Strategies Used to Improve the Quality of Citopathological Examinations

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Estratégias Utilizadas para Melhorar a Qualidade dos Exames Citopatológicos

Estrategias Utilizadas para Mejorar la Calidad de los Examenes Citopatológicos

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Abstract

Introduction: The cytopathological examination is used for early detection of cervical cancer precursor lesions. **Objective:** Evaluate the quality indicators according to the Quality Management Manual for the Cytopathology Laboratory. **Method:** The results of the request forms of cytopathological examinations of the Clinical Laboratory of the Pontifical University of Goiás (LC-PUC-Goiás) were verified between January 2013 and December 2017. **Results:** Of 6,809 diagnoses in total, 99.4% (6,768/6,809) were satisfactory, 91.3% (6,215/6,809) were negative, 8.1% (553/6,809) presented cytological abnormalities and 0.6% (41/6,809) were unsatisfactory. The Positivity Index from 2013 to 2017 was 10.5%, 7.9%, 8.6%, 6.8% and 5.3%, respectively. The percentage of examinations with high-grade intraepithelial lesion (HSIL) among satisfactory examinations in 2013 was 1.3%, in 2014, 1.0%, in 2015, 0.5%, in 2016, 0.6 % and in 2017, 0.7%, results within the established ≥ 0.4%. The atypical squamous cells (ASC)/satisfactory ratio showed values above the standard figures in 2013 with 6.8% and 2015 with 6.1%. According to the Quality Control Management Manual, it is expected that, at the most, 4% to 5% of all exams be classified as ASC. Values above 5% demand differentiated attention. **Conclusion:** It is of the utmost importance the continued education of professionals who participate in all stages of the process, from the pre-analytical to the analytical phase, so that possible errors can be avoided and preventive measures taken for better quality interpretation of the cytopathological examinations.
Key words: Cell Biology; Quality Control; Uterine Cervical Neoplasms.

Resumo

Introdução: O exame citopatológico é utilizado para detecção precoce das lesões precursoras do câncer do colo uterino. **Objetivo:** Avaliar os indicadores de qualidade de acordo com o Manual de Gestão da Qualidade para Laboratório de Citopatologia. **Método:** Verificaram-se os laudos das fichas de requisição dos exames citopatológicos do laboratório clínico da Pontifícia Universidade de Goiás (LC-PUC-Goiás) entre janeiro de 2013 e dezembro de 2017. **Resultados:** Do total de 6.809 diagnósticos, observaram-se 99,4% (6.768/6.809) satisfatórios, sendo 91,3% (6.215/6.809) resultados negativos, 8,1% (553/6.809) diagnósticos com anormalidades citológicas e 0,6% (41/6.809) de exames insatisfatórios. O índice de positividade dos anos de 2013 a 2017 foram 10,5%, 7,9%, 8,6%, 6,8% e 5,3%, respectivamente. O percentual de exames compatíveis com lesão intraepitelial de alto grau (HSIL) entre os exames satisfatórios no ano de 2013 foi de 1,3%; 2014: 1,0%; 2015: 0,5%; 2016: 0,6%; e 2017: 0,7%, resultados dentro do estabelecido, ≥0,4%. A relação de células escamosas atípicas (ASC)/satisfatórios demostrou valores acima do estabelecido nos anos de 2013 com 6,8% e 2015 com 6,1%. Segundo o Manual de Gestão para Controle de Qualidade, espera-se que, no máximo, 4% a 5% de todos dos exames sejam classificados como ASC. Valores acima de 5% necessitam de uma atenção diferenciada. **Conclusão**: É de suma importância a educação continuada dos profissionais que participam de todas as etapas do processo, da fase pré-analítica à analítica, para que possíveis erros possam ser corrigidos e medidas preventivas tomadas para uma melhor qualidade na interpretação dos exames citopatológicos.
Palavras-chave: Biologia Celular; Controle de Qualidade; Neoplasias do Colo do Útero.

Resumen

Introducción: El examen citopatológico se utiliza para la detección temprana de lesiones precursoras de cáncer cervical. **Objetivo:** Evaluar los indicadores de calidad de acuerdo con el Manual de Gestión de Calidad para el laboratorio de citopatología. **Método:** Se verificaron los informes de los formularios de solicitud para los exámenes citopatológicos del Laboratorio Clínico de la Pontificia Universidad de Goiás (LC-PUC-Goiás), de enero de 2013 a diciembre de 2017. **Resultados:** Del total de 6.809 diagnósticos, se observarán 99,4% (6.768/6.809) diagnósticos satisfactorios, 91,3% (6.215/6.809) resultados negativos, 8,1% (553/6.809) diagnósticos con anomalías citológicas y 0,6% (41/6.809) exámenes insatisfactorios. El índice de positividad de 2013 a 2017 fue de 10,5%, 7,9%, 8,6%, 6,8% y 5,3% respectivamente. El porcentaje de exámenes compatibles con lesiones intraepiteliales de alto grado (HSIL) entre los exámenes satisfactorios en 2013 fue de 1,3%; 2014: 1,0%; 2015: 0,5%; 2016: 0,6%; y 2017: 0,7%, resultados dentro de lo establecido, ≥0,4%. La relación células escamosas atípicas (ASC)/satisfactorio fue más alta que la establecida en 2013 con 6,8% y 2015 con 6,1%. Según el Manual de Gestión de Control de Calidad, se espera que un máximo del 4% al 5% de todos los exámenes se clasifiquen como ASC. Los valores superiores al 5% requieren una atención diferente. **Conclusión:** Es de suma importancia la educación continua de los profesionales que participan en todas las etapas del proceso, desde la fase preanalítica hasta la analítica, para que se puedan corregir los posibles errores y se tomen medidas preventivas para una mejor calidad en la interpretación de los exámenes citopatológicos.
Palabra clave: Biología Celular; Control de Calidad; Neoplasias del Cuello Uterino.

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INTRODUCTION

Cervix cancer, except non-melanoma skin cancer is considered the third tumor most frequent in women, being the fourth cause of death of the Brazilian female population. According to the National Institute of Cancer José Alencar Gomes da Silva (INCA), in Brazil, the estimated incidence for 2018 is 16,370 new cases[1]. This is caused by the etiologic agent called human papillomavirus (HPV)[2].

The precursor lesions of cervix cancer in the cytopathological diagnosis classified as high-grade squamous intraepithelial lesions (HSIL) and adenocarcinoma *in situ* (AIS) are provoked by the persistent infection by several types of oncogenic high-risk HPV[3]. There are risk factors that favor the infection and/or its persistence such as: initiation of early sexual activity, number of partners, high parity, use of oral contraceptives and tobacco addiction that facilitate its infection and persistence[4].

Another factor that can contribute for the infection by HPV is the zone of transformation, also called cervical transformation zone (squamocolumnar junction) where there is the column and/or metaplastic epithelium, increasing the probabilities of micro traumatism and carcinogenesis. This physiological process is called ectopy, the area of the cervix that is more able of being infected with high number of young cells in replication and differentiation, therefore, more possibility of encountering precursor lesions of cervix cancer[3,5].

The analysis of a proper sample is a fundamental quality indicator, therefore, a sample is considered satisfactory when it contains squamous, glandular and/or metaplastic cells, that is, of the transformation zone in representative quantities and well distributed, fixed and, stained that allows the diagnosis[6].

The World Health Organization (WHO) recommends the utilization of the cytopathological exam adequately, reaching 80% of coverage and performed within the parameters of quality. In these conditions, it is believed that the occurrences of cervix cancer diminish between 60% to 90%[7].

In order to have a good performance in cervix screening, it is necessary that high sensitivity methods are used, good specificity and of easy implementation. In the last years, the cytopathological test has been object of several criticism because of its low sensitiveness[8-10]. The rates of false negatives vary between 6% to 56%, that can occur in pre-analytic and analytic phase[11,12]. Some of these motives may be related to problems of collections and others in the processing and analyzes like the procedure of staining, scrutiny and interpretation[12].

According to Resolution -RDC number 302, October 13, 2005[13], programs that have as objective the internal and external quality control, must be implemented and executed in clinical laboratories to avoid errors of diagnosis and reductions of false-negatives[14]. The methods of evaluation recommended by Directive number 3.388, December 30, 2013, which redefine the national qualification in cytopathology for prevention of cervical cancer are called National Qualification in Cytopathology (QualiCito) for prevention of cervix cancer. QualiCito consists in establishing standards and evaluate the quality of the Papanicolaou test of the cervix, monitoring the performance of the healthcare providers in public and private laboratories of the National Health System (SUS). In this year, it was created the first edition of the Manual of Quality Management for Cytopathology Laboratory[14].

This Manual consists of the internal quality monitoring (IQM) and external quality monitoring (EQM) to allow the improvement of the analysts, unifying the cytomorphological criteria and improvement of the quality of the samples to be analyzed[14].

The objective of this study was to evaluate the quality indicators according to the Manual of Management of Quality for Cytopathology Laboratory[14].

METHOD

Analytic, descriptive, retrospective study where the results of the cytopathological tests shipped to the Cytopathology Sector of the Clinical Laboratory of the Catholic University of Goiás (LC-PUC-Goiás) from January 2013 to December 2017. The Institutional Review Board of PUC-Goiás approved the study, protocol number 235,376, titled "Investigation of communicable and non-communicable diseases in the clinical laboratory of the Catholic University of Goiás (PUC-Goiás), Laboratory of the "Santa Casa de Misericórdia" of Goiânia, Laboratory of the Hospital of Military Police of Goiás and Collection Unit of UABSF Vila Mutirão, Northwest Region of Goiânia-GO", that ensures the collection of sample data in the mentioned sites.

The result of the cytopathological test was categorized according to the Brazilian Nomenclature for Cervical Results and Recommended Conducts[15], based in cytopathological criteria defined in the System of Bethesda[6]. The cytologic results encountered were categorized according to the grade and nature in the following manner: atypical squamous cells of undetermined significance possibly non neoplastic (ASC-US); high-grade atypical squamous cells of undetermined significance not excluding intraepithelial lesion (ASC-H); low-grade squamous intraepithelial lesion (LSIL); HSIL;

atypical glandular cells (AGC); AIS; invasive carcinoma and adenocarcinoma.

The data was added to a databases in the program *Excel 2013.* Further, it were calculated the indicators of quality according to the Manual of Management of Quality for Cytopathological Laboratory according to Chart 1.

RESULTS

In this study, it were evaluated the cytologic tests of the clinical laboratory of PUC-Goiás, during the period from January 2013 to December 2017. Of the total of 6,809 cytopathological diagnosis, it was observed 99.4% (6,768/6,809) satisfactory diagnosis, being 91.3% (6.215/6,809) negative results, 8.1% (553/6,809) diagnosis with cytological abnormalities and 0.6% (41/6,809) of unsatisfactory exams (Table 1).

Table 2 shows total of 8.1% of cytological abnormalities (553/6,809). Among the abnormalities, it was encountered prevalence of 2.40% (162/6,809) of ASC-US*;* 2.80% (193/6,809) of ASC-H; 1.50% of LSIL (101/6,809); 0.90% of HSIL (64/6,809); 0.50% of AGC (31/6,809)*;* 0.015% of carcinoma (1/6,809); and 0.015% of adenocarcinoma (1/6,809).

The results of IQM are demonstrated in Table 3. The Positivity Index of the years 2013 to 2017 are within the expected values, 10.5%, 7.9%, 8.6%, 6.8% and 5.3%, respectively. In 2013 alone, it was observed a little above what is recommended for the laboratories that provide services for the National Health System (SUS). The percent of compatible with HSIL presented in 2013 as 1.3%, 2014, 1.0%, 2015, 0.5%, 2016, 0.6% and 2017, 0.7%. These values are within what is established by the rates of screening ≥ 0.4%. The relation of ASC/satisfactory

Chart 1. Formulas and descriptions for evaluation of the internal quality indicators of cytopathological exams

Indicators of Quality	Formula	Description
PI	Number of results altered in determinate place and period x 100 / Total satisfactory exams performed in the same place and period	Percent of exams classified as altered (ASC-US; ASC-H; LSIL; HSIL; HSIL not excluding (microinvasion); invasive epidermoid carcinoma; AGC; AIS, invasive adenocarcinoma, atypical cells of undefined origin and other neoplasms) among the satisfactory. PI expresses the prevalence of cellular alterations in the exams and the sensitiveness of the tracking process in detecting lesions in the population examined. Must be reviewed together with the indicators related to the atypia of undetermined significance. The results of PI are categorized in: very low (PI below 2%); low (PI between 2% and 2.9%); expected (PI between 3% and 10%); below expected (PI above 10% 10%, considering that these providers can attend secondary reference services in cervical pathology)
Percent of exams compatible with ASC among the satisfactory exams	Number of cases with ASC-US and ASC-H x 100 / Total of satisfactory exams	Cases of doubtful diagnosis where the cytological findings are insufficient for the diagnosis of intraepithelial lesion. Include the cases of ASC-US and ASC-H. It is expected that, at the most, 4% to 5% of all tests are classified as ASC
Percent of exams compatible with HSIL among the satisfactory exams	Number of exams HSIL x 100 / Total of satisfactory exams	This indicator measures the capacity of the laboratory to detect truly cervix cancer precursor lesions, that is, HSIL. Its result must be ≥0,4%
Ratio ASC/SIL	Number of exams compatible with ASC-US and ASC-H / Number of exams with LSIL and HSIL	The result must be <3

Captions: AGC: atypical glandular cells; AIS: adenocarcinoma *in situ*; ASC-H: atypical squamous cells of undetermined significance not excluding high-grade squamous intraepithelial lesion; ASC-US: atypical squamous cells of undetermined significance possibly non neoplastic; HSIL: high-grade squamous intraepithelial lesion; PI: positivity index; LSIL: low-grade squamous intraepithelial lesion.

Table 1. Prevalence of the results of negative, unsatisfactory cytopathological tests and abnormalities performed in the clinical laboratory of PUC-Goiás from 2013 to 2017

Year	Negatives		Unsatisfactory		Cytological abnormalities		Total	
	n	%	n	%	n	%	n	%
2013	1,622	89.2	5	0.3	191	10.5	1,818	100
2014	1,547	91.4	12	0.7	133	7.9	1,692	100
2015	1,035	90.2	15	1.3	98	8.5	1,148	100
2016	1,007	93.2	0	0	74	6.8	1,081	100
2017	1,004	94.0	9	0.8	57	5.2	1,070	100
Total	6,215	91.3	41	0.6	553	8.1	6,809	100

Table 2. Prevalence of the cytopathological tests performed in the clinical laboratory of PUC-Goiás from 2013 to 2017

Year	Negative		Unsatisfactory		ASC-US		ASC-H		LSIL		HSIL		AGC		Carcinoma		Adenocarcinoma		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
2013	1,622	89.20	5	0.30	49	2.60	76	4.20	38	2.10	25	1.40	3	0.20	0	0.00	0	0.00	1,818	100.00
2014	1,547	91.40	12	0.70	32	2.00	53	3.10	26	1.50	18	1.10	4	0.20	0	0.00	0	0.00	1,692	100.00
2015	1,035	90.20	15	1.30	39	3.40	31	2.70	17	1.50	6	0.50	4	0.30	1	0.10	0	0.00	1,148	100.00
2016	1,007	93.20	0	0.00	24	2.20	20	1.90	12	1.10	7	0.60	10	0.90	0	0.00	1	0.015	1,081	100.00
2017	1,004	94.00	9	0.80	18	1.70	13	1.20	8	0.70	8	0.70	10	0.90	0	0.00	0	0.00	1,070	100.00
Total	6,215	91.30	41	0.60	162	2.40	193	2.80	101	1.50	64	0.90	31	0.50	1	0.015	1	0.015	6,809	100.00

Captions: ASC-US: atypical squamous cells of undetermined significance possibly non-neoplastic; ASC-H: atypical squamous cells of undetermined significance not excluding high-grade intraepithelial; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; AGC: atypical glandular cells.

Table 3. Indicators of internal quality of cytopathological exams performed in the clinic laboratory of PUC-Goiás in relation to the index of positivity. percent of compatible exams with ASC among the satisfactory exams and ratio of ASC/SIL no period from 2013 to 2017

Year	Positivity Index	% Compatible withHSIL	% ASCsatisfactory	RatioASC/SIL
2013	10.5%	1.3%	6.8%	1.9
2014	7.9%	1.0%	5.0%	1.9
2015	8.6%	0.5%	6.1%	3.0
2016	6.8%	0.6%	4.0%	2.3
2017	5.3%	0.7%	2.9%	1.9

Captions: HSIL: high-grade squamous intraepithelial lesions; ASC: atypical squamous cells; SIL: low-grade squamous intraepithelial lesions.

demonstrated values above to the established in the years 2013 with 6.8% and 2015 with 6.1%. According to the Manual of Management for Quality Control[14], it is expected that, at the most, 4% to 5% of all the exams are classified as ASC, values that are above 5% need differentiated attention.

DISCUSSION

The evaluation of the quality of the exams analyzed in the clinical analysis laboratory of PUC-Goiás occurred with the analysis of four indicators, according to the Manual of Management of Quality for Laboratory of Cytopathology[14]. In relation to the PI, that determines the prevalence of cellular alterations and indicates the sensitiveness of the exam in the screening of the lesions in the period from 2013 to 2017, it was 7.8%. This result is within the expected values and recommended, which is from 3% to 10%, indicating good performance of the screening process for detection of precursor lesions of cervix cancer. In the study of Plewka et al.[16], it was observed a PI of 5.1% in a laboratory in the State of Maranhão in the period of January 2010 to December 2012.

In the study conducted by Paula et al.[17], in the laboratory of clinical analyzes of PUC-Goiás, it was encountered, during the period from 2009 to 2013, PI of 5%, 4%, 7%, 7% and 11%, respectively, with mean of 7% of the years evaluated. In the same study, it stands out the concurrence with the results of EQM, varying in 85.6%, 87.2%, 95.9%, 86.9% and 90.6%. Actually, EQM is essential to ensure the continuous improvement of the quality of cytologic exams.

The percent of HSIL evaluates the capacity of detecting precursor lesions of cervical cancer in the attempt to diminish its incidence and mortality[12]. In this study, in the period evaluated, HSIL obtained a percent of 0.9%, showing it is within the recommended value which is ≥ 04%. According to Bortolon et al.[18], the percent of HSIL for the great Regions and for Brazil, was below 0.5%, among the States, only Roraima and Federal District presented results above the established. Indeed, the correct identification of HSIL, in combination with diagnostic confirmation, proper treatment and follow up can prevent the evolution of the lesion to cervix cancer [19,20].

The mean of ASC/satisfactory during the period evaluated, was 5.0%. This value is compatible with the established, which is a percent of until 5%. This rate forms a condition of diagnosis suspicion, since the diagnosis of ASC is more variable than the diagnosis of SIL of high and low grades[14]. Bortolon et al.[18] observed a percent of ASC among the satisfactory exams of 1.1% in the laboratories of Paraná, 1.1% in Rio Grande do Sul and 1.3% in Santa Catarina, all below the mean.

The ratio ASC/SIL reveals that the percent of the years evaluated are within the recommended, < 3, and may suggest that, in this study, there was no unexpected event with the technical aspect of the cytological samples, however, continued education can't be waived since improvement ensures the quality of the cytopathological diagnosis[14].

The quality of the sample plays a key role in the diagnostic results of the precursor lesions of cervix cancer[21-24]. Many factors that can reduce the accuracy of the cytopathological test for the diagnostic of the precursor lesions and cervix cancer are the factors considered obscuring, harming partially and/or totally the smears such as blood, leukocyte infiltrate, thick areas, desiccating, stretching artifacts, lubricant and contamination, according to the indication of the System of Bethesda[6], in addition to the non-representativeness of the zone of transformation. These problems occur in the moment of collection, which result in false negatives results[14].

The total of cytopathological results, 99.4% was of satisfactory diagnosis; of these, 91.3% were diagnosed negatives and 8.1%, with cytological abnormalities. In relation to the prevalence of unsatisfactory, it was 0.6% with greatest percent in 2015, 1.5%. Among the abnormalities, it was encountered a prevalence of 2.4% of ASC-US, 2.80% of ASC-H, 1.50% of LSIL, 0.90% of HSIL, 0.50% of AGC, 0.015% of carcinoma (1/6,809) and 0.015% of adenocarcinoma (1/6.809). The fact of these results of carcinomas and adenocarcinomas are little expressive can be explained because of the period analyzed and because these are results of a population who realizes the cytopathological exam with the finality of tracking.

The MIQ in the cytopathological laboratories[14] is important, since errors can occur in the moment of scrutiny, some motives can lead to diagnostic sub-evaluation of the neoplasm cells that are present in the smear, but are not acknowledged by the reviewer[25,26]. The lack of attention and concentration, the reduced time to exam the blade, mental exhaustion, overload of working time and absence of professional experience contribute for this to happen[27], which reinforces the necessity of MIQ in the cytopathology laboratories[14,20].

CONCLUSION

Because the method of cytology of the cervix is subjective, the implementation of the internal quality control must be effective, utilizing the standardized methods and the quality indicators must be always evaluated and interpreted by the entire lab team. The quality indicators are a tool that indicates the necessity of improving the cytomorphological criteria among the reviewers.

However, it is very important the continuous education of the professionals who participate of all stages of the process, from pre-analytic to analytic for possible errors to be corrected and preventive measures to be taken for improved quality in the interpretation of cytopathological exams.

CONTRIBUTIONS

Mackson Jardel Silva Santos contributed for the planning of the study, gathering, analysis and interpretation of the data, wording and critical review of the text. Andrea Alves Ribeiro contributed for the planning of the study, orientation of the gathering, analysis and interpretation of the data, wording and critical review of the text. Both approved the final version to be published.

DECLARATION OF CONLICT OF INTERESTS

There is no conflict of interests to declare.

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