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ORIGINAL INVESTIGATION

Prevalence of human papillomavirus infection among women presenting for cervical cancer screening in Chile, 2014–2015

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Abstract Cervical cancer is the fourth most common malignancy in women worldwide. In Chile, cervical cancer is the second leading cause of death among women of reproductive age, causing more than 600 deaths annually. This study was carried out to determine the burden and confirm the predominant human papillomavirus (HPV) genotypes among women presenting for cervical cancer screening in public health services in Chile. Women aged 18–64 years residing in the north and central areas covered by six primary care centers of Santiago, Chile, were invited to participate from March 2014 to August 2015. Cervical swabs were examined both HPV genotyping by PCR and Reverse Line Blot, and cervical cytology by Pap testing. A total of 1738 women were included in this study: 11.1 % were HPV positive, 9.7 % were high-risk types positive, 3.2 % were low-risk types positive, 1.4 % were Pap positive and 0.9 % were positive by both tests. The four most predominant genotypes were 16, 66, 51 and 59, with prevalence of 2.8, 1.4, 1.2 and 1.2 %, respectively. Multiple HPV infections were detected among 3.8 % participants. Age-specific prevalence of HPV showed a peak in HPV infection at younger ages (≤30 years), declining to a plateau in middle age. Among women with normal cytology, the 9.4 % were HPV positive, while 58.3 % of women with abnormal cytology were HPV positive. These findings show new epidemiological data confirming HPV 16 and 66 as the most predominant genotypes in Chile. These data are important for design successful strategies for prevention of cervical cancer in Chile.

Keywords Human papillomavirus · Prevalence · Genotypes · Cervical cytology · Cervical cancer

Introduction

Human papillomavirus (HPV) infection has been established as the main cause of cervical squamous intraepithelial lesions and invasive cervical cancer. From the more than 100 types of HPV described, about 40 are known to infect the genital tract and about 20 have been classified as oncogenic to humans [1–3]. Epidemiological information allows to distinguish as high-risk HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 [1, 2]. Persistent infection with high-risk HPV has been considered as the necessary condition for malignant transformation of the cervical epithelium. In most studies, HPV-16 and HPV-18 are the predominant genotypes: they cause about 70 % of precancerous lesions and cervical cancer [4].

Cervical cancer is the fourth most common cancer women worldwide, with an estimated 527,624 new cases and 265,672 deaths in 2012 [5]. About 86 % of the cases occur in developing countries, accounting for 13 % of all cancers affecting women. South America has some of the highest cervical cancer incidence and mortality rates in the world, surpassed only by most regions of Africa and South-Central Asia [6].

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In Chile, cervical cancer causes the death of more than 600 women each year, mainly of low socio-economic level, and is the second most common cause of cancer death for Chilean women aged 20–44 years [7]. The current country's mortality rate of 7.6/100,000 is four than that of developed countries [8, 9]. These facts emphasize the need to improve the effectiveness and equitability of the national cervical cancer prevention program.

About 15.6 % of Chilean women are estimated to harbor cervical HPV infection at any given time [10]. These estimates came from women residing in Arica [11] and the south of Santiago [12, 13] cities, with HPV prevalence values ranging from 2.6 to 28.0 %, respectively. These data would indicate the heterogeneous character of HPV prevalence throughout the country and highlight the need for further studies about exposed women living in other areas of Chile.

Here, we report the first type-specific prevalence of HPV infection in sexually active women recruited during a routine gynecological visit to six public health centers located in north and central Metropolitan Area of Chile. These epidemiological findings may provide guidance for HPV testing in the routine clinical practice of public primary health centers in Chile.

Materials and methods

Study population and specimen collection

We carried out the present survey from March 2014 to August 2015 in north and central from Santiago city, Chile. Six public health care centers and their referral hospital participated in the study, using the infrastructure, personnel and protocols already in place under the national cervical cancer prevention program. We recruited women aged 18–64 years residing locally, excluding women who were pregnant, hysterectomized or virgins. Women were invited to participate through an outreach campaign in the catchment area of each health center and, if interested, received an appointment with the health center midwife. Eligible women who agreed to participate signed an informed consent form and entered the study.

Exfoliated cervical cell samples were obtained by a gynecologist or a midwife according to the routine procedures in the health center. For each patient, two separate specimens were collected independently for cytological diagnosis and HPV genotyping assay.

Pap smears were stained and read by trained cytopathologists and were classified according to the Bethesda classification. Women who had an inadequate cytologic result were excluded from the analysis. Women with abnormal cytology were followed, according to the guidelines of the National Cancer Program of Chile.

Detection and typing of HPV

HPV DNA testing was done on exfoliated cell samples at the Seccion Virus Oncogenicos of the Instituto de Salud Publica de Chile. DNA was extracted from cells according to a commercial and automated method (NucliSENS® easyMAG®, cat 280140, bioMérieux, France). Three extraction controls used identical procedures: without cells, negative control (K-562 HPV non-infected cells), and positive controls (SiHa HPV-16 and HeLa HPV-18 infected cells).

HPV DNA was measured using Brilliant II SYBR® Green QPCR Master Mix (Agilent Technologies, cat 600828, La Jolla, California). We amplified the following genomic regions: 450 bp of HPV L1 gene with primers PGMY 09/11 [14], and 141 bp of albumin gene with primers ALB-Fw and ALB-Rv for internal calibration [15]. PCR conditions were as follows: 100 ng DNA was added to 20 μL reaction mixture containing 1x Brilliant II SYBR® Green QPCR Master Mix, 0.5 mM each primer. Thermocycling was performed in a Stratagene Mx3000P (Agilent Technologies) under the following conditions: 10 min at 95 °C (hot start), and then 45 cycles of 10 s at 95 °C (denaturation) followed by 10 s at 56 °C (annealing) and 60 s at 72 °C (extension). Purity of amplified products was checked by observation of a single melting peak in HPV PCR.

HPV genotyping was performed by PCR and Reverse Line Blot (PCR-RLB). PCR using PGMY09 and biotin-labeled PGMY11 generic HPV primers was performed to amplify 450 bp in the L1 viral region. PGMY-PCR-positive samples were typed by reverse line blot hybridization using 6, 11, 16, 18, 26, 31, 33, 34, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 55, 56, 57, 58, 59, 69, 66, 68, 70, 73, 82, 83, and 84 type-specific oligoprobes [16]. Positive reactions were revealed by chemiluminescence using AmershamTM ECLTM Detection Reagents according to manufacturer recommendations (GE Healthcare, Little Chalfont, UK).

Statistical analysis

We calculated crude and age-adjusted prevalence of HPV infection, using Chilean population and the world standard population as the reference. The HPV infection rate was estimated within 6 age groups (<20, 21–30, 31–40, 41–50, 51–60, and >60).

A binomial 95 % confidence interval (95 % CI) was estimated, and *P* values for age trends of HPV infection were analyzed using the linear-by-linear association test.

Differences between each pairing of two age groups were compared by the Chi-squared (χ^2) test.

The frequency of each high-risk HPV (HR-HPV) and low-risk HPV (LR-HPV) genotype was presented in HR-HPV-positive samples and LR-HPV-positive samples, respectively. All statistical analyses were performed using Prism 6.04 software (GraphPad Software, Inc., San Diego, CA, USA). Values of p lower than 0.05 were considered to be statistically significant.

Results

Prevalence of HPV infection

A total of 1738 samples were obtained during this study. The presence of HPV genome was evaluated in these specimens, and genotyping was carried out in all positive samples. One hundred ninety-three samples were HPV infected. Thus, total HPV prevalence was 11.1 % (193/1738). It was detected 9.1 % samples with normal cytology and simultaneously infected with HPV: 7.8 % HR-HPV and 2.5 % LR-HPV infected. The 65.3 % (125/193) samples were infected with a single viral type, and 34.7 % (67/1393) samples were simultaneously infected with multiple viral types (Table 1). The most prevalent single infections were produced by the following viral types: HPV-16 (34/2.0 %), HPV-66 (11/0.6 %), HPV-52 (8/0.5 %), HPV-51 (7/0.4 %), and HPV-31, HPV-33, HPV-39 and HPV-59 (6/0.3 %) (Table 1). Single infections were detected in 62.7 % (106/169) and 27.1 % (20/56) HR-HPV and LR-HPV infected samples, respectively. Single infections were detected with all HR-HPV, except HPV-35 and HPV-82. Also, single infections were only detected with some LR-HPV (HPV-6, HPV-42, HPV-44, HPV-53, HPV-54, HPV-55, HPV-83 and HPV-84).

Another ten LR-HPV caused only multiple infections. Similarly, the most prevalent multiple infections were produced by the following viruses: HPV-16 (15/0.9 %), HPV-51 and 59 (14/0.8 %), HPV-66 (13/0.7 %), HPV-31, HPV-42, HPV-52 and HPV-58 (11/0.6 %). Besides, 169 and 56 samples were infected with HR-HPV and LR-HPV, respectively (Table 1).

On the other hand, when single and multiple infections were analyzed together, the most prevalent HR-HPV were the following types: HPV-16 (2.8 %), HPV-66 (1.4 %), HPV-51 (1.2 %), HPV-59 (1.2 %), HPV-52 (1.1 %) (Fig. 1a). Moreover, HPV-18 was found in very low frequency in this population (0.6 %). Similarly, the most prevalent LR-HPV were the following types: HPV-42 (0.8 %), HPV-6 (0.7 %), HPV-53 (0.4 %), HPV-54 (0.3 %) and HPV-44 and 55 (0.3 %) (Fig. 1b). Also, HPV-11 was found in very low frequency (0.1 %). It was detected three H-SIL cases associated with a single infection of HPV-16 or HPV-33 or HPV-73. Another H-SIL case was multiple infected with HPV-26 and HPV-31.

Prevalence by age of HPV infection

We calculated crude and age-adjusted prevalence of HPV infection in this studied population. According to age, patients were classified into six groups (<20, 21–30, 31–40, 41–50, 51–60, ≥60 years). Number of HPV infection was counted in each of these groups. The prevalence of HPV by age showed the highest levels at 21–30 and ≤20 age groups with 22.9 and 19.5 %, respectively (Table 2). In addition, the age-adjusted prevalence showed that positivity rates of HPV infections decreased as the age of women increased. Thus, viral prevalence in women ≥60 years old was below 5.0 and 4.0 % for HR-HPV and LR-HPV, respectively (Fig. 2). The prevalence of infections with HR-HPV by age of women remained in a high level at <20, 21–30, 31–40, 41–50 years group (24.7, 18.5, 13.3 and 14.4 %, respectively) (Fig. 2a). The age-specific prevalence of HR-HPV (24.7–18.5 %) and LR-HPV (2.7–6.4 %) showed a sharp high level at the youngest age group. Besides, LR-HPV infections occurred in a low prevalence. These infections reached a peak level (6.4 %) in women at 21–30 years (Fig. 2b). Consequently, the prevalence by age high- and low-risk HPV showed a peak in HPV infection in younger age (≤30 years), decreasing with a plateau in middle age. For both types of viruses, HR-HPV and LR-HPV, the curve shape resembled a reverse J-curve.

HPV type distribution according to cytology

We compared the analytical results of detection of HPV genome and cervical cytology in all studied cases in order to evaluate the correlation between both assays. Normal or negative cytology was found in 1678 (96.5 %) cases (Fig. 3a). In this group, it was detected 6.7 % (112) and 1.4 % (23) HR-HPV and LR-HPV infected, respectively (Fig. 3b). Furthermore, it was found 9.2 % (154) cases infected with any HPV; of which 72.7 % (112) cases was exclusively infected with HR-HPV. On the other hand, it was determined 60 (3.5 %) women with an abnormal result by cytology: 35 ASC-US, 16 L-SIL, 8 H-SIL and 1 CCI (Fig. 3a). Among women with abnormal cytology 19 ASC-US, 12 L-SIL, 7 H-SIL and 1 ICC were detected HPV positive. Thus, specific HPV prevalence in each type of lesion was 54.3, 75.0, 87.5 and 100 %, respectively (Fig. 3b). Abnormal cytology was caused by both single HR-HPV and LR-HPV infections as well as multiple infections with both groups (Fig. 3b). Consequently, 43.3 % (26), 1.7 (1) and 20.0 % (12) of abnormal cytology were associated with single HR-HPV, single LR-HPV and multiple HR-HPV/

Table 1 Overall HPV prevalence, type distribution and multiplicity of infection, and cytological findings among 1738 Chilean women (2014–2015)

HPV type	Cytology *n*(%)				Total		
	Normal	ASC-US	L-SIL	H-SIL	Single	multiple	Total
HPV −	1520 (87.5)	16 (0.9)	4 (0.2)	5 (0.3)			1545 (88.9)
HPV +	158 (9.1)	19 (1.1)	12 (0.7)	4 (0.2)	126	67	193 (11.1)
HR HPV+	136 (7.8)	19 (1.1)	11 (0.6)	3 (0.2)	106	63	169 (9.7)
LR HPV+	44 (2.5)	7 (0.4)	3 (0.2)	2 (0.1)	20	36	56 (3.2)
HR infections							
16	38 (2.2)	6 (0.3)	4 (0.2)	1 (0.1)	34	15	49 (2.8)
18	8 (0.5)	2 (0.1)	0	0	5	5	10 (0.6)
31	13 (0.7)	1 (0.1)	1 (0.1)	1 (0.1)	6	11	17 (1.0)
33	2 (0.1)	5 (0.3)	0	1 (0.1)	6	2	8 (0.5)
35	3 (0.2)	1 (0.1)	0	0	0	4	4 (0.2)
39	11 (0.6)	2 (0.1)	0	0	6	7	13 (0.7)
45	6 (0.3)	1 (0.1)	0	0	3	4	7 (0.4)
51	17 (1.0)	3 (0.2)	1 (0.1)	0	7	14	21 (1.2)
52	16 (0.9)	3 (0.2)	0	0	8	11	19 (1.1)
56	6 (0.3)	1 (0.1)	3 (0.2)	0	5	5	10 (0.6)
58	9 (0.5)	1 (0.1)	4 (0.2)	0	5	11	14 (0.8)
59	16 (0.9)	4 (0.2)	0	0	6	14	20 (1.2)
66	19 (1.1)	2 (0.1)	3 (0.2)	0	11	13	24 (1.4)
68	5 (0.3)	0	0	0	3	2	5 (0.3)
73	7 (0.4)	0	0	1 (0.1)	1	7	8 (0.5)
82	2 (0.1)	0	0	0	0	2	2 (0.1)
LR infections							
6	9 (0.5)	1 (0.1)	2 (0.1)	0	5	7	12 (0.7)
11	2 (0.1)	0	0	0	0	2	2 (0.1)
26	0	1 (0.1)	0	1 (0.1)	0	2	2 (0.1)
32	1 (0.1)	1 (0.1)	0	0	0	2	2 (0.1)
34	2 (0.1)	0	0	0	0	2	2 (0.1)
40	3 (0.2)	0	0	0	0	3	3 (0.2)
42	11 (0.6)	1 (0.1)	1 (0.1)	0	2	11	13 (0.8)
44	5 (0.3)	0	0	0	3	2	5 (0.3)
48	0	0	1 (0.1)	0	0	1	1 (0.1)
53	7 (0.4)	0	0	0	5	2	7 (0.4)
54	4 (0.2)	2 (0.1)	0	0	1	5	6 (0.3)
55	5 (0.3)	0	0	0	1	4	5 (0.3)
57	1 (0.1)	0	0	0	0	1	1 (0.1)
69	1 (0.1)	0	0	0	0	1	1 (0.1)
70	2 (0.1)	0	0	0	0	2	2 (0.1)
72	1 (0.1)	0	0	0	0	1	1 (0.1)
83	1 (0.1)	1 (0.1)	0	0	1	1	2 (0.1)
84	4 (0.2)	0	0	0	2	2	4 (0.2)

LR-HPV infection. A positive correlation between single HR-HPV infection and cytological diagnosis severity was determined. Difference of single HR-HPV infection in normal and abnormal cytology was significant: 6.7 % (112/1678) and 43.3 % (26/60), respectively ($\chi^2 = 69.2$; $p < 0.0001$). Prevalence of single HR-HPV infection was 34.3 % (12/35), 50 % (8/16), 62.5 % (5/8) and 100 % (1/1) in ASC-US, L-SIL, H-SIL and ICC, respectively. The only case of ICC was associated with a single HPV-16 infection. However, prevalence of single LR-HPV infection in normal and abnormal cytology was not significantly different: 1.4 % (23/1678) versus 1.7 % (1/60). Further, prevalence of LR-HPV infection varied between 0.0 and 25.0 % regardless of the severity of lesions.

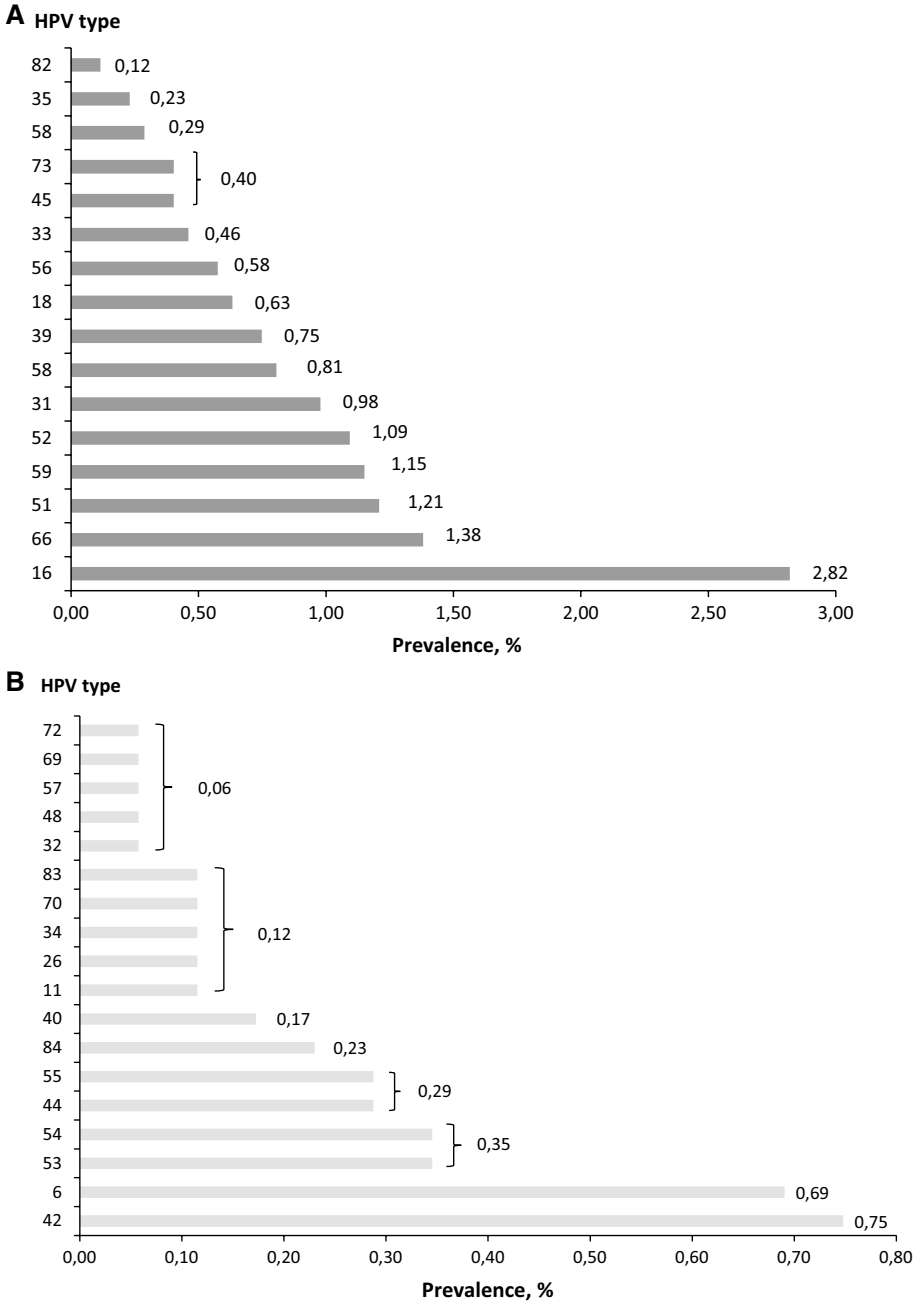

Fig. 1 Frequency of HPV types among HPV positive samples from 1738 Chilean women. **a** High-risk HPV genotypes. **b** Low-risk HPV genotypes

Table 2 Prevalence of HPV by age groups among 1738 Chilean women

Age (y)	HR-HPV (+)		LR-HPV (+)		Any HPV (+)		Total cases *n*
	n	%	*n*	%	*n*	%	
<20	7	17.1	1	2.4	8	19.5	41
21–30	73	18.2	19	4.7	92	22.9	401
31–40	34	7.7	16	3.6	50	11.3	443
41–50	36	7.1	12	2.4	48	9.5	504
51–60	15	5.4	8	2.9	23	8.2	279
>60	4	5.7	0	0.0	4	5.7	70
Total	169	9.7	56	3.2	225	12.9	1738

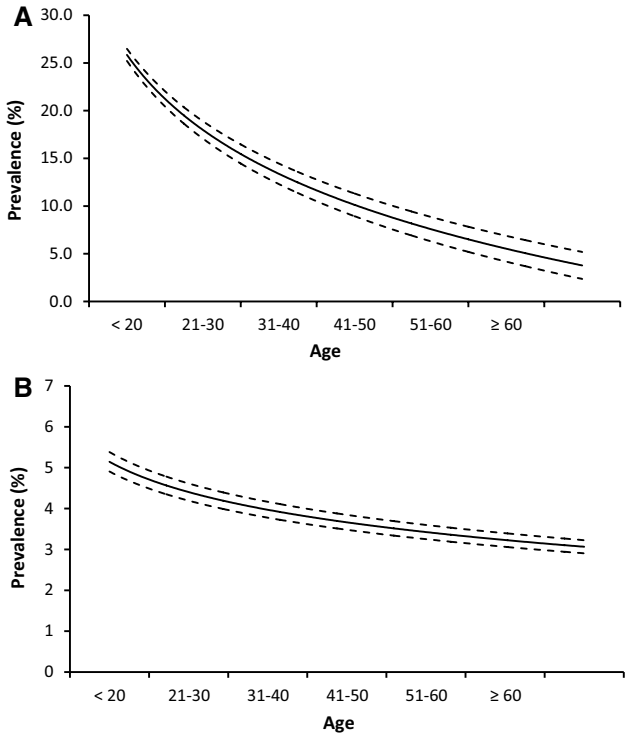

Fig. 2 Age-adjusted prevalence of HPV infection among 1738 Chilean women and 95 % confidence intervals (*dotes lines*). **a** High-risk HPV genotypes. **b** Low-risk HPV genotypes

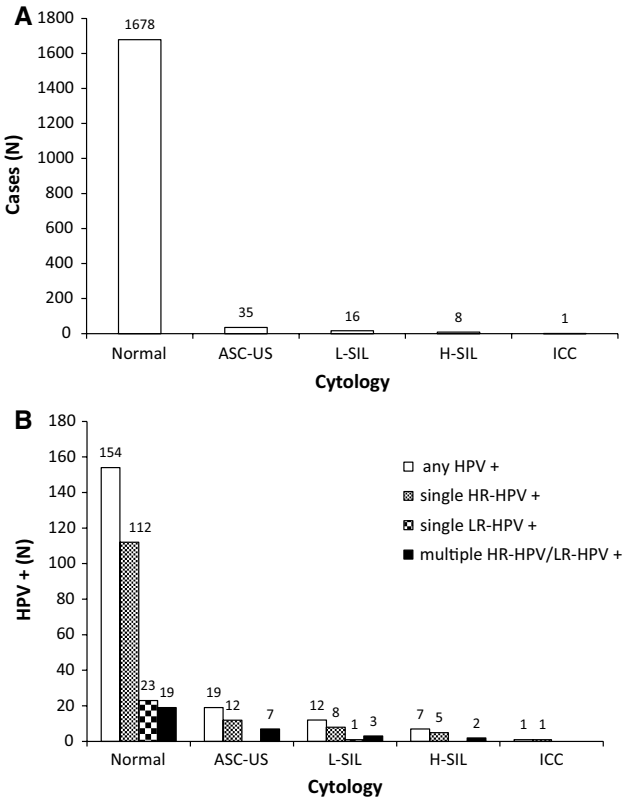

Fig. 3 Overall HPV, HR-HPV and LR-HPV prevalence by cytological category. **a** Distribution of cytological categories. **b** HPV infections by cytological categories. Normal, negative for intraepithelial lesion or malignancy; *ASC-US* atypical squamous cells of undetermined significance, *L-SIL* low-grade squamous intraepithelial lesion, *H-SIL* high-grade squamous intraepithelial lesion, *ICC* invasive cervical cancer

Discussion

Cervical cancer ranks fifth in frequency among women in the world [17]. It was estimated 528,000 new cases during 2012. However, this cancer has a heterogeneous distribution because it is more common in underdeveloped regions. It is estimated 266,000 women died for cervical cancer worldwide during 2012. Almost 90 % of these deaths occurred in less developed regions. Cervical cancer is the second most common cancer among women between 15 and 44 years old in Chile. Annually, it is estimated that 1450 new cases are diagnosed with cervical cancer and 734 die from the disease [5].

Here, samples of 1738 women attending at primary care centers from north and center of Santiago were analyzed. We found that total HPV prevalence was 11.1 %, considering both HR- and LR-HPV. This rate agrees well with HPV prevalence previously reported (10.7–11.8 %) in the south of Santiago [12, 13]. The level of HPV infection (11.1 %) among Chilean women is similar to the prevalence previously reported in other Latin American countries among women from routine cancer control program: Mexico, 8.6–14.5 % [18, 19]; Brazil, 10.5–12.3 % [20, 21]; Argentina, 16.6 % [22], Peru, 12.6 % [23]; Colombia 14.6 % [24], but higher than in many parts of Europe [25–27] and Asia [28, 29].

In this study, HPV-42 was the most prevalent type of LR-HPV. HPV-6 and HPV-53 were the second and third common types, respectively. In addition, the HPV-11 was the ninth prevalent LR-HPV. Similar low prevalence of HPV-6 and HPV-11 were previously reported in Chile [12]. In our study, the frequency of HPV-6 and HPV-11 were 0.7 and 0.1 %, respectively. Previously, frequency of HPV-6 and HPV-11 was 0.2 and 0.4 % [12]. This situation seems to be different worldwide and Northern America, where the prevalence of HPV-6 and HPV-11 was 0.8–5.9 and 0.5–2.9 %, respectively [30, 31]. However, the prevalence of HPV-6 and HPV-11 infection among Chilean women is similar to the prevalence previously reported in other Latin American countries among women from primary health care centers: Mexico, 0.4–1.9 % HPV-6 and 0.2–1.0 % HPV-11 [18, 32, 33]; Brazil, 0.5–2.1 % HPV-6 and 1.6–2.3 % HPV-11 [34, 35]; Argentina, 0.0 % HPV-6 and 0.4 % HPV-11 [22]. Furthermore in Spain, the CLEOPATRE study reported prevalence of 0.4 and 0.3 % for HPV-6 and HPV-11, respectively [36].

We found that HPV 16 was the most frequent viral type. This result agrees with those found in most other countries. However, we detected a very low HPV-18 prevalence unlike what it has been reported in many South America countries [30]. We determined HPV-66, HPV-51 and HPV-59 were second, third and fourth place of the most prevalent types in Chile, respectively. This finding is different than previously reported in Santiago 12 years ago [12]. It was previously reported that the most prevalent types, in decreasing order, were HPV-16, 56, 58, 31 and 59 (12). In both studies, HPV-16 was reported to be the most prevalent type in different areas of Santiago. However, finding HPV-66 as one of the most frequent type in Santiago was an unexpected result. Moreover, the HPV-66 frequency that was found in this study was higher than reported worldwide [5, 30, 37], and also it was similar among the recently published prevalence studies in which this type was identified in normal cytology [36, 38]. It is very necessary to know on the epidemiology of different HPV types to implement appropriate prevention strategies for cervical cancer in a region or country. There are currently two effective vaccines to prevent HPV infections associated with cervical cancer: the bivalent vaccine, which targets HPV-16 and HPV-18, and the quadrivalent vaccine, which also targets HPV-6 and HPV-11. The quadrivalent vaccine is currently used in Chile. However, it seems that this vaccine is not enough to confer optimal protection because HPV-18 infections are infrequent in Chilean women, and other HR-HPV (e.g. HPV-51, HPV-59 and HPV-66) are much more prevalent than VPH-18. Furthermore, it was reported that the cross-protective efficacy of quadrivalent HPV vaccine against high-grade lesions was only significant for HPV31 among non-vaccine HPV types [39]. Other studies have indicated that quadrivalent vaccine would confer significant cross-protection for HPV31, HPV58 and HPV59 [40]. Consequently, the new epidemiological data on HPV prevalence in South America should be considered for the design of future prophylactic HPV vaccines.

On the other hand, epidemiological information on HPV infection prevalence by age range is also important to define appropriate vaccination strategies in order to prevent cervical cancer. In our study, it was found the highest levels of HPV prevalence in youngest women. Later, a steady decrease of HPV infection was detected as age of women increased. This epidemiological profile found in Chilean population is the typical pattern previously detected in Northern America, Europe and China [30, 41, 42]. However, it is different from the pattern found in several Latin American countries, in which a modest second peak is detected in middle-aged women [43]. This Chilean pattern is different from that reported 15 years ago, where the prevalence by age showed a bimodal distribution. Therefore, a peak in HPV infection was found at younger ages (<25 years), declining to a plateau in middle age, and a second peak was observed at age ≥45 years [12]. Our new findings suggest that over the last two decades have produced a change in the prevalence of HPV by age in Chile. The decrease of HPV after age 50 could be the result of the selective elimination of HPV by treatment or the reflection of successful impact of cancer prevention program in this group of Chilean women during the last decade [44, 45]. It is necessary to perform new studies with larger populations to confirm our preliminary results. It seems that sex education program has had a positive impact on Chilean women at age ≥50 years. These women have been treated by national health insurance system through last 20 years. This could explain the new epidemiological pattern observed in women at age ≥50 years. However, new sexual behaviors in younger women (i.e. younger age at first sexual intercourse and a greater number of sexual partners) suggest that it is necessary to establish more aggressive and earlier educational programs in Chilean schools.

Persistent infection with HR-HPV is the etiological factor for development of cervical cancer. Previously, it has reported that the severity of lesions in the cervix is directly related to the increased prevalence of HR-HPV infections [46]. Here, we have confirmed that the most serious cervical lesions were associated with higher frequency of HR-HPV infections. Among the 1738 Chilean women, 154 cases were any HPV positive with normal cytology and 21 cases were HPV negative with abnormal cytology. Low number of viral copies in the early stages of HPV infection may be an explanation for women with HPV positive and normal cytology [42]. Besides, it is known that a vast majority of HPV infections are transient; they are cleared by immune response within 6–8 months post-infection [44]. However, alternative explanation may be related with low sensitivity of cytology. It has been reported that this test has lower sensitivity to detect HPV infection than molecular biology assays [47]. Furthermore, the sensitivity of cytology is affected by multiple factors such as quality of sampling, staining technique, training of professional staff, etc. [48]. Consequently, sensitivity of cytology has great worldwide heterogeneity, which varies between 30 and 87 % [49]. Finally, we detected few HPV negative with abnormal cytology women. It was reported that HPV infections may be confused with non-specific cytological abnormalities produced by follicular cervicitis, other inflammation processes or bacterial and/or viral infections [42, 50–52].

On the other hand, the HR-HPV infections more frequently associated with cervical cancer are types HPV-16, 18, 31, 33, 35, 45, 52 and 58 [31, 53]. A meta-analysis about prevalence of HPV type in Latin America indicated that HPV-16, 18, and 31 were among the three most common type in H-SIL and ICC [54]. In this work, high-risk

HPV-16, 31, 33, and 73 were the most prevalent genotypes in H-SIL. Also, HPV-18 was detected in very low prevalence in cases with abnormal cytology. It was recently found in Mexico a minor prevalence of HPV-18 as reported worldwide and that HPV-58 and 52 also were genotypes with an important prevalence in ICC [32]. Moreover, in Argentina HPV-66 and 16 were the most prevalent HPV types in abnormal cytology [55]. These new findings suggest that HPV-18 in HSIL may be less prevalent as previously reported in some regions of Latin America. These data would indicate the heterogeneous prevalence of HPV types in Latin America and highlight the need for further studies about abnormal cytology cases.

Consequently, knowledge of prevalence of high-risk HPV associated with abnormal cervical cytology is very important for the design of successful strategies for control and prevention of cervical cancer in Chile and South America.

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