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Short Communication

An Index to Assess Integrative Health Status in Human Studies

Mohammad-Reza Vaez-Mahdavi[1], **Leila Nasiri**[1*]

1. Health Equity Research Center, Shahed University, Tehran, Iran.

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ABSTRACT

Background: Conventional metrics for assessing biological aging, like allostatic load or telomere length, have limitations in providing a comprehensive picture, especially across diverse populations exposed to chronic stressors like sulfur mustard.

Materials and Methods: This study proposes a novel composite index the Biological Health Score (BHS)-to-telomere length ratio. It integrates a multisystem BHS (from non-invasive biomarkers) with leukocyte telomere length, applicable to various epidemiological studies.

Results: The composite ratio demonstrated greater explanatory power than its individual components. It more successfully predicted injury severity in sulfur mustard-exposed veterans and showed a stronger association with biological aging markers.

Conclusion: This feasible, integrative index is a promising tool for epidemiological and clinical research to identify individuals at risk of accelerated aging and health disorders resulting from chronic stress exposure.

*** Corresponding Author:**
Leila Nasiri, Assistant Professor.
Address: *Health Equity Research Center, Shahed University, Tehran, Iran.*
Phone: *+98 (902) 8101600*
E-mail: *l.nasiri@shahed.ac.ir*

Introduction

Various studies on chemical warfare survivors, affected by sulfur mustard gas during the Iraq-Iran war, have indicated evidence of premature aging, mitochondrial dysfunction [1], and attrition in the telomeres of immune cells in the affected individuals [2-10]. The pathological effects of sulfur mustard exposure across diverse organs mimic the chronic stress milieu within cells, characterized by a sustained elevation in glucocorticoids unaccompanied by regulatory feedback mechanisms on adrenocorticotropic hormone (ACTH) and corticotropin-releasing hormone (CRH) secretion. Consequently, this heightened glucocorticoid state precipitates Th1 process suppression, triggering a cascade of health consequences among affected individuals [11, 12]. Glucocorticoids play a crucial role in inhibiting leukocyte migration and diminishing the Th1 response in conditions, such as Takayasu's arteritis, due to their anti-inflammatory properties and immunosuppressive effects [11]. Glucocorticoids affect immune cells, including T cells, by blocking cytokine production by Th1 cells and inducing cell death, highlighting their role in modulating immune responses [12].

Glucocorticoids regulate fundamental processes in the human body and control cellular functions, such as metabolism, growth, differentiation, and apoptosis. Additionally, endogenous glucocorticoids link the endocrine glands and the immune system, ensuring the proper functioning of inflammatory responses during tissue repair, remodeling, and pathogen clearance through genomic and rapid non-genomic pathways. Glucocorticoids demonstrably improve quality of life for a substantial cohort of patients with immune system disorders, through their suppressive, anti-inflammatory, and anti-allergic properties on cellular, tissue, and immune organ function [11, 13].

Exposure to pathogens triggers a rapid immune response. Glucocorticoids modulate the inflammatory response by suppressing the expression of pro-inflammatory cytokines in immune cells [14]. Furthermore, glucocorticoids can suppress the expression of adhesion molecules, preventing neutrophils from adhering, sticking, and migrating to the site of inflammation. Glucocorticoids also induce annexin-1 expression, leading to neutrophil detachment and apoptosis. Chronic exposure to glucocorticoids alters the gene expression profile of resident macrophages toward an anti-inflammatory state and enhances macrophage phagocytic activity. Finally, glucocorticoids act on T cells by blocking cytokines production derived from both Th1 and Th2 cells and inducing cell death [12].

The chronic glucocorticoid milieu, as observed in conditions, such as sulfur mustard exposure, thus establishes a pro-aging environment at the cellular level. It is characterized by immune dysregulation and accelerated cellular senescence. A key biomarker of this senescent state is telomere attrition, the protective caps at the ends of chromosomes [3, 5, 9, 10]. Telomere shortening is a hallmark of cellular aging and is exacerbated by chronic inflammation and oxidative stress, both of which are influenced by prolonged exposure to glucocorticoids. This mechanistic link between systemic stress (reflected in physiological dysregulation) and cellular aging (reflected in telomere length) [10] provides a strong rationale for integrating both levels of analysis into a single, comprehensive metric [15, 16].

Allostatic load is a composite metric that quantifies physiological aging-related impairments over an individual's lifespan [17], principally associated with responses to stress [18]. Its evaluation is facilitated through a metric known as the allostatic load score. The allostatic load score is a comprehensive index used to assess the cumulative physiological load imposed by chronic stress on the body. This score reflects the pressure and weariness on various physiological systems caused by repetitive or sustained exposure to stressors. The allostatic load score usually comprises several biomarkers from various physiological systems, including cardiovascular, metabolic, immune/inflammatory, coagulation, and neuroendocrine systems. The allostatic load score provides an overall assessment of the impact of chronic stress on physiological functions and can be effectively used to identify individuals at risk of stress. This scoring method is often used in basic studies of the relationship between stress and health, as well as in clinical settings to guide targeted interventions to reduce stress and improve health [2, 19, 20].

Accordingly, this short communication aimed to introduce and conceptually justify a composite index based on the biological health score (BHS) and telomere length for integrative assessment of health status in human studies.

Materials and Methods

The integrative assessment methodology for stress injuries involves deriving a composite index, the BHS. This index reflects the functioning of key physiological systems, including cardiovascular, endocrine, metabolic,

hepatic, renal, and immune response regulation. The BHS index assesses the functioning of multiple systems and organs, the dysfunction of which disrupts homeostasis and, consequently, leads to the onset of allostatic load in the body. This index can be used in many examinations aimed at assessing overall health status [2, 21]. Additionally, measuring telomere length in white blood cells is a recognized indicator of cellular health and of aging [3]. The combination of BHS and telomere length indices has led to novel quantitative calculations that demonstrate enhanced efficiency and explanatory power compared to either BHS or telomere length indices alone. This is a consequence of the significant variability in findings across demographic groups and the limitations of the aforementioned indicators [6]. The BHS-to-telomere length ratio mitigates these limitations by integrating a systemic, multi-organ physiological state (BHS) with a fundamental, cell-intrinsic marker of aging (telomere length). This composite index is hypothesized to have greater explanatory power because it captures a broader biological reality: an individual with a high allostatic load (high BHS) and compromised cellular integrity (short telomeres) is likely to experience a more advanced state of biological aging than either measure alone would indicate.

Results

Empirically, this ratio has demonstrated a stronger association with injury severity among chemical veterans than either component in isolation [6], suggesting it reduces noise and enhances the signal of biological aging across diverse demographic groups. In other words, the computation of the BHS to telomere length ratio has provided transparency power as a determinant for assessing the overall health level of study subjects, which can be used in various studies.

Conclusion

Considering that the variables required for calculating BHS are all non-invasive and their measurement can be included in regular health assessment programs, and also measuring telomere length in white blood cells through simple peripheral blood sampling is feasible, measuring and calculating this index in cross-sectional, cohort, and population-based epidemiological studies is easy and relatively inexpensive. This index (BHS-to-telomere length ratio) can be an influential and efficient indicator for human studies dedicated to assessing individuals' health levels and evaluating the impact of various risk factors on the health of individuals and communities.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

Conceptualization: Leila Nasiri and Mohammad-Reza Vaez-Mahdavi; Supervision: Mohammad-Reza Vaez-Mahdavi; Data analysis and writing the original draft: Leila Nasiri; Review and editing: Mohammad-Reza Vaez-Mahdavi.

Conflicts of interest

The authors declared no conflict of interest.

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