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Research article

PATTERN OF EXTRA-PULMONARY TUBERCULOSIS IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION, AT A TERTIARY CARE CENTRE IN EASTERN INDIA

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ABSTRACT

Introduction: Tuberculosis and Human Immunodeficiency Virus (HIV) co infection is becoming one of the most important public health issues in India. In some developing countries, 40% of all tuberculosis cases are attributed to HIV infection and in more than 50% of cases, tuberculosis is the first manifestation of HIV infection. **Materials and methods:** A cross sectional study was done among the in-patients of a tuberculosis ward in a tertiary care hospital in Eastern India. Fifty patients with HIV and tuberculosis infection of an extra pulmonary site, were included in the study. **Results:** A vast majority of the participants were young males. More than 80% were using intoxicants like alcohol or tobacco, 76% admitted exposure to commercial sex workers and 12% were intravenous drug users. Twenty five (50%) of the participants had disseminated tuberculosis, that is tubercular infection of more than one anatomical site. Maximum (62%) participants had tubercular infection of lymph nodes, followed by pleura, abdomen and central nervous system. **Discussion and conclusions:** The socio-demographic correlates of participants were similar to that seen in similar studies in other parts of the world. But in our study, tubercular lymphadenitis was the most common extra-pulmonary manifestation and proportion of disseminated tuberculosis cases was as high as 50%. Both these findings are different from studies from other parts of the world. These findings warrant a larger research study and programmatic changes to address issues of HIV/TB co infection.

Keywords: Tuberculosis epidemiology, Tuberculosis diagnosis, Risk factors, HIV Infections/epidemiology

INTRODUCTION

Tuberculosis in India is characterised by high incidence and prevalence of both tuberculosis infection and disease. Different disease surveys have yielded varied results, the prevalence of smear positive pulmonary tuberculosis ranged from 0.6-7.6 per 1000 population while that of culture positive tuberculosis was in the range 1.7-9.8 per 1000 population.^[1] There is also a problem of high transmission rates and is indicated by a very high Annual Risk of Tuberculosis Infection (ARTI) of around 1.5%.^[1] Fittingly, India is classified along

with sub-Saharan countries in terms of the effectiveness of tuberculosis control.^[2] Even though some studies have demonstrated a small downward trend over a long period of time, especially after the launch of the Revised National Tuberculosis Control Programme (RNTCP), most of the tuberculosis researchers and epidemiologists refuse to believe that the peak of infection has already been crossed.^[2] According to a global consensus effort by World Health Organisation (WHO) in 1997, the estimated number of new cases for the year was around 8

million and more than 50% of it was contributed by 5 countries of the WHO's South East Asian Region (SEARO). They concluded that the burden of tuberculosis is remaining so enormous, as the control efforts have failed in South-Asia, sub-Saharan Africa and Eastern Europe.^[3] Since the global consensus effort by WHO, Indian health authorities have stepped up efforts to expand the RNTCP programme. By 2005, RNTCP was successful in initiating treatment for over 3.5 million patients and avoided premature mortality in 600,000 patients.^[4] Though this renewed interest in tuberculosis control and heavy investment in Directly Observed Treatment, Short course (DOTS) strategy has yielded results in urban and rural areas of the country, the tuberculosis situation in Tribal areas have worsened over the last few years.^[2] In a state like Orissa, where Scheduled Tribes (STs) form over 22% of the total population, the ARTI was estimated to be 1.7% to 1.8%, much above the national average rates.^[5] The reasons for this high infection load can be many; the poor penetration of healthcare delivery infrastructure coupled with low awareness levels among people can be the main ones. In a study done in Orissa, only 16% of the respondents knew about the cause of Tuberculosis while 31% knew the correct mode of spread of the disease. This is much lower than the statistics from other parts of the country, derived from similar surveys.^[6]

Human Immunodeficiency Virus (HIV) infection is an independent risk factor for tuberculosis and is considered as a cause for the resurgence of tuberculosis in many industrialised countries. The high incidence of tuberculosis (almost 290/100,000 population) in Africa is also attributed to the high prevalence of HIV infection in that part of the world.^[7] In some countries like Tanzania, over 40% of the tuberculosis cases are attributed to the presence of HIV infection in those patients.^[8] In most of the developing countries, Tuberculosis is considered as the most serious opportunistic infection among those people with HIV infection and is the first manifestation of Acquired Immunodeficiency Syndrome (AIDS) in over 50% of the cases.^[9] India has the third most number of HIV patients with 2.1 million people living with HIV/AIDS. Though the HIV epidemic in India is slowing down with a 57% reduction in new HIV infections over a period of 2000 to 2011, it has the potential to explode into

gargantuan proportions. These points towards the need for sustained investment in research activities on HIV and allied subjects.^[10] Diagnosis of tuberculosis among HIV affected individuals pose a dilemma for clinicians as most of the cases tend to be extra-pulmonary and the routine sputum testing may prove to be ineffectual.^[11] The sites for extra-pulmonary tuberculosis among HIV infected individuals seem varied; according to a study from New Delhi, abdomen (70%) is the most common site for extra-pulmonary tuberculosis, followed by lymph nodes (22%), pleura (15%) and Central Nervous System (3%).^[11] Another study from Shimla, Himachal Pradesh showed that CNS tuberculosis constituted over 33% of the extra-pulmonary tuberculosis cases in HIV patients and was followed by abdominal tuberculosis (26%). The study also found out that disseminated tuberculosis was seen only in patients with CD4 count of less than 200/cmm.^[12] In a study from Gujarat, it was found that among HIV patients, 60% of the tuberculosis disease was extra-pulmonary in site and mediastinal tuberculosis constituted about 34% of them, followed by extra-thoracic lymphadenopathy in 18% of the patients.^[13] Conversely, the prevalence of HIV infection among those with tuberculosis is also much higher when compared to general population. In a study done in Agra, Uttar Pradesh, it was observed that the 4.3% of the adults and 8.5% of the children attending a tuberculosis clinic were HIV infected.^[14, 15]

Tuberculosis and HIV are converging dual epidemics and constitute the greatest public health challenge of our time. The diagnosis and treatment of HIV-Tuberculosis co-infection is a difficult task and understanding the pattern of disease in such cases may help to identify patients who may need treatment for both infections.^[16]

MATERIALS AND METHODS

Study design: Cross-sectional, observational study

Inclusion criteria: Patients admitted with a diagnosis of tuberculosis of any site were screened for HIV infection using Enzyme Linked Immunosorbent Assay (ELISA). Those patients, who had positive results on ELISA, were tested and confirmed using Western Blot technique.^[17] All the patients who had a positive test in ELISA and Western Blot, and having suspicion of extra-pulmonary tuberculosis were included in the study.

Exclusion criteria: Those patients admitted in intensive care units or on assisted ventilation were excluded from the study

Ethical approval: Clearance was obtained from the Institutional Review Board of SCB Medical College, Cuttack, before the start of the study. Also, written informed consent was obtained from all participants.

Duration of study: January 2004 to December 2005.

Methodology: Extra-pulmonary tuberculosis was confirmed by mycobacterial and histopathological examination of the relevant samples. For lymph node tuberculosis, a lymph node biopsy or a Fine Needle Aspiration Cytology (FNAC) was done to obtain samples. Ascitic fluid or pleural fluid was taken to confirm pleural or abdominal tuberculosis respectively. Cerebro-Spinal Fluid (CSF) was taken and examined to diagnose Central Nervous System tuberculosis. Radiological investigations like contrast enhanced CT scans were used for diagnosis when mycobacterial and histopathological examination was inconclusive or when appropriate samples were not obtained.

The participants were administered a standardised, pilot-tested questionnaire to find out their socio-demographic correlates, risk factors, symptoms, past history and treatment history. A focussed clinical examination was done to elicit all the associated clinical signs. A sputum sample was collected for Ziehl-Neelsen(ZN) staining^[18], to rule out pulmonary tuberculosis and a venous blood sample was collected for measuring CD4 (Cluster of Differentiation 4) counts, which is a surrogate marker for disease activity in HIV infection^[19].

RESULTS

A total of 50 patients with HIV/TB co-infection and with extra-pulmonary manifestation of tuberculosis infection, were included in the study. The maximum numbers of participants were from the age group 25-34 years (44%) and 35-44 years (44%). Males constituted 92% of the total study participants and 82% of the participants were married. Most of the study participants were manual labourers (54%) and drivers (22%). Twenty four (58.5%) of the currently married participants had their spouses with a positive HIV status, while it was negative for 29.2% and unknown for 12.2%. [Table 1]

Table 1: Baseline characteristics (n=50)

Attribute	Characteristics	Number	%
Age (in Years)	15-24	3	6%
	25-34	22	44%
	35-44	22	44%
	45 and above	3	6%
Sex	Male	46	92%
	Female	4	8%
Marital Status	Married/ Unmarried/ Separated/Divorced	41	82%
	Spouse died	9	18%
		0	0
Occupational status	Manual labourer	27	54%
	Driver	11	22%
	Small business	5	10%
	Army/Police	1	2%
	Housewife	4	8%
	Others	2	4%
HIV status of spouse(n=41)	Positive	24	58.5%
	Negative	12	29.2%
	Unknown	5	12.2%

A vast majority of the participants were using intoxicants regularly. Forty four (88%) of the participants admitted using Alcohol, 40(80%) said they use tobacco in some form and 4(8%) used cannabis/cannabinoids. Among the other social risk factors for HIV infection, 35(70%) had history of migration from the place of birth and 5(10%) had history of imprisonment or incarceration by a court of law. A vast majority of the participants (38, 76%) admitted having contact with commercial sex workers and 6(12%) have used intravenous drugs in the past. Interestingly, none of the participants were homosexuals [Table 2]

Table 2: Social risk factors for HIV infection (n=50)

Risk factor	Characteristic	Number(%)
Use of intoxicants	Alcohol	44(88%)
	Tobacco	40(80%)
	Cannabis	4(8%)
	Hallucinogens	6(12%)
History of Migration	Yes	35(70%)
	No	15(30%)
History of Imprisonment	Yes	5 (10%)
	No	45(90%)
Contact with Commercial Sex Worker	Yes	38(76%)
	No	12(24%)
Men Having Sex with Men (MSM) (n=46)	Yes	0
	No	46(100%)
Intravenous drug user	Yes	6(12%)
	No	44(88%)

Twenty five (50%) of the participants had disseminated tuberculosis, that is tuberculosis infection of more than one anatomical site. The rest of the participants had tuberculosis limited to one extra-pulmonary site. Lymph nodes were the most

common site (62%) followed by pleura (32%), abdomen (22%), Central Nervous System (8%) and bone marrow (2%). None of the participants had tuberculosis infection of the spine or the mediastinum. [Table 3]

Table 3: Pattern of Extra-pulmonary tuberculosis (n=50)

Extra-pulmonary site	Number	Percentage
Lymph node(s)	31	62%
Pleura	16	32%
Abdomen	11	22%
Central Nervous system	4	8%
Bone marrow	1	2%
Spine	0	0
Mediastinum	0	0

Among the 25 participants with disseminated tuberculosis infection, 7(28%) had infection of lymph nodes and lung, 5 (20%) had infection of lymph node and pleura and 4(16%) had infection of lymph nodes and abdomen. One (4%) participant each had tuberculosis infection of bone marrow and miliary tuberculosis. [Table 4]

Table 4: Pattern of Disseminated tuberculosis (n=25)

Sites of Dissemination	Number	%
Lymph node and lung	7	28%
Lymph node and pleura	5	20%
Lymph node and abdomen	4	16%
Lymph node, pleura and abdomen	1	4%
Lymph node and CNS	1	4%
Lymph node, CNS and lung	1	4%
Pleura and abdomen	2	8%
Pleura and lung	1	4%
Abdomen and lung	1	4%
Bone marrow	1	4%
Miliary	1	4%

Among the 25 participants where the tuberculosis infection was limited to one extra-pulmonary site, 12(48%) had infection of the lymph nodes, 8(32%) had infection of the pleura, 3(12%) had abdominal tuberculosis and 2(4%) had Central Nervous system tuberculosis. [Table 5]

Table 5: Pattern of isolated extra-pulmonary tuberculosis (n=25)

Extra-pulmonary site	Number	Percentage
Lymph node	12	48%
Pleura	8	32%
Abdomen	3	12%
Central Nervous System	2	4%

DISCUSSION

The study reveals a familiar trend seen in other parts of the world, where HIV infection and tuberculosis are generally considered as a disease of social inequities. The participants in our study are from occupations which are relatively lowly paid, a large number of them are migrants, and the use of intoxicants is very high. A similar finding is seen in studies done in other parts of the world, especially South Asian nations and African countries.^[20] A vast majority (76%) of the participants reported exposure to commercial sex workers and this may be the reason behind the baseline demographic correlates being skewed in favour of young males. This finding is also in concordance with the results of similar studies from other parts of the country which states that commercial sex is the primary mode of HIV infection for males and sexual relations with the infected husband is the most important mode of acquiring infection for females.^[21]

In our study, the most common site of extra-pulmonary tuberculosis infection was lymph nodes, followed by pleura and abdomen. Tubercular lymphadenitis was seen commonly in disseminated tuberculosis infection as well as in isolated extra-pulmonary tuberculosis. This finding is quite different from the findings in other parts of the country which stated that infection of the abdomen and Central Nervous System were the most common extra-pulmonary sites in HIV/TB co infection. The proportion of disseminated tuberculosis cases among all the extra-pulmonary tuberculosis patients was as high as 50%, and this is much higher when compared to data from other parts of the world.^[22] This may be due to the late diagnosis of tuberculosis and HIV infection, Orissa being a relatively backward state in socio-economic progress and healthcare delivery indicators.

CONCLUSION

This study points towards the need to do more extensive research in HIV/TB co-infection. All the stakeholders of the Revised National Tuberculosis Control Programme (RNTCP) and the National Aids Control Programme (NACP) needs to be sensitised on the need to screen for the other infection when one of it is diagnosed in a patient. Since the diagnosis of extra-pulmonary tuberculosis is difficult and

expensive, it poses a clinical dilemma to the treating doctors. Diagnostic protocols and cost-effective techniques need to be formulated in diagnosing and treating these conditions when both the infections occur together.

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Conflict of interest: Nil

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