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PREVALENCE OF EXTRAPULMONARY TB IN CLINICALLY SUSPECTED PATIENTS IN A TERTIARY CARE CENTER IN LUCKNOW: A PROSPECTIVE STUDY

Medical Microbiology

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ABSTRACT

Background: Tuberculosis (TB), caused by Mycobacterium tuberculosis, Extra Pulmonary Tuberculosis (EPTB) results from hematogenous spread of bacillus to various organs. EPTB constitutes about 15-20% of all the cases of tuberculosis (TB), In HIV patients the frequency is higher about 20-50% of all cases of TB. **Objective:** This study aims to estimate the prevalence of EPTB among clinically suspected patients in a tertiary care center in Lucknow, and to identify demographic and clinical factors associated with EPTB. **Methods:** A prospective cross-sectional study was conducted from September 2023 to March 2024 in the Department of Microbiology, IIMSR, Lucknow. Clinically suspected TB patients were included based on specific criteria, and data were collected through demographic information, clinical history, and laboratory investigations including acid-fast staining for EPTB diagnosis. A total of 52 samples were analyzed. **Results:** The prevalence of EPTB among the study population was found to be 9.62%. A higher proportion of cases were observed in males (57.7%) compared to females (42.3%). Age distribution revealed the highest prevalence among adults aged 19-60 years (36.54%) and children aged 2-10 years (25.00%). Pus samples had the highest positivity rate (40.4%). Lymph node TB being the most common form, followed by pleural and abdominal TB. **Conclusion:** The study highlights significant gender and age disparities in EPTB prevalence and underscores the importance of comprehensive diagnostic approaches. The findings emphasize the need for targeted public health interventions and interdisciplinary collaboration to improve EPTB diagnosis and management,high-risk demographic groups and also highlight the burden of EPTB in tertiary care center.

KEYWORDS

Extra Pulmonary Tuberculosis, Prevalence, Acid-Fast Staining, Tertiary Care Center, Lucknow, Epidemiology.

INTRODUCTION

Tuberculosis is an infectious disease without widely effective treatments available, caused by Mycobacterium tuberculosis and infecting about a quarter of the world's population with more than 10 million new TB cases every year.(Singh et al., 2019) Tuberculosis continues to be a major global health problem.(Dawani et al., 2019). India accounted for the highest number of TB cases in the world in 2022, with 2.8 million TB cases, representing 27% of the global burden. The TB incidence rate, which measures new cases per 100,000 population per year, increased by 3.9% between 2020 and 2022.(WHO, 2023)

TB incidence for the year 2021 is 210 per 100,000 population. compared to the baseline year of 2015, the incidence was 256 per lakh of population in India; there has been an 18% decline which is 7 percentage points better than the global average of 11%.(Mitra, 2022) Despite being preventable and often treatable, tuberculosis persisted as a significant global health threat in 2022, ranking as the second leading cause of death from a single infectious agent worldwide, following COVID-19. Shockingly, it claimed nearly twice as many lives as HIV/AIDS. With over 10 million new cases annually, urgent measures are imperative to combat TB and achieve the shared objective of ending the global epidemic by 2030. This target has garnered unanimous support from all United Nations (UN) Member States and the World Health Organization.(WHO, 2023)Tuberculosis is one of the leading causes of death from a single infectious agent, ranking above HIV/AIDS.(Paudel & Shrestha, 2022)Tuberculous meningitis (TBM) causes death and disability, with especially high rates of poor outcomes in children and individuals with an HIV-1 co-infection Important risk factors for poor outcome are delayed diagnosis, delayed treatment, advanced disease, and antitubercular drug resistance. (Wilkinson et al., 2017)

The disease is spread when people who are sick with TB expel bacteria into the air (e.g by coughing). TB typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB). Pulmonary tuberculosis (PTB) encompasses cases of TB confirmed by bacteria or diagnosed clinically, affecting either the lung parenchyma or the tracheobronchial tree. Miliary TB is considered PTB due to the presence of lung lesions. Extrapulmonary TB is defined by tuberculous intra-thoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without observable radiographic lung abnormalities. Patients with both pulmonary and extrapulmonary TB are classified as having PTB. Extrapulmonary tuberculosis (EPTB) involves TB affecting organs beyond the lungs, such as the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, and meninges.(Lee, 2015) Although TB mainly affects the lung parenchyma, Mycobacterium tuberculosis can spread to extra-pulmonary sites. On average, extra-pulmonary TB (EPTB) accounted for 16% of active cases of TB reported in 2019.(Chakaya et al., 2021) Extra-pulmonary tuberculosis (EPTB) occurs when tubercle bacilli spread via the bloodstream to various organs, comprising approximately 15-20% of all tuberculosis (TB) cases. This incidence is notably higher among HIV-positive individuals, where it accounts for 20-50% of TB cases. EPTB can affect virtually any organ system, with tuberculous lymphadenitis being the most common form, affecting 35% of EPTB cases. This form primarily targets the posterior cervical and supraclavicular lymph nodes, presenting as painless swelling in the neck without warmth or color change. Pleural tuberculosis, accounting for 20% of EPTB cases, is often associated with pleural effusion. Tuberculosis can also impact the upper airways, including the larynx, pharynx, and epiglottis. In the genitourinary system, renal tuberculosis and genital tuberculosis are notable, with the latter potentially affecting the fallopian tubes and endometrium in females, leading to infertility, and the epididymis in males. Skeletal tuberculosis commonly involves weight-bearing joints such as the spine, hips, and knees, and may lead to complications like vertebral body collapse, kyphosis, and paravertebral 'cold' abscesses. Tuberculosis of the central nervous system is most prevalent in children, manifesting as tuberculous meningitis or tuberculoma. Tuberculous pericarditis can occur due to direct extension from adjacent lymph nodes or hematogenous spread. Gastrointestinal tuberculosis often affects the terminal ileum and cecum, caused by swallowing infected sputum, hematogenous spread, or ingestion of M. bovis -contaminated cow's milk. Skin manifestations of tuberculosis include scrofuloderma, which involves the skin through direct extension from underlying lymphadenitis, and lupus vulgaris, characterized by apple jelly nodules on the face. Miliary or disseminated tuberculosis results from hematogenous spread and is marked by yellowish granulomatous lesions resembling millet seeds in various organs. Additionally, post-TB aspergillosis can occur, characterized by chronic pulmonary aspergillosis due to Aspergillus fumigatus colonization in residual TB cavities. This overview underscores the diverse manifestations of EPTB and its significant impact on multiple organ systems. (Sastry, Apurba S bhat, 2023). Diagnosing EPTB is challenging due to its diverse clinical manifestations and low bacterial count. Traditional diagnostic methods like acid-fast bacilli staining, mycobacterial cultures, and clinical assessments have limitations, including low

sensitivity, long result times, and often requiring invasive procedures . Accurate and rapid diagnosis is critical for timely treatment and reducing complications and fatalities associated with EPTB .

Aim and Objectives

To estimate the prevalence of EPTB and positivity of different EPTB in various samples among clinically suspected patients in a tertiary care center in Lucknow and also cover potential demographic and clinical factors associated with EPTB.

MATERIAL AND METHODOLOGY

Study Design and Study Period

This cross-sectional study This study employs a prospective cross-sectional design to to estimate the prevalence of EPTB received ethical clearance from the Institutional Research Committee and Institutional Ethical Committee (IEC/IIMSR/2023/38). It was conducted at the Department of Microbiology, IIMSR, Lucknow, over a period of eight months (October 2023 to March 2024).

Data Collection

A total of 52 tb patients attending the Tertiary care hospital were included demographic information (age, gender, residence), clinical history, presenting symptoms, and laboratory investigations, including acid-fast staining for EPTB diagnosis. Inclusion Criteria: Patients with clinical symptoms suggestive of EPTB. Exclusion Criteria: Patients or their guardians who do not consent to participate.

Laboratory examination: Diagnostic material collection involved using a 22-gauge needle and syringe for patients with superficial masses, enlarged lymph nodes, and abscesses, applying minimal negative pressure to ensure sample quality and reduce tissue damage. CSF samples were obtained via standard lumbar puncture techniques for suspected EPTB affecting the CNS. Tissue biopsies were taken from patients showing clinical signs of EPTB, involving careful surgical removal of small tissue samples from infection sites like lymph nodes or organ lesions to preserve integrity were collected and transferred to the microbiology laboratory for diagnosis. The collected material was smeared onto glass slides and stained using Ziehl-Neelsen (ZN) staining, which stains acid-fast bacilli (AFB), including Mycobacterium tuberculosis (MTB), red against a blue background to aid in TB diagnosis.

Data Analysis and Interpretation

A preformed proforma was used to capture the demographic details and clinical history, and physical examination findings were recorded for each enrolled patient at the time of their initial presentation to Integral hospital. Statistical analysis of the diagnostic test results was performed using MICROSOFT EXCEL 2016. The demographic and clinical characteristics of the study participants were summarized using descriptive statistics. This included calculating frequencies, and percentages where appropriate to describe the patient population. The diagnostic performance of the EPTB by Acid -fast stain was evaluated in terms of sensitivity, specificity and diagnostic accuracy.

RESULTS

The prevalence of extra-pulmonary tuberculosis (EPTB) among the clinically suspected patients in the study was found to be approximately 9.62%. Out of the 52 clinically suspected cases evaluated using acid-fast staining, 5 cases tested positive for EPTB.

This is the images of positive case of findings of mycobacterium tuberculosis bacillus in Pus samples

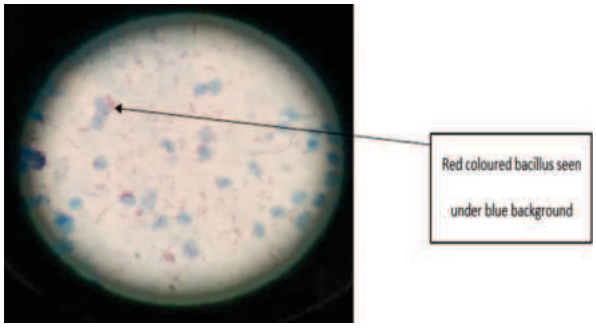

Figure 1:- This Is The Images Of Positive Case Of Findings Of Mycobacterium Tuberculosis Bacillus In Pus Samples

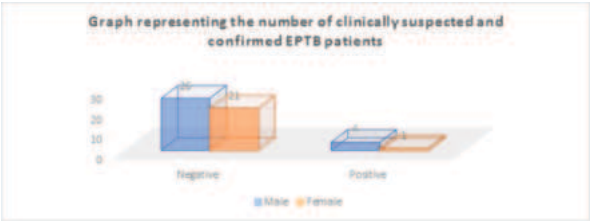

Figure 2:- This Is The Graph Representing The Number Of Clinically Suspected And Confirmed EPTB Cases

Table 1.Characteristics Of The Study Population (clinically Suspected Patients In A Tertiary Care Center In Lucknow (n= 52).

Gender		
	Male 30 (57.70)	4 (Positive)
	Female 22 (42.30)	1 (Positive)
Age (years)		
	Infant (0-1)	4 (7.69)
	Child (2-10)	13 (25.00
	Teenage (11-18)	6 (11.54)
	Adult (19-60)	19 (36.54)
	Old aged (60+)	10 (19.23)
Domicile		
	Urban	27 (51.92)
	Rural	25 (48.08)
Specimen		
Samples from different sites	Ascitic fluid	2
	Cervical lymph node	1
	Internal cranial fluid	1
	CSF	12
	Gastric aspirate	1
	Pleural Fluid	3
	Pus	23 (4 positive)
	Vaginal swab	3 (1 positive)
	Vitreous tap fluid	6
Symptoms		
	Fever	35 (67.30)
	Cough	25 (48.07)
	Chest Pain	11 (21.15)
	Loss of appetite	19 (36.53)
	Weight loss	36 (69.23)
	Lymphadenopathy	16 (30.76)

This indicates that a notable proportion of clinically suspected patients in the tertiary care center in Lucknow were confirmed to have EPTB.

Gender analysis revealed a higher proportion of male cases (57.7%) compared to female cases (42.3%), highlighting a gender disparity in TB susceptibility. Age distribution showed that suspected EPTB cases were most prevalent among adults aged 19-60 years (36.54%) and children aged 2-10 years (25.00%), indicating significant impacts on both productive adults and pediatric populations.

Departmental distribution indicated that neurology (23.1%) and orthopedics (21.2%) were the departments most involved in diagnosing suspected EPTB cases, reflecting the diverse clinical manifestations of the disease across different body systems. A variety of diagnostic samples were collected, with pus, CSF, pleural fluid, and vitreous tap fluid being the most common, illustrating the multisystem nature of EPTB and the need for comprehensive diagnostic approaches.

Positivity rates for different samples showed that pus samples had the highest positivity rate at 40.4%, underscoring the importance of meticulous clinical evaluation and sample collection techniques in detecting EPTB. Demographically, urban residents and males exhibited slightly higher positivity rates, suggesting that socio-economic and gender-specific factors may influence TB positivity rates. These findings emphasize the need for tailored interventions to address disparities among different demographic groups.

DISCUSSION

Prevalence of EPTB cases of 52 individuals, the prevalence of extra-pulmonary tuberculosis (EPTB) was found to be 9.67%, with 5 out of the 52 samples testing positive and most common affected site was

Lymph node. In contrast one of the retrospective cohort survey study done in Africa published less percentage of EPTB prevalence and the most common affected site was disseminated TB followed by pleura. This study is different than our study as it has more immune compromised HIV positive patient(Ohene et al., 2019)This finding underscores the presence of EPTB in a significant minority of cases, reflecting the importance of considering EPTB in diagnostic evaluations. Although this prevalence rate is slightly lower than the global average of 15-20%, it highlights the variability of EPTB occurrence in different populations and settings. The observed prevalence aligns with the understanding that EPTB, while less common than pulmonary TB, remains a critical aspect of tuberculosis management, particularly in populations with heightened vulnerability, such as those with HIV. This data underscores the need for heightened vigilance and comprehensive diagnostic approaches to identify and treat EPTB effectively.

Gender Disparity in EPTB Suspected Cases

In this study gender distribution of suspected EPTB cases reveals a higher proportion among males (57.7%) compared to females (42.3%), indicating potential gender-specific differences in TB susceptibility. The result of our study is contrast to the retrospective study done in Pakistan's different level Level-I (Primary HCF/clinics), Level-II (secondary HCF/specialized TB hospitals) and Level-III (tertiary hospitals) however the authors found high prevalence in female as compare to male(Tahseen et al., 2020) This disparity might be influenced by social and behavioral factors, such as males engaging in occupations or behaviors that increase TB exposure, like working in poorly ventilated environments or spending time in crowded settings. Additionally, biological differences, including hormonal influences on immune responses, might also contribute to variations in TB susceptibility. Recognizing these gender disparities is crucial for tailoring public health interventions to effectively reach and serve at-risk populations through targeted TB awareness campaigns, early diagnosis promotion, and improved healthcare access.

Age Distribution

In this study Suspected EPTB cases are distributed across different age groups, providing insights into the age-specific burden of the disease. Adults aged 19-60 represent the largest group (36.54%) of suspected cases, indicating a significant impact on the productive adult population. Children aged 2-10 constitute a substantial proportion (25.00%) of suspected cases, highlighting the importance of pediatric TB screening and management. The result of our study is similar to the study done in Manipal Medical College, however the author has distributed population in 25, 25-50 and more than 50.(Bhalla et al., 2015) These distributions underscore the need for age-specific approaches in EPTB diagnosis, treatment, and prevention, with special considerations for pediatric cases due to differences in disease presentation, diagnostic challenges, and treatment regimens compared to adults.

Departmental Involvement

Multiple hospital departments are involved in diagnosing suspected EPTB cases, reflecting the disease's multisystem nature. Neurology (23.1%) and orthopedics (21.2%) contribute the highest proportions of suspected cases, highlighting the diverse clinical manifestations of EPTB affecting the central nervous system and musculoskeletal system. This involvement underscores the importance of interdisciplinary collaboration in EPTB diagnosis, treatment, and management, ensuring comprehensive patient care and optimized treatment outcomes through teamwork among healthcare professionals from various specialties.

Positivity Rates

In this study the positivity rates of EPTB vary across different sample types, with pus samples showing the highest positivity rate (40.4%). Similar study in done in Pakistan's tertiary care hospital, Authors found high positivity Pus samples 19 out of 40 confirmed EPTB cases(Iram et al., 2015), often collected from abscess formation or tissue inflammation sites, may have a higher concentration of TB bacilli. This higher positivity rate emphasizes the importance of thorough clinical evaluation and proper sample collection techniques in detecting EPTB. The variation in positivity rates across sample types highlights the need to consider sample selection and diagnostic methods when interpreting test results, as different samples may have varying sensitivities and specificities for TB detection.

Demographic Representations

The demographic analysis of positivity cases based on residence and gender provides insights into TB positivity rates among different population groups. Urban residents exhibit slightly higher positivity rates compared to rural residents, while males show a higher proportion of positive cases compared to females. Socioeconomic factors, living conditions, and healthcare access may contribute to these variations. Gender disparities in TB positivity rates emphasize the need for gender-sensitive approaches in TB control and prevention efforts, including targeted interventions to improve TB awareness, healthcare access, and addressing gender-specific risk factors to reduce the TB burden among both males and females.

In summary, examining these factors provides a comprehensive understanding of the epidemiological, clinical, and demographic influences on clinically suspected EPTB cases, informing TB control and prevention strategies.

CONCLUSION

In conclusion, the analysis of clinically suspected EPTB cases highlights significant epidemiological and demographic disparities, particularly in gender and age distribution. These findings suggest the need for gender-sensitive and age-specific TB control strategies. Temporal trends in EPTB incidence emphasize the importance of timely public health interventions. The multisystem involvement of EPTB necessitates interdisciplinary collaboration for accurate diagnosis, while disparities in diagnostic positivity rates call for improved diagnostic methods. Addressing socioeconomic and gender-specific factors is crucial for equitable TB care. These insights are vital for shaping evidence-based strategies to reduce TB burden and improve diagnostic and treatment outcomes.

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