

CLINICAL DIFFERENCES BETWEEN PULMONARY AND EXTRAPULMONARY TUBERCULOSIS: A 5-YEAR RETROSPECTIVE STUDY

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This article describes the clinical, epidemiologic, laboratory, and treatment characteristics of pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB) in Eastern North Carolina, a primarily rural area. The database was obtained for 1988-1992 from the University Medical Center of Eastern North Carolina-Pitt County and East Carolina University School of Medicine (the tertiary care referral center for this region). One hundred thirty-eight culture-positive patients were enrolled in the study; 56% were PTB and 44% were EPTB. African-American males constituted 59% of the population. Sixty-nine percent of the patient base were uninsured. There was a bimodal age distribution of <40 and >60 years of age. Factors associated with PTB (reported as odds ratios) were white males (2.5), diabetes mellitus (5.4), and cancer (5.1). Factors associated with EPTB (reported as odds ratios) were African-American females, positive human immunodeficiency virus (HIV) serology (8.7), low hematocrit (32.6), and elevated alkaline phosphatase (199). This study emphasizes that in the latest

resurgence of tuberculosis, impoverished rural areas, which have been ignored in earlier and present control efforts, are important reservoirs of disease. (*J Natl Med Assoc.* 1995;87:187-192.)

Key words • pulmonary tuberculosis • extrapulmonary tuberculosis

Compared with the remainder of North Carolina, tuberculosis in eastern North Carolina is an important disease with a high morbidity and mortality that constitutes a significant financial burden to this region. The incidence of tuberculosis in this region is two to five times that of the rest of North Carolina (Figure 1). This high incidence is only partly explained by the region's racial and economic demographics. Moreover, extrapulmonary tuberculosis (EPTB) is often difficult to diagnose and manage. Also, early recognition of the signs and symptoms of this disease would help to reduce the morbidity and cost of treating this disease.

This retrospective study was designed to characterize and define the demographics and clinical presentations of pulmonary and extrapulmonary tuberculosis in eastern North Carolina. Hopefully, this information will point out another aspect of the latest resurgence of tuberculosis, namely that pockets of high endemicity in impoverished rural areas in states with an overall low incidence of disease still constitute an important health problem.

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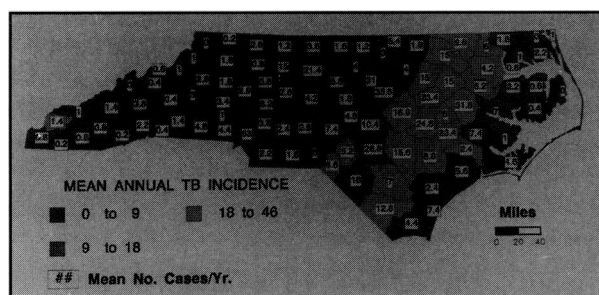


Figure 1. Mean annual tuberculosis incidence in North Carolina, 1988 to 1992.

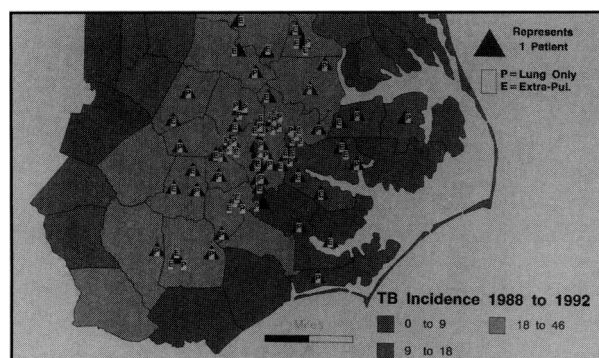


Figure 2. Pulmonary versus extrapulmonary tuberculosis at the UMCEC-PC catchment area, 1988 to 1992.

METHODS AND MATERIALS

Medical records of all patients with a positive culture for *Mycobacterium tuberculosis* from both pulmonary tuberculosis (PTB) and EPTB sites between 1988 and 1992 were reviewed. Culture results were obtained from the clinical microbiology laboratory of both components of the University Medical Center: East Carolina University School of Medicine and Pitt County Memorial Hospital. University clinics serve as outpatient referral facilities for much of eastern North Carolina, which has a population of approximately 1.5 million, while the hospital is a 750-bed tertiary care referral center for the same area.

Data collected from the patients' charts were analyzed for the following: demographics, clinical features, personal characteristics, sites of acid fast bacillus (AFB), comorbid disorders, laboratory data, and treatment regimens. Logistic regression modeling was used to determine comorbidity factors for tuberculosis, PTB, and EPTB by comparing these factors for our patients with those from all University Medical Center and eastern North Carolina residents. Unpaired *t*-tests were used to determine the differences in the white blood cell

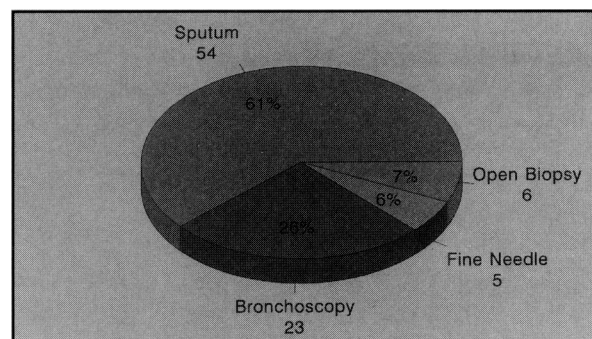


Figure 3. Characteristics of patients with culture-positive *Mycobacterium tuberculosis* (PTB) from 1988 to 1992, with sources of PTB included.

count and logistic regression modeling was used to determine the characteristics of the hematocrit and alkaline phosphatase.

RESULTS

Characteristics of AFB Cultures

One hundred thirty-eight culture-positive cases were enrolled in the study; geographical distribution is shown in Figure 2. Seventy-seven patients had a total of 88 positive specimens for *M. tuberculosis*, all obtained from the lung (Figure 3), which were reported at the medical center during the time of the study. Sixty-one patients had positive *M. tuberculosis* cultures obtained from extrapulmonary sites. Of these patients, 18 had positive pulmonary cultures. *Mycobacterium tuberculosis* was recovered from 67 specimens from extrapulmonary sites (Figure 4).

Demographics

Compared with the population figures for eastern North Carolina, which has an incidence of 1.8 to 2.9 times that of the western section of the state (Figure 1), the patient population with tuberculosis had a greater proportion of African-American males (59%) and individuals who were uninsured (69%). There was a bimodal age distribution with peaks <40 years of age and >60 years of age. Fifty-three percent of the patients were under 60 years of age (Figure 5). There is a tendency for a clustering of EPTB in the northern counties of the region.

Comparison of Factors Associated With PTB and EPTB

Logistic regression modeling was used to identify comorbidity factors associated with PTB and EPTB.

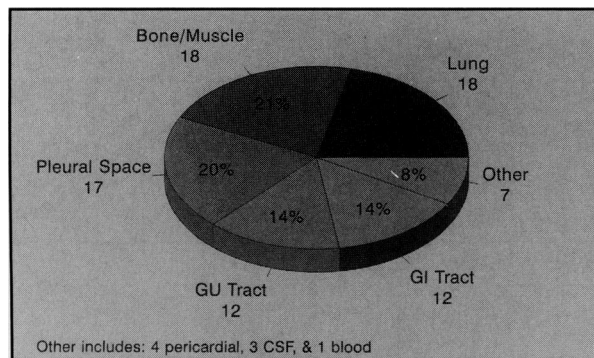


Figure 4. Characteristics of patients with culture-positive *Mycobacterium tuberculosis* (EPTB) from 1988 to 1992, with sources of EPTB included.

Factors associated with EPTB included female sex, African-American ethnicity, and positive human immunodeficiency virus (HIV) serology ($P < .05$). Factors independently associated with PTB included male sex, white race, diabetes mellitus, and cancer from any site (Table 1). Eight patients tested positive during the study. The association of diabetes with tuberculosis (odds ratio 5.4) appears to be a significant finding.

Laboratory Parameters

Logistic regression modeling also was used to identify laboratory parameters of serum alkaline phosphatase levels and hematocrit that were significantly different among PTB and EPTB. The mean serum alkaline phosphatase level of 199 μ /L was higher in patients with EPTB than in patients with PTB (147 μ /L; $P \leq .05$). The mean hematocrit also was significantly lower in patients with EPTB (32.6%) than the mean hematocrit in patients with PTB (35.4%; $P \leq .05$). Using unpaired t -tests, the mean white blood cell count of patients with EPTB was significantly lower than the mean white blood cell count of patients with PTB ($P < .05$) (Table 2).

Treatment Modalities

Ethambutol was prescribed more frequently to elderly patients and vitamin B-6 more frequently to patients with insurance; no other difference could be detected in the treatment regimens prescribed to these groups of patients. Information on the number of treatment failures during the study period was not obtained.

DISCUSSION

Tuberculosis continues to be a major health problem despite advances made in the understanding of the

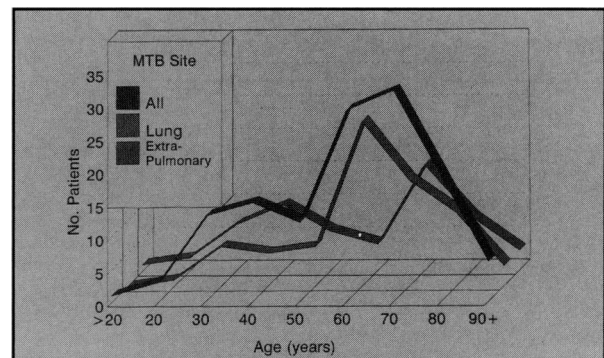


Figure 5. Age distribution of patients with PTB and EPTB, 1988 to 1992.

pathogenesis and management of the disease. In the United States, there had been a steady decrease in the incidence of incidence since the early 1900s with a slight increase between 1979 to 1981 due to the influx of Indonesian refugees. Unfortunately, since 1990, the incidence of tuberculosis has increased 9.4% annually. This is thought to be the result of the increased prevalence of HIV infection.¹⁻⁴ California and New York appear to have the largest increase in new tuberculosis cases. However, in most states in the southeast, the number of new cases has remained about the national average.² This is probably due to the large migrant, immigrant, minority, and elderly population in these regions.⁵⁻⁹ This is especially true for North Carolina, which has a large, rural, elderly population with a higher minority population consisting mostly of African Americans and Hispanics. North Carolina also has a higher incidence of tuberculosis in the eastern section of the state when compared to the western section of the state.¹⁰

Certain patient populations such as African Americans, males, economically disadvantaged, inner-city residents, and nursing home residents appear to show susceptibility to tuberculosis.¹¹ Some groups such as African Americans, Hispanics, immigrants, alcoholics and intravenous drug abusers have a disproportionately higher incidence of tuberculosis.¹²⁻¹⁵ Most of these factors, with the exception of inner-city and nursing home residents, are probably responsible for the higher incidence of tuberculosis seen in this region.

Several theories have been put forth regarding racial susceptibilities to tuberculosis, especially in the African-American population. These include deficiency of vitamin D and genetic differences.¹¹ In addition, an increased rate of tuberculosis in African Americans and

TABLE 1. COFACTORS ASSOCIATED WITH PULMONARY AND EXTRAPULMONARY TUBERCULOSIS

	PTB	EPTB
Sex	Male (2.5)*	Female
Ethnicity	White (3.0)	African American
Human immunodeficiency virus infection	No	Yes (8.7)
Diabetes	Yes (5.4)	No
Cancer†	Yes (5.1)	No

Abbreviations: PTB=pulmonary tuberculosis and EPTB=extrapulmonary tuberculosis.

*Number in parentheses is adjusted odds ratio of characteristic occurring for this site. Estimated from logistic regression procedures using the parameter estimate.

†Any site.

TABLE 2. MEAN LABORATORY DIFFERENCES BETWEEN PULMONARY AND EXTRAPULMONARY TUBERCULOSIS

	PTB	EPTB
White blood cell count*	9330 ± 5280	7700 ± 3650
Hematocrit†	35.4 ± 6.7	32.6 ± 7.0
Alkaline phosphatase‡	147 ± 130	199 ± 145

Abbreviations: PTB=pulmonary tuberculosis and EPTB=extrapulmonary tuberculosis.

*Given as cells/ μ . Unpaired t-test; $P \leq .05$.

†Given as % volume. Logistic regression modeling; $P \leq .05$.

‡Given as U/L. Logistic regression modeling; $P \leq .05$.

Hispanics in the 25- to 44-year-old age group compared with whites in the same age group has been noted.³ The increased incidence of tuberculosis in African Americans between 20 and 54 years of age in New York appears to be related to the current HIV epidemic.^{3,16,17} In North Carolina between 1989 and 1990, 22% of the tuberculosis patients were tested for HIV infection; a total of 26% were found to be HIV-positive.¹⁸ We and investigators at other centers have noted a significant association of EPTB, but not PTB with positive HIV serology ($P \leq .05$).

In addition, the high incidence of poverty and homelessness among African Americans appear to play a role in the high incidence of tuberculosis.^{12,18} Moreover, the risk of contracting tuberculosis and its poor outcome among native born African Americans exceeds the risks of the same outcomes in other groups.⁵ Transmission in infected farm workers is thought to be an occupational hazard and may play an important role in the spread of the disease in this region.^{2,5} These factors translate to approximately a three to seven times higher morbidity rate among

nonwhites and accounts for almost 50% of all new cases of tuberculosis diagnosed in whites.⁵

In whites, tuberculosis is a disease of the elderly with a mean age of 62 years. However, in minorities, it is a disease of the young with a mean age of 39 years. This may be due to reasons such as time of initial infection and opportunity for exposure to infection.¹⁹ Our population had a higher association of PTB in white males, which is unusual and cannot be explained on the basis of racial or demographics factors. In African-American males, age-specific risk has a marked first peak in the 35- to 44-year-old group and is lower in the 54- to 64-year-old group. Males are twice as likely to contract tuberculosis than females with African-American males having a 6.4 times overall risk of developing tuberculosis compared with the general population. This may be due to the differences in exposure opportunities such as site of employment or even unexplained genetic differences.³ In our population, 59% of new cases were African-American males. Extrapulmonary tuberculosis accounts for approximately 20% to 37% of all new cases diagnosed with tuberculosis.^{20,21} It can be difficult to make a diagnosis of EPTB because almost 50% of these patients have negative chest radiographs and may present with either single or multiorgan involvement. The most commonly involved organs include the genitourinary tract, musculoskeletal system, and reticuloendothelial system.²¹ Tuberculosis meningitis is being seen more commonly in the elderly,^{22,23} whereas tuberculosis pericarditis occurs more often in the young and middle-aged.^{24,25} In addition, EPTB occurs in up to 70% of acquired immunodeficiency patients (AIDS) with tuberculosis with the likelihood rising as the CD4 count falls so that the 70% rate of EPTB occurs mostly in severely immunocompromised patients, such as those with AIDS.¹⁸

Our findings of EPTB concur with those reported in

the literature with involvement of the musculoskeletal system in 21%, genitourinary tract in 14%, and gastrointestinal tract in 14%. Involvement of the musculoskeletal system is most likely due to haematogenous spread resulting in the Potts abscesses, paraspinal abscesses, gibbus formation, and vertebral collapse.²⁶ Pulmonary tuberculosis is still the most common form of tuberculosis and occurs in 60% to 70% of all presenting cases. Fifty-six percent of our patients presented with PTB as the initial manifestation of the disease. The association of diabetes with PTB appears to be a significant finding as the Centers for Disease Control had identified diabetics as persons at increased risk for tuberculosis; however, no studies to date have convincingly supported that recommendation. Pulmonary tuberculosis may present as atypical pneumonia, pleuritis, upper lobe involvement, or in combination with EPTB.¹⁶ When associated with HIV, its presentation may be atypical.

Laboratory parameters associated with tuberculosis may vary tremendously with patients presenting with laboratory evidence of anemia (usually anemia of chronic disease), leukocytosis with relative monocytosis, thrombocytosis, and hypergammaglobulinemia. Hyponatremia and increased alkaline phosphatase usually reflect extrapulmonary involvement.²⁶

CONCLUSION

This study demonstrates that tuberculosis still presents itself as a health problem in eastern North Carolina. The disease was seen predominantly in African-American males with a bimodal age distribution of >60 years or <40 years of age. The uninsured population formed a large percentage of the population. In this study, PTB as an initial presentation of the disease is associated with white males, diabetes, and cancer from any site. Extrapulmonary tuberculosis as an initial presentation of the disease is associated more often with African-American females, positive HIV serology, elevated alkaline phosphatase, and lower hematocrit. These latter findings suggest multiple sites of involvement in extremely sick patients who are immunocompromised.

This study points out the unusual demographic and clinical manifestations of pulmonary and extrapulmonary tuberculosis in the region. In addition, clinicians should be aware of the association of diabetes with pulmonary tuberculosis so that adequate measures can be taken to test for the disease. It also should be noted that the ratio of pulmonary to extrapulmonary tubercu-

losis is different from the urban-based population and therefore merits a different clinical approach.

Acknowledgments

The authors thank Dr R. Turner (general medicine) and Drs Y. Kataria and A. Driver (pulmonary medicine) for their suggestions and Nancy Hamm for her help in preparing the manuscript.

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