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RESEARCH ARTICLE

IMMUNOGLOBULING (IGG) STATUS IN PULMONARY AND EXTRA PULMONARY TUBERCULOSIS

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ABSTRACT

During active phase of tuberculosis, antibodies especially IgM and IgG are developed against different mycobacterial antigens and these can be detected in patients' sera. Patients with confirmed tuberculosis reporting to the Department of Thoracic Medicine and General Medicine of Govt Rajaji Hospital, Madurai were taken up for the present study. Of the 80 patients, 50 were (M=38, F=12) in PTB group and 30 (M=19, F=11) in EPTB group. Their age ranged from 19 to 45 years. Blood samples from 21, age and sex matched healthy control were included. IgG test was positive in 20 (8 PTB & 12 EPTB) of the 80. In the present study, IgG positive status was more among EPTB and it was significant (P<0.001).

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INTRODUCTION

Immunoglobulin G (IgG) is the major antibody containing protein fraction of blood. With significant decreases in IgG level, on either a congenital or acquired basis, there is an increased susceptibility to infectious processes ordinarily dealt with by humoral antibody (ie, bacterial infection). During the active phase of tuberculosis, antibodies especially IgM and IgG are developed against different mycobacterial antigens and these can be detected in patients' sera within a month after the development of the disease (Karen, 2011). There is promise in serodiagnostic tests such as Enzyme-Linked Immuno Sorbent Assay (ELISA) which is of value in early diagnosis of the disease because of its sensitivity and reliability and less costly diagnostic methods for the detection of pulmonary tuberculosis (Maekura, 2001). Commercially available controls of the mycobacterium tuberculosis antibody kit are defined and expressed in arbitrary units (U/ml). Diagnosis of extra pulmonary tuberculosis is often difficult to establish using standard methods (Marco, Marco, 1998). The purpose of the present study was to evaluate the usefulness of detection of serum immunoglobulin G (IgG) antibodies directed against the mycobacterial antigen for the diagnosis of active pulmonary tuberculosis (PTB) and extra pulmonary tuberculosis (EPTB) among symptomatic individuals, and for the detection of *Mycobacterium tuberculosis* infections among close contacts of PTB patients.

MATERIALS AND METHODS

The patients with tuberculosis reporting to the Department of Thoracic Medicine and General Medicine of Govt Rajaji Hospital, Madurai who satisfied the inclusion and exclusion criteria were included for the study. The work was carried out after getting Institutional Ethical Committee clearance and written informed consent from the patients.

Inclusion criteria: Patients presenting with persistent cough for more than two weeks, and those presenting with typical clinical features suggestive of tuberculosis were included for the study. Standard methods were followed to confirm tuberculosis. The pulmonary and extra pulmonary tuberculosis were considered only if the patients had microbiological and or histological evidences. All the patients should have received BCG vaccine.

Exclusion criteria: Patients with malignancy, diabetes mellitus, thyroid or other endocrine disorders, chronic respiratory disorders with acute exacerbations, other end organ disorders, pregnancy and on immunosuppressives or antimicrobials were excluded. Similarly, patients with HIV infection, other dual infection and under nutrition were also dropped. Thus, there were 80 newly selected patients with TB (50 with PTB and 30 with EPTB). BCG vaccinated age and sex matched persons 21 who have close contacts of PTB patients, healthy volunteers without any other illness kept as control. Fasting blood samples were collected in the vacutainer. Serum samples were separated under sterile precautions. Commercially available spot enzyme immunoassay TB RAPID IgG-SPOT-test (Span Diagnostics) was used in a blinded fashion by using stored serum samples as per the guidelines of suppliers. One drop of serum was added in RAPID IgG-SPOT device and observed for the band. All the data were recorded and analyzed using chi-square test.

RESULTS

Of the 80 patients studied, there were 38 males and 12 females in (50) PTB group and 19 males and 11 females in (30) EPTB group. Their age ranged from 19 to 45, and the median, mean ages were 34 and 36 years respectively. IgG test was positive in 20 of the 80 patients with tuberculosis and negative in all the 21 close contacts who were free from tuberculosis or other diseases. Among the 20 positive, eight belonged to PTB and 12 to EPTB. The IgG positive status among patients and controls could not be compared since the IgG was negative in all the healthy controls.

Table 1. IgG status among Tuberculosis patients

Nature of Tuberculosis	No of persons for IgG Positive (%)	No of persons for IgG Negative (%)	Total no of persons Examined
PTB	8 (16)	42 (84)	50
EPTB	12 (40)	18 (60)	30
Total	20 (25)	60 (75)	80

Using 2 × 2 table the IgG positive status was more among PTB and EPTB was compared. IgG positive status was more among EPTB and the difference was significant statistically ($P<0.001$).

DISCUSSION

In TB patients mycobacterial infection elicits humoral immune response leading to the production mainly of IgA, IgM and IgG antibodies in patients and the relationship between IgG levels and the previous TB disease was also shown earlier by (Charpin, 1990). Charpin and colleagues. The infections responsible for IgG status are activity of the diseases (Jackett, 1998), duration of illness, stages of diseases (Karen, 2011 and Martin, 1992), lymphocyte activity (Rabia, 1995), cross specificity to previous BCG status (Rosen, 1996), site of lesion and genetic nature composition of the individual (Maekura, 2001) harboring tuberculosis. From the result, it is observed that presence of IgG is associated with TB cases only. In the present study IgG positive status was lower in PTB 16% (8/50) patients when compared with EPTB 40% (12/30). Whereas other workers from India several studies (Jha, 1974; Agnihotri, 1978 and Skvor, 1975), have reported a high level of IgG among PTB patients. The rise of total IgG in pulmonary tuberculosis was interpreted as humoral response to myobacterial antigen however (Grange, 1980), Grange and colleagues observed that there is no relation between the various Immunoglobulin and mycobacterial antigen level. Martin and colleagues (Martin, 1992), observed low antibody titers when the disease is first discovered. Hence, it is more likely that a much less specific stimulation of Immunoglobulin synthesis is occurring possibly due to adjuvant activity of mycobacteria and the patients exhibited secondary response as reported (Rosen, 1996). The present report is different from a Pakistan study (Karen, 2011) in which high level of antibody was reported in TB patients 84.4% were attributed to evolution of diseases. Kaplan and colleagues (Jha,1974) observed that IgG level is valuable in differentiating patients with positive and negative cultures and with no prior history of tuberculosis and also due to treatment, presumably as a result of mycobacterial inactivation due to the treatment and release of the antigen in blood stream. Turneer (Turneer, 1988) and Gupta (Gupta, 1995), observed significant elevation of IgG in highly smear positive patients. On the other hand [16] showed raised IgG levels in health care workers. However, IgG measurement alone, cannot differentiate patients with active disease from those who had TB in the preceding few years.

IgG profiles in extra pulmonary tuberculosis patients: IgG was found to be positive in 40% of EPTB in the present study. Similar observation was made by [7] from Karachi and Addis Ababa, from Ethiopia recent study[17] who observed raised IgG in all tuberculosis patients irrespective of disease localization (lymph node versus pulmonary) when compared with healthy controls, and noted IgG antibodies only with disease establishment and not to infection alone. The factors that regulate IgG subclass are not well characterized and could well determine the disease progression in other mycobacterial infections. IgG antibodies do not show any association with lymphocyte blastogenic responses which are suppressed in pulmonary tuberculosis but not in tuberculosis lymph node (LN). Patients with both pulmonary and LN involvement also showed a trend toward higher response in IgG3, IgG4 and IgE subclasses as observed (Rabia, 1995). The strength of the present study was that all cases were confirmed cases of tuberculosis by microscopy and the individuals who performed the laboratory tests were blinded on the clinical history. The limitations are the cases were not further classified as per stage of the disease, culture status etc., as the numbers became smaller for statistical analysis.

Conclusion: Various factors influence the IgG level in patients with tuberculosis alone with site of the lesions. Hence, it is suggested to screen large number of cases and clarify them in relation to various factors and ascertain the status statistically.

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