ORIGINAL ARTICLE

Clinicopathological profile of significant cervical lymphadenopathy and effectiveness of CBNAAT in diagnosis of tubercular lymphadenitis under 18 years of age – A cross-sectional study

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Background: Lymph node enlargement is a prevalent issue in children and evaluation of a child with lymphadenopathy is a usual clinical scenario for the pediatricians. **Objective:** The aim of the study was to determine the etiological factors in Pediatric significant lymphadenopathy, to study the prevalence of tubercular lymphadenitis in children of different age groups, and to correlate the effectiveness of cartridge based nucleic acid amplification test (CBNAAT) versus histopathology in diagnosing tuberculosis (TB) lymphadenitis. **Methodology:** The present cross-sectional study was carried out at the Paediatrics Department of Rohilkhand Medical College and Hospital in Bareilly, Uttar Pradesh. **Results:** In our study, out of 80 cases, fever was most common complaint when presenting in 35.0% of cases followed by cough in 32.6% of cases and neck swelling in 20.0% of cases, and anterior Cervical involved in 43.8% of cases, whereas posterior Cervical involved in 30.0% of cases. Out of 80 cases in our study, maximum 52.5% of cases have reactive lympadenitis in fine needle aspiration cytology (FNAC) report, 21.3% of cases have granulamatous lympaphadenitis, 13.8% of cases have caseous necrotizing lympaphadenitis, and 12.5% of cases have suppurative lymphadenitis in FNAC report. CBNAAT has high sensitivity of 82% and specificity of 100% in samples diagnosed for TB lymphadenopathy by cytology. **Conclusion:** The procedure known as FNAC is quick, safe, inexpensive, repeatable, and does not require anesthesia; open biopsy, anesthesia, and hospitalization are eliminated by FNAC. Due to its early diagnosis, FNAC is useful as an outdoor diagnostic procedure. Our study, therefore, showed that CB-NAAT is a useful tool to diagnose TB lymphadenopathy in sample positive by cytology. It has high sensitivity of 82% and specificity of 100% in samples diagnosed for TB lymphadenopathy by cytology.

KEY WORDS: Cartridge-based nucleic acid amplification test, cervical lymphadenopathy, fine needle aspiration cytology, lymph nodes

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INTRODUCTION

Lymph node enlargement is a common problem in children and evaluation of a child with lymphadenopathy is a common clinical scenario for the pediatricians. Lymph nodes in children may be palpated as early as in the neonatal period.[1] Palpable nodes in the cervical region are found in about 80–90% of children. The

nodes have considerable capacity for growth and change, and with continued antigenic exposure, as in children, the lymphoid tissue continues to proliferate and enlarge through puberty. Participating in the reticuloendothelial system, lymph nodes serve as the termination point for lymphatic vessels that drain lymph from most tissues of the body. The presence of abundant phagocytic cells, antigen presenting cells and lymphocytes provides ideal first line of defense against pathogens.

Lymphadenopathy is defined as an abnormality in the size or character of lymph nodes. In a situation where lymph node is considered as abnormally enlarged if it measures more than 10 mm in its longest diameter in cervical and axillary region, whereas more than 15 mm in inguinal region.[2] Palpable supraclavicular nodes are always considered abnormal. Majority of these are due to benign self-limited disease process because self-limited viral or bacterial infections are the most prevalent causes. However, some children with underlying serious systemic disease or malignancy may present with lymphadenopathy. Sometimes, it is difficult to determine whether adenopathy is simply a normal response to frequent viral or bacterial infections or, if it is significant enough to consider more serious underlying disease process.

The possible diagnoses of lymphadenopathy are numerous. To narrow this differential, a thorough medical history and clinical examination are essential.[3] The distribution of the enlarged lymph nodes is important in the evaluation of children with lymphadenopathy. Enlargement of two or more non-contiguous lymph node regions is known as generalized lymphadenopathy.[4] Causes include systemic infections (viral, bacterial, fungal, or protozoal), malignancies, autoimmune diseases, benign hyperplasia, drug reactions, histiocytoses, and storage diseases. Systemic infections are the most prevalent causes. Majority being systemic viral infections.

Although simple self-limited infection is frequently the underlying cause, more serious underlying causes must be promptly identified and appropriately treated. Important considerations include cancer and serious infections, which should not be missed. Therefore, an understanding of the differential diagnosis is critical in directing an appropriate and timely evaluation. If doctor do not want to miss a serious disease process or attempt to diagnose it too quickly or aggressively, there is need to follow a methodical and step-by-step approach.

Until recently lymph node biopsy was the investigation of choice for cases with lymphadenopathy, especially when malignancy is suspected.[5] However, "fine needle aspiration cytology" (FNAC) has been advocated as an alternative procedure in recent times. It has been found to be a useful adjunct diagnostic technique especially in children. Over the years, there has been an increase in the use of this technique. It is a simple, rapid, reliable, safe, and cost-effective technique with good diagnostic accuracy. It can obviate the need for a biopsy done surgically. There are few studies on the same from Western Uttar Pradesh region. Hence, we intend to conduct this study at our hospital. Routinely, "Cartridge Based Nucleic Acid Amplification test" (CBNAAT) of FNAC specimen was not being done routinely in our institution. Hence, we also intend to study the utility/ effectiveness of CBNAAT in diagnosis.

MATERIALS AND METHODS

The index cross-sectional research study was carried out at Department of Paediatrics, "Rohilkhand Medical college and Hospital," Bareilly, Uttar Pradesh, for all the children with significant cervical lymphadenopathy attending Paediatric OPD and admitted in Paediatric department at "Rohilkhand Medical College and Hospital," Bareilly, U.P. from November 1, 2020, to October 31, 2021. Ethical approval derived from "Institutional Ethical Committee" of the institute.

Sample Size

In our study, a total of 80 patients were taken which was calculated by the following formula-

$$n = [(z_{\alpha/2})^2 \text{ X P X } (100\text{-P})]/e^2$$

The participants in this study were 80 children. The study technique that was carried out was carried out in compliance with the ethical standards that were accepted by the "Rohilkhand Medical College and Hospital Ethics Committee" in Bareilly, Uttar Pradesh (Human).

Inclusion Criteria

Patients younger than 18 years old[6] were included for the study, which had cervical lymphadenopathy with lymph node size of 1 cm or more in the cervical region, and whose parents were willing to give informed consent.

Exclusion Criteria

Patients already on specific and empirical treatment for lymphadenopathy and those with lymphadenopathy in regions apart from the cervical region were not included in the study. Predesigned proforma for data collection (Semi structured Clinical Data Sheet) was made for the study, and consent from the attendants was taken.

Methodology

All children meeting the inclusion criterion were involved in the study. Informed consent was taken from the accompanying parent or guardian for inclusion into the study. The clinical and laboratory data of these patients were recorded on a structured proforma. A detailed history was taken, which included the duration and course of swelling, and associated general symptoms such as fever, cough, weight loss, loss of appetite, history of respiratory tract infection, ear discharge, presence of wound, or skin lesion. Contact history with pet animals at home or with a person with infectious tuberoculosis was enquired. Immunization status, socioeconomic history, and antibiotic therapy received was also be recorded. The area drained by enlarged lymph nodes was examined for presence of features

of inflammation or infection such as tonsillitis, pharyngitis, ear infection, dental infection, and wound or pyoderma lesions over the skin. Systemic examination was done including respiratory, cardiovascular, abdominal, and central nervous system. Significant findings were recorded.

Technique of CBNAAT

The automated cartridge-based molecular technique known as the CBNAAT (CB-NAAT, GeneXpert) has been approved by the World Health Organization (WHO) as an initial diagnostic test for children who are suspected of having tuberculosis (TB), including pulmonary and specific forms of extrapulmonary TB. It not only detects *Mycobacterium tuberculosis* but also rifampicin resistance within 2 h. Globally, the use of rapid molecular tests is increasing. A significant portion of TB cases reported to the WHO are still clinically diagnosed rather than bacteriologically confirmed, despite advancements in diagnostics. As a result, we are presenting a case series in which CB-NAAT assisted us in timely diagnosis and treatment. Sputum, gastric aspirate, or FNAC aspirate is collected and is sent for CBNAAT investigation. Our hospital is a hospital with tertiary care and a designated medical center for directly observed treatment, short-course but CB-NAAT testing facility is not available in our center. We shipped the samples to the closest MDR treatment center in Bareilly, where the government pays for CB-NAAT testing.

Table 1: Region of the largest lymph node involved

Region of the largest lymph node involved	Percentage	Percentage
Anterior cervical	35	43.8
Occipital	5	6.3
Posterior auricular	6	7.6
Posterior cervical	24	30.0
Submandibular	7	8.8
Supraclavicular	3	3.8
Total	80	100.0

Table 2: FNAC report

FNAC report	Percentage	Percentage
Caseous Necrotizing Lympaphadenitis	11	13.8
Granulamatous Lympaphadenitis	17	21.3
Reactive lympadenitis	42	52.5
Suppurative lymphadenitis	10	12.5
Total	80	100.0

FNAC: Fine-needle aspiration cytology

Technique of FNAC

The largest lymph node is selected. Aspiration of the selected lymph node takes place under strict aseptic conditions. The lymph node is grasped between the index and thumb of the left hand, stretching the underlying skin; A 5–10 mL syringe with a sterile 22 or 23 gauge needle is inserted obliquely into the lymph node. The needle is removed after entering the lymph node mass, and the syringe's negative pressure causes the needle to move back and forth several times while maintaining suction. The needle is taken out of the mass and the negative pressure is let go. The needle containing the aspirated material is then detached and air is drawn into the syringe. After reattachment of needle, content of the needle is ejected out on the clean, dry, and grease free glass slides. Smears are made by lightly pressing a second glass slide. The aspirate is examined for the amount and nature of the aspirated material, and then several smears are prepared. Excess of blood if present is removed using blotting paper. Caution is exercised to minimize the cell damage and preserve cell distribution. Smears are immediately fixed with ethyl alcohol containing 95% and stained with hematoxylin and eosin. Wright's stain is also used to prepare and stain smears that have been air-dried. Smears can also be stained with Zichl-Neelsen stain for the cases where necrotic material is aspirated or TB suspected, for the demonstration of acid-fast bacilli. Smears are examined under microscope for the cytological picture. Data were analyzed with SPSS version 23.0 ("Statistical Package for the Social Sciences") for calculation of means and SDs. T-test and Chi-square test were used and $P < 0.05$ was considered statistically significant.

RESULTS

In our study, out of 80 cases, maximum 33.8% of cases were in age group of 9–12 years followed by 31.3% of cases were in age group of 5–8 years, 22.5% of cases were in age group of 13–17 years, and 12.5% of cases were in age group of 1–4 years. Mean age of study subjects was 9.34 ± 4.2 years. In our study, out of 80 cases, 53.8% of cases were female and 46.3% were male. In index study among the 80 cases, fever was most

Table 3: Correlation of FNAC report with CBNAAT report

FNAC report	CBNAAT					
	Positive		Negative		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage%
Caseous Necrotizing Lympaphadenitis	10	90.9	1	9.1	11	13.8
Granulamatous Lympaphadenitis	13	76.5	4	23.5	17	21.3
Reactive lympadenitis	0	0	42	100	42	52.5
Suppurative lymphadenitis	0	0	10	100	10	12.5
Total	23	28.75	57	71.25	80	100

FNAC: Fine-needle aspiration cytology, CBNAAT: Cartridge based nucleic acid amplification test

common presenting complaint in 35.0% of cases followed by cough in 32.6% of cases and neck swelling in 20.0% of cases.

Anterior cervical involved in 43.8% of cases, posterior cervical involved in 30.0% of cases Table 1.

Out of 80 cases in our study, maximum 52.5% of cases have reactive lympadenitis in FNAC report, 21.3% of cases have granulamatous lympaphadenitis, 13.8% of cases have caseous necrotizing lympaphadenitis, and 12.5% of cases have suppurative lymphadenitis in FNAC report Table 2.

CBNAAT has high sensitivity of 82% (10 cases of caseous necrotizing lympaphadenitis and 13 cases of granulamatous lympaphadenitis) and specificity of 100% in samples diagnosed for TB lymphadenopathy by cytology Table 3.

DISCUSSION

In index study, 12.5% of patients were in 1–4 year age group, 31.3 patients in 5–8 years age group and 33.8% in 9–12 years age group whereas Mishra and Garg[7] in their study observed 36.5% of patients in 5–8 years age group and 24.1% in 8–12 years age group. In our study, incidence in females (53.8%) was more than that in males (46.3%). In the study by Ingale and Boghavar[8] incidence in males (68.57%) was more than that in females (31.42%) with male to female ratio 2.18:1. El-Sheikh *et al*.[9] observed higher incidence in males (55.6%) as compared to females (44.4%). In majority of patients, fever (87.5%) was present and cough was there in 85% of patients. In study by Bhogavar *et al*.,[8] majority of patients had fever (90%), but cough in relatively lesser number of patients (48.5%). In the index study, upper anterior cervical nodes were commonly involved (43.8%) cases, followed by posterior cervical (30%) cases. In the study by Bhogavar *et al*.,[8] anterior cervical nodes were the most commonly involved (44.28%) cases. Knight *et al*.[10] did a study of 239 children with lymphadenopathy, out of which 47% of the children had involvement of anterior cervical lymph node. In our study, more than 50% of the study group had reactive lymphadenits as the cytopathological finding (52.5% cases), 21.3% had granulomatous lymphadenitis, 13.8% as caseous nectrotizing lymphadenitis, and 12.5% patients of suppurative lymphadenitis. In the study Kumar and Kiran,[3] reactive lymphadenitis was the most common cytopathological finding (74.4% cases), followed by granulomatous (15%) and suppurative lymphadenitis (6.9% cases). According to our study, total 28 patients of TB lymphadenitis were diagnosed by FNAC, out of which 23 were also positive for CBNAAT. It has high sensitivity of 82% and specificity of 100% in samples diagnosed for TB lymphadenopathy by cytology.

CONCLUSION

The cervical lymph node's anatomical details are uncovered. TB cervical lymphadenitis's history, pathogenesis, pathology, clinicopathological agents, diagnosis, and treatment are discussed. The study looked at 80 cervical lymph node cases. The results were looked at and talked about. TB cervical lymph nodes are prevalent in the first and second decade of life, based on age incidence. Therefore, this is mostly a childhood disease, but no age group is immune. Females have a higher incidence of TB cervical lymph node than males do. The most common complaint included a fever, a cough, and neck swelling. In a few instances, appetite, night sweats, and weight loss were present. Multiple groups of cervical lymph nodes are frequently involved, with the Jugulo-digastric group and submandibular nodes being the most common. A positive Mantoux test and a raised ESR both favor a TB cervical lymph node diagnosis. Positive Mantoux reactions are not diagnostic, and negative reactions do not exclude TB. However, only on "Histopathological ground" can the disease process be used to diagnose TB in cervical lymph nodes. The present study aims to prove that TB is a disease process in the cervical lymph nodes. The majority of TB lymph nodes were single, mobile, and firm. The procedure known as FNAC is quick, safe, inexpensive, repeatable, and does not require anesthesia; open biopsy, anesthesia, and hospitalization are eliminated by FNAC. Due to its early diagnosis, FNAC is useful as an outdoor diagnostic procedure. Our study, therefore, showed that CB-NAAT is a useful tool to diagnose TB lymphadenopathy in sample positive by cytology. It has high sensitivity of 82% and specificity of 100% in samples diagnosed for TB lymphadenopathy by cytology.

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