

## Extrapulmonary tuberculosis epidemiological characteristics

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### Abstract

**Background:** Tuberculosis is a highly contagious disease that is prevalent in underdeveloped countries. According to the World Health Organization (WHO), this disease is defined by its anatomical location.

**Methodology:** A narrative review was conducted using various databases from 2017 to 2021; the search and selection of articles was carried out in indexed journals in English and Spanish. The following keywords were used: tuberculosis, extrapulmonary, characteristics, epidemiological.

**Results:** The main epidemiological characteristics aim to quantify the evolution of extrapulmonary tuberculosis within a certain time frame in a specific geographical area or population.

**Conclusion:** Patients diagnosed with extrapulmonary tuberculosis may present different clinical manifestations depending on where the tuberculosis has spread, but this does not differ from the global epidemiological context.

**Keywords:** Tuberculosis; Extrapulmonary; Characteristics; Epidemiological

### 1. Introduction

Tuberculosis is a highly contagious disease and is prevalent in underdeveloped countries, according to the World Health Organization (WHO). This disease is defined by the anatomical location in which it is found. Extrapulmonary tuberculosis is considered to be that which is produced by clinically diagnosed *Mycobacterium tuberculosis*, which involves not only the lungs but also organs such as the pleura, abdomen, lymph nodes, and genitourinary tract, among others. This disease spreads hematogenously and lymphatically. (1)

This disease has different clinical manifestations, which makes its diagnosis difficult. It usually occurs in immunocompromised patients or those with diseases that affect or weaken their immune system. (2)

In Colombia, more than 2,385 cases of tuberculosis were reported in 2015, with TBE having the highest incidence. (3) Diagnosis requires additional tests such as a liver function test, which is not highly sensitive, but if clinical manifestations are suspected, granulomas, appropriate epidemiology, and diagnostic imaging tests can be evaluated to confirm the diagnosis and establish strategies for timely treatment, which should be started as soon as possible to

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reduce mortality and morbidity rates. We must bear in mind that the presence of granulomas is also due to other conditions that are not related to TB. Therefore, special importance is given to the determination of adenosine, as it allows for early treatment. (4)

Treatment will depend on the patient's clinical characteristics, but it is generally the same as the system used for TBP, a drug treatment lasting around 6 months that includes isoniazid, rifampicin, ethambutol, and pyrazinamide. Unless it is the meningeal form, in which case treatment is extended to 7 months. (5)

Despite new prevention updates, the total number of tuberculosis cases has decreased, but the decrease in TBP has not been as noticeable. One of the reasons for this may be the reduced use of vaccination (BCG) or the generation of real changes in the most socioeconomically vulnerable populations. Risk factors to be evaluated for the spread of tuberculosis include age, HIV disease, female gender, and the presence of comorbidities such as diabetes. (6)

The objective of this research is to compile the epidemiological characteristics that are commonly found in patients who contract extrapulmonary tuberculosis.

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## 2. Materials and methods

This research involved a literature review, searching databases such as PubMed, Scielo, and ScienceDirect, among others. The collection and selection of articles was carried out in indexed journals in English and Spanish from 2019 to 2022. The following terms were used as keywords in the databases according to the DeCS and MeSH methodology: tuberculosis, extrapulmonary, characteristics, epidemiological. This review identified 40 original and review publications related to the topic studied, of which 25 articles met the specified inclusion requirements, such as articles published no earlier than 2017, full-text articles, and articles reporting on extrapulmonary tuberculosis epidemiological characteristics. Exclusion criteria included articles that did not provide sufficient information and were not available in full text at the time of review.

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## 3. Results

TBE is defined according to classification criteria as a contagious infection caused by *Mycobacterium tuberculosis* that affects tissues and organs outside the lung parenchyma. Globally, this represents 15 to 20% of tuberculosis cases. (7)

When tuberculosis occurs extrapulmonarily, it makes microbiological sampling difficult, which means that diagnostic imaging tests such as magnetic resonance imaging or computed tomography can be of great help in reaching a diagnosis. (8)

### 3.1. Lymph node tuberculosis

This is one of the most common forms of TBE and usually occurs mainly in children and young adults. The most common location is cervical lymphadenopathy, but it can also affect the axillary, thoracic, abdominal, and supraclavicular lymph nodes. It does not usually present with symptoms, but over time a series of clinical features may develop, such as necrosis, ulceration, and fistulization, among others. Lymph node growth may also cause compression symptoms in neighboring organs, such as tracheal obstruction, among others. (9)

### 3.2. Tuberculosis in the central nervous system

This type of TBE is caused by hematogenous spread from a distal focus, has a high mortality rate, and between 25% of patients who suffer from it are left with some type of sequela, while 40% may die despite timely initiation of treatment. It occurs mainly in the meninges, but it can also manifest as brain abscesses or vascular thrombosis with a high probability of infarction. (10)

### 3.3. Intestinal tuberculosis

This form of TBE can affect any part of the gastrointestinal tract, but the most common location is the ileocecal region. In these cases, the bacteria penetrate the mucosal tissue and initiate an inflammatory reaction that can lead to the formation of ulcers, scars, fibrosis, and other types of lesions. (11) The clinical manifestations are not specific, as they have a chronic and slow progression, although the most characteristic symptom is severe abdominal pain. Weight loss to the point of developing anorexia, sweating, high fever, diarrhea, and constipation may also occur. In the most advanced cases, serious complications such as intestinal obstruction may develop. (12)

### 3.4. Urinary tuberculosis

This is caused by hematogenous spread and accounts for 6.5% of cases, usually occurring mainly in men. In its early stages, it tends not to present symptoms, but later spreads to the ureter and bladder, developing symptoms of urinary syndrome with the presence of microhematuria and sterile pyuria. (13)

### 3.5. Pleural tuberculosis

This is the most common form of TBE and occurs when microbacterial antigens enter the pleural space, producing a hypersensitivity reaction to these same antigens. It is unilateral and in most cases resolves on its own or without prior treatment. For diagnosis, a microbiological analysis of the pleural fluid is performed by thoracentesis, as smear microscopy is not very useful for this form of TBE. (14)

### 3.6. Risk factors for extrapulmonary tuberculosis

- Smoking
- COPD
- Alcoholism
- contact with TB
- other chronic diseases
- immunosuppression
- malnutrition
- HIV carrier
- no identified risk factors
- diabetes mellitus

### 3.7. Epidemiological characteristics of TBEP

As it is an infectious disease transmitted by microorganisms, in order for it to spread from person to person, contact with the population susceptible to the disease is necessary. (15)

The most profitable form of tuberculosis transmission is through healthy infected individuals, as they carry the bacillus in their bodies without showing any signs that would identify the presence of the disease. It is when the disease develops that they become a source of infection. (16)

The main epidemiological characteristics aim to quantify the evolution of TBEP within a given time frame in a specific geographical area or population. Certain epidemiological parameters are used, such as those mentioned in Table 1 below:

**Table 1** Epidemiological parameters

Annual incidence rate	This is the number of new cases of tuberculosis that appear in a year, generally expressed per 100,000 inhabitants.
Annual incidence rate of bacilliferous cases	This is the number of new cases or recurrences of tuberculosis with positive sputum smear microscopy, expressed per 100,000 inhabitants. This data is particularly relevant as it corresponds to the sources of infection.
Prevalence rate	This is the number of cases of tuberculosis at a given time expressed per 100,000 inhabitants.
Annual mortality rate	This is the number of deaths from TB per 100,000 inhabitants in a year. Since the advent of anti-tuberculosis chemotherapy, it is not considered a good parameter for estimating the evolution of the disease, but it serves to draw attention to its vital importance in many regions of the world.
Case fatality rate	This is the number of deaths per 100 cases of tuberculosis. Taking into account the WHO estimates for 2005, we still a global case fatality rate of 18%, ranging from 14% in some WHO regions in Europe and America to more than 20% in Africa and Eastern Europe.

Prevalence of latent TB	This is the number of people who react to the tuberculin skin test, expressed as a percentage.
Annual risk of infection	This expresses the percentage of the population that will be infected (or reinfected) in the course of a year. There are many factors that influence its calculation, so the data obtained from this parameter should be treated with caution and its use is not usually recommended
High-risk group	is defined as more than 100 cases per 100,000 individuals per year.

Globally, it is difficult to obtain consistent figures and information on the incidence of TB, as diagnostic tests are not routinely performed in impoverished areas where the disease may have a high probability of transmission. The WHO states that one-third of the population has some form of latent tuberculosis. (17)

### 3.8. Cases of tuberculosis by type and condition in Colombia in 2020

In Colombia in 2020, cases of TB and EPTB were reported in most of the country's territorial entities. The places with the highest incidence of extrapulmonary tuberculosis were Bogotá (34%), Vaupés 22%, and Cartagena and Casanare 20.2%. During this year, it was reported that the most common types of EPTB were pleural, meningeal, and lymph node. (18)

## 4. Discussion

Given that the diagnosis of extrapulmonary tuberculosis is often difficult due to the different symptoms, these can be associated with other pathologies such as fever, sweating, weight loss, among others that may occur depending on the site where the tuberculosis has developed. The diagnosis will depend on the availability of diagnostic and imaging tests. (19)

In general, the incidence of extrapulmonary tuberculosis is lower than that reported for pulmonary cases, tending to represent 14% of tuberculosis cases worldwide. (20)

In this regard, several studies were consulted in the medical literature that refer to an expansion of the topic, as pointed out by Donel González-Díaz et al. in their research for the year 2019-2020, where patients diagnosed with extrapulmonary tuberculosis at the Benéfico Jurídico Pulmonary Hospital in Havana, characterized from a clinical-imaging perspective, where the results obtained predominantly involved male patients between the ages of 26 and 35 (29.4%). Seventy-three point five percent of patients presented risk factors for this disease, the most frequent being: being contacts of tuberculosis patients (29.4%), ex-prisoners (17.6%), and alcoholics (14.7%). Fifty-eight point eight percent presented with fever and general symptoms or signs such as anorexia (44.1%), weight loss (41.2%), and asthenia (38.2%). The most common radiological finding was pleural effusion (47%), and the most frequent extrapulmonary form, with 15 cases (44.1%), was tuberculous pleurisy. The most relevant clinical manifestations were fever, weight loss, and asthenia. (21)

On the other hand, in the study conducted by Dora Montiel et al., the clinical-epidemiological characteristics of adult patients diagnosed with TB admitted to the National Hospital of Itauguá between January 2008 and March 2018 were determined. A total of 72 patients between the ages of 18 and 86 were included. Eighty-seven point five percent had some type of comorbidity, including HIV infection (55.5%); systemic lupus erythematosus (6.3%); type 2 diabetes mellitus (6.3%); malnutrition (15.8%); alcoholism (9.5%); smoking; and corticosteroid use (14.2%); prolonged fever (63.8%), acute fever (36.2%), pulmonary tuberculosis (50%), miliary tuberculosis (11.1%), and extrapulmonary tuberculosis: pleural (9.7%), meningeal (8.3%), central nervous system (tuberculoma) 9.7%, digestive (8.3%), lymph node (6.9%), spinal column (2.7%), skin (2.7%), urogenital (1.3%). Associated tuberculosis: miliary-cutaneous (10%), pulmonary-lymph node (10%), pulmonary-digestive (20%), pulmonary-pleural (10%), pulmonary-tuberculoma (40%). Tuberculosis revealed HIV infection in 15.1% of cases, with a mortality rate of 6.9%. There was an association between miliary tuberculosis and mortality. (22)

These results are similar to those found by Mamani Loza et al., where the main objective of the study was to determine the clinical and epidemiological characteristics of adult patients diagnosed with extrapulmonary tuberculosis at the Hipólito Unanue Hospital in Tacna between 2016 and 2018. This study also found a predominance of males, who represented 64.2% of the study population and most were between the ages of 20 and 29. Many of them had non-modifiable diseases or conditions, compromising systems such as the respiratory system (14.17%), the peritoneal

system (13.33%), and the central nervous system (9.16%), among others. The most predominant clinical characteristics were fever, weight loss, hypoxia, and cough with expectoration. (23)

A strength of the current study is the methodology implemented with regard to the literature search and steps in the selection of relevant articles, quality assessment, and data extraction. However, this study has several limitations that should be taken into account before reaching a conclusion, including the lack of evidence related to extrapulmonary tuberculosis epidemiological characteristics. [24, 25]

## 5. Conclusion

It is very important to emphasize that both the clinical and epidemiological characteristics in patients diagnosed with extrapulmonary tuberculosis can present different clinical manifestations depending on the location where the tuberculosis has proliferated, even so, it does not differ from the global epidemiological context.

We must point out that, according to the medical literature consulted, there is a high incidence in younger age groups, and immunosuppressive diseases such as HIV are not a determining factor, but they do enable a high probability of contagion.

In the event of clinical and epidemiological suspicion, which would indicate a high rate of possible extrapulmonary tuberculosis, it is extremely important to make a timely diagnosis following the protocol, as this remains a cornerstone for reducing mortality, especially in high-risk populations.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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