

Review

Cervical Cancer in Latin America and the Caribbean: The Problem and the Way to Solutions

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Abstract

Latin America and the Caribbean have one of the highest incidence and mortality rates from cervical cancer in the world. In this region, age-adjusted incidence rates range from 20 to 80 per 100,000 women per year. Overall, the mortality rates are extremely high in spite of the availability of Pap screening in several countries. Women from lower socioeconomic status, often less educated, are unaware of cervical cancer screening or have no access to it. Despite the efforts to reorganize screening programs in the region, in a few countries, only a slight decrease in cervical cancer mortality has been observed. New modalities for primary and secondary screening should be evaluated and disseminated, including HPV testing and vaccination against the most common HPV types. HPV prophylactic vaccines were approved in most Latin American countries, but only few are considering its implementation in national immunization programs. Besides cost and other logistical issues, lack of recommendation by policy makers or lawmakers is deterring the introduction of HPV vaccines in the region. Furthermore, studies conducted in the region have indicated that HPV vaccination only or vaccination supplemented with screening may be considered a cost-effective strategy to reduce mortality by cervical cancer. *Cancer Epidemiol Biomarkers Prev*; 21(9); 1409–13. ©2012 AACR.

Introduction

The World Health Organization (WHO) and the International Agency for Research in Cancer (IARC) estimate that cervical cancer is responsible for approximately 1% of all causes of female mortality worldwide, killing more than 273,000 women per year (1). About 80% of those cases occur in women living in developing countries, including several Latin American countries from Central America, South America, and the Caribbean (LAC; refs. 2 and 3). Breast and cervical cancers are the most frequent cancers among Latin American women, followed by colon, stomach, and lung (Table 1). Moreover, cancer burden is projected to increase significantly in the region due to population aging, epidemiologic transition, and lack of efficient and widely available healthcare systems, including screening tools and adequate treatment (4).

LACs exhibit large within-country variation in cervical cancer incidence and mortality, reflecting differential access to cervical cancer screening and treatment. The highest incidence rates are observed in Haiti (87/100,000),

Bolivia (55/100,000), Peru (48/100,000), and Nicaragua (47/100,000), whereas Argentina (23/100,000) and Uruguay (19/100,000) have the lowest rates (1, 4). Overall, the mortality rates are extremely high, particularly in young women, being the first cause of death by cancer in several countries of the region (4). These high rates occur in spite of the availability of Pap screening in most LAC countries. However, cervical cancer screening has achieved limited success due to lack of organized screening programs, the limitations of techniques, poor quality control, low population coverage, insufficient monitoring, treatment, and follow-up for women with abnormal cytology results, among other difficulties (3, 5). Women from lower socioeconomic status, often less educated than their higher socioeconomic status counterparts, are unaware of cervical cancer screening or have no access to it (5). Therefore, despite the efforts to organize screening programs in the region, only a slight decrease in cervical cancer mortality has been observed, for example, in Mexico, Costa Rica, Chile, and in some regions of Brazil (5). The Pan American Health Organization (PAHO), in its proposed plan of action for cancer prevention and control in LAC countries for 2008–2015, mentions that despite the fact that cervical cancer screening is widespread in the region, screening coverage is reported to be less than 50% in the majority of these programs (6). Importantly, this plan of action aims to disseminate information to health professionals and the public in general about cancer causes, risk factors reduction, cancer screening, and effective interventions for cancer control. In fact, there is a widespread lack of knowledge about HPV infections, cervical cancer and its precursors, screening, and effective treatment, which

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Table 1. Population and cancer statistics in Latin America and the Caribbean

	Male	Female	Both
Population (thousands)	284,592	291,508	576,101
Number of new cancer cases (thousands)	444.8	461.2	906.0
Number of cancer deaths (thousands)	279.5	262.6	542.1
5 most common frequent cancers	Prostate	Breast	Prostate
	Lung	Cervix uteri	Breast
	Stomach	Colorectum	Lung
	Colorectum	Stomach	Cervix uteri
	Leukemia	Lung	Stomach

NOTE: Source: Globocan 2008, IARC (1).

contributes to the observed high incidence and mortality rates of cervical cancer (7–9). Many do not comprehend the cause and burden of cervical cancer and may not be able to understand the value of HPV vaccines for improving the current situation (7). Efforts to improve awareness of women and health providers' knowledge of prevention options are critical to achieve a successful cervical cancer prevention program.

New Screening Tools

To meet the demand generated on their health systems from cancer and other chronic diseases, governments are challenged to introduce new strategies for prevention as well as diagnosis and treatment. It is clear that screening programs in Latin America should have a wider coverage, especially reaching those women who have never had a Pap test and are at higher risk of developing cervical cancer. As in other developing countries, the proportion of women never screened in LAC is considerable. However, coverage rates do not always reflect a decrease in mortality rates of cervical cancer (5). A comprehensive evaluation of cervical cancer screening programs is ongoing in several LAC countries (10, 11). Of note, Chile, Colombia, Mexico, Peru, and more recently Argentina, are actively engaged in evaluating and proposing new strategies for cervical cancer control. In consequence, countries such as Chile, Colombia, and Costa Rica are registering reductions in mortality rates for cervical cancer (5).

New modalities for primary and secondary screening should be evaluated and disseminated. Evidence is accumulating of the feasibility and cost-effectiveness of alternative screening tools, particularly HPV testing, in different settings (12–13). In recent years, highly sensitive and reproducible laboratory techniques to detect oncogenic HPVs have been developed and are now being used or considered to replace cervical cytology for primary screening (14). Different methodologies and algorithms have been proposed; several studies are ongoing in LAC, but the overall experience is incipient to impact public health decisions in most countries of the region (15–16). Recent reports indicate that HPV testing could be more cost-effective than cervical cytol-

ogy in large health delivery organizations such as those existing in the larger LAC countries, for example, Mexico (17). Furthermore, new technologies can be applied to vaginal self-collected samples, which may increase participation in cervical cancer screening. Evidence is accumulating in the region with positive indications for the application of self-sampling in large communities of low resource settings (18–20).

HPV Prophylactic Vaccination

The recent introduction of prophylactic vaccines against some of the more oncogenic HPV types (HPV 16 and 18) is considered as a step forward in the prevention of cervical cancer. Two vaccines composed of HPV L1 proteins self-assembled into virus-like particles (VLP) have been developed: one containing VLPs of HPV types 6, 11, 16, and 18 (Merck & Co. Inc.), whereas the other vaccine is composed of HPV 16 and 18 VLPs (GlaxoSmithKline). Large phase II and III clinical trials to assess prophylactic efficacy have been conducted in which both HPV infection endpoints and disease endpoints were evaluated, particularly high-grade cervical intraepithelial neoplasia (CIN2 or CIN3) as well as vulvar and vaginal intraepithelial neoplasias (VIN or VaIN), and genital warts for the quadrivalent vaccine (21). Very high efficacy rates were observed in different populations that included young women between 16 and 26 years of age, and older (up to 55). More recently, the quadrivalent vaccine has been shown to be efficacious in men to prevent genital and anal infection and disease caused by the types included in the vaccine (21). On the basis of shown clinical efficacy and favorable safety profile, HPV prophylactic vaccines are being introduced worldwide. While the vaccines are now given routinely in the United States, Canada, Australia and several European countries, with various degrees of coverage, the Latin American region has not yet seen wide distribution of prophylactic HPV vaccines. Importantly, several clinical trials of HPV prophylactic vaccines were conducted in LACs with clear demonstration of the safety, immunogenicity, and efficacy of such recombinant vaccines among Latin Americans (22). Furthermore, data gathered during these clinical trials concerning the

incidence and prevalence of genital HPV-associated infection and disease provided important insight into the burden of genital HPV in the region (22). A systematic review and meta-analysis on type-specific HPV prevalence in cervical cancer and high-grade lesions from LACs was recently published (23). Seventy-nine studies from 18 countries were identified, which included 2,446 cases of high-grade cervical neoplasia and 5,540 invasive carcinomas. HPV 16 and 18 were the most prevalent types in both high-grade lesions and cancer, followed by HPV types 31, 58, 33, 45, and 52. Therefore, the presently available prophylactic vaccines could have a significant impact in reducing the burden of disease caused by HPV 16 and 18 in the region. Moreover, these results are relevant for monitoring and surveillance of HPV infections and diseases after vaccine implementation in LACs.

HPV vaccination's target population is children and adolescents before sexual activity onset. Most LACs present a well-developed public immunization infrastructure including vaccination of adolescents. However, strategies to reach adolescents and ensure a 3-dose regimen vaccine need to be implemented. There is a need to evaluate HPV vaccine acceptability and develop programs to increase awareness among young Latin Americans, particularly considering the large social, cultural, and economical differences existing in LACs (24). Seminal demonstration studies and surveys have shown that the HPV vaccine acceptability is very high in the region (25–27).

HPV vaccines were approved in most LACs, but only few are considering its implementation in national immunization programs (Table 2). Panama was the first Latin American country to introduce HPV vaccination in national immunization programs and since 2008, is vaccinating 11- to 12-year-old girls in a school-based program. Other countries are following, including Mexico,

Peru, Colombia, and more recently Argentina. Interestingly, a broad evaluation of the programs is leading to a revision of the entire cervical cancer control strategies adopted by each country, which includes HPV vaccination for female adolescents and cytology/HPV testing for adult women. Unfortunately, however, several governments of LACs are deterring the introduction of HPV vaccines mostly because of lack of political decision and other logistical issues.

Implementation of effective vaccine programs might seem straightforward and obvious in light of the vaccines' efficacy and lack of serious adverse events to date; nonetheless, significant challenges remain. Cost concerns as well as the logistical challenge of getting the vaccines to their intended population have hindered their use, even though this region is among the most likely to benefit from such vaccines. Organizations such as the United Nations Children's Fund (UNICEF), the Global Alliance for Vaccines and Immunization (GAVI), and the revolving fund of PAHO may contribute to accelerate HPV vaccine introduction in LACs. Importantly, studies conducted in the region have indicated that HPV vaccination only or vaccination supplemented with screening may be considered a cost-effective strategy to reduce mortality by cervical cancer (depending on vaccine cost and delivery; refs. 28–30).

Concluding Remarks

The prevalence and incidence of HPV-related infection and disease in Latin America and the Caribbean underscores the importance of supporting cervical cancer prevention strategies in the region. Cervical cancer rates are among the highest in the World: decades of Papanicolaou-based screening have had little or no impact in several LACs. Hence, the opportunity to define a more comprehensive cervical cancer control approach is required, where primary and secondary prevention strategies are

Table 2. HPV vaccination in Latin America and then Caribbean by country and selected characteristics

Country	Year of implementation (licensed)	Setting	Population target (geographic scope)
Argentina	2011	Public	Females, 11 y (national)
Bolivia	(2007)	Private	
Brazil	(2006)	Private	
Cayman Islands	2011	Public	Females, 11–17 y (national)
Chile	(2007)	Private	
Colombia	2011	Public	Females, 10 y (partial)
Mexico	2008	Public	Females, 9–12 y (partial)
Panama	2008	Public	Females, 11–12 y (national)
Paraguay	(2010)	Private	
Peru	2011	Public	Females, 10 y (national)
Uruguay	(2007)	Private	

NOTE: Source: CDC (26); http://www.who.int/immunization/GIN_February_2011.pdf.

implemented with high coverage and sustainability. Moreover, the relative nonexistence of organized cervical cancer screening programs in the Latin American region should not hinder the implementation of primary prevention strategies such as vaccination. Vaccination of adolescents/young adults before exposure to HPV will likely provide the maximal benefit against cervical cancer. All efforts are justified to alleviate the burden of cervical cancer and other HPV diseases, particularly among those who are in most need. Fortunately, the first initiatives to

vaccinate young cohorts of women from Latin America and the Caribbean have been launched.

Disclosure of Potential Conflicts of Interest

L.L. Villa has an honoraria from speakers bureau and is a consultant/advisory board member of Merck and Sharp & Dohme for the Quadrivalent HPV vaccine. L.L. Villa is also a consultant/advisory board member in BD and Roche for HPV DNA diagnostic tests.

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