

## Short Communication

# Effect of measles infection on cellular immunity in tuberculosis patients

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Accepted 7 June, 2011

This study was applied on 60 TB patients admitted in the Babylon Center of Tuberculosis and Chest Diseases in Hilla, Iraq. TB patients consisted of 38 males and 22 females with 40 healthy individuals as control group. Blood samples were collected from patients and control group to estimate phagocytic index, interferon gamma (IFN- $\gamma$ ), and anti-measles IgG level. The level of anti-measles IgG showed a significant increase (27.9 DU,  $p < 0.05$ ) in comparison to control (18.9 DU). The cell mediated parameters showed a significant decrease ( $p < 0.05$ ) in phagocytic index (7.3%) with no significant increase in IFN- $\gamma$  level (0.123 IU/ml,  $p > 0.05$ ) compared to the control group.

**Key words:** Measles, cellular immunity, tuberculosis, Iraq.

## INTRODUCTION

Tuberculosis (TB) is considered as one of the most important infectious diseases in the world, and one third of the world population are infected with *Mycobacterium tuberculosis* (Forbes et al., 2007). It is a leading global cause of morbidity and death (Dye, 2006) and it is acquired by inhalation of droplets containing *M. tuberculosis* bacilli (MTB). Tuberculosis is an immunological disease and the clinical manifestations of tuberculosis are the functions of the immune status of the host (Singh, 2000). Measles remain an important cause of child mortality, particularly in Africa and the Asian subcontinent, and most deaths are due to secondary infections resulting from the accompanying immunosuppression (Moss et al., 2002). There is belief that measles activates tuberculosis, either by converting a latent infection to active disease or by aggravating an active one. This is based on several epidemiological reports, and the plausible mechanism is the suppression of delayed type hypersensitivity after Measles (Lee et al., 2008). In the course of natural measles infection, the potentiating of other infections, including tuberculosis, is common (Cheong et al., 2010). This study was designed to highlight the association between measles infection and the level of cell mediated immunity in TB patients.

## MATERIALS AND METHODS

A total of 60 TB patients consisting of 38 males and 22 females were involved in this study. Their age ranged from 9 to 60 years. They were admitted to Babylon Center of Tuberculosis and Chest Diseases during the period October 2009 to January 2010. A total of 40 apparently healthy subjects (25 males and 15 females) were involved as controls group. The age range of controls was matched to the patients (10 to 60) years. 3 ml of blood were collected by vein puncture, 2 ml of them were left for 2 to 4 h, then, the serum was collected in clean test tube and stored at  $-20^{\circ}\text{C}$  until use for serological tests. The remaining 1 ml of blood was put in another test tube containing anticoagulant EDTA and used for assessment of phagocytic activity (Lewis et al., 2001).

## RESULTS AND DISCUSSION

The mean of titer of anti-measles IgG in TB patients sera was 27.9 DU, while in control subjects, it was 18.9 DU. The titer of control represents the base line titer. This study significantly showed differences between TB patients and controls ( $p < 0.05$ ). Depending on the fact that IgG antibodies elevates and persists for long time as an indicator for chronic or previous infection, the results of this work explained that TB patients may be suffering from previous infection with measles virus. Al-Salihy (2008) found that 50 cases of measles infection were admitted to Marjan teaching hospital in Babylon province-Iraq.

This finding indicates the persistence of measles infection

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**Table 1.** Levels of anti-measles IgG and phagocytic index.

Subject	Anti measles (Mean(DU) $\pm$ SD) (IgG)	Phagocytic index (Mean (%) $\pm$ SD) (%)	IFN- $\gamma$ (Mean $\pm$ SD) (IU/ml)
Patients (n = 60)	27.9 $\pm$ 4.07	7.3 $\pm$ 2.1	0.123 $\pm$ 0.071
Controls(n = 40)	18.9 $\pm$ 5.85	11.6 $\pm$ 1.9	0.071 $\pm$ 0.070

Phagocytic index for neutrophils was estimated according to Furth et al. (1985), Serum gamma interferon (IFN-  $\gamma$ ) and anti-measles virus IgG antibody were estimated using ELISA methods according to the manufacturer manual (Biosource) and DRG Instruments GmbH respectively.

as one inhibitory mechanism for cell mediated immunity against TB infection. These findings support Flick in 1976 who mentioned several reports regarding the relationship between measles and tuberculosis. These results also provide a suggestion that measles activates tuberculosis from latent to the active form. This is based on several epidemiological reports, and the plausible mechanism is the suppression of delayed type hypersensitivity after measles infection (Lee et al., 2008). Thus, depending on the results of this work, measles virus infection leads to immune suppression causing decreased CMI, and at the same time, increased susceptibility to TB infection during immune suppression.

In this study, the level of anti-measles IgG for TB patients was increased (27.9 DU), whereas the mean of phagocytic index was significantly ( $p < 0.05$ ) decreased (7.3%) in patients when compared to control (11.6 %) (Table 1).

This result was matched with previous studies which reported that adult measles patients in the acute phase of the disease are accompanied with severe immunosuppression of both innate and adaptive responses (Yu et al., 2008). Moreover, Fugier-Vivier et al. (2010) mentioned that measles virus suppresses cell mediated immunity. The enhanced MV replication during antigen presenting-T cell interaction, leads to a decrease in the IL-12 production, and which may be the essential mechanism of immunosuppression induced by MV. In measles, T cell skewed from type 1 responses (cell-mediated immunity) towards type 2 responses (antibody mediated immunity). Also, Al-Sa'adi (2004) reported that TB patients in Babylon/Iraq were characterized by a decreasing level for neutrophil activity.

The level of IFN- $\gamma$  which represents another indicator for cell mediated-immunity against *M. tuberculosis* was insignificantly decreased ( $p < 0.05$ ) for patients when compared to controls. The results indicated the presence of reduced cell mediated immunity in TB patients, with increased level of anti-measles IgG. This finding was matched with Fugier-Vivier et al. (2010) who mentioned that measles virus suppresses cell-mediated immunity by interfering with the survival and function of dendritic cells and T cells. Carsillo et al. (2009) mentioned that there is *in vivo* and *in vitro* evidence of Th2 polarization in cytokine responses during and after measles: production of IL-4 increases while production of IL-2 and IFN-  $\gamma$

decreased. The hallmark of normal immune response in TB patients IS elevation on the level of Th1 cell cytokines mainly IFN-  $\gamma$  to an amount that much greater and significant than normal subjects, whereas in this study there is no significant differences ( $p < 0.05$ ) between two groups. This means that TB patients involved in this study have a low level of IFN- $\gamma$  that may be insufficient to be able to activate the mycobactericidal activity of alveolar macrophages.

The results obtained in this work indicated the presence of reduced cell mediate immunity and increased Anti-Measles IgG in TB patients. This finding was matched with Yu et al. (2008) who found that reduced CMI was caused by MV infection. MV caused up regulate of CD4+ CD25+ T reg and that CD4+ CD25+ T cells contribute to the increased IL-10 and found significantly increased sustained IFN- $\gamma$  and IL-10 secretion.

Previous studies have shown that the monocytes play a key role in MV infection and decreased cell-mediated immune responses has been observed during measles (Fugier-Vivier, 2010). Thus, depending on the results obtained, increases of TB cases in Babylon, Iraq as a result of viral infection, is difficult to control due to their difficulties in the prevention, diagnosis, and treatment. Moreover, there is no strategy for the follow up of vaccination program, so that viral infection especially measles can break down the CMI, making the persons more susceptible to TB infections. Thus checking for TB infections for persons suffering from recurrent viral infections and the periodic evaluation of cell mediated immunity may aid in the monitoring of TB infections.

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