

RESEARCH ARTICLE

Screening Cervical Cancer by the Pap Test – Relevance of Age Ranges Recommended by the Brazilian Programme for Prevention and Control

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Abstract

Objective: To evaluate screening by the Papanicolaou smear (Pap) and the frequency of cervical abnormalities in the age range recommended by the Brazilian programme for prevention and control of cervical cancer (CC) in the years 2012 and 2013 in a high prevalence city. **Methods:** This retrospective study covered results of Pap examinations performed on women aged ≥ 12 years residing in urban areas of the city of Maringá, Paraná in Brazil. The examinations were performed in the years 2012 and 2013 for the System of Public Health (SPH) which maintains a city database. The age ranges were grouped as recommended into $<15-24$, $25-64$, and >64 years. **Results:** A total 40,866 women were screened, 19,606 in 2012 and 21,260 in 2013. The Pap exams performed for the age range 25-64 years accounted for 80.7% of the total in 2012 and 80.3% in 2013 ($p=0.13$), while those for <15 to 24 years accounted for 11.7% and 11.3%, respectively. There were more tests performed in the >64 years age group in 2013 (8.46%) than in 2012 (7.52%) ($p<0.001$). A total of 1,354 (3.31%) women presented with abnormal test results, with atypical squamous cells of undetermined significance (ASC-US) as the most prevalent finding (2.12%) in 2012, while in 2013 it was LSIL (1.56%) ($p<0.001$ for both). Women with ASC-US showed a lower mean age than did those with other lesions in both years. **Conclusions:** This study detected a significant expansion of women screened for CC in age ranges not recommended by the Brazilian government.

Keywords: Age ranges- cervical cancer- Pap smear- public health- screening

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Introduction

Cervical cancer (CC) is still an important public health problem in the world. Even after its prevention was implemented in recent decades with exams for cervical cytology or Papanicolaou smear (Pap) tests and, more recently, with molecular tests for the detection of human papillomavirus (HPV) and the advent of vaccines against this virus, its incidence remains high (Globocan, 2012; Amaro-Filho et al., 2013). CC is the fourth most common cancer diagnosed in women in the world, with an estimated 528,000 new cases occurring per year. CC represents the fourth most common cause of death by cancer in women, with approximately 266,000 deaths occurring annually (Globocan, 2012; Koh et al., 2015).

CC's incidence varies between the different regions of the world, but it is well-established that more than 85% of the new cases of CC and more than 87% of deaths occur in developing countries as a result of the frailty of screening programmes (Ferlay et al., 2010; Sudenga et al., 2014).

In 2016, there were an estimated 16,340 new cases and 5,430 deaths resulting from CC in Brazil (Mayrand

et al., 2007). CC is also the third most common tumour in the Brazilian female population and is preceded only by cancers of the breast, while colorectal cancer is the fourth leading cause of cancer death in the population of women. CC presents differences in its incidence in the various regions of the country and is more prevalent in the North, Northeast and Midwest followed by the Southeast and South. While the mortality by CC has decreased in developed countries, it has increased in Brazil according to data from 2000 through 2012 (INCA, 2014). The natural history of CC reveals that despite its high incidence, this cancer stands out among those with a great potential for prevention. The progression of cervical lesions to invasive cancer usually takes years or decades, which enables the detection of the lesions in the premalignant stage (Cuzick et al., 2008).

The Pap exam is one of the most efficient and successful methods of CC screening (INCA, 2015). This examination is an essential component for women with access to medical care and is the most commonly used CC-screening method in the world (Roland et al., 2011). Despite the Pap exam's benefits, many women in

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developing countries have never been screened or are not selected at regular intervals; thus, cytological screening programmes have not reached the desired impact in reducing the incidence and mortality resulting from CC (Aniehue and Aniehue, 2010; Villa, 2011).

Brazil has not implemented an organized population-based CC screening program, and not even a universal system to invite all women to realize these examinations. However, the government has designed a program to identify and control the Pap exams performed in opportunistic screening at no cost to the population (INCA, 2015; Lorenzi et al., 2015). The Ministry of Health recommends the Pap exam to identify CC precursor lesions, targeted to women from 25 years (sexually active) to 64 years, repeated every 3 years for women who had two consecutive negative smears within five years. Unfortunately, the population coverage of the Pap examination did not reach the desired indices (>80% of women in the age range recommended) because approximately 40% of the women never had the procedure (INCA, 2009).

The establishment of the potential to high-risk HPVs in carcinogenesis and the aetiology of CC led to the introduction of molecular testing for HPV in the primary screening in many countries, but this testing has not been adopted to date in Brazil. Considering the variations in the Pap screens throughout the world and, many times, in different regions of the same country, the objective of this study was to assess the frequency of the cervical abnormalities in the age ranges recommended by the Brazilian Programme for Prevention and Control of CC in the years 2012 and 2013 in a city with a high prevalence of this type of cancer.

Materials and Methods

This was a retrospective study that included the Pap examination results from women ≥12 years old residing in the urban area of the city of Maringá, Paraná State, Brazil. These women had Pap exam in the years 2012 and 2013 in the Public Health System. According to census conducted in the year 2010, Maringá has a population of 357,077 residents, with approximately 102,200 women living in its urban area and in the age range recommended for performing the Pap exam (IBGE, 2010).

Conventional cervical smears were collected from women by physicians or nurse practitioners in primary health care units. Those health professionals also identified and recorded clinical data on the patients. Opportunistic and no cost screening is performed, although national recommendations prioritize women ages 25 to 64 years and with sexual activity, and is conducted every 3 years after 2 annual Pap exams with a normal result (INCA, 2015). An ectocervical and endocervical samples are collected and Pap smears are mounted on slides and stained using with Pap, which were interpreted and classified according to the 2001 Bethesda System (INCA, 2011). The Pap smears were categorized in negative for intraepithelial lesion and malignancy (NILM), atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells that cannot rule out a high-grade

lesion (ASC-H), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL) and cervical carcinoma (CC). In accordance with the national ages for Pap screening recommendations, we stratified the women into three years of age sub-groups as follows: <15-24; 25-64; and >64 years.

The data were obtained between the months of December 2014 and September 2015 from the databases of primary health care units (29 in the total), in the Central Laboratory of Clinical Analysis and in the Technical Area of Coordination of Women's Health in the city. Subsequently, the data were compiled in Microsoft Office Excel® 2013. We performed the statistical analysis (mean and distribution of frequency) and the Fisher's exact test using the Epi Info statistical programme 3.5.1. Values with p<0.005 were considered to be significant.

The study was approved by the Standing Committee on Ethics in Research Involving Humans of the State University of Maringá (COPEP/UEM) number 089627/2014 and observed all ethical principles established.

Results

The total number of women screened for CC in the city of Maringá was 40,866, which included 19,606 in 2012 and 21,260 in 2013 (p>0.005). The Pap exams performed in the age range recommended in Brazil (25-64 years old) corresponded to 80.74% of the total tests performed in 2012 and 80.28% of those performed in 2013 (p=0.130). The Pap exams performed in the age range of <15-24 years totalled 11.74% in 2012 and 4.83% in 2013 (p=0.250). There was a higher number of exams in the age range of >64 years in 2013 (8.46%) than in 2012 (7.52%) (p<0.001) (Table 1). A significant number of women were screened in the age groups not recommended by the country (n=7,969; 19.5%).

Table 2 shows that 3.31% had an abnormal Pap exam. During the study period, the majority of the abnormal results were ASC-US (1.68%), followed by LSIL (1.12%), ASC-H (0.36%), HSIL (0.24%) and CCS (0.002%). Comparing the prevalence of the abnormal cases in the two years studied, in 2012, the prevalence of ASC-US at 2.12% was higher than in 2013 at 1.27% (p<0.001). In addition, in 2013, the prevalence of ASC-H (0.33%), LSIL (1.56%), and HSIL (0.38%) was higher than in 2012 (0.20%, 0.64%, and 0.09% respectively) (p=0.008

Table 1. Pap Exams Were Performed in the City of Maringá, Brazil According to the Age Ranges During the Years 2012 and 2013

Age ranges	Pap screening 2012		Pap screening 2013		*p	Total Pap screening 2012 and 2013	
	n	%	n	%		n	%
	<15-24	2,302	11.74	2,395		11.26	0.25
25-64	15,830	80.74	17,067	80.28	0.13	32,897	80.5
>64	1,474	7.52	1,798	8.46	<0.001	3,272	8.0
Total	19,606	100	21,260	100	-	40,866	100.0

*Fisher's exact test

Table 2. Results of the Pap Exams for the Years 2012 and 2013

Pap findings	2012		2013		*p	2012 and 2013	
	n	%	n	%		n	%
NILM	19,007	96.94	20,505	96.45	-	39,512	96.69
ASC-US	416	2.12	271	1.27	<0.001	687	1.68
ASC-H	40	0.2	72	0.34	0.008	112	0.27
LSIL	125	0.64	331	1.56	<0.001	456	1.11
HSIL	17	0.09	81	0.38	<0.001	98	0.24
CC	1	0.005	-	-	-	1	0.002
Total	19,606	100	21,260	100	-	40,866	100

*Fisher's exact test; NILM, negative for intraepithelial lesion and malignancy; ASC-US, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells cannot rule out high-grade lesion; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; CC, cervical carcinoma.

to ASC-H and $p < 0.001$ to LSIL and HSIL).

Considering only the abnormal cases in 2012, the total was 599 and the ASC-US cases represented 69.4% followed by LSIL at 20.9%, ASC-H at 6.7%, HSIL at 2.8% and CCS at 0.2%. In 2013, the number of abnormal cases was greater ($n=755$), and there was a decrease in the prevalence of ASC-US (35.9%) and an elevation of LSIL (43.8%), HSIL (10.7%) and ASC-H (9.5%) (Table 3).

Table 3 also shows the mean age of the women affected by the different cytological abnormalities. Women with ASC-US had lower mean age (36.68 ± 6.33) than those with ASC-H (45.20 ± 6.04), LSIL (43.28 ± 6.52) and HSIL (42.70 ± 5.67) in 2012. We observed in 2013 that the average age of the women with ASC-US was lower (38.76 ± 6.90) than those with ASC-H (42.97 ± 6.13), LSIL (41.68 ± 7.04) and HSIL (43.50 ± 5.16). There was no significant difference between the mean ages of the women with ASC-H, LSIL and HSIL in the two years studied ($p > 0.005$).

Discussion

This study evaluated the prevalence of abnormal Pap exams according to the age ranges recommended by the Brazilian Programme for Prevention and Control of CC in a city with a high prevalence of this type of cancer. The results of Pap exams were evaluated in two consecutive years, 2012 and 2013. The data showed a significant number of women screened for CC in age ranges that are not recommended in the country ($<15-24$ and >64 years), corresponding to 7,969 women and 19.5% of the total number of women. Considering the two years assessed, there was a significant greater number of Pap exams in women >64 years old in 2013 (8.46%) compared to 2012 (7.52%), which seems to be an expansion of even more screening of CC in women outside the age range recommended in the country (INCA, 2015).

The results for the age ranges noted that in the city of Maringá, the Pap exams are performed by spontaneous demand, and as in other regions of Brazil, patients seek health services for various reasons that are not covered by CC screening (INCA, 2015; Lorenzi et al., 2015). This

Table 3. Prevalence of the Abnormal Pap Results and the Mean Ages

Results	2012		Ages		2013		Ages	
	n	%	Mean age \pm SD	n	%	Mean age \pm SD		
ASC-US	416	69.4	36.68 ± 6.33	271	35.9	38.76 ± 6.90		
ASC-H	40	6.7	45.20 ± 6.04	72	9.5	42.97 ± 6.13		
LSIL	125	20.9	43.28 ± 6.52	331	43.8	41.68 ± 7.04		
HSIL	17	2.8	42.70 ± 5.67	81	10.7	43.50 ± 5.16		
CC	1	0.2	71.00	-	-	-		
Total	599	100	-	755	100	-		

ASC-US, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells cannot rule out high-grade lesion; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion; CC: cervical carcinoma.

fact has consequences on the screening of CC because financial resources are spent in age ranges that do not affect the reduction of CC. The guidelines (national and international) do not recommend screening women under the age of 25 by a Pap exam because majority of cervical lesions are resolved spontaneously due to the high rate of HPV elimination in young women (Smith-McCune et al., 2010; Stormo et al., 2014; INCA, 2015). Furthermore, for women aged 65 years or older who have been screened according to recommendations and have prior normal test results, the burden of continued screening due to false-positive test results (including unnecessary colposcopies) is predicted to be high relative to further benefits (Kulasingham et al., 2013).

The prevalence of an abnormal Pap exam in 3.31% of the women screened for CC in this study was similar to the prevalence in studies in other parts of the world, such as in Turkey (2.5%) (Nayir et al., 2015), South Africa (4.69%) (Fonn et al., 2002) and in the United Arab Emirates (4.86%) (Al Zaabi et al., 2015). However, other studies show higher rates of prevalence, with a rate of 7.8% being observed in Egypt (El-All et al., 2007) and a rate of 9.8% being observed in Russia (Shipitsyna et al., 2011).

Among the 3.31% abnormal Pap exams in our study, the greatest portion was ASC-US (1.68%), which was similar to that described in another Brazilian study (Xavier-Júnior et al., 2015). Similar rates of ASC-US were found in recent studies from other parts of the world, showing 1.7% (Nayir et al., 2015) and 2.48% (Al Zaabi et al., 2015). However, the results of studies in which the Pap exams were performed by conventional and non-liquid cytology showed a wide variation in the prevalence rates of ASC-US, which are as high as those found in Russia (7.2%) (Shipitsyna et al., 2011), in the United States (9.8%) (Bukhari et al., 2012) and Egypt (15.3%) (El-All et al., 2007) or as low as in India (0.3%) (Bal et al., 2012).

The second most frequent result of the Pap exam was LSIL (1.12%), which was similar to those observed in another Brazilian study (Xavier-Júnior et al., 2015), in the USA (Insinga et al., 2004), in India (Gupta et al., 2013), in Nigeria (Schnatz et al., 2008) and in Kuwait (Kapila et al., 2006), where the prevalence of LSIL was 0.8%, 1.2%, 1.36%, 1% and 1%, respectively. Other studies show higher rates, such as 2.42% in South Africa (Fonn

et al., 2002), 2.5% in Russia (Shipitsyna et al., 2011) and 2.7% in India (Gupta et al., 2013).

In our study, the rate of ASC-H was high (6.7%), and there are few studies similar to our report on the prevalence of abnormal cytological. Nayir et al. (2015) observed a lower prevalence of ASC-H (0.2%) than we did. However, this study was carried out in Turkey where the Pap screening is organized differently from our study.

Results of LSIL accounted for 2.8% of the total cases altered. Another Brazilian study showed a much lower rate at 0.4% (Xavier-Júnior et al., 2015). The results of studies whose populations were evaluated with the CC screening also by spontaneous demand and not organized as in our study, report prevalence that vary greatly, such as 5.2% in Egypt (El-All et al., 2007), 1.8% in South Africa (Fonn et al., 2002) and 0.9% in India (Gupta et al., 2013). For CCS, our study detected 0.2%, which was similar to a report in Turkey (Sengul et al., 2014).

This study detected a significant number of women screened for CC in age ranges not recommended by the Brazilian government (<15 to 24 years, and >64 years), (n=7,969; 19.5% of the total). Additionally, in the two years evaluated, there were made more exams in women >64 years old in 2013 than in 2012, suggesting that an expansion in the number of tests in this age group, which is not recommended in the country.

Statement conflict of Interest

The authors declare that they have no competing of interests.

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