

SHORT COMMUNICATION

Precision Medicine in Resource-Limited Settings: The Central Role of Pathology

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Precision medicine (also known as individualized or personalized medicine) is a novel approach that integrates genetic, environmental, and lifestyle data to drive medical care decisions. It aims to give more precise approaches to illness prevention, diagnosis, and treatment.(1) In oncology, precision medicine is based on the premise that malignancies are not all the same, and people may respond differently to therapies depending on their genetic, environmental, and lifestyle variables.(2) In high-income countries, precision medicine is frequently associated with genomics and molecular profiling. The most common cancers (lung, breast, colorectal, prostate, stomach) all require histopathological diagnosis and immunohistochemistry (IHC) (e.g. ER/PR/HER2 in breast cancer) as part of the WHO Essential Diagnostics framework. Therefore, precision medicine does not have to include expensive whole-genome sequencing. Accurate pathology, basic immunohistochemistry, morphology, and low-cost molecular diagnostics can all provide precision treatment.(3,4)

Immunohistochemical methods identify antigens in tissue slices using immunological and chemical responses. This approach is very sensitive and specific, detecting a wide range of antigens.(5) For example, IHC for ER, PR, and HER2 in breast cancer identifies molecular subtypes that guide treatment decisions. A recent study conducted in

Thailand determined that HER2 IHC (3+) predicted HER2 gene amplification with 94% specificity and 88% sensitivity and a positive IHC test result (score 3+) could potentially stand alone for commencing anti-HER2 therapy. IHC tests are inexpensive and simple, hence suitable for a developing country. In situ hybridization (ISH) or gene testing, on the other hand, turns out to be substantially more complex, time-consuming, and costly than IHC for HER2 status.(6) Therefore, IHC could serve as a powerful tool for precision medicine in resource limited countries like Pakistan, as it not only provides the diagnosis but also guides therapy. Another study by Gilani et al., reveals that a thorough histological examination of tumors, aided by immunohistochemistry surrogate markers and expert advice, can provide clinically useful precision medicine. Their findings show that just 10 of the 57 clinically significant genetic changes revealed could not be detected by IHC, allowing expensive genomic technologies to be saved for a limited proportion of undiagnosed neoplasms.(7)

While IHC provides a strong backbone for the diagnosis and treatment of cancer in resource limited settings, the scarcity of histopathological services in these countries raises serious concerns. A study by Zehra et al. reveals that only about 338 certified histopathologists serve the country (≈1 per 450,000 people). There are just 18 large histopathology labs in the country, the bulk of

which are situated in major cities, further delaying diagnosis for patients in remote locations.(8) Furthermore, in many lower middle income countries, pathology services are of poor quality. It has been demonstrated that poor pre-analytical control, especially delayed fixation and prolonged cold ischemia, seriously impairs immunohistochemical biomarker expression, leading to false-negative or deceptive results for clinically significant markers, such as ER, PR, HER2, and PD-L1.(9) Pathologists in low- and middle-income countries have insufficient control over cold ischemia time, resulting in protein breakdown and misleading IHC findings. The turnaround time substantially exceeds the two-day guideline suggested by the College of American Pathologists.(10)

For precision medicine to be successful in environments with limited resources, expensive genomic technologies are not necessary. As previously mentioned, precise histopathology can provide meaningful, practical precision care for common cancers when it is backed by basic immunohistochemistry and reasonably priced molecular tests. Research indicates that most clinically significant tumor changes can be detected by careful morphological evaluation in conjunction with IHC, saving costly genomic testing for a few complex cases. However, significant systemic obstacles, such as a lack of qualified histopathologists, inadequate laboratory infrastructure, subpar specimen handling, and lengthy turnaround times, limit the full potential of this pathology-lab-based precision medicine approach. It is crucial to close these gaps by funding pathology services, quality control, education, and decentralization. Improving pathology labs can turn precision medicine from a theoretical idea into a reality.

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