OPEN ACCESS

International Journal of Applied Medical and Health Sciences

Int J Appl Med Health Sci | Vol-1, Iss-2, Sept-Oct., 2026
e-ISSN: XXXX-XXXX
Homepage: https://ioasdpublisher.com/ijamhs

Inflammation, Metabolic Dysfunction and Biological Aging: The Relevance of Exploring Laboratory Biomarkers

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ABSTRACT

Review Article

Aging is a multifaceted physiological process characterised by gradual decline in cellular, metabolic, inflammatory and overall physiological functions. Chronological age is an imperfect indicator of the body's functional state since individuals of the same age can demonstrate a wide spectrum of physiological capabilities and predispositions towards disease. It is now postulated that low-grade inflammation, metabolic dysfunction, insulin resistance, lipid abnormalities and other age-associated disruptions are closely linked to the phenomenon of biological aging. Laboratory inflammatory and metabolic biomarkers can help evaluate such alterations for the early detection of disease. Traditional biomarkers include C-reactive protein, interleukin-6, tumour necrosis factor-alpha, fasting glucose, insulin, glycated haemoglobin, lipids and adipokines, whereas novel approaches concern telomere biology, epigenetics, proteomics and metabolomics. At the same time, no specific laboratory abnormality can fully represent the complex nature of biological aging. A comprehensive assessment of inflammatory and metabolic biomarkers, along with other relevant parameters, may offer valuable insights into biological age and mechanisms of healthy aging. This article aims to discuss the interrelationships between inflammation, metabolic dysfunction and biological aging, as well as the relevance, opportunities and limitations of laboratory biomarkers for studying healthy longevity.

Article History
Received: 03-07-2026
Accepted: 25-08-2026
Published: 05-09-2026

Keywords: Biological aging; Inflammation; Inflammaging; Metabolic dysfunction; Laboratory biomarkers; Insulin resistance; Longevity; Healthy aging.

INTRODUCTION

Aging is a universal physiological process that involves gradual deterioration in cellular, metabolic, inflammatory and overall body functions. Chronological age is a conventional indicator of human aging since it generally reflects how old a person's body is. However, chronological age is only a crude metric since individuals of the same age may have diverse physical performances and susceptibilities to disease. In other words, a person's health status and physiological functionality can be estimated using the concept of biological age. Biological age reflects cumulative alterations in body functions that determine the individual's resilience and vulnerability to disease. Therefore, studying biological age in relation to physiological functions is essential for understanding the mechanisms of healthy aging and promoting longevity [1].

Inflammation is an integral part of the aging process, and researchers have proposed the concept of inflammaging to explain how low-grade, persistent inflammatory responses contribute to immunosenescence and chronic diseases. Inflammaging is characterized by increased levels of pro-inflammatory cytokines and acute-phase proteins due to deregulated innate and adaptive immunity. Various cellular mechanisms, including cellular senescence, mitochondrial dysfunction, reduced autophagy, intestinal microbiota dysbiosis and others, can contribute to inflammaging. Inflammation drives atherosclerosis, diabetes, neurodegeneration, frailty and other age-associated conditions [2]. Chronic, low-grade inflammation is often accompanied by metabolic impairments, which in turn promotes further pro-inflammatory responses, and inflammaging is increasingly recognised as a key driver of metabolic dysfunction. Insulin resistance is another crucial component of metabolic dysfunction, and its role in inflammation is complex, multifaceted and bidirectional [3].

Assessment of inflammatory status, particularly biomarkers of chronic, low-grade inflammation, is essential in studying biological aging and associated conditions. Laboratory tests allow for the quantitative analysis of inflammatory biomarkers, including C-reactive protein, interleukin-6, tumour necrosis factor-alpha and others. At the same time, standard blood tests

can provide insight into metabolic dysfunction by estimating fasting glucose and insulin levels, haemoglobin A1C, lipid profile and other conventional biomarkers. Adiponectin and leptin are adipokines with anti-inflammatory properties that can also serve as predictive biomarkers of aging. On the other hand, a single parameter cannot reflect the global effects of biological aging, and a comprehensive panel of tests is often required to estimate the risks of age-associated diseases [3].

More advanced technologies, including telomere length measurements, epigenetic clocks, proteomics and metabolomics, are now used to study the mechanisms of biological aging. Epigenetic clocks, in particular, offer a simple and reliable way to estimate biological age across diverse populations. Nevertheless, many of these technologies still require further validation and optimization before they can be used in large-scale epidemiological studies or clinical settings [4].

The study of laboratory biomarkers of inflammation and metabolic dysfunction is crucial in the context of biological aging. Individual measurements of inflammatory and metabolic biomarkers can help evaluate a person's current functional state and predict future health outcomes. The implementation of lifestyle interventions, including physical activity, healthy eating, drug therapy and other evidence-based measures, can help promote healthy aging and prevent chronic diseases. Additionally, population-specific variations in biomarkers and biological aging are of particular relevance to epidemiological studies [4]. Many previous investigations primarily concerned high-income countries, whereas the aging process in Nigeria and Africa in general is different. Therefore, expanding the knowledge base regarding biological aging is essential for developing preventive strategies and improving healthcare in local populations. This article will further explore the interconnections between inflammation, metabolic dysfunction and biological aging and discuss the relevance of laboratory analysis in this context.

Inflammation, Metabolic Dysfunction and the Biology of Aging

Aging is a complex biological process that involves gradual structural and functional changes in cells, tissues, and organs. Chronological age is the most basic indicator of aging, but it only provides a limited understanding of the process. Individuals who are the same chronological age can have vastly differing levels of cardiovascular, metabolic, and cognitive health, as well as variations in immune function and susceptibility to disease. This has led to the concept of biological aging, which is related to the gradual decline of physiological function that occurs over time [5].

The distinction between chronological and biological aging is crucial to modern longevity science. Chronological aging is linear, while biological aging is influenced by genetic, environmental, and lifestyle factors, among others. This means that some individuals may experience accelerated or delayed biological aging compared to their chronological age, which can have significant implications for health and disease risk [6].

Biological aging is a multifaceted process that involves various physiological systems and mechanisms. Some of the most well-established processes include genomic instability, deregulated nutrient sensing, cellular senescence, mitochondrial dysfunction, proteostasis decline, impaired stem cell function, and chronic inflammation. These processes are intricately linked and contribute to the development of age-related diseases. For example, mitochondrial dysfunction can lead to cellular damage, which can trigger cellular senescence. Senescent cells, in turn, can contribute to chronic inflammation, which has been implicated in a wide range of age-related conditions [7].

Inflammation plays a particularly important role in the aging process. The term inflammaging refers to the chronic, low-grade inflammation that occurs with aging and is associated with increased morbidity and mortality. There are several mechanisms that contribute to inflammaging, including cellular senescence, mitochondrial dysfunction, oxidative stress, altered gut microbiota, and changes in adipose tissue function. Inflammaging is characterized by the production of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), as well as acute phase proteins such as C-reactive protein (CRP). Inflammaging is associated with a wide range of age-related conditions, including cardiovascular disease, diabetes, frailty, and neurodegenerative disorders [8].

Metabolic dysfunction is another key contributor to biological aging. Aging is often accompanied by changes in glucose and lipid metabolism, as well as alterations in adipose tissue function. These changes can lead to insulin resistance, dyslipidemia, and obesity, which are major risk factors for a variety of age-related diseases. Insulin resistance is a particularly important factor in the interaction between metabolic dysfunction and inflammation. Chronic inflammation can contribute to the development of insulin resistance, while insulin resistance can, in turn, promote inflammation [9].

Adipose tissue is a key player in both metabolic and inflammatory processes. It is an endocrine organ that produces a wide range of hormones and cytokines, including adiponectin and leptin. Adiponectin has anti-inflammatory and insulin-sensitizing effects, while leptin is involved in the regulation of appetite and energy expenditure. Dysregulation of adipose tissue function can contribute to both metabolic and inflammatory dysfunction [10].

The interconnectedness of metabolic and inflammatory processes is further demonstrated by the fact that alterations in lipid metabolism can contribute to both. Elevated triglycerides and low-density lipoprotein (LDL) cholesterol, as well as decreased high-density lipoprotein (HDL) cholesterol, are associated with an increased risk of cardiovascular disease and other age-related conditions. Chronic inflammation can also contribute to dyslipidemia [11].

Indeed, the evidence suggests that inflammation and metabolic dysfunction are two of the most important drivers of biological aging. These processes are closely intertwined and can interact synergistically to promote the development of age-related diseases. The assessment of inflammatory and metabolic biomarkers can provide valuable insights into an individual's biological age and health status [12].

Laboratory Biomarkers for Exploring Biological Aging

The search for biomarkers of aging is a major area of research in modern longevity science. Ideally, biomarkers of aging should be able to predict health and mortality outcomes and be sensitive to interventions that influence the aging process. However, there is no single biomarker that meets all of these criteria, and the field is still in the early stages of development. There are several laboratory biomarkers that can provide valuable insights into the aging process.

C-reactive protein (CRP) is one of the most commonly used biomarkers of inflammation. It is produced by the liver in response to inflammation, typically as a result of IL-6 signaling. High-sensitivity CRP can be used to assess low-grade inflammation, which has been linked to a variety of age-related conditions. However, CRP is a non-specific marker of inflammation, and its levels can be influenced by a variety of factors, including infection, obesity, autoimmune disease, and trauma [13].

Interleukin-6 (IL-6) is another important inflammatory biomarker. It is a pro-inflammatory cytokine that plays a role in the acute phase response to infection and injury. Chronically elevated IL-6 levels are associated with aging, frailty, and a variety of age-related diseases. TNF-alpha is another pro-inflammatory cytokine that is involved in the regulation of immune response and inflammation. It has been implicated in the development of insulin resistance and metabolic dysfunction [14].

Metabolic dysfunction is another key contributor to the aging process, and there are several biomarkers that can be used to assess metabolic health. Fasting glucose and hemoglobin A1c (HbA1c) are standard tests for assessing glucose metabolism, while fasting insulin and homeostatic model assessment of insulin resistance (HOMA-IR) can be used to assess insulin sensitivity. Dysregulated glucose and insulin metabolism are major risk factors for a variety of age-related diseases, including diabetes, cardiovascular disease, and dementia [15].

HOMA-IR is a particularly important biomarker of aging because insulin resistance is a key driver of metabolic dysfunction and inflammation. However, it is a relatively crude measure of insulin resistance that can be influenced by a variety of factors, including ethnicity and assay methodology. Other important metabolic biomarkers include adiponectin and leptin, which are hormones produced by adipose tissue that play a role in regulating metabolism and inflammation [16]. Lipid metabolism also plays a crucial role in the aging process. Total cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) can be measured to assess lipid metabolism and cardiovascular risk. Dyslipidemia is a major risk factor for cardiovascular disease, which is one of the leading causes of mortality in older adults [17].

In addition to these conventional biomarkers, there are a number of emerging approaches to assessing biological aging. Telomere length is a promising biomarker of aging that has been extensively studied. Telomeres are protective caps at the ends of chromosomes that shorten with age. However, telomere shortening is a complex process that is influenced by a variety of factors, and its relationship to health and mortality is still not fully understood [18]. Epigenetic clocks are another area of active research. These are mathematical models that use DNA methylation patterns to estimate biological age. There are several different epigenetic clocks, and they can provide valuable insights into the aging process. However, they are still relatively new, and their clinical utility is still being evaluated.

Proteomic and metabolomic approaches are also being used to study aging. These approaches can provide a comprehensive view of the proteins and metabolites that are present in the body, which can be used to identify biomarkers of aging. However, they are still relatively complex and expensive. Cellular senescence is another important aspect of aging. Senescent cells are cells that have stopped dividing and are no longer functional. They can accumulate with age and contribute to inflammation and tissue dysfunction. There is growing interest in developing senolytic drugs that can selectively remove senescent cells, but more research is needed to fully understand their potential benefits and risks.

The study of biomarkers of aging is a complex and multidisciplinary field. There are many different approaches that can be used to assess biological aging, but each of them has its own limitations. A combination of different biomarkers is likely to be the most effective approach for assessing biological aging and predicting health outcomes [19].

Clinical Relevance, Opportunities and Challenges of Biomarker-Based Aging Assessment. The exploration of laboratory biomarkers of aging has significant clinical relevance and offers numerous opportunities for advancing preventive medicine and longevity science. One of the most promising aspects of biomarkers of aging is their potential to identify individuals who are at increased risk of developing age-related diseases. This information can be used to develop personalized prevention and intervention strategies that can help to delay the onset of age-related conditions and improve health outcomes [20]. For example, an individual who is classified as metabolically healthy based on conventional criteria may still have subtle abnormalities in glucose metabolism, lipid metabolism, or inflammatory markers that could increase their risk of developing diabetes, cardiovascular disease, or dementia. By identifying these individuals, healthcare providers can recommend lifestyle changes or interventions that can help to reduce their risk.

This approach can help to shift the focus of medicine from disease management to risk reduction and prevention. Lifestyle modifications such as regular physical activity, a healthy diet, and adequate sleep can have a profound impact on metabolic and inflammatory health. Physical activity, for instance, can improve insulin sensitivity, reduce inflammation, and promote cardiovascular health. A healthy diet can help to regulate glucose and lipid metabolism, while sleep deprivation has been linked to increased inflammation and impaired glucose metabolism [21]. In addition to lifestyle modifications, biomarkers of aging can also be used to evaluate the effectiveness of different interventions. For example, changes in inflammatory markers or glucose metabolism can be used to assess the impact of a particular intervention on health outcomes. However, it is important to note that biomarkers should be used in conjunction with other clinical assessments, rather than in isolation.

The clinical relevance of biomarkers of aging extends beyond individual health outcomes. By identifying patterns and trends, researchers can gain valuable insights into the aging process and develop new interventions that can slow down or even reverse the effects of aging. For instance, senolytic drugs are being investigated as a potential way to remove senescent cells that contribute to inflammation and tissue dysfunction [22].

However, it is important to recognize that biomarkers of aging are not a panacea. While they can provide valuable information, they should be used as part of a broader approach to health and aging. For example, while a particular biomarker may be associated with increased mortality risk, an individual's overall health and functional status should also be taken into account when developing a treatment plan. Another challenge in the field of biomarkers of aging is the need for standardized criteria for defining accelerated aging. The concentration of a particular biomarker can be influenced by a variety of factors, making it difficult to interpret results in the context of an individual's overall health status. For instance, levels of CRP can be elevated in response to infection or obesity, which may confound the interpretation of results. Similarly, insulin resistance can be influenced by a variety of factors, including diet and physical activity [23]. A related challenge is the issue of biological variability. Many biomarkers can fluctuate over time in response to changes in health status or lifestyle. As a result, it can be difficult to obtain accurate measurements, and multiple tests may be needed to obtain reliable results.

Finally, it is important to consider the practicality and accessibility of different biomarkers. Some of the most promising approaches, such as epigenetic clocks and proteomic profiling, require specialized equipment and expertise that may not be available in all settings. This is particularly relevant in low- and middle-income countries, where access to healthcare services and diagnostic technologies can be limited [24]. The exploration of laboratory biomarkers of aging has the potential to revolutionize medicine and extend human healthspan. However, it is a complex and multidisciplinary field that presents numerous challenges. By understanding the strengths and limitations of different biomarkers, clinicians and researchers can harness their potential to improve health outcomes and advance the field of longevity science.

CONCLUSION

Inflammation and metabolic dysfunction are two of the most important processes that contribute to biological aging. These processes are closely intertwined and can interact synergistically to promote the development of age-related diseases. Chronic low-grade inflammation, insulin resistance, dysregulated glucose metabolism, dyslipidemia, and adipose tissue dysfunction can all contribute to accelerated aging and increased mortality risk. Laboratory biomarkers can provide valuable insights into these processes and help to identify individuals who may be at increased risk of developing age-related conditions. Conventional biomarkers such as CRP, IL-6, TNF-alpha, fasting glucose, insulin, HOMA-IR, HbA1c, lipid profile, adiponectin, and leptin can be used to assess inflammatory and metabolic status. Emerging approaches such as epigenetic clocks, telomere length measurements, proteomic profiling, and metabolomic analyses offer additional opportunities to study biological aging.

However, it is important to recognize that no single biomarker can fully capture the complexity of the aging process. A combination of different biomarkers, as well as clinical and functional assessments, should be used to obtain a comprehensive understanding of an individual's biological age and health status. The study

of laboratory biomarkers of aging has significant clinical relevance and offers numerous opportunities for advancing preventive medicine and longevity science. By identifying individuals who are at increased risk of developing age-related diseases, clinicians can develop personalized prevention and intervention strategies that can help to improve health outcomes. However, further research is needed to fully understand the potential of these biomarkers and to develop effective interventions that can slow down or even reverse the aging process.

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