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RISK FACTORS OF EXTRA PULMONARY TUBERCULOSIS IN BASRAH

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Abstract

This article aimed to study the risk factors of extra pulmonary tuberculosis (EPT) in Basrah. A case-control study of 78 known cases of extra pulmonary tuberculosis (EPT) and 156 control subjects studied in "TB and Respiratory Diseases Center" in Basrah from December 2014 to March 2015.

Forty four (56%) of EPT cases were females (P>0.05) and the males were 34 (44%). Lymph nodes were the commonest site for EPT (33%), followed by tuberculosis pleural effusion and osteal tuberculosis (19% each). 34.6% of EPT patients consume raw milk while only 4.5% of the control group (free from EPT) consume raw milk with an odds ratio of 11.2, P<0.01. Some 6.4% of EPT patients had family history of having tuberculosis, and the odds ratio is 10 and P<0.01. The risk of development of EPT in people of less than 120.000 ID monthly incomes is 3.2 times greater than those with higher income, P<0.01. Regarding Body Mass Index (BMI), when comparing people having normal BMI (18.5-25 Kg/M^2) with people having subnormal BMI, the risk of having EPT is 3.9 times in underweight patients, P<0.01.

In conclusion, risk factors for EPT are; consumption of raw milk, family history of TB, BMI<18 (Kg/M^2) and a monthly income <120.000 ID.

Introduction

Tuberculosis (TB), a multisystemic disease with different presentations, and according to the WHO Global Tuberculosis Report 2014, 9 million new cases of TB were reported in 2013 and it is considered the second fatal infectious disease after HIV, with 1.5 million people deaths from TB in 2013[1].

HIV infection leads to emergence of drug resistant cases[2]. Moreover, some studies found that HIV infected patients are more likely to develop extra pulmonary tuberculosis (EPT) rather than pulmonary TB[3,4]. And one of the causes of increased incidence of TB in the United States in the early 1990s was the epidemic of HIV infection[5,6].

The causative agent of tuberculosis is Mycobacterium tuberculosis, a tubercle bacillus (T.B.), which belongs to a group of closely related organisms including M. africanum, M. bovis, and M. microti[7].

Infection with M. tuberculosis results most commonly through exposure of the lungs or mucous membranes to infected aerosols with M. tuberculosis, when inhaled, they deposit in the mucous membranes of the lungs, most of the bacilli are destroyed, the remaining live bacilli may spread to other body organs[8].

The lungs are the most common site for the development of TB; 75-85% of patients with TB have pulmonary complaints. An extrapulmonary location may also serve as a reactivation site; extrapulmonary reactivation may coexist with pulmonary reactivation[9,10].

The study of extra pulmonary tuberculosis (EPT) is quite important because of the serious complications and the high risk of

morbidity and mortality of EPT patients. TB meningitis has a mortality rate of 35% and potentially permanent neurological sequele[11]. In the setting of delayed therapy (more than 6 weeks), mortality from TB peritonitis approaches 60%[12].

Necessity of EPT study is not only due to the deficient data regarding the incidence and risk factors of EPT in our locality but it is also due to the difficulties which face the physicians during diagnosis as obtaining material for culture confirmation in ETB is often challenging because of smaller number of bacteria which produce poor yield on culture, and it is difficult to access organs such as retroperitoneal tissue, mediastinal glands and occasionally a non-approachable window in the spine[13]. EPT diagnosis based on clinical ground is also difficult because of the different presentations which may face the surgeons, physicians, gynecologists, and other clinical specialities[14]. And some studies found that 20-50% of EPT cases were diagnosed postmortemly[15-17]. So, high index of suspicion is needed to diagnose EPT.

The most common sites of extrapulmonary disease are as follows (the pathology of these lesions is similar to that of pulmonary lesions)[10]:

- Tuberculous lymphadenitis
- Tuberculosis pleural effusion
- Skeletal Tuberculosis
- Genital Tract Tuberculosis
- Urinary Tract Tuberculosis
- CNS Tuberculosis
- Gastrointestinal Tuberculosis
- Adrenal Tuberculosis
- Peritoneal TB
- Cardiac Tuberculosis
- Miliary TB

Strategies for prevention of TB include preventing HIV infection and intravenous drug use. BCG vaccine is a live attenuated strain of Mycobacterium bovis that is used in many parts of the world. BCG vaccination is effective in prevention of TB meningitis and disseminated TB in infants and young children, although its efficacy in older patients is unknown[18].

Methods

A case-control study involving a total of 78 diagnosed CASES of extra pulmonary TB in "TB and Respiratory Diseases Center" in Basrah from December 2014 to March 2015.

And 156 subjects who are apparently free from extra pulmonary TB, were matched to their corresponding cases according to age and sex from the same place and period of time of the cases, and were considered as CONTROLS.

The two groups (cases and controls) were put into a questioner study of the expected risk factors of extra pulmonary TB, including:

Age, Sex, Marital status, Address, Current job, Educational level, Smoking habit, Alcoholism, Drug addiction, Consumption of raw milk, History of previous imprisonment, Overcrowding, Income, History of contact with T.B. patients, Family history of T.B., History of chronic steroids use, BMI, BCG vaccine, Past history of T.B., Chronic medical illness.

EPT patients were diagnosed histopathologically, acid-fast bacilli (AFB) smear and culture, and GeneXpert MTB/RIF test. All EPT patients were screened for HIV infection.

The results were analyzed calculating exposure percentage, Chi-square and odds ratio using IBM SPSS Statistics v20. The results were considered significant when $P<0.05$, and highly significant when $P<0.01$.

Results

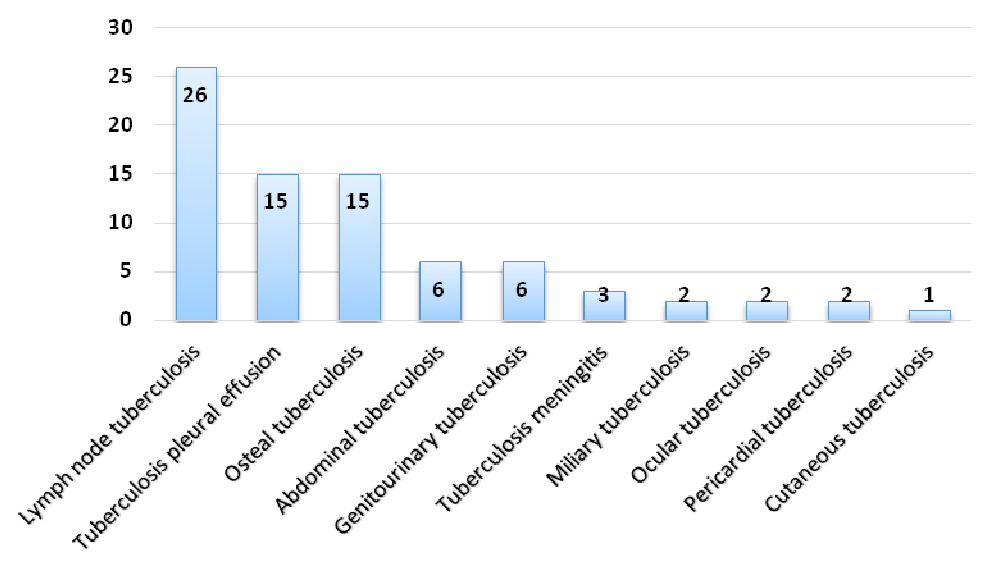
Of the 78 collected cases of extra pulmonary TB, 44 (56%) of them were females and the males were 34 (44%). While the age groups had a variable distribution. Table (I)

Table I: Demographic distribution of cases according to age and sex

Age	Males	Females
0-4	9.0% (7)	0.0%
5-14	7.7% (6)	3.8% (3)
15-24	9.0% (7)	11.5% (9)
25-34	6.4% (5)	9.0% (7)
35-44	3.8% (3)	6.4% (5)
45-54	3.8% (3)	6.4% (5)
55-64	1.3% (1)	6.4% (5)
65 and above	2.6% (2)	12.8% (10)
Total	43.6% (34)	56.4% (44)

Lesion sites were also variable, most lesions were lymph node tuberculosis (33%) followed by tuberculosis pleural effusion and osteal tuberculosis (19% each). The frequencies of other types are listed in the chart below. Figure 1.

Figure 1: Bar chart showing the frequency of each encountered type of EPT.



All the 78 cases of EPT were screened for HIV infection, and all of them were negative. 34.6% of EPT patients consume raw milk while only 4.5% of the control groups (free from EPT) consume raw milk with an odds ratio of 11.2, i.e. the risk of having EPT is 11.2 times greater in those who consume raw milk than those who do not. ($P < 0.01$)

As the efficacy of BCG vaccine lasts for 10-15 years[19], so data analysis will be in two categories; those under 15 years old, and those who are above 15-year old. 16.7% of EPT patients who are under 15 years old hadn't received BCG vaccine compares to 8.3% of the control group are BCG vaccinated ($P > 0.05$), so there is no association. While the above 15-year old EPT patients, the risk is unexpectedly increased to 7.4 times in those who hadn't received the vaccine before ($P < 0.01$).

6.4% of EPT patients had family history of having tuberculosis, and the odds ratio is 10 and $P < 0.01$.

The risk of development of EPT in people of less than 120.000 ID monthly incomes is 3.2 times greater than those with higher income, $P < 0.01$.

Regarding Body Mass Index (BMI), when comparing people having normal BMI (18.5-25 Kg/M^2) with people having subnormal BMI, the risk of having EPT is

3.9 times in underweight patients, P<0.01. On the other hand, having a BMI above the normal has a risk but with less association, P<0.05.

Table II: Risk factors for developing extrapulmonary tuberculosis

Possible risk factors	% among cases (n)	% among controls (n)	p-value	Odds ratio
Consumption of raw milk	34.6% (27)	4.5% (7)	p < 0.01	11.2
Family history of T.B.	6.4% (5)	0.6% (1)	p < 0.01	10
Non BCG vaccinated > 15 years old	51.7% (31)	12.5% (15)	p < 0.01	7.4
BMI < 18 (Kg/M2)	31.9% (15)	10.6% (10)	p < 0.01	3.9
Monthly income < 120.000 ID	42.3% (33)	18.5% (29)	p < 0.01	3.2
BMI > 25 (Kg/M2)	49.2% (31)	34.1% (43)	p < 0.05	1.8
Overcrowding	57.7% (45)	37.2% (58)	p < 0.01	0.43
Smoking	12.8% (10)	39.1% (156)	p < 0.01	0.25
Living in rural area	32.1% (25)	28.2% (44)	p > 0.05	
Being illiterate	32.9% (23)	27.5% (39)	p > 0.05	
Alcohol drinking	3.8% (3)	1.9% (3)	p > 0.05	
Having history of contact with T.B. patients	5.1% (4)	1.9% (3)	p > 0.05	
History of chronic steroids use	3.8% (3)	3.2% (5)	p > 0.05	
Non BCG vaccinated ≤ 15 years old	16.7% (3)	8.3% (3)	p > 0.05	
Having T.B. previously	2.6% (2)	1.3% (2)	p > 0.05	
Diabetes mellitus	7.7% (6)	12.2% (19)	p > 0.05	

Discussion

There is no doubt that TB is major health problem being a fatal infectious disease[1], nevertheless, it is preventable and curable, if the risk factors are avoided properly, diagnosed thoroughly and well treated[20].

Although all the cases of EPT were HIV negative, but many studies found that being an HIV positive is a great risk factor[9,10,14,21].

Female patients were 56.1% (44) of EPT , and it is not considered as a risk factor for having TB (P > 0.05); but other studies show that being a female is a risk factor for EPT[12,14,22].

As shown in table I, the variability of EPT patients' ages doesn't indicate any association of the age group and getting infected with Mycobacterium which is similar to another study done in the United States[14], but other studies found that being less than 15 years of age is more likely to have EPT[22,23].

Lymph nodes were the commonest site for EPT (33%), followed by tuberculosis pleural effusion and osteal tuberculosis (19% each). Which greatly resembles the results of other studies[10,14].

Consumption of raw milk is a significant risk factor of EPT (P < 0.01) with 11.2 times more risk to have the disease than in those who don't consume it. Although milk pasteurization is well known and widely used, but there are many in our

community who still consume unpasteurized milk, which makes them susceptible of being infected with M. bovis. Raw milk consumption is not only restricted to people living in rural areas, with 48.1% (13) of EPT cases who consume it live in the center of the city, mostly as a therapeutic agent in cases of bone fracture. Unfortunately, there are deficient data worldwide to compare with regarding the relationship between EPT and raw milk consumption, mainly due to eradication programs in many parts of the world[24] which makes it unlikely to have TB from animals in these countries.

Having family history of TB, is of great significant to have EPT ($P<0.01$), many studies found that there are genetic factors which determine the susceptibility to have TB, although an exact mechanism has not yet been found[9,25].

Poverty is of great importance in encountering EPT ($P < 0.01$). Exactly how poverty may lead to tuberculosis remains unclear. It may be due to poor education which is associated with poor knowledge of TB, risks of infection and dissemination, and with inadequate and/or delayed availability of health care. Poverty also results in poor nutrition and low body weight, which are likely to render the immune system more vulnerable to the invading organisms[26].

Underweight patients (BMI < 18 Kg/M^2) are of high risk of developing EPT ($P < 0.01$). And to a lesser extent overweight and obese patients (BMI > 25 Kg/M^2) also develop EPT ($P < 0.05$). Many studies also show that having a BMI < 18 (Kg/M^2) is considered as a risk factor for developing TB, contrarily, having a BMI > 25 (Kg/M^2) has a protective effect against TB[27,28]. It is well known that nutritional status influences the functioning of the cell-mediated immune system. Though the exact pathways are not fully understood, there is no doubt that several nutritional factors also influence the capacity of the cell-mediated immune system to fight TB bacilli[29].

Although diabetes affects the immunological status of the individual, but in this study it was found that it has no association with EPT ($P > 0.05$), which is comparable to the results of other studies. It is obvious in these studies that D.M. mostly increases the risk of having pulmonary TB but not extra pulmonary TB[30-32].

In conclusion, risk factors for EPT are; consumption of raw milk, family history of TB, BMI < 18 (Kg/M2) and a monthly income < 120.000 ID.

The commonest types for EPT lesions are; lymph node tuberculosis, tuberculosis pleural effusion and osteal tuberculosis.

Health education programs are needed in order to educate people about tuberculosis in general, risk factors, importance of milk pasteurization, and BCG vaccination of newborns.

Another study is needed to include more cases for a period of at least 1 year to look for other risk factors, to study individual risk factors, to study the efficacy of BCG vaccine along time, and to know the prevalence of EPT in Basrah.

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