Original Article

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Pathology Section

Inter-Observer Variation in Reporting of Pap Smears

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ABSTRACT

Introduction: The Papanicolaou smear is one of the most important tests in preventive health care which helps to identify women at risk of developing cervical cancer. The use of the test is increasing because of more awareness. But the validity of the test has always been questioned because reporting of Pap smears is known to have inter-observer and intra-observer variation, which can affect the prognosis of the patients or sometimes create legal issues too.

Aim: To assess the frequency of discordant diagnosis between the pathologists in reporting of conventional Pap smears using the Bethesda System of reporting.

Materials and Methods: A total of 200 cases of Pap smears with each case having 2 slides (ectocervix and endocervix) which were received, are labelled and stained using Papanicolaou stain. The slides are reported by a pathologist using the Bethesda System of reporting Pap smears. The reported slides are then reviewed by the second pathologist with the same level of experience and again reported following the same protocols. For those cases which had disagreement, the reports were confirmed by biopsy. If the biopsy could not be obtained, opinion was taken from the senior pathologist whose report was considered as a tie breaker.

Statistical Analysis: Statistical analysis was done using Kappa statistics for all cases which had epithelial cell abnormality.

Results: Among 200 cases, 22 cases had epithelial cell abnormality. The degree of agreement between the results obtained in the first and second assessment between the observers was analysed, with the overall Kappa of 0.61, indicating a moderate agreement.

Conclusion: Inter-observer variation is a common screening error in reporting of Pap smears. It is necessary to implicate corrective actions to reduce such error which ultimately helps in detecting the cervical lesions in its earliest, which in turn affects the prognosis of the patients.

Keywords: Cervical cancer, Cytology, Disagreement

INTRODUCTION

Carcinoma of cervix is the second most common cause of death in women worldwide and the most common cause in developing countries [1]. Papanicolaou smear is one of the established components in preventive health protocols for women [2]. None of the other tests have been as successful as Papanicolaou smear in preventing cancer [3]. Cervical intraepithelial lesions is a morphologic continuum that is divided into number of categories. Whenever we assess the severity of a morphological abnormality, whether in a biopsy sample or in cytology smears, there can be significant inter-observer variation [4]. To improve the communication between the pathologists and clinicians, Bethesda System of cytopathologic reporting was designed. When compared with other taxonomies, the Bethesda System helps in distinction between changes associated with inflammation, infection and those reflecting squamous cell atypia and dysplasia [2].

Due to high degree of accuracy, Pap smear is considered one of the best screening tools for women in health care system, but problems such as false positive and false negative interpretations, as well as inter-observer have questioned its validity [1]. Inter observer variability means the disagreement among the different medical observers who consistently may score patients at various risk levels. Despite differences in cytological interpretation, which may lead to false negative results, the inter-observer variability and its implication in patient's care justify the need for planning a routine laboratory system for quality assurance [5].

The quality of a cervical cytology report depends on pool of factors like adequate handling and staining of the samples, screening and interpretation of the slides and reporting of the results [6].

Inspite of critical presumption of reliability, standards of inter pathologist agreement have not been well defined for interpretation of cervical pathology specimens [7].

It is important to educate the public about the importance and limitations of cervical cancer screening by Pap smears and to develop reasonable practitioner standards for the performance of the test. The present scenario of increasing litigation over alleged false-negative Pap smears has the potential to reduce the use of this test which is still considered the most effective screening test devised [8].

Though the Pap smears lack the sensitivity, it must be always remembered that it still has significant utility worldwide. The Pap test will have importance as a diagnostic triage tool because of its greater specificity compared with HPV testing [9].

This study was conducted to assess the degree of inter-observer variation between two pathologists in reporting of pap smears.

MATERIALS AND METHODS

A prospective study was conducted at the Department of Pathology, Bangalore Medical College & Research Institute, Bangalore between December 2015 and February 2016 after the ethical committee clearance from the institute. Based on the inclusion and exclusion criteria, 200 consecutive Pap smear cases, received from the Gynaecology Department were studied.

Inclusion criteria

All Pap smears received at Department of Pathology, Banglore Medical College and Research Institute, Bangalore were studied.

Exclusion criteria

1. Cases without a request form
2. Cases with unlabelled slides
3. Broken slides.

A total of 200 consecutive cases of Pap smears with each case having 2 slides (ectocervix and endocervix) were received. The slides are first labelled, then fixed in 100% methanol for 15 minutes and stained using Rapid Papanicolaou staining. The slides are first placed in Nuclear stain for 60 seconds, then in Scott's tap water for 10 seconds, followed by dehydrant for 30 seconds, then again in Scott's tap water for 10 seconds, followed by cytoplasmic stain for 60 seconds, finally in dehydrant for 30 seconds. Slides are then air dried, dipped in xylene, which are then mounted.

The slides were first reported by a pathologist using The Bethesda System of reporting Pap smears. The reported slides were then reviewed by second pathologist with the same level of experience who was blinded to the first pathologist's report and again reported following the same protocols. The cases which had discordance between the two reports, diagnosis were confirmed with cervical biopsy or third opinion was taken from the senior pathologist when the biopsy was not available. The reports were then compared and analysed using Kappa statistical method.

RESULTS

A total of 200 cases were analysed to check for the degree of agreement between the first and second pathologists reports [Table/Fig-1]. The mean age of the 200 patients was 33.2 years (19-71 years). Among 200 cases, 22 cases had epithelial cell abnormalities which included Atypical squamous cells of undetermined significance (ASCUS), Low-grade squamous intraepithelial lesion (LSIL), High grade squamous intraepithelial lesion (HSIL), Squamous cell carcinoma(SCC) and Atypical glandular cells (AGS) as illustrated in [Table/Fig-2]. The mean age of these 22 cases was 45.1 years (28-70 years). Though there was disagreement in reporting of cases regarding the adequacy of the smears, inflammatory smears, specific infections or atrophic smears, importance was given for those cases which had epithelial cell abnormality as it needs careful patient follow-up.

Among these 22 cases, 9 cases had disagreement between the two reports [Table/Fig-2]. Biopsy was obtained in four cases which had disagreement. Discordant cases in which biopsy could not be obtained, opinion was taken from the senior pathologist whose report was considered as a tie breaker.

One case which had epithelial cell abnormality was missed by the first pathologist, while both the pathologist had one each case of over diagnosis for ASCUS and AGS respectively.

Kappa statistical analysis was done only on the cases which had epithelial cell abnormality (22 cases). The degree of agreement between the results obtained in the first and second assessment between the observers was analysed, with the overall Kappa of 0.61 indicating a moderate agreement.

	1st Pathologist	2nd Pathologist
Inadequate	25	25
Inflammatory smear	110	122
Candida	02	02
Trichomonas vaginalis	02	01
Bacterial vaginosis	07	03
Atrophic smear	09	09
ASCUS	08	11
LSIL	04	03
HSIL	05	03
SCC	01	01
AGS	02	02
Normal smear	25	18
Total	200	200

[Table/Fig-1]: Summary of data given by two pathologists.

S. No.	1st Pathologist	2nd Pathologist
1	HSIL	HSIL
2	Inflammatory smear	ASCUS
3	LSIL	HSIL
4	HSIL	HSIL
5	ASCUS	ASCUS
6	ASCUS	ASCUS
7	ASCUS	ASCUS
8	ASCUS	ASCUS
9	SCC	SCC
10	ASCUS	ASCUS
11	ASCUS	ASCUS
12	ASCUS	ASCUS
13	LSIL	ASCUS
14	AGS	AGS
15	HSIL	LSIL
16	ASCUS	Inflammatory smear
17	HSIL	LSIL
18	LSIL	LSIL
19	AGS	ASCUS
20	HSIL	ASCUS
21	LSIL	LSIL
22	Inflammatory smear	AGS

[Table/Fig-2]: Summary of cases with epithelial cell abnormality given by two pathologists.
*ASCUS-Atypical squamous cells of undetermined significance, LSIL-Low-grade squamous intraepithelial lesion, HSIL-High grade squamous intraepithelial lesion, SCC-Squamous cell carcinoma AGS-Atypical glandular cells.

DISCUSSION

In a study done by Izadi-Mood N et al., 162 cervical smears were retrieved that had been originally interpreted as ASC-US, ASC-H, LSIL, HSIL, SCC, AGC and adenocarcinoma which were rescreened by an experienced pathologist and reclassified. All the 162 slides were reviewed by three more pathologists to evaluate inter-observer reproducibility and obtained slight inter-observer agreement (k=0.26). The greatest agreement was seen among the invasive category (SCC in addition to adenocarcinoma) and the least agreement was seen for HSIL (k=0.19) [1].

Gatscha RM et al., solely studied on ASCUS who rescreened 632 cases previously diagnosed as ASCUS, to compare initial and rescreen diagnosis, and to analyse agreement with follow-up.Complete agreement was found in 200 cases constituting 32% cases with 31 (15%) cases being WNL; 91 (45%) cases of ASCUS; 77 (38.5%) cases SIL; and one (0.50%) case of carcinoma. Follow-up showed no abnormality among 67% of the cases reclassified as WNL, 49% of the cases which were reclassified as ASCUS, and 48% of the cases reclassified as squamous intraepithelial lesions (SIL). SIL was found among 29% of cases reclassified as WNL, 29% of specimens re-diagnosed as ASCUS, and 34% of cases reclassified as SIL. Partial agreement was found in about 391 specimens (62%) [10].

Simsir A et al., studied exclusively on inter-observer variation of 23 cases of glandular lesions which was reviewed by 6 observers with the lesions ranging from benign to malignant and found that inter-observer agreement for site was poor (kappa < 0.4) especially in the AGC category. Definite prediction of the final histologic diagnosis by observers varied from 30% to 87% and did not actually correlate with the experience [11].

In a study done by Young NA et al., 20 slides were distributed among 5 panellists who were considered experts in the field of cytopathology. Only 7/20 (35%) cases showed unanimous agreement. Participants disagreed within one category of magnitude for 7 (35%) cases. In 6 (30%) cases there was a range of more than one category disagreement. A greater degree of subjectivity exits in classifying squamous abnormalities without classic morphology despite standardization of Pap smears reports by the Bethesda System. The lack of reproducibility should always be considered in cytology proficiency testing [12]. Even the experienced cytopathologists can show poor Inter-observer agreement in classifying squamous metaplastic lesion [13].

Hatem F et al., conducted a review Pap smear study on 17 cases of cytology negative smears and histopathology proved HSIL. Upon review, 16 of 17 “negative” smears contained a cytological abnormality [14].

Sherman ME et al., conducted a study using web-based format to compare assessments of 77 images demonstrating a range of classical and borderline cytological changes by cytotechnologists and pathologists and found that a higher sensitivity is obtained for identifying high-grade squamous lesions than they did for high-grade glandular lesions [15].

Performance of external quality control becomes necessary for the standardisation of diagnostic criteria, accuracy of screening and to improve the quality of cytopathology test results [16].

It is impossible and unreasonable to have zero error screening in standard practice. But unfortunately the practise standards have not been well defined in cytology. Errors of 5% to 10% may be an excellent target and below 15% to 20% a possible standard for Pap smear accuracy [17]. Inter-observer variability significantly plays a role for patient care, diagnostic error and medical litigation. Biologic role as well as diagnostic accuracy becomes important in the management of cervical epithelial abnormality [13].

Inter-observer variation is inevitable in reporting of Pap smears. Similar findings are observed in several studies conducted all over the world [Table/Fig-3].

S. No.	Study	Number of Cases	Results
1.	Izadi –Mood N et al., [1]	162 cases	0.26 (kappa value)
2.	Simsir A et al., [11]	23 cases	<0.4(kappa value)
3.	Young NA et al., [12]	20 cases	7/20 cases (unanimous agreement)
4.	Hatem F et al., [14]	17 cases	1/17 (unanimous agreement)
5.	Gatscha et al., [10]	632 cases	200/632 (unanimous agreement)
6.	Ázara CZS et al., [16]	10,053 cases	0.81 (kappa value)
7.	Present study	200 cases (22 cases of epithelial abnormality)	0.61 (kappa value)

[Table/Fig-3]: Comparision of findings with similar studies.

LIMITATIONS

It was a small study group without randomisation. Hence further randomized studies with a larger group would be taken up for more reliable results.

CONCLUSION

Inter-observer variation is a common screening error in reporting of Pap smears. Many studies have been published regarding the same, but very few laboratories have taken steps to correct them. Hence, it is necessary to study and document these inter-observer variations to implicate corrective actions like routine screening of all cases by more than one person or to implement external quality control, so that errors can be reduced which finally helps in detecting the cervical lesions in its earliest, ultimately affecting the prognosis of the patients.

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