ANALYSIS OF CANCER TRACE CANCER OF THE UTERUS COLUMN OF A MUNICIPALITY OF THE SOUTH OF BRAZIL

Análise do rastreamento do câncer do colo do útero de um município do sul do Brasil

Análisis del rastreo del cáncer del colo del útero de un municipio del sur del Brasil

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ABSTRACT

Objective: to analyze the cervical cancer screening of a municipality in the South of Brazil. **Method:** A retrospective descriptive quantitative study was performed by analyzing the reports of the cytopathological exams registered in the Cancer Information System. **Results:** It was identified that the majority of the exams were performed in women targeted by the program, despite the low coverage of the screening. The small number of unsatisfactory samples represents a positive aspect. In contrast, a considerable number of samples obtained not representative of the squamocolumnar junction, this is a critical point to be improved in the efficiency of the examination, since it was found a significant association between the representation and the abnormal changes epithelia. **Conclusion:** the findings of this study reinforce the importance of the evaluation and constant monitoring of the quality of the exams collected, so that they are effective in tracking the lesions that are precursors of cervical cancer.
Keywords: Papanicolaou test; Neoplasms of the cervix; Women's health; Nurses; Family health strategy.

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RESUMO

Objetivo: analisar o rastreamento do câncer do colo do útero de um município do Sul do Brasil. **Método:** realizou-se um estudo quantitativo descritivo retrospectivo pela análise dos laudos dos exames citopatológicos registrados no Sistema de Informação do Câncer. **Resultados:** identificou-se que a maioria dos exames foram realizados em mulheres alvo do programa, apesar da baixa cobertura do rastreamento. O reduzido número de amostras insatisfatórias representa um aspecto positivo. Em contrapartida, um número considerável das amostras não obteve representatividade da junção escamo-colunar, este constitui um ponto crítico a ser melhorado na eficácia do exame, uma vez que, verificou-se associação significativa entre a representação dos epitélios e alterações anormais. **Conclusão:** os achados deste estudo reforçam a importância da avaliação e do monitoramento constante da qualidade dos exames coletados, para que sejam efetivos no rastreamento das lesões que são precursoras do câncer do colo do útero.
Descritores: Teste de papanicolaou; Neoplasias do colo do útero; Saúde da mulher; Enfermeiros; Estratégia saúde da família.

RESUMÉN

Objetivo: analizar el rastreo del cáncer del cuello del útero de un municipio del sur de Brasil. **Método:** se realizó un estudio cuantitativo descriptivo retrospectivo por el análisis de los laudos de los exámenes citopatológicos registrados en el Sistema de Información del Cáncer. **Resultados:** se identificó que la mayoría de los exámenes se realizaron en las mujeres objetivo del programa, a pesar de la baja cobertura del rastreo. El reducido número de muestras insatisfactorias es un aspecto positivo. En cambio, un número considerable de muestras no obtuvo representatividad de la unión escamoso-colunar, éste constituye un punto crítico que debe mejorarse en la eficacia del examen, ya que se ha observado una asociación significativa entre la representación de los epitelios y las alteraciones anormales. **Conclusión:** los hallazgos de este estudio refuerzan la importancia de la evaluación y del monitoreo constante de la calidad de los exámenes recogidos, para que sean efectivos en el rastreo de las lesiones que son precursoras del cáncer del cuello del útero.
Descriptores: Prueba de papanicolaou; Neoplasias del cuello del útero; Salud de la mujer; enfermeras; Estrategia de salud de la familia.

INTRODUCTION

Cervical cancer is a serious public health problem due to its high incidence and mortality, therefore epidemiologically and socially relevant. This situation requires managers and health professionals to combine actions aimed at control through early detection and access to timely diagnostic and therapeutic procedures of high quality.[1]

According to the National Cancer Institute (INCA), this cancer represents the third most common type of cancer in the female population, after breast and colorectal cancer. It is the fourth leading cause of death for women in Brazil.[2]

Relevant regional and intraregional differences are observed in Brazil. Regions with less favorable socioeconomic conditions have poor performance in terms of indicators for cancer control. The persistence of high mortality rates in some regions suggests gaps in the effectiveness of the program, including failures in capturing women, in population coverage, and in the quality of exam samples collected.[3]

Cervical cancer usually begins at the age of 30, with its risk increasing up to the age of 50 and older.[4] With the onset of increasingly early sexual activity in adolescence, women are increasingly exposed to sexually transmitted diseases (STDs) thus increasing vulnerability to human papillomavirus (HPV) infection.[5]

HPV represents the main risk factor for the development of cervical cancer. HPV infections have a high chance of spontaneous evolvement in more than 90% of cases. However, persistent lesions can lead to the development of cancer precursor intraepithelial lesions and, if not detected and treated appropriately and in a timely manner, may progress to cancer. Risk factors such as smoking and immunosuppression contribute to the onset of this cancer.[4]

Although the risk of HPV infection is high, most women do not develop the disease.6 Nevertheless, the natural course of the disease is characterized by a long interval between infection and the onset of cancer precursor lesions.[5] Due to slow progress, the cellular changes caused precede cancer in many years, around 10 to 20 years, in most cases. This is the period when timely screening and treatment of women is possible.[3]

The HPV vaccine for adolescents was implemented in Brazil in 2014 as a contribution to the fight against cervical cancer.[4] Given that the results of this action will be collected in a few decades, the cytopathological exam is the main screening method for cervical cancer and its precursor lesions.[7]

As the professional nurse is responsible for collecting the exam in the Primary Health Care establishment(PHC), they should lead planning of actions that promote strengthening of the work process, considering the importance of quality screening and timely diagnosis of cancer.[8]

Thus, it is important to analyze cervical cancer screening based on the characteristics of the exams collected, so that they can detect cells with altered characteristics early and therefore be effective in cancer screening. Given the above, the objective of this study was to analyze the cervical cancer screening of a municipality in southern Brazil using data from the Cancer Information System (SISCAN).

METHODOLOGY

A descriptive retrospective quantitative study was performed by analyzing the reports of cytopathological examinations registered at SISCAN, in the municipality of Três Passos, Rio Grande do Sul. According to the last census, this municipality has an estimated population of 24,640 inhabitants, of which 12,214 (49.5%) are women and of these, 6,684 (54.7%) are among the target population for screening for cervical cancer, between 25 and 64 years old.[9]

The reports covered a period of one year from February 13, 2015 to February 12, 2016. Data collection took place in July and August 2017. The following variables were selected: date of birth, date of collection, adequacy of sample, reasons for unsatisfactory sample, epithelia represented, microbiology, normal cell abnormalities, abnormal cellular alterations and diagnostic conclusion. Ages were categorized into pre-established age groups (under 25, 25 to 64 and 65 or older). The suitability of the cellular material was rated as satisfactory or unsatisfactory. Epitheliums were identified in the examination reports as squamous, glandular and/or

metaplastic (individual or associated). Microbiology was analyzed separately for each microorganism, so mixed flora could occur. For the classification of cervical lesions, the Brazilian Nomenclature for Cervical Cytopathological Reports recommended by INCA[10] was used. Quantitative data were transferred to a spreadsheet using Microsoft Excel®. Descriptive data analysis was performed, with distribution of absolute and relative frequencies, using the Statistical Package for the Social Sciences (SPSS) ® software, version 23. Pearson's chi-square test evaluated the association between age and abnormal results as well as the association between epithelia and abnormal results, considering the significance level of 95%.

The research complied with the ethical precepts provided for in the Resolution No. 466/2012 of the National Health Council.[11] The study was approved by the Research Ethics Committee of the Federal University of Health Sciences of Porto Alegre, through Decision No. 2,033,967.

RESULTS

1,583 cytopathological exams were analyzed. The age ranged from 14 to 84 years, with a mean of 43.9 years (standard deviation = 14.42). Figure 1 shows that most of the tests, 1,271 (80.3%), were performed on women aged 25 to 64 years. The age group from 45 to 54 years old was the one that most sought the cytopathological exam.

Figure 1 - Distribution of cytopathological exams according to age group. Tres Passos , RS, Brazil, 2015 - 2016
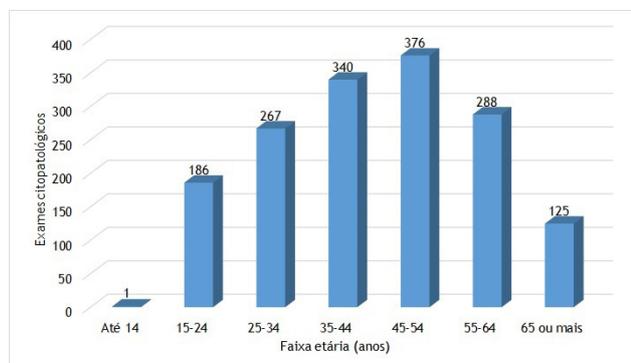
Source: SISCAN/MS, 2017.

Regarding the adequacy of cellular material, 1,566 samples (98.9%) were considered satisfactory and 17 (1.1%) unsatisfactory. Of the unsatisfactory samples, the reasons were: acellular or hypocellular material in less than 10% of the smear; reading impaired by blood, piocytes, desiccation artifacts and intense cell overlap, and in some samples, there were associations; two samples were rejected for absence or misidentification of the slide or form; and three because the slide was damaged or missing. Even though some variables were associated, the presence of piocytes dominates as the reason behind reading impairment.

Of 1,566 satisfactory samples for evaluation, the following are the epithelial representation, microbiological agents, results and cellular alterations found.

Table 1 - Epithelial distribution, microbiology, results and cellular alterations represented in the cytopathological sample of the studied population. Tres Passos, RS, Brazil, 2015-2016

Variables	n	%
Epitheliums		
Scaly	881	56,3
Squamous / Glandular	411	26,2
Scaly / Glandular / Metaplastic	249	15,9
Scaly / Metaplastic	25	1,6
Microbiology		
Lactobacillus SP	872	55,7
Gardnerella	248	15,8
Flora not displayed	194	12,4
Other bacilli	182	11,6
Cocos	71	4,5
Candida	32	2
Trichomonas vaginalis	4	0,3
Leveduriform cells	1	0,06
Results and cellular alterations		
Within the limits of normality	594	37,9
Normal cell alterations		
Benign cell alterations with inflammation	643	41,1
Immature squamous metaplasia	56	3,6
Reparation	12	0,8
Atrophy with inflammation	308	19,7
Other: keratotic cell alterations	1	0,1
Abnormal cell alterations		
Atypical findings of undetermined significance in squamous cells		
Probably not neoplastic (ASC-US)	27	1,7
High grade lesion can not be discarded (ASC-H)	4	0,2
Atypical findings of undetermined significance in glandular cells (AGC)		
Probably not neoplastic	9	0,5
High degree lesion can not be discarded	1	0,06
Atypical findings in squamous cells		
Intraepithelial low grade lesion (LSIL)	4	0,2
Intraepithelial high grade lesion (HSIL)	9	0,5
Invasive squamous cell carcinoma	1	0,06

* The sum exceeds 100% because some variables are repeated.

Source: SISCAN / MS, 2017.

It was observed that 881 (56.3%) exams presented only the squamous epithelium. The most frequent microbiological agents were *Lactobacillus sp* (55.7%) and Gardnerella (15.8%). Among the cellular alterations considered normal, the most frequent were benign (reactive or reparative) cellular alterations with inflammation (41.1%), followed by atrophy with inflammation (19.7%). There were 49 (3.1%) abnormal cell alterations on cytopathological examination that require further investigation.

It follows that the association between abnormal changes and the age range of women recommended for follow-up was not significant, however, there is a significant association between the variables epithelial representation and abnormal changes.

Table 2 - Relationship between recommended age range and abnormal cellular alterations. Relationship between epithelial representation and abnormal cellular alterations. Tres Passos, RS, Brazil, 2015-2016

Variables	N	%	N altered	%	p-value
Age group					
< 24 yrs	187	11,8	3	6,1	0,379
25 to 64 yrs	1271	80,3	43	87,8	
> 65 yrs	125	7,9	3	6,1	
Epitheliums					
Scaly	881	56,3	6	12,2	<0,001
Squamous / Glandular	411	26,2	16	32,7	
Scaly / Glandular / Metaplastic	249	15,9	25	51	

* Pearson's chi-square test (p <0.05)

Source: SISCAN / MS, 2017.

DISCUSSION

The method available in Brazil for screening cervical cancer and its precursor lesions is cytopathological examination. According to the Brazilian Ministry of Health (MS), women between 25 and 64 years are the target population. Screening before the age 25 has very limited impact as the incidence of cervical cancer is considered to be very low. Earlier initiation of screening would make it possible to diagnose low-grade non-cancer precursor lesions with a high probability of spontaneous regression; resulting in additional examinations and unnecessary interventions. Furthermore, there is no evidence of the usefulness of screening after age 65.[1]

Despite the recommendations of the MS, the study revealed that 19.7% of the exams were performed outside the recommended age range, which suggests unnecessary public expenditure. A similar result was identified in the state of Maranhão, in 2011, where 23.2% of the exams were performed outside the recommended age range.[12]

Of the tests performed outside the target population, 11.8% were performed before 25 years of age. A study conducted in the city of Novo Cruzeiro in Minas Gerais (MG) revealed that 4.5% of the exams were under the age of 19.[13] This age group should receive counseling on contraception, STDs and safe sex, without the need for unnecessary interventions.[1]

The mean age of 43.9 years (SD = 14.42) differs from that found in a study conducted in the city of Rio de Janeiro, where 3,425 examinations were analyzed, with a mean age of 39.0 years.[14] It is farther away still of the average of 30 years (SD = 13,25) found in a study carried out in Minas Gerais, with the sample of 8,281 exams.[13] Our survey demonstrated that older women in the municipality in question do the exam more often.

The indicator "Ratio between Cervical Cytopathological Exams and Target Population" expresses the production of cytopathological exams in the 25-64 year-old female population, allowing to evaluate the offer of exams to cover it .The proposed parameter for this indicator is the ratio of 0.30, since the recommendation is that the examinations be performed every three years and in case of two consecutive negative results, performed at an interval of one year.[1]

Considering the target population of 6,684 women residing in the municipality studied and a total of 1,271 tests performed on women aged 25 to 64 years in a one-year period, 0.19 exams were performed during this period in the target population, well below the recommended by the MS. This difficulty in achieving the recommended goal suggests failures in the capture of women and possibly the influence women going to supplementary health institutions for the examinations.[1]

Of the target set in the country (ratio of 0.3 examinations / woman/ year) in 2009, nine states did not reach the agreed goal. Thus, the periodicity of examinations with unnecessary repetitions, the increase in the percentage of unsatisfactory samples and the concentration of examinations performed outside the recommended age range interfere with the performance of the healthcare network.[3]

To be considered a satisfactory smear for oncotic evaluation, the presence of well distributed, fixed and stained representative cells, whose visualization allows a diagnostic conclusion is essential. According to the World Health Organization (WHO), the maximum limit of unsatisfactory samples expected is 5% of the total tests performed.[1]

Notably, in this study, only 1.1% of the samples were unsatisfactory for oncotic evaluation, showing the potential of the collection made by the health professionals of the municipality studied. A better percentage was found in a study conducted in the state of Santa Catarina in 2014 with 0.3% samples described as unsatisfactory.[6] Approximate values were identified in a study conducted Pernambuco with 0.92% of unsatisfactory samples.[15]

Another study pointed out that the three most frequent causes of unsatisfactory samples were: presence of acellular or hypocellular material (in less than 10% of the smear); absence or error in identification of the slide, bottle or form; and presence of desiccation artifacts.[15] In the present study, the main reasons that compromised the reading of the sample were the presence of desiccation and pyocytes. In these cases, the MS recommendation is to repeat the exam between six and 12 weeks, with corrections, when possible, of the problem that led to the unsatisfactory result.[7]

In the cytopathological sample, representative cells of cervical epithelia may be present, namely: squamous cells, glandular cells (except endometrial epithelium) and metaplastic cells. Although only the presence of squamous

epithelium characterizes the sample as satisfactory, the presence of metaplastic or endocervical cells, representative of the squamocolumnar junction (SCJ), has been considered an indicator of quality of collection. This is because it is in SCJ that almost all cervical cancers are located. Thus, it is very important that professionals pay attention to the representativeness of SCJ in cervicovaginal smears, at risk of not providing women with all the benefits of prevention.[1]

In the present study, in 56.3% of the sample there was only the representation of the squamous epithelium and absence of the transformation zone (ZT) in more than half of the samples. In the others, the representation was distributed between glandular and metaplastic epithelia associated with squamous epithelium.

A similar result was identified in the western region of Minas Gerais, with 99.1% representing squamous epithelium, followed by the glandular with 57.9%, and the metaplastic with 34.2%.[16] For adequate quality of examination the representation of glandular and / or metaplastic epithelia is expected to be at least equal to squamous, and their absence is considered normal only in hysterectomized women.[12] In this regard, information on women who underwent hysterectomy was not available in the reports of the exams analyzed.

The absence of both epithelia in the cytopathological specimens from the ectocervix and endocervix may contribute to the incidence of false negative results, as well as delaying the early diagnosis of cervical cancer precursor lesions.[8] In addition, age between 25 and 64 years, oral contraceptive use, hormone replacement therapy (HRT) and metaplastic epithelium are facilitators for capturing ZT cells.[8] In contrast, weakness in the technique of collection may be linked to failures in the effectiveness of actions, corroborating the findings of this study, where less than half of the samples had cellular elements representative of ZT.

According to the sensitivity analysis performed in one study, the frequency of atypical findings was shown to increase to 46.4% when simulated increase in the presence of representative ZT cells to 43.0%. Thus, the presence of cellular elements representative of ZT, such as glandular and metaplastic epithelial cells, can be used as a quality parameter for cytopathological examination collection.[14]

The main microbiological findings, Lactobacillus sp. and Gardnerella, respectively, were also found in a study in Santa Catarina.[8] The microbiological findings of this study, with the exception of Trichomonas vaginalis, are considered normal, and it is recommended to follow the cytological screening routine and treat only in case of complaints about vaginal discharge.[7] In asymptomatic women, these agents can usually be identified due to the presence of a large variety of bacteria in the cervicovaginal content, forming a mixed flora.[12]

A small amount of microbiological agents such as Trichomonas vaginalis (0.3%) were identified indicating STDs. Given the unavailability of more sensitive and specific methods to confirm the presence of these microorganisms, such findings are an opportunity to identify agents that should

be treated.[7] The presence of STD-related microorganisms is a factor that masks cellular atypicalities due to the infectious process.[14]

Considering the negative psychological effects evidenced in many women after receiving the result of an altered exam, it is up to the health professional during the service to explain in detail the abnormal meaning. In addition, they should advise on recommended conduct, necessary referrals, and possible procedures.[1]

The result of 3.1% of abnormal alterations was higher than that found in a study conducted in Santa Catarina, where the result was 2.1%.[6] Among the possible changes that may or may not progress to cervical cancer, atypicalities of undetermined significance in squamous cell (ASC-US), probably non-neoplastic, were the most prevalent (1.7%). This result was also identified in the study mentioned above, in which the diagnosis of ASC-US was the most frequent (1.3%). However, this result represents a mixture of differential diagnoses and diagnostic difficulties, not considered abnormality, but cytopathological ambiguity. Thus, they are neither quantitatively nor qualitatively sufficient for the definitive diagnosis, and subsequent or immediate diagnostic definition is required depending on the severity of the suspicion.[1]

In this study, low-grade squamous intraepithelial lesions (LSIL) compatible with the cytological manifestation of HPV infection were found in 0.2% of cytopathological examinations, lower than in Maranhão (0.6%)[12] and Minas Gerais (0.5%)[16] The recommendation for women with this diagnosis is to repeat the exam in six months. Understanding the slowly evolving natural history of HPV infection leads to the postponement of repeated cytology research to avoid unnecessary costs.[1]

High grade squamous intraepithelial lesions (HSIL) and invasive squamous cell carcinoma are considered the precursor lesions of cervical cancer if they are not detected and treated in a timely manner. In such cases, patients should be referred for colposcopy in secondary care. Nevertheless, lesions can be totally curable most of the time.[1] In this study, 0.5% of HSIL and 0.06% of invasive squamous cell carcinoma were identified. Lower results were found in Minas Gerais, with 0.2% and 0.008%, respectively.[16]

In the present study we observed that the association between abnormal changes and the age range of women recommended for follow-up was not significant. However, for the cross-referencing of the variables, the severity of the lesions was not considered. According to the literature, the diagnosis before 25 years is higher for low-grade lesions.[1]

On the other hand, a significant association between epithelial representation and abnormal alterations was identified. In 32.7% of the samples with abnormal cellular alterations, the representation of the glandular squamous epithelium was verified. This percentage went up to 51% with the presence of squamous, glandular and metaplastic epithelia. Thus, the study suggests that samples with representation of the glandular and / or metaplastic

squamous epithelium are more likely to detect precursor lesions.

In a retrospective study conducted in Rio de Janeiro, it was found that the chance of finding atypia in the presence of ZT cell elements was 5.19 times higher than in the absence of these cell elements.[17] Considering that over 90% of lesions precursor or malignant lesions of the cervix are located in the ZT, it is understood that their absence in the smear may cause false negative results and delay timely diagnosis and treatment.[1]

However, the representativeness on the slide of ZT cellular elements as an indicator of exam quality should be evaluated, in order to optimize the benefits of cervical cancer prevention. Thus, it is essential that all professionals involved ensure the availability of this information, both those who accompany the woman and perform the collection of the exam, as well as those who interpret the exam.[17] In this sense, the nurse needs to feel prepared to perform the procedure. In addition to the search for constant professional development, it is recommended to adopt a protocol of care to women, with guidance to schedule cytopathological examination.

FINAL CONSIDERATIONS

Based on the results presented in this study, most of the exams were performed on women targeted by the program, which underscores the potential of the service, as well as the small number of unsatisfactory samples. On the other hand, a considerable number of samples did not include ZT. This is a critical point in the collections made by the municipality's professionals, since a significant association between epithelial representation and abnormal alterations was identified.

Considering that the PHC protocols establish the importance of the representation of the two epithelia as an indicator of the quality of the collection in the municipality in question, the collection of material with epithelial representation is still a point to be improved in the efficacy of the exam. The findings of this study reinforce the importance of constantly evaluating and monitoring the quality of the exams collected, so that they are effective in tracking lesions that are precursors of cervical cancer.

Among the limitations found in the study, the lack of identification in the examination report of hysterectomized women prevented effective measurement of women with the possibility of having epithelial representation but did not have it. Another limitation refers to the fact that the existing reports in SISCAN are restricted to women who performed their examinations in the basic health network. Thus, tests performed in supplementary health services were not accounted for to calculate coverage in the municipality, which means a partial view of reality.

For further studies, an evaluation of the follow-up performed for women who presented alterations in their exams is recommended, with the objective of increasingly approximating the care strategies with the recommended improvements of the care provided.

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