Increased mycobacterium tuberculosis antigen-induced gene expression of interferon-gamma, tumor necrosis factor alpha and interleukin-6 in patients with diabetes

Kiran I. Masood  
*Aga Khan University*

Muhammad Irfan  
*Aga Khan University, muhammad.irfan@aku.edu*

Qamar Masood  
*Agha Khan University, qamar.masood@aku.edu*

Bushra Jamil  
*Aga Khan University, bushra.jamil@aku.edu*

Shoaib Rao  
*Aga Khan University*

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Increased *Mycobacterium tuberculosis* antigen-induced gene expression of interferon-gamma, tumor necrosis factor alpha and interleukin-6 in patients with diabetes

Kiran I. Masood a,*, Muhammad Irfan a, Qamar Masood b, Bushra Jamil b, Shoaib Rao a, Maryam Rahim a, Zahra Hasan a

a Department of Pathology and Laboratory Medicine, The Aga Khan University, Karachi, Pakistan
b Department of Medicine, The Aga Khan University, Karachi, Pakistan

**Introduction:** Pakistan ranks fifth in high tuberculosis (TB)-burden countries and seventh among countries with high prevalence rates of diabetes mellitus (DM). DM is a risk factor for TB and worsens disease outcomes. Furthermore, *Mycobacterium tuberculosis* (MTB) infection can induce glucose intolerance and worsen glycemic control in diabetes. Suppressor of cytokine signaling (SOCS)-1 and -3 molecules regulate cytokine signaling and are important in maintaining an immune balance. In TB, interleukin (IL)-6 upregulation induces SOCS3, which is also a negative regulator of insulin signaling. This research focuses on the mechanism by which SOCS1 and SOCS3 affect insulin resistance and increased susceptibility to TB.

**Methods:** We studied gene expression in peripheral blood cells of patients with diabetes (n = 10) and healthy endemic controls (EC, n = 11) both with and without MTB infection. Mycobacterial antigen (PPD) and mitogen-stimulated SOCS1, SOCS3, interferon-gamma (IFN-γ), IL-6, and tumor necrosis factor alpha (TNFα) mRNA expression levels were determined using real-time polymerase chain reaction.

**Results:** MTB antigen-stimulated mRNA levels of IFN-γ was 10-fold higher, SOCS1 was 4 times greater, TNFα was 10-fold higher, and IL-6 was 2-fold greater in patients with DM than in ECs. Overall levels of PPD-stimulated IL-6 was higher in patients with DM than in ECs (p = .036). Mitogen-induced mRNA levels of IFN-γ were 30-fold higher, SOCS3 was 20 fold higher, and SOCS1 was 4-fold higher in patients with DM than in ECs.

**Conclusion:** Increased proinflammatory cytokine production in response to MTB antigens in diabetes would lead to exacerbated pathology and reduced inflammatory control at the site of MTB infection. This would in turn hamper the resolution of inflammation, resulting in unfavorable disease outcomes.

**Conflicts of interest**

The authors have no conflicts of interest to declare.

* Corresponding author at: Department of Pathology and Laboratory Medicine, The Aga Khan University, P.O. Box. 3500 Stadium Road, 74800 Karachi, Pakistan.

E-mail address: kiran.iqbal@aku.edu (K.I. Masood).

Peer review under responsibility of Asian African Society for Mycobacteriology.

http://dx.doi.org/10.1016/j.ijmyco.2016.09.001