Pathology Services in Nigeria: Cross-Sectional Survey Results From Three Cancer Consortia

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abstract

PURPOSE Cancer incidence is increasing in sub-Saharan Africa, yet there is little information on the capacity of pathology laboratories in this region. We aimed to assess the current state of pathology services in Nigeria to guide strategies to ensure best practices and improve the quality of surgical specimen handling.

METHODS We developed structured pathology survey to assess tissue handling, sample processing, and immunohistochemistry (IHC) capabilities. The survey was distributed electronically to 22 medical centers in Nigeria that are part of established cancer consortia. Data were collected between September and October 2017.

RESULTS Sixteen of 22 centers completed the survey in full. All 16 institutions had at least one board-certified pathologist and at least one full-time laboratory scientist/technologist. The majority of responding institutions (75%) reported processing fewer than 3,000 samples per year. For sample processing, 38% of institutions reported manual tissue processing and 75% processed biopsies and surgical specimens together. The average tissue fixation time ranged from 5 to more than 72 hours before processing and paraffin embedding. Half of the institutions reported having no quality assurance processes to evaluate hematoxylin and eosin–stained slides, and 25% reported having no written operating procedures. Half of the participating institutions have a facility for routine IHC staining, and among these there was considerable variability in processes and validation procedures. External proficiency testing was not common among surveyed sites (38%).

CONCLUSION Data from 16 Nigerian medical institutions indicate deficiencies in standardization, quality control, and IHC validation that could affect the reliability of pathology results. These findings highlight addressable gaps in pathology services that can ensure accurate diagnosis and follow-up for the growing number of patients with cancer in this region.

INTRODUCTION

Poor quality and limited access to pathologic and laboratory medicine in low- and middle-income countries (LMICs) can result in delayed and inaccurate cancer diagnoses. Pathology inadequacies can have serious consequences, including inappropriate follow-up, delayed or ineffective treatment, and poor patient outcomes. Despite its important role in guiding clinical care, pathology fails to receive the necessary investment and attention needed to perform its essential functions in LMICs.1,2 Given the projection that approximately 80% of the global cancer burden will be in LMIC by 2030 (WHO, 2010), addressing fundamental gaps in cancer diagnosis is an essential component of a cancer control strategy in resource-limited settings.

Pathology laboratories struggle to meet the growing needs of patients with cancer in Africa.3 In sub-Saharan Africa (SSA), most countries have under-invested in pathology services, despite having the highest age-standardized breast cancer mortality rate in the world.1,4 Many pathology laboratories in SSA do not have the infrastructure or technologies that are available in high-income countries. The need for pathology improvement in SSA has been recognized by several groups,5-8 who point to necessary systems, quality assurance (QA; established processes to meet quality requirements), and workforce improvements as well as the need for technical standards for tissue handling and processing and standard operating procedures (SOPs) for pathology laboratories. International Standards Organization (ISO) 15189:2012 is the international reference for best laboratory practices.9 ISO 15189:2012 is not required in most countries, but it is the most common reference for quality in pathology laboratories and includes
technical specifications for personnel, environmental conditions, laboratory equipment and consumables, examination processes, quality control, reporting, release of results, and information management. However, accurate data and standards pertaining to the current state of pathology services to work toward these standards are lacking in SSA. To date, studies that have assessed pathology needs in the region have focused on the total number of pathologists and the lack of necessary resources that would otherwise ensure accurate testing and reporting. These include essential infrastructure, basic equipment, skilled personnel, equipment maintenance,5,6,10,11 training materials and services,5,11,12 and the quality of pathology reports.13,14 A more detailed look at current minimum standards, QA processes, use of SOPs, and sample handling procedures, with consideration of ISO standards, is warranted.

Nigeria leads the WHO African region in cancer burden, with breast, prostate, cervical, colorectal, and liver as the top cancers by incidence.15 Clinicians depend heavily on pathologic findings to assess severity, prognosis, and potential treatments for these cancers.1,16 Nigeria has seen an improvement in the number of pathologists per population17,18; however, the majority of pathology services remain rudimentary compared with high-income countries, and access to high-quality pathology services is still lacking. Here, we report the results of a survey conducted to assess the current state of surgical pathology laboratory practices from a subset of cancer consortia–affiliated institutions in Nigeria to guide future efforts to ensure best practices and improve the quality of surgical pathology specimen handling.

**METHODS**

**Participants**

A convenience sample of 22 Nigerian medical institutions that are members of either the African Research Group for Oncology, the Prostate Cancer Transatlantic Consortium, or the Nigerian Breast Cancer Consortium were selected to complete an electronic survey on pathology practices and capacity. The institutions represent a cross-section of Nigeria’s health care centers. Targeted study participants were pathologists, administrators, or designated individuals with knowledge of the pathology services of their institution. Surveys were electronically distributed to participants using each consortium’s listserv. Data collection took place from September to October 2017. This study occurred before a pathology training workshop held in November 2017 in Lagos, Nigeria, that focused on developing SOPs to improve pathology practice in West Africa, with a focus on Nigeria.

**Survey Instrument**

A 40-item, English-language, structured pathology survey instrument was developed by the investigators using expert opinions on quality pathology laboratory services and best practices for surgical specimen handling. An independent group of pathologists, histotechnologists, and administrative personnel tested the questionnaire to establish content validity. Information requested related to tissue handling and processing, immunohistochemistry (IHC), and quality control (QC; processes to fulfill quality requirements). Survey questions are provided in the Data Supplement. Qualtrics software (Qualtrics, Provo, UT) was used for survey administration and data management.

**Data Analysis**

Data analysis was performed using SPSS version 23.0 (SPSS, Chicago, IL). The nominal variable yes/no was used as a data point for each question. Due to the small sample size, no comparative statistical analyses were performed. Binary data are reported as number and percentage for each question.

**RESULTS**

Twenty-two institutions completed the survey. Information was missing in the responses from six institutions, and these were excluded from analysis, making the final response rate 73%. Characteristics of the respondent institutions are listed in **Table 1**. Thirteen (81%) of 16 institutions were university hospitals, two (13%) were private or independent hospitals, and one (6%) was a proprietary hospital. Approximately 94% of responding
TABLE 1. Characteristics of Participating Institutions

| Characteristic                                                                 | No. of Institutions (N = 16; %) |
|-------------------------------------------------------------------------------|---------------------------------|
| Fully functional anatomic pathology laboratory to handle pathology needs       |                                 |
| Yes                                                                           | 15 (94)                         |
| No                                                                            | 1 (6)                           |
| No. of board-certified pathologists                                           |                                 |
| 1-4                                                                           | 10 (63)                         |
| ≥ 5                                                                           | 6 (37)                          |
| No. of anatomic pathology (physician) trainees                                |                                 |
| 1-3                                                                           | 3 (19)                          |
| ≥ 4                                                                           | 11 (69)                         |
| Unknown                                                                      | 2 (12)                          |
| No. of full-time laboratory scientists/technologists                          |                                 |
| 1-6                                                                           | 10 (63)                         |
| 7-12                                                                          | 6 (37)                          |
| Anatomic pathology services offered                                           |                                 |
| Surgical pathology only                                                       | 1 (6)                           |
| Surgical pathology and autopsy                                                | 7 (43)                          |
| Surgical pathology, autopsy, and immunohistochemistry                         | 4 (25)                          |
| Surgical pathology, autopsy, intraoperative frozen section, and immunohistochemistry | 2 (13)                       |
| Surgical pathology, autopsy, immunohistochemistry, brightfield in situ hybridization, and tissue-based polymerase chain reaction | 2 (13)                       |
| Average annual volume of cases and tissue blocks prepared                     |                                 |
| ≤ 1,000                                                                       | 5 (31)                          |
| 1,001-2,000                                                                   | 2 (13)                          |
| 2,001-3,000                                                                   | 5 (31)                          |
| ≥ 3,001                                                                       | 3 (19)                          |
| Unknown                                                                       | 1 (6)                           |

We also assessed the standard tissue processing procedures at the institutions (Table 2). Approximately 88% of respondents fix tissues in 10% neutral buffered formalin. Whereas 38% of institutions reported manual tissue processing, others used an automated tissue processor, such as those from Leica Biosystems (Wetzlar, Germany) or Thermo Fisher Scientific (Waltham, MA). In terms of processing, 75% of institutions process biopsies and surgical specimens together, whereas 25% process them separately. All centers use xylene as a clearing agent, and 56% use ethanol for dehydration.

Reported average tissue fixation time at the centers ranged from 5 hours to more than 72 hours (Table 2). For biopsies, 81% of institutions reported formalin fixation of 6 to 72 hours, 6% fix tissues for less than 6 hours, and 13% fix tissues for more than 72 hours. Half of the institutions fix surgical specimens for 6 to 72 hours, and 50% fix tissues for more than 72 hours.

Three fourths of institutions have written SOPs for tissue processing, whereas others (25%) reported no SOP manual. Half of the institutions reported the use of a QA process to evaluate hematoxylin and eosin (H&E)–stained slides on a daily basis. Of these eight institutions, 88% report that H&E QC evaluations are performed by both laboratory scientists and pathologists. One institution reported the use of a QA process but could not indicate whether it was performed by laboratory scientists or pathologists (Table 2).

The survey also assessed IHC services and techniques (Table 3). Approximately 47% of respondents send their IHC to reference laboratories, and eight institutions reported having a facility for routine IHC staining. Of the institutions performing IHC on-site, three fourths cut IHC sections at 3 to 5 µm; one center (13%) reported requiring 2-µm sections for IHC staining. Most institutions (63%) use low-pH antigen retrieval solutions, and retrieval time varied between 15 minutes and more than 60 minutes (Table 3). Approximately 88% of institutions perform IHC manually; one institution (13%) reported the use of a Ventana autostainer (Ventana Medical Systems, Oro Valley, AZ). All institutions reported using heat-induced epitope retrieval solutions to unmask antigen binding sites. The majority of institutions (75%) perform antigen retrieval using either a steamer (25%), pressure cooker (25%), water bath (25%), or microwave oven (13%). All laboratories reported the use of 3,3′-diaminobenzidine chromogen for IHC staining.

The expected turnaround time for IHC requests varied across institutions from 25 to 48 hours to more than 72 hours. Although 63% of respondents performing IHC on-site have written procedures to validate predictive IHC makers, none of these institutions tests a minimum of 20 cases for validation of nonpredictive markers. It is important to include a sufficient number of patients in validation studies to ensure accurate results.
studies for proper characterization of the antibody, performance parameters, and interpretation criteria. Approximately 75% of the laboratories do not perform IHC on cytologic specimens, and 75% do not include decalcified specimens in the validation. Final IHC protocol approval—ie, antigen retrieval, antibody dilution, and incubation time—at 75% of the institutions is made by laboratory scientists/managers, not pathologists. Only 38% of the institutions reported external proficiency testing, a quality assessment tool that aids in evaluating current knowledge, standardizing processes, and identifying areas for improvement. Most institutions (75%) have a process to investigate cases that did not meet the expected turnaround time.

DISCUSSION

The need for oncology services in SSA has increased in recent years, and the demand is projected to continue to rise in the foreseeable future. Pathology laboratories in the region provide a critical service that guides both clinical decision making and cancer research initiatives. Accurate diagnosis and high-quality tissue preservation are important for immediate and long-term patient outcomes. Reliability and validity of pathology laboratory processes are paramount. Our survey assessed pathology capacity and practices in cancer consortia–affiliated institutions in Nigeria and identified several areas for improvement in pathology laboratory practices, including variability in adequacies in tissue handling and processing, standardization, QC processes, and IHC procedures and validation.

Many prior studies report a shortage of pathologists in SSA, an observation consistent with our survey findings—63% of the institutions reported four or fewer certified pathologists. A 2011 to 2013 survey that assessed pathology capacity in SSA found that pathologists per population ranged from 84,133 persons per pathologist in Mauritius to 9,264,500 persons per pathologist in Niger compared with 5.7 pathologists per 100,000 persons in the United States. In addition to clinical responsibilities—that

### TABLE 2. Tissue Processing and Hematoxylin and Eosin Staining

| Variable | No. of Institutions (N = 16, unless otherwise noted; %) |
|----------|------------------------------------------------------|
| Use of quality assurance process for evaluating hematoxylin and eosin stains daily | 8 (50) |
| Performed by | 0 |
| Pathologists | 0 |
| Laboratory scientists | 0 |
| Both | 7 (88) |
| Unknown | 1 (12) |
| No | 8 (50) |
| Type of fixative for specimen processing | 10% neutral buffered formalin 14 (88) |
| Commercial formalin alternative | 2 (12) |
| Laboratory method for processing specimens | Manually 6 (37) |
| Automated tissue processor | 10 (63) |
| Type of processor (N = 10) | Shandon 4 (40) |
| Leica | 5 (50) |
| Unknown | 1 (10) |
| Available written standard operation manual for tissue processing | Yes 12 (75) |
| No | 4 (25) |
| Separation of small size specimens (biopsies) from larger tissue samples for processing | Yes 4 (25) |
| No | 12 (75) |
| Average length of fixation for biopsies, hours | 5 1 (6) |
| 6-72 | 13 (81) |
| > 72 | 2 (13) |
| Average length of fixation for larger tissue samples, hours | 5 0 |
| 6-72 | 8 (50) |
| > 72 | 8 (50) |
| Dehydration reagent | Alcohol blend 0 |
| Ethanol | 9 (56) |
| Isopropanol | 2 (13) |
| Reagent alcohol | 5 (31) |

(Continued in next column)
without adequate QC processes, laboratory staff may not identify nonconformance events and address them promptly. Moreover, more than 60% of institutions surveyed reported no external proficiency testing. This finding is consistent with prior observations that indicate that more than 75% of SSA countries had pathology laboratories that failed to meet internationally recognized QA standards.29 External proficiency testing ensures that laboratory practices conform to required quality standards needed for patient care. Lack of external quality assessment not only impedes the identification of discrepant laboratory processes and systemic errors, but may also affect the quality of patient results and ultimately patient management.

The process of producing formalin-fixed, paraffin-embedded tissue blocks and sections requires the standardization of all preanalytical and analytical processing stages by individual laboratories. Wide interlaboratory variation in sample handling, processing, and/or methodology may adversely affect the reliability of downstream assay results and tissue quality for future research use. Our study demonstrates that 75% of surveyed institutions process biopsies and surgical specimens together, a practice that can result in either overprocessing of small samples or underprocessing of larger surgical specimens.30 Such suboptimal processing can affect tissue morphology, quality of stains, and ancillary testing, and ultimately lead to delays in reporting and/or diagnostic errors.31-33 In addition, approximately 40% of laboratories in our study reported processing samples manually. Routine manual tissue processing can introduce variation and is less consistent and reproducible than automated methods.34 Manual tissue processing also requires close monitoring of factors, such as reagent quality, temperature, solution pH, and time. Finally, 50% of sites reported having no QA process to assess the quality of basic H&E stains, a type of stain that is easily influenced by the nature of tissue handling and processing.35,36 Widespread manual tissue handling and processing, processing of biopsy and surgical samples together, and insufficient reagent QC all represent significant sources of variability that could critically affect formalin-fixed, paraffin-embedded tissue block quality.

Most pathology laboratories in SSA operate from 9 AM to 5 PM, yet 81% of respondents reported fixation and

### TABLE 3. Immunohistochemistry Services and Techniques

| Variable                                      | Institutions With IHC Staining Facility (N = 8; No., %) | Institutions Without IHC Staining Facility (N = 8; No., %) |
|------------------------------------------------|--------------------------------------------------------|-----------------------------------------------------------|
| Frequency of IHC staining                     |                                                        |                                                           |
| Daily                                         | 2 (25)                                                 |                                                           |
| Weekly                                        | 3 (37)                                                 |                                                           |
| Biweekly                                      | 1 (13)                                                 |                                                           |
| When needed                                   | 2 (25)                                                 |                                                           |
| How IHC needs are handled                     |                                                        |                                                           |
| Block sent to an outside laboratory for specific antibodies, without interpretation | 1 (13)                                                 |                                                           |
| Block sent to an outside laboratory for specific antibodies, with interpretation | 7 (87)                                                 |                                                           |
| Availability of antibody validation process of reference laboratory |                                                        |                                                           |
| Yes                                           | 0                                                      |                                                           |
| No                                            | 8 (100)                                                |                                                           |
| Specific tissue/block submission requirements by reference laboratory |                                                        |                                                           |
| Yes                                           | 3 (37)                                                 |                                                           |
| No                                            | 4 (50)                                                  |                                                           |
| Not sure                                      | 1 (13)                                                  |                                                           |
| Method of IHC staining                        |                                                        |                                                           |
| Automated staining                            | 1 (13)                                                 |                                                           |
| Manual staining                               | 7 (87)                                                 |                                                           |
| Antigen retrieval method                      |                                                        |                                                           |
| Protease digestion                            | 0                                                      |                                                           |
| HIER, steamer                                 | 2 (25)                                                 |                                                           |
| HIER, microwave                               | 1 (13)                                                 |                                                           |
| HIER, pressure cooker                         | 2 (25)                                                 |                                                           |
| HIER, water bath                              | 2 (25)                                                 |                                                           |
| HIER, automated stainer                       | 1 (13)                                                 |                                                           |
| Buffer type (HIER usage)                      |                                                        |                                                           |
| Low pH                                        | 5 (62)                                                 |                                                           |
| High pH                                       | 2 (25)                                                 |                                                           |
| Unknown                                       | 1 (13)                                                 |                                                           |
| Total retrieval time (HIER usage), minutes    |                                                        |                                                           |
| > 15 to < 30                                  | 2 (25)                                                 |                                                           |
| > 30 to < 45                                  | 2 (25)                                                 |                                                           |
| > 45 to < 60                                  | 2 (25)                                                 |                                                           |
| > 60                                          | 1 (13)                                                 |                                                           |
| Unknown                                       | 1 (13)                                                 |                                                           |

(Continued on following page)
TABLE 3. Immunohistochemistry Services and Techniques (Continued)

| Variable | Institutions With IHC Staining Facility (N = 8; No., %) | Institutions Without IHC Staining Facility (N = 8; No., %) |
|----------|--------------------------------------------------------|----------------------------------------------------------|
| Cut thickness, µm | | |
| 2        | 1 (13)                                                 | 1 (13)                                                   |
| 3-5      | 6 (75)                                                 | 3 (38)                                                   |
| Unknown  | 1 (13)                                                 | 4 (50)                                                   |
| Detection reagent | | |
| HRP polymer kit with DAB | 8 (100) | |
| Available written procedures to validate predictive and nonpredictive antibodies | | |
| Yes, for predictive markers only | 5 (63) | 1 (13) |
| Unknown | 3 (37) | |
| Include a minimum of 20 cases in nonpredictive antibody validation | | |
| Yes | 0 (0) | |
| No | 8 (100) | |
| Include cytology specimens in antibody validation | | |
| Yes | 1 (13) | 1 (13) |
| No | | |
| Include decalciﬁed specimens in antibody validation | | |
| Yes | 1 (13) | 1 (13) |
| No | | |
| Expected turnaround time, hours | | |
| < 24 | 0 (0) | |
| 25-48 | 3 (38) | |
| 49-72 | 2 (24) | |
| > 72 | 3 (38) | 8 (100) |

Abbreviations: DAB, 3,3′-diaminobenzidine; HIER, heat-induced epitope retrieval; HRP, horseradish peroxidase; IHC, immunohistochemistry.

IHC provides diagnostic conﬁrmation and it is important to control parameters that could affect protein preservation to minimize false-negative staining. Accurate IHC results rely largely on slide preparation techniques—that is, tissue ﬁxation, processing, antigen retrieval, primary antibody incubation, reagent pH, and environmental factors—and interpretation of the staining pattern.5 Antigen retrieval time, for instance, depends on ﬁxation type and length, detection system sensitivity, retrieval solution pH or enzyme concentration, and intended antibody target.46,47 Our study found a number of gaps in technical and QC measures that would ensure the standardization, reproducibility, accuracy, and validity of IHC results. The majority of the surveyed laboratories with IHC capabilities perform tests manually using a variety of appliances (steamer, microwave, pressure cooker, and water bath) for heat-induced epitope retrieval. Some of these appliances are not ideal. Microwaves tend to produce uneven heat distribution and steamers or pressure cookers may cause temperature variations and tissue disruption.48,49 Approximately one third of laboratories perform IHC on 2- to 3-µm sections, even though the recommended thickness is 4 to 5 µm; inappropriate section thickness can negatively affect the proportion of positive and negative cells and ultimately affect diagnostic accuracy.50 More than 40% of surveyed laboratories have no written procedures for basic antibody validation. Lack of validation procedures accompanied by suboptimal section thickness could affect staining quality and the interpretation of results. We also found that the ﬁnal antibody working protocol—that is, retrieval and incubation time, antibody dilution, and staining intensity—at most sites is determined by a non-pathologist. Only 25% of participating laboratories reported ﬁnal approval by a pathologist or a designee. IHC staining interpretation requires the integration of multiple parameters,
including demographic information, tumor location, potential tumor biology, the antigen’s expression in normal versus neoplastic tissues, and pertinent clinical history. Although there are no known criteria with which to assess the competency of nonpathologist staff for IHC protocol approval, integration of pertinent clinical information may not be well understood by nonpathologists. Approval of IHC working protocols by nonpathologists may indicate insufficient clinical oversight of laboratory services.

Limitations of the current study include the cross-sectional nature and small sample size obtained by convenience sampling. Caution must be exercised in generalizing the findings. Most of the participating centers are in the southwest part of Nigeria, and the findings may not reflect the conditions in the entire country. Tissue size and types were not captured in the survey; thus, a correlation between tissue size/type and fixation time could not be established to aid in the interpretation of the fixation issues identified. There was a high representation of tertiary hospitals, likely because of the higher likelihood of such institutions to offer pathology services in LMICs. In addition, the analysis is based on information reported by surveyed sites and its accuracy might have been influenced by response bias. However, the current study demonstrates the feasibility and value of a pathology survey in this region. A larger-scale survey that addresses additional pathologically relevant areas is warranted to further evaluate gaps in pathology services that can ensure accurate diagnosis and quality specimen handling in Nigeria.

A strength of this study is the identification of gaps in pathology services that would be inexpensive to address. On the basis of our findings, we recommend the creation of internal standards and guidelines to ensure high-quality pathology practices. Transitioning to the use of tissue processors over manual tissue processing would improve consistency. In the absence of financial resources for such a transition, establishing SOPs and providing relevant training in manual tissue processing, guided by pathologists, is critical. Furthermore, we recommend routine external quality assessment—proficiency testing—to validate that processes are correctly followed and technical and diagnostic standards are routinely achieved. Ultimately, these steps are essential for ensuring best histopathologic practices to support quality cancer care in Nigeria and guide quality improvement efforts, such as enrollment in the WHO Stepwise Laboratory (Quality) Improvement Process Toward Accreditation (SLIPTA) program.

In conclusion, key themes highlighted in the current study are the inadequate standardization of protocols and processes within the preanalytical, analytical, and postanalytical phases of pathologic analysis. There is also evidence of a lack of adherence to guidelines across institutions in the region with a potential impact on quality, reliability, and pathology results. These are addressable gaps in pathology services that can ensure accurate diagnosis and quality specimens handling in Nigeria.

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REFERENCES

1. Fleming KA, Naidoo M, Wilson M, et al: An essential pathology package for low- and middle-income countries. Am J Clin Pathol 147:15-32, 2017
2. Sayed S, Lukande R, Fleming KA: Providing pathology support in low-income countries. J Glob Oncol 1:3-6, 2015
2a. World Health Organization: Global status report on non-communicable diseases. 2010. http://www.who.int/nmh/publications/ncc_report_full_en.pdf
3. Dafaallah K, Awedekarim A: Role of pathology in sub-Saharan Africa: An example from Sudan. Pathol Lab Med Int 2:49-57, 2010
4. Azubuke SO, Muirhead C, Hayes L, et al: Rising global burden of breast cancer: The case of sub-Saharan Africa (with emphasis on Nigeria) and implications for regional development—A review. World J Surg Oncol 16:63, 2018
5. Adesina A, Chumba D, Nelson AM, et al: Improvement of pathology in sub-Saharan Africa. Lancet Oncol 14:e152-e157, 2013
6. African Pathologists’ Summit Working Groups: Proceedings of the African Pathologists Summit; March 22-23, 2013; Dakar, Senegal: A summary. Arch Pathol Lab Med 139:126-132, 2015
7. Ezzelle J, Rodriguez-Chavez JR, Darden JM, et al: Guidelines on good clinical laboratory practice: Bridging operations between research and clinical research laboratories. J Pharm Biomed Anal 46:18-29, 2008
8. Hewitt SM, Lewis FA, Cao Y, et al: Tissue handling and specimen preparation in surgical pathology: Issues concerning the recovery of nucleic acids from formalin-fixed, paraffin-embedded tissue. Arch Pathol Lab Med 132:1929-1935, 2008
9. International Standards Organization: ISO 11518:2012: Standardization of medical laboratories—Requirements for quality and competence. https://www.iso.org/standard/56115.html
10. Stalsberg H, Adjei EK, Owusu-Afriyie O, et al: Sustainable development of pathology in sub-Saharan Africa: An example from Ghana. Arch Pathol Lab Med 141:1533-1539, 2017
11. Wilson ML, Ayers S, Beney D, et al: Improving anatomic pathology in sub-Saharan Africa to support cancer care. Am J Clin Pathol 139:310-315, 2018
12. Sabageh D, Daramola AO, Rotimi O: Histopathology practice and training in Nigeria: A model. Niger J Med 25:197-200, 2016
13. Atanda AT, Atanda JO: Audit of histopathology reports for breast cancer in Aminu Kano Teaching Hospital. West Afr J Med 29:174-177, 2010
14. Daramola AO, Banjo AA, Bennett A, et al: Breast cancer reporting in Lagos, Nigeria: Implications for training and education in Africa. J Glob Oncol 2:397-402, 2016
15. Bray F, Ferlay J, Soerjomataram I, et al: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68:394-424, 2018
16. Rohr UP, Binder C, Dieteler T, et al: The value of in vitro diagnostic testing in medical practice: A status report. PLoS One 11:e0149856, 2016 [Erratum: PLoS One 11:e0154008, 2016]
17. Adeyi OA: Pathology services in developing countries: The West African experience. Arch Pathol Lab Med 135:183-186, 2011
18. African Strategies for Advancing Pathology Group Members: Quality pathology and laboratory diagnostic services are key to improving global health outcomes: improving global health outcomes is not possible without accurate disease diagnosis, Am J Clin Pathol 143:325-328, 2015
19. Meera JG, Leather AJ, Hagander L, et al: Global Surgery 2030: Evidence and solutions for achieving health, welfare, and economic development. Lancet 386:569-624, 2015
20. Sayed S, Cherniak W, Lawler M, et al: Improving pathology and laboratory medicine in low-income and middle-income countries: Roadmap to solutions. Lancet 391:1939-1952, 2018
21. Fitzgibbons PL, Bradley LA, Fatheeree LA, et al: Principles of analytic validation of immunohistochemical assays: Guideline from the College of American Pathologists Pathology and Laboratory Quality Center. Arch Pathol Lab Med 138:1432-1443, 2014
22. Howat WJ, Lewis A, Jones P, et al: Antibody validation of immunohistochemistry for biomarker discovery: Recommendations of a consortium of academic and pharmaceutical based histopathology researchers. Methods 70:34-38, 2014
23. Olsen M: Cancer in Sub-Saharan Africa: The Need for New Paradigms in Global Health. Boston, MA, Boston University, 2015
24. Stefan DC: Cancer care in Africa: An overview of resources. J Glob Oncol 1:30-36, 2015
25. Kaschula RO: The practice of pathology in Africa. Arch Pathol Lab Med 137:752-755, 2013
26. Nelson AM, Milner DA, Rebeck TR, et al: Oncologic care and pathology resources in Africa: Survey and recommendations. J Clin Oncol 34:20-26, 2016
27. Robboy SJ, Weintraub S, Horvath AE, et al: Pathologist workforce in the United States—Development of a predictive model to examine factors influencing supply. Arch Pathol Lab Med 137:1723-1732, 2013
28. Mesfin EA, Taye B, Belay G, et al: Factors affecting quality of laboratory services in public and private health facilities in Addis Ababa, Ethiopia. JIFCC 28:205-223, 2017
29. Schroeder LF, Amuleke T: Medical laboratories in sub-Saharan Africa that meet international quality standards. Am J Clin Pathol 141:791-795, 2014
30. Bindhu P, Krishnapillai R, Thomas P, et al: Facts in artifacts. J Oral Maxillofac Pathol 17:397-401, 2013
31. Apple S, Pucci R, Lowe AC, et al: The effect of delay in fixation, different fixatives, and duration of fixation in estrogen and progesterone receptor results in breast carcinoma. Am J Clin Pathol 135:592-598, 2011
32. Ekundina V, Eze G: Common artifacts and remedies in histopathology (a review). African J Cell Pathol 4:6-12, 2015
33. Srinivasan M, Sedmak D, Jewell S: Effect of fixatives and tissue processing on the content and integrity of nucleic acids. Am J Pathol 161:1961-1971, 2002
34. Bancroft JD, Gamble M: Theory and Practice of Histological Techniques. New York, NY, Elsevier, 2008
35. Wynnychuk M: Minimizing artifacts in tissue processing: Part I. Importance of softening agents. J Histotechnol 15:321-323, 1992
36. Patents, Royalties, Other Intellectual Property: Coinventor on several patents assigned to Riptide Bioscience
37. Consulting or Advisory Role: Ashion Analytics
36. Wynnechuk M: Minimizing artifacts in tissue processing: Part 2. Theory of tissue processing. J Histotechnol 16:71-73, 1993
37. Bass BP, Engel KB, Greystak SR, et al: A review of preanalytical factors affecting molecular, protein, and morphological analysis of formalin-fixed, paraffin-embedded (FFPE) tissue: How well do you know your FFPE specimen? Arch Pathol Lab Med 138:1520-1530, 2014
38. Engel KB, Moore HM: Effects of preanalytical variables on the detection of proteins by immunohistochemistry in formalin-fixed, paraffin-embedded tissue. Arch Pathol Lab Med 135:537-543, 2011
39. Hammond ME, Hayes DF, Dowsett M, et al: American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. Arch Pathol Lab Med 134:907-922, 2010
40. Wolff AC, Hammond MEH, Allison KH, et al: Human epidermal growth factor receptor 2 testing in breast cancer. American Society of Clinical Oncology/College of American Pathologists clinical practice guideline focused update. Arch Pathol Lab Med 142:1364-1382, 2018
41. Iyengar JN: Quality control in the histopathology laboratory: An overview with stress on the need for a structured national external quality assessment scheme. Indian J Pathol Microbiol 52:1-5, 2009
42. Barbé B, Verdonck K, Mukendi D, et al: The art of writing and implementing standard operating procedures (SOPs) for laboratories in low-resource settings: Review of guidelines and best practices. PLoS Negl Trop Dis 10:e0005053, 2016
43. Guindo MA, Shott JP, Saye R, et al: Promoting good clinical laboratory practices and laboratory accreditation to support clinical trials in sub-Saharan Africa. Am J Trop Med Hyg 86:573-579, 2012
44. Agarwal R: Quality-improvement measures as effective ways of preventing laboratory errors. Lab Med 45:e80-e88, 2014
45. Alves VA, Bacchi CE, Vassallo J: Manual de Imuno-Histoquímica. São Paulo, Brazil, Sociedade Brasileira de Patologia, 1999, pp 64-67
46. Shi SR, Shi Y, Taylor CR: Antigen retrieval immunohistochemistry: Review and future prospects in research and diagnosis over two decades. J Histochem Cytocem 59:13-32, 2011
47. Kim SW, Roh J, Park CS: Immunohistochemistry for pathologists: Protocols, pitfalls, and tips. J Pathol Transl Med 50:411-418, 2016
48. K R V, Jones D, Udupa V: A simple and effective heat induced antigen retrieval method. MethodsX 3:315-319, 2016
49. Ramos-Vara JA, Miller MA: When tissue antigens and antibodies get along: Revisiting the technical aspects of immunohistochemistry—The red, brown, and blue technique. Vet Pathol 51:42-87, 2014
50. McCampbell AS, Raghunathan V, Tom-Moy M, et al: Tissue thickness effects on immunohistochemical staining intensity of markers of cancer. Appl Immunohistochem Mol Morphol 27:345-355, 2017