.

Finally, a study performed in Denmark in 1998-2008 by Nielsen et al.[16] considered important features regarding intra-anal neoplasms. The incidence of HPV-related cancer has increased, being more common among 60 years-old, that's why there is a benefit in the use of preventive methods, including HPV vaccine.

CONCLUSION

Research show that the risk of HPV anal lesions in women with HPV cervical lesions is high[1,2,4,5,8-12,14]. Genital infection by HPV is the main predictor for anal infection, and a significant correlation has been found between the types of HPV identified in anal lesions and those found in cervical lesions[2].

Considering these associations between anal and cervical infections, as well as an apparent cause-effect relation, ASIL screening in women with GSIL should be mandatory. Screening indication seems to be a Public Health issue, once it would probably mean prevention of intra-anal neoplasms, which are more frequent each year.

The most appropriate and cost-effective method for screening nowadays is an important matter of questioning. Further studies comparing data regarding different techniques are needed to establish the best one.

Conflict of interests

The authors report no conflict of interests.

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Address for correspondence:
FRANCISCO EUGÊNIO DE VASCONCELOS FILHO
Rua João Cordeiro, 949, apto 601 – Praia de Iracema
Fortaleza (CE), Brazil
CEP: 60110-300
Tel: +55 (85) 9962-3220
E-mail: eugeniovasc@gmail.com

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The influence of the usage of the male condom by seniors in the vulnerability to HIV: a systematic review with meta-analysis

Influência do uso da camisinha masculina por idosos na vulnerabilidade ao HIV: uma revisão sistemática com meta-análise

Marcella Alves da Paz[1], João Márcio Nunes de Alencar[1], Cláudia Layse Almeida Sousa[1], Ulisses Umbelino dos Anjos[2], Jordana de Almeida Nogueira[3], Jailson Alberto Rodrigues[4]

ABSTRACT
Introduction: Brazil has presented a rise of the population aged over 60 years. In addition to this change in demographic profile, there is an epidemic of worldwide, HIV infection. **Objective:** Was to ascertain the influence of the use of male condoms by seniors in vulnerability to virus infection. **Methods:** We developed a systematic literature review and meta-analysis of observational studies, research being conducted in the following databases: SciELO, LILACS, electronic library at UFMG and USP and Google Scholar. Results: A number of 38 articles were selected and after evaluation and application of the Physiotherapy Evidence Database (PEDro) scale, 6 of them were elected to compose the study sample. The statistical analysis obtained a summary measure (*odds ratio* − OR=1.643). **Conclusion:** From the analysis of the database, one realizes that the indicator found (summary measure), the condom use is ratified as a factor or protection against HIV infection, in other words, its adoption makes the individual less vulnerable.
Keywords: elderly; HIV; condoms; acquired immunodeficiency syndrome.

RESUMO
Introdução: O Brasil vem apresentando ascensão da população com idade igual ou superior a 60 anos. Além dessa mudança no perfil demográfico, há uma de caráter epidemiológico de âmbito mundial, a infecção pelo vírus da imunodeficiência humana (HIV). **Objetivo:** Averiguar a influência do uso da camisinha masculina por idosos na vulnerabilidade à infecção pelo vírus. **Métodos:** Desenvolveu-se uma revisão sistemática da literatura, com meta-análise, entre estudos observacionais, sendo realizadas pesquisas nas seguintes bases de dados: *Scientific Electronic Library Online* (SciELO), Centro Latino-Americano e do Caribe de Informação em Ciências da Saúde (LILACS), biblioteca eletrônica da Universidade Federal de Minas Gerais (UFMG) e da Universidade de São Paulo (USP) e Google Acadêmico. **Resultados:** Foram selecionados 38 artigos e, após avaliação e aplicação da escala *Physiotherapy Evidence Database* (PEDro), foram eleitos 6 deles para compor a amostra do estudo. Mediante análise estatística, obteve-se uma medida sumário (*odds ratio* − OR=1,643). **Conclusão:** A partir da análise dos dados, percebe-se, que a partir do indicador encontrado (medida sumário), o uso do preservativo é ratificado como um fator ou comportamento de proteção contra a infecção pelo HIV, ou seja, sua adoção torna o indivíduo menos vulnerável.
Palavras-chave: idoso; HIV; preservativo; síndrome da imunodeficiência adquirida.

INTRODUCTION

The increase of the life expectancy of the general population may be related to the quick advance of the therapeutic,pharmaceutical and technological sciences, which is providing the elderly with a better quality of life in the physiological and psychological aspects and also has increased their sexual longevity; Such event brings out the necessity from the health care professionals involved directly or indirectly with the care of the elder to address this matter, and aim not just to treat but also prevent the occurrence of such diseases.

Whereas there were medicine development and hardware technologies to improve the sexual performance of the elderly population, little has been done by the health care services and the media to address the issues of the sexual life of the elderly, approaching it in a casual way and as a legitimate right [(1)].

Despite of the significant increase in the number of elderly people infected with the human immunodeficiency virus (HIV), usually this population is not considered vulnerable to this kind of infection, specially a stigmatizing sexually transmitted infection (STI) Therefore this way of approach can set a vulnerable behavior on the elderly population[(2)].

This negligent situation reaches a binomial situation between the Acquired Immunodeficiency (AIDS) and the elderly population, and it gets worse facing the stigmas related to the acceptance and perception of the sexuality of this group. The growing number of occurrences of STIs like the HIV the causative agent of AIDS

[1]Underdgraduate student from the nursing school of the Universidade Federal do Piauí (UFPI) – Floriano (PI), Brasil.
[2]PhD in Statistics from the Universidade de São Paulo (USP); Professor of the Graduate Program in Health Decision Models and the Universidade Federal de Paraíba (UFPB) – Floriano (PI), Brazil.
[3]PhD in Nursing from USP; Coordinator of the Graduate Program in Nursing UFPB - João Pessoa (PB), Brazil.
[4]Master in Decision Models and Health UFPB; Professor of Nursing CAFS/UFPI – Floriano (PI), Brazil.

among the elderly has come into special attention, affecting both men and women, casting out the idea that old people are asexual[3].

These prejudices tend to difficult the contact between the health care professionals and the elderly and they are responsible for the lack of attention regarding the forms of prevention, which is reflected in the growing number of AIDS infections among the elderly. With the discriminatory character and the professional negligence in not addressing properly the use of preventive methods, regarding the sexual conducts of the elderly, this is not yet a common practice between sexual partners during intercourse, even after the known effectiveness in preventing HIV. Thus, the need of a multi professional care focused in the ways that the sexual practices are experienced in old age is utterly necessary, and with this minimizing the vulnerability during sexual intercourse.[4].

This restricted view related to sexuality, old age and unprotected sexual exposure is currently the main way of encouraging HIV infection among older adults. Among the various factors that can influence the non-use of condoms by this group, we highlight the lack of knowledge about the disease and the availability of condoms, cultural, social, economic and educational factors, Like the omission of health professionals and family on addressing the issue and providing information during consultations , and many other factors. However, the prejudice regarding the fact that elderly have an active sex life awakens in people a discriminatory exhaustive look, since they regard this act as something amoral, causing in the elderly a sense of shame in seeking information and prevention materials[5].

Sex and old age most of the time seem as incompatible themes, because people never imagine that the elderly can maintain sexual relations with his(her) partner or outside their relationship. Because of that, it is possible to see the importance of research on how the preservatives, specially the male condom contribute to help the elderly prevent infections such as HIV. Thus, the following question comes into attention: what has been the influence of the use of the condom regarding the HIV infections in the elderly?

OBJECTIVE

The goal is to research of the use of male condom by the elderly in vulnerability to HIV infections.

METHODS

This is a review of the literature on the systematic type with a meta-analysis of observational studies. Meta-analysis is an appropriate statistical technique for combining results from different studies, thus producing estimates that summarize the whole, called meta-analytical estimates. In order to get a meta-analysis with a meaningful applied significance, the studies that compose the data of such technique should be the result of a systematic review[6].

The research for articles to compose the sample was done with databases Scientific Electronic Library Online (SciELO), Latin American and Caribbean Center on Health Sciences for Health (LILACS), Medical Literature Analysis and Retrieval System Online (MEDLINE) and Excerpta Medica Database (EMBASE).

The study population was of a finite type, composed by all the articles found in the period from September to November 2013 in these databases and are focused on the same theme: influence of condom use by the elderly in vulnerability to HIV infection. The sample was not probabilistic, defined from the inclusion criteria.

The following inclusion criteria were used:

- Being ranked in the magazine as abstract or full-text research article;
- Is available for free *online* access in any database mentioned in item type and location of the study of the methodology;
- Have been published by the magazine ranked by *qualis* Coordination of Improvement of Higher Education Personnel (CAPES);
- Have been published in the period 2005-2014;
- Articles that offered at least two comparative groups are sufficient to calculate the estimate or measure of effect, (*odds ratio* – OR) data;
- Have at least two strata;
- Have passed the qualifying criteria set by the scale *Physiotherapy Evidence Database* (PEDro)[7] and have obtained a score equal or greater than four

The following exclusion criteria was used:

- Works that did not address the theme or the influence of the use of male condoms by seniors in vulnerability to HIV infection;
- Duplicated articles in the databases;
- Deleted when found in the second database.

An instrument for assessing the quality of the selected articles was used. The value 1 was assigned to each item that was evaluated and approved. Thus, the total score achieved may vary from zero (poor quality paper) to seven (good quality article).

The selection of articles was initially based on the analysis of the summary. After that, it is filtered by checking the inclusion criteria. Finally, the decision regarding the inclusion or exclusion was made jointly by the researchers involved in the application of quality of the PEDro scale.

All selected studies were presented descriptively in tables of descriptive statistics. We conducted meta-analysis by the methods of random effects considering as hypotheses to be tested:

H_0:the male condom influence, regardless of the size and characteristics of the sample, the vulnerability of the elderly to HIV; Likewise, in all situations (fixed effect model).

H_1:male condom influences, in different ways, considering the size and characteristics of the sample, the vulnerability of the elderly to HIV (random effects model).

The database of the study, containing estimates or measures of effect, was developed in *Excel for Windows* 2007 and converted to tab-delimited text (.txt). We used the R *software* to conduct the statistical procedures and the elaboration of the *forest plot*. This, indicated the extent meta-analytic estimates and their respective statistical significance.

We took on consideration the significance level of 5% (α=0,05). And we used the Cochrane Q statistic and the I^2 test of Higgins and Thompson.

RESULTS AND DISCUSSION

These papers were researched in the health sciences databases, by the descriptors combination and selected in case they

showed any relation regarding the theme of the use of condom by the elderly. Initially it was found a number of 17.898 articles according to **Table 1**. From these articles, just 191 were selected to further research, using the inclusion criteria to compose the final sample narrowing down the process with the use of the PEDro scale in 42 scientific articles.

After the evaluation of the papers that fitted in the established inclusion criteria and the theme of the study, from the 38 articles found, just 6 contained sufficient and consistent data to conduct the meta-analisys procedures.

The meta-analysis is a statistic technique fit to combine results from different studies, thus producing the estimative that can summarize the whole, that is why it is the best statistical method to be used after a systematic review in order to integrate the results of the studies analyzed. To summarize, the meta-analysis is a efficient way to combine results from different studies allowing the researchers to combine the data and analyze them like they were part of a single large work[6].

Table 1 – Scientific publications on the use of the male condom by the elderly, HIV/AIDS and sexuality of the elderly.

Database	Articles (n)	Sorting (n)	Articles to evaluate
SciELO	1,055	50	06
LILACS	98	46	12
UFMG	677	20	02
USP	591	15	02
Google Scholar	15,477	60	16
TOTAL	17,898	191	38

SciELO Scientific Electronic Library Online; LILACS: Latin American and Caribbean Center for Information on Health Sciences; UFMG: Universidade Federal de Minas Gerais; USP: Universidade de São Paulo

That brings out perspectives on the realization of meta-analytical procedures in different studies with different clippings of time and space and even different methodological approaches, as we can see in **Chart 1**.

The values of preservative usage by the eldery were extracted from the articles utilized in the meta-analysis. We used the age-range of "equal of 50 years or older" because the latency period of the HIV virus. This age definition aims to include the individuals of between the ages of 50 and 60 and the ones that got infected with more than 60 years of age.

Besides, the international age classification criteria was respected, since in some of the countries where the studies on HIV/AIDS are conducted, the life expectancy is lower than the one in developed and developing countries.

It is important to pay attention to the fact that the systematic review aims to map a knowledge on an issue; however, this question cannot be as detailed. A fact that occurred regarding the requirements to compose the sample in some studies selected for review from the PEDro scale. Quoting:

- Rocha FCV, Freitas Filho FC, Macêdo Júnior JA, Rosa YRD. Entitled: Conhecimento dos idosos sobre HIV/AIDS. 2013. Reason of exclusion: Because it is a review on literature, conducted through the methodological approach suggested by Marconi and Presotto.
- Serra A, Sardinha AHL, Lima SRCS, Pereira ANS. Entitled: Perfil comportamental de idosos com HIV/AIDS atendidos em um centro de referência. Reason of exclusion: low score on the PEDro scale
- Alencar RA. Entitled: O idoso vivendo com HIV/AIDS: a sexualidade, as vulnerabilidades e os enfrentamentos na atenção básica. Reason for the exclusion: Qualitative focus.
- Garcia GS, Lima LF, Silva JB, Andrade LDF, Abrão FMS. Entitled: Vulnerabilidade dos idosos frente ao HIV/AIDS: tendências da produção científica atual no Brasil. Reason of exclusion: An integrative review of the literature

Chart 1 – Characteristics of the articles selected for the meta-analysis.

Author	Year	Title	Target of study
Lima TC e Freitas MIP	2012[8]	Health behaviors of the population with HIV / AIDS	Identifying health behaviors in a population aged 50 years or older with HIV / AIDS and analyzing the association of these behaviors with sex.
Melo HMA *et al.*	2012[9]	The knowledge about AIDS in elderly and young adult men: a study on the perception of this disease	Compare the perception of elderly to young adults about AIDS men considering the level of education.
Araújo VLB	2009[10]	Targets people aged 50 years old and older living with HIV / AIDS in Ceará, Brazil	It aims to describe the epidemiological characteristics of people aged 50 and older living with HIV / AIDS attending a tertiary hospital of Ceará, in the period 1983-2008.
Olivi M *et al.*	2008[11]	Targets behaviors, knowledge and risk perception of sexually transmitted diseases in a group of people aged 50or more	It describes characteristics of sexual behaviors, knowledge about STD / AIDS and risk perception in people aged 50 years and older and assess the association between risk perception and aspects of behavior and knowledge.
Sormante M and Shibusawa T	2007[12]	*Predictors of condom use and HIV testing among midlife and older women seeking medical services*	Aims to examine correlates and predictors of sexual HIV risk reported by a sample of middle-aged and older women.
Brazil	2006[13]	Analyses sexual behaviors of the Brazilian Population and Perceptions of HIV / AIDS	Identifying representations, behaviors, attitudes and sexual practices of the Brazilian population, and knowledge about HIV / AIDS, with a view to developing strategies for preventing STDs and HIV.

HIV: human immunodeficiency virus; AIDS: Acquired immunodeficiency syndrome; STD: Sexually transmitted diseases.

- Melo HMA. Entitled: O conhecimento sobre AIDS de homens idosos e adultos jovens: um estudo sobre a percepção desta doença. Reason of exclusion: no present data on condom use.
- Melo MC, Pimenta AM. Entitled: Característica epidemiológica da AIDS na população com mais de 50 anos em Betim e microrregião. Reason of exclusion: no present data on condom use.
- LPS Souza Oliveira MVR, Silveira WRM, Figueiredo MFS, Messias RB, Silva JR. Entitled: Análise da clientela idosa portadora de HIV atendida em um centro ambulatorial em Montes Claros, Minas Gerais. Reason of exclusion: low score on the PEDro scale
- Baldoni AO, Pereira LRL. Entitled: O impacto do envelhecimento populacional brasileiro para o sistema de saúde sob a óptica da farmacoepidemiologia: uma revisão. Reason of exclusion: narrative review, with a qualitative synthesis
- Baptist AFO, APO Marques Leal ACC, Marino JG, Melo HMA. Entitled: Idosos: associação entre o conhecimento da AIDS, atividade sexual e condições sociodemográficas. Reason of exclusion: low score on the PEDro scale
- Frugoli A, Magalhães-Junior CAO. Entitled: A sexualidade na terceira idade na percepção de um grupo de idosas e indicações para a educação sexual. Reason of exclusion: A research with a qualitative exploratory approach.
- Laroque MF, Affeldt AB, Cardoso DH, Souza GL, Santana MG, Lange C. Entitled: Sexualidade do idoso: comportamento para a prevenção de DST/AIDS. Reasons of exclusion: It is a qualitative, exploratory and descriptive study.
- Maschio MBM, Balbino AP, De Souza AFR, Kalinke LP. Entitled: Sexualidade na terceira idade: medidas de prevenção para doenças sexualmente transmissíveis e AIDS. Reason of exclusion: A prospective, quantitative and descriptive study.
- Moraes KM, Vasconcelos DP, Silva ASR, RCC Silva, Santiago LMM, Freitas CASL. Entitled: Companheirismo e sexualidade de casais na melhor idade: cuidando do casal idoso. Reason of exclusion: a case study with a qualitative approach.
- DC Oliveira, Oliveira EG, Gomes AMT, Teotônio MC, Wolter RMCP. Entitled: O significado do HIV/AIDS no processo do envelhecimento. Reason of exclusion: a case study with a qualitative approach.
- Santos AFM, Assis M. entitled: Vulnerabilidade das idosas ao HIV/AIDS: despertar das políticas públicas e profissionais de saúde no contexto da atenção integral: revisão de literatura. Reason for the exclusion: It is a non systematic review of the literature
- Souza NR, Bernardes EH, Carmo TMD, Nascimento E, Silva ES, Souza BNA, et al. Entitled: Perfil da população idosa que procura o centro de referência em DST/AIDS de Passos/MG. Reason for exclusion: no present data on condom use.
- CC Torres, VP Bezerra, Pedroza AP, Silva LM, Roberts TP, Coutinho NJM. Entitled: Representações sociais do HIV/AIDS: buscando os sentidos construídos por idosos. Reason for exclusion: no present data on condom use.
- Andrade HSA, Sharma SK. Entitled: AIDS em idosos: vivências dos doentes. Reason of exclusion: a study with a qualitative approach.
- Garcez BS, Garcez JS, Paixão MRP, Fernandes ACV, Santos RB. Entitled: Conhecimento e percepção do grau de risco sobre DST e HIV/AIDS e a utilização do preservativo entre idosos: o autocuidado sadio e a enfermagem neste contexto. Reasons for exclusion: It is a cross-sectional descriptive and retrospective study.
- Lopes FMVM. Entitled: Vulnerabilidade da mulher idosa frente ao HIV/AIDS. Reason of exclusion: a case study with a qualitative approach.
- Pereira GS, Borges IC. Entitled: Conhecimento sobre HIV/AIDS de participantes de um grupo de idosos, em Anápolis-GO. Reason for exclusion: low score on the PEDro scale
- Silva SFR, Pereira MRP, Neto RM, Ponte MF, Ribeiro IF, Costa PFTF, et al. Entitled: AIDS no Brasil: uma epidemia em transformação. Reasons for exclusion: It is a retrospective, descriptive and observational study.
- Toledo LSG, Maciel ELN, Rodrigues LCM, Tristão-Sá R, Fregona G. Entitled: Características e tendência da AIDS entre idosos no Estado do Espírito Santo. Reason for exclusion: no present data on condom use.
- AC Sousa, Suassuna DSB, Costa SM. Entitled: Perfil clínico-epidemiológico de idosos com AIDS. Reason for exclusion: no present data on condom use.
- Veras R. Entitled: Envelhecimento populacional contemporâneo: demandas, desafios e inovações. Reason of exclusion: a study with a qualitative approach.
- Berquó E, Barbosa RM, Lima LP. Entitled: Uso do preservativo: tendências entre 1998 e 2005 na população brasileira. Reason for exclusion: low score on the PEDro scale
- Lazzarotto AR, Kramer AS, Hädrich M, Tonin M, Caputo P, Sprinz E. Entitled: O conhecimento de HIV/AIDS na terceira idade: estudo epidemiológico no Vale dos Sinos, Rio Grande do Sul, Brasil. Reason for exclusion: no present data on condom use.
- Souza JL. Entitled: Sexualidade na terceira idade: uma discussão da AIDS, envelhecimento e medicamentos para disfunção erétil. Reason of exclusion: a case study with a qualitative approach.
- Souza CF. Entitled: O uso/não-uso de preservativo entre mulheres residentes em Belo Horizonte e Recife, 2002: um estudo de fatores associados. Reason for exclusion: low score on the PEDro scale
- Zornitta M. Entitled: Zornitta M. Os novos idosos com AIDS: sexualidade e desigualdade à luz da bioética [tese]. Reason of exclusion: a study with a qualitative approach.
- Castro MP. Entitled: O viver com HIV/AIDS na perspectiva das pessoas idosas atendidas em ambulatório especializado da cidade de São Paulo. Reason for exclusion: low score on the PEDro scale
- Cunha JVQ. Entitled: Vulnerabilidade, gênero e HIV: um estudo sobre mulheres e homens heterossexuais, Brasil-1998. Reason for the exclusion: Qualitative focus.

After reviewing the selected articles, the ones without enough descriptive information that their results could allow the OR calculation were excluded. Likewise, the ones evaluated by the PEDro scale in order of eligibility to compose the sample were excluded if they obtained a low score facing the criteria that the scale dictates. Also excluded among the studies evaluated are the ones without

data regarding the use of male condom by the elderly during sexual intercourse.

In other words, the systematic review using the meta-analysis, aims to put together the results and compare it with the results of many studies correlated. the relevant ones are quantified in a way that the resulting values are displayed in a common scale. Given that, it is necessary that the selected studies have a quantitative character, not just qualitative[14].

The data analysis was based in a model of fixed effects, where the statistical inference is conditioned on previous studies, the study has a retrospective characteristic. In order to do that, we present a summary measure of the Mantel-Haenszel OR, with confidence intervals (CI), the significance level of 0.05, as shown in the forest plot (**Figure 1**).

Using the *forest plot* (**Figure 1**), It is possible to see that the summary measure (OR=1.643) supports the use of condoms as a factor or behavior of protection against HIV infections, and the usage of such measures makes the individual less vulnerable . With this synthetising measure, it is possible to note that the non-use of condoms may increase by 1.64 times the chances elderly people being infected with HIV.

The elderly are a minority group regarding the use of condom, as common use or in case of a "casual relation". This fact corroborates the study by Pereira and Borges[15], showing the results that 69% of elderly people with an active sexual life will never use condoms, and that 15.5% do so occasionally.

When it comes to condom usage among the most recent sexual intercourses, 82.2% of older people do not use condoms, 16.8% that are adopting this method of sexual prevention[15].

The professionals who are assisting the elderly person with the possession of a scientific knowledge and are aware of studies that prove a patient can be senile due to HIV infection, should know how to connect this clientele with the health service and pay attention to the social, economic and cultural factors that may mask the real situation of sexuality experienced by this group, implying the low adherence to condom use.

Facing the importance of the use of the condom as a preventive way of HIV infections, the individualizing approach given by the risk view and, it's influence on the vulnerability, we can see the necessity of avoid tendentious ways(bias) in the studies. In this scenario of controversies and uncertainty, the statistical validation of the results can direct the scientific thought towards a better interpretation of the results.

With this in mind, we used a statistical method to test the heterogenity of studies data based on the general variant, calculating the statistical value Cochrane Q (sorting the test of χ^2 with different levels of freedom — total number of studies minus one) to the chosen group of studies. The significance value of 0.05 was fixed in order to reject the hypothesis of homogeneity in the studies[16].

There were a statistical significance of the summary measure (IC 0.952–2.836 ; p<0.001), the latter with a significant at 99%. Furthermore, the test for the heterogeneity of the studies, from the value of χ^2 test, rejected the null hypothesis (H_0) of uniformity, with p <0.0001, accepting that there are significant differences at the level of 99%. . Therefore, the selected studies present different measures of the OR for condom use by seniors.

The Q value obtained from the Cochrane heterogeneity test was 31.9026 with 2 degrees of freedom. There was a Q value = 83.989 for the general heterogeneity test, and the same amount of degrees of freedom.

The I^2 test also showed statistical evidence of heterogeneity. However, the existing portion between the sample studies (I^2 = 94%)

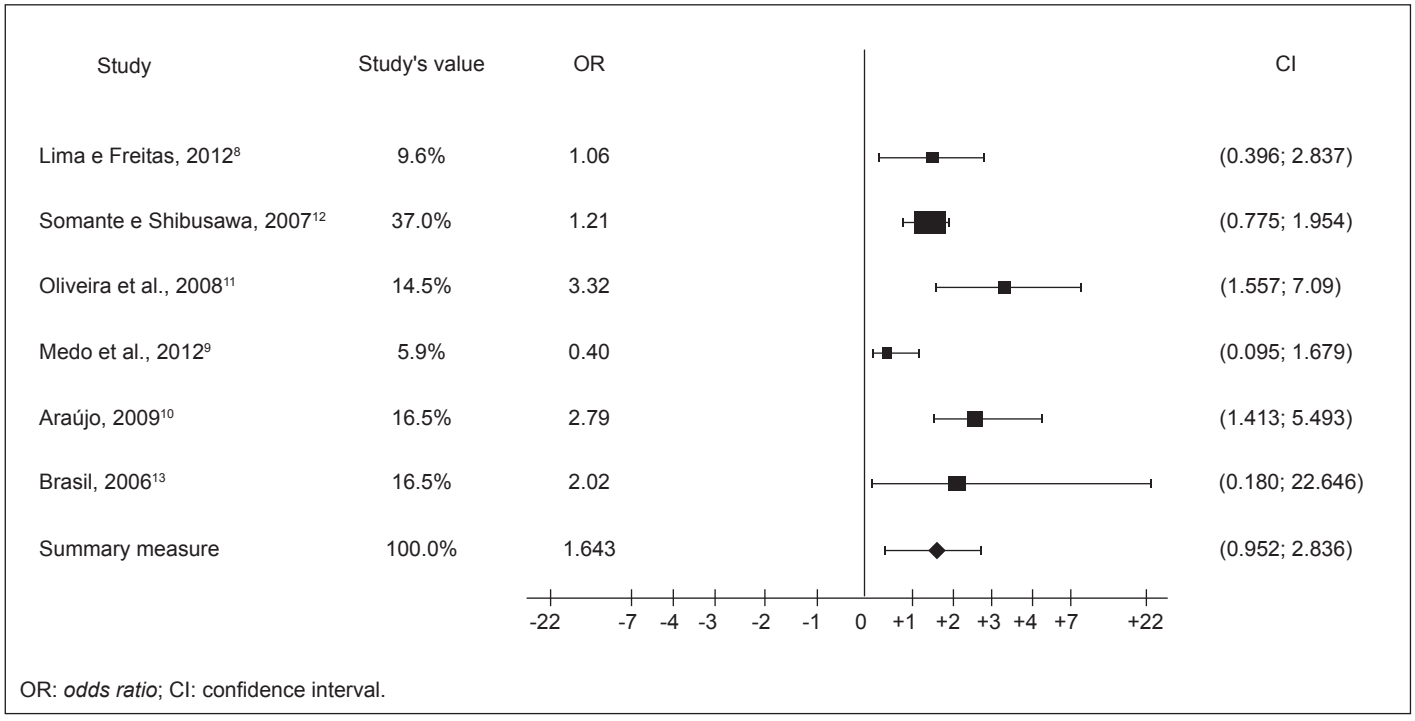

Figure 1 – Displaying a *Forest plot* with the estimated extent of the hazard ratio for non-condom use among elderly.

difference may be caused by methodological heterogeneity or by chance. This indicator (I^2) could be minimized by the inclusion of other studies, with less distinct objects of study.

The heterogeneity of effect measure found in the study is established from the test Cochrane Q or by the statistic I^2 of Higgins and Thompson[16]. The calculated p value indicates whether the heterogeneity is significant or not, if different from zero. The Q value can vary between 0 and infinity, while the I^2 statistic may vary from negative values to 100%. An I^2 value close to 0% indicates no heterogeneity between studies, close to 75 or 100% indicates high heterogeneity, and when the value is negative, it is set equal to 0[6].

All studies selected after application of the PEDro scale, evidence the no condom use as a risk factor for HIV infection, except Melo et al. (2012)[9], which may be related to the sample size and have significantly contributed to the increased heterogeneity. Another factor that may have influenced this result is that the study sample includes young and old adults.

There is another important interpretation to be made regarding the ICs. These results, while very comprehensive, may indicate inadequate sampling of case studies and representativeness of the deviation indicator for less, reflecting possibly a low level of test power (β value).

All measurements, including meta-analytic showed positive values. The analysis of ICs, can infer that none of the studies was found possible to introduce the OR value equal to zero. However, the analysis of ICs, there is a possibility of the studies that compose the sample had an OR equal to one, indicating no relationship between the factor studied (condom use) and the outcome (HIV infection), contradicting the causal relationship between non-condom use and HIV infection.

Given this event, it is possible to see, in the *forest plot*, that the IC summary measure includes the value one. This probably is due the effects of heterogeneity and the small number of published studies on the subject, which could constitute the sample

Through the value of OR found it is possible to establish whether the variable studied is a protective factor or not. Regarding the variables found having lower values than one indicates that this is a protective factor, greater than one indicates the variables as risk factors values, and equal to a point that there is no association between the variables.

It is possible to understand that not using condoms makes the elderly vulnerable to HIV. The right to have safe sexual practices whatever kind they may be, with fixed partners, non fixed partners hetero or homosexual is a irrefutable right not only of the elderly, thus, being able to access the health services and to have social condition which allows them to promote prevention practices is also a huge asset in order to exercise safety in sex[17].

The healthcare professionals, do not often see the elderly as a sexually active person, who thinks about sex and is able to arouse sexual desire in other people. To all health professionals, especially those in nursing, it is a more accurate performance in primary care programs, specifically in the Family Health Strategy (FHS), disseminating protection inputs and information on the correct use of condoms and warning that population about the risks of acquiring HIV / AIDS, especially when practicing unprotected sex[18].

There is an urgent need for interaction between health professionals and the elderly, in order to gain understanding of the spreading process of HIV / AIDS in this age group. Understanding the elderly as a sexually active and exposed to risks of unsafe sex allows the execution of actions for the development of preventive conducts[15].

With that said, these professionals will be approach the sexual health of the elderly in a holistic way, thus preventing HIV infection and minimizing biological and social effects of AIDS. Only then, with this dialog,using a common language spoken among professionals, public policies and users, you can change behaviours and improve the adhesion of individuals in this age range to prevention methods.

CONCLUSION

The results were satisfactory in the proof of the usage of the male condom as a positive influence on the prevention of HIV among the elderly. Besides, the statistical tests conducted confirmed the existence of clear evidences on the benefits of preservative usage in this age group, aiming to mitigate their vulnerability towards HIV.

However, there are some considerations to be made, considering most of the academic work developed originated some limitations. There are very few representative studies approaching this issue or making any correlation between the sexual practices of elderly people and the non-usage of condom to prevent HIV/AIDS. These elements permeate the uncertainties and inaccuracies limiting health actions.

Therefore is necessary, a greater scientific production targeting the sexuality of the elderly, given the continuous inversion that the age pyramid is suffering. With this, a new epidemiological characterization has represented and demanding specific interventions for this reality.

Conflict of interests

The authors report no conflict of interests.

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Address for correspondence:
JAILSON ALBERTO RODRIGUES
Rua França, 11 – Jardim Europa
Patos (PB), Brasil
CEP: 58705-090
Phone: +55 (83) 9963-4983
E-mail: jailson_rodrigues@ig.com.br

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HPV INFECTION AND CERVICAL CANCER: A REVIEW OF SCREENING AND PREVENTIVE STRATEGIES IN DEVELOPED COUNTRIES AND BRAZILIAN POLICIES

INFECÇÃO POR HPV E CÂNCER CERVICAL: UMA REVISÃO DE TRIAGEM E ESTRATÉGIAS PREVENTIVAS NOS PAÍSES DESENVOLVIDOS E POLÍTICAS BRASILEIRAS

Guilherme Lucas de Oliveira Bicca[1], Mariângela Freitas da Silveira[2], Kleber Roberto Siguel da Silva[3], Fernando Celso Lopes Fernandes de Barros[1,2]

ABSTRACT

Introduction: Cervical cancer is currently the third malignancy on number of female deaths in the world. Persistent HPV infection is the main agent involved in cervical cancer development, particularly of high risk (HR) HPV types 16 and 18, accountable for approximately 75% of cervical cancer cases. These aspect has increased demand for HPV detection molecular tests. **Objectives:** To summarise and update the current knowledge on HPV and cervical cancer screening techniques and, also, discuss HPV-related data and screening techniques in Brazil. **Methods:** We include articles published in the past 10 years, both in English and Portuguese. Scientific search engines as Scopus, Cochrane Library and Pubmed were used for the terms "cervical cancer", "HPV", "cervical carcinoma", "HPV vaccine". Only research articles and reviews were considered. **Results:** The most used techniques for HPV detection are PCR and Hybrid Capture 2 (HC2). However, techniques for detection of HPV E6/E7 mRNA and p16INK4a have been developed, which are still being validated. These tests may help distinguish transient from persistent HPV infections. **Conclusion:** To reduce the number of cervical cancer cases, screening strategies could be adjusted to contain the best combination of cytological and molecular tests. The ideal screening strategy require high sensitivity to minimize false negative results, and high specificity, to avoid false positives and over referral. Optimization may be achieved by using by co-testing, combining HPV genotyping and cytology triage with low-grade intraepithelial lesions (LSILs) or with atypical squamous cells of undetermined significance (ASC-US). Besides, strategies to prevent cervical cancer cases include HPV vaccination.

Keywords: papillomavirus infections; uterine cervical neoplasms; vaccines; Brazil.

RESUMO

Introdução: O câncer de colo uterino é a terceira causa de morte em mulheres no mundo. Infecção persistente pelo HPV é o principal fator no desenvolvimento do câncer de colo uterino, particularmente HPV de alto risco (AR), tipos 16 e 18, responsáveis por aproximadamente 75% dos casos de câncer de colo uterino. Este conhecimento incrementou a demanda de testes moleculares para detecção de HPV. **Objetivos:** Sumarizar e atualizar o conhecimento atual em técnicas diagnósticas para HPV e rastreamento de câncer cervical, e discutir dados a respeito do diagnóstico de HPV e métodos de rastreamento no Brasil. **Métodos:** Foram incluídos artigos originais ou revisões publicados nos últimos 10 anos, em inglês e português, utilizando as bases de dados Scopus, Cochrane Library and Pubmed, e os termos "*cervical cancer*", "*HPV*", "*cervical carcinoma*", "*HPV vaccine*". **Resultados:** As técnicas mais utilizadas para a detecção de HPV são a PCR e a captura híbrida. Contudo, técnicas para detecção de RNAm de HPV E6/E7 e p16NK4 já foram desenvolvidas estando em fase de validação. Estes testes poderão auxiliar na distinção de infecções transientes e persistentes. **Conclusão:** Para reduzir o número de casos de câncer cervical, estratégias de rastreamento podem ser ajustadas para a melhor combinação de testes citológicos e moleculares. Estratégias de rastreamento ideais requerem alta sensibilidade, minimizando resultados falso negativos e alta especificidade, evitando falsos positivos e excesso de encaminhamentos. A otimização pode ser obtida combinando testes de genotipagem de HPV e triagens citológicas. Além disso, estratégias para prevenção de casos de câncer cervical incluem a vacinação contra o HPV.

Palavras-chave: infecções por papillomavirus; neoplasias do colo do útero; vacinas; Brasil.

INTRODUCTION

Uterine cervical cancer is the third most common malignancy in women, and the seventh overall, with approximately 530,000 new cases in 2008[1] and 270,000 deaths annually[2]. Cervical cancer is responsible for more years of life lost in Latin America and the Caribbean than tuberculosis and AIDS[3]. It is estimated that viral infections are involved in 20% of human cancers worldwide, and just under 25% of cancer cases in developing countries[4]. Epidemiologic studies have shown that infection with high-risk (HR) types of Human Papillomaviruses (HPVs) is the main aetiological factor of cervical cancer[5]. Additionally, previous studies have shown that nearly all of cervical cancer cases test positive for HPV[6].

More precisely, persistent infection with HPV has been explicitly linked to the development of cervical cancer, with between 13 and 18 types of the virus characterized as conferring a high oncogenic risk[7]. Of these, the most carcinogenic, responsible for approximately 70% of all cervical cancers are types 16 and 18 HPV[8].

The better knowledge about the association between HPV and cervical cancer has increased the demand of tests for the presence of HPV for the diagnosis of abnormal cervical smears and screening for cervical cancer[9]. Also, it has led to the development of

[1]Postgraduate Program in Health and Behavior, Universidade Católica de Pelotas (UCPel) – Pelotas (RS), Brazil.
[2]Postgraduate Program in Epidemiology, Universidade Federal de Pelotas (UFPel) – Pelotas (RS), Brazil.
[3]School of Medicine, UFPel – Pelotas (RS), Brazil.

new screening techniques based on molecular biology testing. These strategies include PCR-based diagnosis and, more recently, Hybrid Capture 2 (HC2) assays.

METHODS

In this review we will summarise and update the current knowledge on HPV and cervical cancer screening techniques. Also, we will discuss HPV-related data and screening techniques in Brazil. This work comprises articles published in the past 10 years, both in English and Portuguese. Scientific search engines as Scopus, Cochrane Library and Pubmed were used for the terms "cervical cancer", "HPV", "cervical carcinoma", "HPV vaccine". Only research articles and reviews were considered.

DISCUSSION

Scientific background on HPV

Human Papillomavirus (HPV) are connected to epithelial proliferative diseases, both benign and malignant, with more than 100 types of the virus having been documented. Its genome encodes for only eight genes[10]. A new HPV type is determined by differences on three nucleotide sequences in its genome, namely in genes E6, E7 and L1, when differing more than 10% from those occurring in know HPV types. Two classes of HPV can be distinct, based on the location of the infection: cutaneous types that infect the epidermis, and mucosal types that infect the epithelia of the anogenital or the aerodigestive tract[11]. HPV types related to cervical cancer, termed high risk (HR), act by interfering with the cell cycle regulation. Its primary oncoproteins are E6 and R7, which mediate the degradation of proteins p53 and retinoblastoma tumour suppression protein (pRB)[10].

HPV and cancer

Of the HPV types related to cervical cancer, the 12 most common are included into two species: 7 (HPV 18, 39, 45, 59, 68) and 9 (HPV 16, 31, 33, 35, 52, 58, 67)[7], which convey greatly different risks. Of these, the most carcinogenic, responsible for approximately 60% of all cervical cancers is HPV type 16 (HPV16)[8], regardless of cytological appearance[12]. The second highest risk genotype is HPV18, accounting for 10 to 15% of cervical cancers[8].

Acute infections of these 12 types of HPV are common, particularly at younger ages[12]. The highest prevalence of HPV-positivity occurs in the late teens or early twenties[13]. There is a rapid decline on HPV infection after the age of 25, which continues until the around age 35–40, where they reach a plateau level[14]. However, adolescents have a high prospect of spontaneous clearance of cervical cell abnormalities, therefore a low risk of cervical cancer (HHS 2012). Although common, most HPV infections will be suppressed by the immune system within one or two years without causing cancer. They may, however, cause transient changes in cervical cells.

HPV types are divided into high-risk (HR) and low-risk (LR), where HR HPVs are the ones associated with cervical cancer. Persistent infection with HR HPV genotypes is essential for the development of pre-cancer lesions, cervical intraepithelial neoplasia (CIN) grade 3 (CIN3) and, subsequently, cervical cancer[12]. Although the prevalence of HPV infection tends to decline with age, viral persistency tend to increase, leading to the increase of severe cervical dysplasia to rise on late twenties to early thirties and of cervical cancer in late thirties[13]. Studies have reported a prevalence of HR HPV about two times higher than of LR HPV types[15]. Data suggests that LR HPV infections tend to clear more rapidly than HR HPV infections, and the probability of an infection not clearing increases proportionally to its duration[16].

HPV persistence, from one to two years, particularly by HPV16, increases the prognostic for CIN3 or a more serious diagnosis (CIN3+) in the following years[6]. The risk of untreated CIN3 lesions becoming an invasive cancer goes up to 20% in 10 years and 30% in 30 years. However, when treated, only around 1% of the lesions will become invasive. In cases of women with both minimum disturbance of their lesion and persistent disease, the risk was of about 30% in 10 years, increasing to approximately 50% in 30 years[17]. Also, HPV16 and multiple-type infections have the lowest clearance rate, increasing the probability of cervical cancer[18].

Knowing the precise relation between HPV type specificity that may or not aggravate the risk of HPV infection is important to understand the dynamics of these infections, take actions toward prevention and determine the best course of treatment if they occur.

Development of cervical cancer

Cervical cancer begins with HPV acquisition, followed by viral persistence, proliferation of infected cells to pre-cancer and, finally, invasion[6], as shown in **Figure 1**. As previously seen, not all HPV infections will persist, and some will be cleared by the immune system. A less frequent outcome is the regression of pre-cancer cells to normality. Therefore, early onset of sexual activity and increased number of sexual partners may increase the risk of HPV infection and, possibly, that of cervical cancer[19].

However, there are independent risk factors associated with squamous cell carcinoma and adenocarcinomas[19]. Among them are smoking, number of pregnancies, other infectious agents[20] and early initiation on oral contraceptives[21]. A Finnish study found correlation of an increased risk of incident HPV-infection with the initiation of smoking beyond 13 years of age and for the initiation of oral contraceptives usage before the age of 20[21].

Cervical cancer screening

Cervical cancer screening comprises two types of tests: cytology-based and HPV testing. These tests are a way to detect HPV infections, abnormal cervical cells — including precancerous cervical lesions — and cervical cancers. High-quality screening using cytology has significantly reduced mortality from squamous cell cervical cancer, which constitutes up to 90% of cervical cancers[22].

Cytology-based screening traditionally involves 3 steps: finding cytological abnormalities in a Papanicolaou (Pap) smear; histological confirmation of a biopsy taken under colposcopic control and treatment of the lesion that otherwise could develop into invasive cancer[23]. When *in situ* lesions are confirmed, they are called cervical

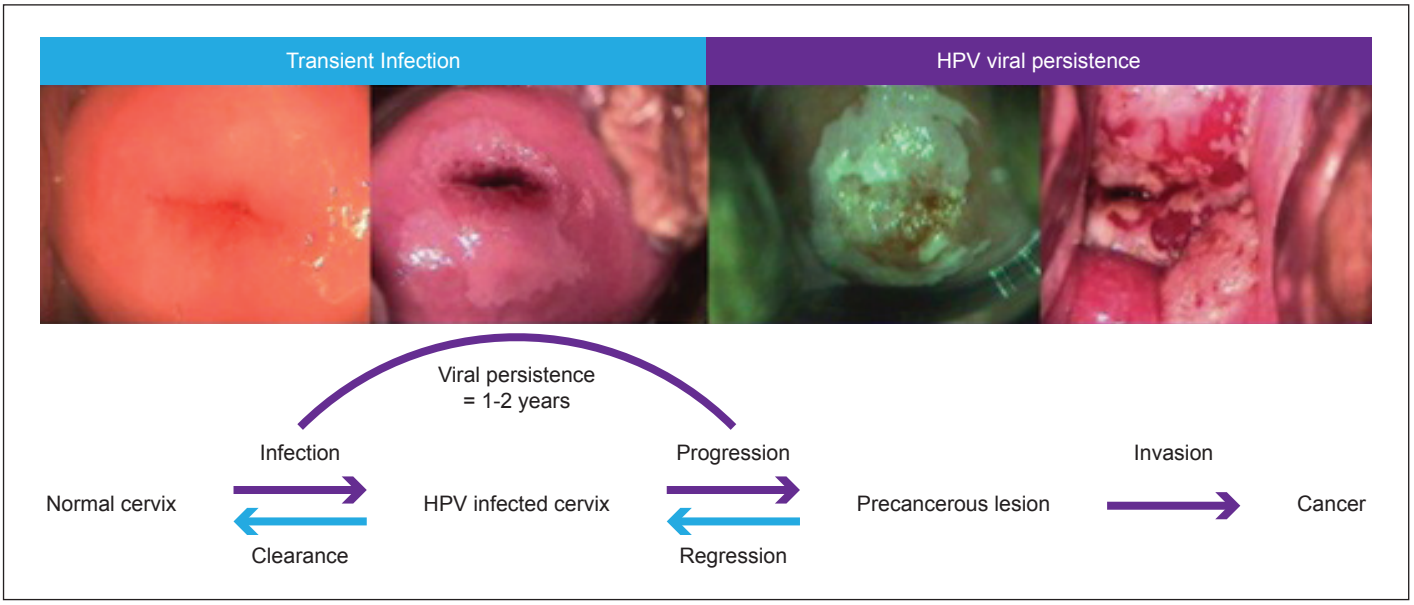

Figure 1 – Critical steps in the development of cervical cancer. Images refer to Colposcopy exams. Adapted from Muñoz et al.[8].

intraepithelial neoplasia (CIN). Depending on the severity of the lesion, it may be denominated CIN1, CIN2 and CIN3, indicating increasing levels of severity. Results from cytology-based tests are classified as LSIL+ for low-grade squamous intra-epithelial lesions or worse, or HSIL+ for high-grade intra-epithelial lesions or worse[23].

Liquid-based cytology (LBC) and Pap tests have similar accuracy as a test for detection of CIN2+. It is a simpler technique when compared to Pap test, its interpretation takes less time, and HPV testing can be performed on the same sample[23]. This could account for LBC replacing Pap tests as cytology exams.

Despite its great benefits toward cervical cancer prevention, cytology tests have weaknesses. In cytology, results are dependent on the collection of high quality sample during examination. Also, requiring identification of morphological changes within cells, interpretation of results is of a qualitative nature, which is subjective. Not only that, but a repetitive method can lead to larger number of interpretation errors[14]. In case of abnormal cytology, colposcopy is recommended as a diagnostic tool. However, shouldn't be considered for screening purposes.

HPV testing has the advantage of being objective (presence or absence of virus), removing the qualitative aspect present in cytology. Below we discuss current strategies of HPV detection in detail.

HPV detection

From the knowledge on the relation between HR-HPV types and cervical cancer came the need to develop new types of molecular detection systems, both for DNA and RNA recognition. Molecular tests offer increased sensitivity although they show lower specificity compared to cytology testing[6].

PCR has been used for over ten years in HPV detection. However, its high analytical sensitivity combined with the potential for contamination is a serious disadvantage for this method, once it may lead to false-positive results. The Hybrid Capture 2 (HC2) assay, a second-generation commercial HPV test, was introduced as a possible routine diagnostic test, including positive and negative controls. HPV DNA tests have been demonstrated to have higher sensitivity for CIN2+ lesions than the ones obtained by cytology in several studies[14].

There is a debate about which of these two tests would be better. On a screening test using both techniques, Kulmala et al.[24] found that the results of PCR and HC2 were consistent for 85% of the samples. However, the sensitivity of HC2 for the detection of high-grade squamous intraepithelial lesions (HSILs) was slightly better[24]. The authors also highlight that the HC2 assay is technically well designed, being easily controlled and performed by lab personal, while PCR needs to have many of its steps optimized, making it more difficult to have rigid standards[24].

Other promising screening techniques being developed detect carcinogenic HPV E6/E7 mRNA and $p16^{INK4a}$, which may help distinguish transient from persistent HPV infections. Molden et al.[25] compared the detection of HPV mRNA from carcinogenic HPV types with the detection of HPV DNA. E6/E7 mRNA expression was detected by the PreTect HPV-Proofer assay, whereas the presence of HPV DNA was detected by Gp5+/6+ consensus PCR followed by type-specific PCR. PreTect HPV-Proofer had lower detection rate of HPV for cases of abnormal cytologic diagnosis; cytologic normal, atypical squamous cell of uncertain significance (ASC-US); and low-grade SIL (LSILs) diagnosis. No significant difference was observed for the detection of high-grade squamous intraepithelial lesion (HSIL) when comparing the tests[25]. Nevertheless, the authors pronounce mRNA detection tool as a promising test as an adjunct to cytology.

The $p16^{INK4a}$ is a cell-cycle regulator that is overexpressed in cervical pre-cancer and cancer cells induced by the deregulated expression of HPV oncogenes. Wentzensen et al.[26] tested $p16^{INK4a}$ levels in lysates of cervical cells that were obtained from a disease-enriched population by using a $p16^{INK4a}$-specific sandwich ELISA. Nonetheless, the overall content of this protein may be higher in specimens derived from patients with high-grade cervical intra-epithelial neoplasias (HGCIN) compared with specimens derived

from patients with low-grade dysplasia or patients without cervical intraepithelial lesions. Still, the authors suggest that ELISA-based quantification of solubilized $p16^{INK4a}$ protein may have high sensitivity for detecting cervical pre-cancer[26].

As there is evidence suggesting that only persistent infections are associated with precancerous lesions, detecting the persistence of HPV — specially types 16 and 18 — would give even more specific markers of clinically significant infections. However, this will require robust assays and feasible clinical protocols[10].

After the treatment of cervical lesions, HPV testing detects residual infection quicker and with higher sensitivity and comparable specificity compared to follow-up cytology[13]. The absence of HPV infection will most likely shorten the follow-up period, yet more data is needed to confirm this hypothesis.

Screening strategies

Cervical cancer prevention programmes vary extensively by country, but most of them could be improved immensely by new techniques. The suitable programme depends on affordability, different social demands for protection against cancer and willingness to prevent complications even at low risk conditions. These will have an effect on when screening begins, the appropriate interval between tests and age to stop assessments. However, studies suggest that screening women within 5 to 10 years of sexual initiation wouldn't be cost effective, as the risk of benign HPV infections is high but the risk of cancer is still low[10]. Overall, evidence suggests that, if screening under the age of 25 is at all valuable, the benefit would be modest at best. It should also be taken into account that women treated for cervical lesions prior to childbearing have preterm delivery chances increased[27].

The ideal cervical cancer screening strategy would require the highest sensitivity to minimize false negative results, as well as the highest specificity, in order to avoid false positives and over referral[28]. Unfortunately, strategies that favour one of these points will inevitably lack in quality for the other. Namely, when maximizing sensitivity, tests have usually presented relatively poor specificity[28].

Incorporating molecular tests into cervical cancer screening strategies may lead to an increase in disease detection and in length of screening intervals. Increase in detections will improve benefits of treatment and longer time between screenings may reduce distresses as the psychological impact of screening positive and proceed with treatment of lesions that might have cleared by themselves[6]. Also, there is evidence that testing for HR HPV is cost effective and sensible for the detection of precancerous lesions in women with ambiguous cytology[13]. HPV testing is more sensible but less specific than Pap tests, can be useful on the follow-up of women post-colposcopy when pre-cancer is not found and can guide an evaluation of cure post-treatment[10]. Testing negative for HR HPV types provides more reassurance against the development of pre-cancer and cancer than cytology-based testing[10].

Precaution should be taken on the use of molecular testing of LSIL lesions. LSIL is usually the manifestation of a current HPV infection with low potential for neoplastic transformation. Consequently, molecular testing of these lesions will frequently produce a positive result, limiting its capacity to discriminate between cases that may lead to severe lesions[13].

Two strategies have been described as being able to optimize the balance between specificity and sensitivity. One consists of cotesting HPV genotyping and cytology triage with low-grade intraepithelial lesions (LSILs), and the other is HPV genotyping and cytology triage with atypical squamous cells of undetermined significance (ASC-US). The authors state that the latter strategy can lead to 50% reduction in the number of required screenings, also being more sensitive and requiring less colposcopies to detect CIN3 or more severe cases[28].

Prevention

Reduction of HPV infection rates can be achieved, to some level, by health education programs and conscientious condom use, decreasing the risk of cervical cancer at the population level. Nevertheless, condom use does not entirely protect against HPV transmission, as the male anogenital skin is not completely covered[29]. For this reason, development of HPV L1 virus-like-particle (VLP) vaccines is a considered a major advance in prevention of cervical cancer. These vaccines are based on the self-assembly of recombinant L1 protein into non-infectious capsids that contain no genetic material[10].

Two types of vaccine against HPV were recently approved: the quadrivalent Gardasil (against HPV types 6, 11, 16, 18) (Merck and Co, Bluebell, PA, USA), and the bivalent Cervarix (against HPV types 16, 18) (GlaxoSmithKline, Rixensart, Belgium). Both vaccines are almost completely effective against HPV 16, and 18 induced CIN2+[30].

In the United States, the federal Vaccines for Children (VFC) program includes HPV vaccination. This program covers vaccine costs for children and teens who don't have insurance and for some children and teens who are underinsured. Vaccination is recommended for girls and boys aged 11 or 12 years. Depending on the jurisdiction, HPV vaccines are also recommended for teen boys and girls who did not get the vaccine when they were younger, teen girls and young women through age 26, as well as teen boys and young men through age 21[31].

Germany has a vaccination program against the most oncogenic types of HPV (namely 16 and 18) since 2007. The Standing Committee on Vaccination (STIKO) recommends vaccination for girls between the ages of 12 and 17 years old[32]. A recent study predicts that, over the next 100 years, HPV vaccination will have prevented approximately 37% of cervical cancer cases even if vaccination coverage is only 50% (as currently observed in Germany)[30]. According to the same study, cross-protection could result in a further reduction of approximately 7% of all cervical cancer cases for the bivalent and about 5% for the quadrivalent vaccine[30].

The Brazilian Department of Health has recently announced that, from 2014, the HPV vaccine will be available free of cost through the National Health System, where girls aged between 10 and 11 years old will be immunized[33]. The aim is to vaccinate 80% of the cohort, approximately 3,3 million people. Federal investments of over R$ 360 million have been announced for the acquisition of 12 million doses of the vaccine. The vaccine, quadrivalent, will be produced in partnership between the Butantan Institute (affiliated to

the São Paulo State Secretary of Health) and Merck (Merck Sharp & Dohme; Merck, Co., Inc. Brazilian subsidiary)[33].

To ensure that a program is cost-effective and vaccination will protect young women through the age of greatest risk of HPV exposure, vaccination durability should be of 10–15 years or greater or that boosting would be safe and effective[10]. Also, HPV vaccines available today would give best public-health benefits when applied to girls who haven't started sexual activity. The determination of the appropriate age to proceed with vaccination will require research on the age of first sexual activity for each region, developing programs that are suitable for the population in question.

HPV in Brazil

There is a need for further documentation of HPV infection, screening processes and treatment options in developing countries. When assessing studies on HPV testing and screening, authors have markedly stated that they did not include developing countries[14]. A program for screening of cervical cancer in Brazil now counts with 17 years of existence[34]. Through its data we see that the number of deaths due to cervical cancer in Brazil are similar to those in developing countries, being far from rates observed in countries where cervical cancer screening is well structured and established[34]. It is estimated that Brazil has over 20,000 new cases of cervical cancer per year[15]. The expected number of cases will increase from 19,603 (estimate for the year 2002) to approximately 36,800 in 2030[1].

In a review regarding HPV infection in Brazil, between the years 1989 and 2008, Ayres and Silva[15] only found 14 articles that met their inclusion criteria. From the data collected in these papers, they could infer that the overall prevalence of HPV cervical infection varied widely from 13 to 54%. When analysing the HPV infection in women with normal cytology results, rates varied between 10 and 24%[15]. Also in Brazil HPV16 was the most prevalent irrespective of cytology results[15].

As stated in previous study, provided that the cost per vaccinated woman is I$ 25 (International Dollars) or below, it appears that vaccination alone would be cost-effective in Brazil. However, there is uncertainty in the price of vaccines and for the programmatic costs related with adolescent vaccination[2]. But if we assume coverage of 70%, HPV16, and 18 vaccination of adolescent girls (before age 12) could reduce the lifetime risk of cervical cancer by 43%. Combining vaccination and three screenings after the age of 30, both at 70% coverage, may lead to a reduction of 53 to 70% in the risk of cancer[2].

Regarding the age indicated for vaccination, a Brazilian report, part of the Latin American Screening (LAMS) study, indicates the ideal age as being 15 years old[19]. This result is based on the average age of the first sexual intercourse of the women interviewed for the study. This differs from the age 12 determined on an international study, where ages 9 to 12 are determined as prior to sexual debut and ideal for vaccination[2].

All this taken into account, the Brazilian Government has decided to drop the age of vaccination from what was recommended in previous Brazilian study, agreeing with the findings of Goldie et al.[2]. The approximate cost of the vaccine in Brazil will be of I$ 28 (accepting the PPP conversion factor (GDP) to market exchange rate ratio in Brazil as I$ 1.07, according to the 2012 World Bank Report[35]). Assuming the PPP rate used by Goldie et al.[2] was I$ 0.8 (PPP rate of 2008[35]), the value of the vaccine in Brazilian Reais, estimated by the group at the time, would be of R$ 31.25. Therefore, with a current cost of R$ 30.05, the program reveals itself to be cost-effective.

CONCLUSION

The ideal screening strategy would require high sensitivity to minimize false negative results, as well as high specificity, in order to avoid false positives and over referral. Optimization may be achieved by using by co-testing: a combination of HPV genotyping and either cytology triage with low-grade intraepithelial lesions (LSILs) or with atypical squamous cells of undetermined significance (ASC-US). It is believed that programmes worldwide are moving from a morphologic prevention model (based on cytology, colposcopy and/or histology) to a model based on HPV virology and its molecular interaction with the human host[12]. Knowing how HPV infections are distributed in the population is key for the development of new tests and for the evaluation of the impact of vaccines in different scenarios[15]. Research and time will tell which screening strategies and programmes are best suited for different regions, adapting them to local resources and collective priorities.

An important measure to reduce cervical cancer cases is prevention of HPV infection through the use of vaccination. Quadrivalent and bivalent vaccines has been approved and are being used in different countries. The Brazilian National Health System has make a huge step in this direction offering the quadrivalent HPV vaccine free of cost for the vaccination of girls aged between 10 and 11 years old.

Conflict of interests

The authors report no conflict of interests.

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Address for correspondence:
GUILHERME LUCAS DE OLIVEIRA BICCA
Rua Padre Anchieta 2396 – Centro
Pelotas (RS), Brazil
CEP: 96015420
Tel: +55 (53) 3222-7398
Fax:+55 (53) 3025-7398
Email: gbicca@yahoo.com

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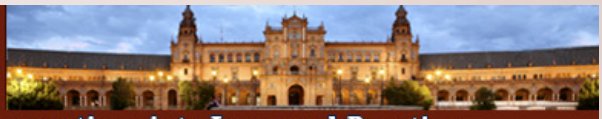

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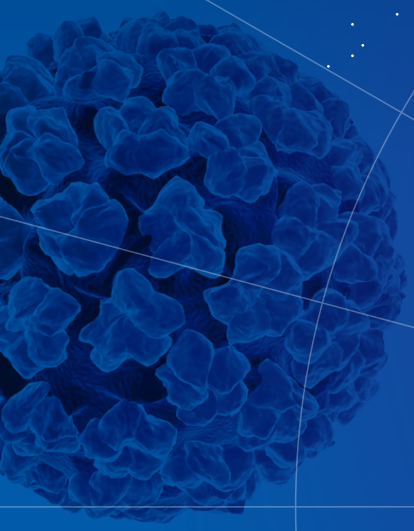

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