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Research Article

A RETROSPECTIVE RESEARCH TO ANALYZE CLINICAL AND DEMOGRAPHIC FEATURES OF EPTB (EXTRAPULMONARY TUBERCULOSIS)

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Objective: This research aimed to establish the association of clinical characteristics and demographic features of patients diagnosed with extra pulmonary tuberculosis along with its changes and developments.

Methods: We conducted this research at Services Hospital, Lahore in the timeframe of February 2017 to December 2017 (while comparing the literature from 2009 – 2012). Data collected was of Descriptive and clinical that included age, gender, site of involvement, diagnostic method and coexisting systemic diseases. Changes were identified in these parameters and were investigated on a yearly basis. Statistical Package for Social Sciences 20 was used for analysis of collected data.

Results: It was found that lymph nodes were majorly affected in 2009 to 2011 and 2012 whereas pleura was most observed in the years 2012 and 2014. No changes were found in varied age and gender. Variation was observed due method of choice and frequency of co-existent disorders.

Conclusion: Rates of morbidity and mortality due to extra pulmonary tuberculosis can be reduced through better conduct of Clinicians in case of uncharacteristically demographic features and clinical characteristics when presented.

Keywords: EPTB (Extra pulmonary Tuberculosis), CGD (Chronic Granulomatous Disease), Diagnosis and Epidemiology.

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INTRODUCTION:

TB (Tuberculosis) refers to a CGD (Chronic Granulomatous Disease) which has remained a major worldwide health issue. In most of the cases, Mycobacterium tuberculosis is a major cause and multisystemic connection may be seen. Any of the organ system in the body may get involved in Tuberculosis. As an established fact pulmonary TB is the most common appearance, extrapulmonary tuberculosis (EPTB) also appears to be a significant clinical entity. An isolated happening of tuberculosis at body sites other than is known as EPTB the lung. Initially, as a result of functional immune system foci of infection may stay inactive. However, the infection may be reactivated at once and anywhere in the body resulting in clinically manifest EPTB. EPTB affects lymph nodes, pleura, skin, gastrointestinal system, bones and joints. It is necessary to have an atypical presentation, diagnostic challenges, increasing prevalence and serious sequelae and complications for timely recognition of EPTB. High rates of morbidity and mortality could be encountered if the diagnosis is not set immediately and treatment is initiated.

The proportion of TB patients with extrapulmonary manifestations was found at 21.6% in Germany. The people of African and Asian countries are more vulnerable for EPTB. Male patients were found more suffering from Pleural TB than females. Children genitourinary system was more likely to be involved with advancing age and they were especially in danger of developing meningeal and lymphatic involvement.

Extrapulmonary and disseminated tuberculosis (cases where pulmonary and EPTB are found in the same patient) has shown an increasing trend worldwide and significantly impacts TB-related morbidity and mortality. There is very less knowledge about the host risk factors for extrapulmonary variety.

It was planned to identify the demographic and clinical features of EPTB in this study whether there were any alterations in terms of these characteristics over a 6-year period has been also investigated.

PATIENTS AND METHODS:

We conducted this research at Services Hospital, Lahore in the timeframe of February 2017 to December 2017. Here d is effect size, Z is critical table value for $\alpha = 0.05$ and p is the proportion of the

event. For this study, Z , p and d values were considered 1.96, 0.5 and 0.06, respectively. Demographical and clinical data was then taken from medical files of the relevant patients. The site of involvement, age, gender, coexistent systemic diseases (CSDs) and diagnostic methods were noted. Definitions from the World Health Organization were referred for establishing Diagnosis of EPTB. When biochemical analyses of fluid samples or fine needle aspiration (FNA) biopsy or other histopathological examinations rendered relevant results, diagnosis of EPTB was confirmed. Simultaneous pulmonary involvement by TB, immune deficiency and age less than 18 or greater than 65 was taken as Exclusion criteria. Data were analyzed using SPSS software tool. Kolmogorov-Smirnov test was used to assess data conformability.

We also used parametric and non-parametric methods for measurements of variables. Related categorical, non-categorical, qualitative and quantitative variables were calculated by Pearson's Chi-square, SPSS and Fisher's exact tests ($P\text{-Value} < 0.05$) and (CI, 95%).

RESULTS:

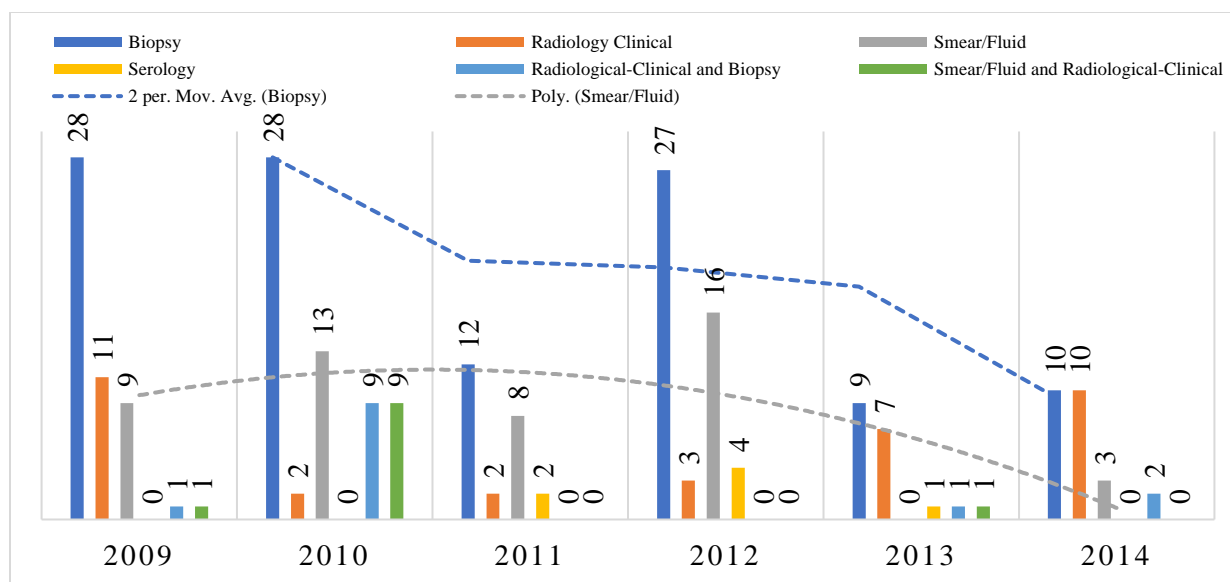
There were 257 cases detected. Of them, 50 (19.45%) related to 2009, 61 (23.75%) to 2010, 24 (9.33%) to 2011, 50 (19.45%) to 2012, 47 (18.28%) to 2013 and 25 (9.72%) to 2014. Sites of involvement from 2009 to 2014 showed notable statistical difference ($p < 0.001$). Lymph nodes were affected frequently in 2009, 2010, 2011 and 2013. Pleura and joints were the most common sites of involvement in 2012 and 2014, respectively. Overall, lymph nodes and pleura were more than half of the organs involved. The median age for EPTB cases found every year did not display any statistically noteworthy difference ($p = 0.503$). In terms of age groups, no particular group displayed any significant differences ($p = 0.431$). Distribution of gender did not reveal any difference ($p = 0.063$). A biopsy was the most used diagnostic method for EPTB ($P\text{-Value} < 0.001$). Most repeated CSD were diabetes mellitus (5.4%), hypertension (1.9%), congestive heart failure (1.5%) and chronic renal failure (3.1%). Distribution of EPTB patients with CSD displayed significant alterations. There were 50 patients with CSDs. Of them, 13 (26%) were from 2009, 21 (34.4%) to 2010, 2 (8.3%) to 2011, 3 (6%) to 2012, 7 (14.9%) to 2013 and 4 (16%) to 2014.

Table – I: Age (Median IQR) 2009 – 2014

Variables	Age (median IQR)
2009	36 – 27.5
2010	36 – 21
2011	32 – 21.25
2012	29 – 17.25
2013	31 – 20
2014	31 – 34
P value	0.503

Table – II: Mode of Injury (2009 – 2014)

Injury Mode	2009	2010	2011	2012	2013	2014	P-value
Biopsy	28	28	12	27	9	10	< 0.001
Radiology Clinical	11	2	2	3	7	10	
Smear/Fluid	9	13	8	16	0	3	
Serology	0	0	2	4	1	0	
Radiological-Clinical and Biopsy	1	9	0	0	1	2	
Smear/Fluid and Radiological-Clinical	1	9	0	0	1	0	

**Table – III:** Age Distribution (2009 – 2014)

Age	2009	2010	2011	2012	2013	2014	P value
< 31 Years	21	24	11	29	21	11	0.431
31 – 50 Years	15	23	11	13	13	7	
> 50 Years	14	14	2	8	13	7	

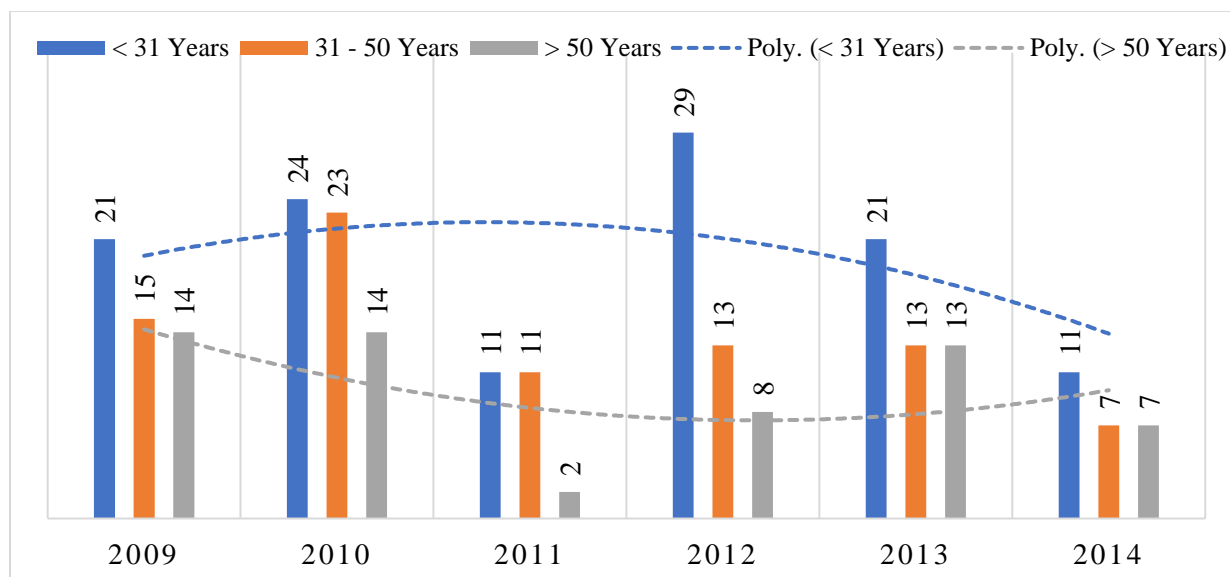


Table – IV: Gender Distribution (2009 – 2014)

Gender	2009	2010	2011	2012	2013	2014	P value
Male	24	29	15	23	30	7	0.063
Female	26	32	9	27	17	18	

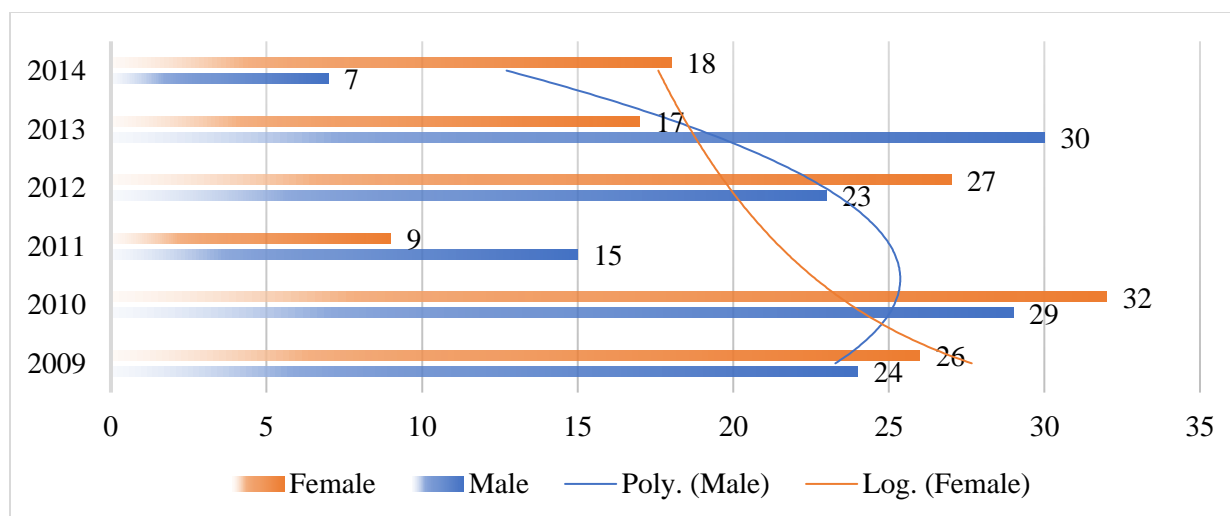


Table – V: CSD Distribution (2009 – 2014)

CSD	2009	2010	2011	2012	2013	2014	P value
Yes	13	21	2	3	7	4	0.002
No	37	40	22	47	40	21	

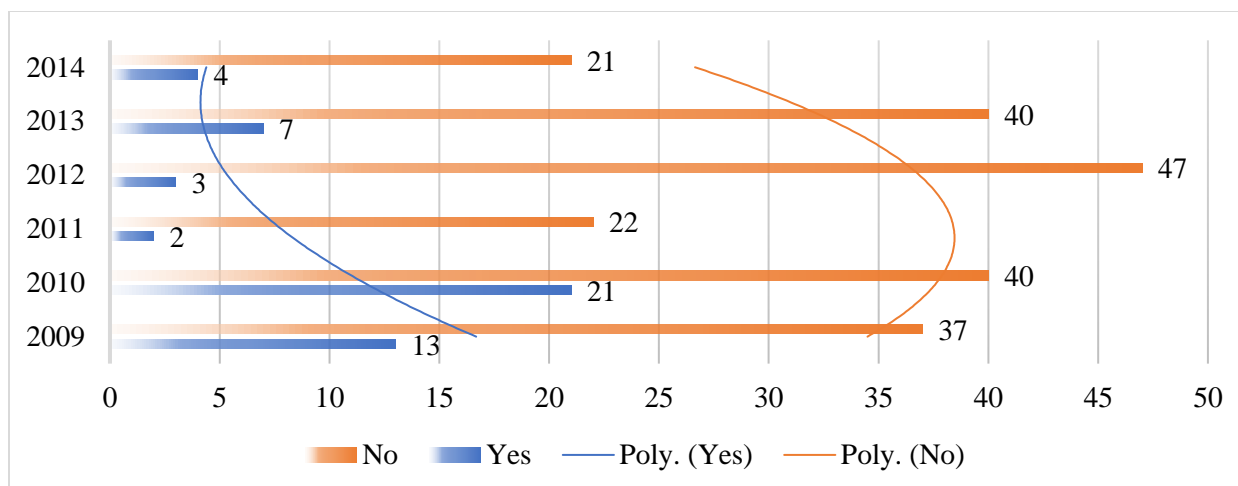
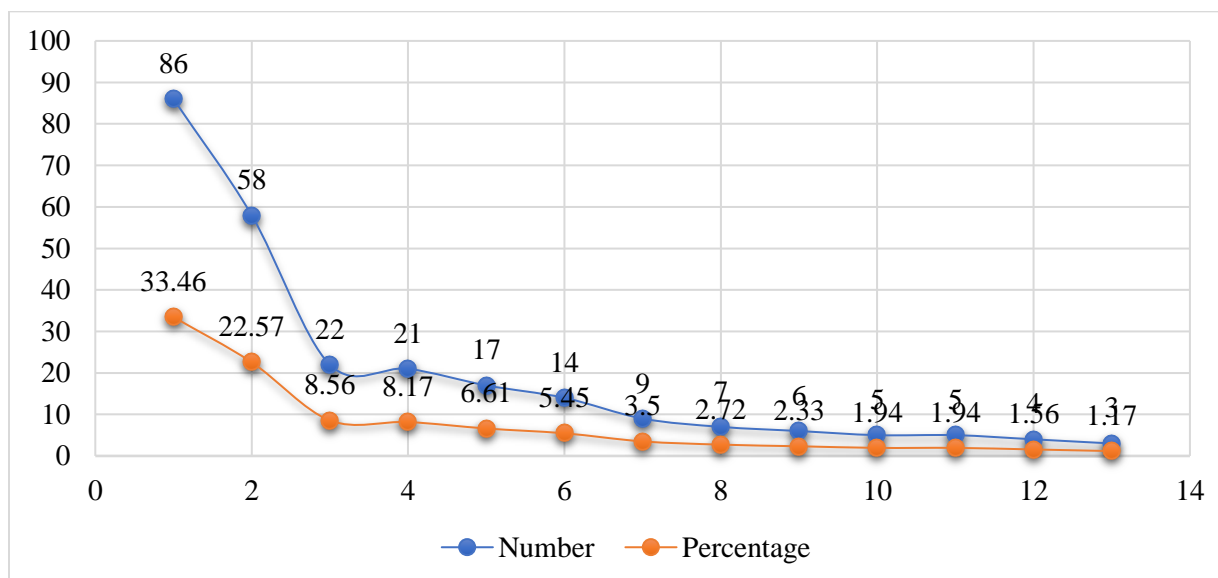
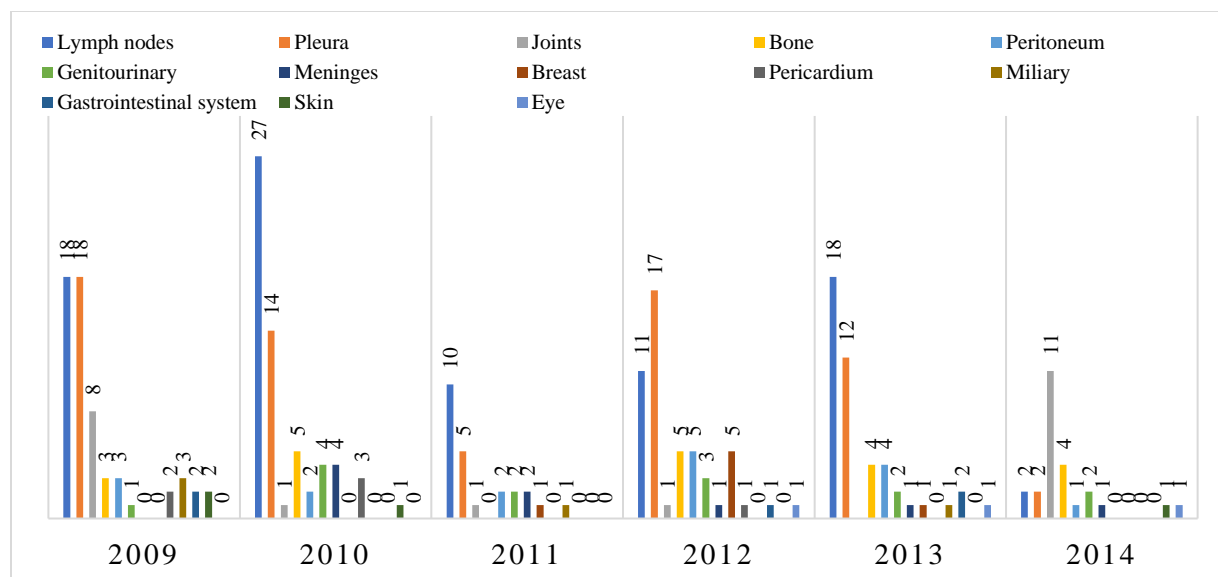


Table – VI: Site of Involvements (2009 – 2014)

Site of Involvement	2009	2010	2011	2012	2013	2014	Number	Percentage
Lymph nodes	18	27	10	11	18	2	86	33.46
Pleura	18	14	5	17	12	2	58	22.57
Joints	8	1	1	1		11	22	8.56
Bone	3	5	0	5	4	4	21	8.17
Peritoneum	3	2	2	5	4	1	17	6.61
Genitourinary	1	4	2	3	2	2	14	5.45
Meninges	0	4	2	1	1	1	9	3.5
Breast	0	0	1	5	1	0	7	2.72
Pericardium	2	3	0	1	0	0	6	2.33
Miliary	3	0	1	0	1	0	5	1.94
Gastrointestinal system	2	0	0	1	2	0	5	1.94
Skin	2	1	0	0	0	1	4	1.56
Eye	0	0	0	1	1	1	3	1.17



DISCUSSION:

The study was aimed to examine the clinical and demographic features of EPTB patients and to appraise whether these features displayed dissimilarity between 2009 and 2014. It was found that diagnostic methods, site of organ involvement and rates of patients with CSD changed notably during the study period. Whereas, in EPTB patients age and gender features seemed to be unaffected. In the disseminated patients of TB, the involvement of Extrapulmonary can be isolated or pulmonary. With the alteration in the epidemiology, the focus shifted to EPTB by current pandemic (HIV). The estimation EPTB was approximately 15% – 20% in the patients of TB with immunocompetent. More

than fifty percent of the patients were also positive for HIV. There was an increased involvement of the lymph nodes by pleural effusion and various body sites. Obtaining tissue samples for confirmation of diagnosis may be difficult as EPTB mostly has an atypical clinical presentation and due to the poor yield of conventional diagnostic methods, the diagnosis may be late. Accessibility of more sophisticated radiological methods and endoscopic interventions has greatly helped in the proper anatomical localization of EPTB. However, a biopsy is generally required to rule in EPTB for initiating the appropriate treatment and to manage complications. It is also another interesting finding to have Involvement of atypical sites such as joints in

combination with the comparatively less amount for lymph node involvement in the last years. Pleura, joints, bone, lymph nodes and peritoneum were the most common sites of involvement for EPTB. Hilar, mediastinal, cervical and axillary lymph nodes were repeatedly EPTB affected entities. Bloated lymph nodes have various sizes and are typically firm and physical findings vary with respect to the stage of the disease. If necrosis and abscess formation take place the consistency may turn into cystic. Likelihood of secondary bacterial infection by the tenderness of lymph nodes reminds.

We didn't find the majority of females for EPTB and both genders seemed to be affected similarly between 2009 and 2014 which was in contrast to the publication by Forssbohm et al. Neither median ages nor age groups varied apparently. ETPB was diagnosed and Biopsy was by far the most useful diagnostic tool for confirmation. Fluid/smear analyses along with Clinical and radiological clues aided for ruling in the diagnosis of EPTB.

Females were more prone to the risk of developing EPTB and five years after the initial contact, the risk of EPTB increased. The reason for this finding could not be explained yet, but endocrine factors may be responsible for this fact. Moreover, in patients from Southeast Asia, polymorphism function loss in purinergic receptor (P2X7) gene elevates the EPTB susceptibility and it also provides a clue about the association of genetic factors with an explanation for few variations.

The involvement of joints and bones is also important despite the agreement of like research outcomes which match with the other published outcomes as repeated lymph node involvement among EPTB patients. According to Yang, joints and bones also had a major involvement in EPTB; whereas, Noertjojo reported genitourinary system and effects on the skin more frequent in comparison to lymph nodes. This pattern may also have an association with environmental and social which is also prominent in different conditions of EPTB.

Histopathological and Biopsy diagnostics are normally mandatory for EPTB ruling despite the fact that fluid/smear analyses and clinical/radiological clues can be helpful in EPTB. In order to ascertain the diagnosis and initiate the treatment immediately improved insight must be supported by selecting suitable diagnostic method. Even though culture for Mycobacterium TB is the old method to establish the definitive diagnosis, culture and other sophisticated microbiological methods have not been used frequently. The reason leading to this finding may be the limitation of technical facilities.

The research limitations include a limited sample, socio-economical status, retrospective design, ethnic

or environmental factors prone to affect the results. Immune compromised patients, Children and elderly (<65 years) were excluded from the study. In the perspective of retrospective design, we may fail to obtain smoking pattern, alcohol and nutrition intake. Therefore, extrapolation of found results must be applied cautiously to larger populations.

CONCLUSION:

It was found that EPTB is having a broad clinical spectrum with nonspecific symptoms that could involve all organs/ systems. In doubt, EPTB diagnosis can be left. Diagnosis and delayed treatment results increase in mortality and morbidity.

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