

**Review of Biomarkers for Gastric Cancer Early Detection
and Current Knowledge of Potential Biomarkers**Aniss Afifa Saidin^a, Tengku Idzzan Nadzirah Tengku Idris^{a*}**Structured Abstract**

Background: Gastric cancer (GC) ranks fifth globally in cancer diagnoses and fourth in cancer-related deaths, which are made worse by late-stage diagnosis. This review discusses the importance of developing better early detection techniques for GC. The review examines the global burden of GC, influenced by lifestyle and microbial factors, as well as genetic changes and abnormalities in molecular pathways that play a major role in GC development and progression. It also explores diagnostic tools, histological classifications, and current biomarkers for GC detection, including HER2, PD-L1, CEA, and CA19-9, as well as novel biomarkers like TRIM3 and GKN1 that show promise for early detection.

Methods: Biomarkers for identifying GC at different stages were analyzed using academic literature and research articles from academic databases such as PubMed, Scopus, ScienceDirect, Web of Science, and Google Scholar. Current biomarkers (HER2, PD-L1, CEA, and CA19-9), and novel biomarkers (GKN1 and TRIM3) were analyzed for their expression, detection stages or GC classification, detection challenges, and their role in GC. An analysis of the advantages and disadvantages of using biomarkers in the early diagnosis of GC was also conducted.

Results: HER2 overexpression is associated with more aggressive GC and poorer prognosis but can guide targeted therapy like trastuzumab. PD-L1 expression inhibits T-cell immunity, allowing it to evade the immune system, and correlates with advanced GC and poor outcomes. CEA levels can indicate cancer progression and metastasis, while elevated CA19-9 is associated with advanced disease and aggressive biological behavior. Novel biomarkers like GKN1, a tumor suppressor, and TRIM3, involved in cancer cell invasion and metastasis, show promise but require further validation. Better patient outcomes, personalized treatments, and less invasive monitoring via liquid biopsies are made possible by biomarkers. However, current biomarkers' limited sensitivity and specificity, heterogeneity of tumors, and interpretation difficulties make them less efficient for early GC diagnosis.

Conclusion: Improvements in diagnostic technologies, such as molecular tumor profiling and non-invasive liquid biopsies, are crucial for enhancing biomarker sensitivity and specificity. Future research should focus on validating novel biomarkers across diverse populations and utilizing advanced genetic and molecular techniques to improve early detection and reduce the global GC burden.

Keywords: Gastric Cancer, Non-Invasive Early Detection, Prognostic Biomarkers, Predictive Biomarkers, Personalized Therapy

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