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Title: Serum and r32kd induced cytokine levels and expression in tuberculosis patients and contacts

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Body: Tuberculosis is a disease caused by Mycobacterium tuberculosis(MTB) whose interaction with the host may lead to a cell-mediated protective immune response. Several cytokines, including IL-6, IFN-g and TNF-a, play important roles in mediating resistance against MTB. The aim was to investigate the candidate cytokines in active pulmonary tuberculosis patients of younger age (15 to 25yrs), their Household Contacts and controls. Levels were estimated by ELISA in pg/ml in serum(n=30) and PBMCs stimulated with r32-kd antigen of M.bovis BCG (n=30). Expression by qRT-PCR in 5 individuals from each group in culture supernatants were studied. In serum IFN-g and TNF-a concentrations were elevated in patients compared with their contacts and controls(24.51±10.60, 20.45±4.93, 14.14±8.22 at p< 0.002), (13.62±8.14, 11.34±5.30, 6.39±4.10 at p<0.003). In contrast, r32kd-stimulated PBMCs from patients produced less IFN-g and TNF-a (36.21±/ - 16.9, 45.57±/ - 41.96, 56.37±/ - 56.37 at P<0.002), (59.74±46.51, 87.28±53.40, 109.2±87.56 at p<0.007), whereas IL-6 concentrations were elevated in controls both in serum and stimulated PBMCs(11.61±6.09, 4.11±3.03, 1.44±1.20 at p<0.0004) (74.49±15.18, 61.21±11.79, 68.66±69.36 at P<0.01). Out of the 30 cases studied 6 contacts behaved similar to the patients in their clinical and Immunological aspects. The cell-associated mRNA in Ag85B-stimulated T cells for IFN-g and TNF-a mRNA was significantly depressed in TB patients. On the other hand, Expression of IL-6 was high in patients. Therefore, in conclusion, IFN-γ, TNF-α and IL-6 production to r32-kd antigen could be used as biomarkers for the clinical status of TB patients and early diagnosis of their contacts.