review articles

Importance of Cytopathologic Diagnosis in Early Cancer Diagnosis in Resource-Constrained Countries

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abstract

PURPOSE The rising cancer burden in low- and middle-income countries (LMICs) stresses already weak health care systems and poses unique challenges. In resource-constrained LMICs and in circumstances where most patients must pay out of pocket for diagnostic tests, these may not be available or affordable for many. Cytopathology provides a simple, inexpensive, standardized, and low-technology diagnostic procedure that is increasingly used as an effective tool to address the hurdles faced in cancer control programs in LMICs. This review explores the potential role of cytopathology in LMICs in reducing the cancer burden.

METHODS This review studied the existing literature across the globe regarding the utilization of cytopathology as a diagnostic or screening tool for various types of malignancies as well as its advantages and disadvantages, depending on the local situation.

RESULTS Apart from the usefulness of cytopathology, this review also sheds light on the barriers to using cytopathology in LMICs. Most recently, SARS-CoV-2 has produced several unique challenges for cytopathology. These are being met with innovative measures to combat the effects of the pandemic and ensure the safe delivery of essential cytopathology services.

CONCLUSION The usefulness of cytopathologic techniques has been demonstrated via various studies, even during the recent pandemic. If cytology is to be used appropriately, the focus needs to be on integrating it into the national cancer screening and diagnostic programs as well as providing well-trained human resources.

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INTRODUCTION

Malignancy is an increasingly prominent cause of morbidity and mortality in low- and middle-income countries (LMICs), which are undergoing an epidemiologic transition from a predominance of infection-related diseases to a broader noncommunicable disease profile, which includes cancer. Nearly 70% of the world's cancer deaths occur in these countries,[1] and this is almost certainly an under-representation because very few LMICs have reliable cancer registries and reporting systems.[2] The rising cancer burden in LMICs stresses already weak health care systems and poses unique challenges. Although there are fewer resources to allocate to cancer,[3] there is a rising rate of cancer incidence because of improvement in life expectancy from reduced infectious disease mortality, and because of exposure to risk factors common in high-income countries (HICs), such as tobacco, physical inactivity, and changes in dietary pattern, heightened by inequalities in the availability of affordable health care.[4]

In poorer countries, here most patients pay out-of-pocket for diagnostic tests, surgical biopsy and pathology are often not readily available and expensive, and precise ancillary diagnostic methods, including immunohistochemistry (IHC) and molecular testing, are rarely available, resulting in many patients being misdiagnosed and treated inappropriately.[5] This further adds to the cancer burden of these countries.

For many LMICs, significant differences between regions, between rural and urban populations, and across social groups remain major challenges for the reorganization of existing health care delivery and the implementation of new structures that enable basic equal access to health care for the entire population. Cancer care represents a major hurdle for universal health coverage in LMICs, mainly because of lack of screening and early detection, poor education about cancer, the cultural taboo of cancer, and the requirement for costly infrastructure for diagnosis and treatment, including educated personnel. This results in an unnecessarily high proportion of patients with metastatic and advanced tumor stages.[6] A study conducted in Cameroon pointed out the magnitude of the difficulties of accessing and receiving cancer care in

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CONTEXT

Key Objective

The key objective of this review is to explore the role and utility of cytopathology for early cancer diagnosis in resource-limited low- and middle-income countries (LMICs).

Knowledge Generated

There are several barriers to using cytopathology in LMICs. However, investment in cytopathology training, research, and implementation at the grassroots levels can alleviate the cancer diagnosis burden to a great extent.

Relevance

Cytopathology is a simple, inexpensive, standardized, low-technology diagnostic/screening tool. In LMICs, it is helpful in the diagnosis and screening of several widely prevalent cancers such as those affecting the breast, cervix, lung, etc. It has the potential to reduce the cancer staging at diagnosis to a great extent.

semiurban areas where only patients 87.30% could pay for biopsy, 26.36% of those did not collect their results, 18.7% denied their results, and only 44 of 110 patients were able to finish their cancer care treatment program.[7] The problem of loss to follow-up (because of the cost of diagnosis and treatment to the patient) is another concern faced by LMICs. Effective cancer prevention and early detection may help in lowering this burden. Patients diagnosed with cancer at an early stage have the best chance of curative treatment and long-term survival. Hence, there is a pressing need to see a paradigm shift in the ability to accurately detect and diagnose cancer at an early stage in LMICs.[8]

Globally also there has been a growing adoption of cytologic tests because of their less invasive nature compared with biopsy and higher reliability.[9] The global histology and cytology market size was valued at 12.35 billion in US dollars (USD) in 2020 and is expected to expand at a compound annual growth rate of 14.74% from 2021 to 2028.[10]

METHODS

Cytopathology Is a Screening and Diagnostic Tool

Diagnostic techniques and procedures need to be reliable, cost-effective, not technology-intensive, and acceptable to patients, and this is markedly accentuated in LMICs. In addition, the facilities and equipment required should be affordable, require minimal maintenance, and have readily available consumables. Cytopathology, as a simple, accurate, standardized low-technology procedure, largely fulfills these criteria and can potentially prove to be one of the most effective tools available to provide the crucial diagnostic component of cancer control programs in low-resource countries.[11] In addition, cytopathology has ease of use, causes minimal patient discomfort, and enables the collection of sufficient material for diagnostic purposes. It is neither time-consuming nor complicated and, in addition to high sensitivity and specificity, has the potential for automation.[12] Studies have also reported that on-site cytologic evaluation of adequacy is a valuable adjuvant diagnostic tool with a success rate of 86%.[13]

A Nigerian study reported that the total cost for fine needle aspiration biopsy (FNAB) procedure and cytologic evaluation of each smear was 1,700 naira (N1,700.00 = $11 USD). The total cost for open surgical biopsy and histopathologic evaluation was 13,600 naira (N13,600 = $88 USD) per patient. It took an average of 2 days ± standard deviation 1 day to obtain FNAB results, whereas, by contrast, it took an average of 28 days ± standard deviation 7 days to obtain a histopathologic diagnosis. FNAB is cost-effective and saves time for the patients when compared with open surgical biopsy.[14]

Cytopathology covers a broad range of diagnostic and screening tests, including the cervical Papanicolaou (Pap) smear, sputum, urine, pleural and ascitic fluids, cerebrospinal fluid, and FNAB.[15] The relatively new kid on the block, interventional cytopathology, combines two techniques, which are fine needle biopsy, with or without aspiration, and ultrasonographic guidance. FNAB has an important role in the diagnosis and management of cancers, not only in the initial diagnosis of patients with palpable and nonpalpable tumors facilitating the planning of appropriate treatment but also in staging—via lymph node FNAB and evaluating the response to treatment, recurrence, and monitoring of disease progression. It can often provide a definitive diagnosis, supported in the clinical context with imaging and ancillary studies. Depending on their availability, flow cytometry, IHC, molecular analysis, genetic studies, culture, and polymerase chain reaction (PCR) for infections can all be performed on the FNAB material, and increase the diagnostic value of the FNAB.[16-18] The use of these ancillary tests is well established and rapidly developing in HIC, especially in the era of personalized medicine.[19]

A study reported that core biopsy is superior to fine-needle aspiration (FNA) in the tissue sampling of lymph nodes regardless of ultrasound-determined risk of malignancy.[20] Another systematic review quoted that, despite recent literature pointing to apparent core needle biopsy (CNB) superiority over FNA, there is no clear and universal answer, as both FNA and CNB can be very good, but in different ways.[21]

Hence, the cost-effectiveness of cytopathology versus histopathology needs to be formally examined in multiple health care settings from low-income countries to HICs.

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However, in most LMICs, the current focus is to develop the ability to provide basic cytopathology services, including FNAB, and the application of ancillary services to mirror those in HIC in almost all cases is very patchy. Rather than trying to catch up with the full broad scope of ancillary methods used in HIC, it appears prudent to adapt to the realities that are specific to the needs and prevalent scenarios of the respective LMIC.

A focused, goal-oriented approach would help in the effective utilization of the limited resources in LMICs. This is feasible for many tumor types, as described below:

- Lung carcinoma: Although histopathology remains the gold standard diagnostic modality, the cytopathologic techniques used for pulmonary and metastatic lesions are less invasive, economical, and yield quicker results. They can be used as a first-line diagnostic and management tool in specific situations. Despite the limitations of the cytopathologic procedures, they can help in diagnosing lung malignancies at the earliest possible time, recognizing that most lung carcinomas present in the late stages as metastatic tumors.[22] Sputum cytopathology has low sensitivity but high specificity for diagnosing lung carcinoma. Facilities to provide bronchial brushing and washings are few in LMICs, but FNAB either transthoracic or endobronchial ultrasound for lung malignancies seen on a chest X-ray shows sensitivity, specificity, and overall accuracy of 84%-96.29%, 95.45%-100%, and 89.55%-95.91%, respectively.[23-28] In a study that reported overall diagnostic characteristics (benign *v* malignant) of FNAB and CNB, the ranges of sensitivity were 81.3%-90.8% and 85.7%-97.4%; of specificity, 75.4%-100.0% and 88.6%-100.0%; and of accuracy, 79.7%-91.8% and 89.0%-96.9%, respectively. However, for specific diagnostic characteristics of FNAB and CNB (identifying the histologic subtype of malignancies or the specific benign diagnoses), the ranges of sensitivity were 56.3%-86.5% and 56.5%-88.7%; of specificity, 6.7%-57.1% and 52.4%-100.0%; and of accuracy, 40.4%-81.2% and 66.7%-93.2%, respectively. Compared with FNAB, CNB did not result in a higher complication rate (pneumothorax or hemoptysis).[29]
- Colorectal cancer (CRC): Brouwer et al[30] reported that brush cytopathology can be nearly as accurate as colonoscopic biopsy for the diagnosis of CRC, and combining these two diagnostic modalities may result in a significant improvement in the definitive diagnosis of cancer, which might reduce the need for further biopsy. They reported that cytopathology alone had a sensitivity of 88.2%, a specificity of 94.1%, a positive predictive value of 98.6%, and a negative predictive value (NPV) of 61.9% for the diagnosis of CRC.[22] Gv et al[31] reported that with careful attention to cytomorphology, coupled with good clinical and colonoscopic correlation, brush cytopathology of large intestine lesions is a reliable diagnostic tool. It categorizes lesions as malignant and benign with high sensitivity, positive predictive value, and NPV. However, adenomas and reparative/regenerative changes seen in inflammatory bowel disease are major pitfalls in the cytopathologic diagnosis of malignancy that may be averted by correlating the colonoscopic findings and clinical history. Cytopathologic diagnosis has the potential of saving time and providing faster feedback to the gastroenterologist. Niedermaier et al[32] suggested that flexible sigmoidoscopy screening reduces CRC incidence/mortality, and its potential to detect proximal neoplasms depends on the colonoscopy referral criteria for detecting CRC and advanced adenomas. Fecal DNA examination is a noninvasive strategy recommended by several medical professional societies for CRC screening in average-risk individuals.[33] The use of imaging in CRC has significantly evolved over the past two decades; however, there are technical, economical, and logistical challenges that need to be considered in LMICs for both fecal DNA testing and imaging.[34]
- Other GI tract (GIT) cancers: Some authors have reported that cytopathology of other GIT lesions can be used successfully to diagnose neoplastic and non-neoplastic conditions, especially when combined with biopsies. Cytopathologic evaluation is widely accepted as a cost-effective method that allows rapid interpretation and triaging of material.[35] Sharma et al[36] reported that the accuracy of brush cytopathology for upper GIT cancer detection was 82.37% and it was found to be a reliable, safe, inexpensive, and rapid method. Watson et al[37] also reported that endoscopic ultrasound-guided FNA is highly accurate for diagnosing GI stromal tumors and has a sensitivity of 82%, specificity of 100%, and overall accuracy of 86%. Brush cytopathology may be considered as an effective diagnostic screening method in poor-resource settings, because of its high sensitivity and specificity, although facilities for endoscopy are required.[38] Sponge cytology of the esophagus may also be used in LMICs for surveillance or diagnosis as an alternative to endoscopy.[39]
- Cervical cancer: The conventional Pap smear is time-tested, validated, and proven as a useful screening tool, and is probably still the most prevalent tool for the prevention of cervical cancer, although this is changing rapidly in HIC, with the introduction of the human papillomavirus (HPV) primary screening.[40] However, establishing cervical cancer screening using Pap smears in LMICs has faced major challenges related to inadequate infrastructure and trained manpower.[41] Other barriers include the financial cost and a lack of political commitment. Studies have reported that liquid-based cytology (LBC) markedly reduced the rate of unsatisfactory cases diagnosed by conventional smears from 22% to 2% of cases and may be used in conjunction with the traditional Pap smear, but LBC is more expensive and the economic implications need to be considered.[42,43] Dykens et al in a systematic review evaluated the implementation of cervical cancer screening programs in low-resource settings globally and found that of the 51

sites, 94.1% were in low-resource settings of middle-income countries, whereas just 9.8% were in low-income countries. Across all studies, visual inspection of the cervix with acetic acid (58.8%) was the most prevalent screening method followed by cytopathology testing (39.2%). Triage with cytopathology is proposed in developing (middle-income) countries where infrastructure exists with experience of screening.[44] Castanon et al[45] found that cytopathology at a cutoff for high-grade squamous intraepithelial lesions or worse had a sensitivity of 79% for cancer. Many HICs are moving to primary screening by HPV testing. However, HPV tests are expensive and require infrastructure, which may not be available in the LMICs, particularly in settings where there have been no previous cervical screening programs. In a meta-analysis, HPV testing has been shown to have greater sensitivity (+37%) but lower specificity (−7%) for cervical intraepithelial neoplastic lesions, and better reproducibility than cytopathology using a positive cutpoint of low-grade squamous intraepithelial lesions.[46] Unfortunately, establishing a cervical cancer screening service using HPV testing as the triage still requires reflex cytopathology and colposcopy, and the need for expert personnel and infrastructural requirements remain barriers to implementation.[47]

- Lim et al[48] in 2016 reported that cytopathology has value beyond screening, and could be used as a diagnostic aid for earlier detection of cervical cancer in young women with gynecologic symptoms. Similarly, Silva et al[49] reported that cytopathology, in addition to its role in cervical cancer screening programs, is also an important tool for controlling the efficacy of treatment in women with cervical cancer by monitoring and early detection of residual or recurrent neoplasms. In resource-limited countries, cytopathology can potentially serve as a useful tool, not only in the early screening of cervical cancer but also in treatment planning and follow-up. It may be particularly useful when only a direct observation method is used for the detection of cervical cancer. The latest WHO guidelines recommend an HPV DNA-based test as the preferred method, rather than visual inspection with acetic acid or cytology (commonly known as a Pap smear), currently the most commonly used method globally to detect precancer lesions.[50]
- Oral cancer: Oral cytopathology is simple, noninvasive, relatively painless, and tolerated well by the patients.[51] Brush cytopathology is valuable to prevent misdiagnosing doubtful oral lesions, that is, those lesions without a definitive etiology, diagnosing large lesions where excision of the entire tissue is not possible or practicable, evaluating patients with recurrent malignancies, and monitoring premalignant lesions.[52] Pereira et al reported that oral rinse-based cytopathology shows an improved quality in cell morphology, cellular clarity, and sample adequacy and, hence, aids in the detection of dysplastic features. The oral rinse-based preparation can thus be considered as a convenient alternative to conventional exfoliative cytopathology whenever a surgical biopsy is not feasible.[53] Shintaro et al in 2020 reported that the liquid-based cytopathology method is superior to conventional methods and in their study, histopathologic diagnosis was less discrepant with cytopathologic classification.[54]
- Breast carcinoma: When breast cancer is detected and treated early, the chances of survival are higher.[55] FNAB has a long and successful history in the workup of breast lesions, including abscesses and palpable or ultrasound-detected mass lesions such as cysts, fibrocystic change, fibroadenomas, proliferative lesions, and cancers. It is inexpensive, accurate, and minimally invasive, as well as a powerful tool in the assessment of these lesions with a high degree of accuracy.[56] In HICs, where mammography is used for routine diagnostics and screening programs, CNB is preferred since many lesions particularly in later screening rounds are calcifications, and CNB has become the more commonly used diagnostic test. In many LMICs, however, FNAB and CNB are regarded as complementary, with FNAB able to diagnose most lesions and triage cases including carcinomas for the more expensive and invasive CNB.[57] The CNB, however, remains an expensive option and is not universally available in LMICs.[58] Godfrey in 2021 reported that in a setting with constrained resources for cancer care in Tanzania, integration of clinical breast examination of palpable lesions with FNAB, rapid on-site evaluation, and rapid PCR testing for estrogen receptor (ER) is feasible in a breast cancer screening program and may be an effective method for triaging patients with breast masses.[59] Similar recommendations have been released in India where early detection of breast lesions is mandated using clinical breast examination followed by ultrasound and FNAB cytopathologic triage.[60,61] A study conducted by Vohra et al supported the equivalency of ER and human epidermal growth factor receptor 2 evaluation performed on FNA cell blocks compared with surgical tissue blocks.[62]
- The use of FNAB material for ER PCR analysis[59] has been demonstrated while using scraped material from direct smear material for hormone receptor analysis. Although this method is eminently technically feasible, it requires an advanced molecular pathology service. Similarly, using LBC material for IHC and immunocytochemistry has shown excellent concordance rates.[63] However, in a resource-constrained setting, reverse transcriptase PCR might be more suitable when compared with IHC.[64]
- Soft tissue and bone tumors: FNAB provides valuable information to the clinician for the diagnosis of soft tissue[65] and bone lesions.[66] To avoid time-consuming and costly investigations, FNAB can be used as the initial diagnostic method to triage cases for more expensive radiologic examinations, laboratory tests, and surgical biopsies that are frequently not available or expensive options in LMICs.[67]

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It is an already widely accepted diagnostic procedure and when used with CNB as required, is gradually replacing open biopsy especially for the initial investigation of deep-seated lesions.[68-70] FNAB can assess with a high degree of accuracy, any palpable lesion, including salivary glands, lymph nodes, thyroid, neck masses, breast (where the most common lesions are cysts, fibroadenomas, and abscesses as well as, carcinoma and proliferative breast lesions), soft tissue tumors, and the skin, including skin tumors, bacterial infections such as leprosy, and disseminated fungal infections.[71-73] FNAB can often confirm mycobacterial infections such as tuberculosis by acid-fast stains on direct smears and provide material for molecular pathology such as GeneXpert, if available. This may help avoid lengthy delays and costs.[74,75]

Barriers to Effective Use of Cytopathology in LMICs

There are several barriers to cancer care in LMICs. Low health literacy, cancer stigma, access to primary care, lack of transportation, geographical limitations, inaccurate diagnoses, poor coordination, loss to follow-up, financial barriers, and sociocultural barriers all contribute to the late presentation of patients at the clinic and delays in diagnostics and treatment.[76]

The major barrier to introducing or enhancing current cytopathology services in LMICs is the lack of well-trained cytopathologists and cytotechnologists, which creates a need for assistance in training the required numbers to allow a service to be established.[77,78] For example, a large country like India, with a population of 1.3 billion people, has a little more than 2000 trained cytopathologists who are members of the Indian Academy of Cytologists. Similar, or even lower, numbers exist in other resource-restrained countries. A second barrier is the lack of awareness among clinicians regarding the potential uses of cytopathology because these services have not been generally available, and there has been limited clinical integration of cytopathology diagnostic services. Anshu et al[79] reported that the main deficiencies in the training of cytopathologists were because of its variability; there were insufficient numbers of pathologists interested in cytology and a consequent lack of training to a high level of competence.

Hence, the utilization of cytopathology to its fullest potential can only be achieved by developing well-trained cytopathologists and cytotechnologists, along with the education of medical professionals about the uses, versatility, and wide applicability of cytopathology in disease management. LMIC trainees and cytopathologists should be assisted to train for short periods or sandwich fellowships in HIC cytopathology departments or LMIC departments that have experience, to gain expertise. This can be counterbalanced by HIC trainees and pathologists spending time in LMIC departments with established cytopathology services where they can gain valuable supervised experience performing and reporting large numbers of FNAB.[77,78] Cytopathology needs to be included in new locally applicable patient management algorithms once the FNAB or other cytopathology services are established, and there is a pressing need for international and national bodies, when establishing best practice guidelines, to ensure that they can be applied in LMICs with management options that recognize the potential lack of medical infrastructure. Clinicians must be made aware of the role of cytopathology so that they can integrate it into their diagnostic and treatment regimens and protocols.

Opportunities to enhance the training of pathologists and allied Pathology and Laboratory medicine (PALM) personnel must be explored and implemented. Rapidly growing populations, increasing disease burdens, and the magnitude of existing gaps in access to PALM services in LMICs mean that substantial progress in addressing these gaps may take years.[80] It is, therefore, crucial not to delay this exercise, because barriers and issues will only increase with time. Investment in human resources will be crucial to overcoming the gap in access to quality PALM services. Given the insufficient awareness of these problems, implementing national and international action will require a major advocacy effort.[81] In Kenya, where the scarcity of pathologists limits patient access to diagnostic tests, Sayed et al[82] demonstrated a successful model of task sharing and shifting from specialist pathologists to medical officers and clinical officers that improved access to important FNAB and bone marrow aspiration and trephine biopsy services in a low-resource setting. In addition, McHugh et al[83] reported that the sensitivity of FNAB for detecting malignancy was 85% and the specificity was 75%. PPV and NPV were 69% and 88%, respectively. Diagnostic concordance between FNAB and histopathology was 79%. This makes it a valuable tool in resource-limited settings for the evaluation of breast palpable lesions. In addition, a multicountry study revealed that the training period for cytopathology lasted 3-12 months vis-a-vis histopathology training, which lasted for 2-3 years.[79]

RESULTS

Role of Cytopathology in Excluding the Cancer Diagnosis

The role of cytopathology is not only important in diagnosing neoplasia, but also in rapidly excluding malignancies; for example, FNAB of a superficial lump suspected to be malignant and demonstrating it to be tubercular in origin by showing classical granulomas, caseation, and acid-fast bacilli could obviate expensive and time-consuming biopsy with histopathology. As reported by one of the present authors, the technique of FNAB can be successfully used to diagnose granuloma in breast aspirates and to demonstrate the presence of acid-fast bacilli. Tuberculosis is rampant in many LMICs, and patients are prescribed antituberculous therapy on the basis of finding granuloma in breast FNAB with or without a culture report, after clinical correlation.[84] This saves time, minimizes costs, and ensures that the treatment of the lesion on an outpatient basis is started immediately, obviating the need for expensive invasive investigations and possible hospitalization—which

further burdens an often overwhelmed, poorly resourced health system. Wright et al[85] reported that incorporating fluorescence in the cytopathologic evaluation of lymph node FNA specimens yielded a sensitivity of 65.9% and a specificity of 73.0%, proving that it is rapid, inexpensive, and cost-effective.

Cytopathology and SARS-COV-2

The current SARS-CoV-2 pandemic has changed much in medical practice, including the way cytopathology is practiced.[86] Ideally, the need to inactivate the SARS-CoV-2 and other viruses in specimens while preserving cytopreparation quality and morphologic details should be balanced.[87] The SARS-CoV-2 health care emergency has also underlined the need to exploit technological advances, particularly to upgrade PCR and other molecular pathology laboratory technologies by promoting automation and automatizing the specimen-to-report workflow.[88] Vigliar et al[89] in a recent study reported that during the pandemic, the percentage of malignant cytopathology samples has increased, as evidenced by higher percentages of breast and lymph node FNAB specimens, effusions, and urine samples, and that cytopathologic examination can be safely carried out in patients at high oncologic risk without the need to be postponed. Not surprisingly, a multicountry study reported that although the SARS-CoV-2 pandemic has resulted in a drastic reduction in the total number of cytopathology specimens regardless of anatomic site or specimen type, there is an increased rate of malignant diagnoses, which reflects the prioritization of patients with cancer who were considered to be at high risk.[90] Rana et al also reported an overall 92.6% reduction in cytopathology samples received and that prioritization of samples, proper precautions, and triaging of patients before procedures helped in carrying out the procedures safely.[91]

Several countries have established national guidelines for cytopathology laboratories for handling suspected and positive SARS-CoV-2 patient samples. In the Indian context, these included protocols for FNAB in SARS-CoV-2–suspected or –confirmed cases, sample processing in the laboratory, sample discarding, management of spills in the laboratory, surface disinfection, and equipment decontamination, care of the laboratory staff, reporting of the cytopathology samples, and training of the cytopathology residents.[92,93]

The safety of patients, health personnel, and the population at large must be ensured during any laboratory test. During the tumultuous times of SARS-CoV-2, laboratories and hospitals have been and continue to be exposed to highly infectious materials. As more and more national and international professional and academic bodies are developing their guidelines that are applicable and cater to the local needs and limitations, the WHO and Centers for Disease Control and Prevention guidelines remain the mainstay for the safety of laboratory professionals.[94]

These testing times of SARS-CoV-2 have necessitated the enhanced use of digital technology while following the social distancing protocol so that the laboratory work can be carried out without risking the lives of the health care professionals in the laboratories.

SARS-CoV-2 has also created an opportunity for telecytopathology to prosper. Several studies have reported that remote facility telecytopathology can be used as an accurate modality in guiding appropriate tissue acquisition and final diagnosis. Dixit et al[95] reported that a total of 154 cases out of 161 were correctly diagnosed on smartphone-assisted telepathology (overall intraobserver concordance of 95.6%). For head and neck swellings, the concordance was 65/70 (92.9%), for breast lesions, it was 23/24 (95.8%), and for miscellaneous swellings, it was 57/57 (100%), whereas for urine cytology, the concordance rate was 9/10 (90%). Another study by Farrell et al[96] reported that the majority (99%) of ultrasound-guided FNAs demonstrated concordant preliminary assessments (using telecytology) with the final diagnoses. Point-of-care digital cytology with artificial intelligence is the new kid on the block and has shown promise to be implementable in rural, resource-constrained areas, and can achieve a diagnostic accuracy close to the level of highly trained experts.[97]

Even for training purposes, a study revealed that the students have responded positively to an online learning cytology program, where remote multiheader sessions were conducted by adapting the telecytology ROSE concept with an attached mobile device to the microscope. Students were keen to attend classes remotely in the future, even when the traditional in-classroom learning option becomes available.[98]

DISCUSSION

In conclusion, cancer is a growing burden internationally. In LMICs, this burden is heavier, mainly because of the need for resource-efficient methods of cancer prevention, diagnosis, and treatment. Cytopathology, if used appropriately, has the potential to lessen this burden, particularly through the accurate and cost-effective early diagnosis of cancer. The usefulness of cytopathologic techniques has been demonstrated via various studies even during the testing times of the COVID-19 pandemic. Additionally, to ensure sustainability, an innovative approach of bringing together local expertise, international technical assistance, and leadership and advocacy from local pathologists to move technical documents into public policy and practice has yielded commendable results.[99] Countries must invest in the future of cytopathology by providing enabling infrastructure and training opportunities for personnel, which ultimately require funding, political will, and good governance. The focus needs to be on integrating cytopathology into international and national cancer screening programs, as well as into diagnostic algorithms, teaching, and treatment programs, but the crucial step is to provide training for and increase the number of cytopathologists and cytotechnologists in LMICs.

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