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Navigating The Complexities Of Extrapulmonary Tuberculosis: Clinico-Epidemiological Profile, Diagnostic & Therapeutic Challenges As Perceived By Treating Doctors In A Tertiary Care Hospital: A Mixed Method Study

Anchu R Nath[1] , Nayanabai Shabadi[2*] , Sana Khader M[3] , Manirsha P V[4]
[1,3,4] *Postgraduate, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara, Mysuru- 570015, Karnataka, India.*
[2*] *Associate Professor, Department of Community Medicine, JSS Medical College, JSS Academy of Higher Education and Research, Sri Shivarathreeshwara Nagara, Mysuru- 570015, Karnataka, India.*
Corresponding author: Dr Nayanabai Shabadi

Abstract
Background:*Extrapulmonary tuberculosis (EPTB) presents unique clinical and diagnostic challenges due to its varied manifestations and often nonspecific symptomatology. Timely diagnosis and effective management are crucial to prevent complications and ensure favorable outcomes. This study aimed to examine the clinico-epidemiological profile of EPTB and explore the diagnostic and therapeutic challenges perceived by healthcare providers in a tertiary care hospital setting.*
Methods:*A mixed-methods study was conducted over a six-month period from June to December 2024. The quantitative component included retrospective data collection from medical records of 90 patients diagnosed with EPTB. Data on demographic characteristics, clinical presentations, and diagnostic methods were analyzed. The qualitative component involved in-depth interviews with eight doctors from various clinical departments to gather insights into their experiences, challenges, and perceptions regarding the management of EPTB.*
Results:*Of the 90 EPTB cases, 40% were in the age group of 35–54 years. Female patients constituted a slight majority (53.3%). Abdominal tuberculosis emerged as the most common form of EPTB, observed in 48% of patients. Interviews with healthcare providers revealed key challenges, including delayed diagnosis due to atypical presentations, limited sensitivity of conventional diagnostic tools, drug resistance, and poor drug penetration in specific tissues. Variability in treatment practices and the need for standardized protocols were also highlighted.*
Conclusion:*The study underscores the complex nature of EPTB diagnosis and treatment. Strengthening clinician training, adopting standardized diagnostic algorithms, and integrating molecular diagnostics are essential to improve patient care. A multidisciplinary and collaborative approach is recommended to overcome existing barriers.*
Keywords:*clinico-epidemiological profile, diagnostic challenges, extrapulmonary tuberculosis, therapeutic challenges, tertiary care hospital.*

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I. Introduction:

Extrapulmonary tuberculosis (EPTB) represents a significant and complex manifestation of tuberculosis (TB), accounting for a substantial proportion of TB cases worldwide. [(1)] Unlike pulmonary tuberculosis, which primarily affects the lungs, EPTB can involve various organ systems, including lymphatic, gastrointestinal, genitourinary, and central nervous systems. This diversity in clinical presentation often leads to diagnostic challenges, as the symptoms may mimic those of other diseases, delaying appropriate treatment and increasing morbidity. [(2)]

The global burden of TB remains a pressing public health concern, with the World Health Organization (WHO) estimating millions of new cases annually. [(2,3)] In many regions, particularly in low- and middle-income countries, EPTB is on the rise, complicating efforts to control the disease. The clinical management of EPTB requires a high index of suspicion, advanced diagnostic techniques, and a tailored therapeutic approach. [(4)]

However, the lack of awareness, inadequate diagnostic facilities, and limited access to specialized care can hinder effective management, resulting in poor patient outcomes. [5,6]

In India, where the TB burden is particularly high, the challenges associated with EPTB are exacerbated by a range of factors, including socio-economic disparities, healthcare system limitations, and the co-existence of other infectious diseases. [7] Despite these challenges, there is a paucity of comprehensive studies examining the clinico-epidemiological profiles of EPTB patients and the specific diagnostic and therapeutic hurdles faced by treating physicians in tertiary care settings.

The increasing incidence of EPTB is particularly concerning among immunocompromised populations, including individuals with HIV/AIDS, diabetes, and those undergoing immunosuppressive therapies. [8] These patients are at a heightened risk for developing EPTB, which complicates their overall health management and increases morbidity and mortality rates. Despite its clinical significance, EPTB is frequently underdiagnosed and undertreated due to a lack of awareness among healthcare providers and limited access to advanced diagnostic modalities.

This study aims to address the critical gap in knowledge regarding the clinico-epidemiological profile of EPTB cases and the perceived challenges in diagnosis and treatment as reported by healthcare providers in a tertiary care hospital. By focusing on the experiences of treating physicians in a tertiary care hospital, the research will provide a comprehensive overview of the challenges in managing this complex disease.

OBJECTIVES:

- To determine the clinico-epidemiological profile of diagnosed Extra pulmonary tuberculosis cases reported in a tertiary care level hospital in Mysuru
- To understand the diagnostic and therapeutic challenges perceived by the treating doctors in managing EPTB cases.

II. Materials And Methods

Study design and setting:

A hospital-based mixed-method study was conducted in a tertiary care hospital, Mysuru, over six months from June 2024 to December 2024, integrating both qualitative and quantitative data collection. The study participants were 90 EPTB patients who were admitted in the last one-year period in the tertiary care hospital. 8 doctors from various departments were interviewed in-depth to understand the diagnostic and therapeutic challenges perceived during the treatment of EPTB.

Method of Data Collection

The data were gathered from patient medical records to assess demographic characteristics, clinical presentations, and diagnostic methods. Concurrently, qualitative data were collected from 8 Doctors from various departments who were treating EPTB cases. The data was collected using in-depth interviews with healthcare professionals to gain insights into their experiences and challenges in managing EPTB cases. A convenient sampling method was used to collect data. The study protocol was approved by the Institutional Ethical Committee and an Informed consent form treating Doctors of EPTB cases was obtained before the commencement of the study.

Study tool:

The questionnaire consists of two parts:

- The first part includes Sociodemographic details like: age, gender, residence, religion, and occupation. Clinical presentations and diagnostic methods like: anatomical sites, comorbidities, complications of EPTB and tests to aid clinical diagnosis.
- The second part includes the qualitative questionnaire consisting of diagnostic challenges encountered with EPTB, role of imaging and advanced tests like Gene Xpert in diagnosis of EPTB,drug resistance ,barriers to accessing care, interdisciplinary collaboration, psycho social support and training on management of EPTB.

Statistical Analysis

The data collected was entered in a Microsoft Excel 2019 spreadsheet followed by analysis using SPSS version 26 (Statistical package for the social science, Licensed to JSSAHER) Windows, Version 26.0. (IBM Corp. Released 2019. IBM SPSS Statistics for Armonk, NY, USA). Descriptive statistics involved reporting of continuous variables as mean ± standard deviation (SD), while categorical variables were reported in terms of frequency (n) and percentage (%). The data distribution was represented using appropriate tables. The qualitative data was imported to Open Code software and analysed using the thematic content analysis. Direct verbatim and results from the coding and categorization were used to develop the narrative, triangulated and synthesized the results.

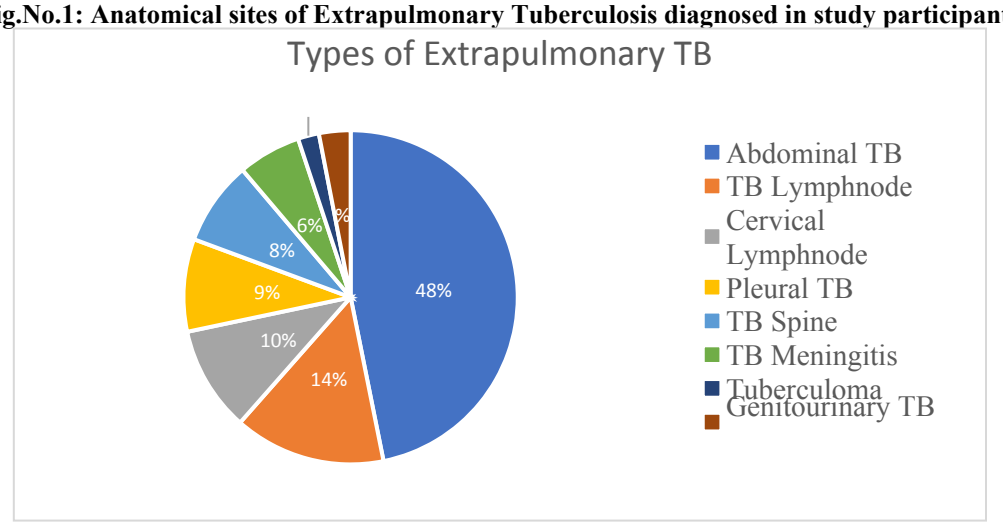
III. Results

Table No. 1: Sociodemographic and Clinical characteristics of the study participants(n=90)

Variables	Category	Frequency,n(%)
Age group	<14 years	8(11.2)
	15-34 years	24(26.6)
	35-54 years	36(37.8)
	> 55years	22(24.4)
Gender	Male	42(46.6)
	Female	48(53.4)
Residence	Urban	32(35.5)
	Rural	58(64.5)
Religion	Hindu	85(95.4)
	Muslim	2(2.4)
	Christian	3(2.2)
Occupation	Unemployed	55(61.1)
	Unskilled	9(10)
	Skilled	20(22.3)
	Professional	6(6.6)
Smoking status	Smoker	16(17.8)
	Non-smoker	74(82.2)
Alcoholic status	Alcoholic	20(22.3)
	Non-Alcoholic	70(77.7)
Family history	Present	4(4.5)
	Absent	86(95.5)
Comorbidities	T2DM	26(28.8)
	Hypertension	19(21.1)
	Hypothyroidism	5(5.5)
	Dyslipidemia	2(2.2)
	Epilepsy	2(2.2)
	No comorbidities	56(62.2)
Complications of EPTB	Developed	17(19)
	Not Developed	73 (81)

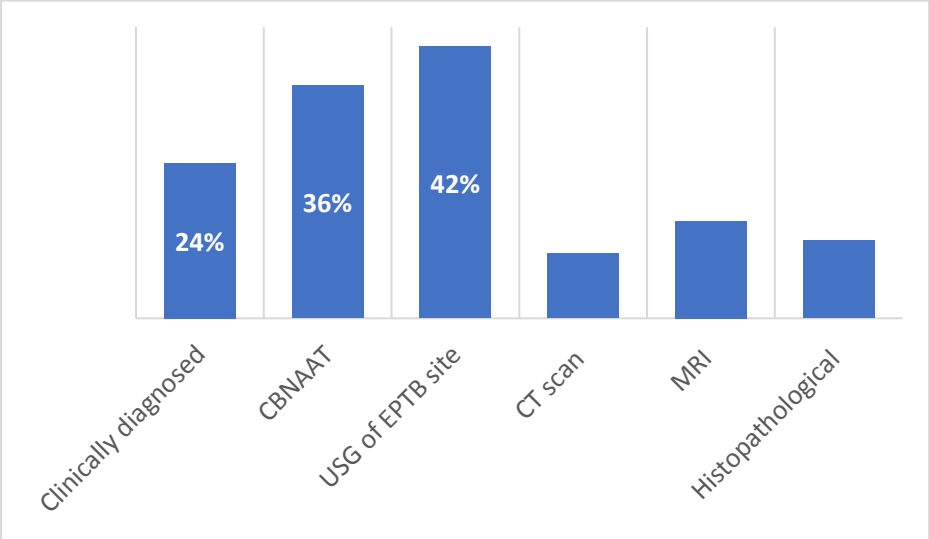
Among the 90 study participants, the majority, 36(3.8%), belonged to the 35-54 age group, followed by 24 (26.6%) in the 15-34 age group. 48 (53.3%) were female, and 42(46.6%) were males. 58 (64.5%) of the study participants resided in rural areas, and 32 (35.5%) lived in urban areas. The majority of study participants were Hindu religion 85(95.4%). 55(61.1%) study participants were unemployed and 20(22.2%) were skilled workers. The majority 86(95.5%) of the study participants had a family history of extrapulmonary tuberculosis. 26(28.8%) were having T2DM, 19(21.1%) with Hypertension.17(19%) had developed complications of EPTB like psoas abscess, TB drug-induced hepatitis, portal hypertension (Table No.1).

Fig.No.1: Anatomical sites of Extrapulmonary Tuberculosis diagnosed in study participants



The most frequent site of EPTB involvement is Abdominal TB 44(48%) & the second most common site is TB Lymph node 13 (14%). 9(10%) of the study participants were diagnosed with Cervical lymph node TB followed by 8(8.8%) with Pleural TB (Fig.No.1).

Fig.No.2: Test to aid clinical diagnosis of EPTB among the study participants



Among the 90 study participants, 22(24%) of extrapulmonary tuberculosis (EPTB) cases were diagnosed clinically, 33 (36%) using CBNAAT, 38(42%) through ultrasonography (USG) of the EPTB site, 9(10%) with a CT scan, 14(15%) via MRI, and 11(12%) through histopathological examination (Fig.No.2)

QUALITATIVE FINDINGS:

Most clinicians involved in EPTB management expressed skepticism about eliminating TB by 2030, citing persistent diagnostic and treatment challenges. Four key themes emerged: diagnostic and therapeutic difficulties, patient and systemic barriers, and the need for interdisciplinary, holistic care, supported by direct verbatim quotes.(Table no.2)

Table No.2 Participant characteristics

PARTICIPANT	AGE	GENDER	SPECIALISATION	YEARS OF EXPERIENCE
Doctor 1	55	Male	Medical Gastroenterology	18
Doctor 2	48	Male	Orthopaedics	13
Doctor 3	42	Female	Paediatrics	10
Doctor 4	56	Male	General Surgery	20
Doctor 5	40	Female	General Medicine	8
Doctor 6	59	Male	Neuromedicine	22
Doctor 7	54	Female	Obstretics & Gynecology	14
Doctor 8	43	Male	Orthopaedics	9

Limited Sensitivity of Diagnostic Tools Doctors reported significant variability in the sensitivity of existing diagnostic modalities depending on the anatomical site of EPTB involvement. A common sentiment was captured in this response:*"The sensitivity of existing diagnostic tools like FNAC and biopsy varies depending on the site of involvement, making it difficult to confirm EPTB.*

Doctors elaborated that while fine needle aspiration cytology (FNAC) and biopsies are widely used, their diagnostic yield depends heavily on the quality and quantity of the sample collected, as well as the expertise of the pathologist. Furthermore, certain forms of EPTB, such as those involving the central nervous system (CNS) or skeletal structures, require invasive procedures to obtain samples, adding to the complexity. *"The prolonged time required for TB cultures, often weeks, was seen as a major bottleneck in initiating timely treatment."* - by a clinician.

Delays in Confirming Diagnosis Participants also highlighted how delays in diagnosis could lead to advanced disease stages, often complicating treatment. These delays were attributed to a combination of factors, including the slow turnaround time of diagnostic tests, the need for referrals to higher centres for advanced imaging or specialized tests, and a lack of awareness among primary care providers. As one doctor noted: *"Delays often lead to advanced disease stages, causing complications such as irreversible tissue damage."*

Doctors expressed concern that late-stage diagnoses not only increased the risk of morbidity but also complicated therapeutic strategies, requiring more aggressive interventions and prolonged treatment duration.

Need for Multi-modal Diagnostic Approaches Doctors emphasized that a single diagnostic tool is often insufficient to provide a conclusive diagnosis of EPTB, especially given the diversity in anatomical involvement. *"GeneXpert is invaluable for rapid detection, especially in lymph node and CNS TB, but imaging techniques like MRI or CT scans are equally critical for localizing lesions."*- reported a General Surgeon

Therapeutic Challenges: Drug Resistance and Side Effects While drug resistance in EPTB is less frequent than in pulmonary TB, it remains a significant hurdle in certain forms such as CNS TB:*"Drug resistance is less common in EPTB compared to pulmonary TB but still poses a significant challenge, especially in CNS TB."*- according to a General Medicine Physician

Adherence to Treatment Side effects, stigma, and socioeconomic factors emerged as key barriers to treatment adherence was a common response *"Side effects like hepatotoxicity and gastrointestinal distress discourage adherence. Social stigma and financial barriers also play a role."*Hepatotoxicity from first-line TB drugs like Isoniazid and Rifampicin, along with gastrointestinal side effects, often leads to fatigue, nausea, and loss of appetite, making treatment adherence difficult.

Monitoring and Follow-Up Doctors emphasized the difficulty of monitoring treatment response, particularly in rural populations:*"Imaging, symptom tracking, and repeat microbiological tests are used, but tracking can be difficult in rural patients."*

Accessibility of Specialized Care Rural patients face significant challenges in accessing specialized care due to geographical and financial barriers, often requiring long and costly travel to distant hospitals, which is further compounded by the lack of specialized providers at local healthcare centers. *"Rural patients often face geographical and financial barriers, and the absence of specialists at primary healthcare centres exacerbates delays."*

Awareness and Understanding Among Patients Many patients, particularly those in areas with limited healthcare education, misinterpret the symptoms of EPTB, confusing them with those of more well-known and often more feared illnesses like cancer. This lack of understanding can lead to a range of negative consequences.*"Awareness is generally low. Many patients confuse EPTB with cancer or other illnesses like autoimmune diseases, or infections., leading to anxiety and non-compliance."*

Systemic Gaps in Health Infrastructure Integrating advanced diagnostics into primary care settings, particularly in underserved areas, would greatly enhance accessibility, particularly for rural patients who face

significant geographical and financial barriers. *"Strengthening DOTS programs and integrating advanced diagnostics into primary care would greatly enhance accessibility."*

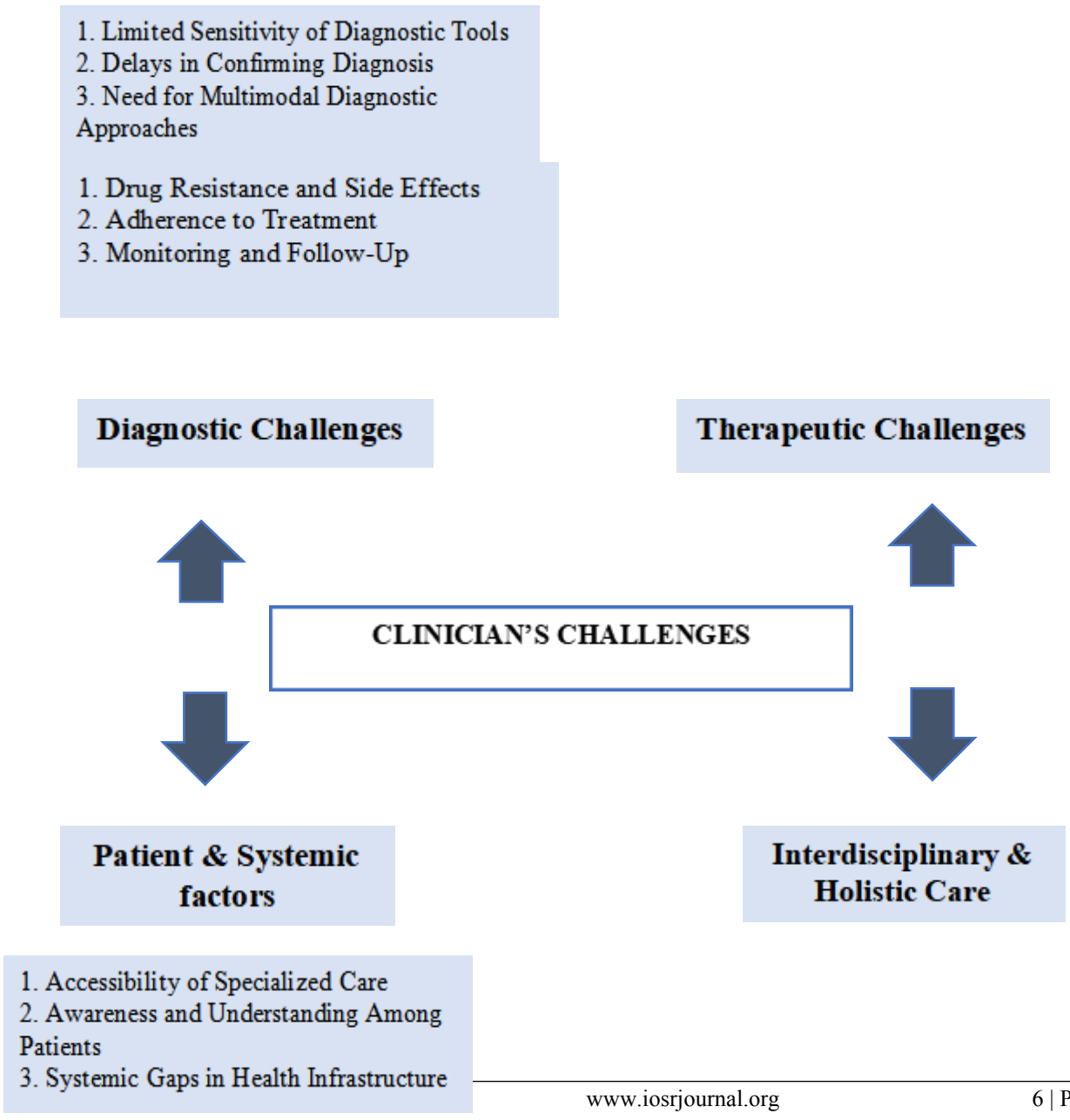
Coordination Between Specialties The multifaceted nature of EPTB often requires a team-based approach to ensure comprehensive care.*"Cases often require input from neurologists, surgeons, and radiologists, emphasizing the need for collaborative care."*

For instance, neurologists are vital for diagnosing and managing CNS TB, while surgeons may be required for biopsy procedures or surgical debridement in cases of skeletal TB. Radiologists play a crucial role in interpreting imaging findings to localize lesions and monitor treatment response.

Psychosocial Support for Patients Psychosocial support was identified as a crucial component of holistic care to address stigma and improve adherence:*"Psychosocial support helps combat stigma, depression, and anxiety among patients, fostering better adherence to treatment."*The stigma surrounding tuberculosis often leads to feelings of shame, isolation, and fear of discrimination, which can negatively impact a patient's willingness to seek treatment or adhere to prescribed regimens.

Training and Skill Development for Healthcare Providers Doctors underscored the need for enhanced training in advanced diagnostics and patient counselling:The complexity of EPTB cases often requires healthcare providers to stay abreast of the latest diagnostic and therapeutic advancements.

Fig 3: Challenges perceived by Clinicians involved in the management of Extra Pulmonary TB



1. Coordination Between Specialties
2. Psychosocial Support for Patients
3. Training and Skill Development for Healthcare Providers

IV. Discussion:

The findings of this study highlight key demographic and clinical characteristics of extrapulmonary tuberculosis (EPTB) patients, underscoring the burden among middle-aged individuals, females, and rural residents. Similar demographic trends have been observed in previous studies, where EPTB was more prevalent among women, possibly due to biological and socio-cultural factors influencing healthcare access and immune response. [8] The substantial proportion of participants with a family history of EPTB suggests a potential genetic or environmental predisposition, warranting further exploration into familial clustering of TB cases.[9]

Diagnostic modalities for EPTB varied, with ultrasonography (42%) and CBNAAT (36%) being the most commonly used methods. Studies suggest that CBNAAT is a highly specific and rapid test for detecting Mycobacterium tuberculosis and Rifampicin resistance. However, its sensitivity varies across different EPTB sites, necessitating adjunct imaging techniques for a more accurate diagnosis. [9] The frequent use of ultrasonography, particularly for abdominal TB, aligns with evidence supporting its effectiveness in detecting peritoneal and lymphatic involvement [10]. MRI and CT scans play a crucial role in identifying complex cases, particularly in CNS and spinal TB, as supported by previous research emphasizing their role in assessing lesion extent and guiding interventions (Huda et al., 2019). Histopathological examination, though less frequently used (12%), remains essential for confirming TB in cases with ambiguous imaging or microbiological findings. These results reinforce the need for a multi-modal diagnostic approach tailored to the EPTB site, ensuring timely and accurate detection to improve patient outcomes.

The variability in the sensitivity of diagnostic tools for EPTB across different anatomical sites presents a significant challenge, with clinicians often relying on FNAC and biopsies, whose accuracy depends on sample quality and pathologist expertise [10]. Additionally, the prolonged turnaround time for TB cultures delays definitive diagnosis, leading to empirical treatment decisions that may not always align with actual pathology [11]. These limitations highlight the urgent need for more rapid and reliable diagnostic modalities to ensure accurate detection and timely management of EPTB cases [12]

Delays in diagnosing EPTB, often due to slow test turnaround times and the need for specialized referrals, contribute to disease progression, complicating treatment and increasing morbidity [12,13]. Given the variability in anatomical involvement, a multi-modal diagnostic approach combining GeneXpert for rapid detection and advanced imaging modalities like MRI and CT scans is essential for precise localization and treatment planning [14]. These findings underscore the importance of integrating molecular, histopathological, and imaging-based diagnostics to ensure early and accurate detection of EPTB, ultimately improving patient outcomes [15,18].

Managing drug-resistant extrapulmonary tuberculosis (EPTB), particularly in cases involving the central nervous system (CNS), presents significant challenges due to the limited ability of many anti-tuberculosis drugs to penetrate the blood-brain barrier, necessitating the use of more toxic second-line treatments with extended durations. Additionally, financial, logistical, and diagnostic hurdles complicate the identification of drug resistance, underscoring the need for improved laboratory facilities and tailored treatment protocols for drug-resistant EPTB[16,17]

Treatment adherence is further hindered by side effects such as hepatotoxicity and gastrointestinal distress, as well as social stigma and financial barriers, including medication costs, travel expenses, and income loss. These factors discourage patients from seeking timely care and maintaining follow-ups, leading to irregular monitoring and delayed detection of treatment failures, particularly in rural populations. [19,20] Improving access to healthcare facilities and providing support to overcome these barriers are essential steps toward enhancing treatment adherence and outcomes.

Integrating advanced diagnostic tools into primary care settings, especially in underserved areas, can significantly enhance accessibility and reduce diagnostic delays for tuberculosis (TB) patients.[21] This approach not only improves early detection and treatment adherence but also strengthens the overall healthcare system, making it more responsive to the needs of underserved populations.A multidisciplinary approach to TB care, involving coordination among specialists such as neurologists, surgeons, and radiologists, is essential for comprehensive management. Additionally, providing psychosocial support addresses stigma and mental health issues, fostering better adherence to treatment regimens.

V. Conclusion:

The challenges of extrapulmonary tuberculosis (EPTB) require a multifaceted approach, incorporating improved diagnostic capabilities, a collaborative care model, and enhanced psychosocial support. Integrating advanced diagnostics into primary care, particularly in underserved rural areas, can reduce diagnostic delays and improve treatment adherence, ultimately strengthening the healthcare system. A team-based approach, involving specialists from various fields and providing psychosocial support to combat stigma, is essential for comprehensive patient management. Furthermore, ongoing training for healthcare providers in advanced diagnostic techniques, patient counselling, and drug resistance management is crucial to ensuring better patient outcomes and reducing the burden of EPTB in vulnerable populations.

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