

CYTOKINE PROFILE FEATURES IN PATIENTS WITH CHRONIC BRUCELLOSIS

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Abstract. Chronic brucellosis remains a global zoonotic health problem, characterised by frequent relapses, long-term complications, and persistent immune dysregulation. Cytokines play pivotal roles in the host immune response and may serve as prognostic markers for chronicity and relapse. This review summarises current evidence on cytokine expression patterns in chronic brucellosis, highlights differences compared to acute infection, explores prognostic implications, and proposes directions for future research and clinical applications. Persistent alterations in cytokine profiles—such as reduced interferon- γ (IFN- γ) responses and elevated regulatory cytokines (e.g., TGF- β , IL-5) in patients with relapsing disease—may underpin impaired pathogen clearance and predisposition to chronic disease. Integrating cytokine profiling into clinical management may facilitate risk stratification and better follow-up of affected patients.

Keywords: chronic brucellosis; cytokine profile; interferon- γ ; TGF- β ; IL-6; relapse; immune dysregulation

Introduction. Brucellosis is a zoonotic infection caused by bacteria of the genus *Brucella*, presenting with a wide spectrum of clinical manifestations, from acute

febrile illness to chronic relapsing disease. Chronic brucellosis, defined as ongoing symptoms or relapse after initial treatment, poses diagnostic and therapeutic challenges. Persistent infection, immune evasion by the pathogen, and host immune dysregulation contribute to chronicity. Cytokines mediate the interplay between innate and adaptive immunity and can reflect disease activity, prognosis, and relapse risk. Understanding the cytokine milieu in chronic brucellosis is essential for improving patient management and prognostic assessment (1).

Cytokine expression patterns in chronic versus acute brucellosis. Acute brucellosis is typically characterised by Th1-type cytokine responses. However, chronic brucellosis often shows a different pattern. Patients with chronic brucellosis have been reported to exhibit significantly lower antigen-stimulated IFN- γ responses, while levels of IL-5 and TGF- β are elevated, suggesting a shift toward a regulatory phenotype (2).

A cohort study in an endemic region analysing IL-4, IL-6, IL-10, IL-17, IFN- γ , and TNF- α in acute and chronic patients found all six cytokines elevated compared to healthy controls; IL-6 and IFN- γ were independent predictors of disease severity (3). This supports IL-6's role in chronicisation. Relapse-focused research revealed that patients with recurrent brucellosis had elevated basal IL-6 and IL-8, as well as increased TNF- α and IFN- γ upon antigen stimulation, distinguishing them from acute-only patients (4). Such cytokine signatures may serve as predictive markers for relapse risk. Older studies measuring IL-12 and IFN- γ in human brucellosis also reported significant elevation compared to controls, reflecting a complex immune imbalance in chronic disease (5,6,7).

Prognostic implications and risk of relapse. Persistent immune dysregulation reflected in cytokine profiles may underlie relapse and chronicity. Elevated IL-6 has emerged as a recurring prognostic marker, correlating with progression to chronic disease (3,8). Baseline and post-treatment cytokine

measurements (e.g., IL-6, IFN- γ) can aid in identifying patients at high risk of relapse. Integrating cytokine profiling with conventional markers (CRP, ESR, serologic titres) may enhance risk prediction and guide prolonged therapy or closer follow-up. (4,5). Patients with persistently elevated pro-inflammatory or regulatory cytokines may require extended monitoring to prevent recurrence.

Clinical and research perspectives. Cytokine profiling in clinical practice is not yet routine due to cost and standardisation challenges. Nonetheless, evidence suggests potential applications:

Stratifying relapse risk for targeted monitoring and follow-up.

Guiding decisions on extended antimicrobial therapy or adjunct immunomodulation.

Identifying candidates for future therapeutic interventions targeting cytokine pathways.

Future research should focus on longitudinal studies correlating cytokine patterns with clinical outcomes, standardisation of cytokine panels (Th1, Th2, Th17, Treg), and multicentre studies in endemic regions to validate prognostic utility(10,11).

Conclusion. Chronic brucellosis is characterised by distinct cytokine alterations, including suppression of Th1 responses (IFN- γ) and elevation of regulatory/pro-inflammatory cytokines (IL-6, IL-8, TGF- β). These immune signatures correlate with relapse risk and may serve as prognostic biomarkers. While routine cytokine profiling is not yet standard, its integration into clinical management could improve personalised care and facilitate targeted follow-up. Expanded research is necessary to validate predictive models and explore immunomodulatory interventions.

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