

Feature Review

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Mechanistic Research and Biomarker Characteristics of Immune Storms in Severe Dengue

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Abstract This study explored the key mechanisms of the immune storm in severe dengue fever, the progress of biomarkers, and potential intervention ideas. Immune storm mainly results from the imbalance between innate immune and adaptive immune responses. Common manifestations include excessive activation of pattern recognition receptor pathways such as TLR, antibody-dependent enhancement (ADE), and abnormal T-cell responses, etc. These changes can cause a large amount of cytokine release, further leading to increased vascular permeability, coagulation disorders, and may develop into multiple organ dysfunction. This study reviewed the research progress of multiple types of biomarkers. The existing evidence suggests that these indicators have application potential in the early identification of severe cases, risk stratification, and monitoring of therapeutic efficacy or disease course. Meanwhile, the research also discussed possible therapeutic exploration directions, such as anti-inflammatory and immunomodulatory therapy, endothelial protection-related drugs, and a comprehensive management model of "supportive treatment+targeted intervention". It should be pointed out finally that the current research on biomarkers still has limitations such as small sample sizes and inconsistent research standards, which affect the comparability and promotion of the results. In the future, larger-sample and multi-center studies should be carried out, more standardized biomarker combinations should be established and clinical applications promoted, so as to achieve more accurate risk assessment and earlier intervention, and reduce the risk of death from severe dengue fever.

Keywords Severe dengue fever; Immune storm; Cytokine; Biomarker; Pathogenesis

1 Introduction

Dengue fever is one of the common mosquito-borne viral diseases worldwide. In recent years, the number of cases has continued to rise and the range of transmission has been expanding, making it a prominent public health issue. As of 2021, there were approximately 59 million new cases and nearly 29 000 deaths worldwide each year (Zeng et al., 2021). This disease has been prevalent for a long time in regions such as South Asia, Southeast Asia and Latin America, imposing a considerable burden on society and the economy. Among them, low-and middle-income countries are more affected. Climate change, accelerated urbanization and increased population mobility have further promoted the spread of diseases (Zhang et al., 2025).

The symptoms of dengue fever virus infection vary greatly. It may have no obvious symptoms or only mild discomfort, or it may develop into a serious condition characterized mainly by blood exudation, massive bleeding and organ function damage. In severe cases, shock or even death may occur (Tejo et al., 2023). The elderly and those with underlying diseases have a higher probability of adverse outcomes (Mendez et al., 2025). In clinical observations, the indicative risk signals mainly include repeated vomiting, abdominal pain, mucosal bleeding, liver enlargement, rapid decrease in platelet count, etc. (Dash et al., 2024; Azra et al., 2025; Jeng et al., 2025). Some patients with mild early symptoms may rapidly worsen within a short period of time, which makes disease assessment more uncertain and continuously increases the pressure on clinical judgment and allocation of medical resources (Tsheten et al., 2021; Yang et al., 2025).

This study will focus on the core cause of severe dengue fever, immune storm (also known as cytokine storm). Simply put, it is an imbalance between innate and adaptive immune responses, releasing a large amount of pro-inflammatory cytokines. At present, there are no specific antiviral drugs for the treatment of dengue fever.