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Evaluation of cytokine levels in active pulmonary tuberculosis patients their household contacts in response to the r32-kilodalton antigen of *M.Bovis BCG*

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Abstract

Household contacts (HHCs) of patients with tuberculosis (TB) are at higher risk of infection as well as the development of active disease. Longitudinal tracking of antigen-specific cytokines with the exposure may significantly help in understanding the dynamic changes in cytokine patterns associated with disease establishment. The aim of the present study is to investigate the role of candidate cytokines stimulated with r32-kDa antigen of *M.bovis* BCG (Ag85A-BCG) in Active Pulmonary Tuberculosis (APTB) patients, their HHC and Healthy Controls (HC) were assessed at 0, 4, 6, and 12 months after exposure. The invitro T cell assays, ELISA of (Interferon gamma -IFN-γ), (Tumour Necrosis factor alpha-TNF-α) and (Interleukin-IL-4) cytokines of culture supernatants were studied in APTB (n=50), HHC who were tuberculin-Purified Protein Derivative (PPD) skin test positive (n =50) and Healthy Controls (HC) n=50, were studied. The mean proliferative responses of stimulation cells was found to be significant between APTB patients at 4M, 6M, HHC at 4M compared to HC (2±0.55,1.061±0.508,0.99±0.3381.518±0.909 at p<0.02,0.01&0.03) respectively. The mean IFN-γ levels were significantly low in Pts/HHC compared to HC (24.5±19.8/33.55±25.44&107.5±59.0)at p<0.0001. APTB Pts at 0M compared to 4M &6M (24.5±19.8,64.13±43.88&81.97±56.22) at p<0.013&0.0008 and HHC at 0M compared to 4M (33.55±25.44&71.6±56.46) at p<0.031.TNF-α levels were significantly low in Pts at 0M compared to 12M(22.82±20.71&40.83±19.09) at p<0.02. IL-4 levels were significantly high at 0M in Pts and HHC compared to HC (7.46±5.826, 7.495±5.568&5.405±4.639) at p<0.01,0.007. The ratios for IFN-γ/IL-4 and TNF- α/IL-4 were significantly increasing from 0 month to 6 months. Five APTB pts were turned into relapse during the follow up, 2 at 4th month and 3 at 6th months of treatment, both IFN-γ& TNF-α levels were decreasing in these patients. Whereas in HHC IFN-γ& IL-4 levels were decreasing during the follow upfrom 0 to 6 months. One of HHC developed the disease at 4th month of follow up. r32Kda M.bovis BCG antigen seems to be immunogenic, stimulating protective immune responses which may help us to assess the treatment outcome. In conclusion, it is important that there is a need to elucidate the mechanism of Th1 and Th2 responses in understanding recurrent TB or susceptibility to disease and also help in identifying the HHC by monitoring their immunological status who are at high risk.