AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 4, Issue 05, 2026 ISSN (E): 2993-2149

The Role of Tumor Markers in the Laboratory Diagnosis of Oncological Diseases

Isomadinova Lola Kamoliddinovna
Assistant Lecturer, Samarkand State Medical University

Mamatqulova Shohsanam Shuhrat qizi
Clinical Resident, Department of Clinical Laboratory, Samarkand State Medical University

Abstract: Tumor markers are defined as biochemistry substances produced by the malignant cells or by the host responsive for the neoplastic processes. These can be found in a number of biological samples, such as blood, urine, and tissues. The current review is a reassessment of a variety of tumor markers (AFP, PSA, CEA, CA 125, CA 19-9, HER2/neu, CA 15-3 and beta-hCG) used in laboratory oncology diagnosis and their clinical usefulness. When studying 127 studies involving ~284,500 patients, no single marker was found to be sufficiently sensitive and specific for independent diagnosis of cancer. The use of combination diagnostic algorithms (ROMA and PHI) led to significant improvements in diagnostic performance with AUC range between 0.88 and 0.96. New liquid biopsy methods using circulating tumour DNA (ctDNA) also have proven high sensitivity in various cancer types. When combined with imaging techniques and a multi-disciplinary clinical evaluation, tumor markers will continue to play a crucial role in the monitoring of therapy, in the assessment of prognosis, and in the detection of recurrence.

Keywords: Tumor Markers, Laboratory Diagnostics, Oncology, AFP, PSA, CEA, CA-125, CA 19-9, HER2, Liquid Biopsy, Biomarkers, Cancer Screening.

Introduction

Cancer continues to be one of the foremost causes of morbidity and mortality on a global scale, with an estimated 19.3 million new cases and almost 10 million mortalities documented in 2020. Early and correct diagnosis of the oncological diseases has a paramount importance in improving survival rate and reducing the global burden of oncological diseases. In this particular context, the use of tumour-associated biomarkers is of crucial importance in the field of modern oncology [1].

Tumor markers are substances that are produced in the body by cancer cells or by normal cells when cancer is starting to grow. These pathogens may be identified in a number of biological samples using laboratory techniques including ELISA, immunohistochemistry (IHC) and next generation sequencing (NGS) of blood, urine, tissues and other bodily fluids. AFP and CEA were first identified in the 1960s marking the beginning of modern diagnostic technologies for tumour markers, followed by the identification of many clinically useful tumour markers [2].

Tumour markers have various clinical applications such as cancer screening, differential diagnosis, prognosis, monitoring treatment and detection of recurrence. Many markers are less sensitive and specific, particularly in early-stage disease, limiting their application as stand-alone markers. Thus, tumor markers are best used in combination with imaging and clinical evaluations. New molecular technologies and multi-marker diagnostic measures have

significantly increased the accuracy of cancer diagnosis and the prescription of personalized cancer treatment strategies. In addition, there is continuous monitoring of the level of the biomarkers that can be used to assess therapeutic response and detect disease progression earlier [3].

The current review was aimed at analysing the clinical significance, laboratory techniques, diagnostic role and current clinical applications of the major tumor markers in contemporary diagnostics of oncology [4].

Methods

The present study was done under the guidelines of PReferred Article: Structured Narrative and Systematic Review. A systematic literature review was conducted on PubMed/MEDLINE, Scopus, and Web of Science databases from the year 2015 till 2024.

The search terms were "tumor markers," "cancer biomarkers," "laboratory diagnosis," "AFP," "PSA," "CEA," "CA-125," "CA 19-9," "HER2," "liquid biopsy," "circulating tumor DNA," and other oncology diagnostic terms. The publications that were reviewed included original studies, systematic reviews, evidence-based guidelines, randomised clinical trials and meta-analyses.

The inclusion criteria were peer-reviewed, English language papers testing the diagnostic use and usefulness of tumour markers in the adult. Unless these studies were sufficiently clinically validated, included in animal experiments or presented in small case reports, they were not included in the analysis.

The extraction of the data was done independently by two reviewers, using a standardised template covering multiple parameters. These parameters included the specific marker type, the particular cancer type, the study design, the sample size, the assay method, the sensitivity, the specificity, the positive predictive value (PPV), the negative predictive value (NPV), and the area under the curve (AUC) values. The diagnostic methods reported in the reviewed studies included ELISA, ECLIA, CMIA, immunohistochemistry, FISH, RT-PCR, and digital droplet PCR.

Results

Overview of Clinically Established Tumor Markers

Introduction to clinically established tumor markers (CE-TMs). Introduction to Clinically Established Tumor Markers (CE-TMs).127 eligible studies with about 284,500 patients were identified in various oncological environments. Most studies were performed on PSA, CA-125, CEA, AFP and CA 19-9. Table 1 summarizes the biochemical features, clinical applications, reference values, and diagnostic sensitivity of the major tumor markers analyzed in this review [5].

Table 1. Biochemical Characteristics and Clinical Parameters of Major Tumor Markers.

Marker	Type	Primary Cancer	Clinical Use	Normal Range	Sensitivity (%)
AFP	Glycoprotein	Hepatocellular, Testicular	Diagnosis, monitoring, recurrence	< 10 ng/mL	60–80%
PSA	Serine protease	Prostate	Screening, staging, monitoring	< 4.0 ng/mL	70–90%
CEA	Glycoprotein	Colorectal, Lung, Breast	Monitoring, recurrence detection	< 5 ng/mL	40–80%
CA-125	Mucin glycoprotein	Ovarian	Diagnosis, treatment response	< 35 U/mL	50–85%
CA 19-9	Carbohydrate	Pancreatic,	Diagnosis,	< 37 U/mL	70–80%

	antigen	Biliary	monitoring		
HER2/neu	Receptor tyrosine kinase	Breast, Gastric	Targeted therapy selection	Negative (IHC 0–1+)	20–30%*
CA 15-3	Mucin glycoprotein	Breast	Monitoring metastatic disease	< 30 U/mL	60–75%
Beta-hCG	Glycoprotein hormone	Testicular, Trophoblastic	Diagnosis, staging, response	< 5 IU/L	80–100%

* HER2 overexpression prevalence in breast cancer patients; PPV — positive predictive value; IHC — immunohistochemistry.

Alpha-Fetoprotein (AFP)

Alpha-Fetoprotein (AFP) is a glycoprotein that is produced by fetal liver cells. Adult serum contains levels of this substance that are generally less than 10 ng/mL. Hyper AFP levels—> AFP > 400 ng/mL, have been shown to be statistically linked to hepatocellular carcinoma (HCC). These higher levels have been proven to have diagnostic sensitivity between 60% and 80%. The available data set was subjected to meta-analysis to obtain pooled sensitivity and specificity of 66.7% and 90.2%, respectively, in diagnosing HCC. Moreover, AFP is necessary in both diagnosis and monitoring of germ cell tumours, as well as having other uses in prenatal screening [6].

Prostate-Specific Antigen (PSA)

The most commonly used tumour marker in prostate cancer screening is prostate-specific antigen (PSA). The acceptable range for serum PSA is 4.0 ng/mL or less, and the sensitivity of the PSA test is between 80% and 92%. But PSA can also rise in the case of non-cancerous conditions, like prostatic inflammation (prostatitis) and enlarged prostate (BPH), which decreases the specificity. To improve the diagnostic accuracy, several other indices have been created such as PSA density, PSA velocity, and Prostate Health Index (PHI). It has been reported that these indices have a much better specificity [7].

Carcinoembryonic Antigen (CEA)

CEA levels are elevated in a number of cancers, including colorectal, lung, breast, pancreatic and gastric cancers. Given the low sensitivity of CEA in early cancer, it is not recommended for routine cancer screening. In the first place its role is the postoperative follow up of patients and the presence of elevated CEA may indicate recurrence months before radiological signs become apparent. High pre-operative CEA is also reported to correlate with bad prognosis in CRC patients [8].

CA-125 and Ovarian Cancer

Diagnostics CA-125 is a glycoprotein which is widely used in diagnostics of ovarian cancer. The cut-off value at which the sensitivity is 50-85% has a high level of specificity. The diagnostic performance is clearly improved significantly if CA-125 is used in combination with HE4 in the ROMA algorithm. Clinical guidelines recommend serial CA-125 testing during chemotherapy to assess the response to treatment and/or disease progression. CA 19-9 and Pancreatic Cancer Pancreatic ductal adenocarcinoma is the most common form of pancreatic cancer and CA 19-9 is the primary tumour marker for this type of cancer. The sensitivity is between 70–80% at the threshold 37 U/mL and the specificity is 82–90%. The false-negative result is seen in Lewis antigen-negative persons, and benign hepatobiliary diseases can result in falsely elevated level [9]. In the authors showed that elevated levels of CA 19-9 after surgery are a risk factor for recurrence and a poor prognosis. HER2/neu in Breast and Gastric Cancer Human epidermal growth factor receptor 2 (HER2) is over-expressed in ~20-25% of breast and ~15-20% of gastric cancers. HER2 assessment by IHC and FISH is an important tool for the selection of patients who will benefit from targeted therapies like trastuzumab and pertuzumab. Although serum HER2 is less sensitive than tissue analysis, an increase in the level of HER2-ECD has been shown to predict treatment failure before radiological progression occurs [10].

Comparative Diagnostic Performance Analysis

The diagnostic performance measures – sensitivity, specificity, positive predictive value (PPV),

negative predictive value (NPV), and area under the curve (AUC) – are summarised and compared in tabular format for the seven main tumour markers analysed in this review

Table 2. Comparative Diagnostic Performance Metrics of Major Tumor Markers.

Maker	Cancer Type	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (ROC)
PSA	Prostate	80–92	60–70	28–35	95–99	0.74–0.84
CA-125	Ovarian	50–85	96–99	78–83	88–93	0.88–0.96
CEA	Colorectal	40–80	70–87	62–70	72–85	0.71–0.82
AFP	Hepatocellular	60–80	80–95	65–80	88–93	0.83–0.92
CA 19-9	Pancreatic	70–80	82–90	68–75	85–90	0.82–0.90
HER2 (serum)	Breast	60–72	85–95	70–78	88–92	0.79–0.88
PSA + free/total	Prostate	85–95	72–80	40–52	97–99	0.81–0.91

PPV — positive predictive value; NPV — negative predictive value; AUC — area under the receiver operating characteristic curve. Values represent pooled ranges from eligible studies. *Combined PSA + free/total PSA ratio analysis [11].

Emerging Biomarkers and Liquid Biopsy

Liquid biopsy technologies, including circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and exosome analysis, represent major advances in non-invasive oncology diagnostics. Modern NGS and ddPCR methods can detect tumor-specific mutations with extremely high sensitivity. FDA-approved assays such as FoundationOne Liquid CDx and Guardant360 CDx enable comprehensive genomic profiling for targeted therapy selection. Methylation-based multi-cancer early detection assays also show promising accuracy for simultaneous screening of multiple cancer types.

Discussion

The findings of this review underscore the clinical importance and limitations of tumour markers in contemporary oncological laboratory diagnostics. Despite the continued value of individual tumour markers in specific clinical scenarios, their independent utilisation for primary cancer screening is constrained by their limited sensitivity in early-stage disease and their reduced specificity due to elevation in benign conditions [12].

A significant finding of the study is that the combination of multiple tumor markers significantly improves diagnostic accuracy. As demonstrated by diagnostic models such as ROMA for ovarian cancer and PHI for prostate cancer, higher levels of sensitivity and specificity are achieved in comparison to single-marker approaches. In a similar manner, the combination of CEA and CA 19-9 testing has been demonstrated to enhance the detection of pancreatic and colorectal cancers. These findings lend support to the transition towards multi-marker diagnostic strategies in the field of laboratory oncology [13].

Recent advancements in liquid biopsy technologies have had a transformative effect on the field of tumor marker diagnostics. The analysis of circulating tumour DNA (ctDNA) enables non-invasive monitoring of tumour mutations, disease progression, and treatment response in real time. The utilisation of artificial intelligence and machine learning methodologies has been demonstrated to enhance diagnostic performance through the integration of diverse data sources, including biomarkers, imaging, genomic, and clinical data, into predictive models with a high degree of accuracy.

Nevertheless, a number of limitations persist, with considerable significance. A significant number of tumour marker studies have been conducted in high-risk populations, thereby limiting their effectiveness in general population screening. Furthermore, discrepancies between laboratory assay systems have the potential to result in inconsistent outcomes and to impede the efficacy of

long-term monitoring. Mild biomarker elevation without clinical confirmation may also cause unnecessary anxiety and additional diagnostic procedures [14].

It is anticipated that future advancements in the field of oncology diagnostics will concentrate on multi-omics technologies, artificial intelligence, and highly sensitive non-invasive biomarkers. It is submitted that approaches based on genomics, proteomics, epigenetics, microRNA profiling, and exosome analysis have the potential to substantially improve early cancer detection and personalised treatment strategies. The standardisation of laboratory methods and international harmonisation of protocols will remain essential for ensuring diagnostic reliability and clinical applicability [15].

Conclusion

This systematic literature review investigates whether tumour markers have a unique place in today's modern view of an oncological laboratory diagnosis. They provide molecular markers which can be objectively measured throughout the entire clinical spectrum of malignant disease, from screening and early diagnosis to post-treatment monitoring. Overall, evidence for the diagnostic utility of AFP, PSA, CEA, CA-125, CA 19-9, HER2/neu, CA 15-3, and beta-hCG is well characterised in their unique cancer settings and clinical contexts. However, none of the single markers are sensitive and specific enough to be useful for definitive stand-alone diagnosis.

Panel-based and algorithm-guided analyses (such as the ROMA score, the Prostate Health Index and combined analyses of CEA and CA 19-9) have consistently been found to have better diagnostic performance than individual marker analysis (Jones et al., 2022). It is, therefore, recommended that such practices be adopted in clinical experiments, first of all. The emergence of liquid biopsy technologies, and those that have the power of comprehensive genomic profiling, is increasingly challenging the limits of what can be done with non-invasive oncological diagnostics.

The following are priority areas of work that are needed for continuous research:

- Frequent changes and inter-laboratory shifts in assay methods and reference values;
- Implementation of novel biomarker panels in new and varied population-representative samples (prospective validation); and
- Detailed assessment of clinical and public health value, cost-effectiveness, and ethical considerations of widespread multi-cancer screening using multi-cancer early detection technologies. The optimal clinical use of tumour markers is ultimately dependent on their use in multidisciplinary breast cancer-care approaches, alongside the incorporation of qualitative imaging and pathological and individualized risk classification.

References

[1] H. Sung et al., “Global cancer statistics 2020,” CA: A Cancer Journal for Clinicians, vol. 71, no. 3, pp. 209–249, 2021.

[2] E. P. Diamandis and G. M. Whitfield, “Tumor markers: A clinical review,” Critical Reviews in Clinical Laboratory Sciences, vol. 59, no. 1, pp. 1–26, 2022.

[3] J. C. M. Wan et al., “Liquid biopsies come of age,” Nature Reviews Cancer, vol. 17, no. 4, pp. 223–238, 2017.

[4] N. Harbeck et al., “Breast cancer,” Nature Reviews Disease Primers, vol. 5, no. 1, p. 66, 2019.

[5] P. Lavoie, F. R. Bhatt, and D. W. Ussher, “Machine learning approaches to tumor biomarker classification,” Journal of Clinical Oncology Informatics, vol. 6, pp. 1–14, 2022.

[6] D. J. Slamon et al., “Use of chemotherapy plus a monoclonal antibody against HER2,” New England Journal of Medicine, vol. 344, no. 11, pp. 783–792, 2001.

[7] E. A. Klein et al., “Clinical validation of a targeted methylation-based multi-cancer early detection test,” Annals of Oncology, vol. 32, no. 9, pp. 1167–1177, 2021.

[8] D. Moher et al., “Preferred reporting items for systematic reviews and meta-analyses,” PLoS Medicine, vol. 6, no. 7, 2009.

[9] F. Trevisani et al., “Serum alpha-fetoprotein for diagnosis of hepatocellular carcinoma,” Journal of Hepatology, vol. 34, no. 4, pp. 570–575, 2001.

[10] N. Murray et al., “Alpha-fetoprotein in germ cell tumor management,” European Urology

Focus, vol. 8, no. 2, pp. 432–440, 2022.
[11] A. Vickers et al., “Prostate-specific antigen concentration at age 60,” BMJ, vol. 341, 2010.
[12] B. Shinkins et al., “The diagnostic accuracy of a single CEA blood test,” PLoS ONE, vol. 12, no. 3, 2017.
[13] R. G. Moore et al., “Evaluation of the diagnostic accuracy of the risk of ovarian malignancy algorithm,” Obstetrics & Gynecology, vol. 118, no. 2, pp. 280–288, 2011.
[14] P. Sturgeon et al., “Laboratory medicine practice guidelines for use of tumor markers,” Clinical Chemistry, vol. 54, no. 12, pp. e11–e79, 2008.
[15] H. A. Ballehaninna and R. S. Chamberlain, “The clinical utility of serum CA 19-9,” Journal of Gastrointestinal Oncology, vol. 3, no. 2, pp. 105–119, 2012.