Cure Rates for Tuberculous Cervical Lymphadenopathy after 6-month or 9-month Anti-tuberculous Therapy

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ABSTRACT

Objectives. The purpose of this prospective case series was to describe the difference in cure rates between a 6-month and a 9-month anti-tuberculous treatment regimen in patients with newly diagnosed tuberculous cervical lymphadenitis.

Methods. Thirty-eight consecutive participants were enrolled in the study. Thirty participants were ultimately analyzed at the end of six months, nine months, and 12 months using serial neck ultrasound to assess for the presence of lymphadenopathy. At the end of six months, participants with residual lymphadenopathy larger than 1 cm extended treatment to complete nine months of treatment.

Results. Among the 30 participants who completed 6-month treatment, 63.3% (n=19) were cured while 36.7% (n=11) had residual lymphadenopathy and extended to 9-month treatment. At the end of 9-month treatment, 36.4% (n=4) were cured while 63.6% (n=7) had persistent lymphadenopathy greater than 1 cm on ultrasound. At 12 months, 15.8% (n=3) of those treated for six months and 45.5% (n=5) of those treated for nine months had recurrent/residual lymphadenopathy. There were no significant differences between cure rates for age, sex, concomitant pulmonary tuberculosis, the number of nodes, skin changes, TB-PCR results, and presence of paradoxical reaction whether at six or at 12 months.

Conclusion. Due to the low cure rates in this study, there was not enough evidence to support current recommendations of a 6-month treatment period for tuberculous cervical lymphadenitis or to claim its effectiveness over a longer treatment duration.

Keywords: tuberculosis, lymph node, antibiotics, antitubercular, paradoxical reaction

INTRODUCTION

Tuberculosis (TB) is an endemic disease in the Philippines and continues to pose a problem for control.[1] Among patients who are newly diagnosed with TB cervical lymphadenitis, the current recommendation for treatment is the same as that for pulmonary TB – two months of isoniazid, rifampicin, pyrazinamide, and ethambutol followed by four months of isoniazid and rifampicin.[2] However, not all cases of cervical lymphadenopathies resolved at the end of a 6-month regimen, and longer treatment durations of at least nine months for unresolved cases are given.[3-7] The cure rates of patients undergoing 6-month treatment versus 9-month treatment have not been studied locally, leaving some ambiguity regarding the optimal management for TB cervical lymphadenitis. The aim of our study is to describe treatment outcomes of patients diagnosed with TB cervical lymphadenitis after a treatment duration of six months and nine months.

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Although the most common site is pulmonary, extra-pulmonary tuberculosis (EPTB) accounts for a significant percentage ranging from 15-34% in high-burden countries, such as India, Pakistan, and Cambodia.[8-10] The most common extra-pulmonary site is the lymph node, accounting for about 40% of EPTB cases.[8] TB lymphadenitis commonly occurs in patients less than 40 years old with a higher predilection for females.[8,9,11] Given the high burden of disease and lack of sufficient local studies regarding the subsite, not much is known regarding incidence, prevalence, associated risk factors, and treatment outcomes of TB lymphadenitis in the Philippines. Only a single large-scale epidemiologic study was conducted in the Philippines which showed a 1.1% prevalence of EPTB.[12] The study admitted that the low detection rate was most likely due to the limitation of the study to primary care centers and the fact that most EPTB cases are detected in tertiary institutions.[12]

There are a few existing local clinical practice guidelines (CPGs) that provide recommendations regarding diagnosis and treatment of TB lymphadenitis.[2,13] Based on several case series cited in published clinical practice guidelines by the Philippine Society of General Surgeons, TB lymphadenitis may be suspected in a patient with non-tender, cervical lymph nodes greater than 1 cm of more than two weeks in duration, and not resolved by antibiotics among patients with prior diagnosis of and/or exposure to TB.[13] Patients may or may not present with systemic symptoms of TB, such as fever, weight loss, cough, and night sweats.[13] For cases suspected of TB lymphadenitis, fine needle aspiration cytology has been recommended to support the diagnosis.[13]

Various CPGs have discussed treatment of newly diagnosed EPTB.[2,14,15] Similar to treatment for PTB, a 6-month regimen with an intensive phase of two months containing isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E), and a continuation phase of four months of isoniazid and rifampicin is recommended for all cases of newly diagnosed EPTB.[2] There is a specified exception for TB involving the central nervous system (CNS), bone, and joints wherein an extension of the continuation phase to 10 months is advised.[2]

The diagnosis of TB cervical lymphadenitis is not standardized due to lack of a single highly sensitive, specific, and cost-effective diagnostic examination. Thus, it has been recommended that combination of tests such as fine needle aspiration and microbiologic studies be used to increase diagnostic accuracy.[16-18] *Mycobacterium tuberculosis* culture studies are considered to be the gold standard for diagnosis. However, this is not the initial test of choice as it is time-consuming and has a low sensitivity of about 30.7%.[17,19]

Fine needle aspiration cytology is a readily available test in low resource settings that is recommended as an initial test to support a clinical suspicion of TB lymphadenitis.[20,21] It has been shown to have a sensitivity ranging from 71.79-96.77% and a specificity about 93-100%.[18,20,21] Various cyto-morphological findings may be seen, but the most suspicious of TB lymphadenitis is the finding of chronic granulomatous inflammation with caseous necrosis.[17,20] In endemic areas, other possible findings suggestive of TB include chronic granulomatous inflammation without presence of necrosis, necrosis with granulomatous inflammation, or caseous necrosis without granuloma formation.[17,20]

Other ancillary tests that are ordered are acid-fast bacilli (AFB) smears, TB polymerase chain reaction (PCR)-based assay, and GeneXpert testing. AFB smears have been found to have the lowest and most variable sensitivity and specificity, ranging from 12.7-77% and 61.5-93.4%, respectively, and a detection rate of 0-77.8%.[17,19,22] TB-PCR has better sensitivity and specificity, ranging from 68-100% and 82.4-96.1%, respectively.[16,22-24] GeneXpert testing has also been shown to have lower sensitivity and specificity, ranging from 33.2-93.5% and 68.2-86.89%, respectively.[16,17,25] Given these findings, combining FNA cytology with TB-PCR test may increase accuracy of detecting TB cervical lymphadenitis cases although some studies have advised the use of TB-PCR for more problematic cases given its more expensive price and higher financial burden on patients.[18,26] Studies showed apparent correlation between PCR positivity and specific cytomorphologic findings, such that there was a significant difference between TB-PCR positivity among those with chronic granulomatous inflammation versus those with chronic inflammation alone.[22,24] One study recommended that patient samples for these ancillary tests be taken prior to the start of any empiric antibacterial treatment which may lead to lower detection rates in AFB and TB culture studies.[27]

In terms of treatment, studies from other countries also reflect local practice guidelines' recommendation of six months (2HRZE/4HR) anti-TB treatment for newly diagnosed cases of TB lymphadenitis.[3-6,15] The ultimate goal of treatment using these four first line drugs is a 95% cure rate.[28] However, studies have also shown that physician practices do not strictly adhere to this as demonstrated by the fact that treatment courses are usually extended among patients who did not show complete resolution by the end of the first six months, especially among those with paradoxical reactions or abscess formation.[3-7] Paradoxical reactions are defined as cases of TB lymphadenitis with either an increase in size or number of lymphadenopathy that occur during the course of anti-TB treatment which have been shown to occur in about 20-25% of TB lymphadenitis cases.[7,29-31]

There have not been enough large-sample randomized clinical studies to show whether there is a clear benefit to prolonging treatment in certain cases since previous observational studies have noted that majority of patients (74.1-93.6%) are cured of the lymphadenopathy upon completion of six months.[11,16,17,32] Furthermore, another study also showed that, among patients with documented post-treatment paradoxical reactions, spontaneous resolution was seen among 92%, all of whom were managed conservatively with observation and no further treatment with anti-TB medication.[33] A few studies done have tried to compare the

efficacy of six months versus nine months in treating TB lymphadenitis which all showed no significant difference between groups. None of the studies used the locally recommended intensive phase regimen of HRZE.[32,34,35] One study used a combination of HRZS (streptomycin).[35] Other studies used either a combination of HRZ or HRE during the first two months.[32,34] A study that attempted to determine risk factors associated with prolonged anti-TB treatment found that male sex, multiple TB foci, and presence of weight loss were associated with treatment regimens more than six months.[4] Because of lack of evidence, treatment of stable, worsened, or incompletely resolved cases of TB lymphadenitis after six months of treatment with HRZE remains controversial. Despite prolonged treatment or work-up of drug resistant TB, persistence of enlarged, palpable lymph nodes has been seen in up to 10-29% of cases.[4,29,32,34]

This study determined cure rates associated with different treatment durations – six months and nine months – of TB cervical lymphadenitis. Identifying the more effective treatment duration can impact physicians' decision making and the development of future guidelines in order to achieve high cure rates while reducing either under- or over-treatment which could promote drug resistance and/or adverse drug reactions.

The main objective was to describe the cure rates of a 6-month and a 9-month anti-TB treatment regimen in patients with TB cervical lymphadenitis. The secondary objective was to identify the presence of statistically significant associations between cure rates at 6, 9, and 12 months and any demographic or clinical characteristics.

MATERIALS AND METHODS

The prospective case series took place in the outpatient department (OPD) of the Department of Otolaryngology – Head and Neck Surgery, Philippine General Hospital. The study protocol was approved by the University of the Philippines Manila Research Ethics Board (UPMREB CODE: 2019-432-01). The study was conducted from November 2019 to August 2021 with consecutive patients recruited from November 2019 until March 2020.

All participants enrolled were exposed to the same intervention at diagnosis with a minimum duration of six months of treatment. This aspect along with the lack of a control group at the beginning led to the study's classification as a prospective case series as opposed to a cohort study. Hence, a computed sample size was not required for this descriptive study.

Inclusion criteria

Patients included were those at least one year in age who presented with at least one cervical lymph node greater than 1 cm for more than two weeks' duration despite antibiotic treatment.

Exclusion criteria

Patients who had another more likely etiology for the cervical lymphadenopathy (e.g., head and neck mass or active infection in the head and neck region or respiratory tract) were excluded. Patients who had been previously treated for TB or who were currently being treated for TB at the time of initial consult were excluded.

Withdrawal criteria

A participant could voluntarily withdraw from the study at any point if he or she desired with no consequence to his or her treatment for the diagnosed disease. Participants were withdrawn if new onset symptoms prompting further diagnostic examinations yielded results of a different etiology such as a malignancy. Participants were withdrawn from the study if found to have poor compliance with treatment defined as stopping medication for more than one month. Participants were withdrawn from the study if they developed an adverse reaction to any of the anti-TB medications which resulted in the alteration of their treatment regimen.

Conduct of the Study

Purposive sampling was done wherein any patient who consulted was eligible for recruitment if they met the inclusion criteria. Informed consent was obtained by the corresponding author. Demographic and clinical information were obtained from the initial interviews done by the resident-on-duty. In the event that the principal investigator was not available, the resident-on-duty at the OPD noted pertinent history and physical examination findings, and personally handled extracting the samples for fine needle aspiration biopsy (FNAB) and/or TB-PCR which were sent to the pathology laboratory and medical research laboratory, respectively, as part of the healthcare procedure. All residents of the department have been equipped to extract samples for FNAB and TB-PCR. In the event that a patient did not consent to participating in the study, due care and proper follow-up were provided by the residents at the OPD.

FNAB was done as part of the initial work-up prior to TB-PCR in all cases. Samples from a patient's lymph node were taken via aspiration using a syringe with either a gauge 23 or 25 needle. The needle was passed through and aspiration was done in multiple directions within the node to increase cytological yield. The sample collected within the needle was ejected onto two glass slides, fixed with 95% ethanol, and dried prior to submission to the laboratory.

Participants were advised to return after two weeks to follow up results of the FNAB. Those with results showing inflammation then underwent extraction of samples for TB-PCR. Fine needle aspiration was again done using a syringe attached to a gauge 23 or 25 needle which was passed through a lymph node. The sample aspirated was ejected into a sterile vial that contained 5mL of saline solution and was then submitted to the laboratory.

The patient participant followed up with the principal investigator to document the results. Cases with cytological findings of "chronic granulomatous inflammation with caseous necrosis," "chronic granulomatous inflammation" without necrosis or "caseous necrosis" without granuloma formation were diagnosed and treated as TB cervical lymphadenitis regardless of TB-PCR results. TB-PCR detection was considered in combination with other cytological findings such as suppurative inflammation and acute necrotizing inflammation. If patients with these FNAB results had negative TB-PCR, they were not diagnosed as having TB lymphadenitis. Those with positive TB-PCR were diagnosed with TB lymphadenitis.

Sputum AFB and chest radiographs were done for all patients to determine if there was concomitant pulmonary TB prior to referral to their TB Directly Observed Treatment Strategy (TB-DOTS) centers. Those with results compatible with TB cervical lymphadenitis were referred to TB-DOTS where they were started on anti-TB treatment for six months. At the end of six months, patients with no detectable lymphadenopathy or with residual lymph nodes 1 cm or less in size as measured by ultrasound were considered cured and stopped treatment. Those with lymph nodes greater than 1 cm on ultrasound extended treatment to complete the 9-month regimen. All patients were followed up using neck ultrasound at 9 and 12 months after start of treatment.

All possible adverse reactions from any of the anti-TB drugs (as stated in the 2016 PhilCAT CPG)[7] were explained in the informed consent and repeated upon referral to TB-DOTS. Minor adverse reactions such as gastrointestinal intolerance, urine discoloration, mild rash, and neuropathic pain were managed conservatively as advised in the CPG.[7] For major adverse reactions, such as severe skin rash, oliguria, shock, anemia, and jaundice, treatment was stopped, and the participant was referred to the allergy service for evaluation. Participants who discontinued certain medications were excluded from the study but continued to be managed according to healthcare standards. Likewise, patients who were later found to have interrupted treatment for more than one month were excluded from the study but were managed according to CPG recommendations.

Statistical Analysis

Baseline characteristics were identified and tabulated. These characteristics were (1) age (with a cutoff of 40 years), (2) sex, (3) concomitant newly-diagnosed pulmonary TB, (4) known co-morbidities (hypertension, diabetes, chronic kidney disease, chronic liver disease, HIV). Clinical characteristics were noted, such as (1) number of lymphadenopathy (single or multiple), (2) neck level location of lymphadenopathy, (3) presence of skin changes or suppuration, and (4) occurrence of paradoxical reaction.

The different outcome categories were (1) cured defined as disappearance of lymphadenopathy or reduction to less than 1 cm in size as measured on ultrasound and (2) not cured defined as the persistence of at least one lymph node greater than 1 cm as measured on ultrasound. The proportions of patients belonging to different outcome categories after 6-month and 9-month treatment were calculated and expressed in percentages. The relationship between patient characteristics and cure rates at six months and at 12 months was assessed using Fisher's exact test. Significance level was set at $p \leq 0.05$. Statistical analysis was carried out by the consultant statistician using STATA 14 (StataCorp, Texas, USA).

RESULTS

A total of 38 patients were recruited from the outpatient department and included in the study. The duration between extraction of lymph node samples and final diagnosis of TB lymphadenitis warranting referral to TB-DOTS centers was one month. Eight patients were withdrawn following withdrawal criteria. Two patients were diagnosed with malignancies after repeat biopsies (nasopharyngeal carcinoma and acute lymphocytic leukemia) and were promptly referred to oncology services for treatment. Two patients experienced urticaria while taking anti-TB medication which warranted a discontinuation in treatment and referral to the allergy service. One patient was found to be non-compliant with medication for more than a month and was subsequently withdrawn. Three patients completed the 6-month treatment but were unable to have any neck ultrasound done and were thus withdrawn from analysis.

Patient demographic and clinical data of the remaining 30 participants are reported in Table 1. The mean age was 25.4 years old (range 8-64) with a ratio of male to female of 1:1.5. All patients were diagnosed with tuberculous lymphadenitis with histopathologic findings consistent with TB (Table 2). Only four patients (13.3%) yielded positive TB-PCR results through fine needle aspiration.

Among the 30 participants who completed 6-month treatment, 63.3% (n=19) were cured. At the 12-month mark, 15.8% (n=3) had documented recurrent lymphadenopathy (Figure 1). One participant had an enlarged lymph node noted at 9 months while the two remaining had recurrent lymphadenopathies at 12 months. None of the measured lymph nodes were greater than 1.3 cm in widest diameter.

At the end of the 6-month treatment, 36.7% (n=11) had residual lymphadenopathy and extended to 9-month treatment (Figure 1). At the end of 9-month treatment, 36.4% (n=4) were cured while 63.6% (n=7) had persistent lymphadenopathy greater than 1 cm on ultrasound. However, despite stopping treatment at nine months, the number of cured participants increased at the 12-month follow up to 54.5% (n=6) and were classified as cured while 45.5% (n=5) had remaining lymphadenopathy. The widest diameter of the remaining lymph nodes ranged from 1 to 5 cm.

At six months, Fisher's exact test showed no significant differences between cure rates for age (p=1.00), sex (p=1.00),

concomitant PTB (p=0.69), the number of nodes (p=1.00), skin changes (p=0.43), TB-PCR results (p=0.27), and presence of paradoxical reaction (p=0.61). The sample of patients treated for nine months (n=11) was too small to generate information on association using the same statistical test. At 12 months, there were no significant differences in overall cure rates for age (p=1.00), sex (p=1.00), concomitant PTB (p=0.67), number of nodes (p=0.68), skin changes (p=0.68), TB PCR results (p=1.00), and presence of paradoxical reaction (p=1.00). No further sub-group analyses could be conducted due to the limitations of sample size.

In total, eight participants had recurrent or residual lymphadenopathy at 12 months – three in the 6-month treatment and five in the 9-month treatment. There was no predilection for a certain type of histopathology among the eight participants (Table 3). They were advised to follow up for further work-up to exclude multiple drug resistant TB or other etiologies. Only one patient returned to the OPD with incision biopsy and immunohistochemical staining revealing reactive follicular lymphadenitis and ruling out a malignancy.

Table 1. Patient Data Summary

	n (n=30)	%
Age (years)		
Mean age = 25.4, SD = 12.56		
<40	27	90.0
≥40	3	10.0
Sex		
Male	12	40.0
Female	18	60.0
Co-morbidities		
Hypertension	2	6.6
Diabetes	1	3.3
HIV	1	3.3
Concomitant PTB		
Yes	9	30.0
No	21	70.0
Number of enlarged cervical lymph nodes		
Single	12	40.0
Multiple	18	60.0
Skin changes/ulceration		
Yes	10	33.3
No	20	66.7
Neck levels involved		
I	2	6.7
II	12	40
III	2	6.7
IV	1	3.3
V	24	80.0
TB PCR result		
Positive	4	13.3
Negative	26	86.7
Paradoxical Reaction		
Present	4	13.3
Absent	26	86.7

Abbreviations: SD, standard deviation; HIV, human immunodeficiency virus; PTB, pulmonary tuberculosis

DISCUSSION

Consistent with previous studies, majority of patients in this study were female and were less than 40 years of age.[8,9,11] The cure rates in this patient sample at the end of six months followed the trend of published randomized controlled trials which found that 6-month treatment was sufficient for tuberculous lymphadenitis.[6,32,34-36] However, long term follow up is needed for these patients since it was noted that the cure rate of the 6-month group at 12 months decreased from 63.3% to 53.5% due to the recurrence of lymphadenopathy in a number of patients. This is far below the target cure rate of 95% stated in the literature and below the cure rates achieved in the previous trials (85-97%).[6,28,32,34-36]

Aside from a longer follow-up period, a larger sample size would also lead to a more precise picture of cure rates among local patients. This study's small sample size prevented the determination of more generalizable or applicable cure rates of the two treatment regimens. It is recommended that a larger sample size and a corresponding control group to be obtained in future studies to assess if this will lead to cure rates closer to those reported in the literature and to determine whether a 6-month or 9-month treatment duration is more effective.

Table 2. Histopathology and TB PCR Results (n=30)

Histopathologic findings*	TB PCR (-)	TB PCR (+)
Chronic granulomatous inflammation with caseation necrosis and Langhans type giant cell	9	0
Chronic granulomatous inflammation with Langhans type giant cells	5	1
Chronic granulomatous inflammation with caseation necrosis	5	0
Chronic granulomatous inflammation with necrosis	2	2
Chronic granulomatous inflammation	5	1

**findings obtained through fine needle aspiration for 28 patients and through incision biopsy for 2 patients*

Table 3. Histopathology among Residual/Recurrent Lymphadenopathy at 12 Months

Histopathologic findings	6-month group (n=3)	9-month group (n=5)
Chronic granulomatous inflammation with caseation necrosis and Langhans type giant cell	1	2
Chronic granulomatous inflammation with Langhans type giant cells	1	1
Chronic granulomatous inflammation with caseation necrosis	1	1
Chronic granulomatous inflammation	-	1

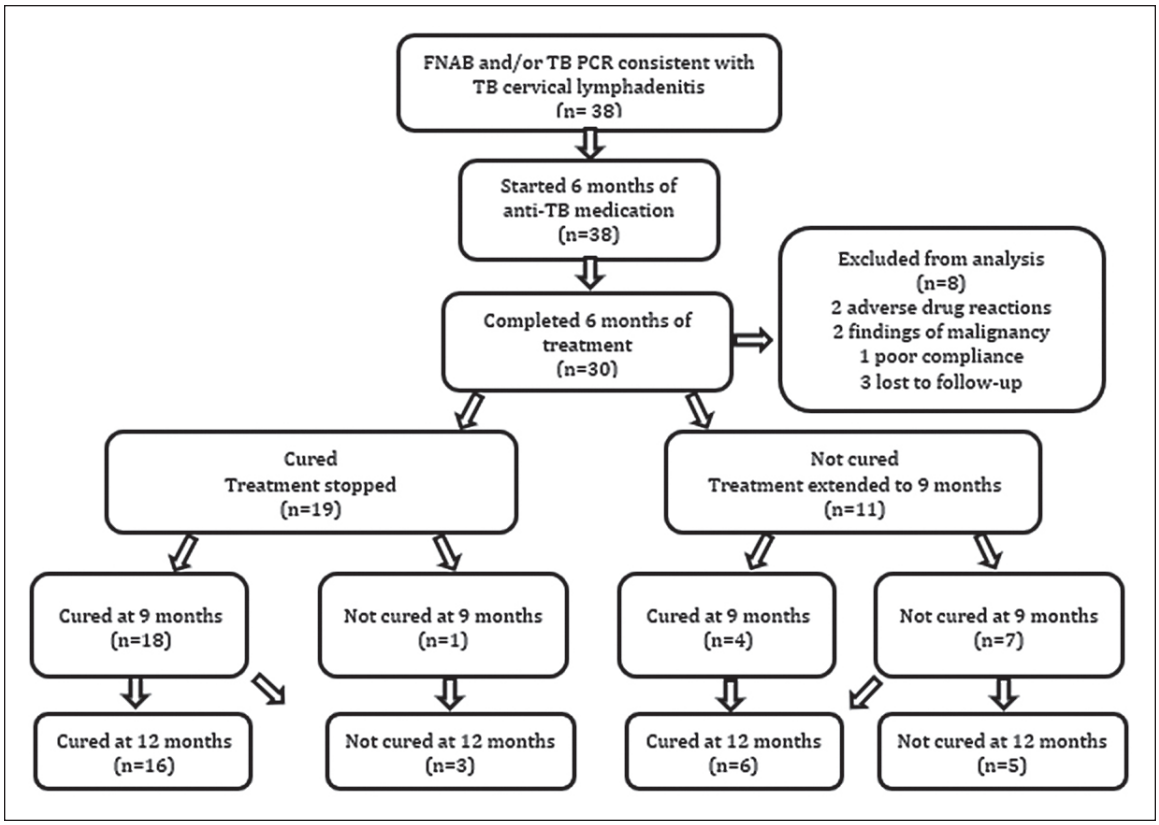

Figure 1. Patient recruitment and treatment response.

No clear guidelines exist regarding the work-up needed for cases of relapse and if they should be treated as cases of reactivated EPTB. Some studies have suggested treatment for those with positive TB cultures.[33,36] Others suggest surgical excision of enlarged lymph nodes, observation, or restarting treatment, depending on the clinical picture of each patient.[3,36,37] It is also not clear how long patients must be followed up to monitor response or recurrent disease as studies had various follow up periods ranging from nine months to 66 months from treatment. [6,32-36]

Even if majority of cases had resolution of lymphadenopathies after completing a 6-month treatment, the benefit of extending to nine months needs to be further investigated. Among the remaining cases who had to undergo a 9-month treatment, more than 50% of them were deemed cured at 12 months. It cannot be concluded at this time if the resolution was a delayed response to the 6-month regimen or if there was an added benefit from extension of treatment. This can only be answered by a locally conducted randomized controlled trial.

Follow-up using ultrasound allows for a more objective documentation of lymphadenopathy over physical examination. This modality is subject to variation since results are operator-dependent.[38] A limitation of this study was that it took place during the COVID-19 pandemic preventing patients from traveling to the study institution for neck ultrasound. All patients had their neck ultrasound done in various diagnostic centers and by different radiologists leading to a source of variation in the measurement of lymphadenopathy. The variation in sonographic results directly affected the outcome classification of "cured" versus "not cured" potentially leading to a source of information bias or measurement error. Controlling for the interpretation of lymph node size and location by a single trained sonologist would have reduced the existing bias introduced by the variety of radiologists who conducted the ultrasounds.

Possible reasons for recurrent or residual lymphadenopathy are drug-resistant TB or another diagnosis, such as malignancy.[3,13] Although more common in countries where TB is rare, other chronic granulomatous diseases such as sarcoidosis, fungal infections, toxoplasmosis, and cat scratch fever may also be considered.[39] Other studies have described the occurrence of post-treatment paradoxical response which is diagnosed if culture or drug-resistant studies yield negative results.[7,39,40] Unfortunately, most participants with residual or recurrent lymphadenopathy at the end of the study failed to follow up for further investigation. Because of this, the cause of lower cure rates in our study could not be determined.[6,32,34-36]

In this study, all patients had findings of chronic granulomatous inflammation with majority having caseation necrosis, Langhans type giant cells, or both. Interestingly,

there was a very low proportion of cases with positive TB PCR results which were also dispersed among the different histopathologic descriptions. This is in contrast to the numerous studies which found that aspirates had comparable or even higher positive TB-PCR results in comparison with tissue samples.[26,39,41-43] Only one study was found to have lower sensitivity for FNA PCR (17.1%) over tissue or biopsy PCR (63.4%).[44] The low yield of TB-PCR positive results in this study is likely due to fine needle aspirate samples being drawn blindly at a separate time from the initial FNAB which had yielded the findings suggestive of TB. This was another possible source of information bias. It is advisable for future studies to obtain samples for both cytology and TB-PCR from the same aspirates by a trained specialist to control for bias and assess if this will yield more congruent results.

Although it was noted that there was no significant difference between cure rates at six and 12 months with respect to TB-PCR results, the sample of patients with positive TB-PCR was too low to be clinically relevant. Still, given the prohibitive cost of TB-PCR in a country where TB continues to be common, it may be recommended for future studies to look into the accuracy and potential benefit of diagnosing and treating tuberculous lymphadenitis using histopathology alone versus in combination with ancillary tests.

This study also had lower rate of paradoxical reactions reported during the participants' course of treatment with a frequency of 13.3% compared with that reported in literature ranging from 20-25%.[7,29-31] If the three cases with recurrent lymphadenopathy at 12 months can be considered as post-treatment paradoxical reactions, this would increase the percentage of paradoxical reactions to 23.33%.[33,40] However, the lack of post-treatment diagnostic work-up and longer follow-up beyond 12 months for these cases to assess for spontaneous resolution preclude the definitive diagnosis of paradoxical reactions. Although Fisher's exact test showed no significant difference in cure rates at six and 12 months with respect to paradoxical reactions, the overall sample size is too small to be able to draw any meaningful conclusion. A larger study is recommended to further study the impact this clinical characteristic may have on treatment outcomes.

CONCLUSION

This study seems to support the recommendation in local clinical practice guidelines of treating newly diagnosed cases of tuberculous cervical lymphadenitis with 6-month treatment. However, cure rate was below the target of 95%. There is currently not enough evidence to determine whether this is more effective than a longer treatment duration of nine months. It is reasonable to initially treat patients for six months and assess for resolution of lymphadenopathy prior to extending treatment. Studies with larger sample sizes and controls are needed for definitive conclusions to be made which can impact guidelines and decision-making.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

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