

Identifying the levels of pro-fibrotic cytokines in pulmonary tuberculosis

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Tuberculosis (TB) is a chronic granulomatous infection, and it is the 9th leading cause of death in the world caused by *Mycobacterium tuberculosis* (MTB).^[1] The disease may involve any or all organs, but the lungs are the most commonly involved (85%).^[2] Pulmonary TB (PTB) is referred as a TB which involves lung parenchyma.^[3] Fibrosis is defined as a structural alteration, with laying down of the collagenous extracellular matrix by fibroblasts and other cell types. It may be interstitial, band like, or a combination of these.^[4] Fibrosis can be caused by a local inflammatory response, and fibrosis-related pathogenesis is associated with dysfunction of many organs such as lungs, liver, and kidneys.

Transforming growth factor- β (TGF- β) is the main cytokine associated with fibrogenesis although other cytokines are also involved: tumor necrosis factor (TNF) and various interleukins such as interleukin (IL)-6, IL-10, IL-13, and IL-17.^[5] TNF- α is associated with multiple roles, for example, fever and wasting in the immune and pathological responses in TB.^[6] MTB induces TNF- α secretion by macrophages, dendritic cells, and T cells.^[6] Insulin-like growth factor-I (IGF-I) is a hormone with antiapoptotic and proliferative activities, which plays an important role in tissue homeostasis.^[7] IGF-I induces an exacerbation of the lesion and thus favors parasitic growth within host macrophages. Wilson and Wynn^[8] demonstrated that pulmonary fibrosis and architectural remodeling of tissues can severely disrupt lung function, often with fatal consequences. Deveci *et al.*^[9] have reported that IFN- γ , TNF- α , and IL-12 stimulate and IL-10, TGF- β , and IL-4 suppress the protective immune response against TB. Several studies have described the role of different cytokines in MTB infection as well as differential cytokine patterns in various clinical phases of PTB.^[5,9,10] However, little information is available regarding possible activities exerted by specific cytokines on specific aspects of the disease, namely lung fibrosis.^[5,8-10]

In this issue of Lung India, Astuti *et al.*^[11] have reported a cross-sectional observational study to evaluate the plasma levels of pro-fibrotic cytokines: TNF- α , IGF-1, and TGF- β 1 in PTB patients with minimal and extensive lesions and healthy controls to explain the process of pulmonary fibrosis in TB. Authors have studied different parameters as sputum smear with direct examination under the microscope, measurement of erythrocyte sedimentation rate (ESR), and chest X-ray.

The investigators have reported no significant difference in terms of gender of the patients suffering from PTB with minimal lesions and extensive lesions. Furthermore, results of sputum smear examination were mostly negative in both groups of minimal and extensive lesions of PTB. The average of ESR was 39.22 mm/h in individuals with a minimal lesion and 69.19 mm/h in individuals with an extensive lesion of PTB; however, normal ESR was found in one patient with a minimal lesion and one patient with an extensive lesion of PTB. The authors have stated that the plasma levels of TNF- α , IGF-1, and TGF- β 1 in TB groups were higher to the healthy controls, although not significant. TNF- α level is nonsignificantly higher in the minimal lesion of TB group than extensive lesion group. IGF-1 is increased as well as TGF- β 1 is decreased significantly in minimal lesion TB group in comparison with their extensive lesion TB group. There are some limitations of the study: due to its smaller sample size, results could not be generalized in a population and there is no information about patients whether they have been previously treated for PTB or not, before enrolling in the study.

In conclusion, pro-fibrotic cytokines play a primal role in the pathogenesis of PTB. Authors have ascribed that there are differences in levels of TNF- α , IGF-1, and TGF- β 1 of extensive lesion of TB group when compared to not only minimal lesion of TB group but also the healthy controls. In addition, the extent of lesions on chest radiograph describes the state of ongoing pulmonary fibrosis which can be shown by the differences in the levels of pro-fibrotic cytokines. Further research is warranted to decipher the roles of cytokines in PTB.

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