DOI: 10.7860/JCDR/2023/59811.17707

Original Article

Pathology Section

Internal Quality Control Indicators in Cervical Smear Screening- Report from a Tertiary Care Centre, India

POONGODI RAJAGOPAL[1], ARUNDHATHI SHANKARALINGAPPA[2], SHARMILA VIJAYAN[3]

ABSTRACT

Introduction: Quality indicators are one of the tools to monitor the Quality Control (QC) system and have revolutionised the field of laboratory medicine. Internal QC helps in identifying the non conformities in lab from the moment sample reaches the lab and till the report is being despatched. This study was performed to evaluate the internal QC indicators of cervical smears with an intent to know where we stand, identify the lacunae and to improve performance of lab services.

Aim: To evaluate the internal QC indicators of cervical smears in an effort to improve performance of lab services.

Materials and Methods: This was a retrospective cross-sectional study conducted in the year 2021. Archived reports of females >18 years of age who had undergone Papanicolaou (Pap) smears between August 2019 and August 2021 were collated from the Department of Pathology, AIIMS, Mangalagiri. Based on these reports, various internal quality indicators, including positivity rate, percentage of Atypical Squamous Cells (ASC) among satisfactory tests, percentage of ASC among abnormal tests {includes Atypical Squamous Cells of Undetermined Significance (ASCUS), ASC-H, Low-grade Squamous Intraepithelial Lesion (LSIL), High-grade Squamous Intraepithelial Lesion (HSIL), carcinoma} ASC/SIL ratio, ASCUS/SIL ratio, percentage of LSIL, percentage of HSIL, percentage of false negatives, percentage of unsatisfactory smears were calculated. Data was analysed by using the Statistical Package for the Social Sciences (SPSS, version 15.0; IBM, USA) and descriptive statistical analysis was calculated for the quality indicators.

Results: A total of 1227 Pap smear cases were analysed in two-year duration, out of which 41 cases were unsatisfactory (3.34%). The annual smear positivity rate ranged from 1.19-1.31%, ASC percentage among the abnormal tests- 40%, ASC percentage among the satisfactory tests- 0.50%, percentage of tests with LSIL- 0.08%, percentage of tests with HSIL- 0.25% and false negative rate- 0.16%. ASC/SIL ratio and ASCUS/SIL ratio were 1.50% and 1.25%, respectively.

Conclusion: The internal QC indicators obtained in the present study were lower than the recommended values by CAP/Bethesda. Thus, achieving benchmark in internal quality indicators is still far from reality as it depends on population, screened incidence of cervical lesions and expertise of sampling team and cytopathologists. Regular audit improves screening ability of the test. Thus, every lab should try to achieve the internal quality indicator goals, which will ultimately result in building a good cervical screening system.

Keywords: Cervical cytology, Intraepithelial lesion, Quality control, Screening

INTRODUCTION

Cervical cancer is the fourth most common cancer in women globally [1]. In India, cervical cancer remains the second most common cause of cancer related deaths among women [2]. Achieving high vaccination rates and implementation of proper cervical screening programs can minimise the incidence of cervical cancer in greater magnitudes. The slow progression of disease in most cases, starting from mild dysplasia to frank invasive carcinoma over a period of 10-20 years gives us the rationale behind screening and detection at preinvasive stage.

Cervical Pap smear remains one of the major screening tools in identifying preinvasive lesions of cancer cervix at the earliest. A standard and uniform system of reporting cervical cytology, officially known as The Bethesda System (TBS) was established for reporting cervical cytology. TBS has introduced a 2-tier system of reporting squamous lesions, namely SIL:LSIL and HSIL, along with other concepts like ASCUS, ASC cannot exclude HSIL (ASC-H) etc., which would convey the cytology findings to clinicians and guide them in patient management [3]. Inspite of being an easy and cost-effective test, the performance of Pap is debated due to high number of false negative results. Approximately, 20% of these errors are attributed to inter and intraoperator variabilities and microscopic errors [4].

Pathologists play a crucial role in providing good quality cervical cytology reports with good accuracy. QC is a set of operational procedures and events that verify the requirement of quality in an individual test/process. In cervical cytology, QC is the design which ensures accuracy of interpretation and reporting of Pap smears [5].

The QC forms a fundamental part of any laboratory system. QC is defined as a system for verifying and maintaining a desired level of quality in an individual test or process [6]. Quality indicators are one of the tools to monitor the QC system and has revolutionised the field of laboratory medicine. Internal QC helps in identifying the non conformities in lab from the moment sample reaches the lab and till the report is dispatched. The main internal QC indicators used in cervical cytology are positivity rate, percentage of tests compatible with ASC among satisfactory tests, percentage of tests compatible with ASC among abnormal tests, ASC/SIL ratio, ASCUS/SIL ratio, percentage of tests compatible with LSIL, percentage of tests compatible with HSIL, percentage of false negative tests and percentage of unsatisfactory smears [7-10].

All the above mentioned quality indicators are of much importance in improving reporting quality of cervical cytology by means of encouraging pathologists to update the cytomorphology, improving accuracy in detection of early preinvasive lesions and reducing the percentage of false negative results and unsatisfactory smear rates. Good quality labs should strive to attain the benchmarks of these quality indicators for providing best services. However, studies concerned with quality of cytopathology reporting are only scarce [8,11,12].

In this study, various internal QC indicators were evaluated. The objectives were to calculate positivity rate, percentage of tests compatible with ASC among satisfactory tests, percentage of tests compatible with ASC among abnormal tests, ASC/SIL ratio, ASCUS/SIL, percentage of tests compatible with LSIL, percentage of tests compatible with HSIL, percentage of false negative tests and percentage of unsatisfactory smears.

MATERIALS AND METHODS

This was a retrospective cross-sectional study conducted in September 2021 at the Department of Pathology, AIIMS, Mangalagiri, where Pap smears reported from August 2019 to 2021 were retrieved from the archives. Since this a retrospective study with an audit of quality of cytopathology reports, IEC review was exempted by competent authority (Approval letter no:F/AIIMS/MG/DIRECTOR/PATHO/2021-22/129).

Study Procedure

The cytology findings and relevant clinical findings were documented in detail and the following internal quality indicators [7-10] were calculated as mentioned below:

Positivity rate

$$\frac{\text{Number of abnormal tests in a particular location and year} \times 100}{\text{Total number of satisfactory tests}}$$

Percentage of tests compatible with ASC among satisfactory tests

$$\frac{\text{Number of tests with ASC-US and ASC-H} \times 100}{\text{Total number of satisfactory tests}}$$

Percentage of tests compatible with ASC among abnormal tests

$$\frac{\text{Number of tests with ASC-US and ASC-H} \times 100}{\text{Total number of abnormal tests*}}$$

*Abnormal tests include ASC-US, ASC-H, LSIL, HSIL, carcinoma

ASC/SIL ratio

$$\frac{\text{Number of tests compatible with ASC-US \& ASC-H}}{\text{No number of tests with LSIL and HSIL}}$$

ASCUS/SIL ratio

$$\frac{\text{Number of tests compatible with ASCUS}}{\text{No number of tests with LSIL and HSIL}}$$

Percentage of tests compatible with LSIL

$$\frac{\text{Number of tests with LSIL} \times 100}{\text{Total number of satisfactory tests}}$$

Percentage of tests compatible with HSIL

$$\frac{\text{Number of tests with HSIL} \times 100}{\text{Total number of satisfactory tests}}$$

Percentage of false negative tests

False negative are the smears that were classified as negative by the routine screening, but which were considered abnormal by the cytopathology quality team in random review of atleast 10% of cases. All positive cases were informed to concerned cytopathologists for further action.

Percentage of unsatisfactory smears

$$\frac{\text{Number of unsatisfactory smears} \times 100}{\text{Total number of Pap tests}}$$

STATISTICAL ANALYSIS

Data was analysed by using the Statistical Package for the Social Sciences (SPSS, version 15.0; IBM, USA) and descriptive statistical analysis was calculated for the quality indicators.

RESULTS

We have analysed a total of 1227 Pap smear cases received over a period of two years comprising of patients ranging in age from 19-87 years. About 18.01% (n=221) of our study population had come for routine cervical screening. Rest of the patients {92% (n=1006)} had varied complaints. Majority of the patients presented with worrisome vaginal discharge {22.70% (n= 279)}. The various reasons for visit to hospital are tabulated in [Table/Fig-1].

S. No.	Reason for hospital visit	Total number of cases (N=1227)	Percentage of cases
1	Routine screening	221	18.01%
2	Vaginal discharge	279	22.74%
3	Itching in private part	31	2.53%
4	Infertility	27	2.20%
5	Irregular periods	256	20.86%
6	Menorrhagia	113	9.21%
7	Postmenopausal bleeding	56	4.56%
8	Delayed periods	19	1.55%
9	Amenorrhoea	5	0.41%
10	Dysmenorrhoea	30	2.44%
11	Other non gynaecological complaints	12	0.98%
12	Frequent and burning micturition	35	2.85%
13	Prolapse and stress urinary incontinence	13	1.06%
14	Lower abdominal pain	130	10.59%

[Table/Fig-1]: Various reasons for hospital visit in cases of Pap smears received in this study.

Out of the total 1227 Pap smear cases that were evaluated, 41 cases were found to be unsatisfactory with an unsatisfactory smear rate of 3.34%. The data collected during this study has been tabulated in [Table/Fig-2].

S. No.	Number of cases	For 2 years together	2019-2020	2020-2021
1	Total number of cases	1227	510	717
2	Total number of satisfactory cases	1186	501	685
3	Total number of unsatisfactory cases	41	9	32
4	Total number of abnormal tests	15	6	9
5	Total number of ASCUS cases	5	3	2
6	Total number of ASC-H cases	1	-	1
7	Total number of ASC cases	6	3	3
8	Total number of SIL cases	4	2	2
9	Total number of LSIL cases	1	-	1
10	Total number of HSIL cases	3	2	1
11	Positivity rate	1.26%	1.19%	1.39%
12	ASC percentage among the satisfactory tests	0.51%	0.59%	0.43%
13	Percentage of tests compatible with LSIL	0.08%	-	0.15%
14	Percentage of tests compatible with HSIL	0.25%	0.40%	0.15%
15	ASC/SIL	1.50	1.50	1.50
16	ASCUS/SIL	1.25	1.50	1.00
17	Percentage of false negatives	0.16%	0.20%	0.15%

[Table/Fig-2]: Various data collected during the study.

The total number of abnormal tests were 15, out of which 6 were ASC cases. Thus, the percentage of ASC among the abnormal tests remained as 40.00%.

Similarly, the authors calculated the various percentages using the formulas and the results and were as follows: ASC percentage among the satisfactory tests-0.51%, percentage of tests compatible with LSIL-0.08%, percentage of tests compatible with HSIL-0.25%. The ASC/SIL ratio and ASCUS/SIL were found to be 1.50 and 1.25, respectively. The annual smear positivity rate ranged from 1.19-1.31% (average 1.26%).

Random slide review of previously negative cases revealed two abnormal cases which were missed during initial reporting. Hence, the false negative rate in this study was 0.16% and the cases were informed to concerned cytopathologist for further action.

DISCUSSION

The Pap smear screening is done extensively nowadays as many females are subjecting themselves to cervical cancer screening due to increased awareness. Maintaining the quality of reporting cervical cytopathology is crucial in providing cytology reports with good accuracy. The quality of cytopathology is maintained by striving to attain proposed bechmarks. However, most of the laboratories are not able to achieve this benchmark due to various reasons like varying incidence of cervical lesions, screening potential of cytotechnologists and sampling errors.

The internal QC indicators were compared with the standard benchmark values provided by CAP/Bethesda and other studies to know where we stand [9,10]. The comparison is shown in [Table/Fig-3] below [9-13]. Comparison between the percentage of false negatives in various studies is shown in [Table/Fig-4] [9,14,15].

S. No.	Parameters	Present study	Davey DD et al., [9]	Bethesda [10]	Crasta JA et al., [11]	Tan KB et al., [12]	Sankaranarayanan R et al., [13]
1	Year of study	2021	1996	1994	2009	2004	2004
2	Place of study	India	America	India	India	Singapore	India
1	Unsatisfactory rate	3.34%	0.5%	-	1.36%	1.3%	4.1%
2	Positivity rate	1.26%	-	3-10%	--	-	-
3	ASCUS	0.42%	4%	-	0.37%	0.9%	8.8%
4	LSIL	0.08%	2.5%	-	0.19%	0.8%	6.2%
5	HSIL%	0.25%	0.6%	>=0.4%	0.61%	0.4%	1.6%
6	ASC/Satisfactory %	0.51%	-	5%	-	-	-
7	ASC/Abnormal %	40%	--	Below 60% (Qualicito)	-	-	-
8	ASC/SIL	1.50	0.4-5.1	2 or 3	-	-	-
9	ASCUS/SIL	1.25	1.8	-	0.5	0.4	0.9

[Table/Fig-3]: Comparison of internal quality control indicators of our study with standard benchmarks and with other studies [9-13].

Studies	Place/Year of study	Percentage of false negatives
Present study	India, 2023	0.16%
Davey DD et al., [9]	Brazil,2015	2.10%
Bonilha JL et al., [14]	Brazil, 2006	2.80%
Currens HS et al., [15]	America, 2012	0.18%

[Table/Fig-4]: Comparison between the percentage of false negatives in various studies [9,14,15].

In the present study, positivity rate, ASCUS, LSIL, HSIL, ASC among satisfactory cases were much below the limits recommended by CAP, Bethesda and other studies [7,10-15]. On analysing the reasons for this marked difference, it was found that 18% of the patients had come for routine medical check-up without any complaints and 55% of the patients had normal cervix appearance on per speculum examination. Supporting this notion, none of the patients with an abnormal smear were asymptomatic in the present study. The complaints were either bleeding, discharge and the per speculum findings were cervical erosion, discharge, bleeding on touch and growth.

Lesser LSIL rates in the present study were comparable with that of study done by Crasta JA et al., in which they attributed lower detection rates to the low-risk urban population and many routine health check-up cases, similar to the present study. This further reinforces the point that cervical lesions are mainly the disease of lower socio-economic status [11].

From previous studies it was known that ASC/SIL ratio is a better-quality indicator than calculating the percentage of ASC alone because the former can act as a surrogate marker by itself to estimate the level of certainty. Ideally, ASC/SIL ratio of less than 2:1 or 3:1 has to be maintained. Kurman RJ and Solomon D [10] proposed that the ASC/SIL ratio must be 2 or 3 and CAP lab accreditation program has recommended between 0.4-5.1 as the acceptable ratio using 5th and 95th percentile limits [9].

The ASC/SIL rates in the present study was almost nearing the benchmark proposed by Bethesda. A study done by Renshaw AA et al., has demonstrated an ASC/SIL ratio of less than 1.5 as a stand-in marker for inadequate screening. This is because a lesser ASC/SIL ratio means a more specific diagnosis was rendered when compared to higher ASC/SIL ratios but this would happen only at the cost of decreased sensitivity. For a screening programme, sensitivity is more important when compared to specificity. Correspondingly, in their study it was suggested that maintaining an ASC/SIL ratio of more than 1.5 would be the best way to ensure acceptable sensitivity and achieving ratios more than 3 would further improve the sensitivity without much compromise on specificity [16].

The percentage of ASC among abnormal tests was well within the limits determined by QualiCito [7]. This parameter has to be assessed in the light of positivity rate. A satisfactory positivity rate with increase in number of ASC cases indirectly points towards the increased number of ambiguous cases. Even though the positivity rate in this study was less, the number of ASC cases was kept within the recommended limits, meaning that the number of cases with uncertainty was less in this study.

In one of the larger studies conducted in Brazil by Tobias AH et al., an attempt was made to evaluate the performance of multiple cytopathology laboratories. The study results demonstrated that 80% of laboratories have an HSIL/satisfactory tests indicator value well below the recommended level, indicating that precancerous cervical lesions were not being detected efficiently. Thereby, Tobias AH et al. highlighted the importance of determining internal quality indicators including rescreening of slides to detect false negatives [17].

Rescreening of slides are done by several methods which includes random rescreening of 10% negative cases, rapid rescreening of 100% of negative cases, and rapid rescreening of all smears [15]. The selection method varies depending upon the sample load and the number of cytopathologists. In high volume labs, it is practically impossible to rescreen all negative cases. In this study, a random rescreening of 10% of the total case numbers was performed, which revealed a false negative rate of only 0.16%. Comparison between the percentage of false negatives in various studies has been tabulated in [Table/Fig-4]. Hence, the possibility of screening/interpretative errors could be eliminated to some extent. Therefore, it is assumed that the lower detection rates of precancerous lesions in this study may be due to the predominance of healthy people in screening.

Unsatisfactory smear reporting rate is a key quality indicator which identifies women who are inadequately screened, the main cause being sampling errors. The unsatisfactory smear rate in this study is much higher when compared to the recommended CAP median of 0.5% and it firmly points out the lack of proper pathologist- clinician feedback system which has to be strongly enforced into action. When compared to the internal quality indicators like positivity rate and percentage of various lesions, which mainly depends on type of population screened, incidence of cervical lesions, and awareness about screening in the population, unsatisfactory smear rate is the one which is independent of all those and it is the relatively easiest parameter to attain benchmark if a proper feedback and periodical training to sampling team is implemented in the system.

In order to maintain accepted figures in internal quality indicators not only in our hospital but also in other hospitals/labs which are striving at it, the following few key areas are to be focused: 1) To ensure proper feedback given to clinicians with respect to unsatisfactory cases and confirm resampling of the same; 2) Scheduling of periodical training for sampling team and cytopathologists; 3) Rescreening of all the doubtful cases by senior most cytopathologist before report release; 4) Periodical review of cytology-histopathology correlation register and discussion with clinicians for discrepancies and further action.

Limitation(s)

The limitations of this study are: 1) No cytology-histopathology correlation was done for the positive cases on cytology, hence we lack the information of number of false positives (though it is known that a good screening method can have some false positives rather than false negatives); 2) Since the positivity rate is low, rescreening of a greater number of cases could have further eliminated the chance of interpretative errors if any to much greater extent; 3) We were unable to track the status of unsatisfactory cases.

CONCLUSION(S)

The figures of many of the internal QC indicators attained in this study are considerably lower compared to the standard values recommended by CAP/Bethesda. So, we assume that achieving benchmarks in internal quality indicators is still a dream come true situation and depends mainly on the type of population screened, incidence of cervical lesions and the expertise of cytopathologists and sampling teams. The evaluation of internal quality indicators plays a major role in identifying the lacunae in cervical smear screening, helps pathologist and sampling teams' self-assessment/ improvement. It is a double-edged sword because in one way, by assessing the past performances it improves the screening ability, but in other way, a greater number of false positives can be obtained in the urge of attaining the benchmark values. For a screening programme to be successful, sensitivity is more important when compared to specificity. Hence, every lab should try hard to achieve the benchmarks, keeping in mind the ground reality. Eventually, in the hands of proper sampling team, good cytotechnologists and a sound quality check system, cervical screening would benefit more people.

REFERENCES

[1] Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86.
[2] Kadam Y, Dhobale R, Gore A, Tripathi N. Barriers for early detection of cancer amongst Indian rural women. South Asian J Cancer. 2014;3(2):122.
[3] Nayar R, Wilbur DC. The Bethesda system for reporting cervical cytology: A historical perspective. Acta Cytologica. 2017;61:359-72.
[4] Gullo CE, Dami AL, Barbosa AP, Marques AM, Palmejani MA, de Lima LG, et al. Results of a control quality strategy in cervical cytology. Einstein (Sao Paulo). 2012;10(1):86-91.
[5] Branca M, Longatto-Filho A. Recommendations on quality control and quality assurance in cervical cytology. Acta Cytologica. 2015;59:361-69.
[6] Krieger PA, McGoogan E, Vooijs GP, Amma NS, Cochand-Priollet B, Colgan TJ, et al. Quality Assurance/Control issues. International Academy of Cytology Task Force summary. Diagnostic Cytology Towards the 21st century: An International Expert Conference and Tutorial. Acta Cytol. 1998;42(1):133-40.
[7] Brazil. Ministry of Health. Jose Alencar Gomes da Silva National Cancer Institute. Quality management manual for cytopathology laboratory. Rio de Janerio: INCA 2012.
[8] Araujo MLC, Santana DA, Almeida LB. Quality in cytopathology: An analysis of the internal quality monitoring indicators of the Instituto Nacional de Cancer. J Bras Patol Med Lab. 2015;51(2):102-07.
[9] Davey DD, Nielsen ML, Naryshkin S, Robb JA, Cohen T, Kline TS. Atypical squamous cells of undetermined significance. Current laboratory practices of participants in the College of American Pathologists Interlaboratory. Comparison Program in Cervicovaginal Cytology. Arch Pathol Lab Med. 1996;120(5):440-44.
[10] Kurman RJ, Solomon D. The Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses. New York, NY: Springer Verlag; 1994:34.
[11] Crasta JA, Chaitra V, Simi C, Correa M. An audit of cervicovaginal cytology in a teaching hospital: Are atypical glandular cells under-recognised on cytological screening? J Cytol. 2009;26(2):69-73.
[12] Tan KB, Chang SA, Soh VC, Thamboo TP, Nilsson B, Chan NH. Quality indices in a cervicovaginal cytology service: Before and after laboratory accreditation. Arch Pathol Lab Med. 2004;128(3):303-07.
[13] Sankaranarayanan R, Thara S, Sharma A, Roy C, Shastri S, Mahé C, et al; Multicentre Study Group on Cervical Cancer Early Detection in India. Accuracy of conventional cytology: Results from a multicentre screening study in India. J Med Screen. 2004;11(2):77-84.
[14] Bonilha JL, Valenca CFM, Micelli JP, Zanovelo EM, Silva J, Cury PM. Quality controlincolpocytology: Visaorapida with marked field. J Bras Patol Med Lab. 2006;42(6):441-48.
[15] Currens HS, Nejkauf K, Wagner L, Raab SS. Effectiveness of rapid prescreening and 10% rescreening in liquid-based Papanicolaou testing. Am J Pathol. 2012;137(1):150-55.
[16] Renshaw AA, Deschênes M, Auger M. ASC/SIL ratio for cytotechnologists: A surrogate marker of screening sensitivity. Am J Clin Pathol. 2009;131(6):776-81.
[17] Tobias AH, Amaral RG, Diniz EM, Carneiro CM. Quality indicators of cervical cytopathology tests in the public service in minas gerais, Brazil. Brazilian Journal of Gynecology and Obstetrics. 2016;38(2):65-70.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, All India Institute of Medical Sciences, Mangalagiri, Vijayawada, Andhra Pradesh, India.
2. Associate Professor, Department of Pathology, All India Institute of Medical Sciences, Mangalagiri, Vijayawada, Andhra Pradesh, India.
3. Additional Professor, Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, Mangalagiri, Vijayawada, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Arundhathi Shankaralingappa,
Department of Pathology, Medical College Building, 2nd Floor, Old TB Sanatorium Road, Mangalagiri-522502, Andhra Pradesh, India.
E-mail: arundhathi19@yahoo.co.in

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 03, 2022
- Manual Googling: Jan 03, 2023
- iThenticate Software: Feb 02, 2023 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Aug 23, 2022**
Date of Peer Review: **Sep 14, 2022**
Date of Acceptance: **Feb 13, 2023**
Date of Publishing: **Apr 01, 2023**