THE ROLE OF BIOMARKERS IN THE DIAGNOSIS AND TREATMENT OF DISEASES

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ABSTRACT

The document provides an extensive review of biomarkers, highlighting their significance in disease detection, care, and observation across numerous illnesses, such as cancer, diabetes, cardiovascular diseases, and neurodegenerative disorders. Biomarkers, defined -as quantifiable biological indicators, perform a pivotal involvement in early disease detection, prognosis, and personalized therapy. The review categorizes biomarkers into diagnostic, prognostic, predictive, pharmacodynamic, and safety types, emphasizing their application in predicting outcomes, monitoring disease progression, and guiding treatment decisions.

For instance, in infectious diseases, procalcitonin (PCT) serves as a biomarker for bacterial infections, aiding in antibiotic therapy. Biomarkers in neurodegenerative disorders such as Alzheimer's disease's tau and amyloid-beta proteins provide early diagnostic insights. Similarly, cancer biomarkers like PSA and circulating tumor DNA enable early detection and treatment personalization. For diabetes, traditional biomarkers like HbA1c and novel ones like miRNAs are explored for better disease management.

The review also discusses advancements in omics technologies and liquid biopsy methods, enhancing biomarker discovery and application. Challenges in integrating multi-omics data and ensuring biomarker validity are acknowledged, pointing to the need for standardized protocols and further research to optimize clinical utility.

Keywords:- *Biomarkers, Personalized Medicine, Diagnosis and Prognosis, Therapeutic Monitoring, Neurodegenerative Disorders, Cancer Biomarkers*

1. INTRODUCTION

Biological markers, also known as biomarkers, are quantifiable indicators of disease states, physiological processes, or reactions to treatment. Their contribution to illness diagnosis, prediction, and treatment has grown dramatically in recent years, transforming personalized medicine and enhancing patient outcomes. These molecular, cellular, or biochemical compounds can be found in tissues, bodily fluids, or imaging investigations. They offer insights into the progression of a disease, its occurrence, and the body's response to treatment. Biomarkers encompass genes, proteins, genetic variations, and metabolic expression differences derived from various sources, including body fluids and tissues [1].

Biomarkers aid in the early diagnosis of diseases, frequently before symptoms appear, allowing for more efficient management and prompt therapies. They might also be crucial in predicting the likelihood of complications, recurrence, or the course of the illness. Biomarkers are used in therapy to help choose the best course of action,

track its efficacy, and modify it according to each patient's unique reaction [1].

As we move toward increasingly tailored therapeutic methods, precise medicine—which optimizes treatment according to each distinctive lifestyle, environmental, and genetic traits of the patient—may benefit from the application of biomarkers in the context of clinical practice. This introduction examines the changing role of biomarkers in medicine, emphasizing their importance in improving diagnosis and treatment as well as their promise to make healthcare a more efficient and individualized system [1][2].

2. AN OVERVIEW OF BIOMARKERS

Biological indicators known as biomarkers offer quantifiable proof of a particular physiological or pathological process or a pharmacological reaction to a treatment. These indicators can be chemicals like proteins, nucleic acids, or metabolites, or they can be more complicated structures like cells or tissue properties. As a result, biomarkers are essential instruments in clinical research, medication development, and medicine [2].

Based on their potential uses, several biomarker subtypes have been identified. Crucially, Just one biomarker may satisfy numerous requirements Regarding several uses for; however, It is essential to establish proof for every definition. Definitions could therefore overlap, but Additionally, they have distinct characteristics that identify specific applications [2].

3. TYPES OF BIOMARKERS:-

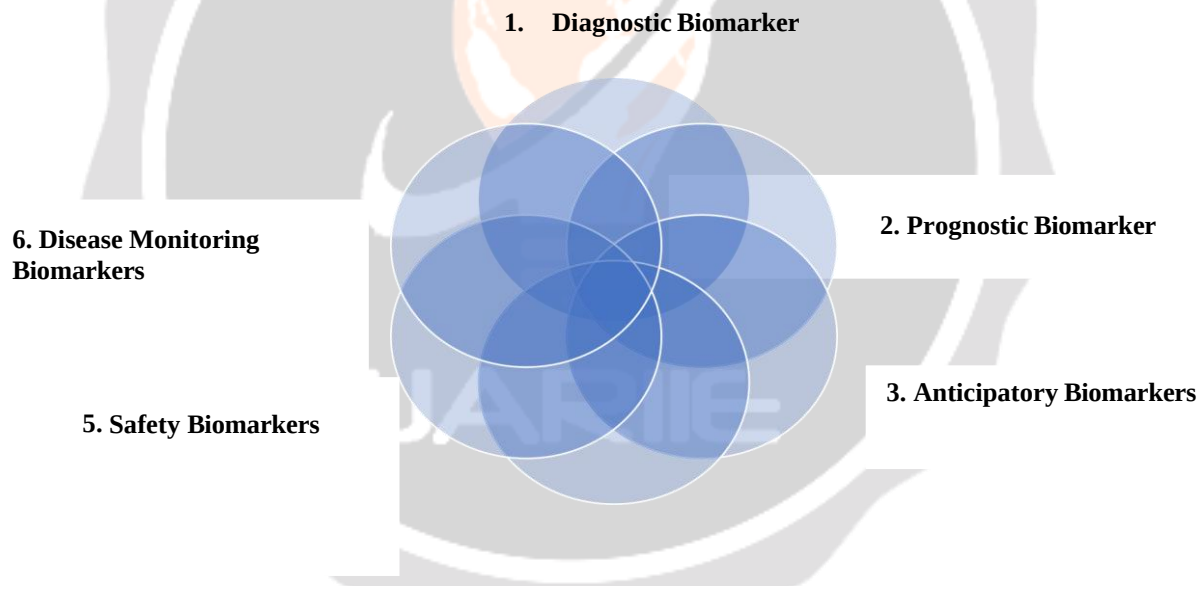

Fig-1: Types of Biomarker

3.1 Diagnostic Biomarkers:-

These indicators are used to find out whether a disease or condition is present, usually early on, before symptoms show up. Tumor markers, such as glucose levels in diabetes or Antigen specific to the prostate (PSA) in cancer of the prostate, are used as diagnostic indicators of these conditions [3].

3.2 Prognostic Biomarkers:-

These biomarkers assist predict outcomes like disease progression, recurrence, or survival by offering information about the likely course of an illness or condition. For instance, some cancer-related genetic abnormalities (such

BRCA1/2) may signal an increased risk of metastasis or disease recurrence, which may have an impact on patient counseling and treatment plans [3].

3.3 Anticipatory Biomarkers:-

Biomarkers for prediction are useful tools for predicting a patient's reaction to a particular treatment. The epidermal growth factor receptor (EGFR) gene's mutations can be used to forecast which cancer patients will profit from tyrosine kinase inhibitors (TKIs) and other targeted medications. These biomarkers are essential for enhancing therapy results and customizing treatment plans [3].

3.4 Pharmacodynamic Biomarkers:-

These indicators show how the body reacts to a medication or treatment. They offer information about the molecular or cellular efficacy of a treatment. Pharmacodynamic biomarkers are frequently used to track treatment effectiveness in real-time and modify treatment as needed [3].

3.5 Safety Biomarkers:-

These biomarkers evaluate a drug's possible toxicity or side effects, assisting in ensuring patient safety throughout therapy. To detect liver damage caused by certain medications, for example, Alcoholic liver enzymes such aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are tested. [3].

3.6 Disease Monitoring Biomarkers:-

Disease Monitoring Biomarkers Used to track disease progression or regression over time, these biomarkers are crucial in chronic diseases like cardiovascular disease, diabetes, and autoimmune disorders. In conditions like rheumatoid arthritis, for instance, Protein C-reactive (CRP) levels are commonly employed to track inflammation [2].

4. BIOMARKER'S FUNCTION IN PARTICULAR DISEASE

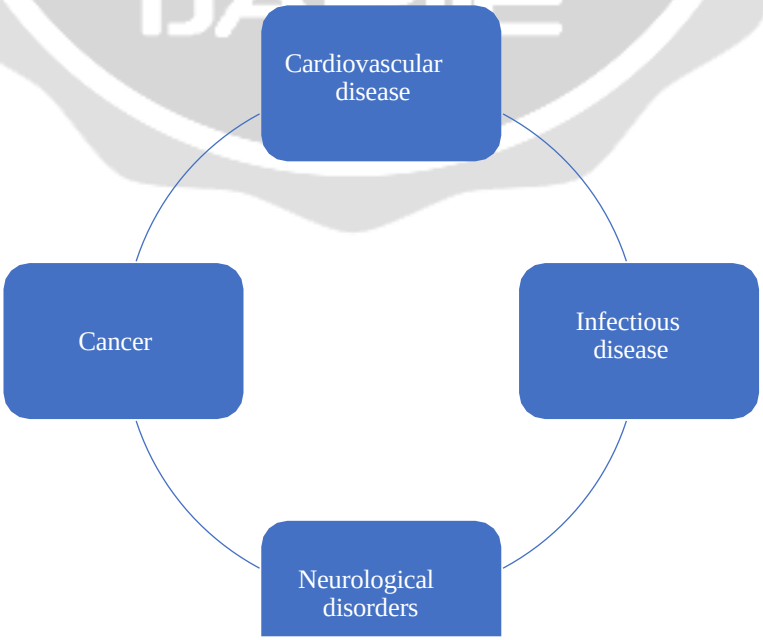

Fig-2: Biomarker's Function in Particular Diseases

4.1 Infectious Disease:-

PCT (procalcitonin) is a beneficial marker for identifying bacteria infections from viral ones and inflammatory disorders. It aids in clinical decisions regarding antibiotic therapy initiation or cessation, with its role in practice still evolving [6]. PCT is becoming more and more seen as a useful method for both identifying infections and encouraging patients with systemic illnesses to use antibiotics responsibly [7]. PCT should be integrated into infection-specific clinical algorithms. While ideal PCT thresholds exist for certain infections, based on randomized trials, their clinical benefits and safety remain unclear for other conditions [8].This study aims to review PCT data across various illnesses, assess its advantages and limitations, and evaluate its reliability When combined with approved algorithms for diagnosis [8].

4.1.1 Using PCT for Treatment with Antibiotics Guidance in Infections of the Respiratory System

Levels of PCT can operate as a surrogate biomarker to direct antibiotic treatment in specific patients because they increase during bacterial infections and fall as recovery progresses [9] [10]. Accurate diagnosis of non-CAP lower respiratory tract infections and CAP relies on sensitive PCT assays. Early low PCT levels (within 4-6 hours) reduce the need for empirical antibiotics and strongly suggest a bacterial infection [14].

4.1.2 PCT in Other Infections for Antibiotic Guidance

Research suggests PCT can differentiate bacterial infections from conditions like arthritis, postoperative fungal infections, fever, neutropenic fever and possible infections of the bloodstream [16][17]. All published research on PCT is observational, and its role in safely guiding antibiotic therapy outside of RTIs, meningitis, and sepsis is still uncertain [8]. PCT may not be sensitive enough for some conditions. It may remain low in subacute endocarditis or viral infections, and rise only after atypical bacterial infections. Elevated PCT in hypothermic cardiac arrest patients suggests inflammation rather than infection, limiting its use for early antibiotic decisions in critically ill cases [13][14].

4.2 NEUROLOGICAL DISORDERS:-

Neurodegenerative diseases involve progressive neural tissue deterioration, with no current treatments Because of the incapacity of central nervous system neuronal regeneration. However, recent stem cell research offers potential for neuroregeneration or neuronal cell replacement [15][18]. Recent efforts focus on finding biomarkers for neurodegenerative diseases to enable earlier diagnosis and intervention. Biomarkers help detect, track progression, and assess treatment efficacy. For Huntington's, Parkinson's, ALS, and Alzheimer's, reliable, specific biomarkers are needed for accurate diagnosis and improved outcomes [19].

4.2.1 Alzheimer's disease

Alzheimer's disease (AD), affecting over four million Americans, is marked by a loss of synapses and neurons, especially in the hippocampus and cerebral cortex, leading to cognitive impairments. The depletion of acetylcholine, crucial for memory and learning, causes the most noticeable symptoms [19]. Patients with AD also exhibit alterations in the levels respectively of butyrylcholinesterase (BuChE) and acetylcholinesterase (AChE) in addition to acetylcholine depletion [20]. When these two indicators are measured together, both the specificity and sensitivity of AD detection are higher than 90% [20].

4.2.2 Diagnostic Criteria

Diagnosing Alzheimer's disease has been challenging since its identification in the early 20th century. The first diagnostic criteria were developed by the DSM-IV and NINCDS-ADRDA towards the end of the century [21].

4.2.3 Biomarkers for Alzheimer's 4.2.4 Disease

4.2.4 Tau as a Biomarker and Ab42:

CSF Aβ42 levels are inversely related to brain amyloid load, with Alzheimer's patients showing lower Aβ42 than healthy individuals. Decreased Aβ clearance into the CSF reflects amyloid plaque formation. CSF Aβ is the earliest known AD marker, becoming abnormal years before memory complaints emerge [22][23].

4.3 Parkinson's disease:

Parkinson's disease (PD), which impacts about 1% of those over 65, is the second most common neurological disorder. It typically develops later in life, gradually impairing motor control. PD was once considered idiopathic, defined by Lewy body pathology and the depletion of the nigrostriatal dopaminergic neuron pathway [24]. Parkinson's disease (PD) is now recognized as a systemic illness, with non-motor symptoms like autonomic disorders, olfactory dysfunction, and cognitive and sleep issues often appearing before motor signs. These may serve as preclinical markers or early indicators of PD [25][26]. An ideal biomarker would enable early treatment, assess neuroprotection, and monitor disease modification. It may be founded on biochemical, genetic, proteomic, imaging, or clinical characteristics or a combination of these [27].

4.3.1 The Various Kinds of Biomarkers and Their Functions:-

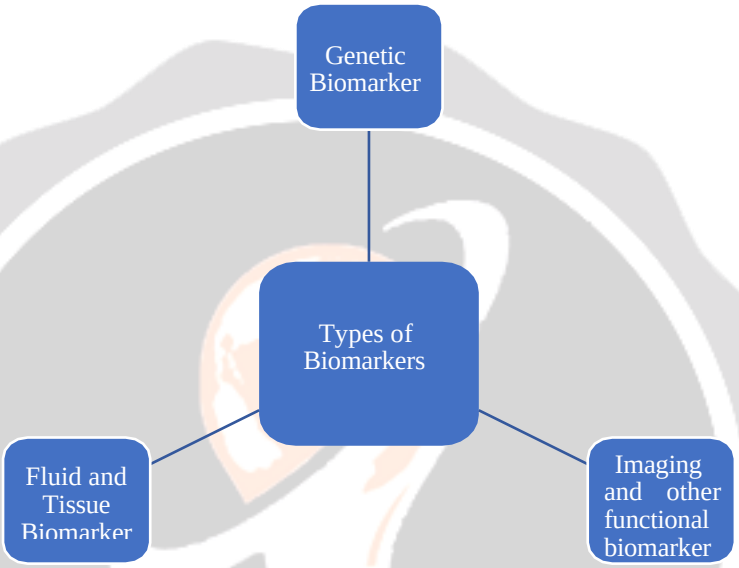

Fig-3: Types of Biomarkers Used in Parkinson's Disease

4.3.2 Genetic Biomarker:-

Genetics was once overlooked in idiopathic Parkinson's disease (PD), but it's now recognized as a factor influenced by environmental, lifestyle, and genetic interactions. While Genes that contain single nucleotide polymorphisms (SNPs) like those Participating in detoxification and dopamine pathways show little correlation with PD risk, genome-wide studies have identified 16 genetic loci linked to the disease. Familial PD, often caused by single gene mutations like in the SNCA gene, has brought genetics to the forefront. Mutations in mitochondrial genes and proteins like α-synuclein, linked to mitochondrial dysfunction and oxidative stress, are being studied as potential PD biomarkers [27].

4.3.3 Fluid and Tissue Biomarker:-

Reliable Neurodegenerative disease biomarkers are challenging to find due to the difficulty in accessing damaged brain tissue, usually only available post-mortem. Cerebrospinal fluid (CSF) is considered ideal for biomarker identification, as it directly reflects brain condition, but CSF collection is invasive. This has led researchers to focus on more accessible fluids like blood and urine. Various potential biomarkers, including α-synuclein, neurofilaments, and DJ-1, have been explored. α-synuclein is especially studied due to its role in Lewy bodies and its genetic link to familial PD. However, variations in fluid collection methods and blood contamination issues pose challenges. Standardizing collection and storage could improve biomarker reliability [27].

4.3.4 Imaging and other Functional Biomarkers:-

4.3.5 Imaging:-

Neuroimaging techniques like SPECT, PET, MRI, and TCS offer valuable insights into brain structure and function in Parkinson's disease (PD), complementing clinical assessments. These methods assess dopamine system

integrity, anatomical changes, and neuron loss over time, often correlating with disease severity. However, they are costly, limiting routine diagnostic use, except for TCS [28]. Neuroimaging techniques, particularly TCS, improve PD diagnosis and help differentiate it from other movement disorders. TCS can detect midbrain hyperechogenicity in early stages, linked to increased iron in the substantia nigra. Although inexpensive, TCS accuracy depends on operator skill and a good acoustic window. Longitudinal studies show little change in the echogenic signal over time, limiting its use mainly for early differential diagnosis. Voxel-based morphometry also aids in distinguishing PD from other motor diseases by highlighting structural and volume changes [27][29].

4.4 Cancer:-

A biomarker is a biological signal that helps identify, describe, and track diseases. It can guide personalized treatments, serve as a prognostic marker, and predict drug side effects. Being aware of the connection between a biomarker and its clinical significance is essential to its effective use [30]. Biomarkers are biological compounds found in tissues, fluids, or blood that indicate either a condition or a procedure, like cancer, is it typical or abnormal [31]. Biomarkers help diagnose diseases, with variations due to post-translational modifications, genetic mutations, and gene expression changes [32]. Biomarkers include proteins, nucleic acids, antibodies, peptides, proteomic profiles, metabolomic signatures, and gene expression patterns. They can be found non-invasively in bodily fluids like blood, urine, saliva, CSF, or through tissue samples [33]. Cancer, a complex disease caused by genetic and epigenetic changes, leads to imbalances in cell division and death. Early detection is key to reducing cancer-related deaths, making reliable biomarkers crucial. Biomarkers such as proteins, lipids, metabolites, and nucleic acids provide valuable insights into cancer onset. Emerging biomarkers like microRNA, circulating tumor cells, and exosomes show promise, while traditional markers like Commonly utilized include CA-125/MUC16, PSA, and CEA [34]. The development of biomarkers in healthcare faces challenges related to clinical utility, validity, and analytical accuracy. Analytical validity ensures reliable biomarker assays, including sample handling and precision. Clinical validity assesses a biomarker's ability to differentiate within target populations, requiring independent validation. Clinical utility evaluates the benefits and risks to justify its use. This review addresses cancer detection challenges, traditional methods, and biomarker types and roles in cancer diagnosis [35].

4.4.1The use of biomarkers in diagnosis, Prognosis, and Detection of Cancer:-

Cancer's unchecked cell proliferation is caused by genetic alterations that support cell survival and growth [36]. Cancer arises from changes to proto-oncogenes, DNA repair, and tumor suppressor genes, disrupting cell division and death. Epigenetic changes, like DNA Histone changes and methylation also have an impact. This section explores biomarker types and detection methods [35].

4.4.2 Biomarkers for Biofluids:-

Biofluids like blood, sweat, saliva, and urine enable non-invasive diagnosis and monitoring of various medical conditions, aiding clinical studies effectively [37]. Each biofluid has unique properties: urine contains urea and salts; saliva has electrolytes like sodium and calcium; and sweat includes urea, lactic acid, and minerals. Biofluids, including blood, urine, saliva, and CSF, are valuable for cancer detection and biomarker discovery [38]. Salivary mRNA biomarkers (e.g., KRAS, MBD3L2) show high specificity for pancreatic cancer. Salivary DNA mutations (e.g., PI3K, CDKN2A) detect oral cancers, while proteins like calprotectin and AZGP1 are effective for lung cancer diagnosis [39]. Techniques like mass spectrometry, ELISA, qPCR, and sequencing are used to identify cancer biomarkers in biofluids. Protein extraction methods include 2D electrophoresis and SELDI, with validation via Western blotting and ELISA. Challenges include sample variability and inter-laboratory differences. Research on hypermethylated cfDNA, such as RPRM and XAF1, shows promise for gastric cancer detection but faces technical hurdles like incomplete cytosine conversion in methylation-specific PCR [35].

4.4.3 Imaging Biomarkers:-

Imaging biomarkers (IBs) are crucial in oncology for tumor staging, assessing treatment response, and monitoring efficacy. Common methods include PET, MRI, CT, and ultrasonography. Validating and qualifying new IBs is essential for broader clinical use [40]. The EORTC and CRUK proposed 14 important suggestions to accelerate the clinical adoption of imaging biomarkers (IBs) [35]. The guidelines emphasize multicenter trials, precision, standardization, accreditation, parallel validation, cost-effectiveness, and alternative validation. Imaging biomarkers (IBs) provide affordable, non-invasive methods for tumor identification, screening, advancement tracking, and treatment reaction. They assess multiple lesions, map tumor heterogeneity, and monitor changes over time while staging methods document tumor size, location, and spread [41]. Accurate assessment of tumors, lymph nodes, and metastases is crucial for cancer diagnosis and prognosis. TNM staging, guided by AJCC standards, uses imaging techniques like CT, MRI, SPECT, and PET to ensure consistent reporting and, in some cases, predict treatment outcomes [42]. Clinical TNM staging, like in prostate cancer, distinguishes between

localized and advanced disease, predicting treatment outcomes such as bicalutamide monotherapy effectiveness. Imaging biomarkers (IBs) are widely used in clinical practice, with response criteria like RECIST 1.0/1.1 assessing treatment effectiveness. Ongoing research aims to refine objective response criteria and evaluate the predictive efficacy of different biomarker versions for clinical outcomes [35].

4.5 Diabetes:-

Diabetes mellitus (DM) affects over 350 million people globally and includes Type 1 (T1DM) and Type 2 (T2DM). T1DM, accounting for 5-8% of cases, involves pancreatic beta cell degeneration, while T2DM, more common, is caused by insulin resistance in tissues like the liver, muscles, and adipose [43]. Microvascular problems, such retinopathy, cardiomyopathy, and nephropathy, are widespread in both both type 1 and type 2 diabetes. Diabetes mellitus (DN), a leading reason for kidney failure, affects about 30% of T1DM patients and 20-30% of T2DM patients [44]. Diabetic cardiomyopathy (DC) involves heart problems and diastolic dysfunction, often not using the typical indications of high blood pressure or coronary artery disease [45]. About one- third of those who have diabetes can develop diabetic retinopathy (DR), with over 10% developing proliferative DR or diabetic macular edema (DME), both of which threaten vision [46-47]. A biomarker is a trait that can be used to identify diseased processes, regular biological processes, or pharmacological reactions to therapy [48]. Biomarkers are classified into traditional (e.g., HbA1c) and novel types (e.g., microRNAs, proteomic markers), with the latter still under investigation for clinical use [49]. This review explores potential research areas on diagnostic molecular biomarkers for T1DM and T2DM, focusing on proteomics and microRNAs [44].

4.5.1 T1dm Related Traditional Proteomic Biomarkers:-

4.5.2 The Decarboxylase of Glutamic Acid (GAD) Enzyme:-

Glutamate is converted by the enzyme glutamic acid decarboxylase (GAD) to GABA, with GAD2 expressed in the pancreas. Autoantibodies targeting both GAD1 and GAD2 are present in Type 1 diabetes (T1DM) patients, and elevated levels of these proteins could serve as biomarkers for the disease [44].

4.5.3 Islet-specific Protein Associated with the Catalytic Subunit of Glucose-6- Phosphatase (IGRP):-

IGRP, a glycoprotein in islet cells, is crucial for glucose homeostasis and linked to the IDDM7 locus for Type 1 diabetes (T1DM). Autoantibodies against IGRP are present in T1DM, making it a potential diagnostic biomarker for the disease [44].

4.5.4 Protein ia-2, Tyrosine Phosphatase-like:-

IA-2 is a transmembrane protein involved in neuroendocrine cell secretory granules. Autoantibodies against IA-2 is able to serve as early biomarkers for the prediction for Type 1 diabetes (T1D), identifying individuals at risk before clinical onset [44].

4.5.5 ZNT8, a Cation Efflux Transporter:-

Transporter of zinc 8 (ZnT8) is a protein in pancreatic cells that transports zinc into insulin granules. Autoantibodies against ZnT8 can serve as a biomarker to distinguish Type 1 diabetes (T1D) patients from healthy individuals [44].

4.5.6 T1dm and the New Proteomic Biomarker Involved CCL3:-

Anti-CCL3 antibodies, found in about 87% of Type 1 diabetes (T1DM) patients, may serve as a useful biomarker for the disease. CCL3, also known as MIP-1α, is involved in inflammation in autoimmune disorders [44].

4.5.7 DOC2B:-

DOC2B, a protein that regulates insulin vesicle fusion in pancreatic beta cells, is found at elevated levels in platelets from people with newly diagnosed Type 1 diabetes (T1D). This makes DOC2B a potential early biomarker for T1D [44].

4.5.8 Key MicroRNAs Associated with Type 2 Diabetes:-

4.5.9 MIR-375 :-

MiR-375, located between the CCDC108 and CRYBA2 genes, plays a crucial function of β- cells in glucose homeostasis growth, and turnover. It targets myotrophin, inhibiting glucose- induced insulin production, and is elevated in response to β-cell death and hyperglycemia, making it a probable biomarker for β-cell loss in Type 2 diabetes (T2DM). miR-375 also affects pancreatic stem cell differentiation and adipocyte development. A 2012 study found higher miR-375 levels in individuals with T2DM compared to healthy controls [44].

4.6 Cardiovascular Disease:-

Globally, cardiovascular diseases (CVDs) constitute the primary cause of death; nonetheless, many are preventable by managing risk factors like smoking, obesity, and diabetes. Biomarkers, including proteins, metabolites, and genetic factors, are crucial for screening, diagnosing, and predicting CVD outcomes. The American Heart Association has categorized cardiovascular biomarkers as screening, diagnostic, or prognostic tools. Blood-based biomarkers help assess health risks and direct resources to those who need them most. This review focuses on blood biomarkers in CVD clinical care [50].

4.6.1 Biomarkers for Cardiovascular Disease:-

4.6.2 Biomarkers Based on Carbohydrates:-

4.6.3 Glycogen Phosphorylase BB (GPBB):-

Due to its high oxygen demand, the heart is vulnerable to hypoxia from carbon monoxide (CO), which can go undetected in cardiovascular patients due to nonspecific symptoms and lack of ECG abnormalities. This highlights the need for early biomarkers to detect myocardial hypoxia. Glycogen phosphorylase BB (GPBB) has become a possible candidate for this purpose [51-53] Phosphorylase BB of glycogen (GPBB) is an encouraging new cardiac biomarker for the early detection of myocardial ischemia [54-56]. Glycogen phosphorylase BB (GPBB) is an enzyme that facilitates the transformation of glycogen to glucose-1-phosphate during hypoglycemia or hypoxia [57] [58] [52].

Humans have three glycogen phosphorylase isoforms: GPMM (muscle), GPLI (liver), and GPBB (brain). While myoglobin and ischemia-modified albumin (IMA) are sensitive diagnostic markers, they lack heart muscle specificity [59]. GPBB, or glycogen phosphorylase BB, is an extremely sensitive biomarker for identifying acute coronary syndrome (ACS), particularly within the first four hours of chest discomfort [52]. Glycogen phosphorylase BB (GPBB) is a highly effective clinical marker for ischemia, with 81% sensitivity and 93% specificity, making it useful for diagnosing acute coronary syndrome (ACS) [59]. Although plasma GPBB levels rise during pregnancy and in the brain, they lack full specificity for cardiac injury. However, it is a reliable potential indicator of acute coronary syndromes in numerous studies [61]. Therefore, GPBB might be used as an additional biomarker to identify an unexpected heart attack [55].

4.6.4 Protein-Based Biomarkers

4.6.5 AST, or Aspartate Aminotransferase:

An amino group is transferred between amino acids and keto acids by intracellular enzymes called aspartate aminotransferases, also referred to as liver transaminases [62]. Aspartate aminotransferase (AST), mainly found in hepatocytes, is a common liver marker. While it can predict cardiovascular risk, it lacks specificity for cardiac tissue, making it ineffective for identifying acute myocardial infarction (AMI) [63] [64]. Total creatine kinase (CK) levels, initially used to predict skeletal muscle injury, were assessed as a diagnostic for acute myocardial infarction (AMI) in 1959 [52]. Acute myocardial infarction (AMI) was first diagnosed using lactate dehydrogenase (LDH) in 1960 [65]. The World Health Organization (WHO) authorized a diagnostic panel for acute myocardial infarction (AMI) that included Lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and creatine kinase (CK) [52].

4.6.6 Biomarkers Derived from Lipid

4.6.7 The proportion of high-density lipoprotein cholesterol to triglycerides:

Key biomarkers for cardiovascular disease (CVD) risk include the triglyceride (TG) TC to HDL-C ratio, HDL-C to total cholesterol ratio, and low ankle-brachial pressure index (ABPI) [52]. Most standard lipid panels may show triglyceride levels, but through their combination with other lipid profile markers, they can also be used to forecast the chance of CVD [52]. Cardiovascular disease risk rises with a ratio of triglycerides to HDL cholesterol above 3.5. In heart failure (HF), LDL-C, HDL-C, lipoprotein A (LPA), and apolipoprotein B (APO-B) are elevated, while APOA1 (apolipoprotein A1), the PON1 activity/HDLC ratio and APOA1/APOB ratio decrease, reflecting disease severity and progression [66]. Individuals who have type 2 diabetes and high levels of total cholesterol, triglycerides, and LDL (hyperlipidemia) have an elevated risk of coronary artery disease, highlighting the importance of controlling cholesterol to reduce cardiovascular risk [67]. Lipoprotein A (LP(A), apolipoprotein B (APOB), total cholesterol, LDL cholesterol (LDL-C), and the APOA1/APOB ratio are key indicators of cardiovascular disease and essential for assessing lipid abnormalities linked to conditions like atherosclerosis [52]. Lipoprotein A (LP(A), apolipoprotein B (APOB), total cholesterol, LDL cholesterol (LDL-C), and the APOA1/APOB ratio are key indicators of cardiovascular disease and essential for assessing lipid abnormalities linked to conditions like atherosclerosis [52].

5. MULTI-OMICS APPROACHES (GENOMICS, PROTEOMICS AND METABOLOMICS)

Omics is the study of molecular systems, including genomics (genes), proteomics (proteins), and metabolomics (metabolites), providing insights into complex biological processes. Unlike classical genetics, genomics analyzes entire genomes, advancing personalized medicine and molecular biology by identifying disease-related genetic variants [68]. Technological advancements, such as cost-effective, high-throughput analyses, have accelerated omics progress. Expression arrays from the late 1990s enabled global gene expression studies and mapping expression quantitative trait loci (eQTLs), enhancing genome-wide association studies (GWAS) and biological network modeling. Modern omics technologies now analyze transcripts, proteins, metabolites, and genomes, broadening molecular and systems biology. Integrating data on molecular variations linked to diseases helps understand disease mechanisms, identify biomarkers, and guide targeted therapies and diagnostics [68]. Recent advancements in omic technologies, including proteomics, metabolomics, and genomics, enable large-scale monitoring of molecular and biological processes. These methods are used to explore biochemical pathways, identify biomarkers, and investigate pathophysiological mechanisms. Despite focusing on genes, RNA, proteins, and metabolites, challenges remain in integrating data across different omic domains [69-70]. Interpreting changes in omic domains is challenging due to complex biochemical regulation, including differences at the cellular, tissue, and organismal levels, in addition to epigenetics and post-translational modifications of mRNA and proteins [71]. This article explores methods for integrating proteomic, genomic, and metabolomic data to reveal hidden biological connections through comprehensive analysis. [72] [70]. Metabolomics analyzes small molecules and metabolic intermediates to study gene, protein, and environmental interactions. It is increasingly used in diseases like cancer and type 1 diabetes to identify biomarkers for prediction, prognosis, and treatment. This approach enhances understanding of disease mechanisms and improves patient care [73]. Metabolomics provides insights into the organismal phenotype by reflecting biological and environmental processes. However, it may not fully capture complex systems or diseases like cancer on its own [70]. A challenge in metabolomics is the difficulty of integrating data when the biochemical domain is poorly understood, leading to fragmented interpretations. This underscores the need for deeper knowledge to improve the utility of metabolomics in disease research [74].

6. LIQUID BIOPSIES:

Liquid biopsies allow the measurement of analytes and biomarkers, initially used to study breast cancer, circulating tumor cells (CTCs), by analyzing non-solid biological tissues [75]. Liquid biopsies use body fluids like urine, saliva, blood, ascitic fluid, cerebrospinal fluid, vitreous fluid, and pleural effusions to evaluate non-invasive circulating biomarkers[76]. Metabolomics studies small molecules to understand gene-protein interactions and environmental impacts, helping identify biomarkers for disease prediction, prognosis, and treatment monitoring [77]. Using a non-invasive technique called liquid biopsy, offers easier sample collection, reduced risk, and real-time profiling, enabling longitudinal monitoring and insights into physiological or pathological conditions [78-79].

6.1 Contents of Liquid Biopsies:

6.1.2 CFRNA, CCFDNA, and CTDNA:

DNA that freely circulates in the bloodstream and can come from tumors or other sources is known as circulating cell-free DNA, or ccfDNA [80]. Tumor-derived ccfDNA shares genetic changes with cancer and is present in a number of bodily fluids, including as urine and brain fluid [81-82]. Circulating fetal DNA (cfDNA) in plasma enables non-invasive prenatal diagnostics, replacing amniocentesis. Cell-free DNA (ccfDNA) is also used to monitor organ transplant rejection. Found in blood, ccfDNA mainly consists of 145–201 base pair fragments, released through apoptosis and necrosis [83]. CcfDNA is often released in trace amounts, making detection and sequencing are difficult and expensive. Standardization between labs and suppliers is needed for reliable results [80]. CcfDNA shows potential as a cancer biomarker, but sensitivity and specificity require analyzing tumor-derived ccfDNA. It is also influenced by various clinical and non-pathological factors [84]. CtDNA can be used for dynamic (real-time) cancer surveillance growth since it is widely split up in body fluids and has a brief Blood half-life (around two hours) [85].

CONCLUSION

The conclusion highlights the transformative potential of biomarkers in healthcare, emphasizing their pivotal role in disease diagnosis, prognosis, and personalized treatment. It acknowledges the rapid advancements in biomarker research and technology, particularly in areas such as omics and liquid biopsies, which enhance early detection, monitoring, and therapeutic decision-making.

Not with standing notable advancements, many obstacles still exist, such as the requirement for uniformity, strong validation procedures, and the incorporation of multi-omics data to enhance clinical dependability and utilization. To fully achieve the potential of biomarkers, interdisciplinary research, and collaboration are necessary to address these issues.

The conclusion underscores that, as we move toward more personalized and precision medicine, biomarkers will continue to play a critical role in optimizing healthcare outcomes, making diagnostic and treatment strategies more efficient, targeted, and patient-centric.

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