DOI: 10.47799/pimr.1003.05

Assessment and Applicability of Various Elements of Quality Assurance in Histopathology Laboratory: A Study from A Tertiary Care Hospital in Eastern Region of India

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Date of Submission: 16/11/2020 Date of Review: 26/03/2022 Date of Acceptance: 17/07/2022

ABSTRACT

Background Quality control in histopathology is relatively newer concept and less understood because of its subjectivity.

Aim: The present study was conducted to assess and determine applicability of the different elements of quality assurance in the histopathology laboratory of a tertiary care hospital in eastern region of India.

Material and methods: An observational, retrospective and analytic study for one year and three months was conducted. 2000 samples were selected by simple random sampling including the biopsy specimens and cell blocks received in the histopathology laboratory.

Results: Of the 2000 samples, 1880 (94%) were accepted and 120 rejected (6%) due to mainly pre analytical factors. Of the rejected samples, 35 samples (29.2%) were without proper fixative, 48 samples (40%) had incomplete requisition forms, 37 samples (30.8%) had incomplete/ absent clinical history. Lack of adherence to standard tissue fixation protocols were observed in 55 cases (2.75%). Inadequate preventive maintenance and delay in renewal of maintenance contracts were the most common cause of failure of maintenance of equipment. Improper staining was found in 35 cases (1.75%). Grossing of specimens were inadequate in 104 cases (5.2%). Concurrence in diagnosis was found in majority cases (1892 cases, 94.6%). Random case review was done with adequate precision (97.5%) and accuracy (96.6 %). Maintenance of turnaround time was found in most cases (1800 cases, 90%).

Conclusion: Standard operating procedures, training of staffs, equipment maintenance, alertness to maintain turnaround time and awareness, proper report documentation and storage are the key factors to successfully uphold quality assurance.

KEYWORDS: Histopathology, Laboratory, Quality assurance, Quality control

INTRODUCTION

Histopathology techniques in clinical laboratories involve the processing of different tissues (obtained by biopsy or autopsy etc) for analysis of morphology. These techniques immensely contribute to the patient care and management especially in a tertiary care hospital. Quality may be defined as measurement of efficiency of the entire laboratory test cycle including pre analytical, analytical and post analytical phases. [1]While Quality Assurance encompasses the procedures from specimen collection to report transmission to the clinician, Quality control includes the operational techniques in day to day workflow meeting the quality standards. To ensure quality assurance standards, all the pre analytical, analytical, and post-analytical parameters have to be maintained. [2]Quality control in histopathology is relatively newer concept and less understood because of the subjectivity of the reports and non-existence of known controls. Similar to other divisions of laboratory technologies, quality assurance is applicable to pre analytical, analytical and post analytical processes in histopathology laboratory also. [3]

The aim of the present study was to assess and determine applicability of the different elements quality assurance in the histopathology laboratory of a tertiary care hospital in eastern region of India. The objective of the study was to identify the errors in the pre analytical, analytical and post analytical processes and suggest recommendations to overcome the same to uphold the quality standards The uniqueness of this study is that it includes assessment of all the important and practically applicable pre analytical, analytical and post analytical factors affecting quality assurance in the histopathology laboratory.

METHODS

A tertiary hospital based retrospective, observational and analytical study was undertaken to study the quality

assurance in the histopathology laboratory in Eastern Region of India. The study was conducted over a period of one year and three months. The Inclusion criteria was all the biopsy specimens and cell blocks (small biopsies, excision biopsies and radical biopsy) from major and minor operation theaters and wards received in the histopathology laboratory. Samples were selected by simple random sampling from the biopsy samples sent to the histopathology laboratory. Exclusion criteria were any sample without any requisition, samples with labeling errors, samples without proper fixative, and samples with transportation errors like spillage signs or mishandling during transport or improperly capped. Study variables are included in Table 1.

Only proper requisition forms duly filled with patient identification details and relevant clinical history were accepted. Accession number was given to each sample which was documented that could be easily traced. The fulfillment of this procedure was noted and number of samples rejected were documented.

Details of type and quantity of fixatives for different specimens in the laboratory as well as their availability in the operation theaters at the site of generation of biopsies were inquired and noted.

Display of standard operating procedures (SOP) for tissue processing and staining protocols were observed. Only standard reagents were purchased. Fresh reagents were used for tissue processing and staining. They were checked periodically and changed when necessary, thereby ensuring the quality of reagents used. Documentation of maintenance of equipment including regular preventive maintenance, downtime maintenance, comprehensive maintenance contract (CMC) or annual maintenance contract of equipment(AMC) and condemnation at regular intervals as required were observed. Regular maintenance of microscopes were assessed. Regular conduction of training and address of troubleshooting of technicians and its documentation were assessed.

Grossing of specimens were done as per Institutional protocols. On receipt of the specimens they were checked for adequate fixative, added if required; requisitions rechecked with sample. Pre grossing with adequate cuts for formalin penetration given on the same day for large specimens. If during grossing the specimen was found inadequately fixed, it was kept for another day for further fixation. On the next working day grossing were done. For resected specimens of malignancy College of American Pathologists (CAP) protocols were followed ensuring international quality standards. [4]For small specimens, sections from representative area were taken or all embedded as was feasible.

Hierarchical reporting, intradepartmental discussions, dialogues with clinicians, correlation with radiology, biochemistry, cytology reports available, use of immunohistochemistry when required were the analytical quality factors. Analytical quality maintenance is difficult to analyze because of subjectivity of histopathological analysis. Random case review were done and sample was reported by same pathologist to determine the precision and by another pathologist to determine the accuracy.

Institutional turnaround time was 5 days for excision and radical specimens. It was 3 days for small biopsies and critical cases. Retrieval time for slide or blocks was half hour and so was for generation for duplicate reports. Overall patient waiting time was fifteen minutes for generated reports maintaining queue system with available waiting area. Deviation from these durations were considered failure of quality maintenance. Monthly clinicopathological meetings were held to discuss interesting cases and overall clinician satisfaction were assessed.

Sample size was calculated using formula $N = \frac{z^2 * P * (1-P)}{d2}$ where z= Confidence level: conventional = 95% = 1 - α; therefore, α = 0.05 and $z_{(1-\alpha/2)}$ = 1.96 ; p= expected Quality assurance from previous studies = 0.95; d= absolute precision = 0.02. Applying this formula the sample size of the study was determined to be 2000.

Data were collected and documented by review of records It was statistically analyzed using Microsoft Excel software. Root causes analysis for the failure of quality assurance variables were done.

RESULTS

Of the 2000 samples 1880 (94%) were accepted and 120 rejected (6%) due to mainly pre analytical factors. 35 samples (29.2%) were without proper fixative, 48 samples (40%) had incomplete requisition forms, 37 samples (30.8%) had incomplete/ absent clinical history. All these samples were sent back for completion of forms and fixing the fixative issues and resubmitted after fulfilling the criteria. Inadequate tissue hampers quality of report and in such cases they were documented during receipt of sample. 20 cases (1%) were inadequate for satisfactory reporting and were mostly small biopsies, commonly endometrium (10 cases, 50%).Table 2

Lack of adherence to standard tissue fixation protocols were observed in 55 cases (2.75%). These sections were sent for recut or thinner section. Inadequate preventive maintenance and delay in renewal of CMC/AMC contract were the most common cause of failure of maintenance of equipment like automated tissue processors, strainers and microscopes. Calibration of equipment were done timely. Improper staining were found in 35 cases (1.75%). Improper quality of slides (8 cases, 0.4%) and improper cover slip application (4 cases, 0.2%) were also found in small numbers. Grossing of specimens were inadequate in 104 cases (5.2%). These were subjected to regrossing from the required areas mostly in cases of endomyometrium in distorted fibroid uterus (52 cases, 50%), suspicious areas of gall bladder (38 cases, 36.5%), pre chemotherapy treated mastectomy specimens (14 cases, 13.5%). Grossing descriptions were inadequate in 48 cases (2.4%). Review of gross specimens

were done in all such cases. Regular technician training were conducted and troubleshooting addressed.

Adequate pathologists were available; however simultaneous leaves, resignation with delay in subsequent appointment were some of the factors for delay in reports. Concurrence in diagnosis was found in majority cases (1892 cases, 94.6%). In discordant cases, intradepartmental discussions were done. Hierarchical reporting was followed mostly (1930 cases, 96.5%) cases. Case discussions with clinical colleagues were done in 150 cases (7.5%). Correlation with other investigations (radiology and biochemistry) and confirmation with immunohistochemistry were required in 126 cases (6.3%). Literature and internet supply were always available for reference. Regular CME were attended by pathologists. Monthly clinicopathological meetings were held for discussing important cases and overall clinician satisfaction were found. Out of randomly selected 100 such case reviews precision was found 97.5% and accuracy 96.6 %. 200 random samples were assessed for histopathological and cytology correlation and concordance were found in most cases (186 cases, 93%). Discordant cases included thyroid cystic lesions (6 cases, 4.3%), lymphomas (5 cases, 3.6%) and proliferative breast lesions (3 cases, 2.1%).

Maintenance of turnaround time was found in most cases (1800 cases, 90%). Downtime of equipment (106 case, 5.3%), delayed supply of reagents (54 cases, 2.7%), tissue processing delay (20 cases, 1.0%), report held for history and other reports (20 cases, 1.0%) were causes of failure of maintenance of turnaround time. Specimens were stored for 5 years, blocks and slides for indefinite period as per the institutional protocol. These were found to be strictly adhered to. Specimens were discarded after stipulated time maintaining biomedical waste management protocols. Retrieval of blocks and slides within stipulated time were found due to systematic storage in slide cabinets.

Report documentation and archiving were done properly enabling retrieval of duplicate reports within stipulated time in most cases (1840 cases, 98%). There were few typographical errors in the signed out reports (4 cases, 0.2%). Staffs were available at report dispatch counter who dispatched reports after checking patient identification and received signature by the patient party. Delay in dispatch of report in some cases (66 cases, 3.3%) for already generated reports. Haphazard arrangement of reports was the major cause in such delays. Patient satisfaction was assessed periodically and majority of patients were found satisfied regarding waiting time, quality of histopathology reports and delivery of reports within stipulated time.

DISCUSSIONS

Pre analytical quality factors starts from sample collection, transport in appropriate fixative, receiving in the laboratory, tissue processing till submission of the slide for reporting. The errors during pre-analytical phase may hamper the quality of histopathology report. [5]Sample identification is one of pivotal aspect which includes specimen labeling and accessioning. [6]Use of Bar Code technology minimizes errors in sample identification and accession. [3]In the present study, 120 (6%) samples were rejected due to pre analytical factors out of which 35 (1.75%) samples were without proper fixative, 47 (2.35%) samples had incomplete requisition form, 37 (1.85%) samples had incomplete/ absent clinical history. Comprehensible documentation and display of standard operating procedures at workplace for sample identification, accession, along with acceptance/rejection criteria may increase awareness of staffs and uniformity in the procedures.

1	Use of disposable blades
2	Cutting of thin sections 2-4 μm
3	Regular calibration of microtome
4	Periodic change of reagents and stains
5	Regular checking of temperature of paraffin embedding bath
6	Proper orientation of small biopsies
7	Proper gradation of alcohol during staining
8	Measures to avoid tissue artifacts and section folding
9	Proper cover slipping to ensure maximum display of the tissue to be analyzed
10	Use of frost free slides with printed accession number

Table 2: Pre analyticalcritical factors of tissue processing and staining

Periodic changing of chemicals used for processing depending on the workload prevents under processing and loss of tissue. [3] Emphasis should be given on use of standard quality equipment, its proper maintenance and periodic calibration. [7]In the present study, lack of adherence to standard tissue fixation protocols were observed in 55 cases (2.75%) Inadequate preventive maintenance and delay in renewal of CMC/AMC contract were the most common cause of failure of maintenance of equipment in the present study. Display of standard operating procedures (SOP), training of staffs emphasizing adherence to the protocols, maintenance of log book of equipment AMC/CMC details may minimize these issues.

Studies have highlighted factors influencing staining like nature of fixatives, treating schedules, section thinness, standardization and regular use of controls. [3, 8]In the present study, improper staining were found in 35 cases (1.75%) These can be minimized by display of standard operating procedure (SOP) of staining at workplace, training of technicians of importance to adherence to timing and change of stains at regular intervals thereby avoiding

Pre analytical Quality factors	
1	Complete requisition form with patient identification and accession no. traceable and generated by the laboratory
2	Appropriate sample fixation including quality, quantity and timing of fixative addition
3	Availability of clinical history
4	Adequacy of the tissue
5	Adherence to tissue processing protocol
6	Availability of standard quality reagents and slides
7	Calibration of instruments
8	Maintenance of automated equipment
9	Adherence to staining protocols
10	Availability of trained technicians
11	Grossing as per protocols including gross descriptions, measurements, weight (where necessary) adequate no. of blocks from representative sections, margins, lymph nodes
Analytical Quality factors	
1	Availability of adequate no. of trained pathologists
2	Concurrence of reports by two pathologists
3	Hierarchical reporting
4	Intradepartmental discussions
5	Expert opinion in controversial cases
6	Case discussions with clinicians
7	Concurrence of histology and cytology reports if available
8	Random case review
9	Use of ancillary techniques (IHC, radiology) for confirmation
10	Availability of literature (internet and books) for reference
11	Regular participation in CME
Post analytical Quality factors	
1	Turnaround time (TAT)
2	Documentation , archiving and retrieval of duplicate reports
3	Storage of specimens as per institutional criteria
4	Discard of specimens as per institutional protocol
5	Proper storage of blocks and slides
6	Retrieval of blocks/ slides when required
7	Availability of staffs for timely dispatch of reports
8	Overall patient satisfaction including wait time, receive of report within stipulated days
9	Clinician satisfaction with the reports generated

Table 1: Study variables including pre analytical, analyticaland post analytical factors

restain; thus helping in maintenance of turnaround time.

Crucial aspect of the histopathology reporting includes precise, complete and systematic gross description, dissection as well as selection of appropriate sections. [8] The present study found inadequate grossing in 104 cases (5.2%) and 48 cases (2.4%) had inadequate grossing descriptions. Depending on the usual type of specimens received, manpower performing the grossing, availability of other tests like immunohistochemistry, need for maintaining the gross anatomy for museum and research work, every laboratory should develop standard operating procedures and display near the grossing station. [9]

Individual judgment and biases makes the analytical phase of quality assurance complicated and difficult. Correlation with other reports (cytology or histopathology), blinded random case appraisal, intradepartmental discussions and evaluation by professionals are helpful to advance the quality. [10]In the present study, concurrence in diagnosis was found in majority cases (1892 cases, 94.6%). Hierarchical reporting, case discussions with clinicians, intradepartmental discussions, correlation of histology and cytology, random case review with precision of 97.5% and accuracy 96.6% were done thereby improvising quality attempting to nullify the grey zone of subjectivity of analytical phase of quality assurance. However, no external quality control was practiced as it was not easily available. [3]

Every laboratory should aim at signing out majority of cases as early as possible maintaining the turnaround time thereby helping in prompt patient management. [11]In study by Ribe et al turnaround times varied according to specimen type. It was ranging from 5.19 days (SD = 2.18) for endoscopic biopsies, 8.11 days (SD = 3.18) for bone biopsies and annual mean turnaround time of 5.7 days for surgical pathology specimens [12] In the present study maintenance of turnaround time was found in most cases (1800 cases, 90%). It was 5 days for excision and radical specimens and 3 days for small biopsies and critical cases. Use of automation in tissue processing, staining, microtomes, paraffin embedding stations, systematic grossing, precise reporting and overall professional attitude of staffs are essential to maintain the turnaround time.

In the present study report, documentation, archival and retrieval were adequate.However, authors recommends that the reports documentation and archival may be done in soft copies with the use of computer, and they may be made available online at different accessible levels. The typographical error should be checked during documentation by the signing pathologists. This will minimize the loss of reports after prolonged period and reduce physical storage area.

In absence of national guidelines regarding retention period of specimens, institutional guidelines have to be followed. [3, 13]In the present study specimens were stored for 5 years, blocks and slides for indefinite period as per the institutional protocol. Specimens were discarded after stipulated time maintaining biomedical waste management protocols.

CONCLUSION

This present retrospective observational study was conducted for assessment and determining the applicability of various elements of quality assurance in histopathology laboratory in a tertiary care hospital. 2000 randomly selected cases were studied for pre analytical, analytical and post analytical quality assurance factors. Most common errors were in pre analytical factors (120, 6%) and maintaining turnaround time was the most crucial among the post analytical factors. Standard operating procedures, training of staffs, equipment maintenance, alertness to maintain turnaround time, proper report documentation and professional attitude are key factors to successfully uphold quality assurance of the histopathology laboratory. Study variables including pre analytical, analytical and post analytical factors.

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How to cite this article: Mallick D, Chakrabarti S, Gayen P. Assessment and Applicability of Various Elements of Quality Assurance in Histopathology Laboratory: A Study from A Tertiary Care Hospital in Eastern Region of India. Perspectives in Medical Research. 2022;10(3):21-26
DOI: 10.47799/pimr.1003.05