



ISSN: 2091-2749 (Print)
2091-2757 (Online)

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Submitted

24 Oct 2020

Accepted

15 Nov 2020

How to cite this article

Reetu Baral, Palzum Sherpa,
Dipti Gautam, Shiva Raj KC.
Histopathology of extra-
pulmonary tuberculosis at
pathology lab of Patan
Hospital, Nepal. Journal of
Patan Academy of Health
Sciences. 2020Dec;7(3):47-53.

DOI:

<https://doi.org/10.3126/jpahs.v7i3.33826>

Histopathology of extra-pulmonary tuberculosis at pathology lab of Patan Hospital, Nepal

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Abstract

Introduction: Tuberculosis is a common condition in underdeveloped countries, with approximately 100,000 cases in Nepal today. Tuberculosis is the 6th leading cause of death in Nepal. This study aims to find out the Extra Pulmonary Tuberculosis in the specimen received in the pathology lab.

Method: This is a retrospective descriptive study of the histopathology database of Extra Pulmonary Tuberculosis at the pathology lab of Patan Hospital, Nepal from 2012 to 2019. Data were analyzed for prevalence, site, and pathology details. Ethical approval was obtained from the Institutional review committee of Patan Hospital.

Result: There were 300(1%) Extra Pulmonary Tuberculosis out of 29629 specimens. The majority 170(57%) were from the lymph nodes, 36(12%) skin, followed by intestine and urogenital each 28 and 26(9%). Male to female ratio was 2:3 (n=116, 39% vs n=184, 61%). The most common age group was 20-39 years comprising 194(64%). Granuloma was present in 288(96%), and 21(7%) tested positive for Acid Fast Bacilli.

Conclusion: Among the Extra Pulmonary Tuberculosis, more than half of them had tubercular lymphadenitis with granuloma present in the majority.

Keywords: acid-fast bacilli, extra pulmonary tuberculosis, granuloma, lymph node

Introduction

Tuberculosis (TB) has existed for epochs and remains a major global health problem, affecting 10 million people annually. As per the report from Nepal Tuberculosis Center in 2019, the Nepalese population accounted for 0.35% of the global population but contributes 0.45% to global TB cases.¹ According to the report from the Ministry of Health in 2020, TB takes up the 6th leading cause of death with approximately 170,000 affected in Nepal today.^{2,3} National TB prevalence survey (2018-2019) suggested that there is an estimated annual reduction of TB incidence by 3% in the last decade which is better than the global annual decline rate of 1.5%-2%. In Nepal and other developing countries, peripheral lymph nodes continue to be the most common form of EPTB.⁴ "Scrofula" meaning "glandular swelling" (Latin)⁵, tuberculous lymphadenitis has been recognized for the last 3,000 years. Peripheral lymph nodes are most often affected; among which cervical involvement is the most common.²⁻⁶

Extrapulmonary tuberculosis (EPTB) is defined by WHO as a case of TB involving organs other than the lungs.

Patan hospital, the university teaching hospital has been providing care for both pulmonary and EPTB using diagnostic criteria of microbial, histopathological, and genetic tests. There are no documented studies on the pattern of EPTB from the institute. This study aims to find out the EPTB pattern that may help to understand the prevalence and disease identification.

Method

This is a retrospective descriptive study where pathology lab database analysis of Histopathology specimens for EPTB at the pathology lab of Patan Hospital, Patan Academy of Health Sciences (PAHS), Nepal, from 2012 to 2019.

The data was searched by primary search key "Tuberculosis" and secondary search keys "Site", "Granuloma", "Caseous" and "AFB". Seven years of data from 2012 to 2019 were analyzed descriptively using Microsoft Excel and SPSS (v16.0).

Variables analyzed were age, gender, site, presence of granuloma, AFB, caseous necrosis.

All entries with the histopathology diagnosis of tuberculosis in organs other than lungs were included in the study.

Ethical approval was taken from the Institutional Review Committee of PAHS.

Result

Out of 29,629 specimens received in the Pathology Department in 7 years, 300 (1%) were Extra Pulmonary Tuberculosis (EPTB). Females were 184(61%) and males 116(39%).

Among 300 EPTB, 170(57%) were lymph nodes, 36(12%) skin, intestine and urogenital TB (UGTB) each 26 and 28(9%) followed by Pott's disease (vertebral TB) 3(1%), Figure 1.

Out of the 170 lymph nodes, the cervical lymph node was 115(68%) followed by axillary 26(15%), supraclavicular 25(15%), and intestinal 4(2%) lymph nodes.

Age-wise, 20-39 years were 192(64%), youngest 3 years and oldest 88 years, Figure 2.

Epithelioid granuloma was seen in 288(96%) with 242(81%) caseous necrosis. Ziehl Neelson stain for acid-fast bacilli (AFB) was positive in 21(7%). Only 4(1%) was not proven as tuberculosis by microbiological (ZN stain -ve) and histopathology (Epithelioid Granuloma absent and Without Caseous necrosis) tests, Table 1.

Table 1. Distribution of histopathology and Ziehl Neelson stain in extrapulmonary tuberculosis (EPTB), N=300

Epithelioid Granuloma	Ziehl Neelson stain	Caseous Necrosis present	Caseous Necrosis absent	Sub-total	Total
Present	+ve	17	3	20	288(96%)
	-ve	217	51	268	
Absent	+ve	1	0	1	12(4%)
	-ve	7	4	11	
Total		242	58		300

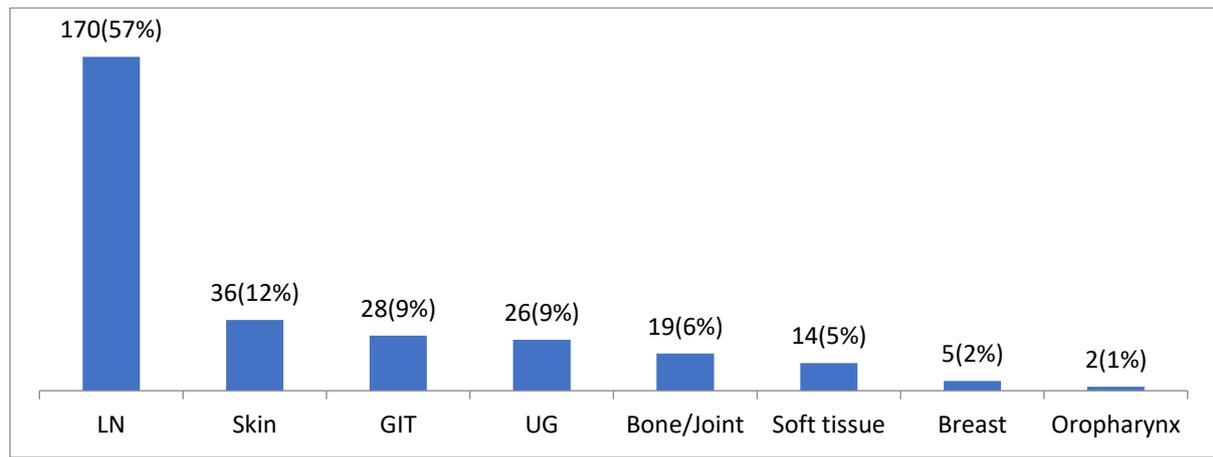


Figure 1. Organs affected by Extrapulmonary Tuberculosis EPTB, N=300

Note: LN- lymph node, GIT- gastrointestinal, UG- urogenital

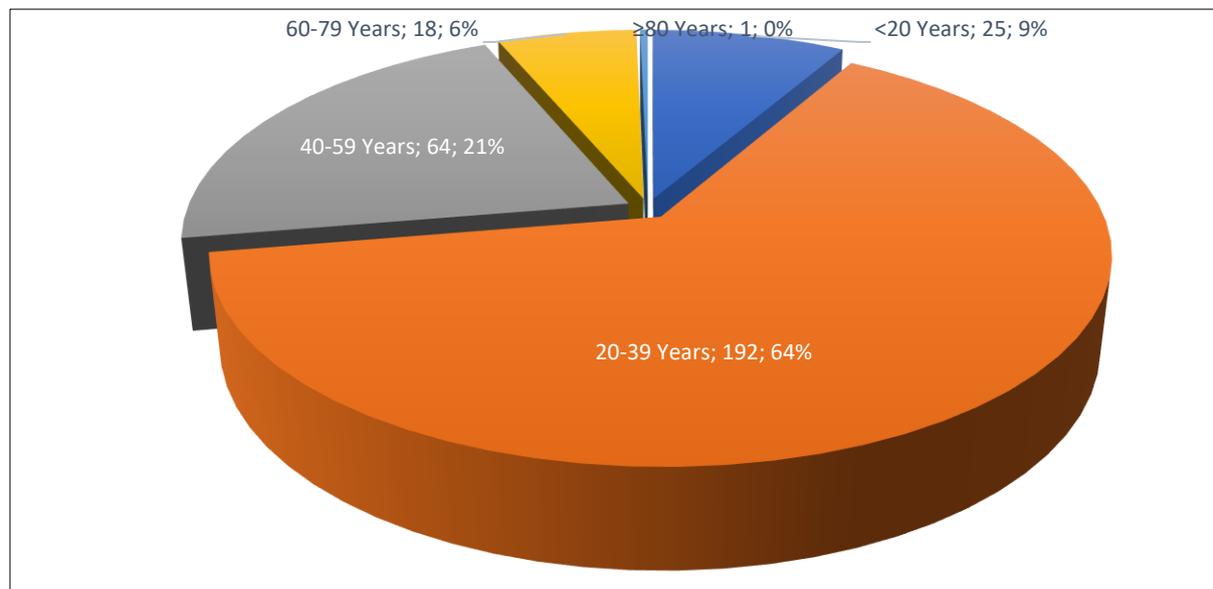


Figure 2. Age-wise distribution of EPTB, N=300

Discussion

This study showed that lymph nodes accounted for more than half, i.e., 57% (170 out of 300) of extrapulmonary TB and 2/3rd (115 out of 170) were cervical nodes. This is consistent with other studies from south Asian countries with similar socio-economic status and health care system.^{2,4,6,7} The similar results are due to the related condition of the host and the environmental association in this region.¹

The most common mode of development of tuberculous lymphadenitis is a reactivation of healed focus and progression of primary tuberculosis. *M. tuberculosis* usually enters the human body via the respiratory tract and forms the primary complex or Ghon's complex in the posterior segment of the upper lobe and undergoes lymphohematogenous dissemination. Because the entry is via the respiratory tract, the first lymphoid tissues encountered are presumably hilar and mediastinal lymph nodes, which are difficult to biopsy. Once the bacilli reach the superficial lymph nodes, the nodes increase in size and number and are detected clinically. Clinically, tubercular lymphadenitis is usually silent without overt symptoms and grows slowly over the months and years. Hence it is important to do a clinical examination of these lymph nodes routinely to find out tubercular lymphadenitis at an early stage.⁸

Abdominal tuberculosis was seen in 25(9%) of the cases out of which 16(5%) were seen in the small intestine and 9(3%) in the large intestine. Intestinal tuberculosis may be due to ingestion of unpasteurized milk from an infected animal (as commonly seen in underdeveloped countries) or as a secondary spread from the lungs by swallowing infected sputum⁹. The ileocaecal region was the most commonly affected site in the small intestine because of the numerous submucosal lymphoid tissues, stasis, increased rate of absorption at this site, and closer contact of the bacilli with the mucosa.¹⁰ Our study showed a female preponderance (F:M=1.2:1) which is similar to other studies done in our region.¹¹⁻¹⁵

Twenty-three cases showed caseous necrosis with epithelioid granuloma while in two cases acid-fast bacilli were seen in Ziehl Neelson stain. Histological appearances reveal classical granulomas with epithelioid cells, Langhan's giant cells, central necrosis, and an outer rim of lymphocytes scattered throughout the layers of the intestine. Caseous necrosis/AFB stains are unique changes in the tissue caused by *M. tuberculosis*. This is especially important in Intestinal TB since it is one of the features which helps in differentiating other granulomatous diseases like Crohn's disease and sarcoidosis which is common in the GIT than in other organs.¹³ The load of the bacilli in the tissue and the tissue fixation, processing, and staining process may affect the visibility of the AFB hence, acid-fast bacilli are not always demonstrable.^{13,16}

In this study, the total number of urogenital tuberculosis was 25(9%) which is similar to studies done in different countries.¹⁴⁻¹⁸ Urogenital tuberculosis is similar to the above discussed Intestinal tuberculosis which can be overlooked owing to the chronic, non-specific symptoms and lack of clinicians' awareness of the possibility of tuberculosis. The age ranged from 19 years to 77 years. The youngest patient was a 19-year female with urinary bladder tuberculosis. A maximum number of cases were seen in the age group of 40-59 years, which is similar to a study done in China with an incidence rate higher in the age group of 40-60 years.¹⁶ Some authors have found that UGTB affects more men than women while others have found exactly the contrary.²⁰ In our study, males were affected more than females.

Out of these 25 UGTBs, the majority were seen in the kidney 8(32%), followed by 6(24%) in the urinary bladder. Other studies have also shown that the majority of the cases in the urogenital category are the kidneys.²⁰ Kidneys are highly vascular organ and hence are seeded more easily by the bacteria which is spread by the lymphatic and hematogenous route.

In this study, we found 18(6%) of EPTB affecting the bones and joints. Bone and joint TB account for 15-20% reported from under-developed countries, particularly in Asia.²¹ In the developed countries like the USA and Europe it is around 2.2-4.7%, seen especially in the immigrants and patients with HIV.²¹ It is more common in the age group of 20-35 years as seen in other studies.^{21,22} Vertebral osteomyelitis (Pott's disease) was seen in 3(1%) only in our study. It could be due to diagnosis using clinical and radiological correlation only. Whereas, other studies show a higher range of 14-27% because of additional diagnostic modalities like Computed Tomography Scan (CT Scan), Magnetic resonance imaging (MRI), Pus/ Tissue culture, PCR, etc.²³

Another common site of tuberculosis seen in this study is the skin. It was seen in 36 (12%) of total EPTB. Our study reveals female predominance with a female to male ratio of 1.9:1 which is similar to other's finding.²⁴ A study done in Western Nepal showed a male predominance with a ratio of 1.5:1.²⁵ The mean age of occurrence was 33 years. However, the mean age of the patients varied in various studies and most of the studies reported greater occurrence in 2nd and 3rd decade which is similar to our study.^{25,26}

The histopathological changes of epithelioid granuloma with central caseous necrosis and granulomas were seen in 288(96%) of cases. Acid-fast bacilli were seen in 21(7%) of cases. Our study shows females are more affected by EPTB than men which is similar to other studies done in South Asia.^{7,27} The age group who are affected by EPTB is of younger age group (20-39 years) especially glandular tuberculosis which is comparable to many studies done around the world.^{7,11}

Center for Disease Control (CDC) recommends genetic tests to be done routinely in patients suspected to have tuberculosis since the results are available within hours which helps in initiating the treatment or if a negative result will help the clinicians to think about

other differential diagnosis and start prompt treatment.²⁸

Limitations of the study are that genetic tests (Nuclear Acid Amplification test) for tuberculosis are not done routinely in the PAHS. In this study, the diagnosis of EPTB was based on histopathological changes and Ziehl Neelson stain for AFB. The gold standard of tuberculosis test is the Culture of the micro-organism which is available only in selected centers around the country.²⁸

Conclusion

This study shows that Extra-pulmonary Tuberculosis is uncommon (1%) among histopathological specimens in a tertiary care hospital. Peripheral lymph nodes were seen affected in half of the cases, two-thirds in the neck. Epithelioid granuloma was seen in the majority (96%) and Acid-fast bacilli rarely (7%).

Acknowledgement

Special thanks to the Department of Pathology, Patan Academy of Health Sciences.

Conflict of Interest

None

Funding

None

Author Contribution

Concept, design, planning – RB. Literature review – RB. Data collection/analysis - RB, PS, DG. Draft manuscript – RB. Revision of draft - PS, DG, SRK. Final manuscript – RB. Accountability of the work - RB, PS, DG, SRK.

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