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Editorial

*Use of placebos and post-trial benefits**

Brazilian legislators have not yet enacted any laws regarding the use of placebos and the duties of assistance to research subjects. As a result of this omission, public administrative authorities have to deal with the subject on a regular basis, oriented by fundamental rights and judicial supervision. Against that backdrop, CNS (National Health Council)[2], speaking through CONEP (National Research Ethics Committee)[3], ANVISA (Healthcare Surveillance Agency)[4], the CFM (Federal Medical Council)[5], the CNJ (National Justice Council)[6] and the STF (Federal Supreme Court)[7] have expressed their opinions on the subject in a consistent manner.

A comparative analysis about the use of placebos and post-trial benefits in Brazil and the United States should therefore re-examine the fundamental rights in question (for example, the right to human dignity), not only according to the 2013 version of the World Medical Association's Helsinki Declaration[8], but also the case law of the Inter-American Court of Human Rights and the European Court of Human Rights, since Brazil is heavily influenced by the public law of Continental Europe.

In addition, certain premises may not accurately reflect Brazilian reality. I wish to point out three of them that might be explored in greater depth:

1. Avoid the possibility of confusion between research and treatment. Indeed, research is not treatment and many believe clinical trials are a sort of game of chance or gamble for volunteers. In fact they may be harmed (adverse events) without any insurance coverage or compensation for damages, or not receive any treatment at all (placebo) and his illness may deteriorate. Why decide to play such "Russian roulette" when well-proven treatments are available from SUS [Unified Health System] at no extra charge?
2. Is all research for the purpose of advancing science? It is undeniable that most research is substantially for an economic purpose. The idea is to maximize the profit of the sponsor (company) at minimal risk, and the subject may be considered a "useful innocent" in this context.
3. Is research in the best interests of governments because it relieves them of the burden of providing care for the subjects in question? Not in Brazil, because the number of volunteers is negligible compared to the 200 million patients funded by SUS, which ends up paying for the costs and consequences of the adverse events that occur in the research, because they do not have real coverage for such claims.

It is also important to remember that the socioeconomic and educational levels of Brazilian research volunteers are fundamentally different from those of their US counterparts, in that the Brazilian government has to provide greater protection for those who are considered psychologically vulnerable. Illiteracy, old age and mental deficiencies make it difficult for subjects to understand the scope and consequences of the study they are undergoing, as well as to understand the Informed Consent Form and consent to participate in a free and informed manner. In general, the insurance provided by the sponsor, which is mandatory according to the manual of good practices in clinical research, is only effective in the sponsor's country of origin and rarely covers adverse events or deaths that occur in the other countries that may participate in a multicenter, multinational research.

There is no specific legislation in Brazil that regulates the funding of research studies by the pharmaceutical industry. However, the notion that administrative authorities must remain independent and impartial is incompatible with the possibility of private financing of any activity that might result in an administrative decision that could directly or indirectly harm or benefit the sponsor.

In any case, it is well known that all the research carried out in order to register a drug is sponsored by the company that holds the patent. It would therefore be important to discuss the topic from a comparative perspective of Brazil and the United States, considering the fundamental principles of administrative law, especially in terms of the independence and impartiality of the authorities. On the one hand, it may seem utopian to expect the State to have specific funds to conduct cutting-edge research; on the other, it is necessary to examine in greater detail whether the authorities in charge of registering new technologies and incorporating them (into SUS) should be dependent on structurally biased technical testing.

Finally, regarding the breakdown of the research committees that monitor the nature and specificities of the project, it is mandatory to examine the type of committee being considered, as suggested by UNESCO[9]: a normative or advisory committee; a committee of professional associations; a hospital or medical ethics committee; or a research ethics committee. The specialisation of committees does not appear to create any great difficulties; however, even subcommittees are acceptable, provided that they are justified by a sufficient number of claims. Whether they are centralised or decentralised and exercise general or specific powers,

*Comments on the paper *Human Subject Protections in the United States: A Model for Brazil?*[1], by Michael J. Werner, on the occasion of the workshop "Brazilian Pharmaceuticals Regulatory Policy Research", of the Health Law Research Center (CEPEDISA) of Health School of São Paulo University, 2014. We wish to thank Alessandra Vanessa Alves, Lígia Bahia, Miriam Ventura and Clarice Petramale for their research and assistance.

it is important for all such committees to maintain structural coherency and, above all, a high level of autonomy, independence, impartiality and technical expertise.

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Prevalence of syphilis, diagnostic methods and associated factors in patients treated in the laboratory of health Foundation of Vitória da Conquista (BA)

Prevalência de sífilis e fatores associados em pacientes atendidos no laboratório da Fundação de Saúde de Vitória da Conquista (BA)

Muccio Costa Gondim Pires[1], Caline Novais Teixeira Oliveira[2], Cláudio Lima Souza[3], Márcio Vasconcelos Oliveira[3]

ABSTRACT

Introduction: In spite been discovered centuries ago, syphilis remains a sexually transmitted infectious disease of major public health impact given the high prevalence found in Brazil and worldwide. The laboratory detection, with subsequent treatment of this disease, can reduce vertical contamination rates among adults and reduce sequelae from its clinical manifestations. **Objective:** To determine the prevalence of syphilis, as well the gestational and congenital forms of syphilis, and associated factors among patients attending the laboratory of Health Foundation of Vitória da Conquista (FSVC). **Methods:** A retrospective cross-sectional study, using secondary data obtained from the system of notification for syphilis, from FSVC laboratory from July 2012 to July 2013, following the ordinance criteria nº 3242 of 2011. **Results:** 134 patients were identified with positive diagnostic tests for syphilis among the 6,699 patients that were tested, revealing a global prevalence of 2%. The prevalence of congenital syphilis was 2.84 and 2.24% for gestational syphilis. It stands out among the positive ones that 19.4% of the patients were aged less or equal to one year old, 37.3% were pregnant women and the vast majority (94%) of them lived in urban areas. 47% of the patients had venereal disease research laboratory (VDRL) titers up to 1:4. Among those patients with primary positive test, 94% got positive results from the confirmatory test. Between newborns that tested positive for syphilis, 60% had titers up to 1:2. **Conclusion:** The prevalence rates are high considering the parameters established by World Health Organization (WHO) and are capable of representing burden for the population. However, they point out good chances of screening the county from the disease, which is an essential step in addressing this serious infection to the Public Health.

Keywords: syphilis, diagnosis, prevalence.

RESUMO

Introdução: A sífilis continua sendo uma doença infecciosa sexualmente transmissível de grande impacto para a Saúde Pública, dadas as elevadas prevalências encontradas no Brasil e no mundo, apesar de ter sido descoberta há séculos. Sua detecção laboratorial, com posterior tratamento, pode reduzir as taxas de contaminação vertical entre adultos, além de reduzir sequelas de suas manifestações clínicas. **Objetivo:** Determinar a prevalência de sífilis, incluindo as formas gestacional e congênita, e fatores associados em pacientes atendidos no laboratório da Fundação de Saúde de Vitória da Conquista (FSVC). **Métodos**: Estudo de corte transversal retrospectivo realizado com dados secundários obtidos do sistema de laudos e norteado pela planilha de notificação para sífilis do laboratório da FSVC no período de julho de 2012 a julho de 2013, obedecendo aos critérios da Portaria nº 3.242, de 2011. **Resultados:** Foram identificados 134 pacientes com provas diagnósticas positivas para sífilis entre 6.699 pacientes testados, revelando uma prevalência global de 2%. A prevalência da sífilis congênita foi de 2,84% e a de sífilis gestacional de 2,24%. Destaca-se entre os positivos que 19,4% dos pacientes tinham idade igual ou inferior a um ano, 37,3% eram gestantes, 94% residiam na zona urbana e 47% tinham títulos de *venereal disease research laboratory* (VDRL) de até 1:4. Desses pacientes com teste primário positivo, 94% tiveram positividade no teste confirmatório. Entre recém-nascidos positivos, 60% tinham títulos de até 1:2. **Conclusão:** As prevalências encontradas estão elevadas levando em consideração os parâmetros estabelecidos pela Organização Mundial da Saúde (OMS) e são capazes de representar ônus para população. No entanto, apontam boa capacidade de triagem do município frente a doença, o que é um passo essencial para a Saúde Pública combater esta grave infecção.

Palavras-chave: sífilis, diagnóstico, prevalência.

INTRODUCTION

Syphilis is a sexually transmitted infectious disease of major impact on public health. According to the World Health Organization (WHO), in 1999, it was estimated 12 million new cases in the world, with the highest incidence seen in developing countries[1]. In Brazil, WHO estimates already indicated, in 1999, more than 937,000 cases of syphilis per year[1]. However, since that became a reportable disease (for cases of congenital syphilis in 1986, gestational syphilis from 2005 and acquired syphilis from 2011) until 2012 there were more than 137,000 cases[2]. In Bahia, according to the Superintendência de Vigilância e Proteção da Saúde (SUVISA – Office of Surveillance and Health Protection), from 2007 to 2013, there were more than 7,000 cases of syphilis, in which the city of Vitória da Conquista appears with 476 cases[3].

The etiologic agent of syphilis is a bacterium called *Treponema pallidum* which was discovered and identified in 1905 by Schaudinn and Hoffmann and since then has been studied in various parts of the world[4]. The transmission mechanism occurs by direct contact with the lesions, by small abrasions caused by intercourse, vertically or through blood transfusions, tattoos or contact with contaminated

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material containing the microorganism – the latter quite unusual today. Once *T. pallidum* infects the individual it may spread through the lymphatic and hematogenous route, and may reach and injure other parts of the body[5].

The natural course of infection may be symptomatic divided into three stages: primary, secondary and tertiary syphilis; and two asymptomatic phases: the early and late latent syphilis. Clinical manifestations occur depending on the stage of the disease[6].

Syphilis in pregnant women can lead to the vertical transmission of the disease at any time during pregnancy, especially when the infection is recent, since *T. pallidum* can reach the placental circulation and reach the bloodstream of the fetus, characterizing congenital syphilis. Possible consequences include premature birth, low birth weight, malformations, miscarriage and, later, dementia, bone, liver and muscle problems[7].

There is a worldwide concern about the control of syphilis, especially in adults. In 2008, WHO drew a target aiming at the eradication of congenital syphilis by the year 2015 and proposed the expansion of access to maternal and child health services, increased detection, treatment and control of the disease, as well as the implementation prevention and counseling activities. Another plan was the reduction of prevalence rates of the disease to levels below 1%, which, according to WHO, does not represent a burden for the population[8].

The acquired form of syphilis occurs primarily in adults and may lead to the tertiary stage of the disease. A person may be evolving symptomatic of the primary phase to tertiary or can be asymptomatic carriers of the infection and, after several years developing cardiovascular syphilis, neurosyphilis, among other complications[9].

The diagnosis of syphilis can be performed easily, following recommendations of the Administrative Rule nº 3,242 of the Brazilian Ministry of Health, from December 2011, which established the laboratory flowchart for the diagnosis of syphilis[10]. **Figure 1** shows the following flow chart of the diagnosis of syphilis.

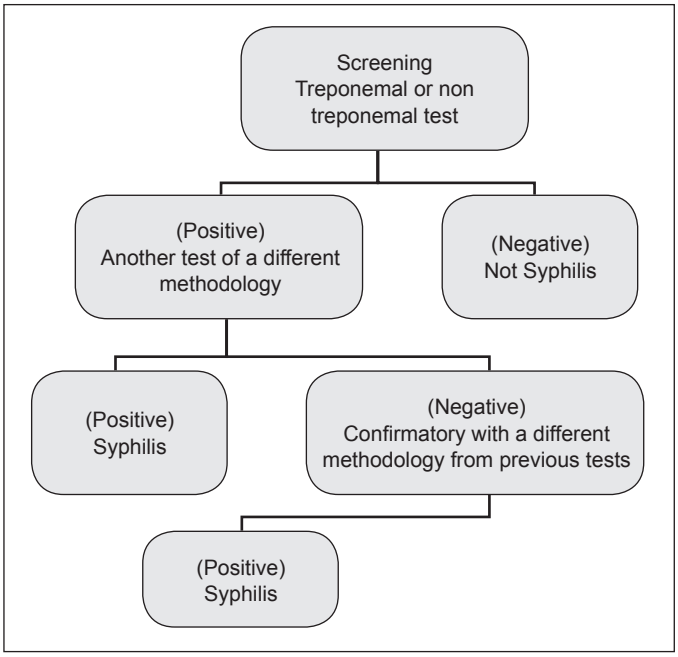

Figure 1 – Flowchart for the laboratorial diagnosis of syphilis. Adapted from regulation nº 3242 of 2011.

Whatever the methodology, the early diagnosis of syphilis can contribute to the reduction of injuries related to the clinical manifestations of the untreated disease, since the treatment is easily accessible and has low cost. Moreover, it can also break the chain of transmission of the disease.

OBJECTIVE

To determine the prevalence of syphilis, including the gestational and the congenital forms, and associated factors in patients treated in the laboratory of the Fundação de Saúde de Vitória da Conquista (FSVC – Vitória da Conquista's Health Foundation).

METHODS

This is a retrospective study of secondary data obtained from the notification system for FSVC Lab syphilis from July 2012 to July 2013.

The FSVC currently manages the largest public health laboratory of the interior of Bahia and figure as the major test maker of the Sistema Único de Saúde (SUS – Unified Health System) in the city and region serving both the needs of patients admitted to the Municipal Hospital of the city of Esaú Matos (maternal and child regional reference) as the patients of the ambulatory net of Vitória da Conquista and region with an average of 55 thousand tests per month. According to the Vitória da Conquista' scheduling system, the laboratory of FSVC is responsible for supplying about 85% of the exams through the city by SUS.

The laboratory of FSVC performs the diagnosis starting from the non treponemal test - venereal disease research laboratory (VDRL) for screening, following with treponemic immunoassay (IC) in case of reagent in any capacity in the screening test. When there is disagreement between the results of the two methods the samples are forwarded to the Care and Life Support Center (CAAV), in that city, where hemagglutination is the methodology of choice for confirmation of results by the *Treponema pallidum hemagglutination* treponemal test (TPHA). The two confirmatory tests are based on detection of IgM and IgG anti-*Treponema pallidum*. In all the diagnostic tests for syphilis the reagents brand WAMA DIAGNÓSTICA® were used. In the laboratory of FSVC, all positive results for syphilis are recorded in the worksheet and hence notified to the surveillance of the municipality obeying the Administrative Rule nº 104, of January 25, 2011, which includes all forms of syphilis as a compulsory notification.

Data collection was done in the period between 05 and 15 September 2013, from the verification of positive cases for syphilis indicated in the notification sheet. Then proceeded to access the registration form of the patients with the laboratory report system of FSVC (COMPLAB®, version 6.9.4) in order to obtain information such as age, sex, pregnancy state and county of origin.

For the purpose of calculation of prevalence of congenital and gestational syphilis it was necessary to obtain, by Serviço de Arquivo Médico Estatístico (SAME – Statistical Medical File Service) of FSVC, data on the number of live births and the number of pregnant women attended by the Health Foundation Hospital of

Vitória da Conquista — reference in maternal and child care and conducting the highest number of deliveries by SUS in Vitória da Conquista and region.

The data were transported to Microsoft Office Excel 2007 spreadsheet and then analyzed using the statistical package *Epi Info* version 3.5.1, where descriptive analyzes were performed.

The data collection was initiated only after signing a confidentiality agreement by researchers delivered to the Teaching and Research of FSVC and after approval by the Research Ethics Committee of the Multidisciplinary Institute of Health (CEP/IMS-CAT) under the nº 442 012, on August 30, 2013 (CAAE: 20541813.3.0000.5556).

RESULTS

Among the 6,699 patients who were tested for syphilis in the laboratory of FSVC from July 2012 to July 2013, 134 were classified as positive, taking into account the Administrative Rule nº 3242, from 2011, resulting in a prevalence of syphilis of 2%. Of these, the majority, 25.39% (n = 34), were aged between 20 and 29 years. He drew attention to the presence of 19.4% (n = 26) of individuals aged less than one year, and its absolute majority represented by newborns (n = 25). Regarding the distribution by gender, 65.7% (n = 88) were female, and 50 of them were pregnant at the time of diagnosis, and 15.7% (n = 21), male. Most individuals studied 94% (n = 126) were from the urban area of Vitória da Conquista. **Table 1** describes the group of individuals involved in the study.

In relation to gestational syphilis and congenital syphilis, prevalence rates were, respectively, 2.24 and 2.84%.

Table 2 shows the distribution of positive cases of syphilis according to the title of VDRL and their occurrence by gender. Most individuals, 47% (n = 63) showed VDRL titers up to 1:2, and only 9.7% (n = 13) of patients had higher titers than 1:64. Among infants, it was observed that 60% (n = 15) had titers up to 1:2.

Among pregnant women involved in the study, there was a more heterogeneous distribution with respect to VDRL titers; however, the majority of 60% (n = 30) showed a title of 1:4.

It was found in this study that all the cases of positive VDRL were subjected to confirmation. **Table 3** distributes all individuals with regency in the VDRL that needed to be confirmed and further reveals cases in need of completion of the second confirmatory test – TPHA. It should be noted that most individuals with positive VDRL, 94% (n = 126) showed positive results in

Table 1 – Descriptive analysis of individuals with positive diagnosis of syphilis in the period from July 2012 to July 2013 (n = 134)

	n (%)
Age group	
≤1 year	26 (19.4)
15 – 19 years	10 (7.46)
20 – 29 years	34 (25.39)
30 – 39 years	30 (22.38)
40 – 49 years	13 (9.7)
≥ 50 years	21 (15.67)
Gender	
Male	21 (15.7)
Female	88 (65.7)
No specification[1]	25 (18.6)[a]
Place of residence	
Urban area	126 (94)
Rural area	5 (3.7)
Another city	3 (2.2)
Pregnant	
Yes	50 (37.3)
No	84 (62.7)

[A]unspecified sex newborn.

Table 2 – Sampling distribution of the individuals according titration of venereal disease research laboratory stratified by gender (n = 134)

Title of VDRL	Gender		
	Female	Male	Unspecified
	n (%)	n (%)	n (%)[a]
01:01	21 (23.9)	1 (4.75)	7 (28)
01:02	18 (20.4)	8 (38.0)	8 (32)
01:04	15 (17.1)	4 (19)	2 (8)
01:08	7 (8)	2 (9.5)	4 (16)
01:16	9 (10.2)	1 (4.75)	3 (12)
01:32	9 (10.2)	1 (4.75)	1 (4)
01:64	4 (4.5)	1 (4.75)	0 (0)
01:128	4 (4.5)	2 (9.5)	0 (0)
01:1024	1 (1.2)	0 (0)	0 (0)
01:2048	0 (0)	1 (4.75)	0 (0)
Total	88 (100)	21 (100)	25 (100)

[a]unspecified sex newborn; VDRL: venereal disease research laboratory.

Table 3 – Sampling distribution of individuals with reaction in the venereal disease research laboratory stratified by immunochromatographic and *Treponema pallidum hemagglutination* confirmatory tests (n = 134)

Title of VDRL	IC		TPHA		
	Positive	Negative	Dispensable	Reagent	No reagent
	n (%)	n (%)	n (%)	n (%)	n (%)
01:01	25 (18.6)	4 (3)[a]	27 (20.1)	0 (0)	2 (1.5)
01:02	34 (25.4)	0 (0)	34 (25.4)	0 (0)	0 (0)
01:04	19 (14.1)	2 (1.5)	19 (14.1)	0 (0)	2 (1.5)
01:08	12 (8.9)	1 (0.8)[b]	13 (9.7)	0 (0)	0 (0)
01:16	12 (8.9)	1 (0.8)	12 (8.9)	0 (0)	1 (0.8)
01:32	11 (8.2)	0 (0)	11 (8.2)	0 (0)	0 (0)
01:64	5 (3.7)	0 (0)	5 (3.7)	0 (0)	0 (0)
01:128	6 (4.5)	0 (0)	5 (3.7)	1 (0.8)[c]	0 (0)
01:1024	1 (0.8)	0 (0)	1 (0.8)	0 (0)	0 (0)
01:2048	1 (0.8)	0 (0)	1 (0.8)	0 (0)	0 (0)
Total	126 (94)	8 (6)	128 (95.5)	1 (0.8)	5 (3.7)

[a]two individuals that should be tested and were not; [b]one individual that should be tested and was not; [c]one individual that should not be tested; VDRL: venereal disease research laboratory; IC: immunochromatography; TPHA: *treponema pallidum hemagglutination*.

the first confirmatory test, and only 6% (n = 8) showed a discrepancy between the initial non-treponemal screening test and the first confirmatory treponemal test. All patients who underwent second confirmation had concordant results with the initial treponemal test. That there were five individuals submitted to a second confirmation, four with VDRL presenting title of up to 1:4 and one with 1:16 titration.

DISCUSSION

In this study, there was a prevalence of 2% for syphilis among patients tested by the laboratory of FSVC. Similar studies with representative samples are still not found in the country, to the point that systematic survey conducted in November 2013 using the bases of PubMed, SciELO and MEDLINE not found any similar study. Probably the fact that the notification of acquired syphilis cases only became mandatory from of Administrative Rule nº 104, from January 2011. However, comparing the prevalence of this study with studies in restricted population groups, it was found that it was smaller. In a study of women from 12 to 63 years in the state of Alagoas, Brazil, there was a prevalence of 2.6%[11], and others held with adults in a university hospital in Rio de Janeiro, Brazil, there was a prevalence of 2.7%[12].

For gestational syphilis the prevalence was 2.24% and is, therefore, higher than the values found in studies such as the Sentinel-blind study in 2006[13], who found 1.1% — a monitoring study of rates prevalence of syphilis in pregnant women in Brazil. It was also higher than the ones found in studies by Guimaraes and Roberts[14], Codes *et al.*[15], Figueiró-Filho *et al* [16] and Macedo Filho[17] — which respectively have prevalence rates of 1.7, 2.0, 0.8 and 1.31%. Regarding congenital syphilis, it was found prevalence of 2.84%, which also exceeded values found by Smith *et al*., in 2013, in Alagoas, and Lorenzi and Madi in 2001, in Niterói (RJ), with prevalence rates, respectively from 0.4 to 1.5%[18,19].

At first sight, it is important to note that the prevalence found in this study are concerning, taking into account the goals set by the WHO to combat and eradicate syphilis in the world and when compared to others prevalences already found in other studies. In further analysis these prevalence values may perhaps be justified in part by the fact that the laboratory of FSVC attends almost all of the municipal SUS demand, including a public hospital in maternal and child reference. The literature points out that low socioeconomic status brings numerous risk factors for infection with *T. pallidum*, resulting in high syphilis prevalence[20,21]. Another issue that may explain the higher prevalence is the fact Vitória da Conquista have a diagnostic network that performs screening satisfactorily, following the Ministry of Health recommendations for prenatal, pre-birth to newborns and general population[22]. In this sense, the more one realizes screening, the more likely to find positive cases, which surfaced a key action in combating the disease, since it allows the identification and treatment of cases, reducing its dissemination.

The literature has shown that one of the major problems for the purposes of diseases prevalence calculations lies in the underreporting[23]. The present study has as one of its strengths information assurance of all positives for syphilis because, since July 2012, the laboratory of FSVC has been performing the notification of all diagnosed cases of syphilis and its main goal is the generation of indicators able to develop policies that aim at the reduction of syphilis cases in the city.

In this study, it was important the fact that the vast majority of the population was living in the city of the municipality, consistent with study in Sobral (CE), Brazil, from 2006 to 2010[24]. Regarding the stratification of patients by age, there was a wide distribution between the groups, revealing an agreement with studies that showed higher prevalence in groups of 20 to 29 years old[24-26]. Another important fact is that over 50% of patients with positive results were pregnant women or newborns. In pregnant women the infection with *T. pallidum* is associated with an increased risk for the occurrence of abortions, malformations, premature birth, among other complications that tend to represent more costs for public health[27]. Within this logic is important to promote health policies that favor the diagnosis and treatment of syphilis to achieve the goal of eradicating congenital syphilis, as established by the WHO. Understanding that this goal will only be reached from a considerable expansion of population access to screening tests for syphilis, especially in the prenatal stage is imperative.

The laboratory screening for syphilis has low cost[28] and does not require sophisticated or widely-equipped laboratories. Depends primarily on the existence of a health network well-structured and imbued in reducing the prevalence of this disease. The laboratory of FSVC screened in a year 6,699 individuals for syphilis, including pregnant women, newborns and individuals in the general population. This number represents the screening of about 3% of the population assisted by the SUS in the city, which shows an enlargement of the service to population, contributing to the reduction of cases of syphilis and perhaps it is why the prevalence rates are higher when compared to the previous studies and the ones that did not meet the requirements of the Administrative Rule nº 3242, of 2011.

Still, it is essential to continue the surveillance of disease and seek to broaden the actions in the diagnosis and treatment in order to see fewer cases, which will help to reduce the prevalence to levels that can not pose a burden for the population (below 1%)[29].

When analyzing the results of confirmatory tests for syphilis in patients with positive VDRL it was observed that in a few cases there had differences between screening and confirmatory test, which could probably be justified in the first instance, by another disease, not syphilis, but which manages production of antiphospholipid antibodies as the VDRL test is not specific and can be present in the reagent of autoimmune diseases, viral, bacterial or parasitic infections[30]. In these cases, the TPHA test performed proved consistent with the initial treponemal, which determines the used tests have good sensitivity and specificity and may be part of the laboratory tests[31].

Although the literature says that only observing the VDRL it can be classified as congenital syphilis when the baby bonds are greater or equal to the mother[32], it is important to note

that most newborns treated at FSVC with positive VDRL have lower titles to the mother, which does not exclude the diagnosis of congenital syphilis. In addition, performing treponemic test in these individuals there was a confirmation of positivity, which can be justified by two situations: either in fact be congenital syphilis, or represent the presence of mother's passive antibodies that have experienced treatment for syphilis[33]; in these cases, appropriate classification should be performed using antitreponemics IgM tests.

It must be considered in the present study a limitation, which is the fact that it was not made as a survey with proportional population calculating interest groups, such as pregnant women, newborns and the general population, coupled to an interview with several socioeconomic, lifestyle, health condition variables, with which it would be possible to do further analysis. Moreover, the number of patients screened and observed within the one year sample period constitutes a significant population for evaluation of the distribution group (pregnant women, neonates, and the general population) since FSVC not only meets ambulatory but all health facilities assisted by the SUS and its prenatal programs, including high risk, and attend a hospital maternal and child reference where is held the largest number of deliveries by SUS in Vitória da Conquista region.

Another important issue is the fact that this is the first study to show the prevalence and control of syphilis in the county, and the chosen period coincides with the moment of greatest surveillance for reporting of cases of the disease in the city.

Finally, it should be noted that this work could serve as developer of future studies of population surveys that can make causal associations and estimate more accurately the prevalence of syphilis, in order to reinforce the importance of the implementation and maintenance of public policies for the reducing the prevalence to levels that no longer will represent a burden on the population[29].

CONCLUSION

Prevalence rates are high taking into account the parameters established by WHO and are able to represent burden for the population. However, they point out good capacity of the municipality for screening when facing the disease, which is an essential step for public health to combat this serious infection.

Conflict of interests

The authors declared no conflict of interests.

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A LOOK AT THE FACTORS OF VULNERABILITY OF ADOLESCENTS TO HIV/AIDS

UM OLHAR SOBRE OS FATORES DE VULNERABILIDADE DOS ADOLESCENTES AO HIV/AIDS

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ABSTRACT

Introduction: Adolescence is considered a phase of intensive biopsychosocial changes. With contemporaneity, you can see teenagers in the splendor of this phase experience sexuality actively, often hiding the practice from parents, guardians, and friends. This fact, coupled with the lack of policies directed to the care of adolescents, has favored the increasing number of cases of infection by HIV/AIDS in Brazil. **Objective**: To identify trends in the scientific literature about the vulnerability factors that predispose adolescents to contracting HIV/AIDS. **Methods**: This is a study of integrative review, conducted by consulting the Virtual Health Library (VHL), the databases are used: Scientific Electronic Library Online (SciELO); Latin American and Caribbean Literature on Health Sciences (LILACS). Articles were consulted covering the period 2009-2014, and they were prepared, analyzed and described in a specific table. **Results**: For the development of the present study, 11 items were selected, respecting the prioritization criteria. Vulnerability factors found in the texts were enrolled satisfactory for the purposes of the study, and therefore elementary to make this review. Among the most commonly found in the performed readings, insufficient or erroneous knowledge of adolescents about HIV infection/AIDS stands out. **Conclusion**: The method used was effective for accomplishment of our objectives. Results presented throughout the review show that knowing the increasing vulnerability of adolescents to HIV/AIDS allows that actions for this audience are guided by integrating family, school, health facilities, and other environments in which adolescents are inserted so that risks are identified and reduced by determining appropriate strategies.

Keywords: Acquired immunodeficiency syndrome, vulnerability, adolescents.

RESUMO

Introdução: A adolescência é considerada uma fase de intensas transformações biopsicossociais. Com a contemporaneidade, é possível visualizar adolescentes que no esplendor dessa fase vivenciam a sexualidade de forma ativa, muitas vezes ocultando a prática de pais, responsáveis e amigos. Tal fato, associado à escassez de políticas direcionadas para o cuidado dos adolescentes, tem propiciado o aumento do número de casos de infecção destes por HIV/AIDS no Brasil. **Objetivo:** Identificar as tendências da produção científica a respeito dos fatores de vulnerabilidade que predispõem os adolescentes a contraírem HIV/AIDS. **Métodos:** Trata-se de um estudo de revisão integrativa, realizado por meio de consulta à Biblioteca Virtual em Saúde (BVS), sendo utilizadas as bases de dados: *Scientific Electronic Library Online* (SciELO); Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS). Foram consultados artigos contemplando o período de 2009 a 2014, os quais foram dispostos, analisados e descritos em uma tabela específica. **Resultados:** Para a construção do presente estudo, foram selecionados 11 artigos, respeitando-se os critérios de priorização. Os fatores de vulnerabilidade encontrados nos textos arrolados foram considerados satisfatórios para os objetivos do estudo e, portanto, elementares para a construção desta revisão. Entre os mais encontrados nas leituras realizadas, destaca-se o conhecimento insuficiente ou errôneo dos adolescentes sobre a infecção por HIV/AIDS. **Conclusão:** O método utilizado mostrou-se eficaz para efetivação dos nossos objetivos. Os resultados apresentados ao longo da revisão mostram que conhecer a vulnerabilização dos adolescentes ao HIV/AIDS permite que sejam norteadas ações voltadas para esse público, integrando a família, a escola, as unidades de saúde e os demais ambientes nos quais o adolescente esteja inserido para que os riscos sejam identificados e diminuídos por meio da determinação de estratégias apropriadas.

Palavras-chave: Síndrome de imunodeficiência adquirida, vulnerabilidade, adolescente.

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INTRODUCTION

Adolescence is the phase of a human being's life when many transformations happen in his/her organism and social environment. According to the Child and Adolescent Statute, adolescent is the subject aged 12 to 18 years; however, the World Health Organization states that adolescence is understood from 10 to 19 years old[(1)].

In this phase, the subject starts to have the ability of generating children, defines his/her ethical and moral values, and molds his/her social and sexual behaviors based on standards defined by society through relations of gender, race, and ethnicity[(2)].

For being in a learning process, the adolescent is able more easily to acquire new habits and behaviors, when compared to adults. Thus, health education actions should be performed so that they can acquire a healthy lifestyle[(3)].

Lack of health education actions aimed at adolescents reflects directly on the increase of their vulnerability before situations like unplanned pregnancy, transmission of sexually transmitted diseases (STDs), use of illicit drugs, violence, among others. In this perspective, one may find the human immunodeficiency virus (HIV) infection: researches point out that even though adolescents know a lot about the Acquired Immune Deficiency Syndrome (AIDS), they have questionings regarding the forms of prevention, which therefore increases the cases of infected adolescents[1].

Recent data from the Brazilian Ministry of Health show that, in the period from 1980 to 2012, there was a total of 2,478 cases of HIV/AIDS infection in subjects aged 10 and 14 years, and 12,246 cases in people aged 15 and 19 years[4].

In 2012, out of the 4,118 cases of AIDS in young people aged 15 to 24 years reported in Sinan, declared in SIM and registered in Siscel/Sisclon, 39.8% were from the Southeast region; 20.3% from the Northeast region; 19.0% from the South region; 12.4% from the North region; and 8.5% from the Central-West region[5].

In addition, according to the Brazilian Ministry of Health, at Sinan, in the year of 2012, 16,464 cases of AIDS were reported for males aged 13 years or older, of whom 18.3% did not have information of the exposure category. Whereas, with regard to the female gender, out of 8,622 cases of AIDS reported at Sinan, in 2012, 91.2% provided the information of the exposure category[5].

Epidemics advance in Brazil shows that there is a very wide need of implementing actions for health promotion, maintenance, and prevention in this population through means of the improvement of access to health services, as well as interaction between the professional and the adolescent[6].

Considering the importance of this theme, sexual and reproductive health of adolescents needs to be further discussed and treated as a priority by health professionals. The principles of confidentiality and privacy must be respected since they are essential for an individualized service, and health education activities concerning contraceptive methods should be feasible. In addition, there is also the need of sexually transmitted infections (STI) prevention.

OBJECTIVE

To identify, based on an integrative review of the national literature, the vulnerability factors that make adolescents more subject to HIV/AIDS infection.

METHODS

This is an integrative review, a methodology that is based on researches of the health area clinical practice through the search of evidence delimited by a theme or question. Its main objective is to expand researcher's knowledge on the investigated theme, reunited and synthesized. This method presents six stages, namely: theme identification and creation of the question that will lead the study; data research and collection (databases choice, year of publication, inclusion and exclusion criteria); evaluation (definition of information to be extracted through the keywords); analysis (aims at elucidating different or conflicting results of the studies included in the research); interpretation of results (critical discussion and evaluation of results); and presentation of results (description of covered stages and exposure of the main research results)[7].

Due to the increase of cases of adolescents infected with HIV/AIDS, the following questioning came into our minds: What are the vulnerability factors that make this group more vulnerable to HIV/AIDS infection?

Reference collection was performed through the Internet, consulting the Virtual Health Library (VHL), and the following databases: the Scientific Electronic Library Online (SciELO) and Latin American and Caribbean Literature on Health Sciences (LILACS). The study was carried out from March 2013 to January 2014. The research was done using the following keywords found in the Health Sciences Keywords (DeCS): acquired immune deficiency syndrome, vulnerability, and adolescent. Furthermore, as inclusion criteria we used: full texts available on-line and articles published in Portuguese from 2009 to 2014, aiming at contextualizing the study.

References were identified and chosen through three stages. Firstly, the keyword "acquired immune deficiency syndrome" was combined with "adolescent" and 952 titles were found. Then, we compared "acquired immune deficiency syndrome" and "vulnerability", and we found 302 titles, in these ones, some of them were already seen in the previous combination. Finally, we used the combination "acquired immune deficiency syndrome", "adolescent", and "vulnerability", where 76 titles were found, in which some of them had already been encountered in previous researches, therefore there were 1,330 texts.

Great part of these productions were excluded after reading their abstracts, since they did not associate with the thematic of this study, thus only 33 articles remained.

After analytical reading of these 33 texts, only 11 articles were chosen since the others did not fit the inclusion criteria that were established nor were they associated with the leading question of this study.

For information analysis and description, the articles were separated in a table (**Table 1**). The variables identified after reading the full texts were: author(s), journal, year of publication, methodology, objectives, and factors that make adolescents vulnerable to HIV/AIDS infection (these are emphatically approached in the topic "Results and Discussion").

RESULTS AND DISCUSSION

When researchers started focusing on the critical analysis of the selected productions, they proved that all of them were published in different journals from the health area; therefore, they are in a simple and determined numeric proportion of 1:1.

After investigating the quantity of published productions per year in the sample, it was seen that in 2011 more articles were found for the study, which may have some association with the Carnival campaign of the Brazilian Ministry of Health. This was released on February 25, 2011, and its slogan was: "Without condom, it will not be possible". This campaign had as its focus adolescents aged 15 to 24 years, and it was carried out in two stages: at the first, adolescents were emotionally moved as to the importance of condom and encouraged to enjoy the festivity using the preservative; at the

Table 1 – Variables included in the study sample

Author(s)	Journal	Year of publication	Methodology	Objectives	Factors that make adolescents become vulnerable to HIV/AIDS infection
Brêtas *et al*.	*Revista da Escola de Enfermagem da USP*	2009	Quantitative and descriptive study	To verify adolescents' knowledge about prevention, transmission, signals and symptoms of STD/AIDS, and collaborate in the elaboration of educational actions of the university extension project "Corporality and Health Promotion"	Limited knowledge about STI/AIDS between adolescents, especially among the male gender (which happens maybe due to the development of each gender)
Nader *et al*.	*Revista da Associação Médica do Rio Grande do Sul*	2009	Cross-sectional and descriptive study, quantitative approach of the investigational type	To investigate the knowledge of a population of adolescents that is inserted in a public school with regard to AIDS, comparing the differences and similarities between genders	Presence of erroneous concepts concerning the STI/AIDS transmission, specially by male gender adolescents
Nunes and Andrade	*Psicologia & Sociedade*	2009	Qualitative research	To better know the reality of adolescents living on the streets involved through business sexual exploration, aiming at improvement of knowledge of this reality and decrease of vulnerability to STD/AIDS	Absence of preservative use and of the adolescent's request of it, be it by the partner's imposition or by the affective need that the girl has
Camargo *et al*.	*Estudos de Psicologia*	2010	Quantitative and comparative study	To investigate the international aspects of AIDS epidemic with afro-descendants and non-afro-descendants adolescents, considering their perception of risk, attitudes, and knowledge on the disease	Low socioeconomic situation predominant in afro-descendent adolescents
Carleto *et al*.	*Jornal Brasileiro de Doenças Sexualmente Transmissíveis*	2010	Descriptive cross-sectional study, with quantitative analysis	To analyze the knowledge, perception, and occurrence with regard to STD/AIDS among adolescents	Limited use of preservative; low knowledge about the forms of STI/AIDS transmission; belief in immunity
Dias *et al*.	*Revista Enfermagem UERJ*	2010	Qualitative research	To report the effects of health education actions at school	Significant knowledge about the importance of preservative, however there is low adhesion from adolescents
Coelho *et al*.	*Revista de Patologia Tropical*	2011	Descriptive, epidemiological, and cross-sectional study	To investigate knowledge and beliefs about STD/HIV/AIDS among adolescents and young subjects aged 15 to 24 years of the male and female genders, from the State Public Network of Teaching in Goiânia, and to identify possible gender differences	Adolescents' unsatisfactory knowledge about questions regarding STI/AIDS infection, as well as presence of erroneous beliefs that put them at risk situations
Costa *et al*.	*Revista Baiana de Saúde Pública*	2011	Descriptive study	To study exposure and risk factors for HIV/AIDS and syphilis among young pregnant women and young adults registered in the STD/HIV/AIDS program in Feira de Santana, Bahia	Trust at partner or his/her refusal in using condom, so that the adolescent decides not to use the preservative; condom unviability; unplanned sexual intercourse
Sampaio *et al*.	*Saúde e Sociedade*	2011	Qualitative study	To analyze the exposure of adolescents to STD/AIDS in the Northeastern semi-arid region	Low educational level; unequal gender relations; absence of prevention policy directed towards adolescents; absence of bound between health professionals and population; visualization of health services as single spaces of health education
Taquete *et al*.	*Revista da Sociedade Brasileira de Medicina Tropical*	2011	Ecological study	To analyze the AIDS epidemics in adolescents from the municipality of Rio de Janeiro	Feminization of HIV/AIDS infection due to inequality of gender and physiological characteristics; hiding from the homosexual adolescents of the first sexual intercourses; lack of access to health services
Toledo *et al*.	*Revista Brasileira de Enfermagem*	2011	Integrative review	To identify scientific evidence from literature about the elements of individual dimension of vulnerability of adolescents to HIV/AIDS	Incorrect or insufficient knowledge about HIV/AIDS infection and risk sexual behaviors

second, those who did not have intercourse with protection were stimulated to go through HIV testing[8].

This emphasis on the bigger number of publications in 2011 can also be associated with the II Meeting of the Formation Program of Young Leaders living with HIV/AIDS, performed by the United Nations Children's Fund (UNICEF) from April 15 to 18, in 2011. Around 20 adolescents from all Brazilian regions participated of this event, which had as its objective the exchange of experiences about the disease and discussion regarding prevention, assistance, and rights of teenagers and young subjects with HIV/AIDS[9].

After observing the methodologies of the chosen publications, it was seen the predominance of descriptive articles represented by 5 articles (45.4%). Furthermore, 4 articles (36.3%) are classified with the quantitative approach.

With regard to the objectives proposed by the investigations identified in scientific journals, it was seen that in 7 of them (63.6%), the authors directed their study towards adolescents' knowledge on HIV/AIDS (what is AIDS, preventive measures, transmissibility, vulnerability, sexual behaviors, among others).

Therefore, the most recurring vulnerability factor to HIV/AIDS infection in the readings performed referred to the insufficient or erroneous knowledge of teenagers about this disease. This is an information that could justify the concern of professionals about the knowledge acquired by adolescents about the epidemics, which directly reflects on the increase of amount of individuals that, by chance, may be exposed and/or infected.

Due to the social existent representations, many adolescents believe that they cannot be infected by HIV/AIDS, naming the infection as "other people's disease", "adult's disease", "of older people" or of specific groups, as prostitutes, homosexual, and drug users[10]. However, this belief in immunity[11] is dangerous, because the infected adolescent may have some difficulties regarding acceptance and fighting the disease.

Researchers also observed that there is a tendency of epidemics feminization due to gender inequality, lack of information and physiological characteristics, according the following discussion.

Many adolescents do not negotiate the preservative use by several reasons, such as: partner does not like; fear of losing the partner, which makes her passive and dependent of sexist convictions; and fear of not being valued or stigmatized because she suggested the use or for having a condom, even when the sexual intercourse was not planned[12,13].

Some adolescents only make use of the birth control pill, so we can assume that they may not know that this method only prevents an unplanned pregnancy or maybe that pregnancy prevention overcomes STDs[14].

Other important factor in the gender issues concerns violence, evidenced and strengthened by sexual abuse report; lower control about the sexual intercourses and use of preservatives; relationships with older partners; and lower acquisitive power[15].

It is also seen inhibition or even adolescents' unawareness on questions concerning sexuality, which is motivated by society and family's super-masculinity, who many times demands prudence and conservatism — a fact that was not seen in male gender adolescents, who, in general, are treated more liberally[12].

With regard to physiological aspects, we can see that adolescents present higher risk of contracting the infection due to more exposure of his/her uterine epithelium[15].

As to the general knowledge about HIV/AIDS, this theme seems controversial: some studies report their knowledge as unsatisfactory; others, however, declared that adolescents present a good knowledge concerning the causes, symptoms, and treatment. Nevertheless, it is important to highlight that the fact of adolescents mentioning infection as a sexually transmitted infection does not ensure that he/she knows or wants to protect him/herself from the contagion[16].

Studies developed by Brêtas *et al*. and Nader *et al*. point that girls have more knowledge concerning STI/AIDS than boys (a fact that maybe happens by the development of each gender). However, one must know that adolescents represent a group with higher risk to exposure and/or infection, since they sometimes feel unable of requesting the use of preservatives during a sexual intercourse[17,18].

Some behaviors mean absence of relevant information regarding the subject and corroborate such information, namely: unawareness of HIV/AIDS transmission by doing anal/oral sex and during menstruation or pregnancy/post-partum; practice of interrupted sexual intercourse; and antibiotic and vitamin intake and, even, washing of the genital areas after sexual practice as a preventive measure[10,17].

We noticed that most adolescents report using condom as HIV/AIDS prevention, however its use is renounced when the partner is well-known, when there is only one partner, and/or when the person trusts his/her partner[11,16]. In addition, it was seen the report of male adolescents stating that they do not use the preservative because this method messes pleasure during the sexual act due to sensitivity decrease (which is a myth infused in society from trivial beliefs, capable of resulting in several risks)[14].

Sexual abstinence as prevention, although it is known, is not considered an usual practice and therefore is not seen as a preventive measure[18].

Other vulnerability factor found in the readings concerns "hooking up". This behavior is common among adolescents and is the representation of affection, caress and many times sporadic sex, which favors the increase of STI cases[19].

However, when religion is present in the lives of adolescents, "hooking up" and sexual existences are less frequent, which makes us believe that the religious practice interferes in their lives[19].

It is important to emphasize the homoaffective relationships among adolescents. Hiding the first sexual experiences from family and/or friends, internal conflicts (causes of psychic suffering), social isolation, and low self-esteem (that makes them susceptible to inequality relations of power, in which there is also difficulty in negotiating the use of preservative) are risk factors pointed as constituents for HIV/AIDS infection[15].

With regard to information sources about STI/AIDS, adolescents look for knowledge in means like school, media (Internet, television, radio, magazines, newspapers), health services, teachers, parents, and friends. The media, although a great information provider, is not considered efficient in the transmission of information about HIV/AIDS to adolescents, because it may cause confusions in their mentality and even value distortion[17,18].

On the other hand, family, besides an important connection link, many times cannot have bounds with teenagers to talk about living a healthy sexuality, therefore they are not part of a sexual education context of these subjects[17,18].

As to health services, adolescents who go to such facilities are few, and usually they are girls. This scenario happens due to several factors, among them: absence of actions directed to adolescents; absence of adhesion to the Adolescent Health Attention Policy, preconized by the Brazilian Ministry of Health; and inexistence of bound between professionals from the health services with teenagers. This is the reason why adolescents do not consider the place efficient to care, reception, and health promotion[12].

Hence, workshops and lectures regarding adolescents' sexuality, not only on health services, where the adolescent will hardly be present, but also in schools and in other living spaces, has been an effective and efficient prevention strategy for it stimulates change of habits and behaviors to avoid HIV/AIDS, as well as other sexually transmitted infections[16,20].

The recent increase of alcohol and drug abuse by teenagers is also a point to be emphasized; this behavior consists on a direct factor of risk to infection by the virus since it does not permit that the adolescent takes sensate and preventive attitudes towards the possibility of contracting the virus[19].

Education was also pointed as a vulnerability risk, since the low educational level difficults adolescents' access to relevant information about STI/HIV/AIDS, making them susceptible. However, it is suggested that the real factor of lack of concern as to the STI prevention is the adolescent's behavior[13].

Finally, it is important to emphasize the vulnerability to which the afro-descendant adolescents are exposed. In Brazil, social and race inequalities have been happening for several years. In addition, it is seen that, summed to the abovementioned vulnerabilities, there are the economical, social, and cultural difficulties from the lowest classes (composed predominantly by black subjects). Thus, it is necessary to create normative and humanitarian policies for the lowest classes, as well as to deepen their knowledge about poverty, ethnicity, equity, discrimination and the connection to risks that adolescents have of becoming infected with the virus[19].

CONCLUSION

In order to meet the strong desire of investigating the vulnerability factors of adolescents before HIV/AIDS, this study enabled fruitful moments with rise of ideas, because through it, we could identify evidence in the national scientific literature of the risks the adolescents are exposed to, as well as to reflect proposals that may decrease the infection.

The used methodology provided the investigation of these factors and the theoretical study about questions concerning the theme, therefore it seems efficient for the objective achievement.

Since remote times, adolescents have been passible of contracting STI. Each period of the Brazilian history brings sexual experiences of adolescents in several ways, depending on their social contexts.

During the Brazilian-colony period until Republic, patriarchalism was the main model of power in the family organization, and sexuality was directed only towards reproduction, with social rules that accepted sexual practice in the marriage and upon men's control. Only from the 1950s, after the appearance of beat and hippie movements, adolescents started to retort the social model under study, which converged in disentail of formerly sexual paradigms and, with this, the right of pleasure, diversification in the way of speaking and acting, use of birth control pills by women and production of pornography[21].

Contemporaneity, still with reflexes of such revolution, brought to the eyes of society the visualization of subjects that, in the splendor of adolescence, lived sexuality in an active manner and many times inconsequent, hiding such fact from parents, guardians, and friends.

This reality, associated with scarcity of policies directed to adolescents' care, has provided an increase in the number of their cases of infection by HIV/AIDS in Brazil.

Thus, knowing adolescents' susceptibility to this infection allows that actions aimed at this audience be developed, integrating family to school, health services, and other environments in which the adolescent is inserted so that risks be identified and decreased through the determination of adequate strategies.

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Relationship between vaginal douching and bacterial vaginosis, sexually transmitted diseases and HIV infection: a systematic review

Relação entre ducha vaginal e vaginose bacteriana, doenças sexualmente transmissíveis e infecção por HIV: uma revisão sistemática

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ABSTRACT

Introduction: Despite of vaginal douching has been strongly condemned by most of health care professionals; this practice remains a very common habit among women for several reasons. **Objective**: To assess if there is any association between vaginal douching and bacterial vaginoses, STD and HIV **Methods:** We conducted a systematic review and metanalysis to evaluate the relationship between vaginal douching and bacterial vaginosis, sexually transmitted diseases and HIV infection. The following databases were searched using Mesh terms: PubMed, Embase, Scielo and Google Scholar. Selection criteria: (1) prospective cohort studies of women using vaginal douching; (2) women 12 years or older and (3) studies published from 2000 to October 2011. Studies involving pregnant women were excluded. Methodological quality was assessed using Newcastle-Ottawa scale. Data collection and analysis: Review Manager 5.1 was used for statistical analysis. **Results**: Seven studies (2 STD, 3 Bacterial Vaginosis and 2 HIV) were included based on the chosen criteria: 9.796 women were enrolled. The global Risk Ratios for Bacterial Vaginosis, STD and HIV acquisition were, 1.24 (95%CI 1.12–1.43), 1.12 (95%CI 0.94–1.32), and 1.36 (95%CI 0.92–2.01) respectively. **Conclusion:** There are few studies checking the association between vaginal douching and STD, BV and HIV infection. A weak positive correlation was found between vaginal douching and bacterial vaginosis, but not to STD and HIV infection.
Keywords: vaginal douching, women, STD, bacterial vaginosis, HIV infection.

RESUMO

Introdução: Apesar de ducha vaginal estar fortemente condenada pela maioria dos profissionais de saúde; esta prática continua a ser um hábito muito comum entre as mulheres, por diversas razões. **Objetivo**: Avaliar se há relação entre a prática de duchas vaginais e vaginose bacteriana, DST e HIV. **Métodos**: Foi realizada uma revisão sistemática e meta-análise para avaliar a relação entre a ducha vaginal e vaginose bacteriana, doenças sexualmente transmissíveis e infecção pelo HIV. Os seguintes bancos de dados foram pesquisados utilizando descritores: PubMed, Embase, Scielo e Google Scholar. Os critérios de seleção: (1) estudos prospectivos de mulheres que usam ducha vaginal; (2) mulheres com 12 anos ou mais e (3) estudos publicados de 2000 a outubro de 2011. Estudos envolvendo mulheres grávidas foram excluídos. A qualidade metodológica foi avaliada usando a escala de Newcastle-Ottawa. Coleta de dados e análise: Review Manager 5.1 foi utilizado para análise estatística. **Resultados**: Sete estudos (2 STD, 3 vaginose bacteriana e 2 HIV) foram incluídos com base nos critérios escolhidos: 9,796 mulheres foram incluídos. A razão de risco global para a vaginose bacteriana, DST e aquisição do HIV foram, (IC95% 1,12-1,43) 1,24 (IC95% 0,94-1,32) 1,12 e (IC95% 0,92-2,01) 1,36, respectivamente. **Conclusão**: Há poucos estudos para verificar a associação entre a ducha vaginal e STD, VB e infecção pelo HIV. Foi encontrada uma correlação positiva entre a ducha vaginal e vaginose bacteriana, mas não para DST e infecção pelo HIV.
Palavras-chave: ducha vaginal, mulheres, DST, vaginose bacteriana, infecção pelo HIV.

INTRODUCTION

Vaginal micro flora (VMF) is the most efficient natural barrier against genital infections. The literature has recently accepted the fact that several factors can influence VMF, allowing science to see the delicate balance of this ecosystem as a result of several variables in a woman's life. These factors include age, pregnancy, menstrual cycle phase, sexual activity, vaginal practices and even diet[1-5]. One of the most important factor which leads to abnormal VMF is vaginal douching[6].

It is known that abnormal VMF raises the risk of acquisition of HIV and other sexually transmitted diseases (STD)[6-14] such as *Chlamydia trachomatis*[10,11] and *Herpes simplex*[12]. Additionally, it is also found to favor pelvic inflammatory disease[13], ectopic pregnancy[14], preterm delivery, Bacterial Vaginosis (BV)[6,7,9] and to increase infertility rates[13-15].

Vaginal douching (VD) is wide spread around the world, and is more common than it is to be expected[15]. VD is defined as the practice of cleaning not only the vulvar introitus, but the entire the vaginal cavity, with a liquid solution for perceived hygienic, therapeutic and/or religious purposes[1,16-18]. VD can also be defined as wiping the internal genitalia with fingers and other substances (cotton, cloth, paper) such to remove fluids. This includes douching, which is the pressurized shooting or pumping of water or any other solution (including douching gel) into the vaginal cavity[19].

The medical community frowns on VD, considered a homemade, self-prescribed household remedy. The majority of women disregards these admonitions, and continues douching regardless. The different reasons listed in recent studies include cleanliness after menses and before or after sexual intercourse, alleviating vaginal symptoms, as well as avoiding pregnancy, genital infections and HIV[17,19,20].

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The douching frequency is affected by such factors as culture and education[17]. Simpson *et al*.[21] observed that douching practices are common in women of low educational and socioeconomic level as well as in young women at risk of STD, including sex workers[1].

Wang *et al*.[10], when studying Chinese sex workers, found that approximately 70% of them made regular use of VD, and came to the conclusion that no association existed between douching and the presence of genital infections. Similar results were observed by Amaral *et al*., where the practice of VD was detected in 60% of sex workers. No significant differences in VMF were found between VD users and non-users[1].

Numerous studies involving douching and genital infections point to the dilemma of establishing a cause and effect relationship. The difficulty lies in knowing whether pre-existing STD induced VD or if VD caused STD. Researchers also question whether VD is only a marker of sexual activity.

OBJECTIVE

The purpose of this study is to evaluate the relationship between VD and BV, STDs and HIV infection.

METHODS

This study used the MOOSE guidelines[22].

Inclusion Criteria

The criteria for studies inclusion were:

- prospective cohort studies of women using VD;
- women aged 12 years old or older; and
- studies published after January 2000 up to October 2011.

Studies in which women were asked to stop using intravaginal practices and those involving vaginal microbicides, placebo products, tampons or other devices to deliver medication, and the ones involving pregnant women, were excluded.

Search and selection of literature

Eligible studies were identified by searching the following databases: PubMed, Embase, Scielo and Google scholar. The studies were identified by a wide literature search of databases following medical subject heading terms and/or text words: “vagina”, “intravaginal”, “vaginal douching”, “cleansing”, “washing”, “intravaginal practices”, “insertion”, “genital lesions”, “HIV”, “STD”, “bacterial vaginosis”, “trichomoniasis”, “candidiasis”, “uterine cervicitis”, “uterine cervicitides”, “cervicitides”, “cervicitis”, “cervicit”, “endocervicit”, “vaginal discharge”, “pelvic inflammatory disease”, “cervicovaginal infections” and “cohort studies”. Reference lists of the identified publications for additional pertinent studies were reviewed. No language restrictions were imposed.

Three researchers searched for articles published up to October 2011. After searching the databases, 248 potentially relevant papers were identified, 185 of which were excluded after the review of both title and abstract. Reviews were done and disagreements were resolved by consensual discussion. Thus, 63 papers met the criteria and were reviewed in full. There were no articles in languages other than English which, based on the abstract analysis, met the criteria. The approved studies had their references researched for potential studies to be added in this meta-analysis. After a full review, 11 papers were included, but four coincident articles were found (they were in more than one database at the same time), remaining, finally, seven studies (**Figure 1**).

Data Extraction

Various study characteristics were extracted from the original reports and included in the meta-analysis. The extracted data included publication data (first authors’ last names, year of publication and country of studied population), number of new cases of specific outcome and follow-up period (**Table 1**). The methodological quality of the studies was assessed independently by three blind reviewers and the studies were given quality points for certain features (such as, type of studies and incidence evaluation), using the Newcastle-Ottawa scale. Disagreements were solved by mutual consensus.

Analysis

Data were entered in the Review Manager (RevMan) 5.1[23]. RevMan allows the user to enter protocols as well as complete reviews, including text, characteristics of studies, comparison table, and study data, and to perform analysis of the data entered. The total Risk Ratio was analyzed overall, using fixed and random effects models and was tested for heterogeneity of effects using the χ^2 test.

RESULTS

Outcomes

We defined STD, BV and HIV infection as the outcomes. Seven reports, involving 12,511 women, were included. The design features of cohort studies of vaginal issues incidence in women who use VD which were approved to the meta-analysis are shown in **Table 1**.

Sexually Transmitted Diseases

Only one study[24] made the relation between VD and Pelvic Inflammatory Disease (PID), *gonococcus* and chlamydial genital infections. It was a multicenter, prospective observational cohort study that happened in the US between 1999 and 2004. Of 2,740 women enrolled at the beginning, 1,541 of them did not meet the inclusion criteria or did not complete the baseline questionnaire. The 1,199 women left were the focus of the analyses; they were followed-up for up to four years.

The data were classified according to the frequency of VD as none (n = 733), once per month (n = 272) and twice or more times per month (n = 194). The four-year incident rate of PID was 10.9% and of gonococcus and/or chlamydial cervicitis was 21.9%. After adjustment for confounding factors, douching two or more times per month at baseline was not associated with PID (HR = 0.76; 95%CI

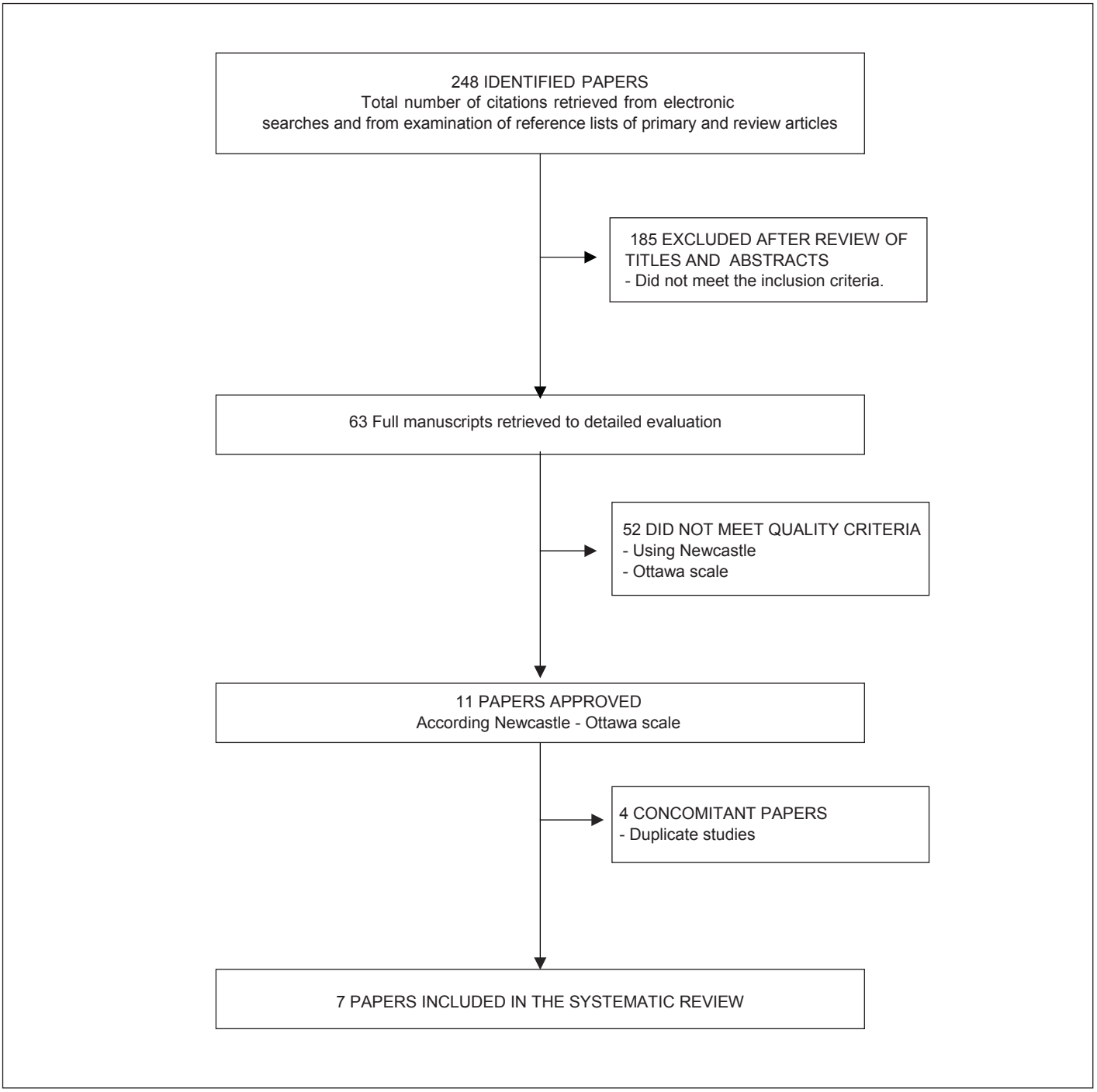

Figure 1 – Study selection process for systematic review.

0.42 – 1.38) or *gonococcus*/chlamydial genital infection (HR = 1.16; 95%CI 0.76 – 1.78)

Tsai *et al*.[25] made the association between douching and four sexually transmitted infections (*Trichomonas vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhea*, and/or HSV-2). The study included 411 high-risk HIV infected and uninfected adolescent females aged 12 to 19 years old. They were enrolled in an observational prospective cohort that occurred in 13 US cities from 1996 to 1999. Out of the 411 adolescents who initiated the study, 43 of them were excluded, remaining 368 subjects who completed the cohort (64.8% were HIV infected). These women were divided into three groups, never douche (n = 88), intermittent douche (n = 230), and always douche (n = 50).

The results demonstrated that, compared to females who never douched, the time to STD was shorter for those who always douched (HR = 2.1; 95%CI 1.2 – 3.4) and for those who intermittently douched

Table 1 – Cohort studies design features of vaginal issues in women using vaginal douching included in the meta-analysis.

Study, year (reference)	Country	Period of follow-up	Number of users/Non users	Outcome and results
Ness, 2005[24]	US	4 years	467/732	STD (PID): Douching once per month aHR = 0.96 (95%CI 0.57 – 1.59) Douching two or more per month aHR = 0.76 (95%CI 0.42 – 1.38) Gonococcal/Chlamydial genital infections Douching once per month aHR = 1.03 (95%CI 0.70 – 1.51). Douching two or more per month aHR = 0.16 (95%CI 0.76 – 1.78)
Tsai, 2009[25]	US	3 years	88/280	STD: Users aHR: 1.8 (95%CI 1.1 – 3.1), Intermittent Users aHR: 1.4 (95%CI 0.9 – 2.0)
Brotman, 2008[28]	US	1 year	1,180/1,555	BV: RR = 1.21 (95%CI 1.08 – 1.38)
McClelland, 2008[29]	Kenya	378 days	130/21	BV -Douching 1 – 14 times per week: aHR = 1.29 (95%CI 0.88 – 1.89) Douching 15 – 28 times per week: aHR = 1.60 (95%CI 0.98 – 2.61) Douching >28 times per week: aHR = 2.39 (95% CI 35 – 4.23)
Rugpao, 2008[30]	Thailand	2 years	182/1,340	BV: HR = 1.30 (95%CI 0.8 – 2.01)
McClelland, 2006[31]	Kenya	468 days	1,199/71	HIV: Women who used water for douching: aHR = 2.64 (95%CI 1.00 – 6.97) Women who used soap for douching: aHR = 3.84 (95%CI 1.51 – 9.77)
Myer, 2006[32]	South Africa	4 years	928/2,642	HIV: aHR = 1.04 (95%CI 0.65 – 1.68)

STD: sexually transmitted disease; PID: pelvic inflammatory disease

(HR = 1.5; 95%CI 1.0 – 2.2). After adjusting for HIV status, race baseline sexual history, and age, the hazard of STI was 1.8 times larger for participants who always douched rather than for participants who never douched (95%CI 1.1 – 3.1), whereas the hazard of STI was 1.4 times larger for participants who intermittently douched than for participants who never douched (95%CI 0.9 – 2.0). Wong *et al.*[26], despite being a prospective study enrolling 503 sex works in Hong Kong, provided only prevalence rates, being excluded from the meta-analysis.

Bacterial Vaginosis

Assessing 1193 women which had vaginal swabs obtained for Gram stain for BV, culture for vaginal microflora, and DNA amplification for Neisseria gonorrhoeae and Chlamydia trachomatis at baseline and 6, 12, 24, and 36 months, Hutchinson *et al.*[27] observed that douching appeared to be associated with BV among women with already imbalanced flora but not among women with normal flora.

Three studies were approved to meet the BV outcome. Brotman *et al.*[28] followed 3,619 women aged 15 to 44 years old. They were recruited between August 1999 and February 2002 when visiting one of 12 clinics in Birmingham, Alabama, US. The presence of BV was evaluated according to Nugent and Gram stain criteria. Participants had a mean age of 23.6 years. The adjusted Relative Risk in those women who had douched was 1.13 (95%CI 1.05 – 1.22) (Table 1).

McClelland *et al.*[29] followed 151 Kenyan female sex workers, mean age 32 years old, with monthly visits, for approximately 378 days. The criteria for Gram stain were present in 56 (37%) of women at baseline. The practice of VD was stratified in the following ranges: 1 to 14 times a week, 15 to 28 times a week and above 28 times a week; finding, respectively, the following HR: 1.29 (95%CI 0.96 – 1.72), 1.47 (95%CI 1.08 – 1.99) and 1.94 (95%CI 1.36 – 2.76) (**Table 1**).

Rugpao *et al.*[30] selected 1,576 Thai women aging 18-35 years between November 1999 and September 2002. Fifty four women were BV positive at baseline and were excluded from analysis, remaining 1,522 of them. Cleaning inside the vagina was not correlated with BV (HR = 1.30, 95%CI 0.83 – 2.01) (**Table 1**).

HIV

In the context of the HIV outcome, two studies were approved. The first of them, McClelland *et al.*[31], analyzed the variations in susceptibility resulting from the practice of VD, following 1,270 Kenyan women for an average of 468 days, with a mean interval between the visits of 35 days. The HIV-1 seroconversion occurred in 222 women. Compared with women who did not undergo vaginal

douche, those who used water had triple the risk of HIV-1 seroconversion (aHR = 2.64, 95%CI 1.00 – 6.97), while those who used soap had a risk about four times higher (aHR = 3.84, 95%CI 1.51 – 9.77). Analyzing the Relative Risk separating those women who had douched from those who did not, we obtained a 2.57 (95%CI 1.09 – 6.03) relation (**Table 1**).

Myer *et al*.[32] noted that 85 of the 3,570 South African participants of their study, all practitioners of intravaginal procedures, tested positive for HIV infection, resulting in an adjusted Odds Ratio of 1.04 (95%CI 0.65 – 1.68) showing that, during the follow-up, there was no association between intravaginal practices and incident HIV.

DISCUSSION

As stated earlier, it is unclear whether VD is a direct cause or a cofactor in the progression of vaginal and/or systemic infections. It may also simply be a risk marker; none of the studies published so far have managed to clarify these possibilities. Given this fact, more recent studies have put this dilemma into question[21,33,34].

It is important to highlight that there are few studies fulfilling methodological queries to check the association between vaginal douching and vulvovaginal and systemic infections. No consensus could be reached regarding the cause-effect relationship between VD and BV acquisition, despite there being a weak positive correlation. Within the three selected studies, a significant positive correlation was observed in only two of them[28,29], specifically in women who douched more than 15 times or up to 14 times a week[29]. The fact that VD could be a risk marker allows us to assume that the risk of acquiring BV could possibly increase with increased vaginal douching frequency. As a result of this train of thought, the studies were used to construct a forest plot graph (**Figure 2**) in order to determine the strength of the correlation[28–30]. The graph weakly suggests that the higher the frequency of VD, the more likely a woman is to develop BV. The global Risk Ratio for BV acquisition for high frequency of VD users is 1.24 (95%CI 1.12 – 1.43), representing a statistically significant result.The data from the Hutchinson *et al*.[27] study could not be included due to the fact that it was incomplete.

On the other hand, no positive correlation was found between douching and STD and/or HIV infection. Two studies evaluated the correlation between VD and STD[24,25] and one[24] did not find a positive correlation. Tsai *et al*.[25] carried out their study over a 3-year period and examined the association between VD and four STDs (*T. vaginalis, C. Trachomatis, N. gonorrhea, and* HSV-2*)* in adolescents at risk of HIV-infection and uninfected female adolescents aged 12 to 19 years old. VD users were found to acquire STDs in a shorter period of time when compared to douching Non-Users. The adjusted hazard for STD was 1.8 times higher for frequent douching Users and 1.4 times higher for intermittent VD users when compared to VD Non-users. However, the results were limited: the study was conducted in a defined population of female adolescents with high-risk behavior, two thirds of which had HIV. These findings may not be generalizable to lower-risk adolescent populations with different sociodemographic, immunological, and/or behavioral characteristics. Furthermore, the study used self-report for the main exposure variable to classify the level of vaginal douching for each female. Additionally and mainly, similar to cross-sectional studies, a limitation of this analysis is that causality is unknown, as vaginal douching could have been precipitated by the STD itself as a response to discomfort or vaginal discharge.

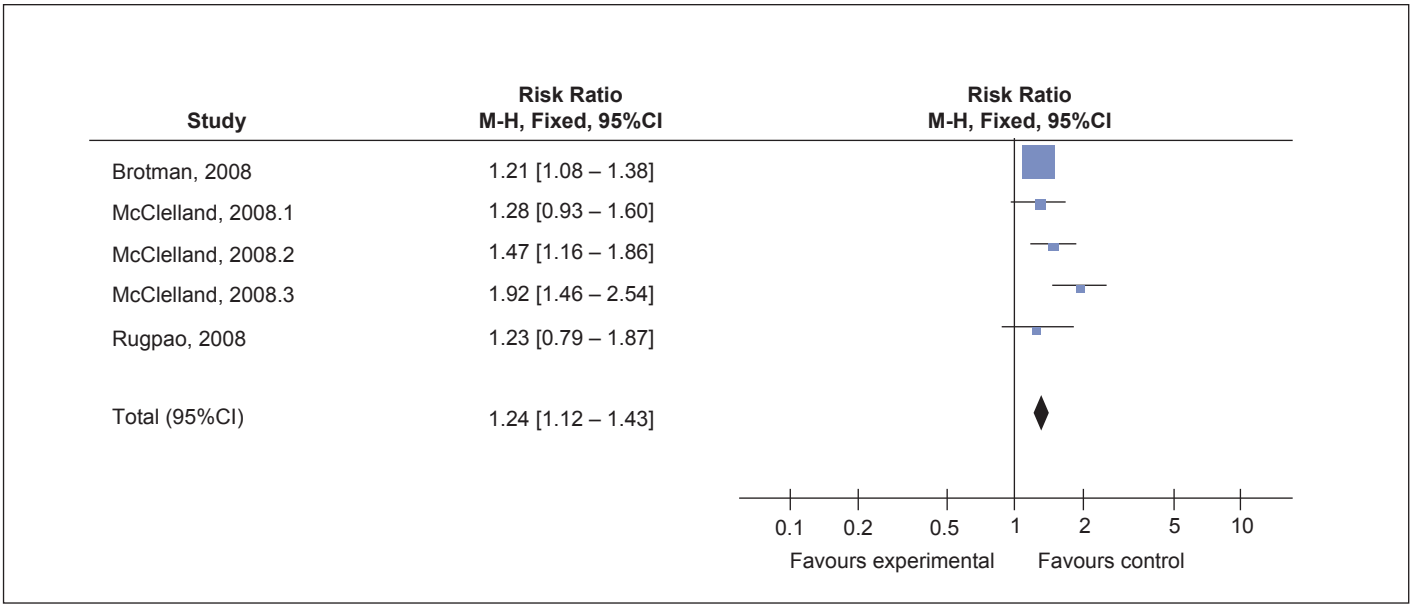

Figure 2 – Forest plot of bacterial vaginosis studies. McClelland *et al.*[31] was separated into three different ranges due to vaginal douching frequency: McClelland, 2008.1 = 1 to 14 times a week; McClelland, 2008.2 = 15 to 28 times a week and McClelland, 2008.3 = more than 28 times a week.

The only study which did not confirm a positive correlation was the one by Ness[24]. After adjusting for confounding factors, this study found that vaginal douching two or more times per month at baseline was not associated with neither PID (aHR = 0.76, 95%CI 0.42 – 1.38) nor *gonococcus*/Chlamydial Genital Infection (aHR=1.16, 95%CI 0.76 – 1.78). These three studies seem to point to the fact that VD frequency is an important factor to the determination of a positive correlation.

Figure 3 evaluates the relationship between VD and STDs. Two studies were included[24,25], one of which was divided in two[24] due to different outcomes (*Gonococcus* and Chlamydial Lower Genital Tract Infection, and PID). Tsai *et al*.[25] had two incidence measures (frequent douching users and intermittent douching users) synthesized into one, using RevMan[23], such to compare with non-users. The final graph shows a non-significant result, similar to HIV.

Similarly to the vaginal douching-BV correlation, disagreement was also found between the two studies regarding the causal relationship between VD-HIV (**Figure 4**). McClelland *et al*.[31] showed a positive correlation between these factors; while Myer *et al*.[32] did not. This might suggest specific mechanisms triggered by vaginal tract washing which could catalyze the process of viral invasion.

CONCLUSION

One of the greatest limitations in our meta-analysis was the scarcity of articles found in the literature considering the possible influence of vaginal douching on vulvovaginal and systemic infections. This gap in the research was also observed in studies specifically evaluating vaginal douching and cervicitis incidence. Only one study[24] addressing the issue in accordance with the inclusion criteria for of this work was found.

More methodologically correct and diversified research is needed to reach conclusive results concerning vaginal douching.

Conflict of interests

The authors declare no conflict of interests.

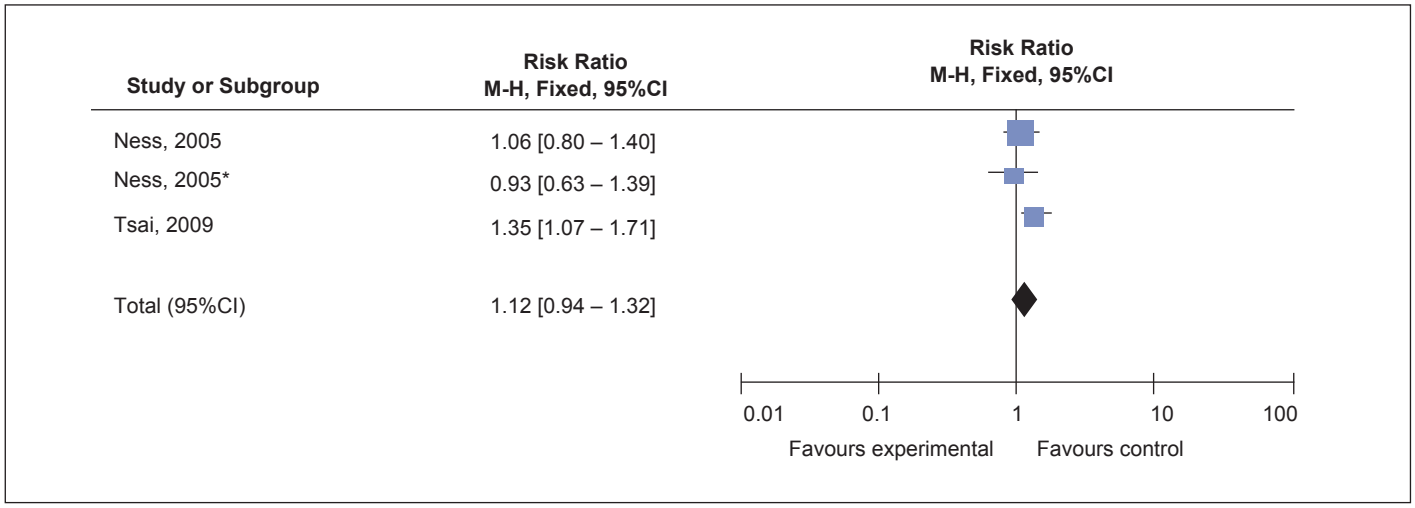

Figure 3 – Forest plot of Sexually Transmitted Diseases studies. Ness (2005) and Ness (2005)* are the same study. The outcome for the first study was Gonococci and Chlamydial Lower Genital Tract Infection while the second evaluated pelvic inflammatory disease.

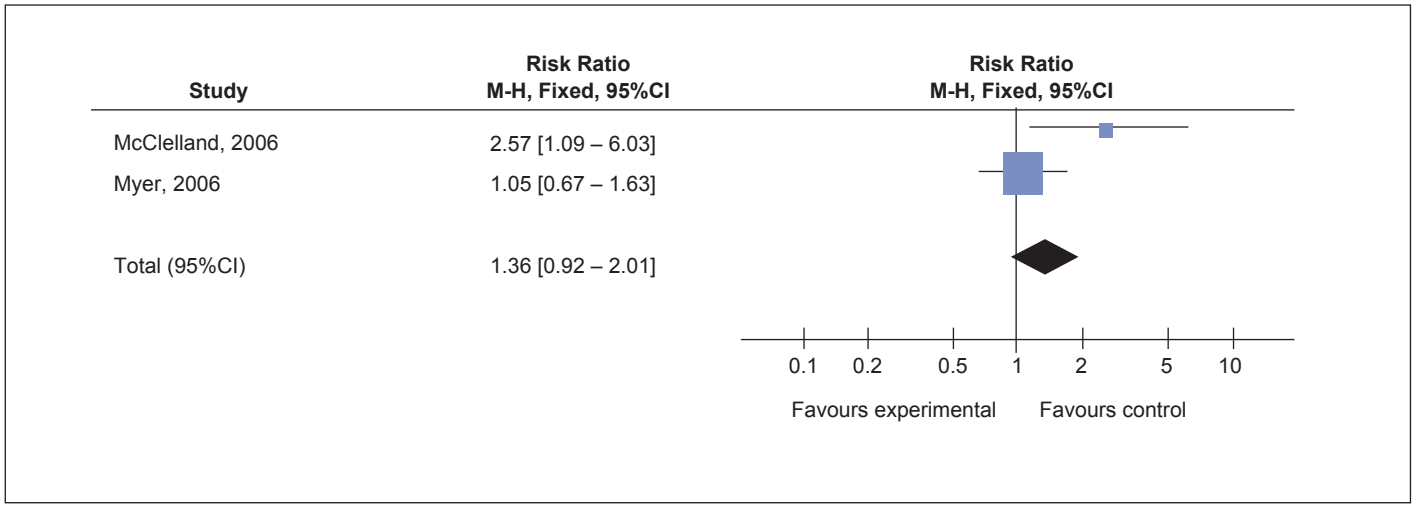

Figure 4 – Forest plot of HIV studies.

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ENDOCERVICAL BIOFILMS IN WOMEN WITH ENDOGENOUS INFECTIONS IN THE LOWER GENITAL TRACT: *IN VITRO* STUDY

BIOPELÍCULAS ENDOCERVICALES EN MUJERES CON INFECCIONES ENDÓGENAS DEL TRACTO GENITAL INFERIOR: ESTUDIO IN VITRO

Alicia Farinati[1], Daniyil Semeshchenko[1], Martín Santalucía[1], Melina Marqués[1], Adrián Orsini[1]

ABSTRACT

Introduction: The biofilm is one life form of microorganisms (MOs). On mucous membranes of women without and with endogenous infections, they are part of the normal microbiota and cause pathologies. We have demonstrated previously the participation of biofilms in chronic forms of vulvovaginal candidiasis (VVC), the influence of other microorganisms in its formation and evolution, in bacterial vaginosis (BV) and aerobic vaginitis (AV). **Objective**: To analyze the endocervical biofilms in women with or without vaginal infections (VI) comparing them with vaginal biofilms. **Methods**: We studied 22 women, 9 non-pregnant (NP) and 13 pregnant (P). Each patient was gynecologically evaluated, and a vaginal sample (VS) was taken with an aspersorium and an endocervical sample was taken with cytobrush (CB). We performed a fresh examination, pH determination and amine test. Both samples were inoculated in suitable culture medium. After each one, Gram staining and optical microscopy with crystal violet were performed for the study of BF. These were put into Sabouraud broth. All samples were incubated at 35°C for 20-24 hours. **Results**: We have discovered 9 women without pathology and with normal microbiota (NM) and 13 with vaginal infections (VI): bacterial vaginosis (BV) – 6 (4P); vulvovaginal candidiasis (VVC) – 4 (3P); vaginitis and intermediate microbiota (IMB) – 3 (1E). The notable differences were: inflammatory response in the cytobrush compared to the one found in the vaginal samples of women with vaginal infections (10/13), including women with bacterial vaginosis who did not have inflammatory response in the vaginal sample. In the cytobrush of women with normal microbiota, this response occurred only in 1 case (1/9). It was also observed the formation of microfilms of Gram-positive cocci (mostly *Enterococcus* spp) in the cytobrush of 84.6% (11/13) of the women with vaginal infections and in 66.6% (6/9) of the women with normal microbiota. Among the latter, mixed biofilms were observed in 3 cases with the presence of Gram-positive Bacilli (*Actinobaculum* (anaerobic) or *Actinomyces*). **Conclusion**: Something that called our attention was that the formation of biofilms of *Enterococcus* and other species of *Streptococcus* and *Satphylococcus* in the cytobrush of women with vaginal infections in whose vaginal samples these microorganisms were not observed nor recovered significantly. This is a risk since they can initiate an upper genital tract infection (UGTI). In the 4 P with BV, this risk is added to the risk associated with the BV. The question is whether the complications arising from this in pregnancy are not a result of such behavior. In the women with normal microbiota, the biofilms that have Gram-positive cocci can also represent a notable risk in the moment of performing instrumental procedures.
Keywords: biofilms, vaginal tract, cervical tract, women.

RESUMEN

Introducción: Las biopelículas constituyen una de las formas de vida de los microorganismos (MOs). En las mucosas de mujeres sin y con infecciones endógenas, integran la microbiota normal y desarrollan patologías. Previamente hemos demostrado la participación de las mismas en las formas crónicas de las candidiasis vulvovaginales (CVV), la influencia de otros microorganismos en su conformación y evolución, en la vaginosis bacteriana (VB) y en las vaginitis aeróbicas (VA). **Objetivo:** Analizar las biopelículas endocervicales en mujeres sin y con infecciones vaginales (IV), comparándolas con las BP vaginales. **Métodos:** Estudiamos 22 mujeres, 9 no embarazadas (NE) y 13 embarazadas (E). Cada paciente fue estudiada ginecológicamente y se tomó muestra vaginal (MV) con hisopo y muestra endocervical con citobrush (EC). Se realizó examen en fresco, determinación del pH y prueba de aminas. Ambas muestras fueron inoculadas en medios de cultivo adecuados. A cada muestra se efectuó la coloración de Gram y se realizó la capa celular sobre el dispositivo de vidrio (DV) para el estudio de las BP. Los DV se colocaron en caldo Sabouraud. Todas las muestras se incubaron a 35°C durante 20-24 horas. **Resultados:** Encontramos 9 mujeres sin patología y con microbiota normal (MN) y 13 con infecciones vaginales (IV): vaginosis bacteriana (VB) – 6 (4E); candidiasis vulvovaginal (CVV) – 4 (3E); vaginitis y microbiota intermedia (VMI) – 3 (1E). Las diferencias notables fueron: hallazgo de respuesta inflamatoria en el EC comparada con la encontrada en la MV en las mujeres con IV (10/13), incluyendo a las mujeres con VB que no presentan respuesta inflamatoria en la MV. En el EC de las mujeres con MN dicha respuesta ocurrió sólo en 1 caso (1/9); y formación de BPs de cocos Gram-positivos (la mayoría *Enterococcus* spp) en el EC del 84,6% (11/13) de las mujeres con IV y en el 66,6% (6/9) de las mujeres con MN. En estas últimas se observaron BPs mixtas en 3 casos con la presencia de bacilos Gram-positivos, (*Actinobaculum* (anaerobio) o *Actinomyces*). **Conclusión:** Llama la atención la formación de BP de *Enterococcus* y otras especies de *Streptococcus* y *Satphylococcus* en el EC de mujeres con IV en cuyas MV no se observan ni se recuperan significativamente estos microorganismos. Esto constituye un riesgo ya que las mismas pueden iniciar una infección del tracto genital superior (ITGS). En las 4E con VB, este riesgo se suma al de la VB y cabe preguntarse si las complicaciones derivadas de la misma en la gestación no son el producto de dicho comportamiento. En las mujeres con MN las BP de cocos Gram-positivos podrían representar un riesgo notable para el desarrollo de ITGS en el momento de efectuar maniobras instrumentales.
Palabras clave: biofilmes, tracto vaginal, tracto cervical, mujeres.

INTRODUCTION

In the lower genital tract, the microorganisms (MOs) that compose the normal or usual microbiota can colonize or infect the vaginal mucosa, making biofilms (BF) of single species or mixed ones[1]. Both the colonizing MOs and those producing vaginal and endocervical infections can determine, in pregnant women during pregnancy and at labor, the contraction of congenital or perinatal infections.

A BF is a very dynamic sessile community of MOs, characterized by cells that are irreversibly joined to a substrate or interface between them, saturated in an extracellular matrix of polymerized substances produced by them and that show a changed phenotype with regard to the growth and gene transcription index[2-5]. They can

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have an important role, both in the infections and for protection. In general, the lower genital tract content is studied taking into consideration the planktonic MOs, but not the BF, since we do not know many physiopathological aspects that happen during the colonization and/or infections.

In the vagina, BFs of lactobacilli are responsible for the wider production of lactic acid that decreases the vaginal pH and prevents, thus, the colonization by pathogenic or potentially pathogenic MOs[6].

The usual endocervical microbiota has not been deeply studied and we can assume that it can allow adherence of other MOs that are different from the vagina, due to its more alkaline pH and histological configuration with the cylindrical epithelium tissue. Therefore, in the pathology due to sexually transmitted infections (STIs), like gonorrhea and chlamydia, produced by *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT), respectively, we know that adherence is produced in the cylindrical epithelial cells instead of in those from the vaginal stratified epithelium[7]. The association of NG with the receptor is essential for the invasion of the epithelial cell. However, this can vary since members of the CD66 receptors family were identified for several Opacity (Opa) proteins of NG, which mediate the interaction with phagocytes and the passage through epitheliums[7,8]. CT is linked through bridges of some polysaccharides that are established between the surface of the elementary body and the cellular receptor[9].

Is has not been reliably known if the same happens to endogenous infections, since it was always investigated the vaginal tract and not the endocervical one. Probably, the establishment of BF of other MOs in the endocervix is mediated by similar mechanisms, which according to environmental conditions can be changed by the presence of some adhesins, such as those we have seen in these STI agents.

OBJECTIVE

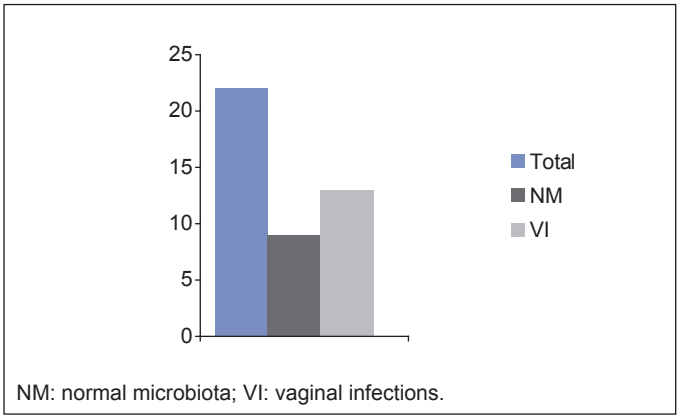
To analyze the behavior of MOs as BF in the endocervix (BFC) in women with and without endogenous vaginal infections (VI) comparing them with the vaginal BF.

METHODS

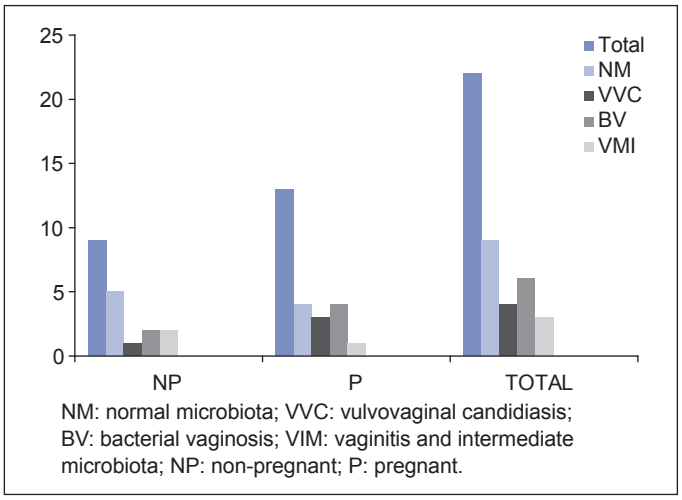
We have studied 22 women, 9 that non-pregnant (NP) and 13 pregnant (P). Each patient was gynecologically studied. It was taken their vaginal sample (VS) with cotton swabs and endocervical sampling with cytobrush (EC). The following exams were performed: wet mount test, pH determination, and amine testing with HOK at 10%. Both samples were inoculated in suitable culture medians: Sabouraud agar, Cystine Lactose Electrolyte Deficient (CLED) agar, trypticase soy agar (TSA). Gram coloration was performed with each sample and the optical microscopy on the glass equipment (GE) for the BF analysis. The GEs were put in Sabouraud broth. All the samples were incubated at 35ºC for 20 to 24 hours.

RESULTS

We found 9 women (5 NP and 4 P) without pathology and NM and 13 with VI: bacterial vaginosis (BV) 6 (4P); vulvovaginal candidiasis (VVC) 4 (3P); vaginitis and intermediate microbiota (VIM) 3 (1P) (**Graphics 1 and 2**).



Graphic 1 – Distribution of patients according to the vaginal content findings.

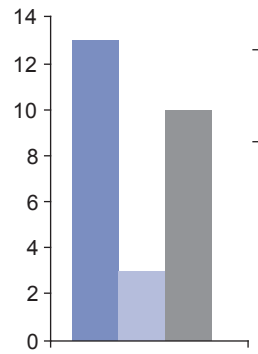


Graphic 2 – Distribution of patients according to their condition and kind of vaginal content.

The most important differences were:

- Inflammatory response in EC comparable to that found in MV in women with VI (10/13), women with BV that did not present inflammatory response in the MV were also included (**Graphic 3 and Figure 1**). In the EC of women with NM, this response happened only in 1 case (1/9).
- Formation of BF of Gram-positive cocci (most of them were *Enterococcus* spp) in the EC of 84.6% (11/13) women with VI and in 66.6% (6/9) women with NM (**Graphic 4**). In the latters, mixed BFs were found in 3 cases with presence of Gram-positive bacilli (*Actinobaculum* (anaerobic) or *Actinomyces*) (**Figures 2 to 4**).

In the cases 12 and 16, one can see the relevant difference on the varied formation of biofilms at vaginal and endocervical levels (**Figures 5 to 12**). In the **Figures 8 and 12**, BF presence of negative *Staphylococcus coagulase* (NSC) (*Staphylococcus epidermidis*) is



	BF Gram positive cocci	
Total of women	22	
Vaginal infections	13	11
Normal microbiota	9	6

Total IV
IR V
IR EC

VI: vaginal infections; IR V: inflammatory response in vagina; IR EC: inflammatory response in the endocervix.

Graphic 3 – Inflammatory response in the vagina and endocervix.

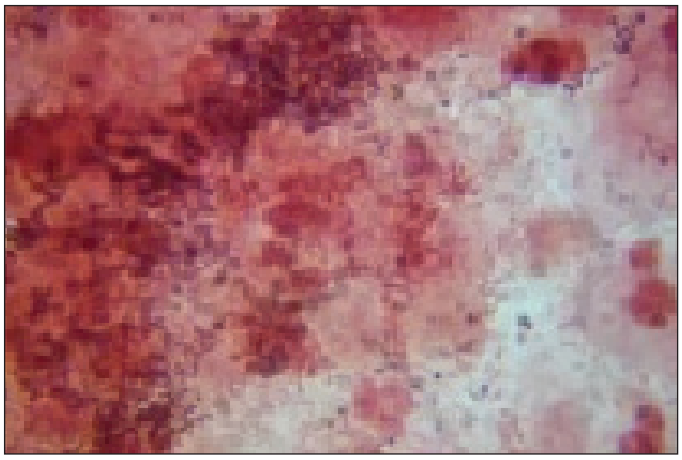
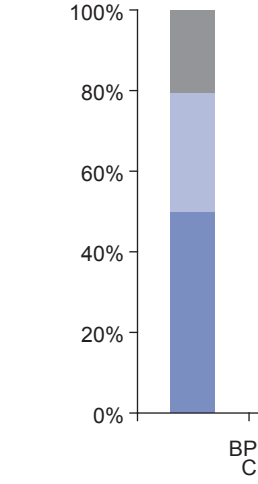


Figure 1 – Bacterial vaginosis – Endocervix – Positive inflammatory answer – Gram staining, 1000x.



Total: total of vaginal infections; BPC C+: biofilms of Gram-positive cocci; NM: normal microbiota; VI: vaginal infections.

Graphic 4 – Biofilms of Gram-positive cocci in the EC of women with vaginal infections and normal microbiota.

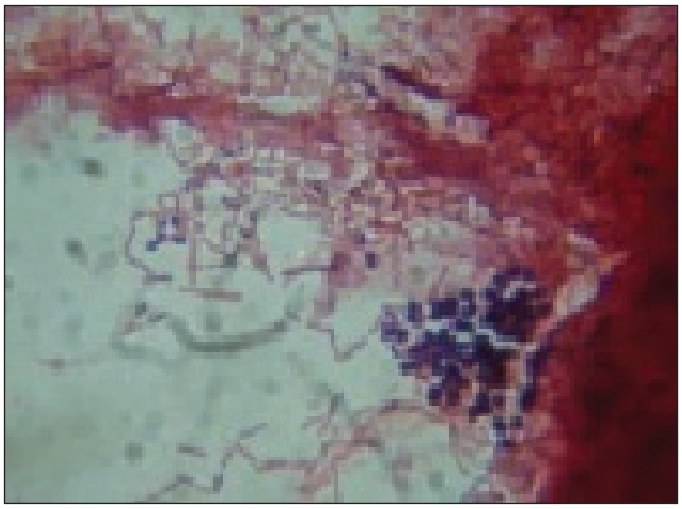


Figure 2 – *Actinobaculum* (anaerobic) or *Actinomyces* – Endocervix – Gram staining, 1000x.

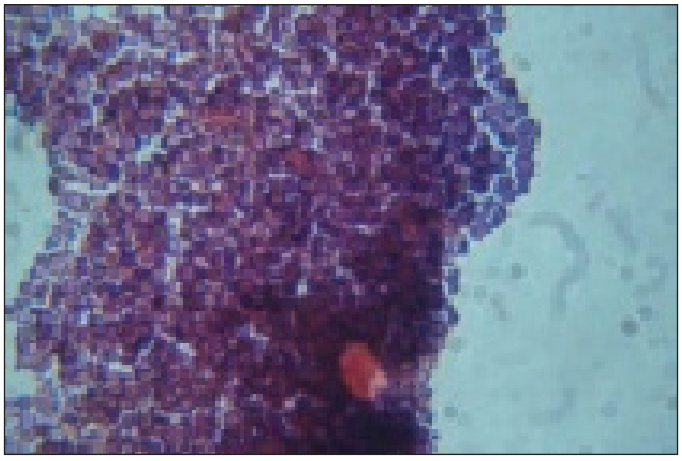


Figure 3 – Endocervical biofilm, Gram-positive cocci. Gram staining, 1000x.

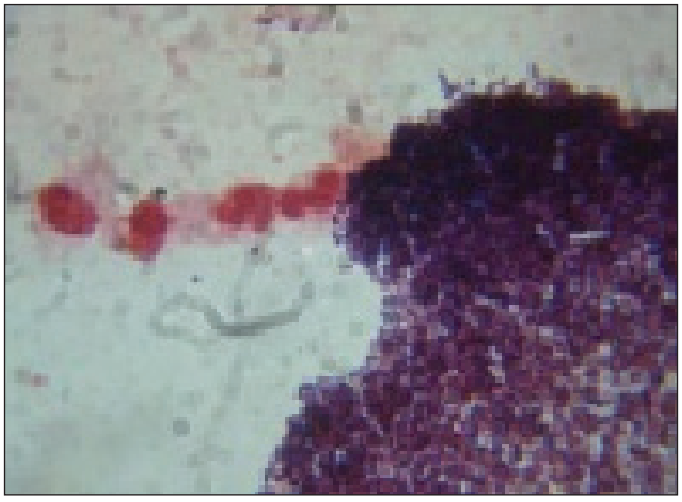


Figure 4 – Endocervical biofilm, Gram-positive cocci. Gram staining, 1000x.

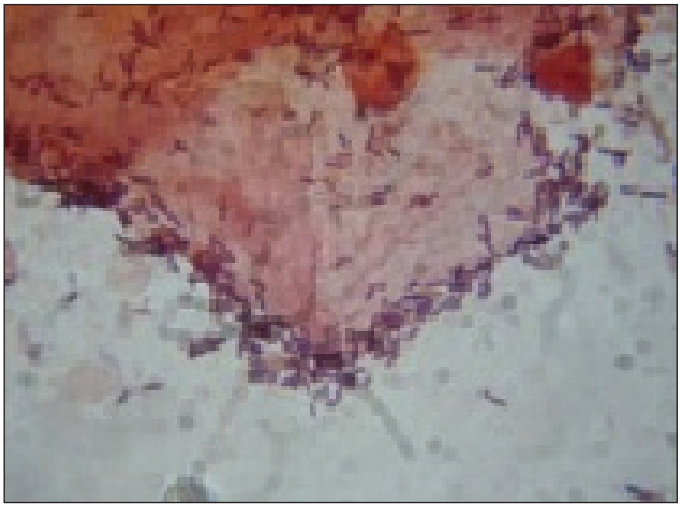


Figure 5 – Case 12: direct vaginal exudate. Gram staining, 1000x.

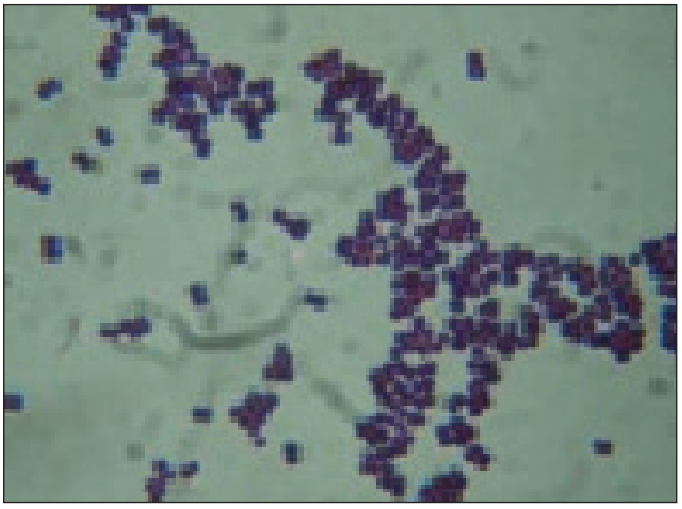


Figure 8 – Case 12: endocervical biofilm. *Staphylococcus epidermidis* (SCN). Gram staining, 1000x.

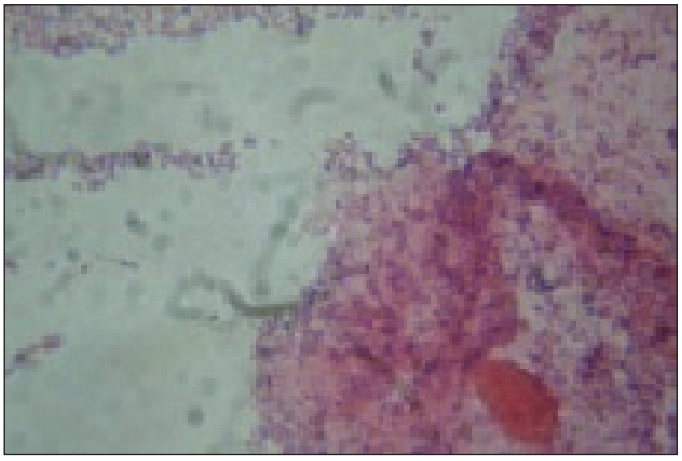


Figure 6 – Case 12: vaginal biofilm. Gram staining, 1000x.

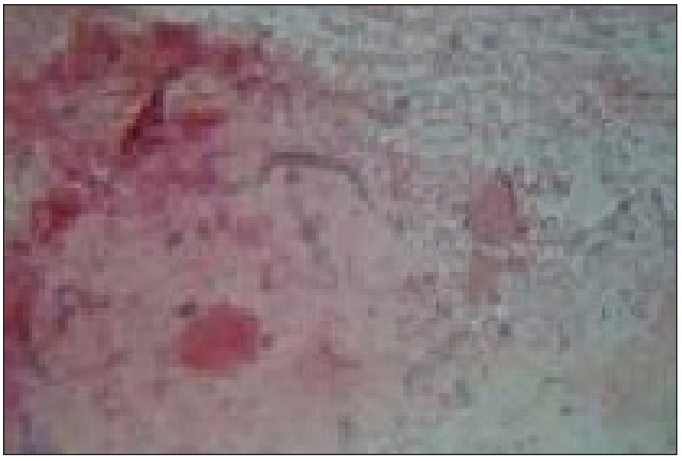


Figure 9 – Case 16: direct vaginal exudate. Gram staining, 1000x.

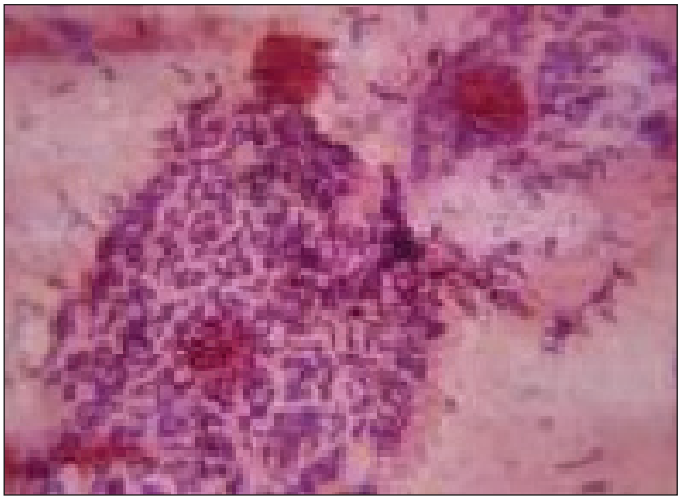


Figure 7 – Case 12: direct endocervical exudate. Gram staining, 1000x.

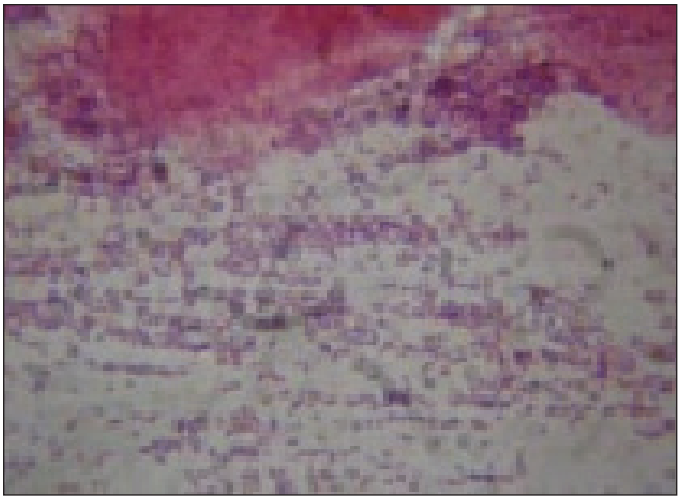


Figure 10 – Case 16: vaginal biofilm. Gram staining, 1000x.

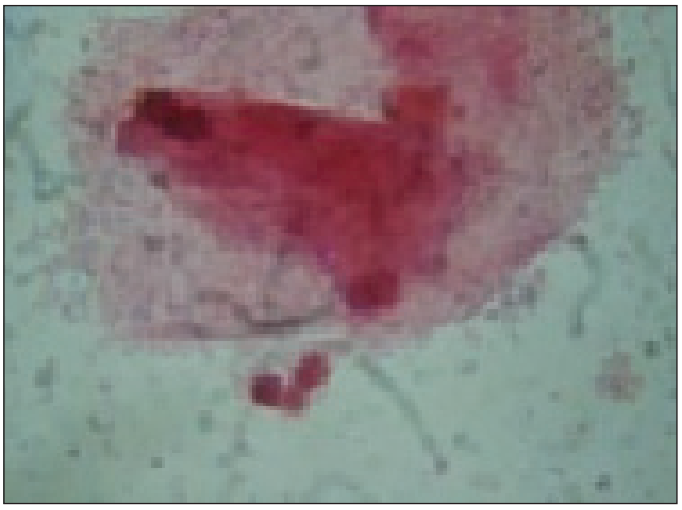


Figure 11 – Case 16: direct vaginal exudate. Gram staining, 1000x.

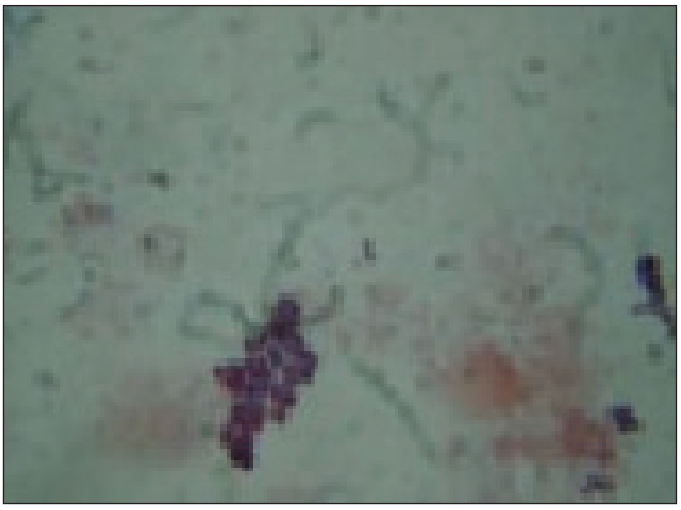


Figure 12 – Case 16: endocervical biofilm. Gram staining, 1000x.

very notable and, nevertheless, these MOs are not seen neither in the vagina nor in their corresponding BF.

DISCUSSION

The formation of BF is an important characteristic of NM constitution from the mucosae in our organism. As it is known, the BFs have two kinds of behaviors in our organism, like NM or a pathogenicity and resistance factor in places that are usually sterile or with prosthesis[10,11]. Their formation participates in the infectious pathology of the lower genital tract together with immunological and allergy factors[12].

We studied the in vitro vaginal BFs both in special equipment and in optical microscopy[13-16]. We have demonstrated that in mixed BFs of yeasts and *Escherichia coli*, the non-albicans Candida species make it easier, due to exuberance of their exopolysaccharide. The bacteria that produce glycocalyx as an adherent material could also have an important role in the pathogenesis of infections by *Candida* spp, not only in the urogenital level but also in other places. These behaviors would explain the almost constant presence of singe species or mixed BFs in the vaginal tract. In the endocervical tract, the possibilities of BFs formation can be different due to some factors, such as the epithelium characteristics, the number of MOs, the pH and the micro-atmosphere. It is known that in the case of NG colonized over the endocervix cells, the anaerobically induced genes and/or those that codify proteins that participate in the anaerobic breathing are needed to form a BF, whereas the genes responsible for the proteins that take part in the aerobic breathing are less abundant in the BF[17]. For all these reasons, the BFs in the endocervix may have a different behavior than the vaginal BFs.

Our findings call the attention to the BF formation of Gram-positive cocci. From the 17 cases of Gram-positive cocci, 11 were of *Enterococcus* spp, 2 of *Streptococcus* spp and 4 of SCN, 3 of which were of women with NM. This is a risk since these BFs may progress to the upper genital tract and create an infection therein, which is usually known as pelvic inflammatory illness or infection (PII) and recently as upper genital tract infection (UGTI). In the 4 P women with BV, this risk is an addition to the one of BV and one may ask if the complications from BV in pregnancy are not the product of the sum of such entities. In women with NM, although Gram-positive cocci BFs happen in lower proportion, they can also represent a risk worthy of consideration for the development of a UGTI when performing instrumental maneuvers.

The inflammatory response in endocervix in BV cases, when absent, could be happening due to the blockage of interleukin (IL)-8 that is in the vagina and not in the endocervix. Although it is increased in the IL-1 β vagina and therefore we expect an inflammatory response, it is not produced through the hydrolytic enzymes of anaerobic bacteria that, together with *Gardnerella vaginalis*, form an abnormal microbiota in the BV[18,19]. We do not know if it happens with such ILs in the endocervix, however there is a different microbiota in the BF with a possible distinct activity compared to them. Data found in literature detail the IL concentrations in cervicovaginal washings and in studies about planktonic MOs[20].

Another theme for discussion with regard to BF from the genital tract is the possible influence in the appearance of late sepsis in newborns. Sepsis in such age range is divided into: early sepsis that is manifested in the first 72 hours for 7 days, and the late one, whose incidence peaks are between the second and third weeks[21]. The Gram-negative bacilli were the most important representations in the 1960s together with emergence of group B *Streptococcus* in early sepsis[22,23]. Recently, Gram-positive MOs represent up to 70% of neonatal sepsis in North America, and SCN is the most prevalent in late sepsis, especially in children born with low gestational age and those with low weight (lower than 1,500 g)[24].

In general, it is confirmed that MOs in neonatal late sepsis come from the environment[25] or the use of central venous catheters, mechanical ventilation, parenteral nutrition or other invasive procedures[26-29]. Few investigators associate the presence of such MOs with a possible colonization from the labor channel.

Detection of SCN BF in the endocervix of a pregnant woman suggests a risk since the MOs that form them may persist, firstly as colonizers and then as infections, in neonates that normally are treated with anti-microbes with difficulties of approaching the BFs.

In the common studies regarding lower genital tract infections and during pregnancy, it is more common to give more attention to vaginal infection and forget about investigating what is happening in the endocervix, with the exception of NG or CT. However, endocervix is part of the labor channel and eventually MOs present may affect the fetus before or in labor.

The described findings allow proposing that further endocervical investigation be performed, independently from the one that is done to investigate NG and CT, especially in women with risks of premature birth or birth of low weight infants.

CONCLUSION

Formation of BF of *Enterococcus* and other species of *Streptococcus* and *Satphylococcus* in the EC of women with VI calls the attention, since in their VM such MOs are not significantly seen or recovered. This is a risk, since they may initiate an infection in the UGTI. In the 4 P with BV, this risk is an addition to that of BV and one should ask if the complications from it in pregnancy are not the product of such behavior. In women with NM, the EC BFs of Gram-positive cocci happen in lower proportion.

Conflict of interests

The authors declared no conflict of interests.

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The psychosocial and economic burden of genital warts among women assisted in six sexual and reproductive health clinics in Brazil

A carga psicossocial e econômica de verrugas genitais em mulheres atendidas em seis clínicas de saúde sexual e reprodutiva no Brasil

Mônica Gomes de Almeida[1], Antônio Márcio Tavares Thomé[2], José Berilo Lima Filho[3]

ABSTRACT

Introduction: World Health Organization estimates that 291 million women worldwide will have a human papillomavirus infection. Treatment for genital warts brings discomfort and may be stressful. **Objective:** The objectives are to estimate the psychological burden of genital warts and to estimate its economic burden in six reproductive health clinics in Brazil. **Methods:** Women visiting BEMFAM's clinics from January 2012 until March 2013 filled a self-administered questionnaire based on psychometric scale. The economic burden was measured with a retrospective study of medical chart review of patients assisted form January 2009 to December 2010. **Results:** A total of 122 individuals filled the psychosocial questionnaire. Women with normal Pap smear presented lower scores of worries and concerns about gynecological health than women with cervical intraepithelial neoplasia (CIN) or GW and higher scores of satisfaction with sexual life than women with CIN or GW. Feelings of anxiety and surprise with the last exam were higher in GW group than for normal Pap smear and CIN groups. Each GW episode lasted on average 132 days, had 6 medical visits and costs US$ 139. **Conclusion:** The economic burden of GW is closely related to psychosocial burden, and the use of health services after a GW episode should be considered in future research. The study of indirect costs is important, considering the number of visits per episode of GW. Additional studies are needed and can help in the advocacy efforts for a comprehensive prevention programs in Brazil.
Keywords: reproductive health, health and costs, genital warts

RESUMO

Introdução: A Organização Mundial de Saúde estima que 291 milhões de mulheres serão infectadas pelo Papilomavírus Humano. O tratamento das verrugas genitais pode ser desconfortável e estressante. **Objetivo:** Estimar a carga psicossocial das verrugas genitais (VG); e estimar a carga econômica das verrugas genitais entre mulheres atendidas em seis clínicas de saúde reprodutiva. **Métodos:** Voluntárias atendidas nas Clínicas da BEMFAM entre 2010 e 2013 preencheram um questionário baseado na escala psicométrica. A carga econômica foi medida através da análise de prontuários de pacientes atendidas entre 2009 e 2010. **Resultados:** O questionário psicossocial foi preenchido por 122 sujeitos. Mulheres com Papanicolaou normal apresentaram menores índices de preocupação quanto à saúde ginecológica e maiores índices de satisfação com a vida sexual do que mulheres com neoplasia intraepitelial (CIN) ou VG. Sentimentos de ansiedade e surpresa com o resultado dos exames foram mais observados entre mulheres com verrugas genitais do que nas com Papanicolaou normal ou CIN. Em média, cada episódio de verruga genital durou 132 dias, demandou seis visitas médicas, e custou US$ 139. **Conclusão:** Houve relação entre a carga econômica e a carga psicossocial das VG. O maior uso de serviços de saúde após um episódio de verruga genital deve ser analisado em estudos sobre a carga econômica das VG. O presente estudo reforça a importância da análise dos custos indiretos, considerando o número de visitas por episódio de VG. Estudos adicionais podem fortalecer os esforços para programas abrangentes de prevenção no Brasil.
Palavras-chave: saúde reprodutiva, saúde e custos, verrugas genitais

INTRODUCTION

The World Health Organization estimates that 291 million women worldwide will have a human papillomavirus (HPV) infection at any given point in their lifetime[1]. Cervical cancer is related to oncogenic types of HPV infection and constitutes a public health issue in Brazil. According to the Brazilian National Cancer Institute 15.590 new cases and a rate of 15,33 cases per 100.000 women are estimated for 2014[2].

Although cervical cancer is the most important public health issue related to HPV infection in women, genital warts (GW), a benign condition related to non oncogenic HPV subtypes, cannot be neglected. In 2008, the Brazilian Ministry of Health published a study on sexually transmitted infections (STI) prevalence in selected populations (pregnant women, men working in industry and people seeking care in STI clinics) in five regions of the country[3]. Genital warts were diagnosed in 5.7% of pregnant women, and 6.5% reported previous episodes. Among women who seek STI clinics, 21% had a GW diagnosis, and 25% reported previous episodes.

Genital warts usually cause stress to the affected individuals. The treatment options bring some kind of discomfort, such as burning sensation and pain. Besides, as a sexually transmitted infection, it may be associated with feelings of shame, anxiety and problems in the relationship with the partner.

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Zhu *et al*.[4] developed a psychometric scale to assess the psychological burden of HPV. The self-administered questionnaire consists of 29 questions designed to capture a wide range of psychosocial consequences of HPV disease, including both cervical cancer precursors and genital warts. The results were sensitive to differences in the psychosocial impact of various HPV-related diseases.

There are studies about costs of GW treatment in many countries; some of them consider only direct costs[5,6] and others include indirect costs such as sick leave[7-9]. Considering the importance of HPV and related diseases in Brazil and the lack of studies about both the psychosocial and the economic burden of these diseases, *Bem Estar Familiar no Brasil* (BEMFAM – Family Wellbeing in Brazil) carried out a study to measure the psychosocial and economic burden of genital warts among two samples of women attending its six reproductive health clinics. BEMFAM is a Brazilian non-governmental organization that provides sexual and reproductive health (SRH) services and technical support to local governments.

OBJECTIVE

There are two objectives in this paper: (i) to estimate the psychological burden of genital warts (GW); and (ii) to estimate the economic burden of GW in six reproductive health clinics in Brazil.

METHODS

The study design comprises two objectives and groups of women assisted in the six BEMFAM's SRH clinics in the Brazilian Northeast States of Maranhão, Paraíba, Rio Grande do Norte, Pernambuco, Ceará and the Southeast State of Rio de Janeiro. All the clinics are located in urban areas of the State capital cities, provide outpatient care and assist both individuals who pay out-of-pocket or with private health plans. All the individuals were assisted by gynecologists. The psychosocial burden was measured by a self-administered questionnaire at the time of the visit and the economic burden was measured with a retrospective study of medical chart review analysis.

Self-administered questionnaire

Women who visited the six BEMFAM's clinics from January 31st, 2012 until March 1st, 2013 were invited to participate in the study. Inclusion criteria were women aged 18–45 years, who had a Pap smear in the preceding 90 days or were diagnosed with genital warts during physical examination, in good health. Women who self-reported to be positive for Human Immunodefficiency Virus (HIV) serology, undergoing antiretroviral treatment, illiterate or pregnant were excluded.

Women who accepted to be a volunteer signed an informed consent and answered a socio-demographic questionnaire and a psychometric scale test applied by nurses. Both questionnaires were pretested through in-depth interviews with clients, to evaluate easy of understanding and adequacy of translations.

All volunteers received written information and an educational counseling session about prevention and treatment of HPV after filling the self-administered questionnaire. Women belonging to the groups with cervical intraepithelial neoplasia (CIN) 1 and CIN 2-3, also had a colposcopy and/or biopsy free-of-charge.

Medical chart review

In order to identify patients with GW, medical records of women who consulted from January 2009 to December 2010 and had undergone one of the procedures that could be related to GW treatment were analyzed. The procedures were provider-applied modalities to treat vulvovaginal or anal lesions. Criteria for enrollment in the study comprise women aged 18 to 45 years, with a GW diagnosis in the preceding twelve months and in good health. Pregnant women, those infected with HIV, women with only vestibular micropapilomatosis and with abnormal Pap smear were excluded.

The individuals were classified as (1) newly diagnosed (never having been diagnosed before with GW); (2) recurrent (those who had previous episodes of GW but who had been free of lesions for at least 12 months); and (3) resistant (those who had previous episodes of GW that remained despite treatment).

All the visits, exams and treatment information were collected by nurses using a checklist form and then sent to the medical department for data review. Cost analysis was carried out considering treatment costs from the payer's perspective. Exams not specific to GW, but performed during the episodes to investigate other HPV related lesions, such as Pap smear and colposcopy were included. Indirect costs were not included. Unit costs for visits and treatments were used to estimate the cost per episode of care, which is defined as the period between the first and the last clinic visit for GW treatment. Costs were based on BEMFAM and private health plans prices in 2013. All costs were converted to US dollars at an exchange rate of 1 US$ = R$ 2.3 (Brazilian reais).

Sample size and statistical analysis

A target sample size of 120 cases for the psychological scale and 100 cases for the medical records review was set. The study aimed at recruiting 30 cases each in the eligibility groups of normal Pap test, CIN 1, 2-3 and GW, for the sample on psychological burden. Due to the low number of cases CIN 1 and 2-3 were regrouped in one single group for analysis. Also, data from all clinical centers was regrouped in one dataset due to small numbers. No systematic differences on samples recruited in the different centers were expected.

RESULTS

Sample characteristics are displayed in **Table 1**.

Mean age was similar for both samples, with a slightly younger population for the sample under medical record review (25.8 *versus* 27.6). Most of the sample enrolled for the psychometric part of the study was married, earning a family income of less than US 11 a day, with one living children and was revisiting BEMFAM clinics. They used modern contraception in larger proportions than women under medical record review (82.8 *versus* 75%). Prevalent methods among the first were pills (43%) and condoms (34%) against pill (35%), condom (29%) and sterilizations (13%), for the second. Fifty three cases were enrolled from the normal Pap smear group, 29 with CIN 1, 6 cases with CIN 2 or 3 and 34 cases with GW. For the psychometric scales, cases with CIN 1, 2 and 3 were regrouped,

Table 1 – Characteristics of participants in the study.

Sample Characteristics	Self–administered questionnaire (n=122)
Mean age at enrollment, years (*) (95%CI)	27.6 (24.3–30.2)
Visit Type (%)	
First	13.4
Revisit	86.6
Mean number of leaving children (min–max)	0.85 (0–9)
Average monthly family income US$ (%)	
<234	11.8
235–335	59.8
336–480	19.6
480–723	8.8
% married or in stable union	90.2
Eligibility groups	
Normal Pap smear	53
CIN 1	29
CIN 2, 3	6
Genital Warts	34
Contraceptive use (%)	82.8
	Medical records (n=102)
Mean age at enrollment, years (*) (95%CI)	25.8 (24.5–27.2)
Mean age at first intercourse (95%CI)	17.8 (17.0–18.6)
Contraceptive use (%)	75.0
First or recurrent episode (%)	
First	90.2
Recurrent	2.0
Resistant	7.8
Mean duration of episodes, in days (95%CI)	132.2 (96.9–76.0)
Mean number of normal deliveries (min–max)	0.18 (0–3)
Mean number of caesarean sections (min–max)	0.16 (0–2)
Mean number of abortions (min–max)	0.22 (0–5)
Payment (%)	
Out-of-pocket	95.1
Private insurance	4.9

(*) Age at first genital warts diagnostic for medical records.

totaling 35 cases. The sample for medical review had the first intercourse at 17.8 years old in average, were experiencing their first GW episode for 90.2% of the total sample, with 2.0% being recurrent and 7.8% resistant cases. In average, women from the medical record sample had 0.18 normal deliveries, 0.16 cesarean sections and 0.22 abortions. Treatment payment with money out-of-pocket represented 95.1%.

The psychometric scale met with asymmetric results, with skewness above 1 for several item scales, as depicted in **Chart 1**. Scale items with skewness above the threshold of 1 were not retained for analysis. Overall, there were very few missing cases to observation.

Four factors were regrouped during exploratory factor analysis (varimax rotation) and are displayed in **Table 2**.

Women with normal Pap smear presented lower scores of worries and concerns about their gynecological health (fear of test results, implications for fertility, fear of no cure for abnormal Pap smear or for cervical cancer, risks of infecting the partner or herself during sexual relations) than the group with CIN or GW. However, there was no significant difference in worries between the groups with CIN and GW. Scores of satisfaction with sexual life (feeling their bodies sexually attractive, satisfied with their sex life, relaxed after last gynecological exam and not disgusted with tests or exams) were also higher for women with normal Pap smear than for the other two groups. Again, differences in feelings about sexual life were not statistically different for women with CIN and GW. Feelings of anxiety and surprise (felt anxious or surprised with last exam or were concerned about GW) were higher for GW group than for the CIN and normal Pap smear group, in that order. All differences for the anxiety and surprise factor were statistically significant. Finally, there were no statistically significant differences in the factor of distress and shame (feeling ashamed, not in control of everyday life or of own health) among the groups.

Medical records analysis showed that each GW episode last in average 132 days (Table 1) and cost US$ 139 with private health plan and US$ 105 with BEMFAM's clinics subsidized tariffs. Cost figures per episode of GW, number of encounters (visits) and cost per procedure are depicted in **Table 3**. Regarding the medical procedures, in 95 episodes, the provider applied trichloroacetic acid as the only treatment. It was also associated with electrosurgery in one episode, with excision and imiquimod in six episodes each. Excision was the only treatment in four episodes. Other procedures described were consultations, Pap smear and colposcopy.

Chart 1 – Scale properties and factor loads.

Scale Items	Factor Loads				n		Mean	Standard Deviation	Skewness
	Wories/ Concerns	Sexual life/ Discomfort	Anxiety/ surprise	Distress/ shame	Valid	Missing			
1. When I think about my recent gynecological exam or test results, I feel good about myself.			-0.588		122	0	5.40	3.461	-0.258
2. When I think about my recent gynecological exam or test results, I feel anxious.			0.814		122	0	5.59	3.440	-0.195
3. I feel my recent gynecological test results were unexpected.			0.537		122	0	4.61	3.928	0.078
4. When I think about my recent gynecological exam or test results, I feel in control of my health.				-0.782	122	0	6.30	3.115	-0.651
5. When I think about my recent gynecological exam or test results, I feel depressed.					122	0	2.45	3.278	1.217
6. After my recent gynecological exam or test result, I feel I can concentrate as well as usual on everyday matters.				-0.631	122	0	6.41	3.055	-0.545
7. When I think about my recent gynecological exam or test results, I feel something is seriously wrong with me.					122	0	2.23	3.109	1.242
8. When I think about my recent gynecological exam or test results, I feel angry.					122	0	1.62	3.065	2.043
9. After my recent gynecological exam or test result, I feel confident my partner will accept me.					121	1	7.19	3.477	-1.188
10. When I think about my recent gynecological exam or test results, I feel my body is sexually attractive.		-0.582			122	0	4.32	3.283	0.045
11. When I think about my recent gynecological exam or test results, I feel ashamed.				0.537	121	1	3.02	3.465	0.906
12. I feel concerned about having genital warts.			0.638		119	3	3.74	4.420	0.490
13. I am worried there are no treatments to cure genital warts.					119	3	3.44	4.096	0.617
14. After my recent gynecology exam or test result, I feel optimistic about my future gynecological health.					122	0	7.50	2.806	-1.012
15. I am worried about having abnormal Pap test results.	0.606				122	0	3.67	3.915	0.418
16. I am worried that there is no cure for what causes an abnormal Pap test.	0.789				122	0	3.95	4.045	0.316
17. I am worried about my fertility because of my recent gynecological health or test results.	0.546				122	0	3.43	3.983	0.577
18. I am concerned I will get cervical cancer in the future.	0.725				122	0	5.83	3.893	-0.430
19. I am worried that there are no treatments to cure cervical cancer.	0.821				122	0	5.84	4.066	-0.396
20. I am worried about having pain during future gynecologist visits.	0.637				122	0	4.26	3.724	0.280
21. After my recent gynecologist exam or test results, I am worried that having sex with my partner may give him/her an infection.	0.607				121	1	4.29	4.226	0.236
22. After my recent gynecologist exam or test results, I am worried that having sex with my partner may give me an infection.	0.704				120	2	4.58	3.972	0.113
23. I felt disgusted by my recent gynecological exam or test results.		0.536			121	1	2.97	3.717	0.887
24. After my recent gynecological exam or test results, I am having less sex.					122	0	2.61	3.491	1.038
25. After my recent gynecological exam or test results, I feel satisfied with my sex life.		-0.755			122	0	5.69	3.700	-0.261
26. After my recent gynecological exam or test results, the quality of my sleep has decreased.					122	0	1.89	3.097	1.465
27. I felt relaxed after my recent gynecological exam.		-0.627			122	0	5.83	3.839	-0.390
28. I felt my recent gynecological procedures were embarrassing.					122	0	1.98	3.033	1.522
29. I felt the medical procedures at my recent gynecological exam were uncomfortable.					122	0	1.57	2.895	1.788

Table 2 – Psychological burden exploratory factors.

Psychological Burdens	Factor Numbers (*)	Normal Pap test	CIN 1, 2–3	Genital Warts
Worries/Concerns	15,16,17,18,19,20,21,22	1.94 (1.12 – 2.75)*	6.58 (5.27 – 7.86)	6.65 (5.45 – 7.85)
Sexual life/Comfort	10, 23, 25, 27	5.56 (4.87 – 6.33)*	4.01 (2.86 – 5.16)	4.21 (2.98 – 5.45)
Anxiety/surprise	2, 3, 12	2.35 (1.55 – 3.16)*	5.92 (4.59 – 7.26)*	7.15 (6.10 – 8.19)
Distress/shame	4, 6, 11	5.52 (4.91 – 6.13)*	4.79 (3.66 – 5.92)	5.38 (4.27 – 6.50)

(*) Significantly different at 95% confidence interval (bootstrap)

Table 3 – Costs of genital warts treatment at BEMFAM clinics.

Type of Payment	Cost per episode (n = 102)	Number of visits per episode	Cost per procedure (n = 613)
Private Health Plans			
Mean	$ 139.45	6.13	$ 23.31
Standard Deviation	$ 62.76	2.77	$ 4.55
Out-of-Pocket			
Mean	$ 105.02	6.13	$ 17.85
Standard Deviation	$ 46.82	2.77	$ 5.15

DISCUSSION

The results of this research are consistent with findings from other studies showing a high psychological and economic burden of the disease. However, the average number of visits per episode is higher than reported elsewhere[8-12]. According to the analysis of medical records, home treatment with imiquimod was also prescribed less often than reported by other studies[7-11]. Most cases of GW were treated with provider-applied trichloroacetic acid that is cheaper than patient applied imiquimod, which is neither provided by public sector nor by private health plans. This probably explains the higher number of mean visits in our study.

Average costs per episode (US$ 105) might also appear low when compared to other countries but it is not when compared with an average monthly income for 91.2% of women enrolled in our study, that is under US$ 480. For this population, about one-week wages is necessary to provide for treatment, indirect and social costs not included.

Woodhall *et al*.[13] wrote that concerns over future recurrence and transmission to new partners could impair the quality of life of subjects after completion of an episode. In our study the results from the psychosocial scale suggest that the psychological burden of GW is at least as distressful and heavy as for the CIN diagnosis and much heavier than for the normal Pap smear group. All the negative feelings associated to GW may lead to sexual dysfunction, low self-steem, risky behavior and the need to use additional health services, increasing the GW related costs.

Those results prompt for practical implications and future research directions. Free access to public healthcare is a constitutional right for all Brazilian citizens. Nevertheless, there are 50.7 million users of private health plans in the country[14], which means that almost 25% of the population is resorting to complementary or substitute sources of healthcare. Low income citizens constitute the majority of users of public primary health care services. Those who cannot afford a private health plan but prefer private assistance pay for low fee private health services, as the clients enrolled in this study did.

HPV is the most common viral reproductive tract infection. Primary prevention includes vaccination, sexuality education and condom promotion[15]. According to the International Federation of Gynecology and Obstetrics[16], all randomized controlled clinical trials provide evidence of a safety profile for the two vaccines against HPV: the bivalent Cervarix (GlaxoSmithKline) and the quadrivalent Gardasil (Merck, Co., Inc.). In Brazil both vaccines are available in the private market and the Ministry of Health included the quadrivalent vaccine in the national vaccination programme since March 2014, for 11–13 year-old girls.

A national study about knowledge, attitudes and practice in the Brazilian population[17], revealed that 26.8% of those who reported at least one sexual intercourse in the last twelve months had had sexual debut before the age of 15. This national study also revealed that only 24.6% of women had free access to condoms in the past year. A survey on adolescent sexual behavior in a public Brazilian high school showed that at the age of 14, 39% boys and 8,5% girls declared being sexually active[18]. Advocacy efforts for the scaling up of the government vaccination program in order to include boys and to expand the age range for the target population of the public vaccination campaigns should be considered. Promoting condom access and use and sexual education cannot be neglected. In addition, the use of imiquimod for treatment should be encouraged and provided through public sector channels. Besides, as the private health plans serve almost 25% of Brazilian population, their contribution to vaccine access should be encouraged.

Despite the relevant results of our study, which shows an excessive psychological and economic burden of GW among the clinics surveyed, there are some limitations to the study that open venues for new research. The main limitations of this study are the analysis of only part of the economic burden of the disease, from the payers' perspective and the fact that the sample is not representative of the country but of BEMFAM's clinics. A comprehensive cost analysis should also include social costs that emerge from the conflict between sexual partners and domestic violence[19]. Finally, the asymmetry in the scales prevented us from analyzing different

psychological burdens of the disease due to the non-validation of some scale items in this study. The expansion of the sample for confirmatory factor analysis is also suggested.

CONCLUSION

Our study shows that the economic burden of GW is closely related to psychosocial burden of disease, and health service use after a GW episode should be considered in next studies. The study of indirect costs is also important, considering the mean number of visits per episode of GW. Additional studies about both the psychological and the economic burden of GW are needed and can help the advocacy efforts for a comprehensive primary prevention program in Brazil, with the participation of the private health sector.

Conflict of interest

The study has received funding from Merck Investigator Studies Program.

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Analysis of related gene of the HLA system class I in women with cervical intraepithelial neoplasia grades II and III

Análise de Gene Relacionado ao Sistema HLA de classe I em mulheres com Neoplasia Intraepitelial Cervical de grau II e III

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Abstract of Master Dissertation submitted to the Graduate Program in Internal Medicine at the Clinics Hospital from Universidade Federal do Paraná, as part of the requirements for obtaining a degree as Master of Internal Medicine and Health Sciences.

Evaluator: Prof. Dr. Luiz Martins Colaço (UFPR) and Profª. Dra. Iara Moreno Linhares (USP).

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ABSTRACT

Objective: To evaluate the *HLA-C* gene in the progression and regression of cervical lesions caused by HPV infection, the present study aimed to analyze the genetic diversity and allelic variants of *HLA-C* gene in women CIN 2 and CIN 3 diagnosed, comparing with those without abnormalities on cervical cytology with and without the presence of infection HPV. **Materials and Methods:** The study group consisted of 84 women with CIN 2 and 90 women with CIN 3; the control group had no abnormality in cervical cytology consisted of 102 women negative for the presence of the HPV and 76 women with positive HPV infection. Samples were obtained from the metropolitan region of Curitiba-PR, Brazil, aged between 15 and 45 years old. The study group was treated in the Department of Pathology of the Cervical Erasto Gaertner Hospital, Curitiba and the control group was recruited in cervical cancer prevention campaigns promoted by public entities in association with the Department of Obstetrics and Gynecology, Hospital de Clínicas, Federal University of Parana and Histocompatibility and Immunogenetics Laboratory, Department of Genetics, UFPR. The HPV detection was performed by the Hybrid Capture 2 (CH2®) methodology. The DNA was extracted from peripheral blood samples and *HLA-C* genotyping was performed PCR-SSOP method. **Results:** Using G test it was observed that alleles *HLA-C* 05:01* (p = 0.0096), *HLA-C * 07:01P* (p = 0.0096), *HLA-C*07:02* (p = 0.0024), *HLA-C*12:03* (p = 0.0010*), HLA-C*15:02P* (p = 0.0176) and *HLAC*16:01* (p = 0.0415) were significantly more frequent in the study. The homozygous genotype *HLAC*04:01P/*04:01P* was the most frequent, reflecting the high frequency in the population studied. Allelic variants *HLA-C*05:01* (p = 0.009; OR = 4.57; 95%CI 0.5749 – 36.3774), *HLA-C*07:02* (p = 0.002; OR = 11.42; 95%CI 1.5173 – 86.2209) and *HLA-C*12:03* (p = 0.001; OR = 7.59; 95%CI 0.9886 – 58.3472) were more frequent in women with CIN than in women with no cytological abnormalities, positive for the presence of HPV. The presence of the *HLA-C*07:02* suggests susceptibility to progression of cervical intraepithelial lesion. **Conclusion:** Additional studies should be conducted to assess the significance of the risk of developing CC, especially in the context of KIR ligand HLA-C interactions in order to evaluate the interaction of immune system with the development of cervical cancer response.

Keywords: HLA-C, HPV, cervical cancer.

RESUMO

Objetivo: Para avaliar os genes *HLA-C* na progressão/regressão das lesões cervicais causadas pela infecção do HPV, *o* presente estudo teve como objetivo analisar a diversidade genética e variantes alélicos do gene *HLA-C* de mulheres com NIC 2 e NIC 3, comparando com aquelas sem anormalidades na citologia cervical com e sem a presença da infecção pelo HPV. **Materiais e Métodos:** O grupo caso foi composto por 84 mulheres com NIC 2 e 90 mulheres com NIC 3; e o grupo controle, por 102 casos controle negativo para a presença do vírus HPV e 76 casos controle positivo para a presença do HPV, sem anormalidade na citologia cervical. As amostras foram obtidas da região metropolitana de Curitiba com faixa etária entre 15 e 45 anos. O grupo de estudo foi tratado no Departamento de Patologia Cervical do Hospital Erasto Gaertner, Curitiba-PR e o grupo controle foi recrutado a partir de campanhas de prevenção do câncer cervical promovido por entidades públicas em associação ao Departamento de Tocoginecologia do Hospital de Clínicas da Universidade Federal do Paraná e Laboratório de Imunogenética e Histocompatibilidade do Departamento de Genética da UFPR. A detecção do HPV foi realizado pela metodologia da Captura Híbrida 2 (CH2®). O DNA foi extraído de amostras de sangue periférico e a genotipagem HLA-C foi feita pelo método PCR-SSOP. **Resultados:** Utilizando o teste G constatou-se que os alelos *HLA-C*05:01* (p = 0,0096), *HLA-C*07:01P* (p = 0,0096), *HLA-C*07:02* (p = 0,0024), *HLA-C*12:03* (p = 0,0010), *HLA-C*15:02P* (p = 0,0176) e *HLA-C*16:01* (p = 0,0415) foram significativamente mais frequentes no estudo. Quanto ao genótipo, o homozigoto *HLAC* 04:01P/*04:01P* foi o mais frequente, reflexo da alta frequência na população estudada. As variantes alélicas *HLA-C*05:01* (p = 0,009; OR = 4,57; IC95% 0,5749 – 36,3774), *HLA-C*07:02* (p = 0,002; OR = 11,42; IC95% 1,5173 – 86,2209) *e HLA-C*12:03* (p = 0,001; OR = 7,59 IC95%: 0,9886 – 58,3472) mostraram-se mais frequentes nas mulheres com NIC do que nas mulheres sem anormalidades citológicas e positivas para a presença do HPV. A presença do alelo HLA-C*07:02 sugere susceptibilidade a progressão da lesão intraepitelial cervical. **Conclusão:** Outros estudos complementares devem ser realizados para se avaliar o significado do risco de desenvolvimento do CC, principalmente no contexto das interações *KIR ligante HLA-C,* permitindo avaliar a interação da resposta imune com o desenvolvimento do câncer cervical.

Palavras-chave: HLA-C, HPV, câncer cervical.

Prevalence of HR-HPV and risk factors associated with the development of lesion cervical precursor of cervical cancer, a sample of the Curitiba Metropolitan Region, case-control study

Prevalência do HPV-AR e fatores de risco associados ao desenvolvimento de lesões cervicais precursoras do câncer cervical, numa amostra da região metropolitana de Curitiba, estudo caso-controle

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ABSTRACT

Objective: Characterize the risk factors associated with the development of cervical intraepithelial neoplasia (CIN) and determine the prevalence of High-risk Human Papillomavirus (HR-HPV) infection in women without cytological abnormalities and women diagnose with CIN 2 and 3, living in metropolitan region Curitiba, Paraná state, Brazil. **Materials and Methods:** Case-control study consisting of 382 women without cytological abnormalities, 233 women with high-grade intraepithelial lesions, which were subdivided in 131 women with CIN 2 and 102 women with CIN 3 diagnose by histological analysis of the cervical segment conical excision material. The age range of the women in the study was 15-45 years old, collected in the period of 2009 to 2012. The detection of HR-HPV DNA was performed by Hybrid Capture 2 test (CH2). An epidemiological questionnaire assessed the risk factors associated with the presence of HR-HPV and CIN 2/3 in each group. Statistical analysis was performed using the Chi-Square test and the G test with significance set at $p<0.05$. To adjust the effect of each variable we used the stepwise logistic regression model. **Results:** The HR-HPV was detected in 12.5% of controls, 87% in CIN 2 women and 93.1% in the CIN 3 women. Risk factors associated with the development of CIN were HR-HPV infection (OR = 62.054; 95% CI: 34.57-111.37), smoking (OR = 1.837, 95% CI: 1.061-3.178), use of hormonal contraceptives (OR = 1.845, 95% CI: 1.034-3.290), first intercourse under 15 years of age (OR = 5.046 95% CI: 2.118-12.019). Regarding the presence of HPV-HR, women under 25 years old are the most susceptible to infection ($p <0.01$), but with less chance of developing CIN (OR =0.256 95% CI: 0.095-0.684). **Conclusion:** the prevalence of HPV-HR in women with normal cytology was higher in those under 25 years of age. The HR-HPV infection, age, smoking, use of hormonal contraceptives and the age of first intercourse, were the predictors associated with the development of CIN. Women within these risk factors group are more susceptible to viral persistence and the development of CIN, therefore the use of methods for the detection of HPV-HR in this population may help reduce the incidence of CC by regular monitoring of these women.
Keywords: Cervical Intraepithelial Neoplasia, HPV, Risk Factor, Prevalence, Hybrid Capture 2.
Keywords: HLA-C, HPV, cervical cancer

RESUMO

Objetivo: Caracterizar os fatores de risco associados ao desenvolvimento de neoplasias intraepiteliais cervicais (NIC) e verificar a prevalência da infecção pelo HPV de alto risco (HPV-AR) em mulheres sem anormalidade citológicas e com NIC 2 e 3, residentes na Região Metropolitana de Curitiba, Paraná, Brasil. Materiais e **Métodos:** Estudo caso-controle, composto por 382 mulheres sem anormalidades citológicas, 233 mulheres com lesão intraepitelial de alto grau, sendo estas subdivididas em 131 mulheres com NIC 2 e 102 com NIC 3 após a análise histológica do material da excisão cônica do segmento do colo do útero. A faixa etária das mulheres do estudo foi de 15 a 45 anos, coletadas no período de 2009 a 2012. A detecção do DNA do HPV-AR foi realizada pelo teste Captura Híbrida (CH2). Um questionário epidemiológico avaliou os fatores de risco associados à presença do HPV-AR e das NIC 2/ 3 em cada grupo. A análise estatística foi realizada utilizando o teste Qui-Quadrado e o teste G com significância estabelecida em $p < 0,05$. Para ajuste de efeito de cada variável empregou-se a regressão logística modelo *stepwise*. **Resultados:** O HPV-AR foi detectado em 12,5% dos controles, 87% no grupo NIC 2 e 93,1% no grupo NIC 3. Os fatores de risco associados ao desenvolvimento de NIC foram: a infecção pelo HPV-AR (OR=62,054 IC 95%: 34,57-111,37),

tabagismo (OR= 1,837, IC 95%: 1,061-3,178), uso de anticoncepcional hormonal (OR= 1,845, IC 95%: 1,034-3,290) e a sexarca com menos de 15 anos de idade (OR= 5,046 IC95% 2,118-12,019). Em relação a presença do HPV-AR, mulheres com menos de 25 anos são as mais susceptíveis a infecção (p< 0,01), porém com menor chance de desenvolvimento de NIC (OR=0,256 IC95% 0,095-0,684). **Conclusão:** A prevalência do HPV-AR em mulheres com citologia normal foi maior naquelas com idade inferior a 25 anos. A infecção pelo HPV-AR, a idade, o tabagismo, o uso de anticoncepcional hormonal e a idade da sexarca, foram os preditores associados ao desenvolvimento das NIC. Mulheres que apresentam esses fatores de risco são mais susceptíveis à persistência viral e ao desenvolvimento de NIC, portanto a utilização de métodos para a detecção do HPV-AR nessa população pode contribuir para a redução da incidência do CC pelo acompanhamento regular dessas mulheres.
Palavras-chave: Neoplasia Intraepitelial Cervical, HPV, Fatores de Risco, Prevalência, Captura Híbrida 2.

HUMAN PAPILLOMAVIRUS PREVALENCE IN THE GENITAL TRACT OF ASYMPTOMATIC MEN: VIROLOGICAL AND EPIDEMIOLOGICAL ASPECTS

PREVALÊNCIA DA INFECÇÃO POR PAPILOMAVÍRUS HUMANO NO TRATO GENITAL DE HOMENS ASSINTOMÁTICOS: ASPECTOS VIROLÓGICOS E EPIDEMIOLÓGICOS

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ABSTRACT

Currently, genital tract infection by human papillomavirus (HPV) is the most prevalent sexually transmitted virosis in the world. However, there are still gaps in knowledge regarding the etiology of penile cancer, and the pathogenic processes of HPV in men are not completely understood, especially in cases of subclinical infections. This study aimed to determine the prevalence of HPV infection in penile swab samples, derived from a clinically asymptomatic male population. For this purpose, 261 samples were analysed, collected between 2010 and 2013 in different institutions of the city of Rio de Janeiro, including hospitals , a laboratory of clinical analysis, and a metallurgical company. Also, we have recorded epidemiological variables of 182 of these individuals, through the application of a questionnaire to aid the investigation of possible risk factors. The viral identification and typing was made by the generic and type-specific Polymerase Chain Reaction and the RFLP (Restriction Fragment Length Polimorfism) techniques, after the extraction of genetic material by the phenol-chloroform technique. The overall HPV infection prevalence was 16.47% (43 individuals). The most prevalent HPV type was the HPV 6 (34.88%), followed by HPV 11 (16.27%), HPV 16 (23.25%) , HPV 45 (9.30%) and HPV 58 (2.32%), so we have found HPV infection by the low oncogenic risk typesin 53.66%, and by the high oncogenic risk types in 46.34% of the infected individuals. The age of the studied subjects ranged between 18 and 65 years, with a mean age of 26.30 years. Among the epidemiological variables, statistical significance was found among the group of men who have sex with men, and the group which declared to have kept anal intercourse during sexual relations. There was no detection circumcised individuals. Two of the three individuals who reported having previous history of Sexual Transmitted Disease were infected. Thus, we could infer that the prevalence of the infection in the asymptomatic male population is considerable, and we believe that the results have contributed to a statistically more clear and realistic view about the behavior and epidemiology of HPV in the general male population.

Keyword: HPV, STD, men, asymptomatic, subclinical infection, PCR.

RESUMO

Atualmente, a infecção do trato genital pelo papilomavírus humano (HPV) é uma das viroses sexualmente transmissíveis mais prevalentes no mundo. Entretanto, ainda existem lacunas de conhecimento a respeito da etiologia do câncer de pênis, e os processos patogênicos do HPV no homem ainda não estão totalmente elucidados, principalmente nos casos de infecções subclínicas. Este estudo teve como objetivo determinar a prevalência da infecção por HPV em amostras de esfregaços de pênis, oriundos de uma população masculina clinicamente assintomática. Para tanto, foram analisadas 261 amostras, coletadas entre 2010 e 2013 em diferentes instituições na cidade do Rio de Janeiro, incluindo hospitais, um laboratório de análises clínicas; e uma empresa metalúrgica. Também contabilizamos variáveis epidemiológicas de 182 destes indivíduos, através da aplicação de um questionário para auxílio na investigação de possíveis fatores de risco. A identificação viral foi feita através das técnicas de Reação em Cadeia da Polimerase genérica e tipo-específica, e RFLP (*Restriction Fragment Length Polimorfism*), quando necessário, após extração de material genético pela técnica do fenol-clorofórmio. Foi encontrada uma prevalência geral para infecção por HPV de 16,47% (43 indivíduos). O tipo de HPV mais prevalente foi o HPV 6 (34,88%), seguido pelos HPV 11 (16,27%), HPV 16 (23,25%), HPV 45 (9,30%) e HPV 58 (2,32%); assim, encontramos infecção por HPV de baixo risco oncogênico em 53,66%, e de alto risco oncogênico em 46,34% dos indivíduos infectados. A idade dos indivíduos analisados variou entre 18 e 65 anos, com média de idade de 26,30 anos. Dentre as variáveis epidemiológicas estudadas, houve significância estatística para o grupo de homens que fazem sexo com homens, e para o grupo que afirmou ter mantido intercurso anal durante as relações sexuais. Não houve detecção em indivíduos circuncidados. Dois dos três indivíduos que afirmaram ter histórico de outras Doenças Sexualmente Transmissíveis se encontravam infectados. Assim, pudemos inferir que a prevalência da infecção na população masculina assintomática é considerável, e acreditamos que os resultados tenham contribuído para uma visão estatisticamente mais clara e realista a respeito do comportamento e epidemiologia do HPV na população masculina geral.

Palavras-chave: HPV, DST, homens, assintomáticos, infecção subclínica, PCR.

Impact of the association of genital infections in HIV-infected women

Impacto da associação de infecções genitais em mulheres infectadas pelo vírus HIV

Newton Sergio de Carvalho[1], Somaia Reda[2], Melissa Mazepa[3], Fernanda Aguiar Gonçalves[4]

Curitiba, November 7, 2014.
Dear Editor-in-chief,

The incidence of human immunodeficiency virus (HIV)-infected women is vertiginously raising. The virus mainly affects women at the reproductive phase, and the presence of genital co-infections is very common[1,2]. These infections may increase HIV susceptibility due to decrease in the amount of lactobacilli in the vaginal flora and consequent loss of H_2O_2 protection, break of continuity of the epithelial barrier, recruitment, and stimulation of cells that are susceptible to infection by the virus or for stimulating HIV replication[1,3]. Among the main co-infections, we have genital herpes, syphilis, bacterial vaginosis, trichomoniasis, chlamydia, gonorrhea, and candidiasis. Genital herpes together with human papilloma virus (HPV) infection is considered the most prevalent agent and, consequently, the one that can most be associated with HIV infection. This is a worsening that, when associated with HIV, has higher rates of recurrence, besides the fact that it increases the replication rate of HIV in the mucus membrane[4]. HIV changes the course of herpes virus infection and may happen in different formats of the usual clinical course[1,5]. Ulcers that persist for longer than a month suggest immunodeficiency, and HIV infection must be investigated. Its treatment should be performed in a diversified manner[6]. Genital ulcers in HIV-positive women will be more present in syphilis, however the treatment is the same as in HIV-negative women[6].

Bacterial vaginosis, depending on the microorganism involved, may increase in up to 100 times the level of genital HIV[7]. The appropriate retroviral treatment is important in these patients, since it improves CD4 cells counting and decreases occurrence of persistent infections. Trichomoniasis does not have its track modified by the HIV, but the proper treatment of this disease reduces the viral load in the vaginal secretion[6]. Chlamydia and gonorrhea are generally asymptomatic infections; however, they may evolve to pelvic inflammatory disease, especially more frequently in HIV-positive women. Furthermore, when such association is present, a clinical presentation with more severe symptoms and higher chances of evolution to ovarian abscess may happen[6].

Finally, vulvovaginal candidiasis is a high-prevalence entity in the female population. In seropositive patients, there is an increase in the frequency and severity of the symptoms[1,8]. CD4 cells counting lower than 200 cells/mm^3 and viral load higher than 10 thousand copies/mL increase the risk of worsening. Persistent forms of vulvovaginal candidiasis and those with weak response to therapy are suspicions for HIV virus co-infection[9]. It is important to emphasize that HIV presence may change the clinical presentation, course and therapeutic response of some infections, mainly in HIV-infected patients with a significant immunologic deficiency and especially in those with AIDS and high viral load.

Therefore, just as it is very important the universal tracking of HIV infection, in these patients tracking of possible genital infections should also be implemented. Thus, we will be increasing protection of HIV-infected women so that infections cannot follow other forms, which can not only deteriorate the HIV course, but also can worsen the evolution of genital co-infection, when associated. Also, by doing this we will be collaborating for decreasing transmission risk of HIV infection and similarly of the genital infections that may be associated.

The authors acknowledge it all.

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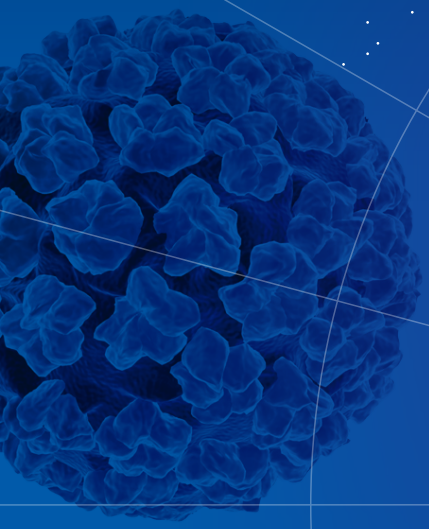

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