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Editorial

Cuba eliminates mother-to-child transmission of HIV and congenital syphilis: a call to action for the Americas Region

On June 30, 2015, the World Health Organization (WHO) validated Cuba as the first country in the world to eliminate mother-to-child transmission of HIV and congenital syphilis as public health problems. What makes this achievement especially laudable is that Cuba is a nation with limited economic resources. With an estimated Gross Domestic Product (GDP) of USD 9,900 (2010), Cuba ranks 114th of 230 nations on this global economic indicator[1].

Following the 2007 launch by WHO of the global initiative on elimination of congenital syphilis as a public health problem, in 2010, the Pan American Health Organization (PAHO) initiated a regional strategy with the broader goal of dual *Elimination of Mother-to-Child Transmission of HIV and Congenital Syphilis* (i.e., "Generations Free of HIV and Syphilis")[2]. The Americas regional initiative supports the integration of HIV and syphilis screening programs in antenatal care and builds on more than 15 years of regional commitment towards congenital syphilis elimination[3,4].

With no vaccine against either HIV or syphilis on the immediate horizon, what does it mean to eliminate mother to child transmission of HIV or syphilis "as a public health problem"? The rationale behind these initiatives takes into account that, for pregnant women with prevalent or new infections, highly effective interventions exist to prevent transmission from mother-to-child. Even when HIV or syphilis transmission continues at low levels within communities, if infections are detected and treated early in pregnancy, infants will be born free of the diseases[5].

Syphilis is an old disease that has fallen off the radar screens of many providers and the funding streams of many health ministries despite the policies for systematic antenatal syphilis screening that exist in most nations[6]. However, syphilis continues to affect about 1.4 million pregnancies each year, including approximately 107,000 pregnancies in the Americas region[7,8]. Untreated syphilis in pregnancy is often devastating, resulting in an adverse pregnancy outcome in more than half of maternal infections[9,10]. Furthermore, since the overwhelming majority of syphilis infections in pregnancy are asymptomatic, many of the perinatal deaths caused by syphilis remain undiagnosed; they are "unexplained" stillbirths, neonatal deaths, or low birth weight infants.

Prevention of mother-to-child transmission of HIV (PMTCT) is a true public health success story. Since the 1994 landmark study proving that antiretroviral medications prevent perinatal HIV transmission, increasingly successful treatment regimens have been identified[11]. Today, using an evidence-based set of comprehensive interventions, HIV transmission from mother to child can be reduced to less than 1%[12]. The situation is even simpler for syphilis: for pregnant women with syphilis, a single maternal dose of 2.4 *mu* intramuscular penicillin before 20-24 weeks gestation can treat the fetus against *T. pallidum*, the causative agent of syphilis[9,10]. Both of these prenatal interventions are recommended by WHO as part of the basic antenatal care package and are national policy in most nations[6,13]. Antenatal HIV screening and treatment are affordable even for low income countries; and antenatal syphilis screening and treatment are almost universally cost-effective and even cost-saving in many countries[14,15].

While integration of HIV and syphilis testing in the perinatal period seems an obviously beneficial approach on the surface, in real-world settings implementation has been more difficult to achieve than expected. HIV is a firmly established priority on the global health agenda, and national HIV programs are often sufficiently well-funded to be carried out to scale. However, the continued stigma associated with this infection, misconceptions about potential transmission risk (even among health providers), and "HIV exceptionalism" have made HIV screening a challenge, even in the context of PMTCT. Integration of PMTCT into routine antenatal services is often limited[16,17]. In some settings, lack of integration of the services has led to egregious missed opportunities for preventing perinatal mortality[18].

Linking antenatal HIV and syphilis screening can be a "win-win" because HIV testing is normalized, leading to higher uptake, and syphilis testing and treatment are not overlooked in poorly funded or weakly coordinated programs[19]. The development of dual rapid tests for both syphilis and HIV on a single device is a recent innovation, and several such tests are already marketed. These dual syphilis/HIV tests allow testing for both infections with a single finger prick during the antenatal care visit; thus, if either test is positive, treatment can be initiated immediately. In addition to limiting patient loss to follow up, such tests are easy to use and interpret, and can save time for busy health providers[20].

In addition to clinic based antenatal clinic services, eliminating MTCT of HIV and syphilis is supported by combined primary prevention of HIV and STIs at the community level and by reproductive health services for women. Equally important is national commitment, because fundamentally EMTCT is a policy issue that requires supportive leaders, continuing visibility, and ongoing justification for sufficient resources to sustain these basic programs. Country programs can benefit from guidance documents using approaches that are standardized and evidence-based. For example, PAHO has developed a set of operational tools to help countries

working on the priority areas of data quality, program organization and services, appropriate attention to human rights, and laboratory quality. For the Americas, laboratory infrastructure continues to be challenging in some settings. A recent survey of laboratory directors from PAHO member countries found more than 30% of laboratories providing syphilis testing for antenatal care settings did not participate in an external quality control program, and about the same proportion did not have a national syphilis testing algorithm for pregnant women. Additionally, half of all participating laboratories serving antenatal clinics reported a stock-out of one or more essential reagents or supplies during the previous year[21]. To address this situation, PAHO, in collaboration with the Ministry of Health in Brazil and the Centers for Disease Control and Prevention (CDC), published in 2015 a guidance document on syphilis testing in Latin America and the Caribbean, aimed at improving uptake, interpretation and quality of syphilis testing in different clinical and laboratory settings[22].

The WHO and PAHO targets for EMTCT of HIV and syphilis are pragmatic rather than onerous, and focus on a platform of basic maternal and child health (MCH) services rather than vertically funded programs. In the Americas, our regional goals are that countries achieve case rates of < 50 congenital syphilis cases per 100,000 live births and < 30 perinatal HIV infections per 100,000 live births, as well as a perinatal HIV transmission rate < 2% (non-breast feeding populations) for at least 2 years. Programmatically, countries must provide compelling data that these benchmarks have been achieved by also providing at least two years of data supporting that more than 95% of pregnant women are screened for HIV and syphilis, and more than 95% of women testing positive are adequately treated, in both the public and private sectors. Countries must show that EMTCT has been achieved not only at the national level but also at the country's lowest performing subnational administrative unit. This helps ensure high coverage and quality of services even among hidden or higher-risk sub-populations in which pockets of MTCT may continue to occur. Countries are also encouraged to provide data indicating that overall STI/HIV prevention services are sufficiently strong to support low community prevalence of these infections. Such programs help ensure that women become aware of their infections prior to conception and can obtain supportive services to prevent MTCT, and that women (and their partners) do not become infected or re-infected during pregnancy.

WHO estimates that each year 350,000 babies die of syphilis infection and another 240,000 are perinatally infected with HIV, dooming most to an early death[6,23]. Most of these infections occurred among women who received antenatal care services, and about one in seven of these perinatal deaths occured in the Americas region[6]. That preventable infant mortality still occurs despite the existence of an effective and affordable public health intervention (i.e., early detection and prompt treatment) is unnerving and supports EMTCT of HIV and syphilis as an appropriate call to action. No public health elimination effort is easy. However, the validation of Cuba as the first country in the world to achieve EMTCT of HIV and syphilis demonstrates the potential for every country, regardless of income level, to achieve the targets set out by WHO and PAHO[24,25]. Cuba's success was realized on the back of its strong primary health care infrastructure, well synergized health systems, and large cadre of well-trained doctors and nurses providing basic health services, free-of-charge, for all. Cuba's organized data monitoring system tracking how well targets are met also played an essential role, as did its compliance with basic human rights principles and involvement with civil society organizations. Evidence-based clinical services, surveillance and data monitoring, program evaluation and continuous feedback, effective commodities distribution, and supportive laboratory infrastructure were all integral in supporting Cuba in achieving EMTCT. These basic public health tools can help other countries in the region achieve elimination.

EMTCT of HIV and congenital syphilis are aspirational goals, but the benefits are enormous and relevant for most countries in our region. Syphilis and HIV screening and treatment are markers of antenatal care quality; and improving quality of basic MCH services supports better maternal and infant outcomes beyond the prevention of perinatal HIV and syphilis. Higher screening coverage ensures services reach the most vulnerable and hidden women who often do not reach antenatal care and contribute disproportionately to poor infant and maternal outcomes. The initiative's demands for robust, high quality interventions, laboratory systems, and data are all necessary elements for any strong national health program. Supporting the dual elimination of MTCT of HIV and syphilis is a bold step in improving health services overall. Let us hope that Cuba is only the first country in the Americas Region to achieve and sustain elimination of MTCT of HIV and syphilis through prioritizing stronger MCH systems.

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Human papillomavirus in head and neck carcinomas: prevalence and clinicopathological relationship

Papilomavírus humano em carcinomas de cabeça e pescoço: prevalência e relação clinicopatológica

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ABSTRACT

Introduction: The human papillomavirus (HPV), associated with other factors such as smoking and drinking, increases the risk of head and neck carcinomas. The presence of the HPV-16 genome, considered as highly carcinogenic, increases the risk by 50%. **Objectives:** To assess the prevalence and clinicopathological relationship of HPV associated with the head and neck carcinomas. **Methods**: This is a systematic literature review, from a bibliographical search on LILACS and MEDLINE databases. **Results:** Thirteen studies were reviewed, which altogether evaluated 1,216 cases of head and neck carcinomas, where HPV was detected, on average, in 36.45% of the cases. HPV-16 was the most prevalent genotype, present in 22 to 100% of positive cases for HPV. A higher prevalence of male subjects was observed in cases where the HPV genome was detected. A lower average age in HPV-positive cases was described in all the studies. An inverse association between the presence of HPV and habits such as smoking and alcohol consumption has been reported, with HPV seeming to be more prevalent in tumors presented by nonsmokers and nondrinkers. **Conclusion:** Despite being associated with smoking and alcohol consumption in some studies, improved prognosis and lower recurrence were reported in head and neck carcinomas with the presence of the HPV genome and a higher prevalence and growing incidence of these tumors in younger individuals.

Keywords: Papillomaviridae; head and neck neoplasm; epidemiology.

RESUMO

Introdução: O papilomavírus humano (HPV) associado a outros fatores, como tabagismo e etilismo, aumenta os riscos de surgimento de carcinomas de cabeça e pescoço, sendo que a presença do genoma do HPV 16, considerado de alto poder cancerígeno, aumenta esse risco em até 50%. **Objetivos:** Avaliar a prevalência e relação clinicopatológica do HPV associado aos carcinomas de cabeça e pescoço. **Método:** Revisão sistemática da literatura, a partir de um levantamento bibliográfico nos bancos de dados LILACS e MEDLINE. **Resultados:** Foram revisados 13 estudos que, em conjunto, avaliaram 1.216 casos de carcinoma de cabeça e pescoço onde o HPV foi detectado, em média, em 36,45% dos casos. Nos 13 estudos, o HPV 16 foi o genótipo mais prevalente, presente em 22 a 100% dos casos positivos para o HPV. Maior prevalência de indivíduos do sexo masculino nos casos em que o genoma do HPV foi detectado. Foi descrito, em todos os estudos, uma menor média de idade nos casos HPV positivo. Associação inversa entre a presença do HPV e hábitos como tabagismo e etilismo tem sido relatada, sendo que o HPV parece ser mais prevalente nos tumores de pacientes não fumantes e não etilistas. **Conclusão:** Apesar de ter sido associado ao tabagismo e etilismo em alguns estudos, foi relatado melhor prognóstico e menor recorrência em carcinomas de cabeça e pescoço que apresentam o genoma do HPV, assim como maior prevalência e uma crescente incidência desses tumores em indivíduos mais jovens.

Palavras-chave: Papillomaviridae; neoplasias de cabeça e pescoço; epidemiologia.

INTRODUCTION

Human papillomavirus (HPV) shows a high prevalence in cervical carcinomas and other genital areas. However, its prevalence and etiological relationship in head and neck carcinomas are still being investigated, and several studies have been carried out in recent years that support this idea[1-3].

Head and neck carcinomas originate from the aggression caused by chemical, physical, or biological agents that lead to the formation of differentiated cells that can develop into a tumor[4]. Changes in cell genetics lead to the formation of an abnormal process that culminates in cell proliferation, which, if not diagnosed and treated in time, cause the formation of a tumor process with unfavorable prognosis for the patient[5].

Its evolution depends on causal factors beyond the affected site. Separately, factors such as tobacco and alcohol consumption and the presence of high-risk HPV can trigger the carcinogenesis but with a lower speed and aggressiveness than when these factors are associated[6].

The prognosis of these tumors is still grim, despite the developments in diagnostic techniques and treatment, because they have low survival rates at 5 years, around 58.3% for oral cavity carcinomas and 52.7% for oropharyngeal carcinomas[7,8]. HPV vaccination campaigns are measures that can influence the natural history of cancers associated with the virus[9].

From a systematic review of literature, this study aims to present articles that investigated the prevalence of samples of HPV in head and neck carcinomas and covering the important aspects about the clinical implications of this relationship.

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METHOD

This is a systematic review of the literature, from a bibliographical search in the LILACS and MEDLINE databases. The following keywords were used: human papillomavirus; head and neck carcinoma; and prevalence. For the construction of the prevalence table, complete studies were included, which used the polymerase chain reaction (PCR) as the HPV detection method and associated findings to the clinicopathological factors of carcinomas.

RESULTS AND DISCUSSION

Studies carried out in different geographical regions have investigated the presence of HPV-DNA in head and neck carcinomas **(Table 1).** The identification of the main HPV genotypes present in these tumors was also performed in order to predict the effects of potential HPV vaccines in head and neck carcinomas.

As described in **Table 1**, the presence of HPV-DNA in the reviewed studies ranges from 5% in a study conducted in the United States that evaluated 29 tumors[13], to 100% in a study that analyzed 20 tumors in Malaysia[11]. A study in Brazil showed the presence of HPV in 19.5% of the cases evaluated[14]. In total, the 13 studies described in **Table 1** evaluated 1,216 cases of head and neck carcinomas, and HPV was detected, on average, in 36.45% of cases. In the 13 studies shown in **Table 1**, HPV-16 was the most prevalent genotype present in 22 to 100% of cases positive for HPV detection.

All the studies shown in **Table 1** used the PCR to detect the HPV genome in the carcinomas evaluated. The PCR method has a high sensitivity for the detection of viral genome, but different results can be obtained as a result of the different sets of primers used in the reaction[19].

Head and neck carcinomas have always revealed smoking and alcohol consumption as the main risk factors. From the studies conducted in the 1980s, HPV has become associated as a risk agent for these carcinomas. However, in the past 15 years, from the numerous antismoking and antialcohol campaigns around the world, many with positive results, the percentage of head and neck carcinomas associated with the virus has increased[20]. In the studies presented in **Table 1**, this relationship is clear, especially, by the presence of HPV-16, considered as of high risk, with high carcinogenic power.

The detection method of the virus genome in the samples is of fundamental importance for the survey of more accurate and reliable results. The PCR is considered a method of high sensitivity and more reliability for this type of study[21,22]. All the studies listed in **Table 1** used the PCR as the HPV detection method.

Wecan observe a high difference in the values presented in different studies, ranging from 5 to 100%. Behavioral and social factors influence the prevalence of the virus in carcinomas of one group studied. In regions where smoking and drinking rates are high, as in some European countries or in some regions within a country, this can influence a lower prevalence of HPV. However, the association between HPV and behavioral factors linked to sexual activity, particularly, oral sex, shows a considerable importance in the prevalence of the virus in these carcinomas[19].

Given the high consumption of alcohol and tobacco by young people and a greater tendency to promiscuity and a greater number of partners, the incidence of these tumors in young people is increasing, as reported in the studies on head and neck carcinomas related to HPV[23].

Studies have shown a better prognosis with greater survival rates among HPV-positive patients when compared with HPV-negative patients. Lower tendency to metastasis and fewer deaths were more common in HPV-positive groups[10]. In all the studies described in **Table 1**, there was a higher prevalence of male subjects.

The association of HPV in head and neck carcinomas reveal an important influence on the profile and clinicopathological characteristics of patients[14]. HPV-positive groups tend to present a lower average age, lower tendency to metastasize, and fewer deaths when compared with HPV-negative groups[7,10]. All the studies surveyed reported a lower average age in HPV-positive groups. HPV was associated with smoking habits in several studies[8,14,16], with no significant values that counteract a higher prevalence of HPV in groups with smoking habits.

Table 1 – Detection of HPV-DNA and genotyping of HPV-16 in patients, with head and neck squamous cell carcinomas in different countries, from 2000 to 2013.

Year	Authors	Country/region	n	HPV (%)	HPV-16 (%)
2000	Gillison *et al.*[10]	USA/Baltimore	253	25.0	90.0
2002	Ringström *et al.*[1]	USA	89	20.0	100.0
2007	Lim *et al.*[11]	Malaysia	20	100.0	30.0
2007	Gonzales *et al.*[12]	Argentina	16	43.7	28.6
2008	Simonato *et al.*[13]	USA	29	5.0	17.2
2008	Oliveira *et al.*[14]	Brazil	87	19.5	22.0
2009	Zhao *et al.*[15]	China	52	40.4	63.5
2010	Montaldo *et al.*[16]	Italy	68	60.3	51.0
2010	Hong *et al.*[6]	Australia	198	42.0	87.0
2011	Snietura *et al.*[17]	Poland	66	14.0	100.0
2011	Elango *et al.*[2]	Asia	60	50.0	96.0
2012	Huang *et al.*[18]	Taiwan	103	30.1	51.6
2013	Quintero *et al.*[8]	Colombia	175	23.9	82.0

CONCLUSION

In the 13 studies analyzed, HPV was detected, on average, in 36.45% of cases, and HPV-16 was the most prevalent genotype, present in 22 to 100% of HPV-positive cases. The highest prevalence of cases was in male subjects, and the same occurred only in cases in whom the HPV genome was detected. Lower average age, in HPV-positive cases, has been reported in all studies. An inverse association between the presence of HPV and habits such as smoking and drinking has been reported (i.e., HPV seems to be more prevalent in tumors in nonsmoking and nondrinking patients). However, HPV was associated with smoking and alcohol consumption in some studies. The best prognosis and lower recurrence are reported for the head and neck carcinomas that reveal the HPV genome and a higher prevalence of tumors in younger individuals.

Conflict of interests

The authors report no conflict of interests.

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Clinical and epidemiological profile and reproductive outcome in HIV-infected pregnant women assisted at a university hospital maternity in Vitória, Brazil

Perfil clínico e epidemiológico e desfecho reprodutivo em gestantes infectadas pelo HIV atendidas na maternidade de um hospital universitário em Vitória, Brasil

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ABSTRACT

Introduction: The infection by the human immunodeficiency virus (HIV), as well as the acquired immune deficiency syndrome (Aids), a worldwide epidemic, may lead to serious consequences in terms of maternal and fetal morbidity and mortality. **Objective:** To describe the clinical and epidemiological profiles and the reproductive outcome in HIV-infected pregnant women. **Methods:** Cross-sectional study, with 109 pregnant women infected by HIV who had their termination in a university hospital maternity in Vitória, Espírito Santo, from November 2001 to May 2012. The data were extracted from medical and public records. **Results:** The most prominent findings among the cases were average maternal age of 28 years, non-white (76.1%), up to 8 years of elementary school (63.3%), housewives (59.4%) and marital status married/cohabitation (70.6%). The nulliparous were 24.1%, and 15.7% had 3 or more childbirths, 33% had a diagnosis of HIV infection during pregnancy, and 53.7% of pregnant women met the criteria for Aids. The cesarean occurred in 82.6% of cases, preterm birth in 17.4%, and low birth weight in 23.9% and perinatal death in 4.6% of the newborns. **Conclusion:** It has been observed, in this casuistry, a pregnant women profile of low socioeconomic level. Preterm birth and perinatal death were more common than in the general population, indicating the need for preventive actions for monitoring the HIV infected pregnant women in order to reduce these events.

Keywords: HIV; pregnancy; health profile; perinatal death.

RESUMO

Introdução: A infecção pelo vírus da imunodeficiência humana (HIV), assim como a Síndrome da Imunodeficiência Adquirida (Aids), uma epidemia mundial, pode acarretar graves consequências em termos de morbidade e mortalidade materna e fetal. **Objetivos:** Descrever o perfil clínico e epidemiológico, e o desfecho reprodutivo em gestantes infectadas pelo HIV. **Métodos:** Estudo de corte transversal, com 109 gestantes infectadas pelo HIV que tiveram terminação na maternidade de um hospital universitário em Vitória, Espírito Santo, entre novembro de 2001 e maio de 2012. Os dados foram extraídos de prontuários médicos e registros públicos. **Resultados:** Os achados mais marcantes entre os casos foram idade materna média de 28 anos, pardas e negras (76,1%), até 8 anos do Ensino Fundamental (63,3%), ocupação do lar (59,4%) e casada/união estável (70,6%). Eram nulíparas 24,1%, e 15,7% com 3 ou mais partos, 33% tiveram o diagnóstico de infecção pelo HIV durante a gestação atual, sendo 53,7% das gestantes com critérios para Aids. O parto cesáreo ocorreu em 82,6% dos casos, parto pretermo em 17,4%, baixo peso ao nascer em 23,9% e morte perinatal em 4,6% dos recém-nascidos. **Conclusão:** Observou-se nesta casuística a ocorrência de um perfil de gestantes de baixo nível socioeconômico. O parto pretermo e a morte perinatal foram mais comuns que na população em geral, sinalizando para a necessidade de ações preventivas durante o acompanhamento da gestante infectada pelo HIV para redução desses eventos.

Palavras-chave: HIV; gestação; perfil de saúde; morte perinatal.

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INTRODUCTION

Infection by human immunodeficiency virus (HIV) is a worldwide epidemic, with serious consequences in terms of maternal-fetal morbidity and mortality, demanding enormous efforts and resources to their confrontation[1]. Women already represent half of people living with HIV in the world, with increasing incidence in many countries[1,2], attributed to biological[2], socioeconomic and behavioral factors[2-4].

The reproductive outcome in pregnant women infected with HIV has been studied, as well as strategies for reducing mother-to-child transmission (MTCT), due to frequent detection of the virus during the gestational period after the implementation of routine serological testing[5,6].

These studies were needed for the elaboration of more suitable care protocols to this population and the actions of information dissemination to the general population, especially women in reproductive period.

This study had as its main purpose to describe the characteristics of these women and the reproductive outcome because of the great relevance of knowing the clinical-epidemiological profile of these pregnant women, as well as the maternal and fetal consequences, in order to guide preventive intervention to reduce the impact of HIV infection on the health of the woman and the child.

OBJECTIVE

To describe the clinical and epidemiological profile of HIV infected pregnant women, as well as the reproductive outcome in them.

METHODS

A cross-sectional study was developed with HIV-infected pregnant women with parturition in the maternity ward of a university hospital, reference in the assistance of HIV infected pregnant women in the municipality of Vitória, Espírito Santo, between November 2001 and May of 2012.

Among the 250 births of HIV-infected pregnant women that occurred in this period, 109 non gemelar pregnancies, with data on gestational age (GA), HIV infection immune state (HIV and Aids) and concept data, were included in the study. It was considered preterm birth those occurred before the 37th week of gestation. The variables of this study were the demographic, clinical, laboratory, obstetric and neonatal data. The data were extracted retrospectively from medical and public records, and tabulated in Excel spreadsheet (Microsoft Office 2010) for simple frequency calculation on each category. There was no patient approach for data collection. This study has been approved by the Institution's Research Ethics Committee.

RESULTS

It was observed a frequency of 1.2% (250) of HIV infected pregnant women out of 20,942 terminations in the analyzed period. In this casuistry, 109 cases whose gestational age was confirmed by ultrasound performed until 20 weeks were included. As for the age group, 50% of pregnant women were between 24 and 32 years and 97% were in the ideal reproductive age.

It was found that 76.1% were black and browns, 63.3% with up to 8 years of elementary education, 59.4% were housewives, 70.6% were married/in stable relationship, and 86.1% were residing within the metropolitan area in Vitória **(Table 1)**.

Smoking was reported by 25.2%, alcohol use by 8.4% and illicit drugs use by 8.5% of the pregnant women. Among the patients, 34.9% made less than 6 prenatal consultations, the same being considered inadequate **(Table 2)**.

Regarding obstetric history, 24.1% were nulliparous and 15.7% had 3 or more childbirths.

As for the moment of diagnosis, it was observed that 33% of pregnant women had diagnosis of HIV infection during pregnancy

Table 1 – Demographic characteristics of HIV/Aids gestations.

Variable	All			HIV(+)			Aids		
	Ef #	F	f %	Ef #	F	f %	Ef #	F	f %
Maternal age	109			50			58		
16 to 35 years		97	89,0		46	92,0		50	86,2
>35 years		12	11,0		4	8,0		8	13,8
Race/ethinicity	109			50			58		
White		26	23,9		9	18,0		17	29,3
Brown		48	44,0		22	44,0		25	43,1
Black		35	32,1		19	38,0		16	27,6
Education	109			50			58		
Illiterate		3	2,8		1	2,0		2	3,4
1 to 4 years		31	28,4		14	28,0		17	29,3
5 to 8 years		35	32,1		18	36,0		17	29,3
9 to 11 years		37	33,9		16	32,0		20	34,5
12 or more		3	2,8		1	2,0		2	3,4
Occupation	107			48			58		
Housewife		64	59,8		28	58,3		35	60,3
Mannual		25	23,4		12	25,0		13	22,4
Other		18	16,8		8	16,7		10	17,2
Marital status	106			49			57		
Married		25	23,6		8	16,3		17	29,8
Stable union		52	49,1		27	55,1		25	43,9
Single		25	23,6		11	22,4		14	24,6
Other		4	3,8		3	6,1		1	1,8
Residence municipality	108			50			58		
Vitória		35	32,4		17	34,0		18	31,0
Others in metro Vitoria		58	53,7		26	52,0		32	55,2
Country		15	13,9		7	14,0		8	13,8

Ef #: Efective number; F: absolut frequency; f: relative frequency.

and 18.8% in previous pregnancies. Fifty-one (46.8%) became pregnant with Aids diagnosis prior. Fifty-eight cases (53.7%) presented Aids defining criteria during the study, 50 (46.3%) did not present it, and in only one case the stage of the disease was unknown. The laboratory findings relating to lymphocytes T CD4 count and viral load are shown in **Table 3**.

Regarding parturition, in 17.4% of cases the birth was vaginal, 41.1% occurred in labor, being 33.3% spontaneous and 2.8% induced. There was spontaneous rupture of membranes in 21.7% of cases **(Table 4)**. Gestational age ranged from 26 to 41 weeks, averaging 37.3±2.9 and 38 median, being 50% of the cases between 37 and 39 weeks. Preterm birth occurred in 17.4% (95%CI 10.3–24.5), and post-term delivery was not found in this study **(Table 3)**.

In the group of patients with a diagnosis of Aids, we observed one case of puerperal infection and one case of maternal death by neurotoxoplasmosis.

It was observed 54.1% of female newborn in this series. The Apgar score of less than or equal to 7 in the first minute was observed in 3.8% (95%CI 0.1–7.5).

Among all the cases, the assistance in the Neonatal Intensive Care Unit (NICU) was needed in 22.3% (95%CI 14.3–30.3). Low birth weight occurred in 23.9%, and perinatal death in 4.6% of newborns (NB) (95%CI 0.7–8.5).

Zidovudine (AZT) intravenous in prepartum was used in 93.2% of women in labour. A follow-up of more than 18 months of postnatal life was observed in 85 cases of RN in pediatric infectious diseases services, and vertical transmission (TV) was verified in 3 cases (3.5%) **(Table 5)**.

Table 3 – HIV Infection characteristics in 109 pregnacies.

Variables	Ef #	F	f %
Diagnosis moment	109		
Previous to gestation		73	
Current gestation		36	
At labour		0	20.8
Sexual partner status	55		79.2
HIV (+)		28	
HIV (-)		27	11.2
Disease duration	108		88.8
<1 year		22	
1 to 3 years		35	17.3
>3 years		51	82.7
Case classification	108		
Aids		58	0.9
Non Aids		50	99.1
Lower CD4 during gestation	93		
0 to 199		10	5.8
200 to 349		19	94.2
350 to 999		63	
>999		1	2.9
Higher viral load during gestation	88		97.1
<1000		50	
1000 to 10000		20	7.8
>10000		18	20.5

Ef #: Efective number; F: absolut frequency; f: relative frequency.

Table 2 – Gestation characteristics and current termination of 109 HIV/Aids pregnant women.

Variable	All			HIV(+)			Aids		
	Ef #	F	f %	Ef #	F	f %	Ef #	F	f %
Prenatal adequability	106			49			57		
Adequate		69	65.1		32	65.3		37	64.9
Inadequate		37	34.9		17	34.7		20	35.1
Prenatal location	104			18			33		
HUCAM		45	43.3		16	88.9		29	87.9
Other institution		59	56.7		1	5.6		4	12.1
Body Mass Index	103			48			55		
Leanness		11	10.7		6	12.5		5	9.1
Normal		64	62.1		29	60.4		35	63.6
Overweight		21	20.4		8	16.7		13	23.6
Obesity		7	6.8		5	10.4		2	3.6
Tabagism	107			50			56		
Yes		27	25.2		13	26.0		14	25.0
No		80	74.8		37	74.0		42	75.0
Ethanol use	107			50			58		
Yes		9	8.4		6	12.0		3	5.2
No		98	91.6		44	88.0		55	94.8
Illicit drug use	106			49			56		
Yes		9	8.5		5	10.2		4	7.1
No		97	91.5		44	89.8		52	92.9
Medical intercorrences	109			50			58		
Yes		51	46.8		25	50.0		26	44.8
No		58	53.2		25	50.0		32	55.2

Ef#: Efective number; F: absolut frequency; f: relative frequency

DISCUSSION

The prevalence of HIV-infected pregnant women in this study (1.2%) was greater than the observed by Miranda and collaborators in a cohort of young pregnant women, with an average of 20.2 years, during labor in Brazilian public hospitals (0.7%)[4].

Sociodemographic characteristics of pregnant women in the study **(Table 1)** make up a typical pregnant women profile seen in Brazilian public maternity hospitals, as reported in other regional studies (7.8) or Brazilians[9,10].

Knowing the sociodemographic and health profile and the prenatal monitoring of pregnant women infected with HIV is of great importance to improve welfare services and tailor strategies for prevention of adverse perinatal outcomes. Socioeconomic conditions can affect the perception of the risks of HIV contamination, which is the main reason to study this variable[11].

In a study of black women living with HIV/Aids in the State of São Paulo, it was observed the occurrence of social inequality of this population, which is seen by low schooling and inequity in accessing health services[9], also observed in our study.

Although it has been found important prevalence of smoking (25%) in this series, it was not possible to compare it with other Brazilian studies due to lack of data on this variable. This limitation has also been found by other authors in order to evaluate prevalence of tobacco, alcohol and drugs use in HIV-infected pregnant women[12].

It is important to highlight that only 65% of the women made the 6 prenatal consultations, being 43.7% at the university hospital where the study was conducted (HUCAM/UFES), and that only 62.1% had good nutritional status assessed by body mass index (BMI) prior to pregnancy (leanness in 10.7%, 20.4% in obesity and overweight in 6.8%). In Brazil, the percentage of pregnant women during prenatal care that held 6 consultation and all basic examinations, including HIV, is around 4%[13].

Taken altogether, these findings reveal several risk conditions of pregnant women infected with HIV and allow characterizing the material as a group vulnerable to bad reproductive outcome, such as prematurity and its consequences, without even considering the assault by HIV. Prenatal care is the moment to approaches for minimizing many of these risks, adopting prevention and care measures.

Table 4 – Gestation characteristics and current terminations in 109 pregnant women.

Variables	All			HIV(+)			Aids		
	Ef #	F	f %	Ef #	F	f %	Ef #	F	f %
Maternal anemia	101			46			55		
Yes		21	20.8		10	21.7		11	20.0
No		80	79.2		36	78.3		44	80.0
Arterial hypertension (chronic or PIH)	107			48			57		
Yes		12	11.2		5	10.4		7	12.3
No		95	88.8		43	89.6		50	87.7
Urinary Infection	104			47			57		
Yes		18	17.3		9	19.1		9	15.8
No		86	82.7		38	80.9		48	84.2
Diabetes mellitus	107								
Yes		1	0.9		-			-	
No		106	99.1		-			-	
Syphilis	104			47			57		
Yes		6	5.8		6	12.8		1	1.8
No		98	94.2		41	87.2		56	98.2
HSV Infection	105			49			56		
Yes		3	2.9		1	2.0		2	3.6
No		102	97.1		48	98.0		54	96.4
HPV Infection	103			47			56		
Yes		8	7.8		5	10.6		3	5.4
No		95	92.2		42	89.4		53	94.6
Labour	107			49			58		
Spontaneous		41	38.3		23	46.9		18	31.0
Induced		3	2.8		2	4.1		1	1.7
No labour		63	58.9		24	49.0		39	67.2
Membrane rupture	106			49			57		
Spontaneous		23	21.7		13	26.5		10	17.5
Artificial		83			36	73.5		47	82.5
Delivery mode	109			50			58		
Vaginal		19	17.4		14	28.0		5	8.6
Cesaerean		90	82.6		36	72.0		53	91.4

Ef #: Efective number; F: absolut frequency; f: relative frequency.

Table 5 – Fetal outcome characteristics in 109 gestations.

Variables	All			HIV(+)			Aids		
	Ef #	F	f %	Ef #	F	f %	Ef #	F	f %
Fetal gender	109			50			58		
Male		50	45.9		17	34.0		33	56.9
Female		59	54.1		33	66.0		25	43.1
Apgar index for 1st minute	104			48			56		
4 ou less		1	1.0		0	0.0		1	1.8
5 to 6		3	2.9		2	4.2		1	1.8
7 or more		101	97.1		46	95.8		54	96.4
NICU attention	103			47			56		
Yes		23	22.3		10	21.3		13	23.2
No		80	77.7		37	78.7		43	76.8
Congenital anomalies	109			50			58		
Yes		2	1.8		0	0.0		2	3.4
No		107	98.2		50	100.0		56	96.6
Perinatal death	109			50			58		
Fetal		2	1.8		1	2.0		1	1.7
Neonatal		3	2.8		1	2.0		2	3.4
Fetal birth weight	109			50			58		
<2,500 g		26	23.9		9	18.0		16	27.6
≥2,500 g		83	76.1		41	82.0		42	72.4
Vertical transmission	98			46			51		
Yes		3	3.1		2	4.3		1	2.0
No		95	96.9		44	95.7		50	98.0

Ef #: Efective number; F: absolut frequency; f: relative frequency.

The considerable frequency of diagnosis of HIV infection during current pregnancy (33%) observed in this series is similar to that described in other studies in Brazil[6,7,9,14-16] due to the practice of routine serological testing. In the study of Stefani[17], it was observed that 70% of pregnant women had the diagnosis of HIV in pregnancy or childbirth.

This fact leads us to reflect on the importance of early diagnosis of HIV infection in women of childbearing age, since some studies show that many women just know their diagnosis during the prenatal period[18].

The national policy for prevention of mother-to-child transmission of the HIV virus recommends systematic testing of pregnant women during prenatal care, as well as the antiretroviral treatment offered by the institution in cases in which the test is considered positive. Pregnant women should be notified, as well as exposed children[6], about favor control and strategizing concerning mother-to-child transmission of HIV.

The proportion of cases of pregnant women with Aids in this study (53%) was greater than the reported by Miranda[7] in the same region (28.8%) and by Lee[9] in another Brazilian State. This finding could point to possible shortcomings of risk-oriented education, being thus recommended the pre and post-conception advice for HIV+ women to opt for getting pregnant or not.[9]

It is worth noting that the largest number of cases of pregnant women with Aids in this series could be justified by a selection bias due in the case of referral hospital for high risk obstetrics.

When assessing the immune status of pregnant women in this study through the lymphocytes T CD4 count less than 200 cells/mm^3, it was observed frequency of 10.8%, less than the proportion of 14.3% reported by Melo et al.[15]; and viral load <1,000/mm^3 was observed in 56.8% of cases, similar to the 60.4% found in the study of Melo et al.[15]. This result is of great importance because in pregnant women with viral load less than 1,000 copies/mL and with more than 34 weeks the mode of delivery can be an obstetric indication.

In the present study, the vaginal birth occurred in 17.4% of cases. Spontaneous rupture of membranes above 4 hours could not be evaluated in this study precisely, which is a recognized factor associated with mother-to-child transmission of HIV, as well as the high viral load and prematurity[6].

The occurrence of preterm birth was higher than the reported in several studies of pregnant women infected with HIV[9,19,20], which

is the Brazilian average occurrence[21] and much higher than the 4.8% of the Live Birth Information System (SINASC) from Vitoria[22], corresponding to a direct increase of 12.6% (Number Needed to Treat (NNT): 7.9, Simple ratio (SR): 3.6 and OR: 4.18 (95%CI 2.37–7.35)). These data indicate the need for preventive actions for the monitoring of pregnant women infected with HIV in order to reduce these events.

In previous studies, it was not found higher frequency of puerperal infection in pregnant women infected with HIV[23,24].

Few studies report higher incidence of birth of female fetuses[25,26], which constitutes a peculiar finding of the present study, maybe relevant because there are more reports of TV for female fetuses[27].

The Apgar score was similar to that observed in SINASC[22] and lower than the 10.5% observed in 2002 Tuomala's study[28]. The occurrence of fetal death was similar to that found in the study of Lee[9] and lower than the observed by Isaacs[25], being greater than the proportion in the SINASC[22]. Several studies have reported lower prevalence of perinatal deaths than the observed in this study[15,28].

Regarding TV cases, it was observed they all occurred with some factor associated with increased transmission (syphilis, without prenatal and without art). This rate is similar to that found in another location study[7] and in other Brazilian cities[10,15,29], however was fewer than the Brazilian rate in 2001 (7.1%) and less than the rate of TV in the Southeast (7.0%)[30].

In Brazil, the rates of HIV mother-to-child transmission had decreased in the last decade due implementation of the measures of the STD/Aids program[6]. Knowing the clinical-epidemiological profile, the prenatal monitoring of pregnant women infected with HIV is of great importance to improve welfare services and tailor strategies for prevention of adverse perinatal outcomes.

CONCLUSION

The epidemiological profile of this series showed the occurrence of categories typical of a low socioeconomic level, such as low schooling and non-remunerated occupation in HIV-infected pregnant women.

Clinical and immunological profile found was of highest number of Aids cases in the HIV-infected pregnant women in this study. Regarding the reproductive outcome in children born to HIV-infected pregnant women, birth and perinatal preterm death were more common when compared with the general population.

Conflict of interests

The authors declared no conflict of interest.

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Detection of *Chlamydia trachomatis* by immunological methods in adult and adolescent female population in Cuiabá, Mato Grosso

Detecção de chlamydia trachomatis através de testes imunológicos em população feminina adolescente e adulta na grande Cuiabá, Mato Grosso

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ABSTRACT

Introduction: Worldwide, *Chlamydia trachomatis* infection remains a major public health problem, especially for sexually active young adults. **Objective:** To investigate the sexually transmitted disease by *Chlamydia trachomatis* in adolescents and young women aged 15–25 years from Cuiabá and Várzea Grande, Mato Grosso, Brazil, through the ELISA and direct immunofluorescence methods. **Methods:** A cross-sectional quantitative study of endocervical samples from 328 nonpregnant, sexually active women who received care in basic health units. Endocervical samples were collected and *C. trachomatis* antigens detected by ELISA and direct immunofluorescence methods. **Results:** A total of 11 positive samples were obtained with ELISA (3.4%) and 69 with direct immunofluorescence (24.4%). The largest number of cases occurred in the 16–25 years age group (24.39%). **Conclusion:** The rate of positive cases observed was representative, similarly to those found in other studies, and, therefore, indicating Chlamydia strains circulating in the population studied. Amplification of prophylactic, diagnostic, and therapeutic measures in public health services will be an important step to counter the spread of sexually transmitted diseases, including genital infection by *C. trachomatis* in the female population.

Keywords: *Chlamydia trachomatis*; enzyme-linked immunosorbent assay; immunologic tests.

RESUMO

Introdução: Mundialmente, a infecção por *Chlamydia trachomatis* continua sendo um importante problema de saúde pública, especialmente para adultos jovens sexualmente ativos. **Objetivo:** Investigar doença sexualmente transmissível por *Chlamydia trachomatis* em adolescentes e jovens do sexo feminino, na faixa etária de 15 a 25 anos de idade em Cuiabá e Várzea Grande, Mato Grosso, através dos métodos imunológicos de ELISA e imunofluorescência direta. **Métodos:** Estudo de corte transversal quantitativo de amostras endocervicais de 328 mulheres sexualmente ativas, não grávidas, que frequentaram as Unidades Básicas de Saúde. Amostras endocervicais foram coletadas, sendo a detecção dos antígenos de *Chlamydia trachomatis* realizada pelos métodos ELISA e imunofluorescência direta. **Resultados:** Foram obtidas 11 amostras positivas por meio do ELISA (3,4%) e 69 pela imunofluorescência direta (24,4%). Observou-se elevado número de casos entre 16 a 25 anos (24,39%). **Conclusão:** O índice de casos positivos observado foi representativo, assemelhando-se aos encontrados em outros estudos e denotando, portanto, uma circulação de cepas de clamídia na população estudada. A amplificação das medidas profiláticas, diagnósticas e terapêuticas nos serviços públicos de saúde será um passo importante para conter o avanço da doença sexualmente transmissível, inclusive a infecção genital por *Chlamydia trachomatis* na população feminina.

Palavras-chave: *Chlamydia trachomatis*; ensaio de imunoadsorção enzimática; testes imunológicos.

INTRODUCTION

The WHO estimates that there are 105.7 million new cases of *Chlamydia* worldwide, with 3 to 4 million of these only in the United States of America (USA), with over 1.4 million cases reported in 2011[1-5], 5 million in Eastern Europe, and 34 million in subSaharan Africa and southeast Asia[5-9]. Worldwide, it occurs more frequently in sexually active young adults, generally aged younger than 20 years, and it is nearly three times higher in the 14–24 years age group[5,7,9,10]. It currently represents the leading cause of female infertility, but the most common infections are urethritis and cervicitis, which, if untreated, can lead to serious consequences in the reproductive tract such as ectopic pregnancy and infertility[6,8-10]. About 50% of infected men and 70 to 75% of infected women are asymptomatic. The infection is transmitted during sexual contact and to the newborn at birth and may cause neonatal conjunctivitis or pneumonia[5,6,8-10]. Over 100 million individuals of both sexes worldwide are infected with *Chlamydia* at some point in their lives[6,9,10]. Among male subjects, the prevalence is comparable with that of risk populations, ranging from 15 to 20%, while in the asymptomatic population, it is between 3 and 7%. In female subjects, the infection rates of asymptomatic populations are between 3 and 10%, while in high-risk populations they are above 20%[1]. Because of this high prevalence, the Centers for Disease and Control Prevention in the United States (CDC) have

Study conducted in MT Laboratório, Health Secretariat of the State of Mato Grosso – Cuiabá (MT), Brazil.

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recommended an annual screening for all sexually active women aged younger than 26 years[1,11].

In Brazil, epidemiological data about the infection are scarce, with variations between 6 and 20% depending on the methodology used for the diagnosis and the population[12-14]. However, according to the STD/AIDS coordination, in Brazil, there are about two million new cases annually[5,7,15]. Although this sexually transmitted disease (STD) often occurs asymptomatically, and despite its high incidence in the human population, it is not communicable in our country[1,7,15].

Cytological analysis for the detection of *Chlamydia trachomatis*, available since 1907, was the first method used in cell samples and inclusion conjunctivitis secretions in infants[1,6]. Other methods, such as complement fixation test, cell culture, and hybrid capture, were subsequently developed, and the last two show high sensitivity and specificity[16-19]. Nowadays, modern laboratory tests are available, using immunological and molecular techniques based on nucleic acid amplification, such as polymerase chain reaction (PCR)[16-19]. Thus, faced with a scenario of limited information on the prevalence of genital CT infection in our country, particularly, in the state of Mato Grosso, this study was conducted.

OBJECTIVE

To investigate the diseases sexually transmitted by *Chlamydia* among sexually active adolescents and young adults of reproductive age, using two methods: enzyme-linked immunosorbent assay (ELISA) and direct immunofluorescence (DIF).

METHODS

Between May 2009 and December 2011, a cross-sectional quantitative study was conducted with a random input of 328 endocervical samples of sexually active young women, aged 15–25 years, who received care in the basic health units (BHU) of Cuiabá (including 56 samples from the municipality of Varzea Grande), Mato Grosso. The sample size calculation was based on the arithmetic average obtained from several prevalence values in Brazil and other Latin American countries, USA, among others, estimated at 15%, obtained in recent articles.

The women who responded to the questionnaire were considered eligible to participate in the study and signed the informed consent (IC) approved by the Research Ethics Committee of Hospital Universitário Júlio Müller da Universidade Federal de Mato Grosso (UFMT) under protocol no. 463 12/03/2008 and of Universidade Federal de São Paulo (UNIFESP) under protocol no. 076208. The patients were approached during the course of their gynecologic cancer preventive examination, according to the individual profile. Antisepsis of the external and internal genitalia was performed, according to the Clinical Microbiology Guide for Infection Control in Health Care[20], e and the STD Control Manual[21] issued by the Ministry of Health. These procedures were performed by nurses and/or nursing technicians responsible for the performance of gynecological cancer preventive examinations, who have received specific training for *Chlamydia* collection, which consisted of inserting a speculum (without lubricant) in the vagina of non-menstruating women, without any other bleeding, with no use of vaginal douches and creams the day prior, with no use of antimicrobials, and at least three days of sexual abstinence. Then, with the aid of an Ayres clamp, with cotton on the tip, moistened with water, the excess mucus was collected from the vaginal opening and the endocervix, proceeding with the further insertion of the dacron swab in the endocervical canal until the tip was no longer visible, gently rotating for a few seconds, scraping the uterine cervix, removing it, and avoiding contact with the vaginal wall. A brush was also used, whose content was deposited in two tubes containing saline solution 0.85%, one of which was used for the ELISA test and the other stored in the Virology Section of MT-Laboratório at a temperature of -70°C for further testing by molecular methods. The endocervical content used in the CT search with ELISA was placed in the refrigerator in health facilities, not exceeding a period of 48 hours, before being transported to the laboratory and stored in saline solution 0.85%. Processing of the samples was performed according to the manufacturer's instructions as described later.

The transportation of clinical specimens was performed according to the usual precautions in a Styrofoam box filled with ice and stored in a refrigerator for 48 hours until being sent to the laboratory. Upon receipt in the laboratory, the samples were placed between 2 and 8°C up to the moment of analysis, within 7 days at the most. The detection methodology employed by ELISA used the miniVIDAS® equipment, a multiparameter automated system for immunoassay that uses the enzyme-linked fluorescence assay (ELFA) technology, combining the ELISA methodology with the final fluorescence reading, which is composed of a multiparameter analytical module, a computer, and a printer.

VIDAS *Chlamydia* CHL is an automated qualitative test on the VIDAS system, which allows the detection of the fixed lipopolysaccharide antigen (LPS) *Chlamydia* from endocervical and urethral specimens using the ELFA technique through the use of specific marked monoclonal antibodies (more than ten known *Chlamydia* antigens are detected). The test exhibits a sensitivity of around 70–100% and specificity of 95%. The beginning of the assay associated an enzyme immunoassay to a final fluorescence detection (ELFA), in which the sample is subjected to suction and dispensation cycles during a given time.

For the DIF test, the endocervical samples were collected as described earlier, using another swab and conducting a smear or imprint on slides for *Chlamydia* DIF and fixed with ethanol. After the complete evaporation of the fixative, the slides were wrapped in aluminum paper and identified. All the samples from each patient, the test tube and the slides were placed in plastic bags and containers and, after identification, stored in a refrigerator until the moment they were sent to the laboratory, for the maximum period of 24 hours. These slides were subjected to the technique using a Pathfinder *C. trachomatis* Direct Specimen kit (BIO-RAD, USA), according to the manufacturer's recommendations and examined with a fluorescence microscope.

The smears were investigated for the presence of fluorescent green elementary bodies (EB). The samples were considered positive if they presented at least five inclusion bodies per slide, cut-off recommended by the manufacturer or, if fewer, when there was no doubt they were inclusion bodies rather than artifact. The absence of *Chlamydia* bodies was considered negative. After the coloration, the slides were examined under fluorescence binocular microscope (Axioscope-A1, CARL ZEISS).

Upon completion of the ELISA and DIF laboratory tests, all the patients with positive results were referred to specialists for medical treatment.

Pearson's χ^2-test, Fisher's exact test, and Student's *t*-test were used for the correlation of variables.

RESULTS

All the specimens collected were tested with the DIF and ELISA methods, with a total of 80 positive cases, of which 11 were detected by ELISA (3.4%) and 69 by the DIF method (24.4%) and 10 positive samples by ELISA were confirmed by DIF. Subsequently, a PCR test was validated using primers to amplify the gene of the major outer membrane protein (MOMP) in the Microbiology Laboratory of Universidade Federal de Mato Grosso, with 50 random samples, of which 15 were positive for CT and showed a positive correlation with the analyzed tests. The positivity rates for the different regions of the Metropolitan region of Cuiabá remained highly homogeneous, except in the western region, where a low percentage of occurrences in the population was observed. The highest number of positive cases (24.39%) occurred in the 15–25 years age group **(Table 1)**.

Variables such as drug use (3.75% of the samples), alcohol consumption (6.25% of the samples), and smoking (7.5% of the samples) and the occurrence of induced abortion (10% of positive cases) were associated with the risk of infection by CT but showed no significant difference for the population **(Table 2)** considering the significance level of 5%.

For other risk factors studied, such as risky sexual behavior, illicit drug use, use of protective barriers, age, socioeconomic status, among others, there was no association with STD positivity for CT.

As for the stratification of income, a significant portion of the positive population was poor or was informally employed **(Table 3)**.

About 50% of the positive cases were found among those who reported living together in formal or informal marriage. With regard to ethnicity, the largest portion of the study population was white, but the greatest number of positive cases was observed in the brown ethnicity (42.5%).

Regarding the number of sexual partners, approximately, 27.4% of patients reported that they possessed more than two sexual partners in the previous 12 months. The largest number of cases, however, was in the group of those with steady partner.

Table 1 – Positivity for *Chlamydia trachomatis* according to age in 328 women assisted from 2009 to 2011 in basic health units in Cuiabá, Mato Grosso.

Age range (years)	n	%	Positive	Intragroup rate (%)	Positive rate (%)
15–16	26	7.9	6	23.0	7.5
17–18	46	14	13	28.3	16.3
19–20	73	22.3	18	24.6	22.5
21–22	62	18.9	20	32.0	25.0
23–24	67	20.4	11	16.4	13.7
25	54	16.5	12	22.2	15.0
Total	328	100	80	–	100

DISCUSSION

CT is the causative pathogen of different clinical infections in humans, especially urogenital which in general are asymptomatic and can occur more frequently in subjects with high-risk sexual behavior. The severe cases are more common in women, especially in adolescents and young people up to 20 years of age [2,10]. The prevalence rates found in Brazil are variable and found by different methods[5,17,18]. According to the reports by the Health Surveillance Secretariat, STD and AIDS Program, the overall prevalence of CT infection, in 2005, was 9.2% for both sexes and 7.3% only in women[15]. The overall rates for each of the cities participating in the study, in descending order, were: Rio de Janeiro (15%), Porto Alegre (12.2%), Vitória (10.7%), São Paulo (9.1%), Manaus (7.8%), Goiânia (7.6% in the female population and 5% in asymptomatic males), and Fortaleza (4.7% for both sexes)[15,22-26]. More recent data have established a prevalence of 56.45% in the endocervical samples from 287 women in São Paulo and Santa Catarina by the PCR method[27]. In another study, conducted in Manaus, with samples from 100 pregnant women by the same method demonstrated positivity of 11%[28]. In this study, there was a high number of positive cases (24.39%) of CT in young people aged 15–25 years. This prevalence was higher than that found by Araújo in the city of Goiania, in adolescents and young women, estimated at 19.6% and lower than those found in São Paulo and Santa Catarina[27,28]. Statistical analyses of this trial demonstrated an association of the variable age with the risk of *Chlamydia* infection (p=0.0060). Therefore, we consider that the prevalence of this STD in all groups was high and, according to numerous scientific publications in this regard, our data reinforce that age is a risk factor for genital CT infection and low socioeconomic conditions.

In the Brazilian midwest, there is little epidemiological data and the number of reported cases is below estimates, suggesting

Table 2 – Positivity for *Chlamydia trachomatis* infection according to the risk factors observed in adolescents and young people assisted from May 2009 to December 2011 in basic health units in Cuiabá, Mato Grosso.

Risk factors	n	%	Positive	Intragroup rate (%)	Positive rate (%)
Drug user	8	2.4	3	37.5	3.7
Alcohol user	21	6.4	5	23.8	6.2
Smoker	19	5.8	6	31.6	7.5
Abortion history	40	12.2	8	20	10
Total	88	26.8	22	112.9	27.4

Table 3 – Positivity for genital *Chlamydia trachomatis* infection in relation to the family income of adolescents and young women served from 2009 to 2011 the basic health units in Cuiabá, Mato Grosso.

Income (R$)	n	%	Positive	Intragroup rate (%)	Positive rate (%)
Up to 700	86	26.2	24	27.9	30.0
Between 700 and 4,000	87	26.5	14	16.0	17.5
Noninformed/no income	155	47.3	42	27.1	53.7
Total	328	100.0	80	71.0	100.0

underreporting of cases. Perhaps, this is owing to the prevalence of self-medication, the lack of specialized diagnostic laboratories, misinformation, or even the lack of a better welfare policy to this STD. In Mato Grosso do Sul, a rate of 6.64% was found in a group of pregnant women using the enzyme immunoassay method[29]. In some groups with high-risk behaviors, the prevalence rates may typically vary between 20 and 30%[15]. Other STDs have been detected at a high frequency in the state of Mato Grosso, such as HIV, syphilis, human papillomavirus (HPV), and gonorrhea, among others. The increased incidence of STDs is, probably, related to a marked migration of young individuals from around the country, particularly, because the state of Mato Grosso, in recent years, has become an attractive region to those searching for better opportunities.

Regarding the use of protective measures and/or contraceptives, the highest percentage of positive cases (75%) corresponded to those who reported using a condom or the pill. Among the supporters of one of the methods, 12.5% of positive cases occurred among those who adopted oral contraceptives, and 7.5% occurred among those who used condoms as a protective barrier. With regard to the number of sexual partners and marital status, there was a higher positivity among patients who reported having a single partner and among those who said they adhered to the protective measures. The lack of association in this case may be related to the fact that women with a regular partner feel safer and do not use condoms. Although the occurrence of STDs is generally associated with sexual promiscuity, currently, there is a larger risk in monogamous individuals owing to occasional contamination of the partner in extramarital relationships. The association observed is related to the southern region of the metropolitan region of Cuiabá, where the highest number of positive cases (54%; $p<0.05$) was found. This region was situated on the outskirts of the capital, where there is a high population density, high demand for care in health centers, and a large number of individuals living in poor socioeconomic conditions.

Among the ethnic group, there was a higher number of positive cases in the mulatto group, perhaps owing to the prevalence of this phenotype in the population of Mato Grosso. However, there were no significant differences between white or black skin groups, although some authors consider the existence of differences in the prevalence of *Chlamydia* infection among ethnic groups[30,31].

Various methods are employed for the diagnosis of *Chlamydia*. Although the cell culture is considered as the gold standard for *Chlamydia* detection, with a specificity of 100%, it is a low sensitivity technique (about 50 to 80%) and complex, costly, difficult to perform, time consuming, and depends on good infrastructure but with a low probability of contamination and the advantage of allowing the performance of antimicrobial susceptibility tests, antigenic characterization, and genotyping[5,13,16-19]. On the other hand, immunological techniques are useful for screening because of their simplicity of execution, good reproducibility, and efficiency and owing to often showing a high sensitivity and specificity[16,17]. Through immunoassays, antigens such as LPS and MOMP can be detected. However, in these tests, the sensitivity, specificity, and predictive values are highly variable, being less sensitive than culture and DIF[3,13,16,19]. The advantage of these techniques takes place in specific cases, because it allows the screening of large numbers of samples, and it is also more constantly suggested for epidemiological studies and diagnoses of systemic infections[17]. In less developed regions, the use of the DIF technique is recommended, because the cold storage during transport is not necessary, and it can be applied to samples from the conjunctiva, urethra, and rectum and endocervical samples. Through this method, the EB are observed directly owing to the specific fluorescein-labeled antibody-antigen reaction[5,16,17,22]. It is a quick technique, in which only 30 minutes are sufficient to diagnose the urogenital infection, thus constituting a useful tool in diagnostic laboratories, where the cell culture and more modern and sensitive methods are not available[6,12,16,17]. As a disadvantage, the DIF exhibits the need for skilled microscopist and expensive fluorescence equipment. Intra- and interspecific cross-reactivity also occur with LPS of Gram-negative bacteria, while false-positive results are rarely observed with the use of the MOMP epitope (species-specific)[5,6,13,16,17]. The combination of two techniques, such as cell culture and immunofluorescence, was recommended as the gold standard, expanded until the middle of 1990. However, the diagnosis by PCR has replaced other techniques for its speed, more reliable reproducibility and, currently, low cost. The methods based on the amplification of nucleic acids have demonstrated a high positive predictive value, presenting the advantage of being usable with urethral, cervical, vaginal, and urine specimens[30,31].

Several factors can interfere with the determination of the prevalence of this STD, such as the laboratory resources available, ecology of the bacteria, the sexual behavior of population groups, therapeutic interference, among others. Thereby, prior studies of the population are advisable, particularly, for adolescents, combined with the choice of sensitive and specific detection methods and individualized analysis of each case[2]. Possible biases regarding our results showing a large discrepancy between the results of ELISA and DIF may be owing to several factors that are difficult to be measured, but some hypotheses can be raised. For example, the false-positive and false-negative results may occur owing to bacterial urinary tract infections, cervical mucus contamination or vaginal secretions, nonspecific antigen–antibody reactions, inappropriate collection, and transport of samples[6,16,17]. A study using the ELISA, DIF, and PCR methods in 100 urethral and endocervical samples of male and female populations under high and medium risk of *Chlamydia* infection detected positivity rates of 3, 11, and 9%, respectively[32]. Of the positive samples for DIF, 72.73% were confirmed by PCR. Further studies regarding the performance of the ELISA test were carried out in different parts of India and the world, reproducing the same results[32]. Previous studies conducted by different authors with different techniques and distinct populations obtained mixed results regarding the observed prevalence. Using the DIF test on the population of both sexes, the lowest prevalence observed was 4.4% in a study conducted in 1987, and the highest, 23.1% in the female population[33]. Using the enzyme immunoassay, the samples were analyzed for endocervical and urethral secretions, obtaining a prevalence that ranged from 1.4 to 32%, both in the male population, in a comparative study conducted in 1992 by the same author. Therefore, we can conclude that enzyme immunoassays can provide low detection rates of *Chlamydia* antigens in symptomatic patients with reduced numbers of microorganism in the secretions, often as a result of previous antimicrobial therapy[32].

CONCLUSION

The rate of positive cases observed was representative, resembling the data found in other studies and denoting, therefore, *Chlamydia* strains circulating in the population studied, which deserves more attention for the control of its spread. The conduction of prophylactic, diagnostic, and therapeutic measures in public health services will be an important step to counter the spread of STDs, including genital CT infection in the female population.

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Conflicts of interests

The authors report no conflict of interests.

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Frequency and genotyping of human papillomavirus in women submitted to citology

Frequência e genotipagem do papilomavírus humano em mulheres submetidas à citologia oncótica

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ABSTRACT

Introduction: Among the sexually transmitted virus, the human papilloma virus (HPV) is the most prevalent and may be detected a considerable number of sexually active women. He is considered the main agent of cervical cancer. Therefore, the high-risk HPV identification can aid in the prevention of cervical lesions. **Objective:** To evaluate the occurrence of HPV infections, comparing different methodologies, as well as some risk factors and their potential association in the development of cervical cancer in women submitted to cytopathology treated in ambulatory Unit Family and Community Health (USFC) of the University of Vale do Itajaí (UNIVALI). **Methods:** 118 samples were evaluated sexually active women who sought care for screening of cervical cancer in USFC and UNIVALI. All samples were subjected to polymerase chain reaction (PCR) and the liquid and conventional cytology. However, only 64 women were subjected to hybrid capture methodology (CH2). **Results:** The prevalence of HPV was 43.22% by PCR and 25% for CH2; analysis of the results was observed association between HPV and the following variables: ethnicity ($p<0.016$), scholarity ($p<0.012$), human immunodeficiency virus (HIV) ($p<0.008$), preservative ($p<0.02$), oral contraceptives ($p<0.03$), younger age at first sexual intercourse ($p<0.07$), conventional cytology ($p<0.002$) and liquid cytology ($p<0.029$). **Conclusion:** The incidence of HPV infection is high and the high-risk HPV was primarily associated with the younger age at first sexual intercourse.
Keywords: papillomaviridae; polymerase chain reaction; sexually transmitted diseases.

RESUMO

Introdução: Dentre os vírus de transmissão sexual, o papilomavírus humano (HPV) é o mais prevalente, podendo ser detectado em considerável número de mulheres sexualmente ativas. Ele é considerado o principal agente causador do câncer do colo do útero. Portanto, a identificação do HPV de alto risco pode auxiliar na prevenção de lesões do colo uterino. **Objetivo:** Avaliar a ocorrência de infecções pelo HPV, comparando diferentes metodologias, assim como alguns fatores de risco e seu potencial de associação no desenvolvimento do câncer do colo uterino em mulheres submetidas à citopatologia atendidas nos ambulatórios da Unidade de Saúde Familiar e Comunitária (USFC) da Universidade do Vale do Itajaí (UNIVALI). **Métodos:** Foram avaliadas 118 amostras de mulheres sexualmente ativas que buscaram atendimento para rastreio do câncer cervical na USFC e da UNIVALI. Todas as amostras foram submetidas à reação em cadeia da polimerase (PCR) e às citologias líquida e convencional. Entretanto, apenas 64 mulheres foram submetidas à metodologia de captura híbrida (CH2). **Resultados:** A prevalência do HPV foi de 43,22% pela técnica de PCR e de 25% pela CH2; na análise dos resultados observou-se associação do HPV com as seguintes variáveis: etnia ($p<0,016$), escolaridade ($p<0,012$), vírus da imunodeficiência humana (HIV) ($p<0,008$), preservativo ($p<0,02$), anticoncepcional ($p<0,03$), início da atividade sexual ($p<0,07$), citologia convencional ($p<0,002$) e citologia líquida ($p<0,029$). **Conclusão:** A ocorrência de infecção pelo HPV é elevada e o HPV de alto risco foi principalmente associado ao início precoce da atividade sexual.
Palavras-chave: papilomavírus humano; reação em cadeia da polimerase; doenças sexualmente transmissíveis.

INTRODUCTION

Cervical cancer is the second most common cancer among women worldwide. In Brazil, cervical cancer is the third most common tumor in women, only surpassed by breast and colorectal cancer, and the fourth leading cause of cancer death in women in the country. In the South region, this type of cancer is the fourth most frequent tumor in women (15.87/100,000); in Santa Catarina, the estimated rate is 14.97/100,000. For 2016, the occurrences of approximately 15,590 new cases in Brazil are estimated[1].

Persistent infection by human papillomavirus (HPV) is considered the main cause of cervical cancer[2] and the main way of acquiring the virus is through sexual intercourse[1]. It is estimated that 75–80% sexually active women will be infected by one or more types of HPV throughout their lives. However, 80% infections are transient and counteracted by the immune system without causing injury. The other 20% can progress to lesions that precede cervical cancer[2]. The relationship between HPV and carcinogenesis depends mainly on the type of virus and its persistence and integration with the host cell[3].

Currently, there are more than 200 known types of HPV, of which about 40 infect the genital tract. They are classified according to their oncogenic potential. Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 are classified as having high oncogenic risk, being directly related to the development of lesions and cancer. Of these, types 16 and 18 are the main etiological agents of this type cancer[4]. On the other hand, types 6, 11, 32, 40, 42, 44, 61, and 62 are

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classified as having low oncogenic risk, as they are associated with benign lesions and condyloma acuminata[5].

HPV plays a central role in the etiology of most cases of cervical cancer. However, although it is a necessary cause, it is often not sufficient for the development of cervical cancer. It is recognized that other factors, such as smoking, alcohol consumption, use of oral contraceptive, use of immunosuppression drugs, number of sexual partners, early sexual activity, and other sexually transmitted diseases (STDs), modulate, jointly with the virus, the transition of the infection to malignancy[6,7].

Histologically, cervical cancer is preceded by a series of cellular changes in the original epithelium characterized by premalignant lesions. Changes can be classified, using the Bethesda system, into atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells that cannot exclude high grade squamous intraepithelial lesion (ASC-H), low-grade squamous intraepithelial lesion (L-SIL), and high-grade squamous intraepithelial lesion (H-SIL)[8].

Papanicolaou stain method was the first way to detect changes consistent with injuries suggesting HPV infection. Even today, it is the most widely used test in screening programs for lesions that precede cervical cancer, given its scope, cost, and ease of implementation. However, it presents false-negative rates ranging from 15% to 50%. Still, over the years, the developed countries that have adopted it as a cervical cancer screening method observed a decrease in the number of cervical cancer cases[9].

To improve the sensitivity of conventional cytology (Papanicolaou), liquid-based cytology has been developed, which can be defined as a means for cell preservation that is capable of improving the quality of cell samples for analysis, as well as enabling the preservation of cell DNA. This methodology allows to automate and standardize the preparation and staining of cytological slides and facilitates molecular analysis[10].

Liquid-based cytology also allows better identification of cellular changes and a decrease in artifacts in the samples, thus reducing unsatisfactory cases. It also allows the possibility of performing additional tests, such as the molecular biology of HPV and other STDs, from the same collection[11].

Colposcopy is another test used as a strategy to detect clinical changes that may indicate possible precedent lesions of cervical cancer. The test allows the visualization of the cervix with a colposcope. It is often used to detect preinvasive diseases to prevent the development of cancer. This test is conducted in situations where the cytology detects abnormal cells, clinical examination presents alterations and in women who already underwent previous treatment for the characteristic lesions caused by HPV[12].

Over the years, the introduction of molecular biology tests with cytology (Pap smear) significantly increased the sensitivity of screening for cervical cancer[13]. Thus, screening for cervical cancer through molecular biology tests began to be considered a strategy for early screening of the virus in women. Among the methods currently available for HPV detection are hybrid capture (HCII), polymerase chain reaction (PCR), solid-phase hybridization (microrrays), and in situ hybridization[14]. Although all methods can be used for this purpose, only the HCII test, a qualitative test, is approved by the Food and Drug Administration and the Brazilian Health Surveillance Agency for the diagnosis of HPV[15].

The HCII is a method based on the hybridization of complementary RNA probes to the genomic sequences of the 18 most common types of HPV that infect the anogenital tract of sexually active men and women. These 18 types are further classified into two groups: high-risk group A (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) and low-risk group B (HPV 6, 11, 42, 43, 44).

PCR is based on the specific amplification of segments of the HPV genome, and has the potential to detect very low levels of viral load in cells and tissues, even in latent infections[14].

OBJECTIVE

To evaluate the occurrence of HPV infections, comparing different methodologies, as well as some risk factors and their potential association to the development of cervical cancer in women undergoing cytopathology, treated at the clinic of the Family and Community Health Unit (USFC) of the University of Vale do Itajaí (UNIVALI).

MATERIAL AND METHODS

A total 118 sexually active women aged 16 years and above participated in this study, randomly selected, who sought outpatient treatment at the clinic of UNIVALI for routine screening for cervical cancer by Papanicolaou (Pap smear) from August 2013 to April 2014. The study was approved by the Research Ethics Committee of UNIVALI, under the protocol number 445.967. Patients who agreed to sign the informed consent were included in the study and had cervical material collected for molecular test and conventional and liquid-based cytology.

Data collection was based on a research protocol by means of a questionnaire with objective questions answered by the patient during the consultation. The variables evaluated were age (stratified every 5 years starting from the age of 15), educational level (primary, secondary, and higher education, without discriminating whether the study was complete or incomplete), ethnicity (white, black, and brown), information on disease (which is cervical cancer, which is HPV, how to prevent), Pap smear, number of sexual partners over a lifetime (up to 5, above 5), age of onset of sexual activity (≤17 years and >17 years), previous pregnancies (none, one, or more), abortion (yes or no), previous history of other STDs, use of hormonal contraceptives and smoking.

Two samples were collected from each patient, the first with an Ayre spatula and CitoBrush for conventional cytology, and the second with the collection kit SurePath™ (BD) for molecular testing and liquid-based cytology. Conventional cytology was performed in the supporting laboratory of cytopathology under a special agreement with USFC. The liquid-based cytology was performed in a fully automated way in the Cytology Diagnostics Laboratory IN CITO (SP).

The colposcopy examination was performed in 95 patients using a colposcope to visualize the cervix under bright light, with 10–40 times magnification. The colposcopic images were analyzed after the collection of Pap smear, with application of a 5% acetic acid and/or 4% Lugol solution (Schiller).

The samples were also subjected to a molecular biology study through the HCII method by Digene & Co. in Laboratório DNAnálise (SC) for the detection of HPV DNA. This method has clinical

sensitivity of 1 pg/mL, equivalent to one virus copy per cell. The test was considered positive when the test's rate of relative light units (RLU) over two positive controls was equivalent to 1 pg/ml of HPV DNA or more. According to recent studies, this cutoff value adds greater sensitivity and specificity to the test[16].

PCR was performed in the Laboratory of Molecular Biology and Mycobacteria of Universidade Federal de Santa Catarina (UFSC-LBMM), Florianópolis. The PGMY0911 primers were used for detection of HPV DNA[17], which amplify a 450 bp segment of the HPV L1 gene. As an internal control, the PCO3/PCO4 primers[18], which amplify a 110 bp segment of the gene of human β-globin, were used. These were used as controls for the presence of inhibitors in the PCR reaction[18].

The data were stored in an Excel spreadsheet and the association between nominal variables and the positive outcome for HPV was performed by Fisher's exact test or χ^2.

To determine the correlation between the methods of diagnosis of HPV and of the lesions that precede cervical cancer (HCII, PCR, liquid-based and conventional cytology), the Kappa test was tested. Thus, the low correlation attributed for Kappa values were between 0.00 and 0.20, fair correlation had values between 0.21 and 0.40, moderate correlation was between 0.41 and 0.60, good correlation had values between 0.61 and 0.80, and excellent correlation had values between 0.81 and 1.00.

RESULTS

The collection of material was performed in 118 sexually active women. The age range was 16–69 years, mean age of 40.4 years. Fifty-two women (44.1%) were aged up to 35 years and the others (66, 55.9%) were above that age. The most prevalent age group was women above 45 years (39.8%).

The prevalence of HPV DNA was 43.22% (51/118) in the sample with PCR and 35% (23/66) with HCII.

Table 1 describes the distribution of the variables studied and their association with the presence of HPV. A significant difference was observed between women that were positive and negative for HPV in relation to the variables: ethnicity (p<0.016), education (p<0.012), human immunodeficiency virus (HIV) (p<0.008), condom use (p<0.02), oral contraceptives (p<0.03), younger age at first sexual intercourse (p<0.07), conventional cytology (p<0.002), and liquid-based cytology (p<0.029).

The frequency of HPV infection measured through the PCR methodology was higher in women aged 25 years or older (47.4%) and over 45 years (53.2%) **(Figure 1)**. Regarding the education level and ethnicity, there was a higher prevalence in brown women with higher education level (**Table 1**).

Among the analyzed patients, 15 (12.7%) did not know what cervical cancer is, 101 (85.6%) did not know what HPV is, and 64 (54.2%) did not know how to prevent themselves. Of the 118 participants, 117 had undergone the Pap smear. Sexual behavior was analyzed by the onset of sexual activity and the number of partners. As for the age of onset of sexual activity, there was a higher, statistically significant prevalence in women who started sexual activity after the age of 17 years (48.8%). Regarding the number of sexual partners, although no statistical significance was observed, a higher

Table 1 – General characteristics and risk factors of the women (n=118).

Variables	PCR-HPV (-) n (%)	PCR-HPV (+) n (%)	p-value*
Ethnicity			
White (n=102)	60 (58.8)	42 (41.2)	0.016
Black (n=12)	6 (50.0)	6 (50.0)	
Brown (n=4)	1 (25.0)	3 (75.0)	
Education level			
Primary (n=53)	33 (62.3)	20 (37.7)	0.012
Secondary (n=58)	32 (55.2)	26 (44.8)	
Superior (n=7)	2 (28.6)	5 (71.4)	
HIV			
No (n=109)	63 (57.8)	46 (42.2)	0.008
Yes (n=9)	4 (44.4)	5 (55.6)	
Smoker			
No (n=101)	58 (57.4)	43 (42.6)	0.465
Yes (n=17)	9 (52.9)	8 (47.1)	
Oral contraceptive			
No (n=77)	41 (53.2)	36 (46.8)	0.003
Yes (n=41)	26 (63.4)	15 (36.6)	
Conventional cytology			
Normal (n=116)	67 (57.8)	49 (42.2)	0.002
L-SIL (n=2)	0 (0)	2 (100.0)	
Liquid-based cytology			
Normal (n=106)	61 (57.5)	45 (42.5)	
L-SIL (n=8)	5 (62.5)	3 (37.5)	0.029
H-SIL (n=3)	1 (33.3)	2 (66.7)	
ASC-US (n=1)	0 (0)	1 (100.0)	
Onset of sexual activity			
≤17 years (n=75)	45 (60.0)	30 (40.0)	0. 07
>17 years (n=43)	22 (51.2)	21 (48.8)	
Pregnancy			
None (n=23)	11 (47.8)	12 (52.2)	0.232
One or more (n=95)	56 (58.9)	39 (41.1)	
Miscarriage			
No (n=84)	48 (57.1)	36 (42.9)	0.530
Yes (n=34)	19 (55.9)	15 (44.1)	
Number of partners			
Up to five partners (n=102)	58 (56.9)	44 (43.1)	0.585
More than five partners (n=16)	9 (56.3)	7 (43.7)	

PCR: polymerase chain reaction; HPV: human papillomavirus; ASC-US: atypical squamous cells of undetermined significance; ASC-H: atypical squamous cells that cannot exclude high-grade squamous intraepithelial lesion; L-SIL, low-grade squamous intraepithelial lesion; H-SIL, high-grade squamous intraepithelial lesion.

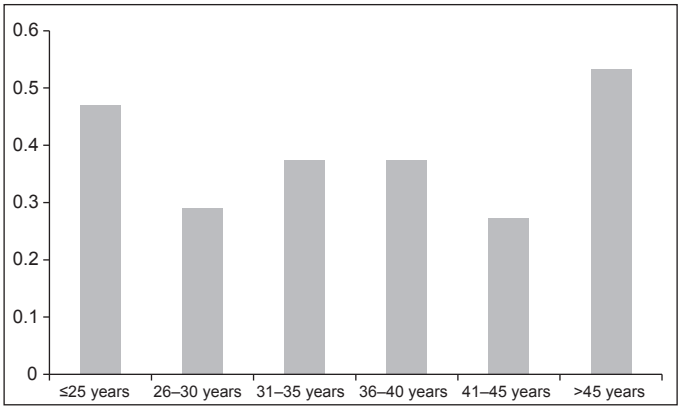

Figure 1 – Percentage distribution by age of the positive cases for polymerase chain reaction of human papillomavirus.

frequency of HPV was observed in women who had more than five partners (43.7%) (**Table 1**).

In relation to parity and abortion, no cases showed statistical significance. However, there was a higher prevalence of HPV in women who have suffered a miscarriage (44.1%) (**Table 1**).

In the assessment of STD history, we observed 55.6% positivity for HPV and HIV, with statistical significance (**Table 1**), and high prevalence of high-risk HPV in patients with STD history (83.3%) (**Table 2**).

Regarding the prevalence of HPV among patients who used oral contraceptives, 46.8% do not use oral contraceptives (**Table 1**). When analyzing only the positive cases for HPV, there was a higher frequency of low-risk HPV in contraceptive users (40%). For high-risk HPV, the frequency was higher in patients who do not use contraceptives, but without statistical significance (**Table 2**).

In relation to smoking, female smokers had a higher prevalence of HPV (47.1%) than nonsmokers (42.6%), but not significantly (**Table 1**).

When observed separately through the HCII technique, high- and low-risk HPV distribution according to age of onset of sexual activity was of 78.6% and 21.4% for women who initiated sexual activity before the age of 17 years, respectively. Regarding the number of sexual partners, between the low-risk and high-risk HPV groups, it is noted that in both categories the prevalence of the high-risk group was higher than the low-risk with statistical significance. There was also a higher prevalence of high-risk HPV (75%) in patients who have suffered at least one miscarriage (**Table 2**).

Of the 118 women, only 95 underwent colposcopy, which was positive in 47.4% of women. Twenty-eight samples (29.5%) were positive for acetic acid, and 35 (36.8%) were positive for the Schiller Test.

Regarding the conventional cytology, the frequency of HPV positivity was 100% for women with abnormal cytology (L-SIL and ASC-US) and 22.2% for women with normal cytology. In the liquid-based cytology, positivity for HPV was shown in 42.2% women with normal cytology, 37.5% women for L-SIL, 66.7% women for H-SIL, and 100% women for ASC-US (**Table 1**).

Regarding the degree of concordance between cytology techniques, there is 0.85% (one sample) of agreement between positive samples for both methodologies and 88.98% (105 samples) between the negative. Discrepancy was observed in 9.32% (11 samples), in which liquid-based cytology was positive and conventional cytology was negative. In one sample (0.85%), the liquid-based cytology was negative and conventional cytology was positive. According to the Kappa association test, there is fair correlation between the techniques (κ=0.224) (**Table 3**).

According to the results found, we evaluated the correlation and/or non-correlation between the samples analyzed. Between the HCII and PCR techniques, there are 17.2% (11 samples) correlation between the samples identified as positive and 35.9% (23 samples) correlation between the negative. Non-correlation was found in 28.1% (18 samples) samples, in which HC2 was negative, whereas the PCR showed to be positive, and 18.8% (12 samples) showed positive HCII and negative PCR. This demonstrated that there is low correlation between the techniques, according to the Kappa association test (0.037) (**Table 4**).

DISCUSSION

Because of the strong association of HPV with the appearance of cervical lesions, there are a great number of studies comparing methods used for screening cervical cancer, linking it with the main risk factors.

According to population estimates, in the general female population, the prevalence of HPV infection varies from 2% to 44%. This wide variation is due to the difference in the mean age of the populations studied and the sensitivity of the methods used to detect HPV infection[7].

These results showed a high prevalence of HPV positivity through both PCR (43.22%) and the HCII methods (35%) in the sample.

Table 2 – Distribution of positive cases for human papillomavirus (high- and low-risk) through the hybrid capture method, according to the risk factors (n=23).

Variables	Low-risk HPV	High-risk HPV	p-value*
	n (%)	n (%)	
STD			
No (n=11)	5 (45.5)	6 (54.5)	0.020
Yes (n=12)	2 (16.7)	10 (83.3)	
Oral contraceptive			
No (n=13)	3 (23.1)	10 (76.9)	0.54
Yes (n=10)	4 (40.0)	6 (60.0)	
Onset of sexual activity			
≤17 years (n=14)	3 (21.4)	11 (78.6)	0.239
>17 years (n=9)	4 (44.0)	5 (55.6)	
Miscarriage			
No (n=19)	6 (31.6)	13 (68.4)	0.085
Yes (n=4)	1 (25.0)	3 (75)	
Number of partners			
Up to five partners (n=18)	5 (27.8)	13 (72.2)	0.053
More than five partners (n=5)	2 (40.0)	3 (60.0)	

STD: sexually transmitted diseases; HPV: human papillomavirus.

Table 3 – Comparison of correlating and non-correlating results between conventional cytology and liquid-based cytology techniques.

	Negative conventional cytology	Positive conventional cytology	Total
	n (%)	n (%)	n (%)
Negative liquid-based cytology	105 (88.98)	1 (0.85)	106 (89.80)
Positive liquid-based cytology	11 (9.32)	1 (0.85)	12 (10.20)
Total	116 (98.30)	2 (1.70)	118 (100)

Table 4 – Comparison of correlating and non-correlating results between the hybrid capture and polymerase chain reaction techniques.

	Negative PCR	Positive PCR	Total
	n (%)	n (%)	n (%)
Negative HCII	23 (35.9)	18 (28.1)	41 (64.1)
Positive HCII	12 (18.8)	11 (17.2)	23 (35.9)
Total	35 (54.7)	29 (45.3)	64 (100)

PCR: polymerase chain reaction; HCII: hybrid capture.

These data corroborate those in the literature, which shows high prevalence and incidence of HPV, according to the population studied and the diagnostic method[7].

Dunne et al.[19] found a higher prevalence in women aged between 20 and 24 years. In another study, the authors observed that there is a peak in women aged below 25 years and that after that age, the prevalence declines gradually[20]. In the sample studied, the prevalence of HPV peaked in patients aged below 25 years, and then there was a new peak in patients older than 45 years. More recent epidemiological studies have described a second peak in the prevalence of HPV infection in the Americas and Africa in older women, aged around 45 years or more[20]. Since this is a cross-sectional study, it is not possible to say whether the prevalence of HPV in women over 45 years is due to the persistence of a previously acquired infection or due to reinfection.

Several sociodemographic and behavioral factors are described as risk factors for cervical cancer. Several authors point to a higher risk for cervical lesions in less educated women[21,22]. In our study, however, we found a higher prevalence of this infection in women with superior education (71.4%), followed by women with secondary education (44.8%). However, Adam et al.[21] found no association between the level of education and HPV infection. These findings demonstrate the difficulty in analyzing an isolated variable, since there are probably a combination of risk factors.

There also seems to be a relationship between early onset of sexual activity and a higher risk of acquiring HPV infection, possibly due to the increase in the exposure time to the virus[23]. In the samples analyzed, the highest prevalence was found among women who initiated sexual activity after the age of 17 years. However, when analyzed separately through the HCII method, there was evidence of a higher prevalence of high-risk group among patients with early onset of sexual activity under the age of 17 years (78.6%).

For Fedrizzi et al.[7], the high number of sexual partners is one of the main risk factors for HPV infection. The relationship between the number of sexual partners and the risk of HPV infection is found in several studies[22,23]. Our prevalence of HPV infection was 43.7% for women with more than five partners. However, it had no statistical significance. When the high- and low-risk HPV groups were analyzed separately, the prevalence of high-risk HPV was higher than the low-risk both in women with few as in those with a high number of sexual partners, with statistically significant results.

HPV infection associated with other sexually transmitted agents has been related to the development of cervical cancer[23]. In a study with Brazilian women, Cavalcanti et al.[9] reported a significant contribution of STDs in the development of cervical lesions, suggesting that they could act as cofactors in the activation of cellular transformation mechanisms or decreased local immunity in the genital tract. In this study, there was a high prevalence of high-risk HPV (83.3%) in women with a history of STDs, as well as a high frequency of HPV in women with HIV (55.6%).

Studies linking the use of oral contraceptives to the risk of cervical cancer are still controversial. It is known that HPV is responsive in vitro to the use of steroids, and that they affect and stimulate the transforming activity of viral oncogenes.

There is evidence that prolonged use of oral contraceptives, for more than 10 years, would increase the risk twice for cervical cancer, but this relationship does not seem to be present for HPV infection[7].

Noronha et al.[24] observed the contrary, women using oral contraceptives had lower risk of cervical neoplasia. In the study population, it was observed that only a small proportion of women surveyed admitted to use oral contraceptives, and the prevalence of HPV found was close to that in the group that denied using this means of contraception (46.8%).

Smoking is considered one of the most important risk factors for cervical cancer. Most of the studies that show the association of this variable with cervical cancer takes into account the duration of smoking and number of cigarettes smoked per day[25]. Moreover, according to Geller et al.[26], the prevalence of HPV in smokers is due to several mechanisms, such as the presence of carcinogenic metabolites from tobacco in cervical secretions, immunosuppression leading to viral persistence, and genomic damage (from genotoxins) to the cell.

Cavalcanti et al.[9] also found that women smokers had a higher risk of developing cervical cancer. Fedrizzi et al.[7], however, found no relationship between smoking and positivity for HPV. In our study, the prevalence of HPV DNA was higher in female smokers (47.1%) when compared to nonsmokers (42.6%), but without statistical association.

Studies comparing the two cytology techniques, conventional and liquid-based, whether with simultaneous collection or with the collection of either technique performed in different comparable patient populations, often present controversial conclusions.

There are several studies, conducted in several countries, pointing to liquid-based cytology as the most sensitive procedure for the detection of ASC-US, L-SIL and H-SIL, with greater suitability of samples and fewer unsatisfactory smears[27]. In this study, there was a similar prevalence of HPV in normal cytology results. However, for L-SIL conventional cytology had a higher frequency of HPV (100%), diverging from the literature. This could be due to liquid-based cytology having been collected after conventional cytology. Studies show that there is an increase of 64.4% in H-SIL detection in BD Sure Path™ blades. Regarding H-SIL and ASC-US, liquid-based cytology showed a higher prevalence of HPV, 66.7% and 100% respectively, confirming the data in the literature.

According to Abulafia et al.[28], the percentage of correlation between the two cytology methods is 92%. These authors also reported a higher sensitivity (76%) in liquid-based cytology than in conventional cytology, which had 68%. The liquid-based method was also more specific (86%) than the conventional method (79%) with specificity ranging from 80% to 90%. In this study, of the 118 samples analyzed by the conventional and liquid-based cytology methods, there was a correlation of 0.85%; according to the Kappa test, this correlation is fair. The samples that were negative for conventional cytology and positive for liquid-based cytology may be false-negatives, probably due to higher rates of errors in the collection and fixation on the blade, because the subject who collects the material has a greater importance in conventional cytology, often determining the quality of the test.

According to Cavalcanti et al.[9] and Jordão et al.[29], it is known that cytology is a method in which the diagnosis is somewhat subjective, and there is significant inter and intra-observer variation in cytological diagnosis, especially in L-SIL. However, the recognition of some non-classical signs in smears, such as bi or multinucleation, perinuclear halo, light dyskeratosis, and hyperchromatic nucleus,

could increase the number of cases of HPV infection diagnosed by cytology. This would be very important, since it has been found that a considerable number of negative swabs in patients showing signs that suggest virus infection, whose diagnosis is confirmed through other methods, such as, for example, biopsy and molecular techniques.

Several studies have demonstrated high correlation between the HCII and PCR techniques, reaching 76.5–90%[30]. To Saini et al.[31], PCR was more sensitive (81.8%) compared with HCII (36.4%) in detecting HPV, though HCII's specificity was much higher (96.6%) than PCR's (58.6%).

In our study, the 64 samples analyzed by the HCII and PCR methods for HPV detection, we demonstrated that HCII and PCR were in correlation in 11 samples, in which, according to the Kappa test, this correlation is low. In a study by Nomelini et al.[30], HCII showed 47.5% of positivity for high-risk HPV in the sample, whereas PCR diagnosed 87.5% of positive cases showing poor correlation between them ($\kappa<0.4$). It is believed that the failure to detect the positive samples through HCII is due to low viral load in samples, occasionally making them false-positives and false-negatives.

The samples that tested positive for the HCII and negative for the PCR techniques can be false-positive results for HCII, probably due to cross-reactivity with HPV types not detected by PCR primers, although this cannot be affirmed. Some studies have attributed these false-positive results to cross reactions with high- and low-risk probe and to the need that some samples remain near the cutoff (1 RLU)[32]. According to the standardization of the HCII test by the manufacturer (Digene), samples with RLU>1 pg/mL should be considered positive. However, some studies show that the test would be more specific if the cutoff value was around 15.56 pg/mL, making it ideal for the detection of lesions, thus reducing the possibility of false-positive results, especially in samples with viral load <100 pg/mL[15].

We also believe that PCR may have been negative due to amplification failure (inefficiency of primers) or even due to mistakes in the extraction. Lonky et al.[33] demonstrated that HCII was negative in 25% cases in which the PCR detected positive results. In situations in which the PCR was positive and the HCII was negative, we considered the PCR results because the technique is performed with primers designed for detection of high- and low-risk HPV.

CONCLUSION

This study shows that HPV DNA tests (both HCII and PCR) show higher sensitivity than the conventional and liquid-based cytology for the detection of HPV. However, if used alone, it has a lower specificity than cytology collection.

Thus, tests for the detection of HPV should be used in a complementary manner to cytology in the early detection of cervical cancer, as well as in the stratification of the risk of development of premalignant lesions. Importantly, health education has a great contribution to the field of prevention through information campaigns about cervical cancer and its risk factors. Adhesion to the monitoring programs, associated with the efficacy of diagnostic methods, is key to the success of new strategies to fight cervical cancer.

Conflict of interests

The authors report no conflict of interests.

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Perceptions about AIDS and sexual behavior among elderly people in the city of Tubarão, state of Santa Catarina, Brazil

Percepções sobre AIDS e comportamento sexual em idosos da cidade de tubarão, santa catarina

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ABSTRACT

Background: With the increase in life expectancy, coupled with the development of new technologies, such as hormone replacement therapy and medications, which help in treating impotence, there have been changes in sexual behavior among the elderly people. **Objective:** To assess the knowledge about AIDS and prevention and to determine sexual behavior and practices among elderly adults living in the city of Tubarão, state of Santa Catarina. **Methods:** A cross-sectional study was conducted on elderly residents in Tubarão, state of Santa Catarina. They received senior care at the municipal Basic Health Units in 2014. The research instrument was a questionnaire adapted from the national "Survey on Knowledge, Attitudes and Practices of the Brazilian Population," used by the Ministry of Health. **Results:** A total of 206 elderly people were surveyed (mean age, 69±6 years). Men showed a less prevalence of stable marital relationship ($p<0.001$) and earlier age at first intercourse compared with women ($p<0.001$). The demand for anti-HIV testing was higher among women than men ($p=0.028$). Of the total sample, 14.1% reported the occurrence of previous STDs, which was associated with early age at first intercourse ($p<0.001$). Regarding knowledge about AIDS and prevention methods, the average score was 15±4 from a total of 25 points. **Conclusion:** There was a greater knowledge about AIDS and prevention methods among persons in stable relationships, among those who experienced their first intercourse with casual partners, and those who underwent HIV testing. However, the average scores for AIDS prevention were low among the surveyed elderly people.

Keywords: aged; acquired immunodeficiency syndrome; HIV; sexually transmitted diseases; knowledge.

RESUMO

Introdução: Com o aumento da expectativa de vida da população aliado ao desenvolvimento de novas tecnologias, como a terapia de reposição hormonal e medicações que auxiliam no tratamento da impotência sexual, houve mudança comportamental da sexualidade entre os idosos. **Objetivo:** Verificar o conhecimento sobre síndrome da imunodeficiência adquirida (AIDS) e prevenção e determinar o comportamento e as práticas sexuais entre idosos residentes em Tubarão, Santa Catarina. **Métodos:** Foi realizado estudo transversal em idosos residentes em Tubarão, Santa Catarina, Brasil, que frequentavam grupos para esta faixa etária em unidades básicas de saúde (UBSs) do referido município no ano de 2014. O instrumento utilizado foi adaptado do questionário utilizado pelo Ministério da Saúde da pesquisa nacional intitulada "Conhecimentos, Atitudes e Práticas da População Brasileira" (PCAP). **Resultados:** Foram estudados 206 idosos com média de idade de 69±6 anos. Os homens apresentaram maior ausência de relacionamento estável ($p<0,001$) e sexarca precoce ($p<0,001$). As mulheres apresentaram maior procura pelo teste anti-HIV ($p=0,028$). Do total, 14,1% relataram ocorrência de doença sexualmente transmissível (DST) pregressa, sendo associada à sexarca precoce ($p<0,001$). Quanto ao conhecimento acerca de AIDS e prevenção, a média de acerto foi de 15±4 de um total de 25 pontos. **Conclusão:** Verificou-se um maior conhecimento sobre AIDS e prevenção em pessoas em relacionamentos estáveis, sexarca com parceiro casual, e naqueles que realizaram o teste anti-HIV. Contudo, a média de acertos relativos à prevenção a AIDS foi baixa entre os idosos.

Palavras-chave: idoso; síndrome de imunodeficiência adquirida; HIV; doenças sexualmente transmissíveis; conhecimento.

INTRODUCTION

According to the 2010 Population Census, the Brazilian population was 190,755,199 million persons, and 10.8% of the total population consisted of seniors (55.5% women and 44.5% men), where seniors are considered as any person aged 60 years or older, according to the National Policy for the Elderly and the Statute of the Elderly[1-3].

The global aging of the population is owing to the decrease in the mortality rates and in the fertility and birth rates, better sanitary conditions, increase in the level of education, nutritional factors, and advances in medicine, which is a fact nowadays[2-4]. This demographic transition causes major changes in the quality of life of this population, given that longevity can be accompanied by increased incidence of noncommunicable and communicable diseases, functional reduction, greater dependence, loss of autonomy, and social isolation[2,4].

Increased longevity, coupled with improved quality of life and health care, with the development of new technologies, such as hormone replacement therapy and other drugs that help in treating sexual impotence, allowed changes in sexual behavior among the elderly people[5,6]. However, this age group showed no sex education on preventive measures for safe sex, as the condom was used only as a contraceptive method. Another factor related to the vulnerability of the elderly people to sexually transmitted diseases (STD) is the myth of the elderly people being seen as asexual, by both the society and the health professionals. This can be attributed to the lack of information, to shame that individuals in this age group may have to seek information, to difficulties in safe sex negotiation, to excess confidence on the sexual partner, to the low level of education, and to the occurrence of extramarital affairs or promiscuity. The elderly people are not considered vulnerable to infection; the use or abuse of

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substances such as alcohol, drugs, and medicines can also occur[5,7-9]. Another associated factor is the postmenopausal period in elderly woman, when they stop using condoms as they no longer present the risk of pregnancy. However, after menopause, they become more vulnerable to infections, dryness of the vaginal walls (with the increase in complaints and the likelihood of wounds), which act as gateways to causative agents of STDs[7,10,11].

STDs make up a group of conditions related to any infectious diseases caused by microorganisms transmitted by sexual contact. Among the most common are syphilis, gonorrhea, chlamydia, human papillomavirus (HPV), and human immunodeficiency virus (HIV). The main way of HIV transmission is through sexual intercourse without condoms. HIV attacks the immune system, especially the TCD^{4+} lymphocyte, destroying them and causing deficiency in the body's immune system, leaving individuals more susceptible to other infections and cancers, which characterizes the acquired immunodeficiency syndrome (AIDS)[12]. According to the Epidemiological Bulletin of the Ministry of Health, in 2012, a total of 39,185 cases of were reported, and the AIDS incidence rate in Brazil was of 20.2 cases per 100,000 inhabitants. There has been a trend of increase in detection rates among individuals in the 15–24 years age group and among adults aged 50 or more, with a detection rate of approximately 20 cases per 100,000 inhabitants[13].

OBJECTIVE

To assess the sexual behavior and the factors associated with the risk of STD infection among persons aged 60 years or older, living in the city of Tubarão (SC). There are few studies involving sexual behavior in this age group, and there are no data in the literature on the sexuality of the elderly people in Tubarão and region.

METHODS

This study was approved by the Research Ethics Committee of Universidade do Sul de Santa Catarina under protocol no. 474.1158, compliant to Resolution 466, of 2012, by the National Health Council. All participants signed an informed consent.

A cross-sectional study was conducted with elderly residents in the city of Tubarão (SC), Brazil, who received senior care in groups for this age group in Basic Health Units (BHU) of the said municipality. According to data from the Department of Health of the Municipality of Tubarão, there were 430 seniors who routinely gathered in 30 BHUs. On the basis of this information, the sample size calculation was done considering the frequency of the outcome of 50% and a margin of error of 1%; the minimum sample required for the study was 204 elderly people, for a 95% confidence level.

We included individuals aged 60 years or older, of both the sexes, residents of Tubarão (SC), who received senior care in groups in BHUs in 2014. An intentional sampling was made among those present in the senior group meetings, and after giving their consent, they were submitted to individual interviews to collect data. The instrument used was adapted from the questionnaire used by the Ministry of Health in a national survey titled "Survey on Knowledge, Attitudes and Practices of the Brazilian Population" (PCAP)[14]. Data were collected between March and August 2014.

The variables of interest were the sociodemographic data (age, gender, race, education, marital status, and religion), knowledge about prevention and AIDS, sexual experiences and sexual initiation, sexual behaviors and practices, HIV testing, and vulnerability. The creation of the variable STD was based on the reports from the participants on the previous occurrence of any of the listed diseases: gonorrhea, trichomoniasis, syphilis, hepatitis, herpes, or some other STD, except candidiasis. With regard to knowledge about AIDS, questions were taken from the questionnaire and assigned a point for each correct answer, and a score of 0 to 25 points was attributed. For the use of the dichotomous variable, the average of correct answers was used.

The sample size was calculated using the OpenEpi software, version 2.3.1. The collected data were registered in a database created with the help of the Epidata software, version 3.1 (EpiData Association, Odense, Denmark), which is public domain, and statistical analysis was performed with the help of Statistical Product for Service Solutions (SPSS for Windows, version 20, Chicago, IL). We used the descriptive epidemiology for the presentation of data; the qualitative variables were expressed as proportions and the quantitative variables as central tendency and dispersion measures. To determine the association between the variables of interest, Pearson's χ^2-test was used for the categorical variables and Student's *t* test for comparison of the averages. The significance level was 5%.

RESULTS

A total of 206 seniors were studied, with a response rate of 100%. However, two seniors reported being virgins and, therefore, were excluded from the analysis concerning questions on sexual behavior. Of the total, 140 (68%) were women and 186 (90.3%) identified as white. The average age obtained was 69 years (SD±6 years), ranging between 60 and 87 years. The Catholic religion was predominant (99%). With regard to education, the median of years of study was 5 years, ranging between 0 and 22 years.

Table 1 shows factors related to marital status, first sexual intercourse, HIV testing, and current consumption of alcohol with distribution according to gender (male or female).

Table 1 – Influence of gender on marital status, first sexual intercourse, HIV testing, and current alcohol intake in elderly respondents (n=204).

	Total n (%)	Men n (%)	Women n (%)	p-Value
Material status				
No stable partner	38 (18.6)	35 (92.1)	3 (7.9)	<0.001
Stable partner	166 (81.4)	31 (18.7)	135 (81.3)	
First sexual intercourse				
≤15 years old	29 (14.2)	22(75.9)	7 (24.1)	<0.001
>15 years old	175 (85.8)	44(25.1)	131(74.5)	
HIV testing				
Yes	41 (19.1)	19 (46.3)	22 (53.7)	0.028
No	165 (80.9)	47 (28.5)	118 (71.5)	
Alcohol consumption (n=167)				
Yes	84 (50.3)	31 (36.9)	53 (63.1)	0.953
No	83 (49.7)	31 (37.3)	52 (62.7)	

HIV: human immunodeficiency virus.

Regarding the number of sexual partners during their lifetime, the median was 1, varying between 1 and 80 sexual partners. Considering the last month, the number of sexual partners ranged between 0 and 1, with a mean of 0 and sexual frequency of 0, ranging from 0 to 20 sexual relationships per month.

Figure 1 shows information related to the genital signs and symptoms among the elderly people according to gender.

Figure 2 shows the frequency of the reported previous STDs according to gender.

Table 2 describes the STD rate (excluding candidiasis) in relation to demographic and sexual data. There was no statistically significant difference between age (p=0.057) and education (p=0.935) compared with the previous occurrence of STDs.

Regarding the knowledge about AIDS and prevention, of the 25 questions contained in the data collection instrument, there was an average of 15 correct responses (SD±4), varying between 1 and 23 correct answers. Considering the dichotomous variable by its average, there was an association between increased knowledge about prevention and AIDS among people in stable relationships (p=0.012), among those experienced had their first sexual intercourse with a casual partner (p=0.030), and those who were already tested for HIV (p=0.009). In addition, there was a higher number of correct answers by the elderly people in a lower average age, 68 years (SD±6 years), than in those with a smaller number of correct answers on prevention and AIDS, 71 years (SD±7 years) (p=0.008). There was no difference between knowledge about prevention and AIDS in terms of education (p=0.655).

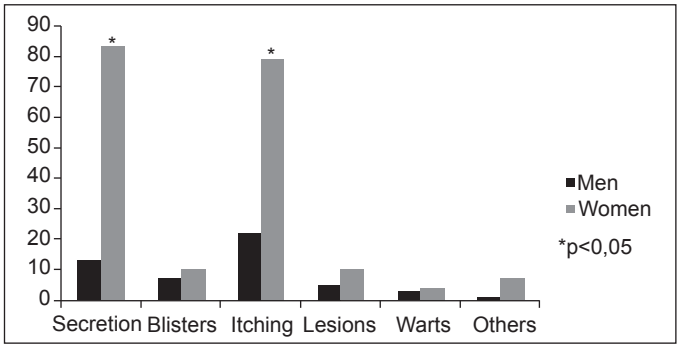

Figure 1 – Signs and symptoms related to the previous genital manifestations among the elderly interviewed people in the study (n=204).

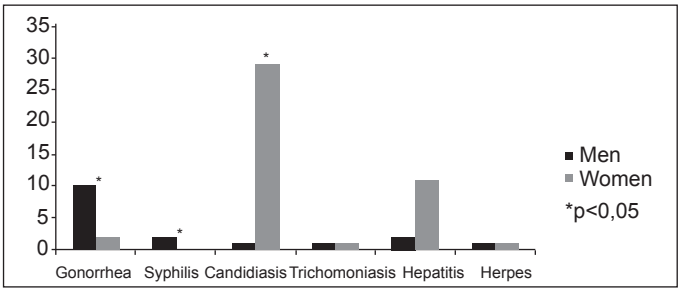

Figure 2 – History of sexually transmitted diseases reported by the elderly people interviewed in the study (n=204).

DISCUSSION

Of the 206 elderly people studied, 68% were women, and this can be explained by some reasons. Men have a higher consumption of alcohol and tobacco, being predisposed to neoplastic and cardiovascular diseases more often, increasing the mortality rate in this gender and causing greater survival among women. In addition, men have a higher exposure to industrial accidents, traffic, homicide, and suicide, and such causes are four times more common in men than in women. Women also have a different attitude toward disease, as they have greater adherence to the proposed treatments and increased demand for health services[15]. However, it is noteworthy that this study sample comes from senior groups whose women often have greater participation, and the external validity of these findings cannot be guaranteed.

Regarding race, 90.3% are self-reported as white and 9.7%, not white. These figures coincide with the National Survey by Household Sampling (PNAD), 2013, which found that the population in the south region comprised 77.8% Caucasian, 17.4% brown, 4.0% blacks, and 0.8% other races[16].

Regarding the level of education in years, the median was 5 years, characterizing a low level of education among the elderly people. Consequently, there may be difficulty in understanding the campaigns related to STDs. In this case, the information for this population should be easily understood and associated with simple vocabulary[17]. According to Souza, the level of education was established as a good indicator of socioeconomic status of individuals and of its impact on health. Throughout life, education shows to be a more stable indicator, being subject to little interference owing to changes experienced by the population or to occasional consequences resulting from sickness[18]. According to Rocha et al., seniors with lower education are more exposed to AIDS, which reinforces the importance of education as a form of preventive measure in

Table 2 – Comparison of demographic and lifestyle factors regarding the reporting of previous sexually transmitted diseases (n=204).

	Yes (%)	No (%)	p-Value
Gender			0.111
Male	13 (19.7)	53 (80.3)	
Female	16 (11.4)	124 (88.6)	
Race			0.901
White	26 (14.0)	160 (86.0)	
Non-white	3 (15.0)	17 (85.0)	
Material status			0.257
No partner	10 (11.0)	81 (89.0)	
Partner	19 (16.5)	96 (83.5)	
First sexual intercourse			<0.001
≤15 years old	12 (41.4)	17 (58.6)	
>15 years old	17 (9.7)	158 (90.3)	
Use of condom			0.532
Yes	1 (20.0)	4 (80.0)	
No	27 (13.8)	169 (86.2)	
Religion			0.262
Catholic	28 (13.7)	176 (86.3)	
Non-catholic	1 (50.0)	1 (50.0)	

combating the disease[19]. However, there was no significance in this study between the knowledge about prevention and AIDS and education level. The same was found in the PCAP survey[14] in which there was no significant statistical differences in level of education of the population aged 15–54 years. This can be explained by Oliveira et al.[20], since in 2009, there was a move toward awareness of the elderly population and a change of the belief of invulnerability, as the AIDS prevention campaigns promoted by the Ministry of Health in Brazil focused on people aged over 50 years.

Analyzing the marital status of the elderly people, it was observed that 18.6% showed no stable relationship, and 92.1% were men. This reveals greater vulnerability of this population to the acquisition of STDs and AIDS, owing to them experiencing casual sex and possibly with multiple partners. In this sense, the epidemiological study by the Ministry of Health[21] showed that the multiplicity of partners is a risk factor for the spread of STDs and HIV/AIDS. It should be noted that, however, in this study, 81.4% of participants possessed a stable partner. In this group, there is a lower perception of vulnerability, as they possess only one partner. In these circumstances, it seems that not using condoms is an option for the elderly people, because they have a stable relationship and share the idea that there is no need for any prevention method and the lack of concern for contraception. Lima[22] explains that the greater the trust between partners, the lower the awareness of vulnerability to AIDS. The author stresses that passion and love produce a favorable assessment of the loved one, inducing a secure perception about disease. In this regard, it is noteworthy that many women refuse to use condoms to avoid conflict with their partners or owing to religious beliefs, establishing a break in the marital trust. The man, when using a condom in a stable relationships, may be building a situation of mistrust, as this may be perceived as questioning loyalty, the latter being a defining and idealized factor of marriage[17].

Regarding the variable first sexual intercourse, 14.2% reported first sexual intercourse before the age of 15 years, of whom 75.9% were men. This result is similar to data found in PCAP, which showed that, in the 50–64 years age group, 20.5% reported first sexual intercourse at the age of 15 years or more, but the data were not broken down according to gender. However, throughout the population interviewed by PCAP — individuals aged 15–64 years — the percentage found of early first sexual intercourse was 36.9% for men and 17% for women[14]. For men, sexual initiation is related to the boy's transition into a man and is considered as a necessary rite of passage for the very confirmation of heterosexual masculinity and to consider oneself as a man[23]. In this study, 41.4% of those who reported early first sexual intercourse reported exposures to STD in the past, which can strengthen the issue of vulnerability in the event of early onset of sexual intercourse, multiple sexual partners, and not using condoms.

As for HIV testing, 19.1% of respondents had undergone the screening test, most of them being women. According to Berquó and Koyama, in Brazil, the adult population tested for HIV has increased from 20% in 1998 to 32.9% in 2005, but the proportion of those tested in both the sexes decreased with the increasing age range. During this period, the prevalence of men tested in the 56–65 years age range increased from 3.4 to 21.8% and women in the same age range, from 1.0 to 12.2%[24]. The low demand for the HIV test in the elderly people may show the barriers in access to early diagnosis, because of both the preconception of the elderly people (who consider themselves invulnerable to disease) and the inability of health teams in dealing with the specificities of this group[17,25]. The investigation of risk situations, especially unprotected sexual intercourse, has not been the subject of counseling actions in health services, especially in the BHU, places where more often the elderly people sought care through the Unified Health System (SUS). Failure to recognize the elderly people as subjects with sexual rights also increases their vulnerability to STD/AIDS, reducing the supply of tests with proper counseling for HIV and other STDs and, hence, early referral for treatment in specialized services[25]. A study conducted in São Paulo observed that the HIV diagnosis time in the elderly people after infection is very high, ranging from 18 months to 17 years, with an average of 8 years[26]. Regarding the greater demand for the HIV testing in women, Berquó and Koyama[24] showed that most of the tested population comprises women aged 25–39 years, a proportion explained by the incorporation of HIV testing in the prenatal care routine. According to Pinheiro et al.[27], a higher percentage of women (62.3%) was observed compared with men (46.7%) in the demand for health services in Brazil. This may often be justified by the woman being responsible for the health of the family, sometimes because of being the main caregiver of a dependent family member, and, therefore, requires greater number of procedures, including laboratory tests[28].

When asked about the signs and symptoms that may be characteristic of STDs, the most cited were genital itching (49%), secretion (46.6%), and blisters/sores/lesions (19%). These data are similar to those of a study conducted in Uberaba (MG), in which the main characteristic signs and symptoms of STDs reported by the elderly people were vaginal itching (65.2%), secretion (57.6%), and ulcers/lesions (21%)[29].

Of the elderly people interviewed, 27.2% reported experiencing an STD in the past, including candidiasis, which was the most frequent, followed by gonorrhea. The Ministry of Health places chlamydia and gonorrhea as STDs with the highest incidence in Brazil, followed by syphilis, HPV, and genital herpes, excluding candidiasis because it is not an exclusive STD[31].

As candidiasis is not always associated with sex, for it can be of endogenous origin, owing to a disruption in the normal balance of the vaginal microbiota or impaired immune system of the host, it was excluded from the analysis when comparing the rates of STDs and demographic and behavioral variables[31]. It was observed that the previous occurrence of STD reported was associated with early first sexual intercourse and multiple casual partners, being more prevalent in men. PCAP data found that the prevalence of STDs is associated with individuals who possessed multiple partners, with coinfection with other STDs and with homosexual relationships[14].

Regarding the knowledge about prevention and AIDS, an association was observed between increased knowledge about prevention and AIDS among people with stable relationships, first sexual intercourse with a casual partner, and those who have undergone HIV testing. According to Rocha et al., when the AIDS epidemic surfaced in the 1980s, the disease was labeled as specific to certain groups of people, such as sex workers, drug users, and gay men, which, thus, helped in the stereotyping of the infection and

the disease[19]. For this reason, the elderly people did not feel vulnerable, because they considered that HIV was far from their reality and ended up not seeking knowledge about this disease. But, with the advance of the epidemic over the years and greater epidemiological knowledge about the infection, the gradual change of the term "risk group" to "risk behavior" and historical context of society are important improvements to its potential for transformative action of the living conditions and health care of the population. The prevention of STD/AIDS of the elderly people depends on their awareness of the risk[27]. With the promotion of knowledge on the disease, mainly those who considered themselves invulnerable to disease are changing their thoughts on it. One example is the increased demand for HIV testing[25] and increased use of condoms. According to Berquó et al.[32], people with stable partners increased the proportion of condom use from 19.1% in 1998 to 33.1% in 2005. Regarding the first sexual intercourse with a casual partner, this was associated with greater knowledge about prevention and AIDS owing to increased vulnerability, as described, because individuals who considering themselves more susceptible to disease end up seeking more knowledge about AIDS and its prevention.

CONCLUSION

On the basis of the data from this study, we conclude that the elderly people in stable relationships, who experienced their first sexual intercourse with a casual partner, and those who have undergone HIV testing showed greater knowledge about AIDS and its prevention. However, the mean score on the prevention of AIDS was low among the elderly people.

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Conflict of interests

The authors report no conflict of interests.

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Management of syphilis in pregnant women and their newborns: is it still a problem?

Manejo de sífilis em gestantes e seus recém-nascidos: ainda um problema?

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ABSTRACT
Introduction: Congenital syphilis (CS) is a preventable disease, but its prevalence is still high in Brazil, with consequent perinatal morbidity and mortality. **Objective:** To evaluate the approach of syphilis in pregnant women and their newborns referred to the referral center of Orestes Diniz, in Belo Horizonte. **Methods:** A cross-sectional study was carried out from March 2012 to April 2013. Data collection was performed on the medical records of patients referred with CS, considering the criteria established by the Ministry of Health. Data were analyzed using SPSS and the study was approved by the Ethics Committee. **Results:** A total of 31 newborns were referred due to a positive result in maternal testing with Venereal Disease Research Laboratory during pregnancy. However, only four women have been adequately treated in accordance with the Ministry of Health. Thirteen newborns presented alterations in blood cells count, one had bone rarefactions, and 28 presented proper information of treatment. **Discussion:** When considering the adequacy of treatment according to the national guidelines, few cases of syphilis during pregnancy can be considered adequately treated. This affects the assistance to the newborn, who is often subjected to invasive investigation and extensive treatment, although most are asymptomatic. **Conclusion:** The follow-up of recommendations for the treatment of syphilis in pregnant women has often been considered inadequate, making CS difficult to eliminate.
Keywords: syphilis, congenital; infant, newborn; maternal serum screening tests; pregnant women.

RESUMO
Introdução: A sífilis congênita (SC) é um agravo prevenível, mas o Brasil ainda apresenta alta prevalência da doença, com consequente morbimortalidade perinatal. **Objetivo:** Avaliar a abordagem de sífilis em gestantes e seus recém-nascidos encaminhados para centro de referência. **Métodos:** Estudo transversal, de março de 2012 a abril de 2013. A coleta de dados foi realizada em prontuários de pacientes referenciados com SC, considerando critérios estabelecidos pelo Ministério da Saúde (MS). Os dados foram analisados pelo *Statistical Package for the Social Sciences* (SPSS) e o estudo foi aprovado pelo Comitê de Ética. **Resultados:** Um total de 31 recém-nascidos foi encaminhado devido à triagem materna com *Venereal Disease Research Laboratory* (VDRL) materno positivo durante a gestação, com 4 mulheres adequadamente tratadas. Treze recém-nascidos apresentaram alteração no hemograma e 1 apresentou alteração óssea, 28 deles com tratamento adequado. **Discussão:** Quando se considera adequação de tratamento de acordo com as diretrizes nacionais, poucos casos de sífilis na gestação são considerados adequadamente tratados. Isso impacta na assistência ao recém-nascido, que, muitas vezes, é submetido a propedêutica invasiva e tratamento extenso, embora na maioria das vezes seja assintomático. **Conclusão:** O seguimento das recomendações para o tratamento da sífilis na gestante tem sido, frequentemente, considerado inadequado, o que dificulta a eliminação da SC.
Palavras-chave: sífilis congênita; recém-nascido; testes para triagem do soro materno; gestante.

INTRODUCTION

Congenital syphilis (CS) is a preventable disease, with effective and broadly available screening, diagnosis by serological confirmation of high specificity as well as low-cost treatment[1,2].

To eradicate CS, the disease became notifiable in Brazil, for surveillance purposes, since 1986[3-6]. Data from the Syphilis Epidemiological Bulletin, 2012[1,2], still present a high incidence rate with 3.3 cases per 1,000 live births. Despite the high reporting rates to the Notifiable Diseases System (SINAN), it shows an estimated 67% of underreporting, largely due to nonuniformity in diagnosis and in conduct, as well as flaws in the notification mechanism[7,8].

But due to the persistence of endemic character of the disease in the country, the Ministry of Health launched, in 2007, the operational plan for the reduction of vertical transmission of human immunodeficiency virus (HIV) and syphilis, which aimed to implement the surveillance of syphilis in pregnant women in all municipalities, with 100% pregnant women diagnosed and treated properly, aiming to achieve less than 1 case per 1,000 live births[1,6]. However, the transmission to the fetus is still an important public health problem in Brazil, and the prevalence of syphilis among Brazilian pregnant women is 1.6%, four times higher than HIV infection, since it displays high rates of fetal impairment, with about 50% abortions, in addition to high rates of perinatal morbidity and mortality[1,9-12]. Unfavorable outcomes amount up to 66.5% cases with 4.5 times greater chance of maternal and fetal affection compared to pregnancies without the disease[13,14].

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The World Health Organization considers as part of the Millennium Development Goals the reduction of the incidence of CS, aiming at its eradication by 2015, contributing to a significant reduction in maternal and child mortality[2]. Brazil is considered a priority due to the number of pregnant women and the high prevalence of maternal syphilis[3,13].

OBJECTIVE

To evaluate the approach of syphilis in pregnant women and their newborns with a diagnosis of CS referred to the referral center in the city of Belo Horizonte, aiming at the adequacy of the procedures recommended by the Ministry of Health.

METHODS

A cross-sectional study was conducted in a referral center in Belo Horizonte from March 2012 to April 2013.

The identification of cases was carried out daily by active surveillance of patients seen at the clinic with evaluation of medical records. Data collection was performed by trained scholars in a form elaborated with information required for diagnosis, propedeutics, and treatment of syphilis in pregnant women and newborns.[1]

The study included all children who met the diagnostic criteria for CS established by the Ministry of Health in 2005. All individuals whose data collected showed inconsistencies or presented no information were excluded.

Data were collected by analyzing the medical records and were later digitized for analysis in the Statistical Package for Social Sciences (SPSS)® software, version 19.0. The project was approved by the Research Ethics Committee of Universidade Federal de Minas Gerais (UFMG).

RESULTS

A total of 31 patients with CS were reported, according to the criteria set by the Ministry of Health.

As for the serological tests conducted with pregnant women during prenatal care, we also considered 4 cases of acute infection during pregnancy, 8 cases of latent infection, and in 19 cases it was not possible to define the status of maternal infection. Variations in titers were found among positive qualitative tests of up to 1:256. There was confirmation via treponemic test in nine of those cases.

In maternity, the titers of Venereal Disease Research Laboratory (VDRL) tests of newborns in three cases were higher than the mother's, but only one such value was four times higher (**Table 1**).

In relation to maternal treatment of syphilis, 23 women were treated with penicillin during pregnancy, 22 of which used benzathine penicillin. Of the women treated with penicillin, 17 received the recommended proper dose. Only five pregnant women received treatment at least 30 days before delivery and 14 of 18 women had a decrease in VDRL titers after treatment. The partner of the pregnant woman was treated in 7 of 16 cases. Thus, four pregnant women diagnosed with syphilis were treated properly (**Table 2**).

The Fluorescent Treponemal Antibody Absorption Test (FTA-ABS) was performed in seven pregnant women. Of these, six showed positive result with VDRL titers ranging from 1:2 to 1:128. However, the patient had a negative FTA-ABS titer of 1:32.

Two children were classified as premature, with gestational age below 37 weeks. During the consultations, some alterations of the physical examination were described, but the hepatomegaly identified only in one patient was associated with CS.

Considering the complementary exams for the investigation of CS, changes were found in the blood count in 13 cases, and in the X-ray of the long bones in only 1 case. No changes were found in the cerebrospinal fluid.

In the treatment of 31 newborns, penicillin was used in 10 cases, benzathine penicillin in 7 cases, and procaine penicillin in 11 cases. In three cases, there was no information on the treatment of the child.

Serologic monitoring of newborns with CS found that only 15 patients had negative VDRL in two samples (**Table 3**).

DISCUSSION

VDRL is the method of choice for screening during pregnancy and it has high sensitivity. Any titration should be considered for confirmation with treponemic test or treatment of the pregnant women, in case confirmation and timely treatment are not possible[4,15-17]. VDRL titers may remain positive even after treatment for a long period, even after the infection was cured, due to an existing immunological memory process[15]. In this study, it was observed that, despite showing positive VDRL at some point in their pregnancy, eight patients showed no record of the treatment.

Table 1 – Venereal Disease Research Laboratory (VDRL) titrations of pregnant women during childbirth and of the first VDRL of newborns, Belo Horizonte (MG), 2012–2013.

Maternal VDRL titrations	VDRL titrations of newborns	Absolute value	%
Nonreactive	Nonreactive	1	3.2
Nonreactive	1:1	1	3.2
Qualitative reactor	1:2	1	3.2
1:2	Nonreactive	4	12.9
1:2	1:2	2	6.4
1:4	1:2	1	3.2
1:4	1:4	1	3.2
1:8	1:2	2	6.4
1:8	1:4	2	6.4
1:8	1:32	1	3.2
1:16	Nonreactive	1	3.2
1:16	1:1	1	3.2
1:32	1:4	1	3.2
1:32	1:8	6	19.2
1:32	1:16	1	3.2
1:64	Nonreactive	1	3.2
1:64	1:8	1	3.2
1:128	1:32	1	3.2
No titration	–	2	3.2

Proper treatment of pregnant women considers the following: the use of penicillin, correct dose of medication, treatment finalized 30 days before delivery, drop in VDRL titers, and partner treatment[4,5,17].

In this study, the majority of pregnant women made use of penicillin for treating syphilis, as recommended by the Ministry of Health[4,18]. Penicillin G Benzathine is more effective and more cost-effective, being the drug of choice for treatment[9,10]. Only one pregnant woman used erythromycin stearate and was considered inadequately treated. In such cases, the entire propedeutics of the newborn must be performed to begin the treatment according to the focus affected[2,4,5,10,11].

The dosage of the medication depends on what stage syphilis is[2,4,5,17]. Five cases were treated with incorrect dosage, which may be related to the use of a single dose scheme, recommended for cases of primary syphilis, similarly to the study by Mesquita et al.[11]. However, when considering the diagnosis of latent syphilis without definition of the disease stage, three doses should be administered[2,4,17].

The treatment was completed 30 days before delivery in only five cases of the eight in which this information was available. Its completion before the last month of pregnancy is of great importance to decrease transplacental transmission rates due to drug hemodilution and due to the time of action[4,11]. This reveals the importance of early diagnosis and early treatment of pregnant women.

The decrease of VDRL titration was not investigated in four pregnant women. This finding may be associated with no partner treatment, the possibility of reinfection, inadequate coverage of syphilis present in the central nervous system (CNS), or even insufficient time to check the drop in titers[4,17]. The mother's partner was treated only in seven cases, in spite of the recommendation by the Ministry of Health to treat all partners, regardless of the outcome of the VDRL. The rapid diagnostic test and treatment in Basic Health Units (BHU) aims at the ease of treatment for the mother and her partner, with increased coverage and, therefore, increased treatment efficacy[4,18,19]. In Mexico, a study showed sensitivity and specificity of 100% for the rapid test in confirmed cases with FTA-ABS[16].

Thus, only four women were found to be adequately treated, according to the criteria of the Ministry of Health. According to a study by Mesquita et al.[11], up to 14% pregnant women showed failure in the treatment due to factors such as coinfection with HIV, very high VDRL titers at baseline or childbirth, treatment started after 24 weeks, and use of inappropriate treatment regimens.

Considering the classification of the newborn, only prematurity could be related to CS. There were two cases of prematurity, below the preterm rate, with CS confirmed in the meta-analysis by Gomez et al.[13].

Of the alterations found on the physical examination, hepatomegaly is most common in infants with CS, possibly due to liver involvement by systemic dissemination of Treponema[9,10].

Up to 50% newborns with CS may be asymptomatic at birth. Because of this, serological monitoring with VDRL is recommended at 1, 3, 6, 12, and 18 months of age, and two consecutive negative serology results are required[4,17], which was observed in only 15 children. It also highlights the large percentage of children who were not kept under monitoring in referral center, for the current follow-up found consultations within 1 year of admission into the

Table 2 – Adequacy of treatment of syphilis in pregnant women, as recommended by the Ministry of Health, Belo Horizonte (MG), 2012–2013.

Category	Absolute value	%
Medication used in maternal treatment		
No	3	9.7
Crystalline penicillin	1	3.2
Erythromycin	1	3.2
Penicillin benzathine	23	74.2
Treated, no information on medication	3	9.7
Use of penicillin in the treatment		
Yes	24	77.4
No	1	3.2
No information	3	9.7
Not treated	3	9.7
Correct dose of penicillin		
Yes	17	54.8
No	5	16.1
No information	8	25.6
Penicillin not used	1	3.2
Treatment completed 30 days before delivery		
Yes	5	16.1
No	3	9.7
No information	23	74.2
Maternal partner treated		
Yes	7	22.6
No	9	29.0
No information	15	48.4
Drop in VDRL rates		
Yes	14	41.9
No	4	12.9
No information	13	42.0
Syphilis adequately treated		
Yes	4	12.9
No	4	12.9
No prior information	23	74.2

VDRL; Venereal Disease Research Laboratory.

Table 3 – Monitoring of Venereal Disease Research Laboratory (VDRL) serology of newborns monitored due to the diagnosis of congenital syphilis, Belo Horizonte (MG), 2012–2013.

Follow-up	Absolute value	%
Follow-up with positive dropping VDRL	2	3.2
Follow-up with 1 negative VDRL	10	32.2
Follow-up with 2 nonreactive VDRL	15	48.3
No VDRL after delivery	4	12.9

VDRL: Venereal Disease Research Laboratory.

service. Only two cases maintained decrease of VDRL titers and continued to follow-up.

It was observed that the majority of infants presenting positive VDRL, but with titer values below the maternal ones. The study by Barsanti et al.[20], conducted in the city of São Paulo, also revealed that there is a high concordance in maternal and newborn positive VDRL, as well as maternal titer values greater than or equal to that of newborns.

Only two cases followed with positive VDRL titers and were still positive in follow-up. None of the children underwent treponemic test at 18 months, as recommended by the Ministry of Health[4,17], which is very important to confirm or exclude the diagnosis.

For the treatment of newborns with CS, the drug of choice again is penicillin. All children of inadequately treated mothers, those who presented reactive treponemal serology or patients with clinical, radiological, or cerebrospinal indication of CS must be treated[4,17]. All newborns monitored met these criteria and were treated with crystalline or procaine penicillin, and procaine penicillin can be used when there was no involvement of the CNS. Benzathine penicillin was used in six cases with nonreactive VDRL, what can be done when propedeutics and laboratory tests for the investigation of target organs do not present changes[4,17].

The laboratory follow-up of CS carriers is an important measure to evaluate the involvement by the disease. Of the haematological abnormalities found, the characteristics of CS are anemia, leukocytosis, and lymphocytosis[4,9,12,19]. There was only one case (3.2%) with thinning of the periosteum. The changes found in the long bones, such as osteochondritis, osteitis, and periostitis, are common in CS and virtually all newborns that were affected but asymptomatic at birth can develop bone deformities in case of late CS[2,4].

The adoption of public health measures, such as diagnosis by rapid test and broad access to treatment with penicillin for the pregnant woman and her partner, is a major breakthrough in trying to eradicate CS[4,10,18]. The difficulty of some primary care centers to manage potential complications of the use of penicillin, such as anaphylaxis, may limit its use, but there is a recommendation that the treatment of pregnant women and their partners be still held in BHU[10,18]. The training of professionals is necessary to expand the access to these services to the users.

CONCLUSION

Despite policies to eradicate CS, inadequate compliance to the recommendations for the treatment of syphilis in pregnant women is still observed, with the need for extensive propedeutics and treatment of the newborn. Considering the epidemiology of the disease, the awareness of professionals and facilitation of the recommended actions are still of utmost importance in eradicating CS.

Conflict of interests

The authors report no conflict of interests.

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KNOWLEDGE AMONG COLLEGE STUDENTS AND EMPLOYEES OF LOCAL HEALTH UNITS ABOUT HUMAN PAPILLOMAVIRUS AND CERVICAL CANCER AND ITS IMPLICATIONS FOR PUBLIC HEALTH STRATEGIES AND VACCINATION

CONHECIMENTO ENTRE ESTUDANTES UNIVERSITÁRIOS E FUNCIONÁRIOS DE UNIDADES LOCAIS DE SAÚDE SOBRE PAPILOMAVÍRUS HUMANO E CÂNCER CERVICAL E SUAS IMPLICAÇÕES PARA ESTRATÉGIAS DE SAÚDE PÚBLICA E VACINAÇÃO

Walkíria Rodrigues de Freitas[1], Edison Natal Fedrizzi[2], Fabiana Gonçalves de Aguiar[3]

ABSTRACT

Introduction: Human papillomavirus (HPV) is the most commonly diagnosed sexually transmitted infection worldwide. It is estimated that 70% of cervical cancer cases are related to high-risk HPV 16 and 18 types; and 90% of genital warts to HPV 6 and 11. Despite its prevalence and significant associated morbidity, the knowledge about the infection and its prevention remain limited. **Objective**: To evaluate the knowledge about HPV, its relation to cervical cancer and genital warts and the HPV vaccine among students of The Federal University of Santa Catarina and employees of local health units in the city of Florianópolis, Santa Catarina, Brazil. **Methods**: A descriptive cross-sectional analysis with 136 college students from the health care area or not and 77 employees from local health units, assessed through questionnaires including demographic data, lifestyle habits, characteristics of HPV infection and HPV vaccine. Data were analyzed using IBM software programs SPSS 20.0 and Epi Info 6.04, and the possible associations between variables were tested using the χ^2 test. **Results**: 94,3% of participants reported knowledge about HPV, and 77,93% about HPV vaccine. HPV was identified as causing cervical cancer by 67,86% of the subjects in school, 55,22% of individuals from higher education without training in health and 94,91% of individuals with training in health. Only 3,75% of the respondents received the vaccine, despite 90,61% saying that would allow their child to receive it. **Conclusion**: Knowledge about HPV infection, its consequences and prevention, both in people in school and in higher education is still very limited.
Keywords: Papillomaviridae; Papillomavirus vaccines; Papillomavirus infections; public health.

RESUMO

Introdução: O papilomavírus humano (HPV) é a infecção sexualmente transmissível mais diagnosticada em todo o mundo. Estima-se que 70% dos casos de câncer cervical estejam relacionados aos tipos de HPV de alto risco 16 e 18 e 90% das verrugas genitais aos tipos 6 e 11. A despeito de sua grande incidência e da importante morbidade associada, o conhecimento sobre a infecção e sobre suas formas de prevenção permanecem limitados. **Objetivo:** Avaliar o conhecimento sobre o HPV, sua relação com o câncer de colo de útero e verrugas genitais e sobre a vacina contra o HPV, entre estudantes da Universidade Federal de Santa Catarina e funcionários de unidades locais de saúde do município de Florianópolis. **Métodos:** Trata-se de um estudo transversal e descritivo, no qual 136 universitários da área da saúde ou não e 77 funcionários de unidades locais de saúde foram avaliados através de questionários incluindo dados demográficos, hábitos de vida, características da infecção pelo HPV e da vacina contra o HPV. Os dados foram analisados com o uso dos programas IBM Software SPSS 20.0 e Epi Info 6.04 e as possíveis associações entre as variáveis foram verificadas com o teste do χ^2. **Resultados:** 94,3% dos participantes afirmaram conhecimento sobre o HPV e 77,93% sobre a vacina contra o HPV. O HPV foi identificado como causador do câncer de colo de útero por 67,86% dos indivíduos de ensino médio/básico, 55,22% dos indivíduos de ensino superior sem formação na área da saúde e 94,91% dos indivíduos com formação na área da saúde. Apenas 3,75% dos entrevistados receberam a vacina, apesar de 90,61% afirmarem que permitiriam que seu(sua) filho(a) a recebesse. **Conclusão**: O conhecimento sobre a infecção pelo HPV, suas consequências e prevenção, tanto entre as pessoas com nível básico/médio quanto entre as pessoas com ensino superior é ainda muito limitado.
Palavras-chave: Papillomaviridae; vacinas contra Papillomavirus; infecções por Papillomavirus; saúde pública.

INTRODUCTION

The Human papillomavirus (HPV) is the most often diagnosed sexually transmitted infection worldwide. The infection is associated to anogenital warts and pre-malignant and malignant lesions of both anogenital (cervical, vaginal, vulvar, penile and anal) and extra-genital areas (head and neck)[1,2].

Currently, there is no doubt that HPV is the cause of cervical carcinoma[3], which was the most frequent malignancy found among women in developed countries, until it was overcome by breast cancer, in the early 1900s. Up until today, it remains at 371 thousand cases diagnosed annually worldwide[1].

There are over 45 genotypes of the virus which may affect the genital area, both for men and women, classified into high and low level[2].

The low-risk oncogenic HPV types 6 and 11 are responsible for over 90% of genital warts cases and for a number of cases of low-risk intraepithelial neoplasia of uterine cervix and vulva[4]. The high-risk oncogenic HPV types 16 and 18 are the most common in cervical cancer, representing 71% of the cases[5].

Study carried out at the Teaching Hospital and Health Centers of Florianópolis (SC), Brazil.
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The high-risk oncogenic HPV show tropism for cells of the uterine ectocervix transitional epithelium, infecting them and inducing neoplastic changes[6]. In this junction region between the endocervical columnar epithelium and the squamous stratified ectocervical epithelium, the constant cell proliferation easily allows the incorporation of the viral genome to the cellular genome[5].

Studies on the epidemiology of the genital HPV infection show a greater prevalence among young women, aged up to 25 years old, and with a trend to decline with advancing age[7]. This standard is possibly explained by the development of an adaptive immune response which could prevent future infections[8].

Although most cases of infection by HPV are related to sexual transmission, it may also occur non-sexually, by contact with skin warts, by fomites (sharing towels, underwear, etc.) and by maternofetal contact (pregnancy, intra- and peripartum)[9].

In most individuals the HPV infection is asymptomatic and transient, considering that 70% of new infections resolve in up to one year and, for the rest of it, about 90% in two years[4]. Epidemiological studies show that a small number of women infected by high-risk HPV will progress to high-degree lesions and cancer. The risk of progression into invasive cancer depends on factors such as the type of HPV, the viral load and the persistent presence of the virus[10]. When that occurs, the mean time between the initial infection and the cervical cancer manifestation is approximately 15 years[11].

The epidemiology of infection by HPV in the genital tract is similar to the one by cervical cancer, including the emerging of intraepithelial lesions before the cervical carcinoma appears[12]. The long interval in the progression of the high-risk cervical lesion into an invasive cancer allows great opportunity of identification of the premalignant lesion by screening programs. Regular Pap smears, as well as the proper follow-up and treatment of the precancerous lesions may help preventing the development of most cervical cancer cases[13].

The expenses involved in the treatment of cervical cancer, the failure to access Pap smears test in various regions and the non-elimination of transmission risk by using condoms[14] reveal the great clinical importance of the development of a prophylactic HPV vaccine. Thus, vaccination appears as a promising tool in the prevention of cervical cancer and other diseases associated to HPV[15].

Two vaccines were developed and approved by the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária* – ANVISA) for primary prevention of HPV an both of them have shown high effectiveness levels. The quadrivalent vaccine protects against anogenital cancer and against genital warts by HPV types 6, 11, 16 and 18, which are responsible for 70% of the cases of cervical cancer and over 90% of the cases of genital warts. The bivalent vaccine, in turn, is exclusively directed for the prevention of cervical cancer induced by HPV types 16 and 18[16].

Studies published by the International Agency for Research in Cancer (IARC) prove the safety and efficacy of the HPV vaccine, able to reduce by 70% the probability of developing cervical cancer[17].

Many countries already introduced the HPV vaccine in their vaccination programs in the public health system[18]. In Brazil, both vaccines are licensed by ANVISA, and the quadrivalent vaccine is in the National Immunization Program (*Programa Nacional de Imunização* – PNI) since 2014 for girls from 9 to 13 years of age.

The popular acceptance to immunization is influenced by different levels of knowledge on sexually transmitted infections, their causes and forms of prevention, as well as particular religious beliefs on practices of health and sexuality[19].

Researches on the acceptance of the vaccine among teenagers, among their legal guardians (parents) and among health professionals show great influence of factors such as cost, existence of medical recommendation and safety of the vaccine[20]. From the parents' point of view, the knowledge on the benefits of the HPV vaccine, the medical history of more than two sexual partners of their children and the recommendations of health professionals emerge as determining factors[21].

Similarly to what was found in other countries, studies developed in Brazil reveal that very little is known about HPV among the general population. It was noticed that, in a group of 204 women in a Brazilian city, two thirds of them did not know what diseases the HPV causes and, despite 73% of women having reported moderate to great fear of having cervical cancer, less than 10% of them knew that the virus could be related to it. Meaning, the lack of knowledge on HPV and its consequences coexist with the perception of high susceptibility to cervical cancer [22].

OBJECTIVE

To evaluate the knowledge on HPV infection, its relation to cervical cancer and the forms of prevention among college students of the Federal University of Santa Catarina, health academics or not, and among employees of the health units in the city of Florianópolis, with college education or not. The data obtained were correlated in order to identify the factors associated to the knowledge on HPV and their forms of prevention, as well as the recognition of barriers to the use of HPV vaccine.

METHODS

It is a descriptive and cross-sectional study carried out in the campus of the Federal University of Santa Catarina (UFSC) and in local health care units (LHU) of Itacorubi, Barra da Lagoa, Campeche and Ingleses, in the period from October 2012 to March 2013.

A structured questionnaire was applied, previously validated, for 51 academics of the first period and 33 of the eighth period of the medical school, 21 academics of the sixth period of the economics course, 18 academics of the sixth period of civil engineering, 13 academics of the sixth period of pedagogy, 17 employees of LHU of Campeche, 14 employees of the LHU of Barra da Lagoa, 20 employees of the LHU of Ingleses and 26 employees of the LHU of Itacorubi. From the total of 213 people who answered the questionnaire, 28 of them had high school/elementary education and 185 of them had complete or incomplete college degree, considering that, from those, 118 of them showed higher education in the health area.

Men and women aged over 18 years old who read, agreed and spontaneously signed the Informed Consent were included in the research. The exclusion criteria were: illiteracy, psychiatric comorbidity or cognitive impairment of comprehension and an appropriate answer to the questionnaire.

The questionnaire by which the participants were evaluated had objective questions, approaching variables on demographics, life habits, characteristics of HPV infection and HPV vaccine.

The data were obtained through the individual answer to the structured questionnaire. The demographic variables approached were: age, gender, marital status, ethnicity, sexual orientation and family monthly income. The family monthly income was analyzed in income groups according to the *Classificação do Centro de Políticas Sociais da Fundação Getúlio Vargas* (CAPS/FGV) in classes A, B, C and D. The variables related to the life habit was the perception of risk of acquiring a sexually transmitted disease (STD).

The knowledge on HPV and the HPV vaccine was approached by 10 questions. The first question referred to having already heard about HPV. In affirmative case, options of knowledge obtaining source could be marked, such as magazines and books, Internet, family and/or friends, academic education and medical consultation. The second question concerned having already heard about HPV vaccine. The third question was about having received at least one dose of the vaccine, and the answer could be yes or no. In negative case, reasons for not doing it could be indicated, such as lack of knowledge on the matter, disbelief in the benefits, not considering indication cases, fear of side effects, and unwillingness to pay and absence of financial good conditions. The fourth question regarded the permission to their kid to being shot with the vaccine. The six following questions were of an objective content about the characteristics related to the HPV and to the vaccine. The question of this last part were about: the possibility of infection by HPV causing genital warts; the sexual relations being a form of contagion; the potential for the infection to cause cervical cancer; the use of HPV vaccine to reduce or not the frequency and needs of gynecological tests; having the HPV vaccine shot to protect against cervical cancer; the vaccine excluding or not the need to use condoms.

The application of the questionnaires was carried out during school year in classrooms of the campus of Trindade of UFSC and in LLHUs, during the monthly meeting of the unit.

The present study followed the criteria of the Research on Human Beings Ethics Committee (CEPSH) of the UFSC, as determined by the Resolution No.196/96 of the National Health Board (*Conselho Nacional de Saúde* – CNS). The final approval by this committee was in February 2013, under the number 209.009.

The analysis of the data was carried out by IBM Software SPSS 20,0® and Epi Info 6.04. The results were obtained by percentage calculations. In order to verify the possible associations between the acceptance of the vaccine, the knowledge about it and the HPV and the variables, a chi-square test (χ^2) and a Fisher's exact test were performed, confidence interval of 95%. The result was considered significant if the probability of an error were 5% ($p<0.05$). When the p-value did not show significance, it was presented as p=ns.

RESULTS

201 participants having knowledge on HPV (94.37%) aged around 27 years old. Of those, 80 individuals were male, 96.38% of the total men, and 121 individuals were females, 93.08% of the total women. Three men and nine women abstained from this answer (**Table 1**).

166 participants claimed knowledge about the vaccine (77.93%) aged 27.91 on average, from which 62 individuals (74.7%) were male and 104 (80%) female. Six females and no males abstained from this answer (**Table 1**).

The correlation between the marital status of the interviewee and the knowledge about HPV and the vaccine do not show statistically significant differences. However, there was a little higher percentage of knowledge on HPV among divorced people, 6 (100%) and single ones, 142 (97.26%), in relation to married ones, 44 (91.67%) (**Table 1**).

As for ethnicity, the knowledge about HPV was seen in 175 (95.11%) of white/caucasian respondents, followed by 15 (93.75%) of brown people, 7 (87.5%) of black and 3 (75%) asians. The prevalence of knowledge about the vaccine was 142 (77.17%) among white/caucasian people, followed by 6 (75%) black, 15 (93.75%) brown and 3 (75%) asian ones. There was a single self-reported indigenous individual, considering that they claimed having knowledge on HPV by ignorance about the vaccine (**Table 1**).

The correlation between sexual orientation and the knowledge about HPV also did not show statistical relevance. From the respondents, 185 (94.87%) of the heterosexual and 11 (100%) of the homosexual stated knowing about HPV. The homosexual showed having more knowledge about the vaccine (81.82%) than the heterosexual group (78.46%) (**Table 1**).

As for the level of school education and the knowledge about HPV and the vaccine, despite having no statistical significance, it was observed that 25 (89.29%) of the individuals with elementary/high school degree and 176 (95.13%) of the individuals with college degree state having knowledge on about HPV. In relation to the vaccine, the higher prevalence of knowledge was in the individuals with elementary/high school degree 22 (78.57%), followed by 144 (77.84%) of the individuals with college education (**Table 1**).

The relation between the social class, the knowledge about HPV and the vaccine showed that from the individuals in social class A, 37 (97.37%) had knowledge about HPV and 29 (76.31%) had knowledge on the vaccine. In turn, individuals in class B, 13 (100%) knew about HPV and 11 (84.61%) knew about the vaccine. Among individuals in class C, 124 (93.94%) knew about HPV and 105 (79.54%) about the vaccine. And in class D, 13 (92.86%) knew about HPV and 8 (57.14%) about the vaccine. Although the relation between the social class, the knowledge about HPV and the vaccine did not show statistically significant differences, it is observed a lower level of knowledge between individuals in classes C and D, specially in relation to the knowledge about the vaccine (**Table 1**).

When questioned about the risk of getting a STD, among the individuals who stated knowing about HPV, 87 of them answered they do not consider themselves at risk (43.28%); 92 consider themselves at low risk (45.77%); 12 of them at moderate risk (5.97%); and 6 of them at high risk (2.98%). There were four abstentions (1.99%). Among those who stated knowing about the vaccine, 71 individuals do not consider themselves at risk (42.77%); 74 consider themselves at low risk (44.58%); 11 of them at moderate risk (6.63%); and 6 at high risk (3.61%). In this group, 4 individuals abstained (2.41%) (**Table 1**).

When we assess the knowledge about HPV, 89.29% of the respondents with elementary/high school education levels have already

heard about HPV, compared to 88.06% with college degree, in this case considering just the individuals without formation in the health area. Among the respondents with elementary/high school level, most of them obtained information through books/magazines (40%) and in their academic formation (40%). In the group with college degree in areas other than health, most people obtained information in books/magazines (45.76%) and with family/friends (35.59%). The vast majority of respondents in the college degree in health group stated knowing about HPV (99.15%), most of them during their academic graduation. It was surprising the little information obtained in medical appointments. In this aspect, more than one option may be signaled (**Table 2**).

When assessing the information about HPV, it was noticed an impressive lack of knowledge of 60% of participants with college education in areas other than health about HPV as the cause of the genital warts and also for college level in health areas (20%). About 15% of the participants in areas other than health believe that HPV is not a STD. Even more alarming is the fact that 28% of the participants with elementary/high school education and 45% of the ones with college degree in other areas than health have no knowledge that HPV is the cause for cervical cancer (**Table 3**). Individuals with college degree in areas other than health have a risk 70% higher of not knowing that HPV causes genital warts in relation to the individuals with elementary/high school education, with relative risk (RR) of 1.72 (p=0.02).

When questioned if they had already heard about the HPV vaccine, 22 individuals (78.57%) with elementary/high school degree stated that yes, while 4 (14.28%) of them claimed not having heard about it. From the individuals with college degree without formation in the health area, 36 (53.73%) of them have already heard about the vaccine, while 29 (43.28%) of them have no knowledge of such. Therefore, the individuals with college degree had three times higher risk of not knowing about the vaccine in comparison to the ones with high school education (RR=2.90; p=0.0008) (**Table 4**).

Of the 28 individuals with elementary/high school education, only one of them reported having used the vaccine and 2 did not answer to the question. As for the justification, 16 people (64%) abstained from answering, most of them did not use it due to the cost of the vaccine (6 participants; 24%) (**Table 4**). None of the respondents marked the option regarding disbelief in the benefits of the vaccine. It should be noted that, in this regard, there was the possibility of marking more than one option. Despite the little use of the vaccine,

Table 1 – Demographic data and information about HPV and HPV vaccine.

Variables	HPV			HPV vaccine		
	n	%	p-value	n	%	p-value
Gender						
Men	80	96.38	ns	62	74.40	ns
Women	121	93.08		104	80.00	
Color						
White/Caucasian	175	95.11	ns	142	77.17	ns
Black	7	87.5		6	75.00	
Sexual orientation						
Heterossexuals	185	94.87	ns	153	78.46	ns
Homossexuals	11	100		9	81.82	
Level of school education						
Elementary/High School education	25	89.29	ns	22	78.57	ns
College education	76	95.13		144	77.84	
Social class						
A	37	97.37	ns	29	76.31	ns
B	13	100		11	84.61	
C	124	93.94		105	79.54	
D	13	92.86		8	57.14	
Consider oneself at risk of having na STD?						
No	87	43.28	ns	71	76.34	ns
Low risk	92	94.98		74	76.29	
Moderate risk	12	92.31		11	84.61	
High risk	6	100		6	100	

ns: non significant

Table 2 – School education and information sources about HPV.

Question	Elementary/high School (n=28)		College (not in a health areas) (n=67)		p-value	College (in a health area) (n=118)	
	n	%	n	%		n	%
Already heard about HPV (where?)	25	89.29	59	78.57	<0.05	117	99.15
Books/magazines	10	40.00	27	45.76	ns	58	49.57
Internet	5	20.00	21	31.34	ns	46	39.32
Family/friends	3	12.00	13	35.59	ns	20	17.09
Academic formation	10	40.00	23	34.33	ns	103	88.03
Medical appointment	5	20.00	14	23.73	ns	20	17.09
Abstention	5	17.8	9	13.43		–	–

ns: non significant

85.71% of the individuals with elementary/high school education answered that they would allow their children to get the vaccine shot (**Table 4**).

Among the 67 individuals with college degree in the health area, only 1 has already been shot with the vaccine and 3 did not answer to the question (**Table 4**). Among the 63 people who claimed not having been vaccinated, 5 people (7.94%) abstained from answering. The vast majority did not use the vaccine because they do not know about it (65,08%). Again, none of the respondents marked the option regarding disbelief in the benefits of the vaccine (**Table 5**). When questioned if they would allow their children to get the vaccine, 57 (85.07%) of them answered they would (**Table 5**).

Few participants in the 3 groups know that the HPV vaccine protects against cervical cancer (17.86% of the group with elementary/high school education, 13.34% of the volunteers with college degree in the health area and 41.52% of the group with college education in a health area). There was no statistically significant difference among these three groups.

When questioned whether women vaccinated against HPV need less frequent gynecological examinations, 10 individuals (35.71%) with elementary/high school education answered no, and 23 (82.14%) answered that the HPV vaccine does not exclude the need to use condom during sex. Among individuals with college degree without formation in the health area, 46 (68.66%) answered that the

Table 3 – Information about HPV and education degree.

Question	Elementary/High School (n=28)		College (not in a health area) (n=67)		p-value	College (in a health area) (n=118)	
	n	%	n	%		n	%
HPV causes genital wart	17	60.71	27	40.30	0.02	95	80.51
Abstention	2	7.14	–	–		3	2.54
HPV causes cervical cancer	19	67.86	37	55.22	ns	112	94.91
Abstention	1	3.57	1	1.49		3	2.54
HPV is an STD	25	89.29	57	85.07	ns	114	96.61
Abstention	1	3.57	–	0		3	2.54

ns: non significant

Table 4 – Information about the HPV vaccine and the education degree.

Question	Elementary/High School (n=28)		College (not in a health area) (n=67)		p-value	College (in a health area) (n=118)	
	n	%	n	%		n	%
Already heard about the HPV vaccine	22	78.57	36	53.73	0.0008	108	91.52
Abstention	2	7.14	6	8.00		2	1.69
Already used the HPV vaccine	1	3.57	1	1.49	ns	6	5.08
Abstention	2	7.14	3	4.48		2	1.69
Would allow their children to get vaccinated	24	85.17	57	85.07	ns	112	94.91
Abstention	4	14.28	4	5.97		2	1.69
The vaccine protects against cervical cancer	5	17.86	9	13.43	ns	49	41.52
Abstention	4	14.28	1	1.49		3	2.54
Vaccinated people =fewer gynecological exams	7	25.00	4	5.97	ns	7	5.93
Abstention	1	3.57	–	–		2	1.69
Vaccinated people do not need condoms use	3	10.71	–	–	ns	1	0.85
Abstention	2	7.14	1	1.49		2	1.69

ns: non significant

Tabela 5 – Motivos para não realizar a vacina contra HPV e grau de ensino.

Alternative	Elementary/High School (n=28)		College (not in a health area) (n=67)		College (in a health area) (n=118)	
	n	%	n	%	n	%
Unknown	2	8	4	65.08	18	16.36
Does not believe in the benefits	–	–	0	–	3	2.73
Does not consider oneself as a suitable indication	–	–	9	14.28	27	24.54
Fear of side effects	1	4	1	1.59	3	2.73
Not willing to pay for it	3	12	8	12.70	31	28.18
Does not have financial conditions	3	12	3	4.70	12	10.90
Abstention	16	64	5	7.90	18	16.30

vaccination should not reduce the frequency of gynecological examinations and 66 (98.51%) believe the vaccine does not exclude the need to use condoms.

In relation to the 118 individuals with college education in the health area, 94 people (79.66%) stated the vaccination against HPV should not be the reason for reducing the frequency of gynecological examinations and 115 people (97.45%) believe the vaccine does not exclude the need to use condoms.

DISCUSSION

Most studies addressing the knowledge about cervical cancer, HPV infection and HPV vaccines focus on a sample of women at a specific age range or focus on the opinion of young parents about the use of the vaccine[20,23]. This specific study included men and women, in different age ranges, from various socioeconomic status and with graduation in the health area or not. Encompassing, thus, a more diversified and heterogeneous sample.

The mean age of the participants in this study was approximately 27 years of age. This data is correlated to the participation in higher number of college students, who, on average, are younger.

Almost 95% of the participants state having already heard about HPV. A lower level of knowledge is found in some researches with the general population[22]. The data obtained are in agreement with other studies carried out with college students and health professionals, that, according to Medeiros et al.[24], would lead to believe that working in the health area and/or having a college education is associated to a greater awareness on the existence of this virus.

All homosexuals who took part in this study claim having heard about HPV and the number of them with knowledge about the vaccine was also higher than among heterosexuals. Maybe this fact is related to a greater knowledge of the STD in general, specially due to HIV infection, whose programs and prevention campaigns focus on the awareness of this group, especially at the beginning of the epidemic.

The discussion about HPV infection, as well as the effects of the vaccine on men is recent[25]. Some studies report men who are sexually active or have already had a STD or who consider themselves under high risk of HPV infection have greater acceptance to the vaccine[26]. An article developed in Australia shows that the acceptance to the vaccine against HPV tends to be higher among men who have sex with men. In this case, the interest for the vaccine could be justified by the higher rates of anal cancer associated to HPV[27].

In other studies, only six participants consider themselves under high risk of having an STD, and all of them state having already heard about HPV and the vaccine against it. Recognizing the risk of having an STD may be involved with knowingly risk behaviors also for the HPV, such as the early beginning of sexual activity, the multiplicity of sexual partners and the lack of use of condoms[28]. The fact of the second greater prevalence of knowledge about HPV is among individuals who consider themselves at low risk of getting an STD supports the initial premise of the study, that the knowledge is connected to the public policies. The people who consider themselves at low risk of having an STD probably believe already using all other possible kinds of prevention, including the use of condoms, so widely spread in campaigns against HIV and STDs in general, though they do not guarantee 100% prevention against HPV[28]. Meaning, possibly, the perception of risk is underestimated among the ones who state knowing about HPV.

The absence of approach about HPV in public STD campaigns may again be noticed due to the lower knowledge among individuals with college education in areas other than health. A college education does not ensure information about STDs, once those are not a part of the curricula of the courses at matter. The source of information would be more related to public policies, which are insufficient for not providing basic information about HPV, about its association to genital warts, STDs and cervical cancer. The limitation of the existing knowledge was even more meaningful in relation to the vaccine, which would already be expected given the little information given out regarding it.

A positive example of the effects of education about this knowledge was highlighted by the research in relation to people with elementary/high school education. In this research, these individuals are LHU professionals and, despite not having a college degree, they work in places where most STD cases in the municipality are taken care of and they have annual trainings provided by the Municipal Health Department (*Secretaria Municipal de Saúde*), with emphasis on infectious diseases, such as STDs[29]. These professionals are daily involved with matters related to information and preventive practices, such as the Pap smear test, which contributed positively for a greater knowledge about HPV, as observed in the 89% of the ones who stated having heard about HPV.

The individuals with a college degree in a health area, as found in other national studies[30], presented greater knowledge about HPV and the HPV vaccine. This is probably due to the curricular formation which approaches the virus, its relation to cervical cancer and other disease and the forms of prevention. As expected, education was relevant as for the knowledge and the vaccination. From the small number of respondents who stated having been vaccinated against HPV, two thirds of them had college education in a health area. These findings are comparable to those seen by Medeiros et al.[31], in their study with college students in Portugal. In this one, 79.3% of the students of health related areas had already heard about HPV, in relation to only 14% of students in other courses. When questioned about the use of the vaccine in case it was available, 89% of them responded positively: 93.4% students of health and 98.3% students of other areas. Similarly to our study, the college education in the health area is associated to a greater knowledge about HPV. Contradictory to our findings, the acceptance of the vaccine was higher among students of areas other than health.

Despite only 6 people among the respondents having received HPV vaccination, over 90% of the participants would allow their children to get it. The belief in the efficacy of the vaccine is confirmed given the reduced mention to the discredit in its benefits as a reason not to do so. The most often reasons mentioned for not doing so were not considering it to be referred as a case and problems to pay. Meaning, the vaccine is greatly accepted and what hinders its use is the high cost and lack of information. Both reasons could be solved in case there were campaigns for awareness about HPV and the inclusion of the vaccine in the public vaccination calendar. It is imperative to change the high numbers of HPV infection, the enlightenment of the population about what is HPV and its relation to cervical cancer, associated to information about

prophylactics action of the vaccine and to the long term immunity, which characterize its indication for teenagers before the beginning of their sexual life, though it does not exclude the possibility of benefits at a later age.

The result is similar to the one found by Black et al.[32], in a study about the acceptance of the vaccine among Americans aged over 26 years old. It should be noted that, in the United States, the HPV vaccine is currently licensed only for women aged between 9 and 26 years old, so that women above this age range would not have free access to the vaccine.

Despite most participants stating having heard about the HPV vaccine, it was noticed in all levels of education, that having information about the existence of something does not mean knowing all its implications. It is alarming the number of participants who state that vaccinated women would require less frequent gynecological exams and who claimed vaccinated women do not need to use condoms during sex. Meaning, claiming having heard of the vaccine does not mean they understand its protection is exclusive to some types of HPV and not for all STDs. The result is common to the one found by Carvalho et al.[30], in a study on the perception of the HPV vaccine among medicine students and doctors affiliated to the Federal University of Paraná. In this one, although all participants had formation in a health area, 75.3% of them do not understand that the vaccine does not cover all types of HPV and that, therefore, the Pap test would still be necessary regardless the vaccination.

The HPV is a STD which has some particularities, thus, despite having a contagion route similar to other STDs, its association to cervical cancer, as well as the particular forms of prevention, require a more unique approach. An example of feasible and relevant public policy would be the creation of compulsory subjects in the elementary and high school curriculum about the use of drugs, sexuality and related diseases. The few existing initiatives in this regard have great resistance of the parents who believe that the approach of these matters would stimulate the early development of sexuality in their children. However, the beginning of an early sex life is a fact and the approach of the matter by professionals, in a proper way, would allow the perception not as a stimulus, but as a guidance.

CONCLUSION

Despite most people having heard about HPV, it is alarming the ignorance of the population, including in the health area, about the relation of this virus to cancer and genital warts, its sexual transmission and the benefits of the HPV vaccine in the prevention. New studies, with different population, must be carried out in order to demonstrate to the government the importance of a form of prevention which is highly effective and safe such as the HPV vaccine in the public system, especially in Brazil, which annually has around 20 thousand new cases of cervical cancer and 8 thousand deaths associated to it.

Conflict of interests

The authors report no conflict of interests.

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Giant condyloma acuminatum: report of surgical treatment and evolution of healing

Condiloma acuminado gigante: relato de tratamento cirúrgico e evolução da cicatrização

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ABSTRACT
Giant condyloma acuminatum, a rare variant of anogenital condyloma, shows rapid growth associated with immunodeficiency. Wound care after resection and outcomes were reported. NGS, black, 55 years, HIV positive, with giant condyloma acuminatum affecting from the groin to the intergluteal groove, which was resected, remaining the wound opened for later skin graft. Topical care included polihexametilene biguanide/betaine solution, essencial fatty acids solution, hydrofiber/silver, and poliuretane film. The wound developed secondary infection, so hidrofiber was replaced by polyurethane foam/silver/ibuprofen. There was improvement in infection and pain, contraction of the edges and the presence of granulation tissue across the lesion. In those conditions the skin graft was performed after 41 days. Despite possible confusion bias, it can be inferred that the care adopted prepared the wound bed to receive the skin graft.
Keywords: Buschke-Lowenstein tumor; wound healing; wound infection; pain; fatty acids, essencial; anti-infective agents, local; betain; silver; ibuprofen.

RESUMO
O condiloma acuminado gigante, variante rara do condiloma acuminado anogenital, apresenta crescimento rápido associado a estados de imunodeficiência. Relatamos os resultados com os cuidados com a ferida operatória. Trata-se de homem de etnia negra, 55 anos, portador do vírus da imunodeficiência humana com condiloma acuminado acometendo desde as regiões inguinais até o sulco interglúteo, que foi ressecado permanecendo a ferida aberta para posterior enxertia. Os cuidados com essa ferida incluíram solução de polihexametileno biguanida/betaína, solução de ácidos graxos essenciais, hidrofibra/prata e película. Evoluiu com infecção secundária sendo a hidrofibra substituída por espuma de poliuretano/prata/ibuprofeno. Houve melhora da infecção e da dor, contração das bordas e presença de tecido de granulação em toda a lesão. Naquelas condições, o enxerto de pele foi realizado no 41º dia. A despeito dos possíveis vieses de confusão, pode-se inferir que esses cuidados prepararam o leito da ferida para receber o enxerto de pele.
Palavras-chave: tumor de Buschke-Lowenstein; cicatrização; infecção dos ferimentos; dor; ácidos graxos essenciais; anti-infecciosos locais; betaína; prata; ibuprofeno.

INTRODUCTION

The giant condyloma acuminatum (GCA) is a rare variation of the anogenital condyloma acuminatum and a sexually transmitted disease related to the human papillomavirus (HPV) (subtypes 6 and 11). The disorder is also known as Buschke-Löwenstein tumor (BLT), Ackerman verrucous carcinoma or Delbaco y Unna precancerous condylomata[1-5].

The GCA was described in 1896 by Buschke and, in 1925, Buschke and Löwenstein reported a case of penile tumor with clinical behavior of malignancy. However, in the histological analysis, it was a condyloma acuminatum. Only then the clinical identity was better defined. The description of the disease when located in the anus was made by Dawson et al., in 1964[3-7]. The incidence of GCA in the population is 0.1%, with post-treatment recurrence of between 60 and 66% of patients[1,3]. It is more common among men, aged 50 years of age[5]. The fast growing of this tumor is usually associated to the immune deficiency[3,5].

Macroscopically, the lesion is large, vegetative, warty, of exotrophytic aspect and slow growth with infiltrative base, affecting the anal and vulvar regions, the penis and scrotum, perineum, the perineal region and the anal canal. Histologically, it presents a chronic infiltrate with thickening of the Malpighian layer, of benign aspect. However, it clinically presents malignant behavior, once it infiltrates the adjacent tissues. The mitosis are rare, there is the occurrence of hyperkeratosis and the basement membrane remains intact[1,3-5,7-9].

The risk factors associated to the development of the GCA are the precarious hygiene habits, sexual promiscuity, chronic irritation, immunosupression by HIV or HTLV-1 and chronic and recurrent genital warts[2,5,7].

There are many therapeutic strategies for the treatment of GCA, among which topical agents are used, immunotherapy, and chemoradiotherapy and surgery, being this last one the most effective once it avoids recurrence and malignancy[1,7].

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After resection, one of the aspects of nursing care is to monitor the progress of healing. The objective is the early identification of possible complications, with periodic evaluation of the wound. This follow-up must be done according to the kind of healing (primary closure, delayed primary or by secondary intention), adopting the appropriate care from the identification of individuals needs and knowing the potential complications[10].

The study has the objective of reporting the healing of the wound resulting from the resection of the anogenital GCA in patients with acquired immunodeficiency syndrome (AIDS), once that we did not find publications on the evolution of healing of this kind of injury in immunosuppressed patients.

The study highlights the importance of a well-planned care, guided by evidence as an important part of the treatment and shows an effective result which may be reproduced by other professionals.

CASE REPORT

All the bioethics principles postulated by the Resolution 196/96, of the National Research Ethics Commission (CONEP), which approaches the research involving human being were respected. The study was submitted to the Research Ethics Committee (CEP), obtaining a favorable opinion (No. 96/2012).

It is about a patient admitted in the hospital wards of the state public network, a reference in care of patients with infectious diseases in the city of São Paulo.

Black man, 55 years of age, single, reported slow growth of a smelly tumor, four years before, affecting his anogenital area. He was HIV positive for three years, making irregular use of antiretroviral medication and a chronic smoker. The physical exam revealed a warty surface, irregular, well delimited and of infiltrative base affecting from the coccygenal area to the base of the penis, including the groin and scrotum. The pre-treatment with topicals did not have total remission of the lesions, leading to surgical resection leaving the wound to be closed later on with rotation of patches and grafts. In the first post-operation day, the evaluation by the Skin Group of the institution found a stable patient, denying pain and without clinical signs of infection. It was about a surgical wound with extensive raw area, beginning at the lower part of the penis, bilateral inguinal region, until the sacral region (**Figure 1**).

The plan for topical care included the selection of the dressing, considering the comfort of the patient, the ease of application and its effectiveness, thus elaborated:

1. Antisepsis with polyhexamethylene biguanide and betaine solution (PHMB);
2. Application of essential fatty acids (EFA) solution;
3. Secondary dressing with silver hydrofiber;
4. Fixation with transparent film.

The change was performed daily, due to the location of the lesion, in order to avoid secondary infections. For the protections of the surrounding skin, we used a barrier cream to each dressing change. For pain assessment, we used the Visual Analogue Scale for Pain (VASP).

In the third post-operation day, signs of local infection were identified, such as putrid odor, pain (score 10 in VASP), increase in the amount of necrosis and slough in the whole lesion and greenish exudate (**Figure 2**).

We collected secretion from the lesion in order to grow a culture and replaced the dressing by polyurethane foam with ibuprofen in the scrotal area, due to intense pain, and polyurethane foam with silver in the rest of the lesion to control the infection and absorption of the exudate. It was decided to replace the silver hydrofiber by the polyurethane foam, which absorbs the exudate without adhering to the injury, keeping it moisturized while avoiding maceration of the edges. The remaining cares were kept with suspension of the use of EFA until the control of the exudate.

It was observed, by the visual analog scale for pain, a reduction of the score (score 5 VASP only to manipulation) with the use of polyurethane foam with ibuprofen, being possible to suspend its use after five days, adopting the polyurethane foam with silver on the whole injury. This way, there was an improvement of signs of infection.

The bacterioscopy of the secretion revealed an infection by *Morganella morganii*, suggesting a change of the systemic antimicrobials.

The conduct regarding topical care was kept during the subsequent period. After five days of suspension of the use of EFA, its

Figure 1 – Initial assessment, first Day post-operation.

use was resumed, once the amount of exudate was already well controlled. Concomitantly there was controll of odor, reduction of the necrosis area and the increase of granulation tissue.

In the 35th post-operation day, the patient reported absence of pain (score 0 VASP). There was granulation tissue on the whole wound, contraction of the edges and absence of sign of secondary infection (**Figure 3**), which allowed its closing with partial skin grafting, removed from the anterior surface of the thigh, in the 41st post-operation day. The post-graft evolution was good. In the hospital return after four months, there was a full healing. Two years after that, there was no recurrence of the lesions.

DISCUSSION

This case report presents the results of the topical treatment adopted for a surgically treated case in our institution. The hospital admittance occurred hours before the surgery, this way, minimizing the risk of infection[10].

The conduct related to the choice of dressings and the frequency of changes were based on publications about the wounds management and international consensus, because we did not find studies reporting topical care after the resection of GCA in which the wound would heal by second intention, probably, because it is a rare disease.

The sequence of the making of the dressing aid, with the respective recommendation, is described up next:

1. antisepsis with PHMB solution, the product indicated in this case following the recommendation of the Consensus Document[11] for the prevention of local infection, due to the location and extent of the wound;
2. application of the EFA, in order to maintain the humidity, promote healing, offering protection against infection and prevent adhesion of the dressing[12-14];
3. secondary cover with silver hydrofiber was indicated with the objective of releasing silver in order to prevent infection. The hydrofiber was used in this moment because of its ease of being shaped to the site of the injury, as well as keeping its fixation due to its thin thickness[15];

Figure 2 – Third Day post-operation, signs of infection.

Figure 3 – Forty-first Day post-operation, grafting programming.

4. fixation with transparent film was used due to its difficult fixation with other products and the need of keeping the dressing still, interacting with the lesion.

The barrier cream was applied at each dressing change with the objective of protecting the adjacent skin, thus avoiding aggression caused by the dressings change or even by the contact with the exudate of the wound[16,17]. Due to the location of the injury, in order to prevent secondary infections, the change was performed daily, once the contact with feces and urine increases this risk[18].

In addition to this risk, there is also the AIDS diagnosis, a disease in which the immune system is severely compromised, the patient being then more likely to develop infection[19].

Initially, we opted for the dressing hydrofiber with ionic silver in order to control the exudate and the microbial burden of the wound, preventing the secondary infection through the dispensation of silver, and at the same time keeping moist to the wound, since the hydrofiber captures the exudate and forms a cohesive gel, retaining it in its structure[20]. Due to its being of discreet thickness material, malleable and easily molded, it was proven ideal to facilitate the making and maintenance of the dressing, without causing discomfort to the patient, considering the place of the wound[20-22].

In the third post-operation day, when identified the signs and symptoms of secondary infection, we proceeded to the collection of the material in order to identify the infectious agent and adequacy of topical conduct, due to the failure of the first dressing in avoiding secondary infections[18].

In the presence of sign of infection in acute wounds[10,18], the recommendation is to collect material for microbiology, one of the techniques used being the one of Levine, in which after appropriate cleaning with saline solution, a sterile swab must be rubbed in rotation in a 1 cm^2 area of the wound, with enough pressure for the interstitial liquid to be absorbed[18]. The swab must be stored and shipped in a Stuart media[23].

The isolated agent in bacteriology, from the culture of the secretion of the wound, was the *Morganella morganii*, which is an opportunistic enterobacteria which may be found in nosocomial settings, and is related to the infection of wounds. When present, it releases toxins and enzymes, activates matrices of metalloproteinases (MMPs) and plasminogen, degrading elastin and thus interfering negatively in the healing process of the wound[24,25]. Most patients affected by *M. morganii* respond well to the antimicrobial treatment; however, mortality rates are high[26].

In this case, the infection was controlled with systemic antimicrobial associated to the topical, recommended in the presence of signs of systemic infection. The topical antimicrobial chosen was silver, set in a preventive way since the first evaluation and adequate its presentation form after signs of secondary infection. The silver is usually the topical antimicrobial of choice, being present in several dressings. This is due to its broad spectrum, acting on yeast, fungi and bacteria, being necessary low concentrations deposited in the lesion in order to achieve this effect[15,27,28].

The choice of the dressing in the presence of infection must be made considering the ideal characteristics for an effective action. These characteristics include promoting a moist mean, though not saturated, in order to stimulate healing, associated to the antimicrobial substance of broad spectrum and low potential for resistance. It is desirable that the antimicrobial activity is given in a controlled way in the devitalized tissue, which is a culture mean for microorganisms; besides being non-toxic, fast-acting, non-irritating/sensitizing, non-adherent and effective even in the presence of abundant exudate[20,24].

The dressings with sustained silver liberation differ from older products, such as silver sulfadiazine and silver nitrate, for releasing ions of the metal in the wound in a more controlled and prolonged way, allowing less frequent changes, a fact which reduces the damage caused to the tissue by the removal of the dressing, the discomfort caused to the patient by the manipulation of the place, the cost of the treatment and the risk of nosocomial infection[27].

For the adequacy of the conduct, we decided to use a thicker dressing, less flexibility, that, however, demonstrated the ability to be molded to the raw wound, avoiding the excess of exudate to be in touch with the wound[29] and at the same time keeping moisture[20,30]. The silver ions in these foams are part of the matrix, and are released as the exudate is absorbed[28].

In addition to all these characteristics, the substitute choice of dressing was based on the effectiveness of polyurethane foams which release silver to control Gram-negative bacteria with reduction of over 99% in 6 hours in *in vivo* simulation; and as in its safety during the healing process, once it was demonstrated that there is no toxicity for the fibroblasts[15,31].

The pain is another relevant aspect that must be a part of the overall evaluation of the patient with wounds, as symptom of infection[10,16,18]. For the evaluation of pain we used the VASP, with which the patient quantifies the symptoms using the scale from 0 to 10, using as a parameter 0 for the absence of pain and 10 for the worst pain ever experienced. In the literature several scales for the evaluation of pain are mentioned; all of them depend on the cognition degree and abstraction ability of the patients in order to be effective, once the pain can only be measured by the report of those who feel it. We elected the VASP for being the most used one, being simple to understand and consistent to the cognitive aspects of the patient. The scale was introduced to the patient and they were requested to position the ruler in the figure equivalent to the pain experienced in that moment[16,32] (**Figure 4**). Due to the pain reported along with the signs of infection, we decided to interlayer the polyurethane foam dressing with sustained silver release and polyurethane foam dressing with sustained ibuprofen liberation, with the objective of helping in the control of pain[16]. Strategically, this foam was placed only in areas in which the patient reported experiencing the highest pain intensity, thus allowing silver to act on the rest of the lesion. At the same time in which the foam exerted its analgesic effect in the lesion, it helped in the control of the infection through the absorption of the exudate by capillarity and its retention in the air spaces of the structure[20].

We can conclude that the conduct adopted, considering the presence of infection in the wound, were appropriate, once it is a immunosuppressed patient, affected by an infection by enterobacteria about which the literature demonstrates high mortality rates[26].

The same way, we may observe the effectiveness of the polyurethane foam with sustained release of ibuprofen helping in the control of the pain, since in only five days of use, there was an important

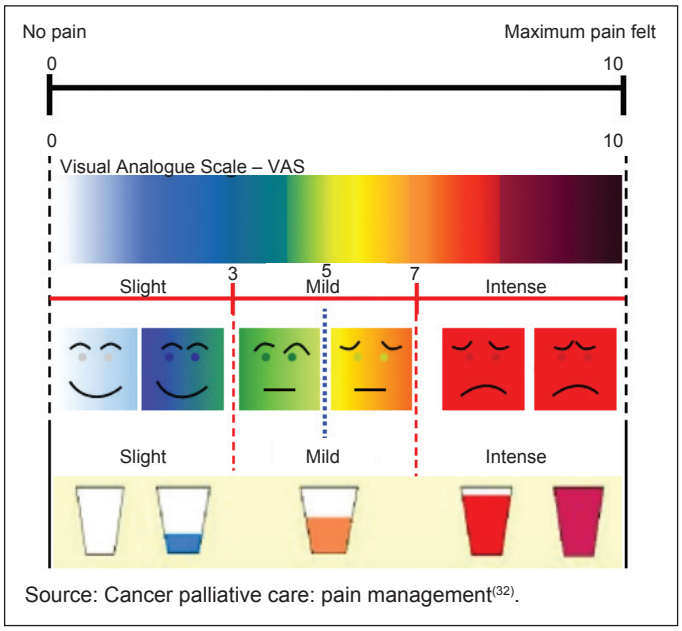

Figure 4 – Visual Analogue Scale.

reduction of the score (from 10 to 5) considering that the pain was reported only during the handling for changing the dressings.

When beginning the use of dressings with silver to control the infection of the wounds, it is recommended the observing of its evolution for 15 days, period in which it is possible to evaluate whether or not the desired effect was achieved, i.e., whether or not the infection was controlled. After this period, if the infection is solved, the use of dressing with silver is suspended and a new strategy is drawn in order to stimulate healing. In case there is improvement in the signs and symptoms of the infection, we can continue the use of silver until it is solved. In case there is no improvement, or even if there is worsening of the infection, the use of the dressing must be suspended and substituted by another one with a topical antimicrobial[15].

In the case reported, we chose to use the dressing with composition and technology different from the first one, because there were no dressings with another associated antimicrobial available in the institution; and after 11 days of use of the polyurethane foam with sustained release of silver it was possible to observe improvement in the infection by reducing the amount of unfeasible tissue in the wound, control of pain and presence of granulation tissue.

The grafting was performed in the 41st post-operation day, remaining with the occlusive dressing associated to the negative pressure wound therapy without changing it for 7 days and evolving with healing of 70% of the grafted area. The remaining 30% of the area of the lesion by second intention with the use of a topical EFA solution and protection with rayon with daily change.

Other studies are necessary in order to confirm the effectiveness of the products used in this kind of lesion, once that we presented one single case in which they were used.

Despite the possible biases of confusion, it can be inferred that the use of PHMB and betaine solution, EFA solution and polyurethane foam on the resulting lesion of GCA resection controlled the secondary infection, the pain, promoted autolytic debridment, increase of granulation tissue and contraction of the edges.

The topical care adopted kept the ideal conditions for healing, preparing the wound to receive the skin graft.

Conflict of interests

The authors report no conflict of interests.

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Diagnosis of secondary syphilis through oral lesions in two patients with negative serology: case reports

Diagnóstico de sífilis secundária através das lesões orais em dois pacientes com sorologia negativa: relatos de caso

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ABSTRACT
Syphilis is a sexually transmitted infection, and oral lesion can be the first manifestation. The serology test, such as Venereal Disease Research Laboratory test, is accepted as an effective testing strategy for detecting syphilis, although false-negative reaction can occur, and oral lesions may be pivotal to achieve the diagnosis. We report two cases of seronegative secondary syphilis, a human immunodeficiency virus positive patient and a no HIV positive patient, whose histopathological exams were pivotal to achieve the diagnosis of syphilis. The serology may be negative in secondary syphilis and the oral lesions may represent the unique method to diagnostic.
Keywords: oral lesion; syphilis; HIV; diagnosis.

RESUMO
A sífilis é uma doença sexualmente transmissível, e a lesão oral pode representar sua primeira manifestação. Testes sorológicos, como *Venereal Disease Research Laboratory,* são rotineiramente utilizados para detecção de sífilis, entretanto, em alguns casos, podem ocorrer resultados falso-negativos. Nesses casos, as lesões orais são essenciais para o diagnóstico. Relatamos dois casos de sífilis secundária com sorologia negativa, em um paciente HIV positivo e um paciente HIV negativo, que obtiveram o diagnóstico de sífilis a partir do exame histopatológico das lesões orais. Os testes sorológicos podem ser negativos na sífilis secundária, e as lesões orais podem representar o único método diagnóstico.
Palavras-chave: lesão oral; sífilis; HIV; diagnóstico.

INTRODUCTION

Syphilis is a sexually transmitted infection caused by *Treponema pallidum*[1]. The number of reported cases still increases around the world, and, in Brazil, the National Program for Sexually Transmitted Diseases and AIDS Control estimates an annual incidence of 937,000 new cases of syphilis in the sexually active population[1,2]. The incubation period for syphilis is 21–30 days after the initial contact with the microorganism and may vary from 10–90 days, depending on the virulence of the parasite, as well as the host response. The disease is classified into early (primary, secondary or latent) and late (also known as tertiary) or early congenital and late congenital syphilis[3,4]. Oral lesions are mainly associated with secondary syphilis and can be the first clinical manifestation[5,6]. Nevertheless, due to its clinical heterogeneity, depending on the stage of syphilis, the diagnosis of oral syphilis lesions can be a challenge to the clinicians[5,6]. It occurs mainly in HIV positive patients that may present typical or atypical oral lesions[7]. A nontreponemal serologic test, such as Venereal Disease Research Laboratory (VDRL) test, is accepted as an effective testing strategy for detecting syphilis, although false-negative reaction can occur, particularly in HIV positive individuals, delayed diagnosis or misdiagnosis of syphilis occurs frequently[6,8,9]. Sometimes, false-negative specific antitreponemal antibodies, such as Fluorescent Treponemal Antibody Absorption (FTA-ABS), can also occur. In such cases, oral manifestations and their histopathological exam may be pivotal to achieve the diagnosis of syphilis[7,10].

The aim of present paper was to report two cases of seronegative secondary syphilis in a HIV positive patient and a no HIV positive patient, who had the diagnosis of syphilis obtained by biopsy of oral lesions.

CASES PRESENTATION

Case 1

A 37-years-old man was referred to the Oral Medicine Service of the Universidade Federal Fluminense with a history of multiple aphthous lesions, which partially resolved in three months. The patient was HIV-positive for four years. The CD4 lymphocytes count was 596 cells/mm^3 and the viral load was 5,838 copies/mL at the time of the first oral evaluation appointment. The patient was not under any medication and a previous VDRL test (performed two weeks before) was negative. The patient had never had any major opportunistic infections since his first HIV positive test.

Oral examination revealed painful smooth ulcerations with slightly raised borders and granular center, as well as erythematous patches, on the buccal mucosa, tongue dorsal surface and soft palate

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(**Figure 1A-F**). The clinical diagnosis was deep mycosis or syphilis. The patient signed the informed consent and an incisional biopsy of the buccal mucosa and tongue was performed.

Histopathological examination revealed hyperplasia, parakeratosis and papillomatosis of the epithelium and mononuclear and polymorphic inflammatory cells exocytosis. Microabscesses were also present. The lamina propria showed a dense and diffuse chronic inflammatory infiltrate composed mainly by plasma cells. The inflammatory infiltrate extended to the deeper area of the lamina propria and also showed a perivascular pattern. Obliterative endarteritis characterized by endothelial swelling was also observed. The Warthin Starry stain showed the presence of spirochetal organisms (**Figure 2**). Neither spores nor hyphae of *Candida spp* were identified in Periodic Acid Schiff (PAS) stain and the cytopathological analysis was negative for candidiasis.

Another VDRL exam was requested, which was again negative. Based on the clinicopathological findings and despite a negative VDRL, the final diagnosis was syphilis. The infectologist initiated a penicillin treatment. A FTA-ABS test and a third VDRL were requested, which were positives. The VDRL presented at titer 1:128. One week after the beginning of the treatment, the oral lesions had completely resolved **(Figure 1 G,H)** and, after two months, the VDRL at titer 1:16.

Case 2

A 29-years-old woman was referred to the Oral Medicine Service for evaluation of pain and migratory oral lesions with two month of duration. Her medical history revealed that she presented hepatitis B in 2009. Extraoral exam was normal, and oral exam revealed erythematous patches on the labial and buccal mucosa (**Figure 3A-D**). The patient presented previous VDRL, FTA-ABS and HIV tests (performed one week before) negatives. The clinical diagnosis was deep mycosis or geographic stomatitis. The patient signed the informed consent, and an incisional biopsy of the buccal mucosa was performed and a new VDRL requested.

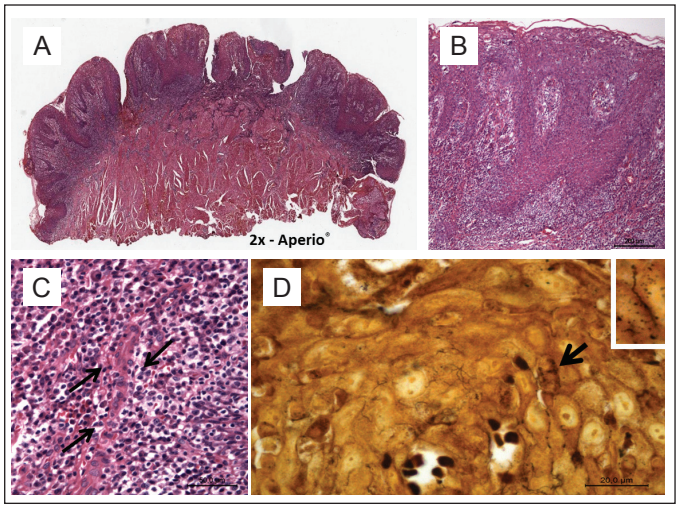

Figure 2 – Histopathological aspects of oral syphilis. Fragment showed hyperplasia, parakeratosis and papillomatosis of the epithelium and mononuclear and polymorphic inflammatory cells exocytosis (A-B). The lamina propria showed a dense chronic inflammatory infiltrate composed mainly by lymphocytes and plasma cells with a perivascular pattern (C). The Warthin Starry stain showed the presence of spirochetes (D).

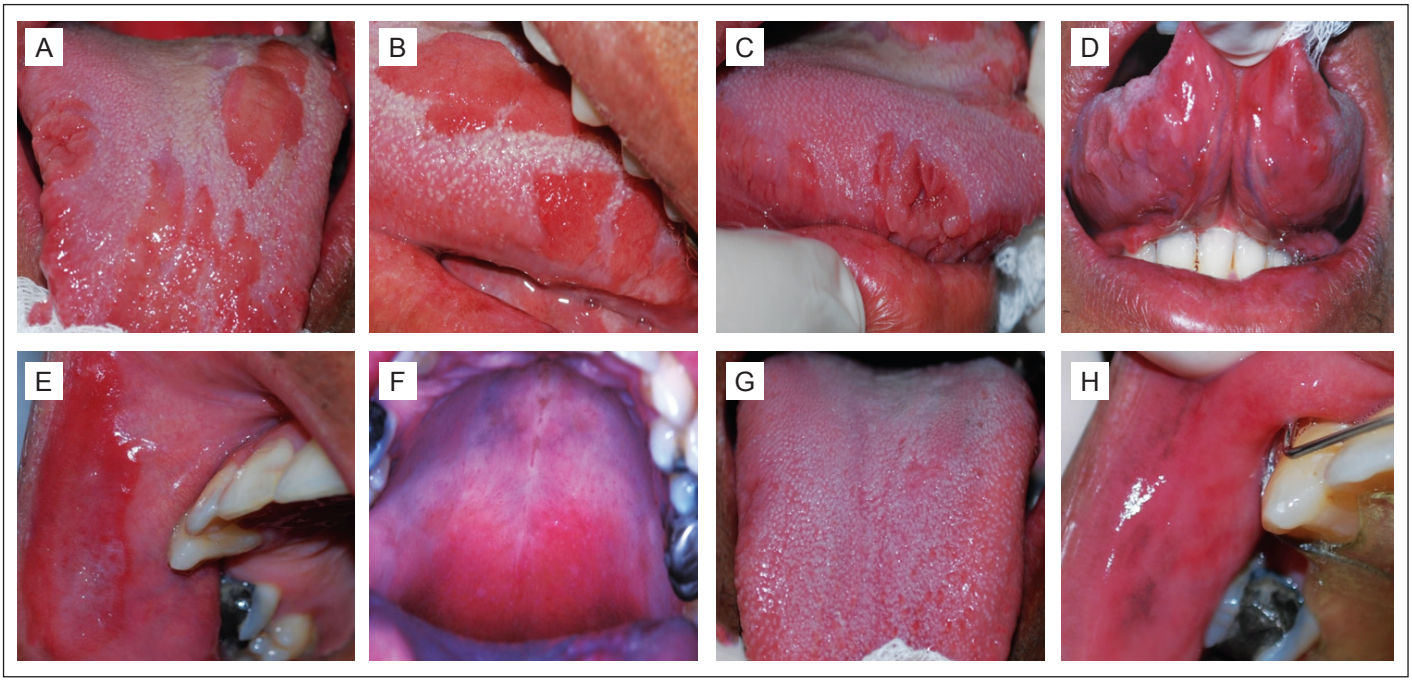

Figure 1 – Clinical aspects of oral syphilis before and after treatment. Ulcers with slightly raised borders and granular center, as well as erythematous patches, on the tongue dorsal (A-C), tongue ventral surface (D), buccal mucosa (E), and soft palate (F). One week after the beginning of the treatment, the oral lesions had completely resolved (G,H).

Histopathological exam revealed buccal mucosa specimen depicting mild architecture changes on the left side and inflammatory changes on the rest of the tissue. Features observed were epithelial hyperplasia, parakeratosis, papillomatosis and neutrophils exocytosis with microabscess. The connective tissue demonstrated superficial and perivascular plasma cell inflammatory infiltrate, and the blood vessels exhibited swelling endothelial cells (**Figure 4**).

Neither spores nor hyphae of *Candida spp* were identified in PAS stain, and the cytopathological analysis was negative for candidiasis.

The histopathological exam suggested syphilis, and the VDRL was positive (titer 1:128). The patient was referred to the Infection Diseases Clinic and initiated a penicillin treatment. After of the treatment, the oral lesions had completely resolved (**Figure 3E-H**).

DISCUSSION

The classical dilemma of the diagnosis of secondary syphilis faced by many clinicians occurs due to the variability of the lesions[1,3,11]. Skin manifestations of secondary syphilis occur in 75% of patients, and the primary chancre is still present in 15% of these patients[11]. Various oral manifestations can be of diagnostic importance and are present in one-third to one-half of patients[12].

The diagnosis of secondary stage can be performed by specific and non-specific serological tests[8,11,12]. Non-specific tests, such as VDRL, are the most common diagnostic tests used to diagnose syphilis and can be useful for screening large numbers of patients[8,12]. VDRL becomes positive in 4 to 8 weeks after acquiring the infection and the sensitivity approaches 100% in secondary syphilis due to the high antibody titers[8]. VDRL is an inexpensive and useful screening test and is reactive in most patients with secondary and latent disease[8]. However, in 1–2% of patients false-negative VDRL can occur due to prozone phenomenon. This occurs due to an inappropriate ratio of antibody versus antigen preventing their agglutination[8,9]. This prozone phenomenon is frequently found in pregnancy and HIV infection. The incidence of prozone phenomenon is very low in non-HIV patients with syphilis, ranging from 0 to 0.4%[9]. Beyond VDRL, which is a non-specific test, other specific tests are used for screening[8]. Generally, FTA-ABS can be considered a very sensitive test in all stages of syphilis, which is still considered the golden standard[8]. Very rare cases (0.35%) of false-negative FTA-ABS can occur and can be found in HIV infection, autoimmune diseases and pregnancy.

In the case 1, patient had two negative VDRL and in the case 2, VDRL and FTA-ABS were negative. The patient 1 was HIV positive,

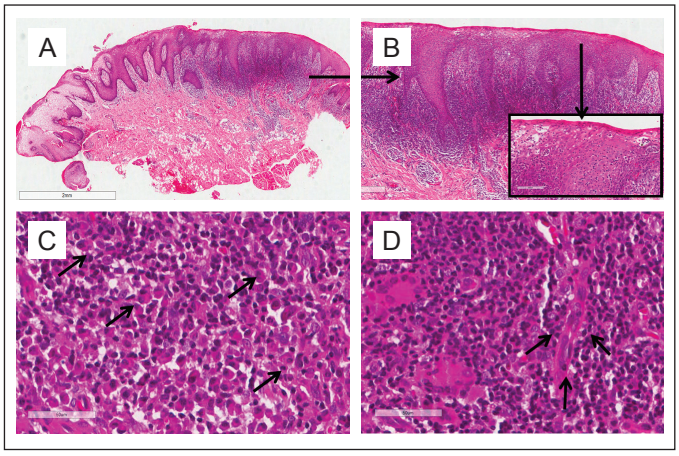

Figure 4 – Histopathological aspects of oral syphilis. Histopathological aspects exhibiting epithelial hyperplasia, parakeratosis, papillomatosis and neutrophils exocytosis (A). On the right side, in a higher magnification, epithelium with microabscess (B). The connective tissue demonstrated an intense chronic plasma cell inflammatory infiltrate on the surface and in depth perivascular (C) and the increased blood vessels with edematous endothelial cells (D).

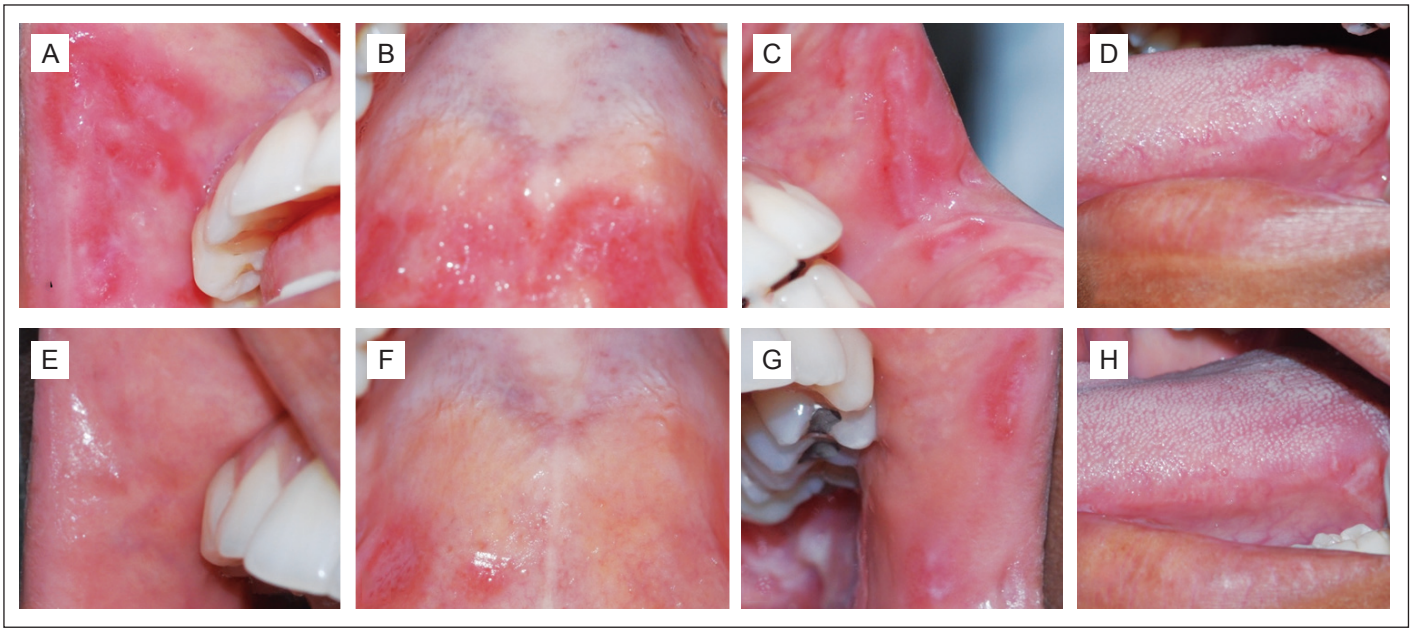

Figure 3 – Clinical aspects of oral syphilis before and after treatment. Erythematous mucosal plaque with mild white ulcerated center on the lip (A), buccal (B), palate (C) mucosa and the tongue (D). E-H pictures demonstrate partial regression of the lesions after seven days of treatment.

which justifies the presence of false-negative results, although they are rare. False-negative results occur because of impaired response of B lymphocytes to *Treponema pallidum*, or due to high antibody titers. However, patient 2 was not HIV-positive neither pregnant, showing that the phenomenon can occur in both tests and in any patient. In the literature, we did not find any case of false-negative in patient with hepatitis B. To our knowledge, this is the first case reported in the literature.

The occurrence of prozone phenomenon may be decreased when laboratories perform appropriate testing and dilutions. This is performed by diluting the patient's serum to bring the antibody concentration into the zone of equivalence. Nevertheless, many hospital laboratories do not routinely test for the prozone phenomenon and, therefore, a laboratory error must also be considered in such cases of false-negative results. In the cases presented in this paper, the exams were performed in different references laboratories[13]. In such cases, oral manifestations and their histopathological exam may be pivotal to achieve the diagnosis of syphilis[7,10]. However, histopathological features are variable and the diagnosis of syphilis may also represent a challenge for pathologists[7,10].

In these present cases, there were no skin lesions, but the patients presented oral manifestations of syphilis, which allowed the diagnosis. Several clinical differences have been described in many case reports of patients with HIV co-infection[14]. Oral lesions at the secondary stage persist from few days up to eight weeks and have a variety of clinical appearance, which may lead to a misdiagnosis[15]. Usually, oral lesions present as multiple painful mucous patches, ulcers, deep ulcers and are located in the soft palate, dorsum of the tongue and vestibular mucosa[5,11,15].

In these cases, the patients were diagnosed with secondary syphilis through the biopsy of oral lesions, which presented different aspects, including erythematous patches and ulcers on the buccal mucosa, tongue and palate. Moreover, oral lesions and histopathological exam may represented the unique method to diagnosis[4,5,10,11].

The histopathological characteristics of secondary syphilis are as variable as the clinical manifestations[10]. Whereas the changes are often non-specific, findings of proliferation and obliterating endothelial, perivascular infiltrates with a preponderance of plasma cells, and epithelium psoriasiform hyperplasia support the diagnosis of syphilis[5,7,10]. Similar histopathological features with the remarkable presence of hyperplasia, papillomatosis and microabscess in the epithelium were observed in these cases. The lamina propria showed a dense and diffuse chronic inflammatory infiltrate composed mainly by lymphocytes and plasma cells. In addition, silver stain and dark-field microscopy are useful to identify spirochetes in tissue sections and are helpful to achieve the diagnosis[7]. In this patient, Warthin Starry stain showed the presence of spirochetal organisms, confirming the diagnosis of syphilis. Based on the histopathological findings, another VDRL and FTA-ABS were requested, which were positive.

CONCLUSION

In conclusion, the serology may be negative in secondary syphilis in HIV patients and no HIV patients, making diagnosis difficult. In these cases, the oral lesions and histopathological exam may represent the unique method to diagnostic.

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SUSCEPTIBILITY OF *NEISSERIA GONORRHOEAE* TO GENTAMICIN, CHLORAMPHENICOL AND OTHER ANTIBIOTICS IN MANAUS, AMAZON, BRAZIL

SUSCETIBILIDADE DA NEISSERIA GONORRHOEAE A GENTAMICINA, A CLORANFENICOL E A OUTROS ANTIBIÓTICOS EM MANAUS, AMAZONAS, BRASIL

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ABSTRACT
We notify the antimicrobial tests of 83 *N. gonorrhoeae* isolates. The results showed that it is not viable to use penicillin and tetracycline to treat the disease. The resistance to quinolones has not precluded therapy yet. All gonococci were sensitive to ceftriaxone, and the low level of resistance to gentamicin and chloramphenicol may suggest their usage as a future therapeutic option.
Keywords: *Neisseria gonorrhoeae*; antimicrobial; gentamicins; chloramphenicol; resistance.

RESUMO
Reportamos os resultados de testes de suscetibilidade realizados com 83 isolados de *N. gonorrhoeae*. Os resultados demonstram que não é viável a utilização de penicilina e tetraciclina para o tratamento da doença. A frequência de resistência às quinolonas detectada neste corte ainda possibilita sua utilização na terapêutica. Todos os gonococos testados foram sensíveis à ceftriaxona. O reduzido nível de resistência à gentamicina e ao cloranfenicol demonstra que esses antibióticos podem ser utilizados como opção terapêutica futura.
Palavras-chave: *Neisseria gonorrhoeae*; antimicrobiano; gentamicinas; cloranfenicol; resistência.

NOTE

In 2008, 106,1 million new cases of gonorrhea in adults were estimated all over the world, out of which 11 million only in the American continent[1]. In 2013, Alfredo da Matta Foundation (FUAM – Manaus, Amazonas, Brazil) reported 3,482 sexually transmitted diseases (STD) cases, out of which 14.6% were gonococcal infection. Currently gonorrhea is the second most common reported disease at FUAM, following condyloma (27.9%) and syphilis (14.2%)[2]. As in vitro susceptibility to oral cephalosporins has declined in several regions[3-5], we evaluated the susceptibility of 83 *N. gonorrhoeae* isolates to different antibiotics, including chloramphenicol and gentamicin as possible future therapeutic options. Through May–November 2009, samples were collected consecutively from 200 patients of both sexes, aged 18 or older, who spontaneously went to the STD clinic at Alfredo da Matta Foundation with urethral or cervical discharge. *N. gonorrhoeae* was identified as described previously[6]. The E-test (bioMérieux AB, Solna, Sweden) method was used for antimicrobial susceptibility tests. The criteria recommended by WHO[6], CSLI[7], EUCAST[8] and Van Dick et al.[9] were applied for the interpretation of the results of susceptibility tests. For the phenotypic characterization of gonococci resistant to penicillin and tetracycline, we used those described by Bhuiyan et al.[10]. Due to the absence of criteria for gentamicin, we used those mentioned by Brown[11], in which Minimal Inhibitory Concentration (MIC) ≤4 mg/L was defined as sensible, 8–16 mg/L as reduced sensitivity and ≥32 mg/L as resistant. Two hundred patients were included in this study (65% male and 35% female) aged from 18–48 (medium of 26 years). After samples were collected, 83 (41.5%) were positive to *N. gonorrhoeae,* out of which 65.5% were urethral and 34.5% cervical. Resistance to azithromycin was of 1.2%; to ofloxacin and ciprofloxacin, 2.4%; to chloramphenicol, 3.6%; to penicillin, 20.5% — 16.7% of which were PPNG (Penicillinase-Producing *Neisseria gonorrhoeae*) and 3.8% CMRNG (Chromosomally Mediated Resistant *Neisseria gonorrhoeae*) —; and to tetracycline, 54.2%, with 4.8% TRNG (Tetracycline- Resistant *Neisseria gonorrhoeae*). All isolates were susceptible to ceftriaxone and gentamicin **(Table 1)**. Resistance reduction of 1.3% to penicillin and of 25.8% to tetracycline was observed when compared with studies carried out in the same region in 2005[12]. The reduction of the resistance of gonococci to both antibiotics may have been the result of some associated factors as follows: those antibiotics are not used at STD clinic in FUAM anymore; governmental measures rule the antibiotic market and the recommendations of standard guidelines[13] to use different kinds of antimicrobials to treat gonorrhea. Regarding quinolones, our findings confirm the presence of resistant gonococci in the region[14], but the frequency of resistance detected does not preclude their usage

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Table 1 – Antimicrobial susceptibility test of 83 clinical isolates of *N. gonorrhoeae.*

Antibiotics	Susceptibility test – Etest								
	Susceptible			Reduced sensitivity			Resistant		
	n	%	mic–µg/mL	n	%	mic–µg/mL	n	%	mic–µg/mL
Azithromycin•	79	95.2	0.16–0.250	3	3.6	0.5	1	1.2	1
Ceftriaxone♦	83	100	0.002–0.032	ND	ND	–	ND	ND	ND
Ciprofloxacin♦	81	97.6	0.002–0.008	0	0.0	–	2	2.4	6–8
Chloramphenicol•	67	80.7	0.047–0.5	13	15.7	0.7–1.5	3	3.6	2–4
Gentamicin∗	83	100	0.016–4	0	0.0	–	0	0.0	–
Ofloxacin♦	81	97.6	0.002–0.125	0	0.0	–	2	2.4	6–8
Tetracycline♦	23	27.7	0.047–0.250	15	18.1	0.380–1	45	54.2	1.5–16
Penicillin♦	23	27.7	0.012–0.064	43	51.8	0.094–1	17	20.5	2–32

• WHO (2013)[6], EUCAST (2014)[8] and Van Dick et al. (2000)[9]; ∗ Brown et al. (2010)[11]; ♦WHO (2013)[6]; CLSI (2013)[7]; ND: not determined. The break-points have not been determined yet.

in therapy. There was no resistance to ceftriaxone in this study, but it is noteworthy that gonococcus with reduced sensitivity to this antibiotic[15] (MIC of 0.064 µg/mL) had been reported in the region before[14]. Concerning azithromycin, the frequency of 1.2% of resistance enables the use of this antibiotic as a therapeutic option at the currently recommended dose[5] if necessary. Thiamphenicol, a chloramphenicol derivate, has been successfully used in Brazil[16] to treat gonorrhea, and its resistance below 5%[17] makes it an alternative therapeutic option. The absence of resistance to gentamicin is encouraging, but an isolate showed MIC of 6 µg/mL, which needed monitoring. Studies with gentamicin were conducted in some countries[18-20] and their good perspectives encourage its use for gonorrhea treatment[21]. Comparing our results with the other countries in South America[22], we notice that decrease of resistance to penicillin and tetracycline has also been detected. However, 11% of resistance to ciprofloxacin has been reported in 8 countries, as well as to azithromycin, gentamicin and chloramphenicol. As in our findings, no gonococcal with ceftriaxone resistance in those countries has been reported either. In Brazil, a single ciprofloxacin oral dose of 500 mg or 250 mg of intramuscular ceftriaxone is currently recommended as first-line treatment for gonorrhea[13]. In spite of the increasing ineffectiveness of antibiotics used in the treatment of gonorrhea in other countries[23], this study demonstrated that quinolones and ceftriaxone are still effective in the therapy of gonorrhea at FUAM. Chloramphenicol and gentamicin might be used as possible future therapeutic option[24] or in cases in which ciprofloxacin is not recommended as: pregnant women, patients under 18 years old and cephalosporin-allergic patients.

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17th IUSTI WORLD CONGRESS

Incorporating the 2016 IUSTI-Africa Regional Conference

MARRAKESH

9th-12th May 2016

ABSTRACT SUBMISSION

to

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INTERNATIONAL UNION AGAINST SEXUALLY TRANSMITTED INFECTIONS

COLLABORATING ORGANISATION

Institut National d'Hygiène Sciences

EUROGIN 2016

International Multidisciplinary Congress

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The EUROGIN 2016 Congress aims at developing a full review of current scientific developments in the field of cervical cancer and human papillomavirus related diseases, raising the public health profile and increasing the need for responsible health services in this area. The event endeavors to translate scientific and evidence-based research into clinical practice while highlighting the following aspects:

- Recent advances and updated scientific insights in HPV screening, testing and management
- The impact of HPV and associated cancers on public health
- Strategies to prevent and treat HPV related diseases
- Exchanging information on early detection, new diagnostic and therapeutic procedures and prevention strategies including screening and HPV vaccination

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