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Predisposing Factors for Pulmonary Tuberculosis

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Abstract:
Aim of The Work: This study was intended to elucidate the role of different risk factors in the development of pulmonary tuberculosis in our locality in order to avoid exposure to possible risk factors, controlling possible risk factors and therefore decreasing numbers of new cases in our locality.
Patients & Methods This study included (150) of patients with tuberculosis (97 males and 53 females) in whom we studied the risk factors that may be of value in developing pulmonary tuberculosis using a special questionnaire asking about smoking status, family history of tuberculosis, impaired immunity, malnutrition, substance abuse, BCG vaccination, over crowding, occupational exposure, consumption of unpasteurized milk, working in residential care facility places, history of asthma, martial status. All patients passed through chest x rays (PA, Lateral views), Sputum smear for AFB positive or sputum culture for AFB if sputum smear was negative, Tuberculin test, Complete blood count, ESR, urine analysis and blood sugar .
Key Words: Risk Factors, Tuberculosis, environmental factors, social factors

INTRODUCTION

Tuberculosis (TB) is a chronic, infectious disease caused by Mycobacterium tuberculosis (MTB)[1]. Currently, TB is the leading cause of mortality among infectious diseases worldwide, and 95% of TB cases and 98% of deaths due to TB occur in developing countries[2]. Due to the inadequacy of disease surveillance in India, it is not possible to present exact data for TB incidence and TB-related mortality. However, based on the results of ad hoc surveys, and using an estimated annual cumulative incidence of TB of 171 cases per 100 000, India has been ranked as one of the top 22 developing countries afflicted by the current TB epidemic[3] (World Health Organization [WHO], 2001 data). High-risk groups for MTB infection in India, like other developing countries, may include people with human immunodeficiency virus (HIV)/AIDS, people with diabetes or cancer, the malnourished, those living with someone who has active TB, poor and indigent people, residents of homeless shelters, and present or former prisoners[4]. The development of tuberculosis in humans is a two-stage process in which a susceptible person exposed to an infectious case first becomes infected and second, after an interval of years or decades, may later develop the disease, depending on a variety of factors. Since the acquisition of infection is often far removed from the development of disease and involves different physiologic mechanisms, the risk factors for infection are quite different from the risk factors for development of disease following infection[5]. This has important implications for tuberculosis prevention and control[6].

Among persons exposed to someone with an infectious case of tuberculosis, the risk of becoming infected is determined primarily by the combined action of three factors: 1) the infectivity of the source case (which is itself a function of microbial virulence and the density of bacilli in the sputum), 2) the intensity of the susceptible person's exposure to the case, and 3) the susceptibility of

the exposed person to infection[7]. Factors reported to influence the risk of mycobacterial infection include age, sex, crowding, socioeconomic conditions, urbanization, racial/ethnic group, and human immunodeficiency virus infection[8]. In patients infected with Mycobacterium tuberculosis, the disease can develop at any time through reactivation of a previously acquired (latent) infection or through exogenous reinfection[9].

The time interval from infection to disease ranges from a few weeks to a lifetime[10]. The risk of developing disease after infection is strongly age and time dependent[11] and has been reported to be much greater in the 5 years following infection and to decline as the time interval increases[12]. In a study of young children who were strongly positive reactors, the lifetime risk was reported to be as high as 10 percent[13]. Any condition modifying the balance established in the body between the tubercle bacilli and the host's immune defenses can have an impact on the risk of developing the disease. Factors that have been shown to influence this balance include age, sex, human immunodeficiency virus infection, immunosuppressive treatment, diabetes mellitus, malnutrition, alcoholism, and Bacillus Calmette-Guérin vaccination[2,6,13]. Any factor influencing the risk of infection and/or the risk of breakdown after infection has an effect on the incidence of tuberculosis[14].

PATIENTS AND METHODS:

Our study included (150) of patients with tuberculosis (97 males and 53 females) between March 2011 and March 2013 in whom we studied the risk factors that may be of value in developing pulmonary tuberculosis .Another 150 healthy persons were studied as a control group. The patients in the study were collected from chest clinic of Bundelkhand Government Medical College, Sagar, Madhya Pardesh. The study defined tuberculosis patients as all adults with sputum or sputum culture +ve for Acid Fasting Bacilli (AFB). While the 2nd group incorporated by normal peoples (controllers) .The study was approved by the ethical committee of Bundelkhand Government Medical College, Sagar.

All patients passed through:-

1- Careful history taking and clinical examination,

2- Radiological investigation included chest x rays (PA, Lateral views).

3- Sputum smear for AFB positive or sputum culture for AFB if sputum smear was negative.

4- Tuberculin test.

5- Complete blood count, ESR, urine analysis and blood sugar .

Then a questionnaire about the risk factors of pulmonary tuberculosis was fulfilled by every case asking about smoking, type and amount per day, family history of tuberculosis, impaired immunity, steroid therapy or history of immunosuppressive drugs, malnutrition, substance abuse, health care workers, BCG vaccination, over crowding, occupational exposure, consumption of unpasteurized milk, working in residential care facility places, history of asthma, martial status.

Smoking:
Non-smoker ( )
Current smoker ( )
Ex-smoker ( )
Stop smoking ( )
Type of smoking (1) Cigarette ( )
(2) Bidi ( )
Amount per day.
Family history of Tuberculosis:
Presence of one of family infected with T.B :
Yes (1)Degree of relation . (2) Duration of contact to the case.
No
Impaired immunity
Presence of disease such as Diabetes mellitus, Renal and Liver disease with special interest in disease duration ,treatment and complications
Steroid Therapy Yes ( ) (1) Duration
(2) Cause of administration
No
History of immunosuppressive drugs
Yes ( ) No ( )
Malnutrition :
Slow recovery from disease Yes No
Under weight Yes No
Malabsorption Yes No
Decrease resistance to infection Yes No
Anaemia Yes No
Substance abuse:
Yes (1) Type. (2) Duration. (3) Amount per day.
No
Health care workers:
Yes (1) Site. (2) Duration.
No
BCG vaccination Yes No
Over crowding
Number of family members.
Number of rooms.
House ventilation : Good Fair Bad
Crowding : Yes No
Occupational exposure:
Yes
(1) Occupation.
(2) Working duration.
(3) Working hours per day.
(4) Chest trouble: Yes No
No
Consumption of unpasteurized milk:
Yes No
Working in residential care facility places :

Yes
(1) Duration
(2) Numbers of working hours per day
(3) History of contact with chest patients.
No
History of asthma:
History of atopy :
Yes No
History of asthma treatment :
Yes No
Family history of asthma :
Yes No
Martial status:
Married Single
Widow Divorced

Statistical analysis:

Data entry and analysis were all done using software SPSS version 13. Graphics were done using Excel. Quantitative data were presented by mean and standard deviation, while qualitative data were presented by frequency distribution. Chi Square, Student t test were used. In addition multiple regression analysis was used to see the combined effect of different independent variables on the target (dependant variable).The probability of less than 0.05 was used as a cut off point for all significant tests.

RESULTS:

Table 1 shows the demo-graphic data of both the tuberculosis and the control groups: as regard the age, sex, residence, marital status, special habits, type of smoking. For both groups, the age range was 11-78 years with the mean age of 42.4±17.6. group 1 or tuberculosis group included 97 males and 53 females and control group included 96 males and 54 females. There was significant

statistical relation between both group 1 and 2 in age (p= 0.0001) residence (p= 0.02) and smoking, and smoking index (p= 0.0001). There was no statistical significance between both groups as regard the occupation.

Table (1):

characteristic data		tuberculosis No=150	Controller No=150	P
Age (years)	Range	11-78	11-78	0.0001**
	Mean ±SD	42.4±17.6	42.4±17.6	
Sex	Male	97(64.7%)	96(64%)	1
	Female	53(35.3%)	54(36%)	
Residence	Urban	136(90.7%)	123(82%)	0.02*
	Rural	14(9.3%)	27(18%)	
Marital status	Single	35(23.3%)	48(32%)	0.2
	Married	106(70.7%)	94(62.7%)	
	Widow	9(6%)	8(5.3%)	
Special habits	Non smoker	63(42%)	68(45.3%)	0.004**
	Current smoker	28(18.7%)	45(30%)	
	Ex-smoker	25(16.7%)	24(16%)	
	Stop smoker	34(22.7%)	13(8.7%)	
Type of smoking	Non smoker	63(42%)	68(45.3%)	0.03*
	Bidi	53(35.3%)	62(41.3%)	
	Cigarette	18(12%)	5(3.3%)	
	Cigarette and Bidi	16(10.7%)	15(10%)	
Smoking index		39.2±78.9	4.4±7.6	0.0001**
Occupation	House wife	45(30%)	34(22.7%)	0.2
	Farmer	54(36%)	36(24%)	0.1
	Student	10(6.7%)	20(13.3%)	0.2
	Not working	8(5.3%)	19(12.7%)	0.2
	Driver	2(1.3%)	7(4.7%)	0.4
	Nurse	9(6%)	6(4%)	0.4
	Teacher	1(0.7%)	5(3.3%)	0.4

Table(2): comparison between tuberculosis and controller regarding occupation, Nutritional Status, history of house hold contact, crowdness, diabetes mellitus, renal disease, liver disease, blood picture, substance abuse, health care workers, BCG vaccine, overcrowdness, occupational exposure, consumption of unpasterized milk, and bronchial asthma. There was a significant statistical relation between the tuberculosis and the control groups as regard the nutritional status, history of house hold contact,, crowdeness, diabetes mellitus, liver disease, subs-tance abuse, health care workers, BCG vaccine, occupational exposure and bronchial asthma. With no significance between both groups in occupation, renal disease and consumption of unpasterized milk

characteristic data	Tuberculosis No = 150		controller No = 150	P
OCCUPATION	House wife	45 (30%)	34 (22.7%)	0.2
	Farmer	54 (36%)	36 (24%)	0.1
	Student	10 (6.7%)	20 (13.3%)	0.2
	Not working	8 (5.3%)	19 (12.7%)	0.2
	Driver	2 (1.3%)	7 (4.7%)	0.4
	Nurse	9 (6%)	6 (4%)	0.4
	Teacher	1 (0.7%)	5 (3.3%)	0.4
NUTRITIONAL STATUS	Malnourished	113 (75.3%)	0	0.0001**
	Nourished	37 (24.7%)	150 (100%)	
History of house hold contact	Positive history	50 (33.3%)	0	0.0001**
	Negative history	100 (66.7%)	150 (100%)	
crowd ness	Over crowdness	106 (70%)	0	0.0001**
	No-crowdness	44 (29.3%)	150 (100%)	
Diabetes mellitus	Diabetic	25 (16.7%)	0	0.0001**
	Non-diabetic	125 (83.3%)	150 (100%)	
Renal disease	Yes	5 (3.3%)	0	0.06
	No	145 (96.7%)	150 (100%)	
Liver disease	Yes	11 (7.3%)	0	0.0001**
	No	139 (92.7%)	150 (100%)	
Blood picture	Lymphocyte	36.2±8.3	5.1±1.5	0.0001**
	WBCs	8.08±4.1	6.5±2.4	0.0001**
	RBCs	4.2±0.5	4.4±0.4	0.0001**
	Hb	10.4±1.5	11.3±1.4	0.0001**
ESR	1st	67.8±24.9	5.3±2.4	0.0001**
	2nd	121.7±30.8	13.9±4.9	0.0001**
Substance abuse	Yes	18(12%)	0	0.0001**
	No	132(88%)	150 (100%)	0.0001**
Health care workers	Yes	9(6%)	0	
	No	141(94%)	150 (100%)	0.003**
BCG vaccine	Yes	150 (100%)	150 (100%)	
Over crowdness	Yes	106(70%)	0	0.0001**
	No	44(29.3%)	150 (100%)	
Occupational exposure	Yes	5(3.3%)	0	0.0001**
	No	145(96.7%)	150 (100%)	
Consumption of unpasterized milk	Yes	39(26%)	0	0.06
	No	111(74%)	150 (100%)	
	No	136(90.7%)	150 (100%)	
Bronchial asthma	Yes	26(17.3%)	0	0.0001**
	No	124(82.7%)	150 (100%)	

Table 1

Table (3): Comparison between tuberculosis regarding residence, marital status, smoking, nutritional Status, crowdness, previous anti-tuberculosis treatment, Duration of diabetes, prolonged steroid therapy: There was a statistical significance inside the tuberculosis group itself: as regard the residence with most of the group of rural origin, the marital status, with 106 out of 150 were married, 35 were single, and only 9 patients were widow. Smoking was found in 87 patients in this group (58.1%). Also there was a significant relation as regard the over crowdness, previous anti tuberculous treatment history, duration of diabetes and prolonged steroid therapy.

Table (3)

SYMPTOMS			
Cough	**Productive**	149 (99.3%)	0.00001**
	Non Productive	1 (0.7%)	
Hemoptysis	**Yes**	70 (46.7%)	0.09
	No	80 (53.3%)	
Dysponea	**Yes**	77 (51.3%)	0.3
	No	73 (48.7%)	
Chest pain	**Yes**	11 (7.3%)	0.0001**
	No	139 (92.7%)	
LABORATORY FINDING			
Tuberculin test	Positive	124(82.7%)	0.00001**
	Negative	26(17.3%)	
Sputum smear	Positive	145(96.7%)	0.00001**
	Negative	5(3.3%)	
Urine analysis	Free	116(77.3%)	0.00001**
	Not free	34(22.7%)	
Chest X ray	Free	20(13.3%)	0.00001**
	Not free	130(86.7%)	
Sputum culture	Done and positive	5(3.3%)	0.00001**
	Not done	145(96.7%)	

Table (4): shows the clinical data, of the tuberculous group with the cough and chest pain was the most presenting symptoms while hemoptysis and dyspnea comes late. Laboratory data: tuberculin test was positive in 124 (p= 0.00001), sputum was positive in 145 patients (p= 0.00001). Chest x- ray was free only in 20 patients while positive finding was detected in 130 (p= 0.00001). Sputum culture was positive in only 5 patients while not done in 145 patients.

Table (4):

Residence	**Rural**	**Urban**	**P**
	136 (90.7%)	14 (9.3%)	0.001**
Marital status	**Single**	**Married**	**Widow**
	35 (23.3%)	106 (70.7%)	9 (6%)
Smoking	**Smoker**	**Non-smoker**	**P**
	87 (58.1%)	63 (42%)	0.02*
Nutritional Status	**Malnourished**	**Nourished**	**P**
	113 (75.3%)	37 (24.7%)	0.0001**
Crowdness	**Over crowdness**	**No-crowdness**	**P**
	106 (70%)	44 (29.3%)	0.0001**
Previous anti-tuberculosis Treatment	**Positive history**	**Negative history**	**P**
	28 (18.7%)	**122 (81.3%)**	**0.00001****
Duration of diabetes	**> 5 years duration**	**< 5 years duration**	**P**
	22 (88%)	3 (12%)	0.001*
Prolonged steroid therapy:	**Positive history**	**Negative history**	**P**
	26 (17.3%)	124 (82.7%)	0.0001**

DISCUSSION:

This cross-sectional community based study aiming at determining the risk factors for development of pulmonary tuberculosis in our locality using sample of 300 case and the diagnosis of tuberculosis was done by different ways and we analyzed the different factors as follow

Our study has shown that Smoking was one of the commonest factor for tuberculosis development, about 58.1 % of the tuberculosis group were smoker in comparison to 42% of the tuberculosis group were non-smoker which related to the dose however this result may be explained by that more than half of studied cases were males. These results are consistent with those reported by who concluded that cigarette smoking was an independent risk factor for TB[14, 15], with a clear dose–response effect with duration of smoking. Our findings thus support the hypothesis of an increased vulnerability of smokers to the infection and development of TB, most probably owing to pathophysiological changes in the lungs induced by chronic smoking. In our study the type of smoking has found that a big ratio among smokers was related to Bidi smoking reached to 35%, 12% in cigarette smoking .

Similar to our study,earlier studies have stated that the risk of prevalence of TB infection is more among current or ex-smoker than never smokers[16]. The biological basic by which smoking increase the TB risk may through decrease immune response, mechanical disruption of cilia functions, defects in macrophage immune response and/or CD 4+ lymphopenia, thereby increasing the susceptibility to pulmonary TB[17]. Our study not included Passive smoking as it was not in general associated with tuberculosis. However, a stratified analysis carried out on households with a patient with tuberculosis demonstrated a significant association between passive smoking and M tuberculosis infection[18].

In our study malnutrition was one of the commonest factors of tuberculosis that about 75% of tuberculosis group were malnourished in comparison to 24.7% of the group who were well nourished .Similar to our study, earlier studies have concluded that patients with tuberculosis from the area of Tanzania frequently have evidence of malnutrition both before and after treatment for tuberculosis[19]. In a trial to explain malnutrition as important character in tuberculosis patients, this have been concluded that the breakdown of protein and other reserve due to fever may also worsen under nutrition and further impair resistance against the infection. There is also good evidence that being underweight, in itself is a risk factor for the development of tuberculosis in infected persons.

Our study has showed that history of contact to tuberculosis case was significant between tuberculosis and controller groups that 33.3% of tuberculosis cases gave history of contact to smear positive case in comparison to 0% that of controller group. But the study did not included the duration of contact to smear positive cases.

Similar to our study, the distribution of tuberculosis infection among households in African communities have observed a consistent effect of former experience of TB within the household, and this effect increased with the number of persons who had TB in the past[20]. It has been reported that the association between contact to positive case and development of tuberculosis could reflect not only the facility of transmission within the household, but also a genetic contribution to the susceptibility to TB[21].

It has been found that the risk of TB was associated with the number of adults in the household, probably related to the particular housing structure in that part of country, with all adults sharing a single airspace[22]. Classically, studies have measured crowding as the density of persons per room in a given household. In our study we did not find an association between TB and the number of persons per room.

It has been concluded that TB transmission occurs with greater prevalence in poorly ventilated and crowded spaces. Similar to this study,earlier studies have stated that sputum smear-positive individual with pulmonary TB is four to six times more contagious than a smear-negative case[23]. However sputum smear-negative, culture-positive patients with pulmonary TB are also infectious to others similar to our study have stated that Crowding has been identified as both a risk factor for TB transmission.

Our study is consistent with earlier studies which have stated that the extent and persistence of contact with an infected person are the main environmental factors for the transmission of TB[24]. Thus, transmission of TB occurs most frequently as a result of prolonged contact in enclosed environments with an infectious person. Persons who are at the greatest risk of exposure to TB are those who live and sleep in the same household as an infected person.

Our study showed that diabetic patients are more susceptible to tuberculosis than others depending on the duration of the disease that about 88% of tuberculosis diabetic patients were treated from diabetes for more than 5 years in comparison to 12% of tuberculosis patients were treated from diabetes for less than 5 years.

Similar to our study ,earlier studies have studied the relative contribution of diabetes mellitus to the increased prevalence of tuberculosis in Hispanics, they concluded that diabetes mellitus remains a significant risk factor for tuberculosis in the United States[25]. Similar to our study earlier studies have noted that the rate of tuberculosis was increased 6.8-fold in patients with diabetes due to increases in both reactivated and recently transmitted infection[24,25]. Co morbidity with diabetes may increase tuberculosis rates as much as co infection with human immunodeficiency virus (HIV), with important implications for the allocation of health care resources. A similar study by have identified statistically significant and clinically important associations between TB and DM, with the increase in risk of TB varying between 1.5- and 7.8-fold for those with DM[26]. Risk was highest at younger ages.

Approximately one-third of the world's population is infected with Mycobacterium tuberculosis, and the majority live in less developed countries where human immuno-deficiency virus (HIV) infection is spreading rapidly. The World Health Organization (WHO) estimates that the number of new cases of tuberculosis and the proportion with coexisting HIV infection will continue to increase.

Our study has also found that HIV infection in our locality is a risk factor for development of Pulmonary Tuberculosis. In accordance to our study WHO (2001) has reported that 30% of TB cases arising among the

15–49-year-old adults in India are attributable to HIV and a continuous 10% per year increase in TB is projected in countries most severely affected by HIV infection[27]. It has been found that HIV infection has emerged as the most important risk factor for the development of TB in individuals infected with M. tuberculosis[28]. It has been documented that the major factors contributing to the HIV associated TB epidemic in Africa are the high risk of reactivation of latent TB infection in HIV infected persons and the high risk of progressive TB disease owing to HIV infection[29].

Other strategies, as early diagnosis and treatment, and BCG vaccination are limited in HIV infection, because of atypical clinical presentations, diagnosis delay and lack of safety data about BCG vaccination.

Our study showed that presence of BCG scar was not indication of protection against infection with tuberculosis .Similar to our study previous studies have stated that the presence of a BCG scar was not independently associated with protection against TB[30]. The sensitivity of scar reading is extremely variable, and BCG scar size has been shown to depend on vaccine strains and doses, prior tuberculin sensitivity, and age. It has been showed that BCG scar was a highly sensitive indicator of vaccination status when vaccine was properly handled and given at over 3 months of age, but in infants <1 month of age vaccinated in health centers, sensitivity of BCG scar had declined to <80% by 4 years post-vaccination[31].

In our study alcohol was significant among tuberculosis group that 12% of tuberculosis cases were alcoholic in comparison to 88% of tuberculosis cases were not ,with duration of administration 5.1 ± 3.3 years and different amounts. Similar to our study it has been stated that there is a strong association between alcohol use and risk of tuberculosis (TB) [32]. Prevalence of alcohol use disorders among TB patients have ranged from 10% to 50% in studies carried out in Australia, Canada, Russia, Switzer-land, and the USA [32].

Alcohol may assert direct toxic effects on the immune system rendering the host more susceptible to TB disease, that cell mediated immunity and macrophage functions (which are essential for the host response to M. tuberculosis infection) are directly impaired by chronic and acute alcohol consumption. Alcohol inhibit tumor necrosis factor (TNF) response. Alcohol may also reduce the NO system response to mycobacterial infection, which may prevent the destruction of mycobacteria., Alcohol can inhibit granuloma formation, IL-2 production, IFN-gamma production, and CD4+ proliferation[33] .

Our study has found out that prolonged steroid therapy was significant between tuberculosis and controller groups.It was about 17.3% of tuberculosis cases in comparison to 0% of that in controller cases had history of prolonged steroid therapy . Similar to our study, previous studies have concluded that patients treated with glucocorticoids have an increased risk of developing tuberculosis[34].

In our study health care shared as risk factor in development of tuberculosis that 6% of tuberculosis cases were workers in medical centers mainly paramedical persons with mean of the duration of working 19.6 ± 6.4 years .In consistent with our study it has been studied among 831 staff under regular chest radiographic survey in the Grantham Hospital, Hong Kong, the cumulative incidence of active pulmonary tuberculosis requiring treatment was 27[35] .Number of cases detected per year ranged from 0 to 3. The mean duration from the beginning of employment to the first evidence of disease was 6.43 years. Although this incidence is low, yet the hospital caters for quite a large number of patients with bacteriologically confirmed tuberculosis, so that the active screening program for hospital staff should be maintained.

Our study showed that a significant difference had been detected in distribution of male and female gender among study population that 64.7% of the tuberculosis group were males and 35.3% of the group were females. The observed association of TB with male sex is in agreement with what has been reported in most countries in Africa and Asia, where notification rates are higher for men than for women as found by WHO, 2001[36].

It has been found that there are considerable sex differences with regard to stigma and its social consequences, which may result in differential health-seeking behavior and access to care between males and females[37].The genome-wide linkage study searching for regions of the human genome containing TB susceptibility genes suggested a linkage between regions of the chromosome X and TB, with a lod score of 1.77, which could contribute to the excess of TB in males in many populations[38].The prevalence of infection with Mycobacterium tuberculosis is similar in males and females until adolescence, after which it is higher in males[39].

In our study renal disease was independent risk factor for development of tuberculosis, that 3.3% of tuberculosis cases had a renal disease but 96.7% of tuberculosis cases had no renal disease in comparison to controller group there was 0% of cases with renal disease.

There is an increased incidence of tuberculosis in patient with end-stage renal disease as compared with the general population[40]. In absolute numbers, this

observation is especially important in areas where the disease is endemic, which is consistent with end-stage renal disease is known to disrupt the cell-mediated immune response that is responsible for the killing of intracellular organisms such as Mycobacterium tuberculosis[41].

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