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Editorial

War-related Psychological Stress and the Rising Concern of Autoimmune Diseases: An Emerging Immunological Challenge

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The recent escalation of wars and armed conflicts across different regions of the world has created an unprecedented humanitarian and psychological crisis affecting millions of individuals. While the immediate impacts of war, including mortality, injury, displacement, malnutrition, and destruction of healthcare infrastructure, are readily observable, the long-term biological consequences of chronic war-related stress remain insufficiently discussed. Increasing evidence from the fields of psychoneuroimmunology and inflammatory medicine suggests that prolonged psychological stress induced by war may profoundly alter immune homeostasis and potentially contribute to the development or exacerbation of autoimmune diseases [1].

Psychological stress is not merely an emotional state; rather, it represents a complex neuroendocrine and immunological response involving activation of the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system. Under acute conditions, these responses may be adaptive and protective. However, chronic and severe stress, such as that experienced during wars, forced migration, bombardment, loss of family members, economic collapse, and persistent insecurity, may lead to sustained immune dysregulation. This dysregulation is increasingly associated with abnormal inflammatory responses and loss of immunological tolerance [2].

Exposure to chronic traumatic stress has been shown to increase circulating levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha, and interleukin-1 beta (IL-1β). Simultaneously, prolonged stress may impair regulatory T-cell activity and alter glucocorticoid responsiveness, thereby disturbing mechanisms responsible for preventing immune attacks against self-antigens. Such inflammatory and immunological disturbances are now considered important contributors to the pathogenesis of autoimmune disorders [3-6].

Several epidemiological studies have demonstrated a significant relationship between post-traumatic stress disorder (PTSD) and autoimmune diseases. Military veterans exposed to combat-related trauma have shown increased incidence rates of rheumatoid arthritis, systemic lupus erythematosus, psoriasis, inflammatory bowel disease, autoimmune thyroid disorders, and multiple sclerosis. Similar observations have been reported among

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civilian populations exposed to war-related trauma and displacement. Although the exact molecular pathways remain incompletely understood, chronic inflammation, oxidative stress, mitochondrial dysfunction, and epigenetic modifications appear to play critical roles in mediating the relationship between severe psychological stress and autoimmunity [6, 7].

One of the major concerns regarding modern warfare is the prolonged psychological exposure. Unlike acute traumatic events, recent conflicts often involve continuous fear, repeated exposure to violence through media and social networks, uncertainty regarding personal safety, and disruption of normal social structures. These conditions may result in persistent activation of stress-response pathways and long-term immune imbalance. Sleep deprivation, anxiety, depression, and social isolation—common consequences of war environments—may further aggravate inflammatory processes and immune dysfunction [8].

Children are among the most vulnerable populations. Early life stress is associated with long-lasting immunological alterations that persist into adulthood. Exposure to war-related trauma may influence immune development during critical periods of maturation, potentially increasing susceptibility to autoimmune and inflammatory diseases later in life. Similarly, pregnant women exposed to chronic stress may experience altered maternal immune responses that could influence both maternal health and fetal immune programming [9].

Another important aspect involves patients already diagnosed with autoimmune diseases. Stress is widely recognized as a potential trigger for disease flare-ups in conditions such as lupus, rheumatoid arthritis, psoriasis, and inflammatory bowel disease. The interruption of medical care during wars, limited access to medications, nutritional deficiencies, and psychological distress may collectively worsen disease severity and negatively affect treatment outcomes. In regions affected by conflict, healthcare systems are frequently overwhelmed or partially destroyed, making long-term management of chronic inflammatory diseases increasingly difficult [3, 6, 10, 11].

Recent advances in psychoneuroimmunology have strengthened the concept that the nervous, endocrine, and immune systems are deeply interconnected. Chronic stress may alter cytokine signaling, impair natural killer cell activity, modify gut microbiota composition, and promote systemic inflammatory states. Emerging evidence also suggests that stress-induced epigenetic changes may contribute to sustained immune abnormalities even after traumatic exposure has ended. These findings raise concerns regarding the potential delayed increase in the prevalence of autoimmune disease among populations exposed to prolonged warfare [12-14].

Moreover, forced migration and refugee crises associated with wars may amplify these biological effects. Refugees often experience repeated traumatic events, poor living conditions, exposure to infectious disease, inadequate nutrition, and restricted access to healthcare. Such combined stressors may synergistically contribute to immune dysfunction and chronic inflammation. Given the growing number of displaced individuals worldwide, understanding the long-term immunological consequences of war has become a global public health priority [14-16].

Despite these observations, the immunological effects of war-related stress remain underexplored in clinical and translational research. Most current healthcare responses to war understandably focus on acute injuries and infectious diseases, while chronic inflammatory and autoimmune consequences receive comparatively limited attention. Longitudinal cohort studies involving trauma-exposed populations are urgently needed to clarify the temporal relationship between psychological trauma and autoimmune disease development. Identification of biomarkers associated with stress-induced immune dysregulation may also facilitate earlier diagnosis and preventive interventions [16, 17].

However, we contend that the current trajectory of merely describing these biological associations—without proposing concrete interventions—represents a missed opportunity for meaningful public health impact. Therefore, in this letter, we advance a clear three-pronged actionable thesis directed at international health authorities, funding bodies, and frontline clinicians [1, 18].

First, we propose the immediate adoption of a minimal, cost-effective, and field-adaptable biomarker panel for routine screening of war-affected populations and refugees. This panel should include: (i) high-sensitivity C-reactive protein as a marker of systemic inflammation, (ii) IL-6 as a key mediator of stress-induced inflammatory signaling, and (iii) serum or salivary cortisol as a reflection of hypothalamic–pituitary–adrenal (HPA)-axis dysregulation. We argue that this trio of biomarkers, selected for their accessibility, well-documented sensitivity to chronic stress, and prognostic value for autoimmune risk, could be feasibly integrated into existing humanitarian health assessments without imposing prohibitive costs or logistical burdens [3-6, 18-20].

Second, we strongly critique the current funding priorities in global health, which disproportionately allocate resources to acute traumatic injuries and infectious disease outbreaks while largely neglecting the long-term immunological sequelae of war. We call upon major international funding agencies—including the Bill & Melinda Gates Foundation, the European Union's Horizon program, and the wellcome trust—to dedicate specific, ring-fenced grant calls to psychoneuroimmunology research in conflict settings. Without such financial commitment, the chronic autoimmune burden of warfare will remain a silent, unaddressed epidemic [21-24].

Third, we issue a direct call to action to the World Health Organization (WHO) and the Office of the United Nations High Commissioner for Refugees (UNHCR). We urge these bodies to incorporate immune monitoring and stress-related inflammatory risk assessment into their official clinical guidelines for conflict zones and refugee camps. This includes recommending the proposed biomarker panel as an optional but encouraged component of routine intake assessments, alongside mental health screening, to enable early identification of at-risk individuals and timely preventive interventions [22-26].

In addition to biomedical investigations, integrating mental health support into humanitarian responses may provide important immunological benefits. Psychological interventions aimed at reducing chronic stress, anxiety, and PTSD may mitigate inflammatory activation and improve immune regulation. Addressing mental health during and after armed conflicts should, therefore, be considered not only a psychiatric necessity but also a broader strategy for preventing chronic immune-mediated disorders [5-7, 27, 28].

In conclusion, war-related stress is not merely a psychological phenomenon but a potent biological driver of immune dysregulation with lasting autoimmune consequences. However, awareness without actionable strategy is insufficient. We argue that the scientific and clinical communities must move beyond descriptive epidemiology toward proactive, implementable solutions. The biomarker panel we propose, coupled with redirected funding priorities and explicit policy integration by the WHO and UNHCR, offers a tangible pathway to mitigate the hidden immunological toll of modern warfare. As global conflicts continue to displace millions, we urge the international community to recognize that failing to address chronic stress-induced autoimmunity today will result in a secondary, delayed pandemic of chronic inflammatory diseases tomorrow. The time for action is now.

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