



Research Article/Özgün Araştırma

Distribution of epidemiological and clinical involvement of extrapulmonary tuberculosis patients in the infectious disease's outpatient clinic by years

Enfeksiyon hastalıkları polikliniğinde ekstrapulmoner tüberküloz hastalarının epidemiyolojik ve klinik tutulumlarının yıllara göre dağılımı

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Abstract

Aim: It was aimed to examine the patients diagnosed with extrapulmonary tuberculosis (EPTB) in terms of diagnostic methods and demographic characteristics.

Materials and Methods: The files of patients with EPTB who were followed up in the infectious disease's outpatient clinic between 2012 and 2022 in our study were retrospectively reviewed.

Results: Of the patients diagnosed with EPTB, 70.8% (102) were female and 29.2% (42) were male. The ages of the patients ranged from 20 to 88, the mean age of women was 54.2, and the mean age of men was 55. The most common site of involvement in these patients was lymph node involvement. This was followed by bone-joint, peritoneal, central nervous system and genitourinary system involvement, respectively. Histopathological methods were used most frequently in 81 (56.5%) of the patients.

Conclusion: The signs and symptoms of EPTB differ according to the organs and tissues involved in the body. We believe that EPTB should be considered in the differential diagnosis in endemic regions.

Keywords: Extrapulmonary tuberculosis; Lymph node; Mycobacterium tuberculosis; Histopathology, Infectious diseases outpatient clinic.

Öz

Amaç: Ekstrapulmoner tüberküloz (EPTB) tanısı alan hastaların tanı yöntemleri ve demografik özellikleri açısından incelenmesi amaçlandı.

Gereç ve Yöntemler: Çalışmamıza 2012-2022 yılları arasında enfeksiyon hastalıkları polikliniğinde takip edilen EPTB tanılı hastaların dosyaları retrospektif olarak incelendi.

Bulgular: EPTB tanısı alan hastaların %70,8'i (102) kadın, %29,2'si (42) erkek olarak saptandı. Hastaların yaşları 20 ile 88 arasında değişmekte, kadınların yaş ortalaması 54,2, erkeklerin yaş ortalaması ise 55 olarak gözlemlendi. Bu hastalarda en sık lenf bezi tutulumu görülmüştür. Bunu sırasıyla kemik-eklem, periton, santral sinir sistemi ve genitoüriner sistem tutulumu izlemiştir. Hastaların tanısında en sık histopatolojik yöntemler 81(%56,5) kullanılmıştır.

Sonuç: EPTB'nin belirti ve bulguları vücutta tutulan organ ve dokulara göre farklılıklar göstermektedir. Endemik bölgelerde ayırıcı tanıda EPTB hastalığının düşünülmesi gerektiği kanaatindeyiz.

Anahtar Kelimeler: Ekstrapulmoner tüberküloz; Lenf nodu; Mycobacterium tuberculosis; Histopatoloji, Enfeksiyon hastalıkları polikliniğinde.

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Introduction

Tuberculosis (TB) remains a serious global public health problem. According to the World Health Organisation (WHO) report (global TB report 2021), an estimated 10 million people are diagnosed with TB each year and approximately 1.5 million people die from TB annually.¹ Although the majority of cases are diagnosed with pulmonary tuberculosis (PTB); pleural tuberculosis, lymph nodes, musculoskeletal system, gastrointestinal tract, meninges, etc. Involvement of other organs and organ systems is classified as extrapulmonary tuberculosis (EPTB).^{2,3}

EPTB causes 15 to 20 % of all TB cases in humans, and this number is reported to have increased in the last decade.⁴ Tuberculin skin test (TST), interferon gamma release test, polymerase chain reaction test, acid-fast bacilli (AFB) smear and culture (gold standard) and radiological imaging, methods are used in the diagnosis of EPTB.^{5,6} There are difficulties in the diagnosis, treatment and follow-up of EPTB due to the fact that it can be seen in almost all organs, has a wide range of clinical symptoms, affects body fluids and settles in hard-to-reach areas in the body.⁷ Due to these difficulties in diagnosis and follow-up, it is thought that EPTB cases are more than previously diagnosed.

The aim of this study was to draw attention to the importance of extrapulmonary tuberculosis, which is an important public health problem, by showing the distribution of organ involvement, demographic characteristics and epidemiological evaluation between 2012-2022 in Adiyaman.

Materials and Methods

Onehundredfortyfour patients diagnosed with EPTB who applied to our outpatient clinic between 2012 and 2022 were included in the study and examined retrospectively. The infectious diseases polyclinic serves a city with a population of six hundred thousand. Cases with at least one of the following criteria were accepted for the diagnosis of EPTB:

- Direct examination of the material taken from the extrapulmonary focus (peritoneal fluid, urine, gastric juice, lymph node

puncture material, etc.) shows the presence or culture growth of AFB.

- Positive TST in patients with caseating granuloma on biopsy.
- The biopsy does not show caseification, granulomatous inflammation is detected and there is clinical findings compatible with TB and other diagnoses are excluded.
- Clinical findings compatible with TB, positive tuberculin skin test and response to treatment.
- TST induration diameter of 10 mm or more in those without BCG scar and 15 mm or more in those with BCG scar were considered positive.

EPTB cases were analysed according to age, gender, organ or organ system involved and distribution rates according to years.

Type of the study

The study is retrospective.

The sample size of the study

Onehundredfortyfour patients aged 20-88 years applied to the infection disease out patient clinic.

Data collection tools

Datas were taken retrospectively.

Data analysis

Analyzes were evaluated in 22 pack age programs of SPSS (Statistical Pack age for Social Sciences; SPSS Inc., Chicago, IL). In the study, descriptive data are shown as n and % values in categorical data and mean±standard deviation (mean±SD) and median (minimum-maximum) values in continuous data. Chi-square analysis (PearsonChi-square) was used to compare categorical variables between groups. The statistical significance level in the analysis was accepted as $p<0.05$.

Ethics committee approval

Ethics committee approval was obtained with the decision of the Ethics Committee for Non-Interventional Procedures of Adiyaman University, dated 13.12.2022, and numbered 2022/9-5. The principles of the Declaration of Helsinki conducted the research.

Results

During the 10-year period of the study, 144 EPTB patients were identified. Among the patients diagnosed with EPTB, 70.8% (102) were female and 29.2% (42) were male. Although the ages of the patients ranged between 20 and 88 years, the mean age of women was 54.2 years and the mean age of

men was 55 years. Considering the annual number of patients followed up, a significant decrease was observed between 2019 and 2021, and it was thought that the reason for this was that patients could not apply to the hospital due to the global COVID-19 pandemic in the specified years. The number distribution of the detected cases according to years is shown in Figure 1.

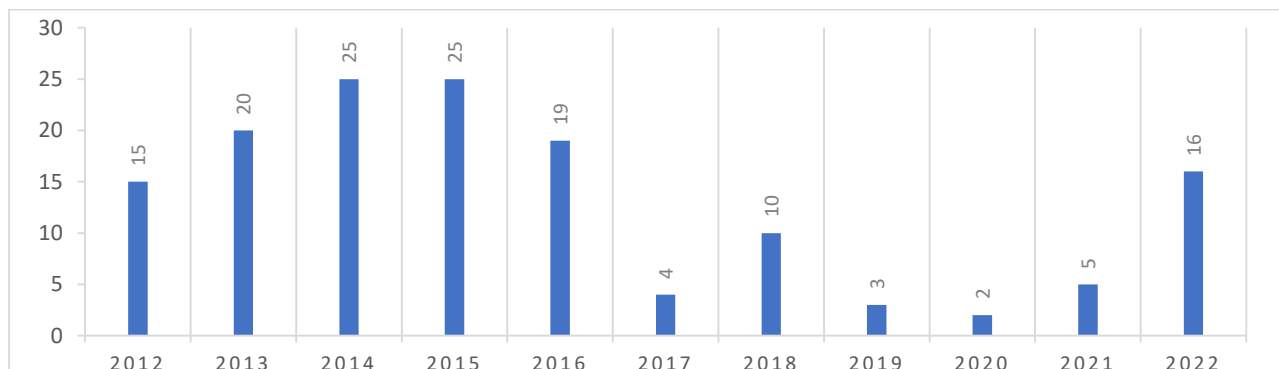


Figure 1. Number of EPTB patients by years.

Among the cases included in the study, histopathological examination was used in the diagnosis of 81 cases, molecular and histopathological diagnosis was made in 7 cases, molecular diagnosis was made in 4 cases, microbiological diagnosis was made in 3 cases and other methods were used in the remaining 49 cases. Diagnostic methods used in EPTB cases are shown in table 1.

Table 1. Methods used in the diagnosis of EPTB.

Diagnosis method	Number of patients(n)	%
Histopathological	81	56.5
Microbiological and histopathological	3	2
Molecular	4	2.7
Molecular and histopathological	7	4.8
Other examinations	49	34

*Other examinations: Radiological examinations, TST, liquid adenosine deaminase, lymphocyte-rich fluid, etc.

When the organ types involved were examined, the most frequently involved organ was the lymph node with a rate of 54.8% (79). This was followed by bone-joint with 18.7% (27), peritoneum with 10.4% (15), and central nervous system with 4.1% (6). Genitourinary system, gastrointestinal system, breast and skin were seen in 2.7% (4). Among the cases, there was one EPTB (0.6%) in the pharynx (Pleural tuberculosis patients were not

included in the study because they were followed by chest diseases departments).

Cervical lymph nodes were most commonly involved in cervical involvement and vertebrae were most commonly involved in bone joint involvement. The organ distribution of the cases is shown in table 2.

Table 2. Involved organ and severity

Organ Involved (n)	Patient (n)(%)
LymphNodes	79 (54.8)
Cervical	53 (67)
Axillary	9 (11.3)
Mediastinal	9 (11.3)
Intra-abdominal	6 (7.5)
Submandibular	2 (1.3)
Peritoneum	15 (10.4)
Genitourinary	4 (2.7)
Ovary	1 (0.6)
Bladder	3 (2)
Central nervous system	6 (4.1)
Pharynx	1 (0.6)
Bone Joint	27 (18.7)
Vertebra	13 (9)
Hip	3 (2)
Spondiliscite	3 (2)
Femur	1 (0.6)
Foot	2 (1.3)
Clavicle	1 (0.6)
Other	4 (2.7)
Gastrointestinal	4 (2.7)
Breast	4 (2.7)
Skin	4 (2.7)

Discussion

In this study, patients who were followed up with the diagnosis of EPTB were analysed. The mean age was 54.4 years and 70.8% of the patients were women. Among the previous studies conducted in Turkey, the mean age was 52.2 years and the female rate was 31% in the study by Sünnetçioğlu et al, the mean age was 64.6 years and the female rate was 40.7% in the study by Binici İ., and the mean age was 52 years and the female rate was 39.2% in the study by Şengül A. et al.^{8,9,10} In a study conducted in Afghanistan, Fader T et al. found that the mean age of the patients was 31.5 years and the female gender ratio was 50.73%.¹¹ In Iran, Fallah et al. observed a different gender ratio of 50.3% females and the mean age was 43.6 years.¹² According to the Tuberculosis War 2020 report in Turkey, the EPTB rate was 47.8% in women and 24.4% in men.¹³ It was thought that the higher average age in our study compared to other studies may be due to the level of development between countries or the fact that young patients did not apply to the hospital.

When the subtypes of EPTB cases were evaluated, lymph node involvement (54.8%) was found most frequently in our study. These results are in agreement with similar studies in the literature.^{8,9,10} In addition, in a study conducted by Lee Jy. in Korea, it was reported that lymph node involvement was the most common after pleura.¹⁴ Similar results were observed by Fader T et al. in Afghanistan, Arega B. et al. in Ethiopia, and Gaifer Z. in Oman.^{11,12,15} In a study conducted by LI L. et al. in Guangxi Zhuang Self-Governing Region, unlike our findings, it was observed that the most common involvement of the pleura followed by the skeletal system and then the lymphatic system in EPTB cases.¹⁶

In our study, cervical lymph node involvement was the most common with 53 (67%) patients, followed by axillary and mediastinal lymph node involvement with 9 (11.39%) patients, intraabdominal lymph node involvement with 6 (7.59%) patients and submandibular lymph node involvement with 2 (2.54%) patients. In Turkey, Sünnetçioğlu A et al. found cervical lymph node involvement in 39.4%, Binici İ. et al. 48.98%, Taşbakan et

al. 61.4%.^{8,9,17} In a meta-analysis study conducted by Mekonnen et al. in Africa on tuberculous lymphadenitis patients, it was reported that cervical lymph node involvement was between 47-98% and cervical lymph nodes were the most commonly involved region.¹⁸ In studies conducted in Guangxi Zhuang Self-Governing Region, Ethiopia, Tunisia and India, cervical lymph node involvement was observed most frequently, similar to our study.^{15,19,20,21}

In our study, bone-joint involvement (18.7%) and peritoneal involvement (10.4%) were the most common after lymph node involvement among EPTB cases. In the study of Binici İ. et al. it was found that peritoneal (13.4%), pleural (9.9%) and spondylitis (9.2%) involvement followed lymph node involvement, respectively (9). In a study conducted by Raval A et al. in India, it was observed that vertebral (20.6%), abdominal (7.84%) and central nervous system (7.35%) involvement followed by lymph node (41.67%) involvement.²¹

Among the methods used in the diagnosis of EPTB cases in our study, histopathological methods (56.5%) were used most frequently, followed by other methods (radiological examinations, TST, liquid adenosine deaminase, lymphocyte-rich fluid, etc.) (34%) and molecular and histopathological methods (4.8%). Similar to our study, the diagnostic methods used in the study by Şengül A et al. were histopathological (68.9%), other tests (adenosine deaminase in fluid, lymphocyte-rich fluid, TST, radiological tests, etc.) (24.8%), microbiological (5.1%), microbiological and histopathological (1.2%).¹⁰ The diagnostic methods used in the study by Raval A et al. were histopathology (48.04%), radiological methods (53.3%), microbiological methods (19.12%).²¹

Conclusion

The signs and symptoms of extrapulmonary tuberculosis (EPTB) vary according to the organs and tissues involved in the body. Epidemiological data on the distribution of EPTB cases were examined. As a result, lymph node tuberculosis and bone joint tuberculosis are the most common forms of EPTB. In our

country where the incidence of tuberculosis is high, tuberculosis can be controlled, and its spread can be prevented by tracking the epidemiological data of tuberculosis cases and their changes over the years.

The limitations of our study are that the study was retrospective, limited to Adıyaman province, there may be missing data in the files, patients travelling outside the province were excluded from the study, and pleural tuberculosis cases were not followed up in the infectious disease's outpatient clinic.

Ethics Committee Approval

Ethics committee approval was obtained with the decision of the Ethics Committee for Non-Interventional Procedures of Adıyaman University, dated 13.12.2022, and numbered 2022/9-5. The principles of the Declaration of Helsinki conducted the research. The study was conducted under the principles of the Declaration of Helsinki.

Informed Consent

Informed consent was obtained from the individuals participating in the study.

Authors Contributions

All of the authors contributed at every stage of the study.

Conflict of Interests

There is no conflict of interest to declare.

Financial Disclosure

No person/organization is supporting this study financially.

Statements

This study was presented as an oral presentation at the 7th. Internal Medicine Academy Congress on 09-12 June 2023 (TAEDER).

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Peer-review

Externally peer-reviewed.

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