CLINICAL AND LABORATORY PARAMETERS AS PROGNOSTIC AND MONITORING BIOMARKERS IN PATIENTS WITH CARDIOVASCULAR AND METABOLIC DISEASES

PARÂMETROS CLÍNICOS E LABORATORIAIS COMO BIOMARCADORES PROGNÓSTICOS E DE MONITORAMENTO EM PACIENTES COM DOENÇAS CARDIOVASCULARES E METABÓLICAS

PARÁMETROS CLÍNICOS Y DE LABORATORIO COMO BIOMARCADORES PRONÓSTICOS Y DE MONITOREO EN PACIENTES CON ENFERMEDADES CARDIOVASCULARES Y METABÓLICAS

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ABSTRACT

Non-communicable chronic diseases represent one of the greatest contemporary challenges to public health due to their high prevalence, impact on morbidity and mortality, and the need for continuous care. In this context, systemic arterial hypertension and type 2 diabetes mellitus play a central role, both because of their frequency in the population and the complexity of their cardiovascular, renal, and metabolic complications. This chapter highlights the importance of using clinical and laboratory biomarkers as tools to support risk stratification, prognosis, and monitoring of these conditions, especially in Primary Health Care. Among the clinical parameters, anthropometric measurements, blood pressure, and cardiovascular assessment stand out, while, in the laboratory field, blood glucose, glycated hemoglobin, lipid profile, renal and hepatic markers, as well as hematological and inflammatory indices derived from complete blood count analyses, gain relevance. The integration of these different parameters makes it possible to increase the sensitivity of clinical assessment, promote the early identification of subclinical alterations, and support individualized management strategies. Thus, the combined use of clinical and laboratory biomarkers constitutes a promising strategy to improve health care quality, especially in resource-limited settings, contributing to the prevention of complications and to better outcomes in patients with chronic diseases.

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RESUMO

As doenças crônicas não transmissíveis representam um dos maiores desafios contemporâneos para a saúde pública, em razão de sua elevada prevalência, do impacto na morbimortalidade e da necessidade de cuidado contínuo. Nesse contexto, a hipertensão arterial sistêmica e o diabetes mellitus tipo 2 assumem papel central, tanto pela frequência com que acometem a população quanto pela complexidade de suas complicações cardiovasculares, renais e metabólicas. O capítulo destaca a importância da utilização de biomarcadores clínicos e laboratoriais como instrumentos de apoio à estratificação de risco, ao prognóstico e ao monitoramento desses agravos, especialmente na Atenção Primária à Saúde. Entre os parâmetros clínicos, ressaltam-se medidas antropométricas, pressão arterial e avaliação cardiovascular, enquanto, no campo laboratorial, ganham relevância a glicemia, a hemoglobina glicada, o perfil lipídico, os marcadores renais e hepáticos, além dos índices hematológicos e inflamatórios derivados do hemograma. A integração entre esses diferentes parâmetros permite ampliar a sensibilidade da avaliação clínica, favorecer a identificação precoce de alterações subclínicas e subsidiar condutas individualizadas. Assim, o uso articulado de biomarcadores clínicos e laboratoriais constitui estratégia promissora para qualificar o cuidado em saúde, especialmente em cenários de recursos limitados, contribuindo para a prevenção de complicações e para a melhoria dos desfechos em pacientes com doenças crônicas.

Palavras-chave: Doenças Crônicas Não Transmissíveis. Hipertensão Arterial Sistêmica. Diabetes Mellitus Tipo 2. Atenção Primária à Saúde. Biomarcadores Clínicos. Biomarcadores Laboratoriais.

RESUMEN

Las enfermedades crónicas no transmisibles representan uno de los mayores desafíos contemporáneos para la salud pública, debido a su elevada prevalencia, su impacto en la morbimortalidad y la necesidad de atención continua. En este contexto, la hipertensión arterial sistémica y la diabetes mellitus tipo 2 desempeñan un papel central, tanto por la frecuencia con que afectan a la población como por la complejidad de sus complicaciones cardiovasculares, renales y metabólicas. El capítulo destaca la importancia del uso de biomarcadores clínicos y de laboratorio como herramientas de apoyo para la estratificación del riesgo, el pronóstico y el monitoreo de estas enfermedades, especialmente en la Atención Primaria de Salud. Entre los parámetros clínicos, se destacan las medidas antropométricas, la presión arterial y la evaluación cardiovascular, mientras que, en el ámbito de laboratorio, cobran relevancia la glucemia, la hemoglobina glucosilada, el perfil lipídico, los marcadores renales y hepáticos, además de los índices hematológicos e inflamatorios derivados del hemograma. La integración de estos diferentes parámetros permite ampliar la sensibilidad de la evaluación clínica, favorecer la identificación temprana de alteraciones subclínicas y respaldar conductas individualizadas. Así, el uso articulado de biomarcadores clínicos y de laboratorio constituye una estrategia prometedora para mejorar la calidad de la atención en salud, especialmente en escenarios con recursos limitados, contribuyendo a la prevención de complicaciones y a la mejora de los desenlaces en pacientes con enfermedades crónicas.

Palabras clave: Enfermedades Crónicas No Transmisibles. Hipertensión Arterial Sistémica. Diabetes Mellitus Tipo 2. Atención Primaria de Salud. Biomarcadores Clínicos. Biomarcadores de Laboratorio.

1 INTRODUCTION

Chronic Non-Communicable Diseases (NCDs) are one of the greatest contemporary challenges for public health. According to the World Health Organization (WHO, 2024) and the Ministry of Health (BRASIL, 2021), these diseases are responsible for approximately 74% of deaths in Brazil and more than 70% of deaths worldwide. This group includes conditions of high social, clinical, and economic burden, with emphasis on cardiovascular diseases, neoplasms, chronic respiratory diseases, and diabetes mellitus, which share widely prevalent modifiable risk factors, such as sedentary lifestyle, inadequate diet, smoking, harmful alcohol consumption, and overweight (WHO, 2024).

Data from the National Health Survey (PNS, 2019) indicate that more than half of the Brazilian adult population has already been diagnosed with at least one NCD, evidencing the magnitude and complexity of this problem in the national scenario (IBGE, 2020). Although advances have been observed in recent decades, such as the expansion of epidemiological surveillance and the implementation of national strategic plans, such as the Strategic Action Plan to Combat NCDs 2021–2030, important inequalities persist in access to prevention, timely diagnosis, and continuous treatment. Such inequities affect populations in situations of social vulnerability more intensely, compromising the principles of equity, universality, and integrality of the Unified Health System (SUS) (MALTA et al., 2020).

Among NCDs, cardiovascular diseases (CVDs) stand out as the main single cause of mortality in Brazil and worldwide, in addition to contributing significantly to morbidity and reduced quality of life. This set of diseases encompasses conditions of great clinical relevance, such as acute myocardial infarction (AMI), cerebrovascular accident (CVA), heart failure (HF) and arrhythmias. Although many of these diseases are preventable through health promotion strategies and control of risk factors, their incidence remains high (PAHO, 2025).

At the same time, type 2 Diabetes Mellitus (DM2) is one of the most prevalent and worrisome metabolic diseases today, with increasing incidence projections on a global scale. In Brazil, it is estimated that 16.6 million adults live with diabetes, and approximately 31.9% are unaware of the diagnosis (IDF, 2024). It is a multifactorial condition, associated with aging, obesity, sedentary lifestyle, and inadequate dietary patterns, with a high potential to trigger micro and macrovascular complications, such as retinopathy, nephropathy, neuropathy, amputations, and major cardiovascular events (IDF, 2021; WHO, 2023).

It is also noteworthy that most of the complications associated with systemic arterial hypertension (SAH) and DM2 can be prevented or attenuated through early diagnosis and adequate longitudinal follow-up. However, because these are diseases with an insidious and

often silent course, late diagnoses and interventions in advanced stages are frequent. This scenario reinforces the need for effective mechanisms for tracking, risk stratification, and continuous monitoring, especially within the scope of Primary Health Care (PHC), the main gateway to the SUS and a strategic level for care coordination (IDF, 2021; WHO, 2023).

In this context, the use of clinical and laboratory parameters as biomarkers of risk and prognosis is a fundamental strategy to qualify care and guide early interventions. Among the clinical parameters, body weight, anthropometric measurements, such as body mass index (BMI), abdominal circumference, and hip circumference, as well as pressure assessment using systolic blood pressure (SBP) and diastolic blood pressure (DBP) stand out. Among the low-cost laboratory tests widely available in the public network, fasting glucose, glycated hemoglobin, lipid profile, renal profile, liver profile, and blood count stand out, which allow not only clinical monitoring, but also the early identification of complications and the implementation of individualized therapeutic approaches (PEIXOTO et al., 2021; WHO, 2016).

However, the underuse of these tests as integrated tools to support clinical decision-making, especially in PHC, still constitutes a relevant gap. The isolated analysis of laboratory parameters often does not contemplate the pathophysiological complexity of NCDs, requiring more sensitive and integrative evaluation models (SCHMIDT et al., 2011; BARRETO et al., 2019).

In this sense, the blood count has stood out as a complementary test of great value, as it enables the identification of subclinical inflammation, hematological alterations, and conditions associated with NCDs. Indicators such as hemoglobin, hematocrit, mean corpuscular volume (MCV), red cell distribution width (RDW), mean platelet volume (MVP), platelet distribution width (PDW), global and absolute leukocyte counts, and cellular relationships derived from the blood count have been associated with outcomes adverse in patients with cardiovascular, renal, and metabolic diseases (ZHANG et al., 2021; LOPES et al., 2022). In addition, immunological biomarkers such as ultrasensitive C-reactive protein (hs-CRP), ferritin, and inflammatory cytokines have been gaining relevance in risk prediction and in the evaluation of low-grade inflammation typical of NCDs (PARK; SHIN, 2021).

The integration between clinical, hematological, and immunological data therefore represents a promising opportunity to improve risk prediction models, qualify prognostic stratification, and personalize the management of NCDs in clinical practice, especially in resource-limited settings. In addition, the use of cell relationships derived from the blood count shows promise in the evaluation of low-grade inflammatory responses, platelet

activation and endothelial dysfunction, constituting an important laboratory parameter for the follow-up and prognosis of hypertensive and/or diabetic patients.

Thus, this chapter aims to describe and analyze the main clinical and laboratory biomarkers applicable to the prognosis, risk stratification and monitoring of people with chronic non-communicable diseases, with emphasis on systemic arterial hypertension and type 2 diabetes mellitus in the context of Primary Health Care. The proposal seeks to contribute to the improvement of care strategies, the prevention of complications and the improvement of the quality of life of affected populations, systematically integrating clinical and laboratory variables as instruments to support decision-making and health care management.

2 CHRONIC NON-COMMUNICABLE DISEASES - NCDs

Chronic Non-Communicable Diseases (NCDs) comprise a group of conditions of prolonged evolution, non-infectious and without transmission between individuals, resulting from the interaction between genetic, physiological, environmental and behavioral factors. They are generally characterized by insidious onset, slow progression, and often absence of signs and symptoms in the early stages (WHO, 2024).

Among the main NCDs, cardiovascular diseases, neoplasms, chronic respiratory diseases, and diabetes mellitus stand out, which, together, represent the highest burden of morbidity and mortality in the global scenario. In addition to their high prevalence, these diseases generate a significant social, economic, and care impact, due to the need for continuous monitoring, prolonged use of medications, and management of acute and chronic complications (MIGOWSKI; COSTA, 2024; WHO, 2024).

The magnitude of this problem is even more evident in low- and middle-income countries, where the highest proportion of premature deaths associated with NCDs occurs. Estimates from the World Health Organization indicate that millions of deaths occur before the age of 70, reflecting inequalities in access to prevention, early diagnosis, and timely treatment (BRASIL, 2021; STOPA et al., 2022; WHO, 2024).

A large part of the burden of NCDs is related to modifiable risk factors, such as inadequate diet, sedentary lifestyle, smoking, harmful alcohol consumption, and overweight. These determinants contribute to metabolic and hemodynamic changes, including arterial hypertension, hyperglycemia, dyslipidemia, and obesity, with a strong association with the development of cardiovascular events and multisystem complications (BRASIL, 2021; VIGITEL, 2023; WHO, 2024).

In this context, systemic arterial hypertension and diabetes mellitus stand out as conditions of high prevalence, high care burden, and important potential for disease prevention. Thus, understanding NCDs and their determinants is essential to guide screening, prevention, and monitoring strategies in Primary Health Care.

2.1 CLINICAL AND LABORATORY BIOMARKERS IN PROGNOSIS AND MONITORING

The follow-up of individuals with systemic arterial hypertension (SAH) and type 2 diabetes mellitus (DM2) requires an integrated approach that includes both clinical and laboratory biomarkers. These indicators play a central role in risk stratification, prognosis assessment, and disease progression monitoring, enabling early detection of complications, optimization of therapeutic interventions, and, consequently, reduction of morbidity and mortality associated with these chronic conditions (MUJADZIC; SKEETE; DIPETTE, 2022; OLIVEIRA et al., 2024).

Clinical biomarkers include parameters obtained during the medical consultation, such as blood pressure, body mass index (BMI), waist circumference, and heart rate, which are indispensable in routine follow-up and identification of additional risk factors. Laboratory biomarkers, on the other hand, include specific tests that allow the evaluation of metabolic control (such as fasting glucose, glycated hemoglobin, and lipid profile) and the early identification of immunohematological, renal, hepatic, and cardiovascular alterations that frequently accompany the course of SAH and DM2 (MUJADZIC; SKEETE; DIPETTE, 2022; OLIVEIRA et al., 2024).

2.1.1 Anthropometry

Anthropometry is a physical assessment method that uses body measurements to analyze the composition and nutritional status of individuals. As it is a non-invasive, low-cost, and easily applicable procedure, it represents a fundamental tool in Primary Health Care, especially in the monitoring of chronic diseases, such as type 2 diabetes mellitus (DM2) and systemic arterial hypertension (SAH) (WHO, 2019; SBD, 2024).

Key anthropometric measurements include body weight, height, waist circumference (WC), hip circumference (HC), body mass index (BMI), and waist-to-hip ratio (WHR). Such parameters allow the identification of both general and central obesity, factors directly associated with insulin resistance, metabolic syndrome, and increased risk of cardiovascular complications (TOMIC; SHAW; MAGLIANO, 2022).

BMI is one of the most used indicators in clinical practice, as it provides an estimate of body weight in relation to height, making it possible to classify it as underweight, normal

weight, overweight and obesity. However, this index has limitations, as it does not differentiate lean mass from fat mass, which can compromise its interpretation in specific groups, such as the elderly and athletes (WHO, 2019). In this sense, waist circumference (WC) has been recommended as a complementary marker, since it reflects visceral fat, whose influence is more significant in the pathophysiology of cardiovascular and metabolic diseases. Elevated WC values are strongly associated with insulin resistance, dyslipidemias, and increased risk of cardiovascular events, regardless of BMI (SBD, 2024).

The waist-to-hip ratio (WHR), obtained by dividing WC by HC, is another robust indicator of cardiometabolic risk, allowing the distinction between central and peripheral obesity. Evidence indicates that visceral fat plays a pro-inflammatory role, stimulating the secretion of inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which contribute to insulin resistance and the progression of microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (coronary artery disease, stroke, and peripheral arterial disease) complications (YOUSEF et al., 2023).

In the context of prognosis and clinical monitoring, anthropometry is a strategic resource for monitoring body changes resulting from therapeutic interventions, such as physical activity programs, dietary modifications, and medication use. In addition, its systematic use contributes to risk stratification and the early identification of individuals susceptible to the development of DM2 and SAH, consolidating itself as an essential tool for health professionals in the context of Primary Care (WHO, 2019; ADA, 2023).

2.1.2 Diastolic and Systolic Blood Pressure

Blood pressure is one of the most relevant clinical biomarkers for the evaluation and follow-up of patients with cardiovascular and metabolic diseases. Its two components, systolic blood pressure (SBP) and diastolic blood pressure (DBP), as well as the calculation of mean arterial blood pressure (MAP), provide complementary information on arterial hemodynamics, playing an essential role in risk stratification, prognosis establishment, and monitoring of clinical evolution (BARROSO et al., 2021; WHELTON et al., 2024). In addition to its clinical relevance in diagnosis and monitoring, blood pressure measurement has high applicability in PHC, being a simple, low-cost, and widely available method. In this context, routine assessment of SBP and DBP is one of the main strategies for screening and monitoring cardiovascular and metabolic conditions, especially in scenarios in which laboratory tests or more complex diagnostic methods are less accessible (WHO, 2023; PAHO, 2022).

SBP, which corresponds to the pressure exerted during cardiac systole, is robustly associated with cardiovascular complications in adults and the elderly, and is considered one of the most consistent predictors of events such as stroke, heart failure, and coronary artery disease. On the other hand, DBP, measured during ventricular relaxation (diastole), has greater prognostic relevance in young individuals, in whom the increase in peripheral vascular resistance is more pronounced. Studies indicate that persistently high levels of SBP and DBP are related to the progression of atherosclerosis, cardiac remodeling, and impaired renal function, and are independent prognostic markers (AMORIM et al., 2024; BARROSO et al., 2021).

Regular blood pressure monitoring is essential both to assess the effectiveness of treatment and to identify pressure patterns that may not be detected in specific measurements performed in the office. In this sense, methods such as Ambulatory Blood Pressure Monitoring (ABPM) and Home Blood Pressure Monitoring (HBPM) have proven to be indispensable tools, allowing the detection of conditions such as masked hypertension and white coat hypertension, in addition to providing more accurate data on blood pressure behavior over 24 hours. This detailed follow-up favors more individualized therapeutic adjustments, with a positive impact on reducing the risk of adverse events (AMORIM et al., 2024; BARROSO et al., 2021).

In addition to the absolute values of SBP and DBP, blood pressure variability (VPA) has emerged as an important prognostic biomarker. APV refers to fluctuations in blood pressure throughout the day, between days, or between months, and elevated levels are associated with a higher risk of cardiovascular events, cognitive decline, progression of chronic kidney disease, and increased mortality. Recent evidence suggests that APC reflects autonomic instability, arterial stiffness, and failures in therapeutic control, constituting a fundamental parameter for risk stratification and longitudinal follow-up. Patients with high variability are more likely to have complications, even when the mean blood pressure is within the reference values, which reinforces the need for an evaluation that goes beyond conventional blood pressure control and considers hemodynamic stability as an indicator of vascular health (LI et al., 2025).

The integration of SBP, DBP, continuous monitoring, and VPA analysis enables a broader understanding of the patient's cardiovascular health. The joint use of these parameters allows for early identification of risk patterns, evaluation of the therapeutic response in a dynamic and personalized way, prediction of cardiovascular and renal complications, and also subsidize Primary Health Care programs, such as HIPERDIA,

optimizing resources and promoting improvements in the management of public health care (PARATI et al., 2023).

In addition, blood pressure should be understood not only as a static indicator, but as a multifaceted biomarker that involves absolute values, circadian patterns, and pressure variability. This integrated approach offers valuable prognostic information, guiding continuous clinical follow-up and therapeutic decision-making more assertively (PEIXOTO et al., 2021; WHO, 2016). Thus, the routine measurement of blood pressure in Primary Health Care assumes a strategic role, as it allows for the early identification of individuals at risk, guide clinical interventions, and subsidize public policies aimed at the control of chronic non-communicable diseases (PARATI et al., 2023).

2.1.3 Cardiovascular Function Assessment

The assessment of cardiovascular function is a central axis in the follow-up of patients with systemic arterial hypertension (SAH) and type 2 diabetes mellitus (DM2), considering that both conditions are closely related to a significant increase in the risk of developing atherosclerotic cardiovascular disease, the main cause of morbidity and mortality in this population group (ADA, 2023; SBD, 2024). Cardiovascular changes resulting from chronic high blood pressure and sustained hyperglycemia can evolve silently, reinforcing the need for clinical and complementary methods that enable the early detection of structural and functional dysfunctions of the cardiovascular system (HERZOG et al., 2025).

The initial clinical evaluation is based on simple, accessible, and non-invasive parameters, such as cardiac auscultation, palpation of peripheral pulses, resting heart rate, and targeted physical examination. These procedures allow the identification of early signs of heart failure, arrhythmias, peripheral arterial disease, and hemodynamic changes. The detection of decreased peripheral pulses, for example, may indicate advanced atherosclerosis, while the presence of peripheral edema suggests possible cardiac or renal dysfunction (BRASIL, 2021; HERZOG et al., 2025).

Among the indirect clinical biomarkers of cardiovascular function, pulse pressure, a marker of arterial stiffness, and the ankle-brachial index (ABI), widely used in the screening of peripheral arterial disease, stand out. Increased arterial stiffness, often observed in hypertensive and diabetic individuals, is associated with a higher risk of adverse events, such as acute myocardial infarction and stroke. Thus, such measures assume relevant prognostic value, allowing not only risk stratification, but also the guidance of preventive conducts (HERZOG et al., 2025).

In the context of longitudinal follow-up, cardiovascular function assessment should be performed periodically and systematically, integrating clinical, laboratory, and imaging data. The combined use of these tools makes it possible to identify subclinical cardiac changes early, allowing the implementation of personalized therapeutic strategies based on the patient's individual risk (ADA, 2023; SBD, 2024).

Thus, the assessment of cardiovascular function transcends the merely diagnostic character and assumes the role of a prognostic biomarker, directly reflecting the impact of metabolic and hypertensive diseases on the integrity of the cardiovascular system. This perspective contributes not only to reducing the occurrence of serious complications, but also to optimizing clinical decision-making and strengthening public health care strategies (ADA, 2023; SBD, 2024).

2.1.4 Regular eye exams

Regular ophthalmologic examinations are an essential strategy in the monitoring of patients with type 2 diabetes mellitus (DM2) and systemic arterial hypertension (SAH), since changes in the retina directly reflect systemic pathological processes. The retina is recognized as a "window to the vascular system", as it allows direct observation of blood microcirculation, making ophthalmological evaluation a non-invasive clinical biomarker, with high diagnostic and prognostic value (CHEN et al., 2024; SBD, 2024).

In the context of DM2, the most relevant ocular complication is diabetic retinopathy (DR), characterized by progressive microvascular changes triggered by chronic hyperglycemia. Among its manifestations are microaneurysms, retinal hemorrhages, hard exudates, and neovascularization, which, when not identified and treated early, can progress to significant visual impairment and even irreversible blindness (ADA, 2023).

In SAH, hypertensive retinopathy stands out, whose alterations include arteriolar narrowing, flame hemorrhages, cotton wool exudates and, in more severe stages, papilla edema. These ophthalmologic signs are directly associated with severity, time of exposure to hypertension, and the extent of systemic vascular involvement, being important markers of disease progression (ALBUQUERQUE, 2024; AMORIM et al., 2024).

Periodic ophthalmologic examinations enable not only the early detection of ocular complications, but also acts as an indicator of systemic vascular health, helping to stratify cardiovascular risk and monitor the efficacy of therapeutic interventions. For this reason, such tests should be incorporated into follow-up routines in Primary Health Care, including national programs such as HIPERDIA, in addition to being part of patients' individualized care plans (BRASIL, 2021; ADA, 2023; SBD, 2024).

Thus, regular ophthalmologic examinations go beyond the dimension of ophthalmologic care alone, configuring themselves as strategic clinical biomarkers in the follow-up of individuals with DM2 and SAH. Its systematic application makes it possible to guide preventive measures, adjust therapies and, above all, reduce the risk of disabling complications, contributing significantly to improving quality of life and reducing morbidity and mortality associated with chronic diseases (CHEN et al., 2024; ADA, 2023).

2.1.5 Biomarkers of the glycemic profile

Glycemic control is a central laboratory parameter in the follow-up of patients with cardiovascular diseases (CVD) and metabolic diseases, especially in Primary Health Care (PHC). From this perspective, laboratory biomarkers of blood glucose have the following purposes: in addition to the diagnosis and monitoring of diabetes mellitus (DM), but can also be evaluated for potential prognosis, contributing to risk stratification and therapeutic decisions that impact clinical outcomes (MUJADZIC; SKEETE; DIPETTE, 2022; OLIVEIRA et al., 2024).

Among the main biomarkers, glycated hemoglobin (HbA1c) is the reference standard for chronic follow-up, reflecting the approximate glycemic mean of the last 2 - 3 months. Persistently high values are associated with a higher risk of microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (acute myocardial infarction, stroke) complications, and can be used in addition to monitoring in the prognosis of diabetic patients (COSTA et al., 2020). It is important to consider factors that affect the accuracy of HbA1c (anemia, hemoglobinopathies, chronic kidney disease, erythropoietin use), which reinforces the usefulness of complementary biomarkers in PHC.

Fasting plasma glucose (FPG) is widely used, reflecting baseline glucose concentration after 8 - 12 hours of fasting. High values are used in the diagnosis of T2DM and predict the progression from prediabetes to diabetes. In addition, fasting hyperglycemia is associated with endothelial dysfunction, subclinical atherosclerosis, and increased risk of cardiovascular events. In PHC, FPG is an accessible and cost-effective marker, but it should be interpreted in conjunction with other indicators for better prognostic accuracy (AHMADIZAR et al., 2021; WANG; FANG, 2022).

Glycemic variability (VG), measured by serial capillary glucose (pre- and postprandial) or by continuous glucose monitoring (GCS), which can be applied as a prognostic biomarker. Recent evidence indicates that greater variability, regardless of the glycemic mean, is associated with oxidative stress, vascular inflammation, and atherosclerotic plaque instability, which may explain the increased risk of micro- and macrovascular complications

even with target HbA1c. In PHC, the structuring of capillary monitoring (e.g., 7-point profiles or sampling focused on critical periods) allows the identification of patterns of metabolic instability and guides early and personalized interventions. When available, GCM metrics such as Time on Target (IRR) and Time Over Target (TAR) add prognostic and monitoring value (SOARES; MOTORCYCLE; CORREA, 2025).

The oral glucose tolerance test (OGTT) maintains high sensitivity to detect glucose intolerance and DM, and also offers prognostic value by capturing postload hyperglycemia - expression of dysfunction of the first phase of insulin secretion and peripheral insulin resistance. These alterations are associated with early cardiovascular risk, including in individuals with normal FPG. Thus, the OGTT contributes to identifying high cardiometabolic risk that could be underestimated by FPG alone, reinforcing its strategic usefulness in public health and PHC surveillance programs (CHEN et al., 2021).

The triglyceride-glucose index (TyG), calculated by: TyG=log (Triglycerides (mg/dL)×Fasting glucose (mg/dL)/2)), has been used as an indirect biomarker of insulin resistance. Population studies have shown that higher TyG values predict a higher risk of T2DM, metabolic syndrome, and subclinical atherosclerosis (TAI et al., 2022), in addition to being associated with cardiovascular events (HUANG; LI; YIN, 2024). Compared to reference methods (e.g., euglycemic clamp), TyG combines simplicity, low cost, and good reproducibility, characteristics that make it especially useful in PHC for monitoring and prognostic stratification. However, the influence of secondary hypertriglyceridemia (alcohol, hypothyroidism, drugs) and the need for contextualized interpretation should be considered (ALOTAIBI et al., 2025; TAO et al., 2022).

In summary, the combined use of these biomarkers becomes very relevant, as the FPG describes the basal state of glycemic homeostasis; glycemic variability captures daily metabolic instability linked to vascular stress; The OGTT detects early glucose intolerance and cardiovascular risk even in fasting normoglycemia and the TyG index is a practical and accessible tool for estimating insulin resistance and cardiometabolic risk. Thus, the integrated evaluation of these markers enables a more comprehensive and prognostically oriented approach to the care of patients with DM2 and CVD, consolidating their role in clinical practice and PHC protocols, with low cost and great applicability (REDDY; VERMA; DUNGAN, 2023; ADA, 2024).

2.1.6 Biomarkers of the lipid profile

Biomarkers of the lipid profile, such as total cholesterol, high-density lipoprotein (HDL-c), low-density lipoprotein (LDL-c), and triglycerides, are fundamental parameters for the

evaluation of cardiovascular risk and metabolic status in individuals with chronic diseases, particularly diabetes mellitus (DM). Among patients with insulin resistance (diabetics and prediabetics), a characteristic dyslipidemic pattern is frequently observed, characterized by increased triglycerides, reduced HDL-c and predominance of small and dense LDL-c particles, forming the so-called atherogenic lipid profile. This metabolic combination plays a central role in the pathophysiology of cardiovascular diseases (CVD), recognized as the main cause of morbidity and mortality in individuals with diabetes (ADA, 2024; CHAIT et al., 2024).

This atherogenic behavior has been widely documented as an expression of interconnected pathophysiological mechanisms, including insulin resistance, chronic low-grade inflammation, and endothelial dysfunction. Alterations in lipid metabolism, especially oxidation and glycation of LDL-c particles, accelerate the atherosclerotic process and promote plaque instability. Thus, the monitoring of lipid profile components is not restricted to cardiovascular risk stratification, but also provides relevant indications on the interaction between metabolic and inflammatory pathways associated with DM and the development and progression of other cardiometabolic diseases. Understanding this set of alterations allows us to design more precise therapeutic interventions that are consistent with the metabolic phenotype of each patient (ADA, 2024; CHAIT et al., 2024).

In the prognostic context, elevated LDL-c and triglyceride concentrations, associated with reduced HDL-c levels, are associated with adverse cardiovascular outcomes, even in individuals with adequate glycemic control. In addition, in people with T2DM and SAH, the coexistence of chronic inflammation, oxidative stress, arterial stiffness, and dyslipidemia synergistically amplifies the risk of macrovascular complications, including acute myocardial infarction and stroke. In this sense, the evaluation of lipid biomarkers assumes a strategic role as a predictive tool and as a parameter for evaluating the therapeutic response to primary and secondary CVD prevention strategies (CHAIT et al., 2024).

In view of this scenario, the importance of periodic and systematic monitoring of the lipid profile is reinforced, since it contributes not only to metabolic control, but also to the in-depth understanding of the progression of cardiometabolic diseases. The strengthening of integrated approaches, which include the joint evaluation of lipid, inflammatory, and glycemic biomarkers, has been pointed out as a central guideline in the most recent international recommendations, highlighting the potential of these biomarkers to guide personalized and evidence-based clinical practices (ADA, 2024).

2.1.7 Renal profile biomarkers

The evaluation of the renal profile by means of laboratory biomarkers plays a central role in the prognostic stratification and longitudinal monitoring of patients with cardiovascular and metabolic diseases. The scientific literature shows that even discrete changes in renal function are associated with higher cardiovascular risk, progression of metabolic complications, and increased overall mortality, highlighting that renal function should be understood as a systemic marker of health and not just as an isolated indicator of renal disease. In this context, widely available biomarkers, such as serum urea and creatinine, qualitative urine testing, albuminuria, and glomerular filtration rate (eGFR) estimation, are indispensable tools for the early detection of kidney lesions and for the integrated management of these patients (KHAN et al., 2026; HASSAN et al., 2025).

Serum urea and creatinine remain among the most commonly used biomarkers for assessing renal function. Creatinine, a product of muscle metabolism, is filtered by the glomeruli, and its elevation indicates a reduction in the glomerular filtration rate. Although influenced by age, sex, race, and muscle mass, serum creatinine remains a key marker, especially when interpreted in conjunction with eGFR equations, as recommended by the KDIGO guidelines (2024). Urea, although less specific, provides complementary information on metabolic and hemodynamic status, reflecting influences such as protein intake, hydration, and catabolism. In Primary Health Care (PHC), the integrated interpretation of these parameters contributes to the early detection of renal alterations in individuals with arterial hypertension, diabetes mellitus, and other cardiometabolic conditions (GUPTA et al., 2024; KDIGO, 2024).

Considering the limitations of the isolated use of urea and creatinine, its joint use is highlighted, which expands the diagnostic capacity of the laboratory evaluation of renal function. In this context, the analysis of the urea/creatinine ratio emerges as an important complementary tool for the differentiation of pathophysiological mechanisms involved in changes in renal function. In addition, the relationship is an auxiliary parameter often used in clinical practice to improve the interpretation of traditional markers of kidney function (LIU et al., 2022).

The urea/creatinine ratio can provide relevant information about the patient's hemodynamic and metabolic status, contributing to the differentiation between prerenal, intrinsic renal, and postrenal causes of renal dysfunction. In prerenal conditions, such as dehydration, hypovolemia, or reduced renal blood flow, there is a disproportionate increase in urea relative to creatinine, resulting in an elevation of the urea-to-creatinine ratio, usually greater than 20:1. On the other hand, in intrinsic renal lesions, such as acute tubular

necrosis, the elevation of these biomarkers tends to occur more proportionally, keeping the relationship within values close to normal. Thus, the evaluation of this ratio, associated with other laboratory biomarkers and the patient's clinical context, contributes to a more accurate interpretation of changes in renal function and helps in clinical decision-making, especially in scenarios of initial evaluation and monitoring of patients with cardiovascular and metabolic diseases (DOSSETOR, 1966; OSTERMANN et al., 2020; KDIGO, 2024).

Among the available biomarkers, eGFR is considered the main indicator of global renal function, being essential for the staging of Chronic Kidney Disease (CKD) and for the assessment of associated cardiovascular risk. Evidence shows that progressive reductions in GFR, even when discrete, are associated with cardiovascular events, recurrent hospitalizations, and increased mortality, reinforcing its clinical relevance. In the context of PHC, eGFR guides therapeutic decisions, drug adjustments, and timely referrals, functioning as a robust prognostic marker in populations with cardiovascular and metabolic diseases (KILLEEN; HOROWITZ, 2022; GUPTA et al., 2024; KDIGO, 2024).

Qualitative urine testing, in turn, stands out as a low-cost, widely accessible tool, and has great clinical sensitivity. Alterations such as proteinuria, hematuria, leukocyturia, or cylindruria allow early identification of kidney lesions even before significant changes in serum creatinine. In patients with metabolic conditions, this test also helps to identify associated complications, such as urinary tract infections, which are often underdiagnosed and can accelerate the progression of renal dysfunction. Thus, the urine test is a complementary biomarker of great value in the global assessment of renal and systemic health (GUTPA et al., 2024; KDIGO, 2024).

Albuminuria stands out as one of the main prognostic biomarkers of kidney injury and cardiovascular risk. Its presence indicates increased glomerular permeability and endothelial dysfunction, and is strongly associated with the progression of CKD and increased cardiovascular events. Recent research has shown that even slightly elevated urinary albumin levels are already correlated with a worse prognosis, regardless of eGFR, reinforcing its role in early risk stratification. Recent guidelines recommend its routine evaluation, especially in patients with diabetes mellitus, hypertension, and metabolic syndrome, as a way to monitor the therapeutic response and the impact of pharmacological and non-pharmacological interventions on PHC (PERILLO et al., 2025; GUPTA et al., 2024; KDIGO, 2024).

The integrated evaluation of these biomarkers enables a more comprehensive, sensitive, and early view of renal function, contributing not only to the diagnosis and staging of CKD, but also to the stratification of cardiovascular and metabolic risk. This approach,

widely recommended by international guidelines, has high applicability in PHC due to its low cost, high availability, and significant clinical impact on the follow-up of vulnerable populations (KDIGO, 2024).

2.1.8 Liver profile biomarkers

Hepatic alterations of metabolic etiology, especially nonalcoholic fatty liver disease (NASH), are a condition of high global prevalence and often underdiagnosed in clinical practice. In the context of cardiometabolic diseases, the monitoring of liver function by means of laboratory biomarkers plays a strategic role in the identification of initial dysfunctions, for risk stratification, and for the longitudinal follow-up of patients. Liver enzymes, bilirubins, and derived indices offer valuable information on hepatocellular, cholestatic, and metabolic alterations, allowing a broad and integrated approach within the scope of Primary Health Care (PHC) (RINELLA et al., 2023; MIN et al., 2024; COUTINHO et al., 2025).

Liver enzymes, including TGO/AST, TGP/ALT, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), and lactate dehydrogenase (LDH), constitute the classic set of biomarkers used to assess hepatocellular integrity and metabolic function of the liver. AST is considered the most specific marker of hepatocellular injury, while OLT, because it is present in other tissues such as skeletal muscle and myocardium, reflects both hepatic alterations and systemic disorders that often coexist in individuals with high cardiovascular risk. Persistent elevation of transaminases has been strongly associated with NASH and cardiometabolic risk, even in the absence of advanced liver disease, reinforcing its potential as an early marker of underlying metabolic changes (GORCZYCA-GŁOWACKA et al., 2023; RINELLA et al., 2023; COUTINHO et al., 2025).

GGT stands out as a sensitive biomarker of both liver injury and cholestasis, showing a robust association with insulin resistance, low-grade systemic inflammation, and oxidative stress, central components in the pathophysiology of metabolic diseases. Recent studies reinforce that GGT is an independent prognostic marker for cardiovascular events and mortality, which gives it expanded clinical relevance in cardiometabolic populations (WANG et al., 2024; AL-SUHAIMI; AL-RUBAISH, 2024). ALP, traditionally associated with cholestatic conditions, has also been related to higher cardiovascular risk when persistently elevated, suggesting interactions between hepatic metabolism, bone remodeling, and systemic inflammation (ADAMIDIS et al., 2024). LDH, on the other hand, although less specific, reflects tissue damage and anaerobic metabolism, configuring a complementary marker in complex inflammatory and metabolic states (PABIN et al., 2025).

Total bilirubin and fractions (direct and indirect) represent essential biomarkers for the evaluation of hepatobiliary function and hemoglobin metabolism. In addition to its role in detecting cholestasis and hepatocellular dysfunction, bilirubin has significant antioxidant properties. Reduced levels were associated with higher oxidative stress and cardiovascular risk, while moderately high concentrations seem to have a protective effect against inflammation and endothelial dysfunction. Thus, its measurement contributes both to liver diagnosis and to the evaluation of redox balance and systemic inflammation in cardiometabolic patients treated in PHC (RINELLA et al., 2023; COUTINHO et al., 2025; AL-SUHAIMI; AL-RUBAISH, 2024).

The TGP/TGO (ALT/AST) ratio is a widely used index for the evaluation of metabolic liver diseases. High values of this relationship suggest the presence of NASH and are particularly observed in individuals with obesity, diabetes mellitus and metabolic syndrome, conditions that make up the cardiometabolic risk spectrum. In addition, it is a useful marker to identify subclinical hepatocellular changes and to monitor therapeutic response to clinical interventions or lifestyle changes (KOUVARI et al., 2023; RINELLA et al., 2023).

In this scenario, recent literature has highlighted the use of derived laboratory indices that integrate liver enzymes and hematological parameters, especially platelet count, expanding the capacity for early identification of hepatic structural alterations and cardiometabolic risk. Among these indices, the ratio between platelets and GO (PLT/TGO) stands out as screening tools for liver fibrosis, especially in metabolic conditions. The reduction in platelet count associated with elevated AST may reflect hepatic structural changes and impaired portal flow, indicating greater disease severity. In this sense, indices such as PLT/TGO have significant applicability in PHC, as they use simple and low-cost laboratory parameters, helping to recognize individuals at increased risk of liver disease progression and cardiometabolic complications (KOUVARI et al., 2023; CASTELLI et al., 2025).

In addition to the isolated use of indices such as PLT/TGO for the evaluation of liver fibrosis, recent evidence suggests that the interaction between liver enzymes and hematological parameters, especially platelet count, reflects complex pathophysiological processes that connect the liver to systemic cardiometabolic risk. Transaminase changes often coexist with chronic low-grade inflammatory states and endothelial dysfunction, conditions that also influence platelet dynamics and inflammatory thrombus activation. In this context, the combination of elevated liver enzymes and platelet changes has been associated with a higher risk of metabolic syndrome, atherosclerotic cardiovascular disease, and progression of metabolic liver disease. Population studies indicate that these

parameters, when evaluated in an integrated manner, can act as indirect markers of systemic inflammation, insulin resistance, and vascular remodeling, reinforcing their usefulness as accessible biomarkers for risk stratification in populations served in Primary Health Care (KOUVARI et al., 2023; LIAO; ZHU; CHANG, 2024; HUANG et al., 2023; LEE et al., 2020; YU et al., 2021).

Among the most commonly used laboratory indices for noninvasive evaluation of liver fibrosis are the APRI (*AST to Platelet Ratio Index*) and the FIB-4 (*Fibrosis-4 Index*), both of which are widely used in clinical practice and in epidemiological studies. APRI is based on the relationship between AST levels and platelet count, whereas FIB-4 incorporates age, GOT, TGP, and platelet count in its calculation. These indices have demonstrated good accuracy in identifying moderate and advanced degrees of liver fibrosis, especially in individuals with hepatic steatosis associated with metabolic dysfunction. In addition to their usefulness in the evaluation of liver, recent evidence indicates that high values of these scores are also associated with a higher risk of cardiovascular events, mortality, and progression of metabolic diseases, reinforcing the interconnection between liver dysfunction, systemic inflammation, and cardiometabolic risk. Because they use widely available and low-cost laboratory parameters, the APRI and FIB-4 represent relevant tools for screening and risk stratification in Primary Health Care (KOUVARI et al., 2023; RINELLA et al., 2023).

The integrated analysis of liver biomarkers, including enzymes, bilirubins, and derived indices, contributes to a broad assessment of the metabolic, inflammatory, and functional status of patients, favoring prognostic stratification and monitoring of clinical evolution in individuals with cardiovascular and metabolic diseases. This multidimensional approach reinforces the importance of the liver as a central organ in systemic metabolism and highlights the relevance of liver biomarkers in PHC (COUTINHO et al., 2025).

2.1.9 Hematologic Biomarkers

Hematological biomarkers, obtained through blood count, are instruments widely used in clinical practice and have significant relevance as prognostic markers in the follow-up of individuals with cardiovascular and metabolic diseases. Because they simultaneously reflect hematological, inflammatory, and immunological changes, these parameters allow for an integrated assessment of the physiological and functional status of patients, contributing to the early detection of diseases and to the monitoring of clinical evolution (LIU et al., 2023).

- *Erythrocyte Parameters*

Erythrocyte parameters, including erythrocyte count, hemoglobin, hematocrit, and hematimetric indices (VCM, HCM, CHCM), provide essential information about the patient's

oxygen-carrying capacity, nutritional status, and metabolic profile. Alterations in these indices allow the morphological characterization of anemias and help in the identification of nutritional deficiencies, chronic inflammation, and metabolic disorders often associated with cardiovascular diseases. Anemia, as well as variations in hematimetric indices, has been associated with a worse cardiovascular prognosis, a higher risk of hospitalizations, and increased mortality, reinforcing the relevance of erythrocyte parameters as complementary markers in the clinical and prognostic evaluation of PHC (SENAPATI et al., 2025; LULE et al., 2026; RESENDE et al., 2026).

The Red Cell Distribution Width (RDW), expressed by RDW-CV and RDW-SD measurements, reflects the variability of erythrocyte size and has emerged as an important prognostic biomarker in different cardiometabolic conditions. High RDW values are associated with systemic inflammation, oxidative stress, nutritional dysfunction, and worse clinical outcome in patients with cardiovascular diseases, regardless of the presence of anemia. Recent evidence shows that RDW has a consistent association with cardiovascular mortality and adverse events, configuring itself as a simple and low-cost marker with high applicability (ARKEW et al., 2022; SENAPATI et al., 2025).

- *Leukocyte Parameters*

The evaluation of the leukocyte profile, by means of the global leukocyte count and the differential count, is a relevant tool for the analysis of the inflammatory and immunological status in patients with cardiovascular and metabolic diseases. The total leukocyte count reflects the activation of the immune system and has been associated with chronic low-grade inflammatory processes, characteristic of conditions such as obesity, T2DM, and metabolic syndrome. Persistently elevated values, even within the upper limits of normality, have been linked to increased cardiovascular risk, progression of atherosclerosis, and worse clinical outcomes (AJOOLABADY et al., 2024; MENSAH et al., 2026).

The differential leukocyte count provides additional and more specific information about the different components of the immune response. Neutrophils play a central role in innate immunity and inflammatory response, and their elevation is often associated with systemic inflammatory activation, oxidative stress, and endothelial dysfunction. In patients with cardiometabolic diseases, neutrophilia has been related to greater instability of atherosclerotic plaques and an increased risk of cardiovascular events (LIBBY et al., 2018; LIAN et al., 2025).

Lymphocytes are predominantly involved in adaptive immunity and modulation of chronic inflammation. Relative lymphopenia has been observed in settings of persistent inflammation and is associated with poorer cardiovascular prognosis and increased mortality.

Changes in lymphocyte count reflect immunological imbalances related to chronic metabolic conditions, reinforcing their prognostic value when analyzed in an integrated manner with other hematological parameters (LIBBY et al., 2018; ZAFRIR et al., 2022; MADJID et al., 2004; SOEHNLEIN; LIBBY, 2021).

Monocytes actively participate in chronic inflammation and atherogenesis, as they migrate to the vascular wall and differentiate into macrophages, contributing to the formation and progression of atherosclerotic plaques. Monocytosis has been associated with a higher inflammatory burden, cardiovascular disease progression, and worse clinical outcome, especially in individuals with diabetes mellitus and dyslipidemias (KOZLOV et al., 2025; MADJID et al., 2004; SOEHNLEIN; LIBBY, 2021).

Eosinophils and basophils, although less frequently altered in cardiometabolic diseases, provide complementary information about the patient's immunological profile. Changes in subpopulations may be related to concomitant inflammatory, allergic, or infectious processes, which influence systemic inflammatory status and should be considered in the global interpretation of cardiometabolic risk (XU et al., 2025; MADJID et al., 2004; SOEHNLEIN; LIBBY, 2021).

- *Platelet Parameters*

The evaluation of the platelet profile, by means of total platelet count and indices related to platelet size and heterogeneity, is an important component in the analysis of cardiovascular risk and systemic inflammatory status in patients with cardiovascular and metabolic diseases. Platelets play a central role not only in hemostasis, but also in the inflammatory response, interaction with the vascular endothelium, and progression of atherogenesis (ZVETKOVA et al., 2024; HAMO et al., 2025).

Total platelet count provides information on hemostatic balance and may reflect underlying inflammatory and metabolic changes. Both thrombocytosis and thrombocytopenia have been associated with chronic inflammatory states, endothelial dysfunction, and increased cardiovascular risk. In patients with metabolic diseases, variations in platelet count may be related to persistent inflammatory activation, liver changes, or impaired platelet production and consumption (SHARMA et al., 2025; HAMO et al., 2025).

Mean platelet volume (MPV) is an indicator of platelet activity and reactivity, since larger platelets are metabolically more active and prothrombotic. Elevated MPV values have been associated with systemic inflammation, platelet activation, and increased cardiovascular risk, including thrombotic events. In individuals with diabetes mellitus and metabolic syndrome, MV has been shown to be a relevant marker of worse prognosis

(DAHAN et al., 2025; CHEN et al., 2025; BRAHMBHATT et al., 2022; BARROS; CARVALHO, 2024).

Platelet distribution width (PDW) reflects platelet size variability and is related to the heterogeneity of the circulating platelet population. Increased PDW indicates higher platelet anisocytosis and has been associated with platelet activation and chronic inflammatory processes. Evidence shows an association between elevated PWD and higher cardiovascular risk, especially when evaluated in conjunction with MV and platelet count (POGORZELSKA et al., 2020; ZHOU et al., 2026).

In addition to reflecting changes in platelet activation, platelet parameters have been progressively investigated as indirect indicators of chronic low-grade inflammation associated with insulin resistance. This systemic inflammatory state is considered one of the main pathophysiological mechanisms involved in the development of metabolic syndrome, type 2 diabetes mellitus, and cardiovascular diseases. Insulin resistance promotes metabolic changes that favor the production of pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha, in addition to increasing oxidative stress and endothelial dysfunction. These processes contribute to platelet activation and morphological modifications of circulating platelets, reflected by changes in indices such as MPV and PDW (DAHAN et al., 2025; CHEN et al., 2025; BRAHMBHATT et al., 2022; POGORZELSKA et al., 2020; ZHOU et al., 2026).

In this context, individuals with obesity, metabolic syndrome, type 2 diabetes mellitus, and hypertension often have increased platelet reactivity, characterized by increased MV and greater heterogeneity in platelet size. Larger platelets have higher granule content, greater capacity to release inflammatory mediators, and greater thrombogenic potential, contributing to the progression of atherosclerosis and increased risk of cardiovascular events. Thus, the integrated evaluation of platelet count and platelet indices derived from the blood count has been proposed as a complementary strategy for the identification of chronic inflammatory states and insulin resistance, especially in populations with cardiometabolic diseases followed up in Primary Health Care (SHARMA et al., 2025; DAHAN et al., 2025).

- *Relationships Derived from Blood Count*

Blood count-derived relationships have gained increasing relevance as indirect biomarkers of systemic inflammation, metabolic stress, and cardiometabolic risk. These indices combine different components of the immune and hematological response, allowing the identification of inflammatory and immunological alterations that are often not detected by the parameters isolated from the blood count. The integration of these relationships has been shown to be useful for prognostic stratification and monitoring of individuals with

chronic metabolic diseases, given its wide availability, low cost, and immediate clinical applicability (SEO; LEE, 2022; NASCIMENTO et al., 2024).

The neutrophil-lymphocyte ratio (NLR) has been validated as an indirect marker of systemic inflammation and immune imbalance. Its usefulness stems from the fact that it integrates the activity of innate immunity, represented by neutrophils, and adaptive immunity, represented by lymphocytes. High values reflect greater neutrophil-mediated inflammatory activation and relative suppression of adaptive immunity, a phenomenon observed in states of chronic low-grade inflammation, such as those that characterize obesity, type 2 diabetes mellitus, metabolic syndrome, and subclinical atherosclerosis. Several evidences demonstrate that NLR is associated with increased cardiovascular risk, progression of atherosclerosis, instability of atherosclerotic plaques, and worse clinical outcomes, configuring a biomarker of high prognostic robustness, simple, reproducible, and with strong applicability in clinical practice (PADILHA et al., 2025; NASCIMENTO et al., 2024).

The platelet-to-lymphocyte ratio (RPL) incorporates elements of platelet activation and adaptive immune response. Platelets participate not only in hemostasis, but also in inflammatory processes, synthesis of prothrombotic mediators, endothelial activation, and progression of atherogenesis. Thus, elevated RPL values reflect a prothrombotic state associated with systemic inflammation and endothelial dysfunction. In populations with cardiometabolic diseases, increased LPR has been associated with a higher probability of cardiovascular events, progression of atherosclerosis, and worse clinical outcome. When integrated with other inflammatory and hematological biomarkers, LPR expands the predictive potential of blood count and contributes to monitoring and risk stratification strategies in Primary Health Care (PADILHA et al., 2025; ZHAI et al., 2021; NASCIMENTO et al., 2024).

The monocyte-lymphocyte ratio (RML) represents another index of increasing relevance, especially in the context of chronic metabolic diseases. The increase in monocytes, associated with the proportional reduction of lymphocytes, indicates activation of innate immunity and reduction of the immunoregulatory mechanisms of adaptive immunity. Monocytes play a critical role in atherogenesis by migrating to the endothelium and differentiating into macrophages, cells that accumulate lipids and contribute to the formation of fatty streaks and the progression of atherosclerotic plaques. Evidence associates high RML values with higher cardiovascular risk, worse clinical outcome, and increased mortality, especially in individuals with diabetes mellitus, dyslipidemias, and other metabolic conditions. Thus, RML is established as a relevant complementary biomarker in the

longitudinal monitoring and prognostic stratification of these patients (NASCIMENTO et al., 2024; VAKHSHOORI et al., 2023).

In addition to the relationships involving leukocytes, indices derived from the platelet profile have also been investigated as markers of systemic inflammation and thrombotic risk. The relationship between mean platelet volume and platelet distribution width (MPV/PDW) provides an integrated assessment of the reactivity and heterogeneity of circulating platelets. VPM reflects the degree of platelet activation, since larger platelets are more metabolically active, while PDW expresses platelet size variability, related to platelet renewal and activation in inflammatory conditions. Thus, changes in this index indicate increased thrombogenic and inflammatory activity, with a consistent association with cardiovascular risk, especially in individuals with chronic metabolic diseases. It is an accessible biomarker of great clinical utility, based on routinely evaluated parameters of the blood count, which facilitates its implementation and interpretation in care practice (KORNILUK et al., 2019; PEREZ et al., 2024; CAKIR; TAYMAN, 2025).

In recent years, in addition to the classic indices, composite inflammatory indices derived from the blood count have been proposed with the objective of integrating multiple components of the immune response and increasing the capacity to detect systemic inflammation, which are widely used in acute inflammatory conditions, but can also be used in chronic inflammatory processes. Among these indices, the *Systemic Immune-Inflammation Index* (SII) and the *Aggregate Index of Systemic Inflammation* (AISI) stand out, calculated from the combination of leukocyte and platelet parameters obtained from the blood count. IBS is generally defined by the formula platelets×neutrophils/lymphocytes, while AISI additionally incorporates monocytes (neutrophils×monocytes×platelets/lymphocytes), more comprehensively reflecting the interaction between innate immunity, inflammatory response, and thrombotic activation. Recent evidence indicates that these indices are associated with systemic inflammatory processes, cardiovascular risk, insulin resistance, and progression of chronic metabolic diseases. Although they are still considered emerging markers, studies have shown that high IBS and SIA values may reflect states of chronic low-grade inflammation, characteristic of conditions such as obesity, type 2 diabetes mellitus, metabolic syndrome, and metabolic liver disease, expanding the analytical potential of the blood count as a tool for inflammatory assessment in clinical practice and in epidemiological studies (ZHAO et al., 2023; BO et al., 2025; XIU et al., 2025).

In general, the relationships derived from the blood count substantially increase the prognostic value of the traditional blood count, allowing the identification of subclinical inflammatory patterns and contributing to a more accurate approach to cardiometabolic risk.

The growing robustness of the available evidence positions these indices as promising tools for clinical practice and for monitoring at-risk populations in Primary Health Care.

2.1.10 Biomarkers of the Inflammatory Profile

Low-grade systemic inflammation plays a central role in the pathophysiology of cardiovascular and metabolic diseases, constituting an important link between insulin resistance, endothelial dysfunction, vascular remodeling, oxidative stress, and progression of atherogenesis. This chronic inflammatory state is underpinned by persistent activation of innate and adaptive immune pathways, mediated by pro-inflammatory cytokines, adipokines, and intracellular metabolic changes that reinforce a continuous cycle of tissue damage. In this context, the use of inflammatory biomarkers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) becomes strategic for the evaluation of systemic inflammation, providing valuable information on inflammatory activity and overall cardiometabolic risk (AJOOLABADY et al., 2024; OU et al., 2024).

Erythrocyte sedimentation rate is a traditional marker of inflammation, widely used in clinical practice due to its technical simplicity, low cost, tracking capability, and wide availability. The increase in ESR is mainly due to the increase in acute phase proteins, such as fibrinogen and immunoglobulins, which alter the electrostatic repulsion between red blood cells, promoting their aggregation and increasing the sedimentation rate. Despite its non-specificity, ESR has relevant clinical utility, especially because it reflects underlying inflammatory processes of slow and prolonged evolution. In individuals with metabolic and cardiovascular diseases, persistently high ESR values indicate a higher systemic inflammatory burden, being associated with the progression of atherosclerotic complications and a worse prognosis, especially when interpreted in conjunction with more specific inflammatory markers (TISHKOWSKI; ZUBAIR, 2025; BROWN et al., 2025).

C-reactive protein is one of the most sensitive and widely validated inflammatory biomarkers in the literature. Produced predominantly by the liver in response to interleukin-6 and other pro-inflammatory cytokines, CRP has a strong ability to detect acute and chronic inflammatory processes, including those associated with cardiometabolic diseases. High CRP values, even at levels considered moderate, have been consistently associated with increased cardiovascular risk, evidencing its relevance as an independent marker of adverse events, including mortality, acute myocardial infarction, and stroke. In addition, CRP integrates the communication axis between inflammation, metabolism, and endothelial function, reflecting the degree of systemic immune activation and contributing to the stratification of metabolic risk in different populations. Contemporary studies reinforce that

high-sensitivity CRP (HSCR-CRP) further enhances the predictive capacity of this biomarker, allowing the identification of subclinical inflammation associated with the early onset of atherosclerotic processes (BROWN et al., 2025; MOISSL et al., 2025).

The combined interpretation of ESR and CRP allows for a more comprehensive assessment of the systemic inflammatory response. While ESR captures sustained and longer-lasting inflammatory phenomena, CRP responds more quickly and sensitively to acute and chronic inflammatory stimuli, reflecting different stages and dynamics of inflammation. This analytical complementarity favors the use of both parameters in clinical practice, especially in Primary Health Care, where low-cost, widely available, and fast-performing tests are essential for risk stratification and longitudinal follow-up. The integration of these biomarkers into the set of clinical and laboratory information contributes to the early detection of relevant inflammatory processes, aiding in decision-making and appropriate management of populations at increased cardiometabolic risk (BROWN et al., 2025).

In addition, the use of inflammatory biomarkers in the metabolic context allows a better understanding of the interaction between chronic inflammation, energy metabolism, and endothelial function. Both ESR and CRP reflect changes in immunometabolic communication, a fundamental characteristic of cardiometabolic diseases, in which changes in adipose tissue, activation of intracellular inflammatory pathways, and immune system dysfunction play determining roles (BROWN et al., 2025). Thus, these biomarkers have not only diagnostic and prognostic utility, but also potential to guide therapeutic interventions and monitor their effectiveness over time.

3 FINAL CONSIDERATIONS

Chronic Noncommunicable Diseases remain among the greatest challenges for public health, due to their high prevalence, multifactorial character and impact on morbidity and mortality. In this scenario, the use of clinical and laboratory biomarkers is essential to qualify risk assessment, support early diagnosis, guide therapeutic conducts, and monitor the clinical evolution of patients.

The integration of parameters such as anthropometry, blood pressure, glycemic, lipid, renal, hepatic, hematological, and inflammatory profiles allows for a broader and more sensitive analysis of health status, favoring safer and more individualized clinical decisions. In addition, the incorporation of these markers into the routine of Primary Health Care strengthens longitudinal care, expands tracking capacity, and contributes to the prevention of cardiovascular and metabolic complications.

Thus, the adoption of low-cost, accessible, and clinically relevant biomarkers may represent a promising strategy to improve care, especially in scenarios with greater social vulnerability and less availability of diagnostic resources. Therefore, the judicious use of these indicators, associated with multiprofessional action and continuous follow-up, is essential for the qualification of care and for the improvement of health outcomes.

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