

QUALITY AND PERFORMANCE OF PAP SMEARS IN A CERVICAL CANCER SCREENING PROGRAM IN A CITY OF SOUTHERN BRAZIL

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ABSTRACT

OBJECTIVE. To estimate prevalence rates and analyze the quality and performance of Pap smears carried out on the Cervical Cancer Screening Program in Maringá, Paraná, Brazil.

METHODS. A retrospective search was run on the Brazilian Ministry of Health SIS-Colo database. Variables such as age, cervical cytology result and district of residence were analyzed. Ages were divided into bands; residence was classified according to the five regional healthcare districts of the city of Maringá. Cervical cytology results were categorized according to the Bethesda System. Cervical screening coverage was calculated by dividing the number of tests within the population aged 25 to 59 by the number of women in that age range.

RESULTS. The 17.664 cervical cytology specimens collected during 2005 by the public health system were distributed across women aged from 12 to 82 years, with 12,961 (73.4%) of these tests being on women in the 25 to 59 range, who are considered at higher risk of cancer. A total of 17,458 (98.84%) cytological examinations were negative for malignancy, and there were 206 (1.16%) atypical results (ASCUS/AGUS, LSIL, HSIL and invasive cancer). The study found a prevalence of 0.85% (151) for ASCUS/AGUS and of 1.14% (203/17,664) for atypical cells, and a ASCUS/atypical cells ratio of 2.75 (151/55).

CONCLUSIONS. The lower than expected prevalence of abnormal cervical cytology results and low proportion of ASCUS, the elevated ASCUS/atypical cells ratio, the insufficient population coverage of that cervical cytology and the elevated cervical cancer mortality rate all compromise the performance of the cervical cancer prevention program. The population with low socioeconomic status need special attention and the more privileged must be better informed about the need for regular tests and which age group is at greatest risk.

KEYWORDS: Intraepithelial cervical neoplasm. Primary prevention. Cytology. Neoplasms of the cervix. Cervical cancer prevention.

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INTRODUCTION

Cervical cancer is very common all over the world, accounting for approximately 10% of malignant neoplasms diagnosed in the female population. It is the second greatest cause of mortality from neoplasm in women; after breast cancer. The incidence of this cancer has been increasing year after year and 80% of new cases are diagnosed in developing countries making it a severe public health problem.¹ In Brazil, the Ministry of Health estimates an incidence of 19.18/100,000, although states in the South administrative region of the country have higher incidence rates, such as the state of Paraná with 25.11/ 100,000, and Rio Grande do Sul with 28.17/100,000.¹

The incidence of cervical cancer is dependent on exposure of women to risk factors and the effectiveness of screening programs.²

In the city of Maringá, which is in the state of Paraná, the coefficient of cervical cancer mortality for the period from 1991 to 1996 was 9.1/100,000 women, which is extremely high when compared with the rates for Paraná as a whole and for Brazil, which were 7.0/100,000 and 5.0/100,000 women respectively, for the same period.³

Because this is a slow-developing disease, mortality from cervical cancer can be avoided when precursor lesions are diagnosed and treated when still in their initial phase. Screening and follow-up of such cases is of fundamental importance to avoiding new cases that will require more complex and expensive treatments. In 1997, the Brazilian Ministry of

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Health inaugurated the National Cervical Cancer Prevention Program (*Programa Nacional de Combate ao Câncer do Colo Uterino*) and chose smear tests (Papanicolaou) as the only method to be used for screening for these abnormalities.¹ The objective of the program is early detection and treatment of the precursor lesions of cervical cancer, giving priority for smear tests to women aged 25 to 59. The program also sets out that, after two normal consecutive test results with a 1 year interval, women should be retested every 3 years, in order to achieve an 80% population coverage. It has been observed that on the public health system there is a predominance of women seeking smear tests because of issues related to childbirth, increasing the demand for cervical cytology tests within an age group younger than that which had been chosen. Furthermore, just 30% of the women in Brazil have had samples taken for the test at least three times during their lives.⁴

Studies have been carried out to evaluate the performance of cervical cytology on the basis of sensitivity and specificity statistics. A systematic review with meta-analysis⁵ found that sensitivity varied from 87% to 99% and specificity from 23% to 87%. Therefore, although it is a relatively simple test, smear testing has its disadvantages in the form of false-negatives and/or positives. Many different stages are essential to achieving a satisfactory cytology specimen, adequate analysis of the sample and a good referral and counter-referral system.

A cervical cytology smear is considered to be both adequate and satisfactory when the sample includes the transformation zone (TZ) and the endocervix, including endocervical or squamous metaplastic cells as evidence of this. Excessive quantities of red blood cells and polymorphonuclear cells, dried or thick areas of material, the presence of artifacts (lubricants and antiseptics) can also interfere with the acceptability of the cytology specimen.⁶

It can be considered that the performance of the program is influenced by three factors: 1) the capacity of each municipal health authority to meet the targets it has agreed to in terms of increasing the population coverage of cervical screening, 2) the operational capacity of the health service network to manage collection, transportation and correct technical interpretation of cytology specimens and 3) the socioeconomic status of women affects whether or not they respond to invitations to join the program.²

In the light of what has been described above, the objective of this study was to analyze the quality and performance of the smear tests carried out by the Brazilian National Health Service (*Sistema Único de Saúde*) through its cervical cancer prevention program within the population of Maringá, which is a city located in the Northwestern part of the state of Paraná in Brazil, taking into consideration the three factors described above.

METHODS

The study design was observational, using data from the cervical cytology samples collected at Basic Healthcare Centers (BHC) and the results entered onto the Cervical Pathologies Assessment System (SIS-Colo) run by the Ministry of Health. Data on cervical cancer for the city of Maringá for

the period between January and December of 2005 were collected by means of an online search via the information portal of the *Secretaria de Saúde do Paraná* (SESA), under *Políticas de Atenção Primária, Busca Ativa*. This time period was chosen because it was the last full year for which all data were available via the portal.⁷

The patient variables age and residency were used in the analysis. Age was categorized into three age groups chosen for this study (15 to 24; 25 to 59 and 60 and over), giving priority to the 25 to 59 band, as recommended by the Ministry of Health.¹ Patient residency was distributed according to the city's five health administration districts: *Pinheiros, Tuiuti, Zona Sul, Quebec and Iguçu*.

The cervical cytology results were classified according to the Bethesda System⁸ and grouped as: atypical squamous or glandular cells of undetermined significance (ASCUS/AGCUS); low-grade squamous intraepithelial lesions (LSIL), which includes HPV and cervical intraepithelial neoplasia (CIN) I; high-grade squamous intraepithelial lesions (HSIL), which includes CIN II and CIN III; and Cancer for invasive squamous cell carcinoma and invasive adenocarcinoma.

All of these results were tabulated using Microsoft Word and Microsoft Excel to calculate prevalence by district and age group. The data were analyzed using Statistica 7.1 and Epi Info version 3.2.2. The confidence interval was set at 95% and the cutoff for rejection of the null hypothesis was set at 5%.

The coverage of the test was calculated by dividing the number of tests within the population of women aged 25 to 59 (12,961) by the number of women within this age range resident in Maringá (81,010), according to data published by IBGE for July 1 of 2005⁹ and then multiplying by 100.¹⁰

This project was submitted to and approved by the Human Research Ethics Standing Committee at the *Universidade Estadual de Maringá* (UEM), in accordance with national legislation. Free and Informed Consent Forms were not used since these were secondary data. Notwithstanding, permission to access the stored data was requested from the 15th Regional Health Authority of the State of Paraná.

RESULTS

During 2005, the public healthcare system performed 17,664 smear tests in Maringá on women aged from 12 to 82 years. Seventy-eight (0.4%) tests were on women in the age group from 12 to 14 years and 3,034 (17.2%) in the age group from 15 to 24 years. There were 12,961 (73.4%) tests on women aged 25 to 59, and 1,591 (9.0%) tests were undertaken on women over the age of 60 (Table 1).

It was observed that the percentage of all tests on women aged 12 to 14 that were performed in the **Tuiuti** district (29.5%) was statistically significant, $p = 0.0221$, $RR = 1.81$ (IC 1.11 - 2.94) when compared with the other districts. At the other end of the scale, the **Iguçu** district exhibited statistical significance with 28.4% of all tests on women aged 60 or more, $p < 0.0001$, $RR = 1.74$ (IC 1.57 - 1.93).

It was observed that the greatest overall number of test specimens were collected in the **Quebec** district with 4,038 (22.8%), followed by the **Zona Sul** district with 3,843

(21.8%), **Tuiuti** with 3,314 (18.8%), **Iguaçu** with 3,283 (18.6%) and **Pinheiros** with 3,186 (18.0%).

A total of 17,458 (98.84%) of the 17,664 tests performed in the city of Maringá (Table 2) were negative for neoplasms, 203 (1.14%) had atypical cells and three (0.02%) cancer.

Of the atypical results (Table 2), 151 (73.3%) test results were ASCUS/AGUS breaking down as 147 cases of ASCUS and four of AGUS. The mean age was 39.1 ± 14 years, with a minimum of 15 and maximum of 82 years. In 22 (10.7%) cases LSIL was identified, where three cases were HPV and 19 were CIN I. The youngest women with an HPV lesion was 18 and the youngest with CIN I was 15 years old. Mean age was 28.2 ± 9.4 years with a minimum of 15 and maximum of 52 years. In 30 (14.5%) tests HSIL were identified, with 23 cases of CIN II and seven cases of CIN III. The mean age in this group was 36.1 ± 14.1 with a maximum of 20 and minimum of 69 years. The youngest woman with CIN II was 20 and the youngest with CIN III was 23 years old. Cancer was found in three tests, with two cases of invasive adenocarcinoma, one in a 21-year-old woman and another in a 53-year-old woman, and one case of invasive squamous cell carcinoma, in a 57-year-old woman, accounting for 1.5% of all abnormalities detected.

The ASCUS/AGUS classification predominated in all age groups (Table 2).

Twenty-three (60.5%) of the cases with abnormalities in the 15 to 24 age group were ASCUS/AGUS, followed by LSIL and HSIL with seven cases of each (18.4%) and one cancer case (2.6%).

The distribution within the 25 to 59 age group was predominantly made up of ASCUS/AGUS with 113 (74.9%) cases, with the remainder comprising 20 (13.4%) HSIL cases, 15 (10.0%) LSIL cases and two (1.3%) cancer cases.

There were 15 (83.3%) cases of ASCUS/AGUS in the over 60 age group, and three (16.7%) HSIL cases. No cases of LSIL or of cancer were detected in this age group.

In terms of the regional distribution of test results with atypical cells, the **Tuiuti** district is of note, with a statistically significant percentage of LSIL and HSIL, in comparison with the other districts, $p=0.0003$, $RR= 2.42$ ($IC= 1.55 - 3.78$) (Table 3). In terms of the total number of abnormal test results, the **Zona Sul** district stands out with 57 (27.7%) abnormal tests, followed by the **Tuiuti** district with 45 (21.8%), **Quebec** with 38 (18.5%), **Pinheiros** with 34 (16.5%) and **Iguaçu** with 32 (15.5%) (Table 3).

The data presented here on 17,664 smear tests corresponds to a 16% cervical screening population coverage on the part of the SUS. Coverage could not be calculated for each of the health districts in Maringá because the exact size of the populations resident in each district was not known. This division into districts is an administrative measure taken by the Department of Health (Secretaria de Saúde) and is used to manage the Family Health Program (FHP); the Health Department holds population data on these districts. However, in several parts of the city, FHP coverage is only partial and a proportion of the population still does not receive care through the program. For this reason the population data offered by the Department was not used in this study.

Table 1. Numbers and percentages of cervical cytology tests performed, by health district and age group. Maringá, PR, Brazil, 2007

Healthcare District	12 to 14 years		15 to 24 years		25 to 29 years		≥ 60 years		Total	
	n	%	n ^o	%	n ^o	%	n ^o	%	n ^o	%
Pinheiros	15	19.2	581	19.2	2359	18.1	231	14.5	3186	18.0
Tuiuti	23	29.5	565	18.6	2423	18.7	303	19.0	3314	18.8
Zona Sul	13	16.7	670	22.1	2847	22.0	313	19.7	3843	21.8
Quebec	14	17.9	755	24.8	2977	23.0	292	18.4	4038	22.8
Iguaçu	13	16.7	463	15.3	2355	18.2	452	28.4	3283	18.6
Total	78	0.4	3034	17.2	12961	73.4	1591	9.0	17664	100.0

Table 2. Numbers and percentages of oncotic cervical cytology test results with abnormal findings, by age group and type of atypical cell detected. Maringá, PR, Brazil, 2007

Age group (years)	ASCUS/AGUS		LSIL		HSIL		Cancer		Total	
	n ^o	%	n ^o	%	n ^o	%	n ^o	%	n ^o	%
15 to 24 years	23	15.2	7	31.8	7	23.3	1	33.3	38	8.4
25 to 59 years	113	74.9	15	68.2	20	66.7	2	66.7	150	72.9
≥ 60 years	15	9.9			3	10.0			18	8.7
Total	151	73.3	22	10.7	30	14.5	3	1.5	206	100.0

ASCUS/AGUS: Atypical squamous or glandular cells of undetermined significance

LSIL: Low-grade squamous intraepithelial lesions.

HSIL: High-grade squamous intraepithelial lesions.

Table 3. Numbers and percentages of oncotoc cervical cytology test results with abnormal findings, by healthcare district and type of atypical cell detected. Maringá, PR, Brazil, 2007

Healthcare District	ASCUS / AGUS		LSIL		HSIL		Cancer		Total	
	nº	%	nº	%	nº	%	nº	%	nº	%
Pinheiros	30	19.9	3	13.6			1	33.3	34	16.5
Tuiuti	24	15.9	10	45.5	11	36.6			45	21.8
Zona South	40	26.5	7	31.8	8	26.7	2	66.7	57	27.7
Quebec	32	21.2			6	20.0			38	18.5
Iguaçu	25	16.5	2	9.1	5	16.7			32	15.5
Total	151	73.3	22	10.7	30	14.5	3	1.5	206	100.0

ASCUS/AGUS: Atypical squamous or glandular cells of undetermined significance

LSIL: Low-grade squamous intraepithelial lesions

HSIL: High-grade squamous intraepithelial lesions

DISCUSSION

In 1997 the Brazilian Ministry of Health launched its *Viva Mulher* program - a national program for the control of cervical and breast cancer. The program is structured with the objectives of prevention and early detection and treatment of the precursor lesions of cervical cancer, among other goals. Therefore, women aged 25 to 59 are given priority for the screening test and it is recommended that, after two normal consecutive test results with a 1-year interval, these women should be retested every 3 years.¹

Of the 17,664 cervical cytology samples taken in the city of Maringá during 2005, 12,961 (73.4%) tests were on women aged 25 to 59, giving priority to this age group, as recommended by the Ministry of Health.¹ In this study, seven (31.8%) and 10 (33.3%) cases, respectively, of LSIL and HSIL, were found outside this age range, supporting the suggestion by Coppell, Paul et al.¹¹ that screening should be widened to cover the younger women, on the basis of the increased incidence of high grade lesions among patients aged 20 to 34.

The **Tuiuti** district tested the greatest percentage of adolescents aged 12 to 14 (RR= 1.81, IC= 1.11 - 2.94) and this district also had the highest proportion of LSIL and HSIL (RR= 2.42, IC = 1.55 - 3.78). The residents of this district have low socioeconomic status¹² and special attention is needed to improve the results of the program here. In contrast, the **Iguaçu** district had a statistically significant percentage of women over the age of 60 (RR = 1.74, IC 1.57 -1.93). The residents of the neighborhoods that make up this district are more privileged¹² and it could be observed that the prevalence of LSIL and HSIL was lower here than in the other districts.

The challenging target accepted by the Paraná department of health was to widen the coverage of screening tests carried out by the SUS from 13% to 80%, to offer appropriate treatment for all cases diagnosed and to set up a epidemiological surveillance system that could efficiently control management of the disease throughout the State.¹ This figure of 80% coverage takes into account the existence of healthcare plans which carry out the other 20% of

oncological cervical cytology tests. The approximate cervical screening coverage calculated in this study was 16%, which is a long way below the 80% target. These data suggest that the majority of cases of cervical cancer are not being detected, being diagnosed only in more advanced stages, thereby elevating the coefficient of mortality in the region.³

With relation to the number of abnormal test results, atypical cells of undetermined significance (ASCUS/AGUS) predominated in all age groups (73.3%) and atypical squamous cells (ASCUS) accounted for the great majority of this group (147 ASCUS and four AGUS).

Faced with these results, the diagnosis rate of ASCUS, even in the presence of rigorous criteria to control adequate clinical management, is disputable. Around 70% of women whose smears have a diagnosis of ASCUS do not have a visible cervical lesion when observed via colposcope.¹³ It should be remembered that around 20% to 40% of patients with a diagnosis of ASCUS will have associated CIN, and in 5% to 15% of cases it will be a high-grade lesion.¹⁴ Although it is a rare event, a smear with an ASCUS result can be associated with the presence of a hidden cancer in around 0.1% of cases.¹⁶

In contrast, the proportion of ASCUS findings after analysis of the smear is considered an indicator of the quality of the tests being done at a center. After recent standardizations of diagnostic criteria, ASCUS should appear in the findings of around 3% to 5% of all smear tests.¹⁶ The appearance of higher percentages would suggest an excess in diagnoses of benign, inflammatory and reparative reactions, leading to unnecessary referrals for cervical cytology.¹⁶ In this study, it was found that the prevalence of ASCUS/AGUS findings was 0.85%, which is well below that which is recommended and may indicate a failure to detect atypical cytology.

The prevalence of atypical cells observed in this study (ASCUS/AGUS, LSIL and HSIL), excluding the three cancer cases, was 1.14% (203/17,664). This figure is also lower than expected by the Ministry of Health's national cervical cancer prevention program, which expects this percentage to be 4%.¹⁷ This is an indirect indication of defective diagnosis of atypical cells increasing the number of false negative

cases. The concern increases when one considers that Neto et al.¹⁸ found major differences between the results of cytology smears and directed biopsies. According to the authors, 12.5% of cases with high-grade cytology findings were low-grade on biopsy, while 27.3% of low-grade cytology findings had missed high grade lesions. They considered that the use of smears alone to screen for cervical abnormalities or high-grade NICs lead to a very rough estimate of the prevalence and severity of disease, thereby failing to treat patients or delaying their treatment.

The ratio between the number of cases of ASCUS and the number of atypical cell findings (LSIL, HSIL and cancer) is another parameter used to control smear test quality. At a wide range of different centers this ratio varies from 0.8 to 1.2.^{19,20} In this study, the ASCUS/atypical cells ratio was 2.75 (151/55), which is above rates that can be found in the literature. Considering that the number of ASCUS is already below what is recommended, it is to be concluded that the number of abnormal cytology results is low and concerns return once more to the rate of false negative test results.

These facts could be considered objectively by means of a systematic review of smear test results and by testing their sensitivity and specificity. The sensitivity of the test, i.e., the proportion of true positive cases it detects, is around 50% and its specificity, i.e., the proportion of true negatives detected by the test, is close to 100%, while false negatives are around 4.8%.²¹ In an earlier study carried out in Maringá, sensitivity and specificity of the smear tests performed here were 66.6% and 81.9 %, respectively, the rate of false negatives was 25.1%.²²

Furthermore, the study in Maringá observed that three cases of invasive cancer were detected, one of which was an invasive adenocarcinoma in a 21-year old woman, accounting for 33.3% of the observed cancer cases, which, in turn, accounted for 1.5% of the 206 tests with abnormal findings in the sample of 17,664 tests. These cancer cases, when compared to the total number of tests performed, do not represent a high proportion. However, when the number of cases of cancer observed is considered, it suggests that the prevalence of invasive adenocarcinoma in young women may be elevated. These results are in line with studies carried out in Switzerland, where an increase in the number of cervical adenocarcinomas was observed among women aged 25 to 39, despite an effective screening program having been in place for several decades.²³ Studies undertaken in Maringá have demonstrated that the mortality rate of cervical cancer is increasing in the over-40 age group, due to failure to diagnose lesions earlier.³

CONCLUSIONS

The lower than expected prevalence of abnormal cervical cytology results and proportion of ASCUS, the elevated ASCUS/atypical cells ratio, the insufficient cervical screening population coverage and the elevated cervical cancer mortality rate are all warnings of poor performance at preventing

this disease. The population with low socioeconomic status need special attention if the results of the program are to improve. Notwithstanding, the more privileged sections of the population must be better informed about the need for regular tests and which age group is at greatest risk.

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