CHAPTER VI
DISCUSSION
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Tuberculosis is a world wide disease and in India it is still the most important bacterial infection. The problem of tuberculosis control is enormous. Approximately one third of the world’s population is infected with mycobacterium tuberculosis. With expected spread of AIDS the prevalence of tuberculosis as a complication is also likely to increase (Sudre et al, 1992).

Early diagnosis of the disease is an important aspect in the control of tuberculosis which is the most cost effective health intervention in developing countries. A definite diagnosis of pulmonary tuberculosis can be made with acid fast bacilli found in sputum smear. Problem arises when sputum smear is repeatedly negative in pulmonary tuberculosis and in extrapulmonary tuberculosis. Chest skiagram provides only a probable diagnosis and culture for tubercle bacilli is both expensive and time consuming (Sachan et al, 1994).

To overcome these diagnostic delay a variety of newer methods have been employed such as RIA, PCR and BACTECH. All these techniques have their limitation being unable to detect many cases, cost effectiveness and too complicated technique (Grange, 1990). But ELISA is less expensive, sensitive, technically simple, easily reproducible and it can measure class specific antibodies and the technique requires only minute
quantities of serum with the additional advantage of quantitating antibodies by testing serum at a single dilution (Young et al, 1980).

With this background in mind this study was undertaken to evaluate the sensitivity and specificity of antigen A60 Specific IgG and IgM in the diagnosis of pulmonary and extrapulmonary tuberculosis.

A total of 150 patients were microbiologically or histologically proven and 100 controls. In the study group 127 patients (84.6%) were had pulmonary tuberculosis and 23 patients (15.3%) were of extrapulmonary tuberculosis.

Our study group compromised of patients between the age of 13-80 years but majority of patients were in the age group of 20-50 years. It indicates that the tuberculosis mainly occurs in the prime years of life.

Summers and McNicol (1980) conducted a study in which they found that 54% of tuberculosis patient being between the age group of 20-40 years.

We also observed in our study out of 150 patients 97 patients (64.5%) were male and 53 patients (36.2%) were female. The ratio of male predominance over female was 2 : 1.
Though tuberculosis is common in younger age group. In our study the serum IgG and IgM were not correlating with the age (Table No.2). p value was not significant (p value 0.539231).

In 1994 Sachan et al conducted a study in which they concluded that the serum IgG titre value was not associated with age.

Eventhough there was male predominance in the occurrence of tuberculosis there was no difference between two sexes in the serum IgG level statistically (p value was not significant - 0.9275). But IgM was high in female than male patients which was statistically significant (p value 0.0045).

Nicholls in 1975 found that ELISA test was more erratic in women, higher titre being found in them.

In our study, of 23 extrapulmonary tuberculosis 14 patients had lymphnode tuberculosis, 3 patients had disseminated tuberculosis, 3 patients had peritoneal, 2 patients had pleural tuberculosis and one patient had pericardial tuberculosis. We concluded that tuberculous lymphadenitis is the most commonest form of extra pulmonary tuberculosis (Table No.5).
In 1986 Nanda et al found that tuberculous lymphadenitis is one of the commonest manifestation of extrapulmonary tuberculosis. It usually affects adolescent and young adult between the age of 10-29 years. Even in our study we found out of 14 patients, 9 patients were below the age of 30 years.

We found that patients who had pleural tuberculosis had high mean IgG titre than pulmonary tuberculosis but patients with other extrapulmonary tuberculosis had low mean IgG titre. The p value was not statistically significant (p value 0.8121).

Wilkins and Ivanyi (1990) found that ELISA test was positive in 70-80% of extrapulmonary tuberculosis unrelated to the organ localisation of the disease. Thus the serological resulting would have obviated the need for the majority of biopsies and allowed chemotherapy to start on average 12.5 days earlier. It could also have prevented the treatment of 14 of 15 patients inappropriately treated for tuberculosis.

Patel et al (1990) and Munshi et al 1993 here found that in extrapulmonary tuberculosis IgG positivity was only in 65-80%. And the mean antibody levels were lower than active pulmonary tuberculosis.
We observed in our study the commonest symptoms were fever in 76% of patients and cough in 74% of patients. In 1963 Banerji and Anderson analysed the symptomatology of tuberculosis patients. They found that 69.4% of patients had cough and 33.2% of patients had fever.

In this study out of 150 patients 87 patients (58%) had positive PPD and 63 patients (42%) had negative PPD. It indicates that it has very limited value in the diagnosis of tuberculosis. Gupta et al (1993) concluded that PPD has limited value especially in India where due to mandatory BCG vaccination in infancy and very high environmental exposure, majority of adults are tuberculin positive. It is however of use as an supportive evidence especially when along with clinical picture either it is stronger positive (induration > 20mm) and or there is necrosis or ulceration. So it has a poor sensitivity and specificity.

We found that patient who had positive PPD test had low mean IgG titre and IgM titre than the PPD negative patients. It indicates that PPD does not affect the antibody formation. But the p value was not statistically significant (p value for IgG 0.3576, IgM 0.3988). In 1993 Banker and Doffery found that ELISA test has no relation with BCG vaccination status or with mantoux test reaction. In 1982 Kardjito et al concluded that previous BCG vaccination (or) mantoux test had no significant effect on the antibody levels.
In our study patients who had radiological evidence of tuberculosis on chest skiagram (cavity, fibrosis and exudate) had high titre of IgG than who had normal chest x-ray. It indicates that the greater radiological extent implies a greater antigenic stimulus which would result in more antibody production. But the 'p' value was not significant statistically (p value 0.2633).

Matti et al (1982) and Cole et al (1972) also found patients who had greater radiological extent of the disease had high titre than lesser extent of disease on chest x-ray.

We also observed patients who had normal chest x-ray had high IgM titre than others who had radiological evidence of tuberculosis. The 'p' value was not statistically significant (p value 0.5838).

We divided this sputum status into 4 groups such as culture negative and smear negative, culture positive and smear positive, culture positive and smear negative and culture negative and smear positive. We compared the IgG and IgM titre between these groups we observed patients were culture positive and smear negative group who had high mean IgG and IgM titre 1250 ± 973.390 and 1.767 ± 0.473 respectively.
But the p value is not statistically significant (IgG p value 0.2525, IgG p value 0.5911).

Sachan et al (1994) observed that patients with high bacillary content in sputum had high titre of IgG value probably because of greater antigenic load causing greater antibody production.

Daniel and Debanne (1987) found that sensitivity of ELISA depends upon the severity of disease and probably reflects the chronicity of disease.

We observed that patients serum IgG titre was higher than the control group. However there was some overlap between the patients and control group.

Narayan et al (1983), Nassau et al (1976) and Grange et al (1980) have reported a significant overlap (20 - 25%) in the ELISA value between control group and patients, thereby indicating that no single value could not be taken as the demarcation line between the patients and normals.

In 1996 Chandersekaran et al concluded that a significant overlap of antibody levels between patients and control group has been observed in their study.
Why this overlap between the controls and patients. The above authors concluded that it is probably due to the high prevalence of tuberculosis country such as ours this finding could be ascribed to circulating antibodies due to subclinical specific infection or infection with environmental mycobacteria.

The second possibility which can explain the overlap is 50% of smear positive patients show low antibody levels. Because of this overlap no single value could be taken as the demarcation line between patients and normals. So we took various titre levels as cut off points which compared between the patients and control group from which we calculated sensitivity and specificity (Table No.17).

The p value was statistically significant (p value 0.000000). We did not analyse the IgM titre value because there is no difference between the control and study group.

Daniel and Debanne (1987) concluded that only measurement of serum IgG antibody against mycobacterial antigens shows potential for diagnostic application using presently available techniques.
In our study we observed there is 23% of overlap between the patients and control it probably due to subclinical infection or environmental mycobacterial infection in control group.

Charpin et al (1990) studied 83 patients of pulmonary tuberculosis found that the sensitivity, specificity and positive predictive value of IgG measurements were equal to 48%, 71% and 50% respectively.

Gevauden and Bouel (1991) had reported the global sensitivity values of 95.5%, 44.0% and 82.5% when the cut-off line was placed at 150, 200 and 300 sero units/ml with the corresponding specificity values being 41.64% and 80.5%.

Baclden et al (1990) set out the baseline at lower level (100 serounits/ml) and reported 78% sensitivity and 86% specificity.

Sachan et al (1994) had reported by a reading 200 sero units/ml was regarded as the dividing line and found that sensitivity of 84.4% and specificity of 100%.

Yu et al (1985) studied and found that measuring IgG titre by using ELISA test the sensitivity and specificity was 89% and 94 to 100% respectively.
Gupta et al (1994) studied A60 specific immunoglobulins IgM, IgA and IgG found that sensitivity of 91.6% and specificity of 90.0%.

Dundar et al (1992) analysed 98 active, 12 inactive and 46 controls found that the ELISA test 60-67% sensitive, 90% specific and 81% positive predictive value.