



To Study The Co-Relation of Tuberculin Test (Mantoux Test) With The Immuno Suppression (Cd4 Lymphocyte Count) in HIV/TB Co-Infection

KEYWORDS

Mantoux test, CD4 count, HIV/TB co-infection, Anergy

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ABSTRACT

AIMS AND OBJECTIVE : 1.) To study the co-relation between Mantoux tests with CD-4+T cell count in HIV/TB co infected patient.2.) To estimate the cut of level of CD4 counts below which anergy is observed.

MATERIAL AND METHODS:- This is a prospective, observational study conducted in the Department of Pulmonary Medicine, Shri Vasantrao Naik Govt.Medical College,Yavatmal , Maharashtra (India) over a period of 2 years from January 2014 to April 2016 . Total 210 HIV proven naive patients with clinical suspicion of Tuberculosis with normal or abnormal chest X-ray were enrolled. Patients already on anti-tubercular and anti-retroviral treatment were excluded. Evaluation of each patient was done which included history, clinical examination, sputum examination, and Tuberculin test, radiological investigational and CD4 T Lymphocytes.

RESULTS:- Out of 210 patients subjected to Mantoux test 60 (28.6%) patients were found to be positive and 150 (71.4%) patients were found to be negative. Anergy (0 mm) was noted in 75 (35.7%) among these 74 (98.66%) patients having CD4 T Lymphocytes count < 200 / cumm , only 1 patient CD4 T Lymphocytes count < 200/ cumm and patients with CD4 T Lymphocytes < 50 were 44(58.66 %).

Out of 60 Mantoux positive patients 30, 28 and 2 had induration of 6-10 mm, 11-20mm and >20mm respectively. Among these 54 were having CD4 T Lymphocytes count < 200/cu.mm, while 6 patients had CD4 T Lymphocytes count of > 200/cu.mm.

CONCLUSION:- Mantoux test and CD4 count matched correlation was found with the level of immune deficiency and hence we conclude that Mantoux test may be incorporated in the clinical management of AIDS patients.

INTRODUCTION:-

Tuberculosis still remains one of the major cause of infectious disease related death worldwide and is one of the commonest opportunistic infection in HIV afflicted patients¹. There is also an increase in the rate of drug resistance tuberculosis, which is difficult to treat further contributing to increase in morbidity and mortality. The risk of developing TB after an infectious contact has been estimated to be 5-15% per year in HIV afflicted patients compared to 5-10% life time risk in HIV non-afflicted patients². Tuberculosis is the prototype of infection that requires cellular immune response for its control.

It has been shown that CD4 + T Lymphocytes are most important in the protective response against mycobacterium tuberculosis³. Increased frequency and severity of tuberculosis in HIV positive patient is another good evidence of importance of CD4 T cells in control of these infection⁴. Tuberculin skin testing is a reliable tool for the detection of tuberculosis infection and its eventual prevention⁵. False negative test may occur in individuals with compromised immune system, including HIV infection, persons taking immunosuppressive drugs, severely malnourished and elderly⁶. It is still useful in detecting infection, which is in close contact with patients with tuberculosis disease. Its prevalence of reactivity is reported to be positively co-related with CD4 count and absolute Lymphocytes counts⁷.

At present there is limited information on delayed type hypersensitivity skin test response in HIV infected patients. The level of immune deficiency in HIV afflicted patients requires not only comprehensive knowledge of possible disease process that may occur but also the ability to deal with the problems of chronic, potentially life-threatening opportunistic infections, so that they can be detected and treated promptly. HIV-TB co infected patient have extremely serious problem in terms of morbidity and mortality requiring immediate action at global, national and local level. The knowledge of various immunological features are important to treat them effectively, considering the public health importance present study was undertaken.

On account of all above points we studied was the existing problem and found the co-relation between Mantoux tests with CD4+T cell count in HIV/TB co infected patients. And estimated the cut of level of CD4 counts below which anergy is observed.

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1.) To study the co-relation between Mantoux tests with CD-4+T cell count in HIV/TB co infected patients.

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MATERIAL AND METHODS:-

This is a prospective, observational study conducted in the Department of Pulmonary Medicine, Shri Vasantrao Naik Govt. Medical College, Yavatamal, Maharashtra (India) over a period of 2 yrs from January 2014 to April 2016. Total 210 HIV proven naïve patients with clinical suspicion of Tuberculosis with normal or abnormal chest X-ray were enrolled. Patients already on anti tubercular and anti retroviral treatment were excluded. Study protocol was approved by the institutional ethical committee and all the patients provided sign informed consent before recruitment. All the analysis were performed SPSS 10.0 (SPSS Inc: Chicago, IL, USA) and SAS Statistical package release 9.1.

Evaluation of each patient was done which included history, clinical examination, sputum examination, and Tuberculin test, radiological investigational and CD4 T Lymphocytes count. The name of patients was not written for sake of confidentiality. The history was included to try and find out the possible risk factor responsible for acquiring the infection.

The clinical examination included general examination and systemic examination. In general examination, body build and nourishment, pulse rate, temperature, blood pressure, respiratory rate were recorded. A special emphasis was made to look for clinical markers of HIV infection like oral candidacies, generalized lymphadenopathy, genital ulcer, rash, molluscum contagiosum, herpes zoster, etc.

HIV patients were confirmed at voluntary counseling and testing center (VCTC). Dept. of Microbiology, Shri V.N. Govt. Medical College using three different methods (ELISA/ Rapid Test/ Simple Test) as per National AIDS Control Organization (NACO) guidelines⁸. CD-4 T Lymphocyte carried out in all the study subject by flow cytometry and result of both were correlated. Mantoux test was performed in 210 patients. Mantoux test was done by intradermal injection of 0.1ml of purified protein derivative containing 5 TU into volar surface of forearm using 26 / 27G needle with plastic disposable syringe and measuring the induration after 48 hours⁹. According to the center for disease control (CDC) and prevention criteria (1987) induration more than '5' mm in HIV seropositive patients and '10' mm in HIV sero-negative patient was considered tuberculin test positive^{10,11}.

RESULTS:-

The age of patient ranged from 21 years (youngest) to 70 years (oldest). In 210 patients, 168 were male and 42 were female. Maximum number of patients, 134 (63.8%) were seen in sexually active and in productive age group i.e. 21-40 years. The male to female ratio was 6.46:1.

TABEL NO-1 GENDER DISTRIBUTION OF STUDY PATIENT.

SR.NO.	Gender	NO.OF PATIENTS	%
1	Male	168	80
2	Female	42	20
	TOTAL	210	100

TABEL NO-2 AGE WISE DISTRIBUTION OF STUDY PATIENT.

SR. NO.	Age Groups	NO. OF PATIENTS	%
1	<20	19	9.04
2	21-30	58	54.6

3	31-40	76	36.1
4	41-50	30	14.2
5	51-60	20	9.52
6	61-70	7	3.3
	TOTAL	210	100

Table no: 3 Mode Of HIV transmission

SR. NO	Mode Of Transmission	Male	Female	Total
1	Unprotected Sexual Contact with CSW	88	0	88
2	Multiple hetero sexual Partners	28	11	39
3	IV Drug Abuser	10	0	10
4	HIV in Spouse	22	17	39
5	CSW(Commercial Sex Worker)	14	9	23
6	Cause Unknown	6	5	11
	TOTAL	168	42	210

TABLE 4:- RESULTS OF TUBERCULIN TEST:

SR. NO.	TUBERCULIN TEST (n= 210)	NO. OF PATIENTS	%
1	Positive	60	28.6%
2	Negative	150	71.4%
	TOTAL	210	100

TABLE NO 5:-Table showing results of Mantoux test in relation to CD-4 count.

Mantoux Test	CD-4 Count					Total
	<50	50-100	100-200	200-400	>400	
0mm	44	12	18	1		75
< 5mm	28	32	14	1		75
6 to 10 mm	6	5	16	3		30
11 to 20 mm	4	16	6	2		28
>20 mm	0	0	1	1		2
Total						210

Out of 210 patients subjected to Mantoux test 60 (28.6%) patients were found to be positive and 150 (71.4%) patients were found to be negative. Anergy (0 mm) was noted in 75 (35.7%) among these 74 (98.66%) patients having CD4 count < 200 / cu.mm, only 1 patient CD4 count < 200/ cu.mm and patients with CD4 < 50 were 44(58.66 %). Out of 60 Mantoux positive patients 30, 28 and 2 had induration of 6-10 mm, 11-20mm and >20mm respectively. Among these 54 were having C4 count < 200/cu.mm, while 6 patients had CD4 count of > 200/cu.mm.

DISCUSSION:-

CD-4 T lymphocytes counts have been shown to be the best marker of disease progression to AIDS¹². Counts below 200 cells / ul are known to be an important landmark. Below this level there are chances of developing life threatening. Opportunistic infections like tuberculosis. The delayed type hyper sensitivity response has been shown to be impaired in HIV infection^{13,14,15}. Various studies concluded that DTH skin response, a major of cellular immunity is an independent predictor of progression to AIDS in

HIV infection¹⁶. Cell mediated immunity is impaired in immune compromise host like HIV infection and the response to PPD and skin test antigens is decreased and Anergy has been observed in progressive immune suppressed patients. An inverse relationship has been found between CD-4 counts and Anergy with concomitant decreases in PPD reactivity with lower CD-4 counts. In our study, male to female ratio was found to be 5.4:1 and dominant age group is 21-40 years which is economically productive age group. NACO has also estimated male pre dominance and similar age group¹⁷. In our study unprotected sexual contact with commercial sex worker was the commonest (41.9%) mode of transmission followed by contact with multiple heterosexual partner¹⁸.

In the present study the immune suppression were demonstrated using parameters like CD- 4 counts, absolute Lymphocytes counts and Tuberculin Test. We observed tuberculin positivity of 45.4 % and 54.6% patients were negative. Similar observations were made by Guteierrez G et.al⁷ with positive rate of 55%. Unnithan S et.al¹⁹ showed in their study Mantoux positivity of 53% and negative in 47 % which is comparable to the present study. We also observed 35 % Anergic to tuberculin test among these 98.66 % patients were having CD4 count < 200/cu.mm, to sub group further significant number of patients that is 58.66 % were having CD4 < 50/cu.mm. Brix et.al²⁰ reported anergy in 10 % of patients when CD-4 count < 500/ cumm. They suggested Cd-4 co related highly with Anergy.

In the present study we also observed direct relation of CD4 count with tuberculin test, interestingly only one patient who was anergic to tuberculin had CD4 count of 240/ cu.mm. All other where having CD4 count of less than 200 / cu.mm. So it can very well inferred from our study that a HIV afflicted patient with tuberculin test showing anergy have '0.9 probability' of having CD4 count less than 200/ cu.mm. At this level of CD4 count which is staged as far advance disease, HIV-afflicted individuals have been shown to develop serious forms of opportunistic infections like pneumocystis carini pneumonia, oesophageal candidiasis and cryptococcal meningitis, so as to merit introduction of prophylactic treatment. Patient at this stage are also at risk of acquiring MAC diseases, cryptococcal meningitis, invasive form of aspergillosis, toxoplasma gondii histoplasmosis, coccidioidomycosis, bartonellosis, penicillium marneffi infection, CMV retinitis, polyoma virus responsible for progressive multifocal leuko- encephalopathy²¹. Also substantial proportional of tuberculosis patients will have PPD anergy if their tuberculosis is concurrent with other HIV-related opportunistic infections. From these observations, hence these conditions should be suspected in any HIV-afflicted patient having anergic tuberculin test, apart from tuberculosis.

CONCLUSION:-

Mantoux test and CD4 count matched correlation was found with the level of immune deficiency and hence we conclude that Mantoux test may be incorporated in the clinical management of AIDS patients. Further studies are needed relating DTH response and biological markers of HIV infection other than CD4 count. Since no comprehensive studies exists on this issue²².

CONFLICT OF INTEREST: NONE

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