



Jornal Brasileiro de Patologia e Medicina
Laboratorial

ISSN: 1676-2444

jbpml@sbpc.org.br

Sociedade Brasileira de Patologia
Clínica/Medicina Laboratorial
Brasil

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Instituto Nacional de Câncer

Jornal Brasileiro de Patologia e Medicina Laboratorial, vol. 51, núm. 2, marzo-abril, 2015,
pp. 102-107

Sociedade Brasileira de Patologia Clínica/Medicina Laboratorial
Rio de Janeiro, Brasil

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Quality in cytopathology: an analysis of the internal quality monitoring indicators of the Instituto Nacional de Câncer

Qualidade em citopatologia: análise de indicadores de monitoramento interno de qualidade do Instituto Nacional de Câncer

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ABSTRACT

Introduction: Quality control programs are required to ensure the effectiveness of Pap smear, which still remain a key strategy for control of cervical cancer worldwide. **Objective:** This study was based on the retrospective and quantitative analysis of the post-analytical phase indicators from the internal quality monitoring (IQM) program for cytopathology laboratories, such as: positivity rate, atypical squamous cell (ASC)/satisfactory exams ratio, ASC/abnormal test results ratio, ASC/squamous intraepithelial lesions (SIL) ratio, percentage of tests compatible with high-grade squamous intraepithelial lesion (HSIL), and total of false negative. **Materials and methods:** The information was extracted from the computerized system of the Section for Integrated Technology in Cytopathology (Seção Integrada de Tecnologia em Citopatologia [SITEC]), a reference institution for cancer cytopathology, from July 2013 to June 2014. From a total of 156,888 Pap smears, 157,454 were considered satisfactory for indicator analysis and 566 were excluded because they were considered unsatisfactory and/or rejected for analysis. The data was organized in tables using Microsoft Excel 2010 software, and categorized as indicators. **Results:** The averages for the indicators were: 7.2% for positivity rate, 56.9 for ASC/abnormal test ratio, 4.1 for ASC/satisfactory tests ratio, 1.4 for ASC/SIL ratio, 0.6% percentage for tests compatible with HSIL, and 2.1% for false-negative rate. **Conclusion:** The results show that an Internal Quality Monitoring Program is essential to ensure quality for cytopathology laboratories, and a randomized review of at least 10% of the negative exams, as recommended by the Brazilian Ministry of Health/Instituto Nacional de Câncer (INCA), since is an effective method, especially for large laboratories.

Key words: cytopathology; Pap smear; cervix; quality indicators.

INTRODUCTION

Cervical cancer appears as a major public health problem and is the fourth most common cancer among women⁽¹⁾. The conventional cervical smear test (Pap smear) is the main strategy of cervical cancer screening programs worldwide. To ensure its effectiveness the structuring of a quality control system is required⁽²⁻⁵⁾.

On December 30, 2013 entered into force on Ordinance N. 3388, which redefines the National Qualification in Cytopathology (Qualificação Nacional em Citopatologia

[QualiCito]) for cervical cancer prevention⁽⁶⁾, under the Health Care Attention for People with Chronic Diseases (Rede de Atenção à Saúde das Pessoas com Doenças Crônicas). QualiCito consists in establishing standards and evaluation the quality of Pap smear of the cervix by monitoring the performance of public and private laboratories service providers to the Unified Health System (Sistema Único de Saúde [SUS]). Its execution occurs through internal quality monitoring (IQM), external quality monitoring (EQM) and compliance with the criteria set out for quality assessment and hiring laboratories⁽⁶⁾.

The Section for Integrated Technology in Cytopathology (Seção Integrada de Tecnologia em Citopatologia [SITEC]) belongs to the Pathology Division of the Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA) and implemented the IQM as a tool to develop the diagnosis, improve the technical procedures, and conduct continuing education. By implementing the quality indicators, we can assess the overall performance of the laboratory, performing individual statistical analysis of professionals, as well as provide the data obtained for conducting internal and/or external audit^(3,5).

This paper presents the quality indicators of post-analytical phase of IQM in SITEC/INCA, which include the positivity rate, the percentage of tests compatible with atypical squamous cells (ASC) among satisfactory tests, the ASC percentage among abnormal tests, the ASC/squamous intraepithelial lesion (SIL) ratio, the percentage of tests compatible with high-grade squamous intraepithelial lesion (HSIL) in addition to the percentage of negative false exams.

OBJECTIVE

To assess the main quality indicators and the percentage of false negative tests by IQM of SITEC/INCA.

MATERIALS AND METHODS

This retrospective and quantitative study, consists in the analysis of the indicators of post-analytical phase of IQM, proposed in QualiCito⁽⁶⁾ and in Quality Management Manual for Cytopathology Laboratories⁽³⁾, whose selected variables are described in their respective formulas as follows:

- 1) positivity rate

$$\frac{\text{n}^\circ \text{ of abnormal tests in a particular location and year} \times 100}{\text{total of satisfactory tests}}$$

- 2) percentage of tests compatible with ASC among satisfactory tests

$$\frac{\text{n}^\circ \text{ of tests with ASC-US and ASC-H} \times 100}{\text{total of satisfactory tests}}$$

ASC-US: atypical squamous cells of undetermined significance; ASC-H: atypical squamous cell, cannot exclude a high-grade squamous intraepithelial lesion.

- 3) percentage of tests compatible with ASC among abnormal tests

$$\frac{\text{n}^\circ \text{ of tests with ASC-US and ASC-H} \times 100}{\text{total of abnormal tests}}$$

- 4) ASC/SIL ratio

$$\frac{\text{n}^\circ \text{ tests compatible with ASC-US e ASC-H}}{\text{n}^\circ \text{ of tests with LSIL and HSIL}}$$

LSIL: low-grade squamous intraepithelial lesion.

- 5) percentage of tests compatible with HSIL

$$\frac{\text{n}^\circ \text{ of tests with HSIL} \times 100}{\text{total of satisfactory tests}}$$

- 6) percentage of false negative tests. False negative are the smears that were classified as negative by the routine screening tests, but which were considered abnormal by the Cytopathology Quality team of SITEC/INCA, in random review of at least 10% of exams. These tests are addressed to cytopathologists to confirm the diagnosis.

The information in this study was taken from the computerized system of SITEC/INCA, a reference institution for cancer cytopathology, including the period from July 2013 to June 2014. From a total of 157,454 cervical smear tests using the conventional method, 156,888 were considered satisfactory for the indicators analysis, and 566 were excluded because they were classified as unsatisfactory and/or rejected.

In SITEC/INCA's first cervical smear test reading is performed by cytotechnologists. Senior cytotechnologists compose the quality control team and they review at least 10% of cases classified as negative and those with information of clinical risk. All positive cases are addressed to the team of pathologists for emit the final report.

All data obtained for analysis were organized in tables using Microsoft Excel 2010 software, in which they were categorized into. The study was approved by the Research Ethics Committee (Comitê de Ética em Pesquisa [CEP]) of INCA, CAAE 32632314.6.0000.5274.

RESULTS

Table 1 shows the monthly percentage of quality indicators in SITEC/INCA. The positivity rates ranged from 3.8% to 9.2%; the ASC percentage among the abnormal tests was between 51.4% - 63.7%; the ASC percentage among the satisfactory tests

present average of 4.1%; the ASC/SIL ratio remained between 1.1-1.9; and the percentage of exams compatible with HSIL showed variation between 0.4%-0.8% during the study period.

The average of each indicator for the assessed period is shown in **Figure 1**.

The false negative rate varies between 1.6% and 2.5% in the period, with an average of 2.1%, as shown in **Figure 2**.

DISCUSSION

Through this study it was observed that the positivity rate (7.2%) of SITEC/INCA in the period remained within the standard recommended by the QualiCito⁽⁶⁾ and the Quality Management Manual for Cytopathology Laboratory⁽³⁾, which is equal to or greater than 3% and between 3%-10%, respectively, as shown in **Table 2**.

Between July 2013 and June 2014 the positivity rate ranged from 3.8% to 9.2%. It is not possible to assert whether the variations among the analyzed months occur by chance or if there is seasonality, since this study is limited to evaluate the data for only one year. The extension of evaluation of these data for other years can help to respond these hypotheses.

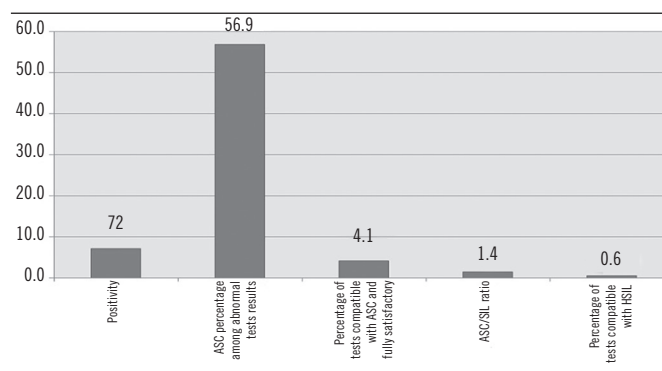


FIGURE 1 – SITEC average July 2013 to June 2014

SITEC: Integrated Section of Technology in Cytopathology (Seção Integrada de Tecnologia em Citopatologia); ASC: atypical squamous cell; SIL: squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion.

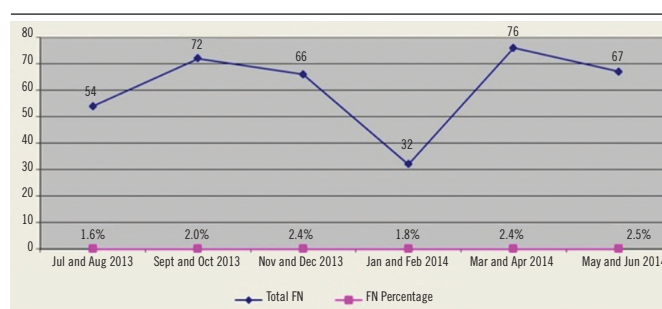


FIGURE 2 – Total and percentage of false negative in the period of July 2013 to June 2014, average 2.1%

FN: false negative.

TABLE 1 – Quality Indicators from SITEC/INCA during the period from July 2013 to June 2014

Indicators	Jul 2013	Aug 2013	Sept 2013	Oct 2013	Nov 2013	Dec 2013	Jan 2014	Feb 2014	Mar 2014	Apr 2014	May 2014	Jun 2014	Mean of period
Positivity rate	3.8	7.6	6.4	8.0	5.8	8.3	9.2	6.2	8.7	6.5	8.2	7.4	7.2
ASC percentage among abnormal test results	51.9	56.8	58.9	53.8	51.4	59.8	56.3	63.7	58.6	58.0	55.3	58.0	56.9
Percentage of ASC compatible test results among satisfactory tests	2.0	4.3	3.8	4.3	3.0	5.0	5.2	4.0	5.1	3.8	4.6	4.3	4.1
ASC/SIL ratio	1.1	1.4	1.5	1.2	1.1	1.6	1.4	1.9	1.5	1.5	1.3	1.5	1.4
Percentage of tests results compatible with HSIL	0.4	0.5	0.4	0.7	0.5	0.6	0.8	0.4	0.7	0.5	0.6	0.7	0.6

SITEC: Integrated Section of Technology in Cytopathology (Seção Integrada de Tecnologia em Citopatologia); INCA: Instituto Nacional de Câncer; ASC: atypical squamous cell; SIL: squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion.

TABLE 2 – Percentage of quality indicators according to QualiCito and the Quality Management Manual for cytopathology laboratories (INCA, 2012)

Indicators	Quality management manual	QualiCito
Positivity rate	Very low: below de 2%	Equal or greater than 3%
	Low: 2% and 2.9%	
	Expected: between 3%-10%	
	Higher than expected: more than 10%	
ASC percentage among abnormal tests	Gradually decrease ASC results	Below 60%
ASC percentage among satisfactory tests	4% to 5%	-
ASC/SIL ratio	Not higher than 3	-
HSIL percentage	Gradually increase the ability to detect HSIL	Equal or greater than 0.4% of the satisfactory tests

QualiCito: National Qualification in Cytopathology in preventing cervical cancer; INCA: Instituto Nacional de Câncer; ASC: atypical squamous cell; SIL: squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion.

The positivity rate expresses the prevalence of cellular changes in the tests and the sensitivity of the screening process to detect lesions in the examined population. When this index is below the recommended, it may indicate that positive tests were not identified, increasing the rate of false negative results⁽⁷⁾.

The literature suggests that countries like the United States⁽⁸⁾, Norway⁽⁹⁾ and the United Kingdom⁽¹⁰⁾ show the positivity rate of 6.8%, 4.9% e 6.4%, respectively. These countries with effective results in cytological screening has been decreased the incidence and mortality rates from cervical cancer. It is important to mention that laboratories need to be alert to keep the positivity rate within the recommended intervals, as the confirmation of this index higher than 3% is one of the parameters discussed in the QualiCito⁽⁶⁾ to contract and/or contract renewal with laboratories providing services to the SUS.

The mean percentage of exams compatible with ASC among the satisfactory in SITEC/INCA in the period was 4.1%, the expected value was between 4%-5% of tests, according to the Quality Management Manual⁽³⁾. The atypical cells of undetermined significance were considered as suspicious cases where the presence of cellular changes are insufficient for the diagnosis of squamous intraepithelial lesions, have their diagnosis variable in relation to the SIL. SIL criteria are clear and well-defined, while the diagnosis compatible with ASC is more variable and less reproducible than the diagnosis of low- and high-grade SIL, meaning that the agreement between the surveyors tend to be higher for SIL than for ASC⁽³⁾.

The mean of ASC percentage among abnormal tests in SITEC/INCA in the period was 56.9%, and the expected value was lower than 60% according to QualiCito⁽⁶⁾. The Quality Management Manual⁽³⁾ recommends that there should be a progressive reduction of this rate. High ASC indices indicate problems in the sample, in the laboratory examination or in both. This indicator comprises an indirect assessment of quality, but does not allow an independent analysis of the quality of the process. The increase of this index is harmful for women as well as the health care network because it leads to an increase in the number of tests intended to repetition⁽³⁾.

The ASC/SIL ratio, in accordance with the Quality Management Manual⁽³⁾, must not exceed three times the SIL rate. Thus, it is possible to identify the low professional performance in the screening. In SITEC/INCA, the average of this indicator was 1.4%, which is within the established limit. According to Türkmen⁽¹¹⁾, ASC/SIL ratio may be lower in high-risk populations and higher in low-risk populations. The 1.4%

ASC/SIL ratio from SITEC/INCA is compared to those found in the study of Renshaw⁽¹²⁾, which corresponds to 1.5%, of Chebib⁽¹³⁾ whose average is 1.15%, and of Catteau⁽¹⁴⁾, which was 1.9%.

The percentage of exams compatible with HSIL in SITEC/INCA ranged between 0.4%-0.8% in the period, which is consistent with QualiCito⁽⁶⁾ that establishes the indice superior a 0.4% index, and the Manual of Quality Management⁽³⁾ recommends gradually increase the ability to detect HSIL. The HSIL percentage for all satisfactory tests reported in the literature was 0.5% for the United States⁽¹⁵⁾, 0.6% in Canada⁽¹⁶⁾, 1.1% in the United Kingdom⁽¹⁰⁾, and 1.14% in Norway⁽⁹⁾. The high-grade lesions represent those which genuinely are precursors of cervical cancer with potential for progression, and its detection is the major goal of secondary prevention of cervical cancer⁽³⁾.

The cervical Pap smear has been criticized because its sensitivity rate is not so high. In the United States, for example, it corresponds to approximately 79% in conventional cytology⁽¹⁷⁾. The false negative exams are mainly related to collecting, screening, and interpretation errors of cytopathological diagnosis^(2-4, 6). The review of cases for quality control is an effective method to minimize the number of negative false diagnosis^(17, 18).

There are several methods of review to monitor the quality of cervical screening, to the discretion of each laboratory to choose the method that better meets its profile. The review methods recommended by the Quality Management Manual⁽³⁾ and QualiCito⁽⁶⁾ include: analysis of cytohistological correlation, retrospective review of the tests, random review of 10%, review of smears selected based on clinical criteria for risk, quick review of 100% of negative smears, fast prescreening of all smears, among others⁽³⁾. The choice of IQM method in the laboratory must be made by evaluating the volume of examination and the quantitative professionals, in order to not exceed the workload^(1, 9, 13).

In SITEC/INCA, the IQM is carried out using the method of random review of at least 10% of negative smears. If the team has found any significant cytomorphological change that changes the diagnostic procedure, the reviewer sends the case with a probable diagnosis to the cytopathologist to the final report.

Analysis of our study results show that the random review method of at least 10% of negative smears is appropriate, especially for laboratories with a large number of Pap smears.

Every two months evaluated had an average of 18000 negative examinations, which make the review of 100% of

smears unfeasible, requiring impractical time and greater quantitative of professionals, not available at the institution.

Using the random review of at least 10% of negative cases, we detected during the analysis period an average of 2.1% of false negative tests. Bonilha *et al.*⁽¹⁹⁾, using the same method obtained a rate of 2.4%. Currens *et al.*⁽²⁰⁾ detected 0.18% false negative cases with the random review of at least 10% by Pap smear, but in liquid-based cytology method.

Through IQM it is possible to assess the causes of false negative exams and to plan actions of continuing education with the professionals. It takes place during the SITEC weekly meeting with the Cytopathology Quality team to discuss scientific articles related to the topic and to propose improvement strategies

of data on the quality of preventive gynecological examinations performed at INCA. In addition, the good practice in IQM gives the laboratory greater credibility with their customers.

CONCLUSION

IQM strategy is essential to ensure quality in cytopathology. We believe that for large laboratories, the random review of at least 10% of exams considered negative, is effective to identify issues that must be addressed in continuing education, in order to obtain reliable indicators that meet the regulations established by Qualicito and by the references in the national and international literature.

RESUMO

Introdução: A estruturação de um sistema de controle de qualidade é necessária para garantir a efetividade do exame preventivo ginecológico, que permanece como principal estratégia para controle do câncer do colo do útero no mundo. **Objetivo:** Análise retrospectiva e quantitativa dos indicadores da fase pós-analítica do monitoramento interno de qualidade (MIQ) para laboratórios de citopatologia, como: índice de positividade, razão atípicas escamosas de significado indeterminado (ASC)/exames satisfatórios, razão ASC/exames alterados, razão entre ASC/lesões intraepiteliais escamosas (SIL), percentual de exames compatíveis com lesão intraepitelial escamosa de alto grau (HSIL), além do total de falso negativos. **Material e método:** As informações foram extraídas do sistema informatizado da Seção Integrada de Tecnologia em Citopatologia (SITEC), instituição de referência em citopatologia oncológica, no período de julho de 2013 até junho de 2014. De um total de 157.454 exames citopatológicos no período, 156.888 foram considerados satisfatórios para análise dos indicadores e 566 foram excluídos por serem classificados como insatisfatórios e/ou rejeitados. Todos os dados obtidos para análise foram organizados em tabelas utilizando-se o programa Microsoft Excel 2010, nas quais foram categorizados em indicadores. **Resultados:** A média obtida dos indicadores foi de 7,2% para o índice de positividade, 56,9 para a razão de ASC/exames alterados, 4,1 para a razão ASC/exames satisfatórios, 1,4 para ASC/SIL, 0,6% para exames compatíveis com HSIL e 2,1% de exames falso negativos. **Conclusão:** Os resultados demonstram que o MIQ é fundamental para manter a qualidade dos laboratórios de citopatologia, e a revisão aleatória de pelo menos 10% dos exames considerados negativos, conforme orientação do Ministério da Saúde/Instituto Nacional de Câncer (INCA), é um método eficaz principalmente em laboratórios de grande porte.

Unitermos: citopatologia; colpocitológico; colo uterino; indicadores da qualidade.

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