BURDEN OF GENITAL WARTS IN ECUADOR: AN OBSERVATIONAL STUDY IN THE PRACTICE OF PHYSICIANS

CARGA DAS VERRUGAS GENITAIS NO EQUADOR: ESTUDO OBSERVACIONAL SOBRE A CLÍNICA MÉDICA

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ABSTRACT

Introduction: Human papillomavirus types 6 and 11 cause 90% of genital warts. Although the epidemiology of cervical cancer and the distribution of human papillomavirus genotypes have been investigated in Ecuador, little is known about the occurrence of genital warts. **Objective:** To estimate the incidence and prevalence of genital warts among patients routinely presenting at the practice of physicians, describe the demographics of genital warts cases and highlight the physician specialties that treat genital warts, including patterns of consultation and referral in Ecuador. **Methods:** Participants were a convenience sample of physicians who treat and/or diagnose genital warts in their practices. Physicians completed a daily log, recording the demographics and diagnosis of genital warts in all patients aged 18 to 60 years seen over 10 days in their practices. Physicians then completed a survey recording their practice characteristics and referral patterns of genital warts. **Results:** A sample of 105 physicians of different specialties participated in the study. Among 12,133 patients, the prevalence of genital warts was 5.5%, and the incidence, 3.7%. Prevalence was 6.9% in men, peaking at 12.6% in those aged from 25 to 29 years old. Prevalence was 5.1% for females, peaking at 6.5% in those aged from 30 to 34 years old. Most women were seen in direct consultations (75%) rather than by referral ones (24%). Most physicians (72%) treated females with genital warts, except for primary care physicians, who referred most cases (88%). **Conclusion:** Cases of genital warts are frequently encountered by physicians in Ecuador and re typically treated by specialists rather than primary care physicians. **Keywords:** Papillomavirus infections; condylomata acuminata; epidemiology.

RESUMO

Introdução: Os tipos 6 e 11 do papilomavírus humano causam 90% das verrugas genitais. Embora a epidemiologia do câncer do colo do útero e a distribuição dos genótipos do papilomavírus humano tenham sido investigadas no Equador, pouco se sabe sobre a ocorrência das verrugas genitais. Objetivo: Estimar a incidência e a prevalência das verrugas genitais em pacientes atendidos rotineiramente na clínica médica, descrever os dados demográficos dos casos de verrugas genitais e determinar as especialidades médicas que tratam as verrugas genitais, incluindo os padrões de consulta e encaminhamento no Equador. Métodos: Foi realizada uma amostragem por conveniência com médicos que tratavam e/ou diagnosticam verrugas genitais em sua clínica médica. Os médicos registraram as suas atividades cotidianas em um diário, anotando dados demográficos e diagnóstico de verrugas genitais de todos os pacientes com idade entre 18 e 60 anos atendidos durante 10 dias em suas clínicas. Posteriormente, os médicos responderam a uma pesquisa sobre as características da conduta tomada e os padrões de encaminhamento médico das verrugas genitais. Resultados: Uma amostra de 105 médicos de diferentes especialidades participou do estudo. Entre 12.133 pacientes, a prevalência de verrugas genitais foi de 5,5% e a incidência foi de 3,7%. A prevalência foi de 6,9% no sexo masculino, atingindo o valor máximo de 12,6% na faixa etária de 25 a 29 anos. A prevalência foi de 5,1% para o sexo feminino, alcançando 6,5% entre 30 e 34 anos. Na maior parte dos casos, as mulheres foram tratadas predominantemente pelo médico que realizou o primeiro atendimento (75%) e não por meio de encaminhamento a outra especialidade (24%). A maioria dos médicos (72%) tratou mulheres com verrugas genitais, exceto os médicos no Equador primária, que em geral encaminharam os casos (88%). Conclusão: Casos de verrugas genitais são frequentemente diagnosticados por médicos no Equador e são mais frequentemente tratados por especialistas do que por médicos de atenção primária.

Palavras-chave: Infecções por Papillomavirus, condiloma acuminado; epidemiologia.

INTRODUCTION

Human papillomavirus (HPV) is a highly contagious DNA virus that infects the skin and mucous membranes, causing genital and other carcinomas, in addition to benign lesions⁽¹⁾. Over 100 different HPV genotypes have already been characterized, of which approximately 30 are responsible for infections in the human anogenital area⁽²⁾. HPV-16, -18, and other oncogenic types are found in cervical precarcinomas, whereas visible anogenital warts (GW) are caused by HPV types -6 and -11⁽²⁾. GW are typically located at sites exposed to epithelial contact during sexual intercourse⁽²⁾; they may be asymptomatic, but can cause discomfort, itching, burning, bleeding, and dyspareunia, in addition to feelings of shame and loss of self-esteem⁽³⁻⁵⁾.

In Ecuador, HPV is highly prevalent in cervical samples with abnormal histology or with precancerous or cancerous lesions^(6,7). The most common viral types in cervical and anogenital samples from women with an atypical Pap test are, respectively, HPV-16 and $-6^{(6,7)}$. HPV is also frequently detected in routine cervical cancer screening samples in Ecuador^(8,9). García Muentes et al. detected HPV in 44% of cervical samples from women undergoing cervical cancer screening from 2008 to 2013⁽⁹⁾. Genotype -16 (5.5%) was the most frequently detected type; HPV-11 (3.8%), the third most frequent; and HPV-6, the eighth, at 2.1%⁽⁹⁾.

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The age-standardized incidence rate of cervical cancer in Ecuador is 17.8 per 100,000 inhabitants, based on GLOBOCAN 2018 data compared with a range of 11 to 38.5 per 100,000 in other South American countries — and approximately 6.5 per 100,000 in the United States⁽¹⁰⁾. Although the incidence of cervical cancer in Ecuador is well characterized, the epidemiology of GW has not been reported, and there is little information about its management by physicians.

OBJECTIVE

The objective of the present study was to estimate the incidence and prevalence of GW among patients routinely presenting at the practice of physicians in Ecuador, describe the demographics of GW cases, and highlight the physician specialties that treat GW as well as their patterns of consultation and referral.

METHODS

Study description

This is an observational, cross-sectional, multicenter study of GW in women and men attending the practice of physicians in Ecuador. The study consisted of two parts: a daily log and a survey, both completed by physicians who typically diagnose and/or treat patients with GW.

The first part of the study involved a self-administered daily log wherein physicians recorded the age, gender, and GW diagnosis of each patient aged from 18 to 60, seen during 10 consecutive workdays. The second part of the study consisted of a self-administered survey of patterns of consultation and referral, by physicians, of male and female patients with GW.

This study was sponsored by Merck & Co., Inc., Kenilworth, NJ, USA, and conducted by a Contract Research Organization (CRO): Centro de Investigación y Docencia en América Latina S.A. (CIDAL). Since there was no intent to alter usual patient care, and no collection of individual patient medical data or patient-identifying information, informed consent from the patients was not required. Approval for the study was obtained in May 2016 from the Ecuador Ministry of Health (Ministerio de Salud Pública, Coordinación General de Desarrollo Estratégico en Salud, Dirección Nacional de Inteligencia de la Salud). Data for the physicians' daily log and survey were collected throughout approximately three months, from July to September 2016.

Study sample

We sought to recruit a convenience sample of physicians from specialties that normally encounter or manage GW cases. Such physicians/specialists included primary care physicians (PCPs), dermatologists, urologists, proctologists, gynecologists, infectious disease specialists, and others. General practitioners and family medicine doctors were included as PCPs. The 'other' category included general physicians, who, in Ecuador, have not completed a residency or specialization, are not general practitioners, nor are internal or family medicine physicians; hence, they were not categorized as PCPs. Physicians were eligible for participation if they had practiced medicine for at least six months, had treated or diagnosed GW, had seen at least 75 patients in their office or outpatient clinic (for any reason) in a typical week, and had practiced in the provinces of Pichincha, Guayas, Azuay, Santo Domingo, Imbabura, or Napo. Physicians were identified from the CRO's internal database of investigators or with local outreach. A total of 100 physicians were targeted for recruitment. It was expected that gynecologists would comprise 50% of recruited physicians; PCPs, dermatologists, and urologists, each, 10 to 20%; and other physicians, each, less than 5%.

Definitions

HPV-caused GW were defined in the daily log and physician survey as gray or flesh-colored growths found in the genital and anal regions in both men and women (genital lesions caused by herpes virus were not considered GW). For inclusion as a GW case, patients had to have visible lesions; an HPV-positive DNA test alone was not enough evidence for inclusion. A *new case* of GW was defined as a case diagnosed in a patient who had never had a previous GW episode or had not had a GW episode in the prior 12 months. This included patients who had a first episode of GW that had lasted six months or less and were captured in the daily log during a follow-up visit to their physician. An *existing case* was defined as a case of GW in which previous episodes of GW (within the last 12 months) had been resolved, with or without treatment, or a case of GW that had lasted longer than six months, despite treatment.

Prevalence was defined as the number of new and existing GW cases divided by the number of all patients logged during the 10 consecutive workdays (Equation 1):

Prevalence = (new + existing cases of GW/All patients seen) in 10 consecutive workdays (1)

Incidence of GW was defined as the number of new cases of GW from the physician's log divided by the number of patients without an existing case of GW seen during the 10 consecutive workdays (Equation 2):

Incidence = (New cases of GW/All patients seen without existing GW) in 10 consecutive workdays (2)

Study instruments and procedures

Physician daily log

Physicians were required to record a daily log of all patients aged from 18 to 60, seen over 10 consecutive workdays. For each patient seen, physicians recorded the patient's age, gender, and current diagnosis of GW (yes or no). If the patient did not have GW, no additional data were collected. For those patients being seen for, or diagnosed with, GW at the clinic visit, physicians recorded the case as new or existing and categorized the duration of the current episode as ≤ 6 months with or without treatment, >6 months without treatment, or >6 months despite treatment. Physicians were urged to keep their regular patterns of practice and to record information only for patients seen during current visit. Completing the daily log was expected to take no more than 5 to 10 minutes.

Physician survey

After completing the daily log, physicians then finished a survey, recording their demographic information, their specialty, and information on their main practice setting type, affiliation, geographic location (urban or rural), and service area population. An urban location was defined as one within 50 km of an urban area, whereas a rural location was one located more than 50 km from an urban area. In addition, the survey queried the physician as to the proportion of male and female patients aged 18 to 60, seen in a typical working week; patterns of consultation, treatment, and referral of their GW patients; and reasons for referring GW cases. The survey was self-administered for one time only and was expected to take no more than 30 minutes.

Procedures

After signing an informed consent release, physicians were provided with written instructions on how to complete the daily log and survey and received training in person or by phone. The daily log and survey were provided in paper copies to be filled out by hand. Physicians were asked to return the completed daily log and survey to the CRO either by fax or mail (prepaid postage) or by e-mail (scanned documents). Data from the physician daily log and physician survey were entered into two dedicated electronic databases, access to which was limited to the project team. All data were coded with an anonymous ID number for each physician. No physician-identifying information was provided to the study sponsor or included in the analytic dataset, and no identifiers of individual patients were recorded.

Data analysis

Physician's daily logs that included seven or more workdays of data were included in the data analysis. All physician surveys were included in the data analysis regardless of the extent of completion. There was no imputation of missing data. A descriptive

Table 1 – Patient demographics, according to physician specialty*.

data analysis was conducted, in which continuous variables were reported as a mean (standard deviation) and median, and categorical data were summarized as proportions or percentages. Patient and physician demographics; physician practice characteristics; GW consultation, referral, and treatment patterns; and proportion of males and female patients seen in a typical week were summarized overall and according to physician specialty. Incidence and prevalence were calculated for the total patient population and stratified by gender.

RESULTS

Patients

Patient demographics

A total of 12,133 patients were seen by the 105 physicians over a 10-day period, as recorded in the daily log, ranging from 79 for the proctologist to 7,017 for the 59 gynecologists. These patients were predominantly female—78% overall, in the range of 59% to 65% for PCPs, dermatologists, and other physicians, but 99% for gynecologists (**Table 1**). Most (58–86%) patients seen by urologists, proctologists, and infectious disease specialists were male. The mean age of patients was 36.2 (**Table 1**).

Incidence and prevalence of anogenital warts

Of the 12,133 patients, 669 (5.5%) had a GW diagnosis, of which 440 (3.6%; 66% of all GW diagnoses) were new cases, and 229 (1.9%; 34% of all GW cases) were existing cases (**Figure 1**).

The overall incidence was 3.7%. As shown in **Figure 2A**, PCPs reported the lowest incidence (0.4%) and the proctologist, the highest (10.4%). The incidence was 4.8% among males and 3.4% among females. The highest incidence was 9.6% in males aged from 25 to 29; in females in that same age group, the incidence peaked at 4.7% (**Figure 3A**).

	Total				DROCT	CVN		Other	
Physicians	10(a) (N=105)			URU (N=12)			ID (N=2)	(N=11)	
Patients	(N=105) (N=12 133)	(N=796)	(N=11) (N=1.434)	(N=12) (N=1.297)	(N=1) (N=79)	(N=7.017)	(N=325)	(N=11) (1.185)	
Gender (%)	(11 12,100)	(11 100)	(,	((11 10)	(11 1,011)	(11 020)	(1,100)	
Male	21.6	39.8	40.9	71.1	58.2	0.8	86.1	35.4	
Female	78.4	60.2	59.1	28.9	41.8	99.2	13.9	64.6	
Age (years)									
Mean (SD)	36.2 (11.9)	37.6 (12.5)	37.1 (12.2)	44.1 (11.2)	39.4 (13.5)	34.5 (11.2)	38.8 (10.0)	35.0 (11.8)	
Age group (%)									
18–24	18.3	17.6	17.8	6.9	21.5	20.9	4.0	20.3	
25–29	15.9	15.3	14.2	7.9	7.6	17.3	15.4	19.4	
30–34	15.5	12.8	13.2	8.6	8.9	17.2	20.3	16.2	
35–39	13.1	11.6	13.8	11.9	8.9	13.4	17.2	12.7	
40–44	10.7	10.2	12.1	12.3	12.7	10.5	14.8	7.9	
45–49	8.5	10.9	7.9	12.3	11.4	7.6	12.6	7.5	
50–54	8.2	8.4	10.0	14.2	13.9	7.0	5.2	7.3	
>54	9.7	13.2	11.1	26.1	15.2	6.1	10.5	8.6	

*Data for all patients recorded in the patient log, presented as percentage of patients unless indicated otherwise; PCP: primary care physician; DERM: dermatologist; URO: urologist; PROCT: proctologist; GYN: gynecologist; ID: infectious disease specialist; SD: standard deviation.

The overall prevalence was 5.5% (Figure 2B). PCPs reported the lowest prevalence (0.6%) and the proctologist, the highest (12.7%; Figure 2B). Prevalence was 6.9% in males overall, peaking at 12.6% in those aged from 25 to 29 (Figure 3B). In females, the prevalence was 5.1% overall, peaking at 6.5% in those aged from 30 to 34 (Figure 3B).



Figure 1 – Overall number of anogenital warts (GW) cases observed in a 10-day observational period in Ecuador.



Figure 2 – Incidence proportion and prevalence of anogenital warts cases, according to physician specialty*.

GW case presentation

Of the 440 incident GW cases, 337 (76.6%) were the first in the patient's lifetime, whereas 103 (23.4%) were new occurrences without lesions in the previous 12 months (see **Figure 1**). About two-thirds (63.5%) of the 669 current episodes (new and existing) had lasted ≤ 6 months, with or without treatment. The remaining episodes had lasted >6 months, either despite or without treatment (17.3 and 19.1% of current episodes, respectively).

Physicians

Physician sample

Of the 204 physicians contacted, 99 (48.5%) declined and 105 (51.5%) agreed to participate in the study: 8 PCPs, 11 dermatologists, 12 urologists, 1 proctologist, 59 gynecologists, 3 infectious disease specialists, and 11 physicians with other backgrounds (2 colposcopists, 8 general physicians, 1 resident). The participating physicians completed all 10 days of the daily log and at least 90% of items in the physician survey.

Physician characteristics

Physician characteristics are shown in **Table 2**. Physicians in each specialty were predominantly men (64–100%), except for



Figure 3 – Incidence proportion and prevalence of anogenital warts cases, by age group*.

dermatologists and physicians with other backgrounds, who were, respectively, 82 and 64% women. Physicians in most specialties were predominantly aged from 30 to 50 (61–91%).

Practice characteristics

The main practice setting was a hospital-based outpatient office or clinic for approximately two-thirds (62%) of all physicians but 100% for the urologists—and a stand-alone primary care office or clinic for about one-fourth (27%) of all physicians. The affiliation was a public/primary care practice for 59% of all physicians and a private/for profit practice for 24%. The geographical setting was almost always urban (97% of all physicians), with a practice service area population predominantly in the range from 5,000 to 50,000 (55%).

Typical patients

The patients seen in a typical working week were predominantly female for PCPs (58%), dermatologists (58%), gynecologists (100%), and other physicians (66%; **Table 3**). Conversely, the patients seen in a typical week were male for urologists (73%), proctologists (57%),

Table 2 - Physician and practice characteristics, by specialty*

and infectious disease specialists (83%). The average for all physicians was 77% female.

Physician consultation and referral patterns

Consultation patterns

Physicians reported that most of their female patients were seen in direct consultation (75%) and only a minority (24%) were referrals (**Figure 4**). Nearly all female GW cases seen by PCPs were in direct consultations (97%); conversely, most female GW cases seen by infectious disease specialists were referrals (90%). Of the cases that were referrals, physicians reported that the referring physician was most often a PCP or gynecologist (39 and 13%, respectively; **Table 4**).

Treatment/referral patterns

Very few PCPs (3%) treated female GW cases themselves, referring most cases (88%) to another physician for treatment. Physicians in most of the specialties reported treating female GW cases themselves: 72% of all physicians treated female GW

	Total (N=105)	PCP (N=8)	DERM (N=11)	URO (N=12)	GYN (N=59)	ID (N=3)	Other (N=11)
Gender (%)							
Male	60.0	75.0	18.2	75.0	64.4	100.0	36.4
Female	40.0	25.0	81.8	25.0	35.6	0.0	63.6
Age group, years old (%)							
<30	7.6	25.0	0.0	0.0	0.0	0.0	54.5
≥30 to ≤50	61.0	62.5	90.9	66.7	61.0	66.7	27.3
>50	31.4	12.5	9.1	33.3	39.0	33.3	18.2
Practice setting (%)							
Stand-alone primary care office/clinic	26.7	37.5	45.4	0.0	28.8	0.0	18.2
Stand-alone HIV/AIDS or sexual/reproductive care office/clinic	1.9	0.00	0.0	0.0	1.7	33.3	0.0
Hospital-based outpatient office/clinic	61.9	50.0	54.6	100.0	57.6	66.7	63.6
Other	9.5	12.5	0.0	0.0	11.9	0.0	18.2
Affiliation (%)							
Public/primary care	59.1	62.5	45.4	75.0	52.5	100.0	81.8
Private/for profit	23.8	25.0	27.3	0.0	28.8	0.0	18.2
Both/mixed	15.2	12.5	27.3	25.0	15.3	0.0	0.0
Other	1.9	0.0	0.0	0.0	3.4	0.0	0.0

*Data from the physician survey, presented as percentage of physicians; PCP: primary care physician; DERM: dermatologist; URO: urologist; GYN: gynecologist; ID: infectious disease specialist; HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome. The characteristics of specialty categories with only one member are withheld to protect confidentiality.

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PCP: primary care physician; DERM: dermatologist; URO: urologist; PROCT: proctologist; GYN: gynecologist; ID: infectious disease specialist; SD: standard deviation; IQR: interquartile range.

The most common reasons physicians (N=40) cited for referring GW cases were "serious cases requiring more specialized treatment," cited by 50% of physicians for female cases, and "lack of resources to treat GW," cited by 30% of physicians for female cases (**Table 5**).



*Data from the physician survey, Question A1: *In general, what percentage of patients with genital warts consult you directly, and what percent are referred to you from another physician*?; PCP: primary care physician; DERM: dermatologist; URO: urologist; PROCT: proctologist; GYN: gynecologist; ID: infectious disease specialist; **data shown for female patients only.

Figure 4 – Percentage of female anogenital warts patients who were seen in a direct consultation or referred by another physician, according to physician's specialty***.



*Data for physician survey Question A3: Among your patients with genital warts, approximately what percentage do you treat yourself, what percentage do you refer to another physician for treatment, what percentage do you treat and then refer to another physician, and what percentage is left untreated for monitoring?; PCP: primary care physician; DERM: dermatologist; URO: urologist; PROCT: proctologist; GYN: gynecologist; ID: infectious disease specialist; **data shown for female patients only.

Figure 5 – Anogenital warts treatment and referral patterns, according to physician specialty*.**.

Table 4 –	Referring	physician	specialty of	referred	female	patients,	according to	consulting p	hysician	specialty*.
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Consulting physician	Total	PCP	DERM	URO	PROCT	GYN	ID	Other
Referring physician								
PCP	39.3 (42.6)	0.6 (1.8)	47.2 (45.9)	45.4 (46.1)	0.0 (-)	46.9 (41.3)	63.3 (55.0)	9.1 (30.2)
DERM	1.9 (6.5)	0.0 (-)	0.9 (3.0)	0.8 (2.9)	0.0 (-)	3.0 (8.3)	0.0 (-)	0.0 (-)
URO	2.8 (7.0)	0.0 (-)	3.6 (9.2)	0.8 (2.9)	0.0 (-)	4.2 (8.1)	0.7 (1.2)	0.2 (0.6)
PROCT	1.4 (4.5)	0.0 (-)	0.0 (-)	0.0 (-)	0.0 (-)	2.5 (5.8)	0.0 (-)	0.0 (-)
GYN	13.3 (26.0)	0.0 (-)	7.8 (12.9)	11.3 (25.6)	100 (-)	16.2 (53.9)	36.0 (53.9)	0.5 (1.5)
ID	0.8 (3.6)	0.0 (-)	2.7 (9.0)	0.0 (-)	0.0 (-)	0.9 (2.9)	0.0 (-)	0.0 (-)
Other	7.2 (22.4)	36.9 (50.9)	1.4 (4.5)	0.0 (-)	0.0 (-)	5.9 (17.5)	0.0 (-)	8.5 (28.0)

*Data presented as mean (SD); PCP: primary care physician; DERM: dermatologist; URO: urologist; PROCT: proctologist; GYN: gynecologist; ID: infectious disease specialist; SD: standard deviation.

Table 5 – Reason for referr	al of female patients,	according to ph	ysician specialty*.
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	Total	PCP	DERM	URO	PROCT	GYN	ID	Other
Cost to your practice associated to the treatment	1 (2.5)	0 (-)	0 (-)	0 (-)	-	0 (-)	0 (-)	1 (12.5)
Time associated to the treatment	1 (2.5)	0 (-)	0 (-)	0 (-)	-	0 (-)	0 (-)	1 (12.5)
Unfamiliarity with the treatment	6 (15.0)	4 (50.0)	0 (-)	0 (-)	-	0 (-)	0 (-)	2 (25.0)
Lack of resources to treat	12 (30.0)	3 (37.5)	0 (-)	0 (-)	-	5 (27.8)	1 (50.0)	3 (37.5)
Serious cases requiring more specialized treatment	19 (49.5)	5 (62.5)	1 (50.0)	1 (50.0)	-	6 (33.3)	2 (100.0)	4 (50.0)
Patient unwilling to engage in treatment	2 (5.0)	1 (12.5)	0 (-)	0 (-)	-	1 (5.5)	0 (-)	0 (-)
Other	11 (27.5)	1 (12.5)	2 (100.0)	0 (-)	-	6 (33.3)	0 (-)	2 (25.0)

*Data presented as N (%); PCP: primary care physician; DERM: dermatologist; URO: urologist; PROCT: proctologist; GYN: gynecologist; ID: infectious disease specialist.

DISCUSSION

Study sample

In this study, 105 physicians, practicing predominantly in hospital-based outpatient office or clinics, recorded 669 GW cases among 12,133 patients seen in a 10-day period. Over half of the physician sample (56%) were gynecologists, whereas the specialties of primary care, dermatology, urology, and 'other' each made up 8 to 11% of the sample. Most of the physicians in 'other' specialties were self-identified as general physicians and not as PCPs.

Referral patterns

Most female GW patients seen by physicians occurred in direct consultations rather than referral ones. Physicians of most types treated most of their female GW patients themselves-except, notably, PCPs, who referred almost all their female GW cases for treatment. In addition, only few infectious disease specialists and physicians in the 'other' category treated female GW cases themselves. This pattern of treatment and referral is like that of other countries, in which GW cases are managed primarily by specialists rather than in primary care. In a study conducted in Peru, 76.7% of physicians reported treating female GW cases themselves, though only about half (52.2%) of PCPs reported treating female GW cases themselves⁽¹¹⁾. In a study carried out in England, only 5% of GW cases were managed by a general practitioner; 22% were seen by a general practitioner before being referred to a genitourinary medicine clinic, and most GW cases (73%) were seen only in genitourinary medicine clinics⁽¹²⁾. Studies of GW management in other countries (Spain and Germany) have been restricted to specialists in Gynecology, Dermatology, and Urology^(13,14).

Epidemiology

Among the patients seen in this study's physician sample, the prevalence of GW was 5.5 to 6.9% in males and 5.1% in females. The incidence proportion was 3.7 to 4.8% among males and 3.4% among females. These values are greater than those reported in a systematic review of population-based studies conducted between 2001 and 2012 in countries world-wide⁽¹⁵⁾. There, the prevalence of GW-based on genital examinationsranged from 0.2 to 5.1%, with a median of 3.2%, and the annual incidence ranged from 0.16 to 0.29%, with a median of $0.2\%^{(15)}$. However, GW prevalence and incidence values reported in studies in Latin American countries cluster at the upper end of the range of those reported worldwide for both men and women. Among men attending vasectomy clinics in Mexico from 2003 to 2004, the prevalence of penile GW was 5.1%⁽¹⁶⁾. In the HPV in Men (HIM) cohort study in Brazil, Mexico, and the United States (Florida) between 2009 and 2013, 4.5% developed GW during a median of 18 months of follow-up⁽¹⁷⁾. Similarly for women, the GW prevalence was reported as 2.4% among adult rural women in coastal, Amazonian, and Andean regions in Peru from 1997 to 1998 and as 3.2% among women attending a Pap screening clinic in Mexico City between 2002 and 2009(18,19). In a cohort of girls aged from 11 to 19, seen at a gynecology clinic in Brazil between 1993 and 2006, 5.6% presented with GW during the first year of sexual activity; the percentage was 1.8% for the second year⁽²⁰⁾. In a cohort of women screened for cervical cancer in 2002 and 2003, a history of previous vulvar warts was reported by 1.1 to 3.4% of them in different Brazilian cities⁽²¹⁾.

Limitations

The estimates for incidence and prevalence presented in this study may not be applicable to the broader population of individuals with GW who are not seen in physician offices, because GW burden in this study was only assessed in patients who sought medical care. Furthermore, this study included a convenience sample of physicians rather than a random sample, consisting of physicians who treat and/or diagnose GW and who were willing to participate in the study. These limitations might conceivably have contributed to a bias in some parameters measured.

CONCLUSION

In this study set in the practice of physicians in Ecuador, the prevalence and incidence of GW were slightly higher than the values reported for other Latin American countries. Female GW cases were treated by gynecologists, urologists, and dermatologists, whereas PCPs referred most of their female cases for treatment. Populationbased studies may be required to establish a more representative estimate of the epidemiology of GW in the general population in Ecuador. Such studies could provide baseline data with which to gauge the effectiveness of HPV vaccination programs. To the best of our knowledge, this is the first report aimed at determining the consultation and referral patterns of physicians toward GW management in Ecuador.

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Participation of each author

Hector Zambrano (HZ), Maria Veronica Petrozzi (MVP), Magdalena Sanchez Aguilar (MSA), Homero A. Monsanto (HAM), Miguel Cashat (MC), Alexandra Altland (AA), and Brianna Lindsay (BL) are responsible for the paper described in the manuscript entitled "Burden of Genital Warts in Ecuador: An Observational Study in the Practice of Physicians." All authors gave their final approval of the version to be published. All authors agree to be accountable for all aspects of the paper in ensuring that questions related to the accuracy or integrity of any part of it are appropriately investigated and resolved. Each author confirmed that their contributions was as follows: Conception, design and planning of the study: BL; Data analysis: HZ, BL; Interpretation of results: HZ, MVP, MSA, HAM, MC, AA, BL; Drafting of the manuscript: HZ, BL; Critically reviewing or revising the manuscript for important intellectual content: HZ, MVP, MSA, HAM, MC, AA, BL.

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Conflict of interests

Hector Zambrano served as a scientific consultant and received research support from Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. María Veronica Petrozzi, Magdalena Sanchez Aguilar, Homero A. Monsanto, and Miguel Cashat are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. Alexandra Altland is an employee of Merck & Co., Inc., Kenilworth, NJ, USA. Brianna R. Lindsay was an employee of Merck & Co., Inc., Kenilworth, NJ, USA at the time of the study.

REFERENCES

- Leto M, Santos Júnior GF, Porro AM, Tomimori J. Human papillomavirus infection: Etiopathogenesis, molecular biology and clinical manifestations. An Bras Dermatol. 2011;86(2):306-17. https://doi.org/10.1590/s0365-05962011000200014
- Tchernev G. Sexually transmitted papillomavirus infections: epidemiology pathogenesis, clinic, morphology, important differential diagnostic aspects, current diagnostic and treatment options. An Bras Dermatol. 2009;84(4):377-89. http://dx.doi.org/10.1590/S0365-05962009000400009
- Insinga RP, Dasbach EJ, Myers ER. The health and economic burden of genital warts in a set of private health plans in the United States. Clin Infect Dis. 2003;36(11):1397-403. http://dx.doi.org/10.1086/375074
- Jeynes C, Chung MC, Challenor R. 'Shame on you'—the psychosocial impact of genital warts. Int J STD AIDS. 2009;20(8):557-60. http://dx.doi. org/10.1258/ijsa.2008.008412
- Piñeros M, Hernández-Suárez G, Orjuela L, Vargas JC, Pérez G. HPV knowledge and impact of genital warts on self esteem and sexual life in Colombian patients. BMC Public Health. 2013;13:272. http://dx.doi. org/10.1186/1471-2458-13-272
- Mejía L, Muñoz D, Trueba G, Tinoco L, Zapata S. Prevalence of human papillomavirus types in cervical cancerous and precancerous lesions of Ecuadorian women. J Med Virol. 2016;88(1):144-52. http://dx.doi. org/10.1002/jmv.24310
- González-Andrade F, Sánchez D. HPV genotyping in anogenital abnormal samples of Ecuadorian women. Cancer Biomark. 2009;5(4-5):225-32. http://dx.doi.org/10.3233/CBM-2009-0107
- Brown CR, Leon ML, Muñoz K, Fagioni A, Amador LG, Frain B, et al. Human papillomavirus infection and its association with cervical dysplasia in Ecuadorian women attending a private cancer screening clinic. Braz J Med Biol Res. 2009;42(7):629-36. http://dx.doi.org/10.1590/S0100-879X2009000700007
- García Muentes GD, García Rodríguez LK, Burgos Galarraga RI, Almeida Carpio F, Ruiz Cabezas JC. Genotypes distribution of human papillomavirus in cervical samples of Ecuadorian women. Rev Bras Epidemiol. 2016;19(1):160-6. http://dx.doi.org/10.1590/1980-5497201600010014

- Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global Cancer Observatory: Cancer Today [Internet]. Lyon, France: International Agency for Research on Cancer; 2018 [accessed on July, 2018]. Available from: https://gco.iarc.fr/today
- García PJ, Carcamo CP, Valderrama M, La Rosa S, James C, Gutiérrez R, et al. Burden of genital warts in Peru: an observational study. Int J STD AIDS. 2018;30(3):264-74. http://dx.doi.org/10.1177/0956462418796088
- Desai S, Wetten S, Woodhall SC, Peters L, Hughes G, Soldan K. Genital warts and cost of care in England. Sex Transm Infect. 2011;87:464-8. http://dx.doi.org/10.1136/sti.2010.048421
- Castellsagué X, Cohet C, Puig-Tintoré LM, Acebes LO, Salinas J, San Martin M, et al. Epidemiology and cost of treatment of genital warts in Spain. Eur J Public Health. 2009;19(1):106-10. http://dx.doi.org/10.1093/eurpub/ckn127
- Hillemanns P, Breugelmans JG, Gieseking F, Bénard S, Lamure E, Littlewood KJ, et al. Estimation of the incidence of genital warts and the cost of illness in Germany: a cross-sectional study. BMC Infect Dis. 2008;8:76. http://dx.doi.org/10.1186/1471-2334-8-76
- Patel H, Wagner M, Singhal P, Kothari S. Systematic review of the incidence and prevalence of genital warts. BMC Infect Dis. 2013;13:39. http://dx.doi.org/10.1186/1471-2334-13-39
- Vaccarella S, Lazcano-Ponce E, Castro-Garduño JA, Cruz-Valdez A, Díaz V, Schiavon R, et al. Prevalence and determinants of human papillomavirus infection in men attending vasectomy clinics in Mexico. Int J Cancer. 2006;119(8):1934-9. http://dx.doi.org/10.1002/ijc.21992
- Anic GM, Lee JH, Villa LL, Lazcano-Ponce E, Gage C, Silva RJC, et al. Risk factors for incident condyloma in a multinational cohort of men: the HIM study. J Infect Dis. 2012;205(5):789-93. http://dx.doi.org/10.1093/ infdis/jir851
- García PJ, Chavez S, Feringa B, Chiappe M, Li W, Jansen KU, et al. Reproductive tract infections in rural women from the highlands, jungle, and coastal regions of Peru. Bull World Health Organ. 2004;82(7):483-92.
- Jimenez-Vieyra CR. [Prevalence of condyloma acuminata in women who went to opportune detection of cervicouterine cancer]. Ginecol Obstet Mex. 2010;78(2):99-102.
- Monteiro DL, Sodré DC, Russomano FB, Trajano AJ, Silva KS. Incidence of genital warts in adolescents and their association with cervical intraepithelial lesions. Eur J Obstet Gynecol Reprod Biol. 2013;168(1):80-2. http://dx.doi.org/10.1016/j.ejogrb.2012.12.032
- 21. Syrjänen K, Naud P, Derchain S, Roteli-Martins C, Longatto-Filho A, Tatti S, et al. Comparing PAP smear cytology, aided visual inspection, screening colposcopy, cervicography and HPV testing as optional screening tools in Latin America. Study design and baseline data of the LAMS study. Anticancer Res. 2005;25(5):3469-80.

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