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The Critical Role of Biochemical Markers in the Early Diagnosis of Chronic Diseases

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Abstract:

Biochemical markers play a pivotal role in the early detection and management of chronic diseases, offering clinicians valuable insights into disease onset, progression, and therapeutic response. This review highlights key biochemical markers commonly used in the diagnosis of cardiovascular diseases, diabetes, liver and kidney disorders, and various types of cancer. The review discusses the long and short-term risk factors for various diseases, disease progression, and prevention. Also, show the extent of the individual's response to treatment, positively or negatively, and the probability of the disease recurrence and progression. Biochemical markers help identify early symptoms and signs by providing a biochemical assessment of various physiological disorders. This review aims at an integrated assessment of the importance of biomarkers in the early detection of chronic diseases by collecting information and evidence and identifying their trend. This review also attempts to demonstrate the diagnostic utility of biomarkers, their clinical applications, and their ability to enhance patient outcomes and improve their response to treatment.

Keywords: Biomarkers, Chronic Diseases, Early Diagnosis, Common Markers, chronic disorders.

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1. Introduction

Biochemical markers are pioneering biophysical and biochemical indicators that precisely measure changes in the concentrations of metabolites, enzyme activities, and levels of proteins secreted during biosynthesis. They track and define various physiological and pathological processes (M. Al-hadlaq et al., 2022). At present, there is a huge volume of information about laboratory and biochemical parameters that are correlated with the onset of various diseases. They reflect short- and long-term exposure to risk factors, early tissue alteration before symptom onset, disease progression, and the effectiveness of early preventive interventions. They are highly specific and sensitive for the early detection of pathological processes, for monitoring therapeutic efficacy, or for use in high-throughput screening platforms (Basgauda Patil & Ramesh Patil, 2011). This review discusses these biomarkers, their clinical limitations, recent advancements in biosensor technology that enable rapid analysis, and the obstacles to commercial adoption of these biosensors.

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2. Overview of Chronic Diseases

Chronic diseases are illnesses that usually have a long duration and whose progression is generally slow. The burden of these conditions has been steadily increasing; for example, they were responsible for 87.4% of all years lived with disability in 2019 (M. Al-hadlaq et al., 2022).

3. Biochemical Markers

Clinical biochemistry, or clinical chemistry, is an essential discipline in medical laboratories that gains clinical information from a patient's body fluids (Turgeon, 2022). Most clinical biochemistry analyses are performed on serum, plasma, and urine, but other body fluids include cerebrospinal fluid, synovial fluid, pericardial fluid, peritoneal fluid, joint fluid, and serous fluid (Leal et al.2025). A key method for characterizing biochemical phenomena involves the analysis of a large group of biological molecules (biomarkers) according to their chemical composition (Ahmad et al., 2023).

A biomarker is a tool used by healthcare professionals to measure and indicate biological processes, pathogenic processes, or responses to interventions. Biomarkers must be non-invasive, inexpensive, and exhibit high specificity and sensitivity to enable early detection and differentiation between normal and diseased states. They are classified into three types: diagnostic, predictive, and prognostic (M. Al-hadlaq et al., 2022). Diagnostic biomarkers assist in identifying diseases and assessing the success of treatments. Predictive biomarkers identify individuals who are more likely to respond positively or adversely to treatments or environmental exposures. Prognostic biomarkers indicate the likelihood of disease recurrence, progression, or future clinical events and are often measured at baseline (Bodaghi et al., 2023).

4. Biochemical Markers in Cardiovascular Diseases

Cardiovascular diseases include heart diseases affecting the vessels or heart structure and thromboembolic diseases, leading to complications like acute coronary syndrome, heart failure, and chronic kidney disease (Robinson, 2021). A recent survey of physicians highlighted the importance of fast biomarker results, especially for Troponin, D-dimers, and Brain Natriuretic Peptide (BNP), which are critical in cardiovascular diagnosis. Faster results can save time, improve clinical decision-making, and enable quicker patient referral (Du et al.2021)(Netala et al.2025) (Abensur Vuillaume et al., 2022).

4.1. Common Markers

Blood glucose is measured as the fasting plasma glucose after 8 hours without food, measured in milligrams per deciliter (mg/dL). Values greater than 125 mg/dL (7.0 mmol/L) trigger further investigation and possible diagnosis of diabetes. Hemoglobin A1C (HbA1C) measures the percentage of hemoglobin carrying glucose. Normal values range from 4% to just below 5.7%. HbA1C above 6.5% indicates diabetes (Walter et al.2025)(Mittal et al.2025).

Because biochemical markers exist for multiple pathways of cellular and systemic dysfunction, they can be used to evaluate conditions such as cardiovascular disease, cancer, arthritis, and so on. For example, prostatic-specific antigen (PSA) may be high during the early development of prostate cancer, but the specificity is poor because PSA can also be elevated by prostatic hyperplasia (Ahmad et al., 2023)(Wang et al., 2021). Although consideration of each marker alone has limitations, a suite of markers, combined with a thorough clinical evaluation, can aid in early diagnosis and continuous monitoring (Sarhadi & Armengol, 2022).

4.2. Diagnostic Implications

Biochemical measurements can indicate healthy or pathological processes, serving as markers for early disease detection. Chronic diseases—conditions persisting over extended periods—underlie a large portion of premature deaths worldwide and manifest with diverse signs and symptoms (Nair et al., 2024). Because symptoms may be non-specific, biochemical markers play an increasingly vital role in diagnosis, prognosis, and long-term monitoring, providing healthcare professionals with indispensable tools (M. Al-hadlaq et al., 2022).

5. Biochemical Markers in Diabetes

Diabetes mellitus, characterized by sustained hyperglycemia, manifests in various forms, including insulin-dependent diabetes mellitus (IDDM) or type 1 diabetes, and non-insulin-dependent diabetes mellitus (NIDDM) or type 2 diabetes. IDDM results from the autoimmune destruction of pancreatic β-cells, leading to insulin deficiency, whereas NIDDM arises due to decreased insulin secretion coupled with peripheral tissue resistance to insulin action (Ahonen et al., 2019) (Yameny, 2024). Early diagnosis of diabetes is paramount for effective management and prevention of complications. Failure in glucose homeostasis may lead to ketoacidosis—a common diabetic emergency signifying disease onset—and subsequent complications that can culminate in multi-organ failure (Hameed et al., 2020) (Yameny, 2025). Biochemical markers for early diabetes diagnosis encompass glucose, fructosamine, glycosylated hemoglobin (HbA1c), β-cell autoantibodies, and lipid profiles (Almheiri et al.2023). They crucially support early identification, patient stratification, and management in the context of a complex syndrome characterized by multiple defects. Metabolite profiling initiatives have identified circulating amino acids, such as 2-aminoadipic acid, alongside lipid species, as early signature biomarkers for type 2 diabetes (T2DM) (Czajkowska et al.2022).

5.1. Key Biomarkers

Biomarkers are tools used by health professionals to measure and indicate pathogenic or biological processes, exposure, or response to interventions. They should be non-invasive, inexpensive, with high specificity and sensitivity to enable early detection and differentiation between normal and pathological states (Al-Hadlaq et al.2022). Biomarkers are classified into diagnostic, predictive, and prognostic types. Diagnostic biomarkers help identify and differentiate diseases. Predictive biomarkers indicate the likelihood of response to environmental or medical interventions, often used in clinical trials. Prognostic biomarkers predict disease recurrence, progression, or future clinical events, and are measured at baseline (Tarighati et al., 2023). Chronic diseases are long-lasting, often progressing slowly, with an increasing burden in terms of disability (M. Al-hadlaq et al., 2022).

5.2. Early Detection Strategies

Early detection is critical for improving the management of chronic conditions. A timely diagnosis enables early intervention, which can slow or halt the progression to disabling complications (Makhmirzaeva et al.2025). However, many chronic diseases remain asymptomatic during their initial stages, creating a need for reliable screening tools and diagnostic tests (Makhmirzaeva et al.2025). Examples include cardiovascular disease, which can be life-threatening, and cancer, where prognosis hinges on the earlyness of detection (Sharma et al.2023).

6. Biochemical Markers in Cancer

Many types of cancer evade detection until the disease has advanced beyond the curable stage (Jiang, 2012). Innovations in microscopic imaging have not improved early detection for most cancers, and screening is accessible or practical for only a small subset (Fitzgerald et al., 2022). Accurately assessing biological alteration could enable earlier

diagnosis, enhancing the effect of current and future therapies (Passaro et al.2024). Cancer biomarkers provide a method to differentiate between healthy and diseased states. They represent cellular, biochemical, and molecular alterations that identify or monitor critical biological processes in the body, including disease presence. A blood or tissue biomarker can be a tumor-secreted molecule or a specific response to the cancerous process. Genomic, transcriptomic, proteomic, and metabolomic changes are found in many cancers, none of which is individually sufficient for cancer detection (Sarhadi & Armengol, 2022)(Das et al., 2023). Combinations of biomarkers have demonstrated utility in the recognition of malignant disease (Das et al., 2023).

Cancer biomarkers appear at all stages of the disease, from initiation through progression, metastasis, and response to therapy. Many individuals succumb to cancers with an undefined primary site, and biomarkers can inform these diagnostic challenges. Far from representing a rigid set of proteins or mutations, cancer biomarkers reflect the physiological status of a cell in a particular phenotypic state during disease progression. They encompass virtually any type of molecular alteration associated with the malignant process (Das et al., 2023).

6.1. Tumor Markers

Tumor markers can be broadly defined as substances produced by either the tumor or host response that indicate the presence of cancer or provide information about the probable behavior of the cancer (J. Duffy, 2012). Such markers might also be used in a screening setting to identify cancers before symptoms become apparent, or to confirm the presence of a cancer when clinical suspicion arises (Crosby et al.2022). An ideal tumor marker has high sensitivity and specificity, is readily and repeatedly measurable by a simple, standardized assay, is acceptable to patients, and has demonstrable clinical utility and validation (Matsas et al.2023). A range of tumor markers has been described, and many are used in routine clinical practice. Carcinoembryonic antigen (CEA), first described definitively in 1965, is one such tumour marker in clinical practice (Sharma, 2009). Other tumour markers commonly used include alpha-fetoprotein (Yameny et al, 2023), human chorionic gonadotropin, CA 15-3, and CA125 (Matsas et al., 2023). A very large number of additional markers, including enzymes, hormones, oncofetal antigens, receptors, and tumor-associated antigens, have been described; their clinical utility remains under investigation (Loi et al.2021).

6.2. Screening and Monitoring

An essential requirement of biomarkers is their capacity to delineate subjects with a normal physiological condition from those with pathology (M. Al-hadlaq et al., 2022). One of their foremost roles is found in screening and monitoring, for which biomarkers should be non-invasive, inexpensive, and sensitive at the early stage of the disease. Biomarkers may be classified into three groups, which are diagnostic, predictive, and prognostic (Saman et al.2022). The diagnostic biomarker may be used for the identification and differentiation of diseased individuals (Dubois et al.2023).

7. Biochemical Markers in Kidney Diseases

Chronic kidney disease (CKD) is characterized by a progressive decline in renal function, ultimately leading to end-stage renal disease (ESRD). The role of biochemical markers is of fundamental importance to allow early diagnosis and to help identify patients with a high risk of progression and complications (Lousa et al., 2020).

Early diagnosis of renal diseases may contribute to the prevention and/or prediction of progression to CKD and ESRD (Lamprea-Montealegre et al., 2021). Initial diagnosis is based on the detection of proteinuria or the elevation of serum creatinine (Ali

et al.2025). Proteinuria has limitations regarding specificity and ability to predict renal injury before the onset of fibrosis (Phanish et al.2021). The creatinine level is greatly influenced by muscle mass and does not accurately represent glomerular filtration rate during the onset of disease and loss of renal mass (De Rosa et al., 2023). An ideal protein marker correlates to early injury, has specificity for renal disease, correlates to the extent of early fibrosis and progression, and can easily be measured (Barinotti et al.2022).

Three biomarkers are being evaluated as potential markers of renal disease: folate receptor alpha (FRA), mesothelin (MSLN), and megakaryocyte potentiating factor (MPF). FRA is a glycosylphosphatidylinositol-anchored membrane protein present at high levels on the apical surface of cells in a limited number of normal tissues. MSLN is also present in a limited number of normal cells, and MPF is the soluble cleavage product of the mesothelin pro-protein. These proteins are produced at high levels in some cancers and are currently being evaluated as serum diagnostic and prognostic markers for several malignancies (Mizdrak et al.2022). These three proteins are filtered by the kidney and are readily detected in human urine (Zhang et al.2022). Preliminary data indicate that the renal clearance of these proteins is reduced and that the serum and urine levels of each increase in subjects with renal disease (Cheng et al., 2023).

Furthermore, these proteins are highly associated with fibrosis, and the level of each protein increases with disease stage (Antar et al.2023). The ability to predict progression of disease was also assessed by evaluating changes in serum level over time during the six-month longitudinal segment of a CKD study, where a systematic rise indicated patients with rapid progression (B Somers & J O'Shannessy, 2014).

7.1. Relevant Biomarkers

A biomarker is used by healthcare professionals to measure and indicate disease processes, exposures, or responses to interventions (Ahmad et al., 2023). It should be non-invasive, inexpensive, with high specificity and sensitivity for early detection, aiding in distinguishing normal from pathological states (Chacko & Ankri, 2024). Understanding disease biology can improve prevention and treatment, emphasizing the need for thorough studies before routine clinical implementation (Horwitz et al.2021). Biomarkers are classified as diagnostic, predictive, and prognostic. Diagnostic biomarkers aid in disease diagnosis and differentiation, while predictive biomarkers identify individuals more likely to respond to specific environmental agents or treatments. Prognostic biomarkers predict disease recurrence, progression, or future clinical events, often measured at baseline (Tarighati et al., 2023). Chronic diseases are long-lasting, usually slow in progression, and have seen increased disability years according to recent studies (M. Al-hadlaq et al., 2022).

7.2. Clinical Applications

In clinical practice, biochemical markers demonstrate promising potential in the early diagnosis of chronic diseases. Before implementation, it is essential to prospectively assess these markers in large populations across extended durations and to validate their correlation with disease severity (M. Al-hadlaq et al., 2022).

8. Biochemical Markers in Liver Diseases

Early diagnosis of chronic liver disease (CLD) is crucial for effective management and potential reversal of fibrosis and cirrhosis (Ginès et al.2022). Proteomic approaches have identified proteins released from the liver into circulation as indicators of liver dysfunction, representing a promising source of biomarkers (Niu et al.2022). Advances in analytical technology enable the generation of

extensive catalogues of biomarker candidates, which require rigorous validation to establish performance characteristics, accuracy, and clinical utility (Ahmad et al., 2023). Controlling critical parameters that affect the validation process is essential to address common pitfalls in biomarker discovery and to facilitate the development of evidence-based markers that satisfy regulatory standards (Ng et al., 2023). Integration of such biomarkers into clinical practice depends on coordinated efforts among research laboratories, the diagnostics industry, and clinical laboratories. Rapid progress in companion diagnostics (CDx) offers cost-effective strategies for the management of CLD (Sumanth Nallagangula et al., 2018).

Liver diseases pose a significant and growing global health burden (Younossi et al.2023). Conventional blood markers, including alanine aminotransferase and aspartate aminotransferase, are limited by suboptimal accuracy (Shipman and Shipman2024). Despite its drawbacks, liver biopsy remains the diagnostic gold standard due to the absence of reliable non-invasive alternatives (Neuberger & Cain, 2021). Liquid biopsy—a minimally invasive technique based on the detection of circulating disease-associated particles such as proteins and RNA molecules in biological fluids—has recently gained attention for its potential in the diagnosis, prognosis, and monitoring of liver diseases (Ma et al.2024). Histones, as the core components of nucleosomes, play important roles in the regulation of fundamental nuclear processes and are released into the circulation following cell death or immune system activation. They exhibit remarkable stability in peripheral blood and retain diverse post-translational modifications. Recent developments in the identification of histone-mediated liquid biopsy approaches for liver diseases are summarized (K. Tsoneva et al., 2023).

8.1. Liver Function Tests

Liver function tests (LFTs) comprise a panel of biochemical assays that provide information on various aspects of hepatic physiology (Lala et al., 2023). Common LFTs include alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), serum bilirubin, albumin, and coagulation parameters such as prothrombin time (PT) and international normalized ratio (INR) (Gupta & Walker, 2021). Monitoring the concentrations of these analytes facilitates the evaluation of hepatocyte integrity, cholestatic processes, synthetic capacity, and disease progression (Tabernilla et al.2021).

8.2. Diagnostic Challenges

Initially, clinical findings and semiological considerations dominated the early disease-diagnosis process (Stempsey, 2024). Pathological anatomy eventually superseded clinical scrutiny by providing evidence of the underlying pattern of disease (Pisapia et al.2022). The advent of radiography and culture techniques added new methods to the diagnostic armory, but pathological anatomy again dominated for many years (Kowalczyk, 2021). Not until chemical analysis became accurate and repeatable, with normal values established, did pathology begin to be overcome (Keren et al.2022).

Chemical testing immediately established itself in the field of diagnosis, yet was rapid and prone to interference and erroneous results (Goumas et al.2025). Although there are various ways to understand and appreciate the medical concept of diagnostic tests, the science of biochemistry is recognized as the highest level for evaluating them (Han et al.2024). The early diagnosis of chronic disease employs the techniques of serum chemical analyses to search for the presence of specific biochemical markers in the system (Al-Hadlaq et al.2022). When detected, they establish, with

reasonable probability, the presence of existing pathology caused by several types of chronic diseases such as diabetes, cirrhosis, acute inflammation, and cardiovascular disease (Sato et al.2023). The presence of these biochemical markers alone allows for the estimation of the nature of the disease without any knowledge of the nature or site of the pathology involved (M. Al-hadlaq et al., 2022).

9. Conclusion

In conclusion, early detection of chronic diseases is a major concern worldwide. Chronic diseases are responsible for around 70% of the deaths worldwide. The use of biochemical markers possesses promising approaches towards the early diagnosis of chronic diseases. Some major chronic disorders, such as cardiovascular diseases, diabetes, cancer, kidney diseases, and liver diseases, are discussed, along with their biochemical marker and diagnostic methodologies. Conventional diagnostic techniques are based on imaging and other clinical investigations. These methods provide specific information about the site and extent of the disease, but most of these are based on major signs and symptoms. Biochemical assessment offers information about the various physiological disturbances, which helps to identify the early signs of the disease. The diagnosis of some major diseases can be improved by the prediction of biochemical markers in various biological fluids that can be used for reliable, accurate, and rapid analysis. Although many strategies are available, early detection of chronic diseases remains a crucial and challenging task for medical researchers and practitioners. Biochemical markers extracted from saliva offer detection and analysis as critical diagnostic fluids; they are easily accessible, non-invasive. In view of these advantages, saliva is a promising diagnostic constituent with the potential to replace conventional strategies. Hence, more attention is required to develop micro- and nano-based biochemical markers for the early diagnosis of chronic diseases for the benefit of human health.

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