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Case Series

Tuberculous lymphadenitis in Baghdad city: A review of 188 cases

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ABSTRACT

Background: Tuberculosis is still a major health problem in the world. Iraq regarded as an endemic country with incidence of 43 tuberculosis cases in 100,000 of the population. Tuberculous lymphadenopathy considered the most common extrapulmonary manifestation of tuberculosis. With cervical lymph node groups most commonly affected. It may confuse by serious aetiology necessitating sophisticated investigations like tissue biopsy to reach a diagnosis. The Surgical role is well established in the diagnosis of tuberculous lymphadenopathy, but still not clear whether surgery plays role in treatment along with antituberculous drugs or not.

Aims: to define the incidence, presentation, investigations, outcome, and the role of surgery in the diagnosis and treatment of tuberculous lymphadenopathy.

Patients and method: A retrospective study performed in the National specialized Centre for Respiratory and Chest Diseases in Iraq-Baghdad, from January until December 2016. One hundred and eighty-eight patients included in the study. The following information were collected from the patient's records: demographic and clinical data; the final diagnostic test; the treatment regimens; the outcome of the antituberculous therapy and the type of surgical procedures used in diagnosis and treatment of the patients.

Result: The diagnosis of Tuberculous lymphadenitis achieved mainly by the clinical with support from results of histopathology after biopsy (74.47%) or FNAC (11.17%). Tuberculous lymphadenitis was seen in 12.34% of all notified TB cases and in 31.87% of extra-pulmonary tuberculosis cases in Iraq 188 patients included in the study, 135 (71.8%) female 53 (28.2%) male patients the mean age was 32.1 ± 18.8 year and cervical region involved in (65.43%).

Conclusion: In Iraqi patients, Tuberculous lymphadenopathy is the most common form of extrapulmonary tuberculosis, with cervical involvement representing the most common site of involvement. Tuberculous lymphadenopathy is a common disease, especially in the endemic area and should put in the differential diagnosis in the aetiology of LAD in different body regions. Its effect female more than male at age of thirty. Diagnosis mainly achieved by the different tissue sampling technique. Surgery role well-established in the diagnosis and treatment of complications, assisting in rapid relief of mass symptoms, but the role in the treatment of TLN with chemotherapy not yet well-known.

1. Introduction

Tuberculosis (TB) is still a major health problem, especially in developing countries. With 10 million people infected each year, it is considered one of ten major causes of death worldwide [1]. Extrapulmonary disease (ET) seen in 20% of patients of TB in the United States. Tuberculous lymphadenitis (TLN) represents a major form of ET seen in 30–40% of all cases of ET [2–4]. TLN occurs due to reactivation of previously latent disease in a previously infected lymph node (LN) or reinfection [5]. Miliary TB is also responsible for a minority of cases of TLN [5–7]. The infection reaches the LN in cervical region hematogenously and to the intraabdominal LN by ingestion of sputum or milk infected by Mycobacterium tuberculosis or Mycobacterium bovis or by contiguous spread, hematogenously or via lymphatic channels from lymphatic nodes elsewhere.

TLN is slightly more common in female than male (1.4:1) with the peak age of incidence between 30 and 40 years [8]. Cervical LN

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most commonly involved in up to 70% [9–12]. However, mediastinal, intraabdominal, axillary and inguinal LN are also involved. TLN usually present as non-tender chronic LN enlargement of single or multiple groups of LN either discrete or matted together, bilateral involvement is not uncommon [13,14]. LN usually up to 3 cm in size, but it can present as a large mass up to 8–10 cm [11]. TLN can be complicated by the formation of abscess (cold abscess) or draining sinus [10,15,16].

The systemic manifestations like fever, night sweat, and weight loss are variably reported in different studies in different countries with weight loss seen in 16%–60% of patients and fever reported in 19%–40% of patients, these constitutional symptoms significantly increased in human immunodeficiency virus (HIV) positive patients. Moreover, pulmonary TB present in 18–42% patient, while chest symptoms such as a cough and dyspnoea were seen in 10–19% [9,13].

Definitive diagnosis of TLN done by culture or by polymerase chain reaction (PCR) showing M. Tuberculosis in involved LN. However, culture need 2–4 weeks to show the results. Specimen for histopathology and acid-fast bacilli (AFB) smear can establish the diagnosis, especially in the endemic area with TB. Histopathological examination shows noncaseating granuloma, lymphoid cell infiltration, or Langerhans giant cell with caseous necrosis.

Fine needle aspiration cytology (FNAC) can be used first as its relatively safe and less invasive and more beneficial in an area where HIV and TB endemic. Excisional biopsy gives more diagnostic material and may give additional symptomatic relief, it's preferred over incisional biopsy, which may increase the rate of sinus tract formation. Chest x-ray (CXR) may show changes consisting with pulmonary TB in 10–40% of patients. Tuberculin skin test (TST) was positive in 74–100% [17,18], but the false positive result may be seen in patients with previous infection of TB or BCG vaccine which may produce reaction of 5–14 mm. HIV testing for a patient with TB should be done.

Treatment of TLN by antimycobacterial multidrug, the World Health Organization (WHO) new guideline for the treatment policy was based on directly observed therapy short course (DOTS). The new TB cases initially treated with 2 months of isoniazid (H), rifampicin (R), Pyrazinamide (Z), and Ethambutol (E) followed by 4 months of isoniazid and rifampicin [19]. the relapse rate after treatment completion may reach up to 3.5% of [20]. Combined surgical excision and antimycobacterial therapy may show better outcome [21,22].

1.1. Aims of the study

To evaluate the patients with tuberculous lymphadenitis and defined their incidence, demography, presentation, approach to diagnosis, the role of surgery in the diagnosis, treatment and outcome in Iraq.

2. Patients and methods

A retrospective study performed in the National specialized Centre for Respiratory and Chest Diseases in Baghdad, Iraq from the period between January to December 2016. The clinical, diagnostic and therapeutic data of 282 patients who were presented to the Centre with TLN. Ninety-six patients are excluded from the study due to incomplete clinical data, results, and investigations e.g. histopathological results.

The following data were collected from patients' records: gender, age, site of involvement of the affected LN, size of LN, characteristic, whether discrete, matted together, mass-like more than 5 cm presentation, abscess, and sinus formation. Systemic signs like fever and weight loss was collected, in addition to chest symptoms (e.g. cough, hemoptysis, and dyspnoea and chest pain).

Ideally the definitive diagnosis of TLN confirmed by the identification of Mycobacterium tuberculosis through culture or PCR. However, in Iraq, culture are highly costly and takes longer time to reach the diagnosis. Furthermore, PCR is not always available and therefore, it is use in the diagnosis of TB is limited. In our Iraqi patients, the diagnosis of TB is mainly done clinically with support from the histopathological examination of the biopsy or the FNAC. Therefore, the final diagnosis based on histopathological tests (excisional biopsy, incisional biopsy, FNAC), TST, and clinical based diagnosis, other ancillary investigations also recorded like HIV test or CXR and use of AFB stain on the pathological specimen.

Treatment regimens used in each patient reported. The treatment policy was based on DOTS course, as recommended by the WHO. For patients who were presented for the 1st time, the treatment regimen was antituberculous drugs for 6 months [2months Isoniazid (H) + Rifampicin (R) + Pyrazinamide (Z) + Ethambutol (E)] then 4 months (H + R). In relapsing patients (defined as those who have the recurrence of the disease after complete course of treatment and become disease-free) or defaulter (patients did not complete their treatment course) the treatment regimen was 2 months HRZES (streptomycin = S) +1 month HRZE+ 5 months HRE.

The information regarding the outcome of antituberculous therapy and types of surgical procedures used in the diagnosis and treatment also collected. Surgical options used in diagnosis and adjuvant to therapy of TLN were complete surgical excision where all the affected LN was excised, incomplete surgical excision used when TLN involve different LN groups which is remote from each other or bilateral or generalized involvement (It is not feasible to excised all LN in different groups so the excised only one or more LN in the accessible LN group), partial excision (incisional biopsy) in a patient where LN was large and adherent to surrounding structures and difficult to excise completely. Surgical drainage and biopsy in patients presented with abscess and aspiration of pus from affected LN. The procedures performed by authorized well trained surgeon from Baghdad city. (All of them have at least 5 years period of surgical training) The mean and the standard deviation were calculated.

3. Result

In Iraq, in the year 2016, the total number of notified patients with TB were 7317. Nearly 39% (2833) of them presented with ET. TLN was seen in 903 patients (represents 12.34% of all notified TB cases and 31.87% of those with ET). Baghdad city reported 282 patients with TLN [23], according to inclusion criteria we include 188 patients in the study, 135 (71.8%) female 53 (28.2%) male patients.

The mean age of incidence of TLN was (32.1 ± 18.8) year and most commonly affected age group by TLN were 25–44 year (67 patients 35.64%) and 45–64 year (41 patients 21.80%) (Table 1). The most commonly affected sites were cervical (65.43%) followed by

Table 1
Gender and age distribution of patients with tuberculous lymphadenitis.

Age group	Female	NO %	Male	NO %	Total	no %
<1 year	5	2.66%	8	4.26%	13	6.9
1–14 year	12	6.38%	11	5.58%	23	12.23
15–24 year	22	11.70%	13	6.91%	35	18.62
25–44 year	53	28.19%	14	7.45%	67	35.64
45–64 year	37	19.68%	4	2.13%	41	21.80
≥65 year	6	3.19%	3	1.606%	9	4.79
Total	135	71.81%	53	28.19%	188	100%

axillary, supraclavicular, intra-abdominal, generalized LN involvement, inguinal and mediastinal LN (Table 2). The most characteristic presenting shape of TLN was discrete LN involvement (59.04%) either single or multiple LN. The TB can affect more than one group of LN or even bilateral, followed by matted together LN in (18.62%) or even presented as a mass more than 5 cm in different sites of body 13.30%, while abscess formation was seen in (7.98%), sinus is seen only in 2 patients (1.06%) (Table 3). Systemic signs like fever seen in 15 patients (7.98%), weight loss 8 patients (4.26%) and Chest symptoms seen in 10 patients (5.32%).

Diagnosis mainly achieved clinically with support from results of histopathology examination obtained by excisional biopsy in 140 patients (74.47%) followed by FNAC in 21 patients (11.17%), incisional biopsy in 17 patients (9.04%), Tru–cut biopsy in 4 patients (2.13%), TST based-diagnosis (in relation to clinical background) in 3 patients (1.6%). Sometimes, clinician based their diagnosis on therapeutic trials (Therapeutic trial used in 3 patients (1.6%). This is accomplished by giving short course of anti-tuberculous drugs and then observe the response to treatment.

Histopathological results obtained in 182 patients in the study all of them showed features suggesting tuberculous infection (noncaseating granuloma, lymphoid cell infiltration, or Langerhans giant cell with caseous necrosis). However, 13 patients (7.14%) did not show all of these features (6 patient show chronic inflammatory infiltrate with non-caseating granuloma (3.23%), 4 patient show chronic inflammatory infiltrate with necrotic caseating material (2.2%), 3 patient show chronic inflammatory infiltrate with giant cells (1.65%).

Chest X-ray (CXR) performed in 75 patients (39.89%) and it was only positive in 8 patients (10.67%). HIV testing performed in 169 patients 89.89% all were negative. AFB stain test performed on the histopathological sample of 53 patients (28.19%), it was positive in 33 patients (62.26%) (Table 4).

The treatment policy was based on DOTS course, as recommended by the WHO. Treatment regimen was antituberculous drugs for 6 months duration (2months HRZE then 4 months H + R) for patients present for 1st time (171 patients, 91%). Patients who were relapsed or defaulter (17 patients, 9%), the treatment regime was 2 months HRZES+1 month HRZE+ 5 months HRE.

Table 2
Site of the tuberculous lymphadenitis involvement.

Site of LN involvement by TB	Patients No	%
Cervical	123	65.43
Axillary	24	12.77
Supraclavicular	17	9.04
Intra-abdominal	8	4.26
Generalized	6	3.19
Inguinal	5	2.66
Mediastinal	5	2.66
Total	188	100

Table 3
Mode of presentation (characteristic of L.N) and systemic signs.

Characteristic of LN	NO	%
Discrete	111	59.04
Matted	35	18.62
Mass like more than 5 cm in size	25	13.30
Abscess	15	7.98
Sinus	2	1.06
Systemic signs	**NO**	**%**
Fever	15	7.98
Weight loss	8	4.26
Chest symptoms	10	5.32

Various surgical options were used in diagnosis and as adjuvant to therapy of TLN. The main indication for surgical intervention was to provide material for histopathological and bacteriological examination when other means failed to reach the diagnosis. In addition, surgical intervention was implemented to give rapid symptomatic relief from the mass effect of the enlarging LN and to control the TLN local complications like abscesses or sinuses formation. The most common surgical option was complete surgical excision (121 patients 73.33%) where all the affected LN was excised followed by incomplete surgical excision in 19 patients (11.52%). Incomplete excision of TLN involved different LN groups which were remote from each other or bilateral or generalized involvement. It is not feasible to excise all LN in different groups so the surgeon excised only one or more LN in the accessible LN group. Partial excision (Incisional biopsy) was conducted in patients (7, 4.24%) who had large and adherent LN to the surrounding structures and difficult to excise completely. Surgical drainage and biopsy have been implemented in those patients presented with abscess formation (10, 6.06%) and those need aspiration of pus (8, 4.85%) (For localized collection of pus) from affected LN (Table 5).

Treatment program completed in 184 patients (97.87%), 4 patients defaulter (2.13%), 13 patients relapse after treatment (4.79%) and only 1 patient died (the cause of death unknown).

4. Discussion

TB is a leading cause of death from a single infectious agent in the world. TLN is the most common form of non-pulmonary TB. It constitutes an important cause of LAD especially in developing world where the tuberculous LN origin present in 22–43% [24,25] of all cases of lymphadenopathy, variation in this figure depending on the prevalence of TB in different countries. It can raise a diagnostic and therapeutic difficulty for the clinician as it may confuse with other serious causes of lymphadenopathy.

In 2016, TLN reported in 903 patients (12.34%) of all cases of TB notified in Iraq, representing 31.87% of all ET cases. While in the United States, in 2016, a total of 9272 TB cases were reported. TLN disease accounts 710 patients (35.8% of ET and 7.66% of all notified TB cases) [26]. Moreover, in Germany approximately 800 new TLN cases diagnosed per year and accounts for about 7.5% of all TB cases [17].

In India, TLN constitutes 35% of extrapulmonary TB, which comprises 15–20% of all cases of TB [27]. We may notice from the above studies that TLN remains the main form of ET disease. However, in developed countries, the percentage of TLN from total TB cases is less than developing countries including Iraq. This difference is due to higher prevalence of ET in Iraq (38.7% of all TB cases) [23] and other developing country in comparison to the developed countries, like USA (about 20% of TB cases were ET) [3]. However, there is a gradual increase in ET and TLN cases in the developed world. The difference in the extent of TLN disease in different geographic settings explained by different genetic groups of *M. tuberculosis* strains [28,29].

Female to male ratio in our study was **2.5:1**. Similarly, previous studies showed a female predominance with a various ratio [3,13,30,31]. However, pulmonary TB is significantly more common among males than females [2,3]. The reason for female predominance is not well known, it may relate to hormonal effect and mycobacteria genotype tropism [8,28,29].

The mean age of incidence of TLN was 32.1 ± 18.8 year with the peak age range of TLN in Iraq was 25–44 year (35.64%) which is compatible with most studies which show peak range from 30 to 40 years [3,11,31,32]. In the past, TLN was more common in children, but age range now shifts toward 30–40 years [33]. While in both Zambia and India (both endemic in TB) mean age of TLN is still in early twenty [13,34].

Table 4
The investigation used in diagnosis of tuberculous lymphadenitis and other supported investigations.

Test used in diagnosis of TLN	NO.		%			
Excisional biopsy	140		74.47			
Incisional biopsy	17		9.04			
FNAC	21		11.17			
Tru −cut biopsy	4		2.13			
TST	3		1.6			
Therapeutic trail	3		1.6			
Supportive investigations	NO. of patients whom performed the test	%	Positive test		Negative test	
Chest x-ray	75	39.89%	8	10.67%	67	89.33%
HIV	169	89.89%	zero		169	100%
Acid fast bacilli test	53	28.19%	33	62.26%	20	37.74%

Table 5
Surgical options used in diagnosis and therapy of tuberculous lymphadenitis.

Surgical option	NO.	%
Complete surgical excision	121	73.33
Incomplete surgical excision[a]	19	11.52
Partial excision (Incisional biopsy)	7	4.24
Surgical drainage and biopsy	10	6.06
Aspiration of pus.	8	4.85
Total	165	100

[a] When TLN involve different LN groups which remote from each other or bilateral or generalized involvement it's not feasible to excised all LN in different groups so the excised only one or more LN in accessible LN group.

In our study, cervical was the most commonly involved region with TB (65.43%). In line with previously published studies (45–79%) [9,24,30,35]. The other involved sites include: axillary, supraclavicular, intra-abdominal, generalized LAD and inguinal or mediastinal. Both Madegedara et al. [30] in Sri Lanka and Chen et al. [35] in Taiwan showed that the axillary region is the next commonly involved after cervical region (14.2%, 12.7%). In contrast, Dandapat et al. [24] showed that inguinal region was the most commonly involved region after the cervical. The possible reason why the cervical was the most commonly involved region is the very rich lymphatics in this area and the wide communication with the pulmonary region.

Physical examination reveals a firm, discrete LN in 59.04% of the patients, matted nodes fixed to surrounding structures in 18.62%. Large mass were reported in 13.30% (more than 5 cm in cervical, axillary, intraabdominal and mediastinal regions), abscesses in 7.98% and draining sinuses in 1.06% of patients. Physical finding of discrete lymphadenopathy was in most of other series representing most common presentation of TLN [8,36]except in Indian series [24,37] which show matted LN is dominant pattern (the natural history of TLN as disease progress to the LN periadenitis and become matted together and adhere to surrounding and later on may complicate by cold abscess which sometimes ruptures to form sinus).

The difference between studies regarding the physical finding of LN may be related to chronicity of disease, immune status of the patient, nutrition status and HIV infection [6,36,38]. Large masses, especially intraabdominal and mediastinal masses may cause diagnostic problem to the clinician because it might be confused with tumors.

Constitutional symptoms such as fever, weight loss, chest symptoms (like cough and hemoptysis) are not common in our patients. Other studies showed a great variation of constitutional symptom, ranging from zero to 40% [13,17,24,30,35,39]. The reason for this variation is not known. However, Shriner et al. report, in HIV-seropositive patients at the time of presentation, there were 63% of patients with fever and 90% with abnormal CXR. Most of these patients had evidence of advanced immune dysfunction, suggesting the role of the immune status of the patient in the development of constitutional and respiratory symptoms [9].

A definite diagnosis of TLN can be done by culture or by demonstration of mycobacteria tuberculosis by PCR from the tissue of affected LN along with histological examination such as lymphoid infiltrate, non-caseating granuloma, multinucleated giant cells or caseating necrosis and AFB test on retrieved specimen.

In Iraq, because bacterial culture might take a long time (2–4 weeks) to give results and our country is still endemic in TB, we depend mostly on histopathology to reach final diagnosis. Thus, most of our patients were diagnosed mainly by histopathological examination of the specimens mainly obtained by excisional biopsy (140 patients, 74.47%). FNAC was used for diagnosis in 21 patients (11.17%), which is less than other studies.

FNAC is appropriate for initial evaluation of cervical LAD to evaluate TLN. The advantage of FNAC appears to be maximized in the setting of HIV infection and in regions where the TB is endemic [9,16,37]. Dandapat et al. [24] showed that FNAC give a positive diagnosis in 83% of cases, a false negative result in 14% and equivocal results in 3%; the technique did not result in complications. Biopsy of the LN gave histopathological confirmation in all cases; 80% of patients had caseating and 20% had non-caseatingesions. In a series in Hong Kong to evaluated TLN, FNAC show a good sensitivity and specificity (77 and 93%, respectively) [40].

In Iraq most of the cases of TLN referred from the surgical unit where most of surgeons preferred to take a biopsy to confirm diagnosis. That gives an explanation why final diagnosis was mostly performed by biopsy (this may be due to stress on the Iraqi surgeon to give definite diagnosis and elimination of serious causes of LAD like malignancy especially in regions like abdomen and mediastinum).

Madegedara et al. [30] in Sri Lanka similar to our study, showed 73% of patients referred from the surgical unit after surgical biopsy while FNAC was performed in 10.53%. The use of PCR in the detection of Mycobacterium tuberculosis in lymph node aspirates increase the value of FNAC in diagnosis TLN [41].

Incisional biopsy performed in our study in 17 patients (9.04%) which is usually not the preferred method in tissue diagnosis as it may cause sinus formation or ugly scar, wound infection [42], in our study incisional biopsy usually reserved to abscesses, large or adherent mass which was difficult to resect completely. Tru cut biopsy performed in 4 patients (2.13%) it seems a promising technique which is less invasive than the surgical biopsy and provides more tissue material for histological and microbiological assessment.

We have 6 patients diagnosed without histopathological confirmations 3 (1.6%) with strongly positive TST combined with clinical feature suggest TLN and 3 (1.6%) patients were diagnosed based on the clinical setting and trial therapy, which was successful, the value of TST in our country, not very high due to wide National program of BCG vaccination and relatively high prevalence of TB in

Iraq (43/100 000). However, strong positive TST may support diagnosis, especially in adult or unvaccinated patients.

The Xpert MTB/RIF assay is a rapid, automated molecular test with high detection accuracy for pulmonary TB, WHO now recommends the use of Xpert for the diagnosis of TB in lymph nodes and other tissues [43].

Acid-fast bacilli stain test performed only in 53 (28.19%) patient samples (FNAC, tissue biopsy, pus) and it was positive in only 33 patient (62.26%), the test yield more in a sample of tissue for excisional biopsy (75% positive AFB) than FANC (23% positive AFB), in other series AFB was performed in only 11%–55% of biopsy specimens; however, positive AFB stain test provides further support for the diagnosis of TLN [18,30,35]. AFB smears of FNA specimens from HIV-seropositive individuals, Usually show the presence of abundant organisms [6].

In our study relapse was relatively low 4.79%, other series show relapse rate slightly lower than our study (3–3.5%) [20,30]with residual node after treatment completion in 7–10% [20,24,30,35], which does not necessarily indicate disease recurrence but it may occur due to host response to dead bacilli [44].

Various surgical procedure performed in our study to reach a diagnosis and assist in therapy in TLN including surgical excision (complete and incomplete) in 73.33%, and 11.52%, respectively, Partial excision (Incisional biopsy) (4.24%), incision and drainage (6.06%) and local aspiration of pus from affected LN (4.85%), The role of surgery well established in diagnosis (especially in intra-abdominal and mediastinal regions) and treatment of local complication like abscess and sinus formation. In another series, there is controversy about the role of surgery, especially in the treatment of TLN, ammari et al. [42] showed that in his retrospective study report 9 patients (15%) were diagnosed by excisional biopsy were complicated by wound infection and deforming scar without defining degree or rate of these complications.

Cheung et al. [45] in his prospective study in surgical treatment of TLN abscess with total period of follow up of 2 years showed that incision and drainage procedure carried a high complication rate (74%) like persistent draining sinus in comparing to local total excision with 94% without local complication, Hawkey et al. [22] show in his series that patients who undergo surgical intervention associated with shorter paradoxical upgrading reaction period than other patients (46 vs. 92 days). Suggesting that surgery is well established in the diagnosis of TLN especially in the equivocal and difficult regions and may help in the treatment of local complications of TLN or persistent LN TO RELIEF discomfort of the patient.

Finally, we state that the work has been reported in line with the SCARE criteria [46].

SCARE 2018 Checklist

Topic	Item	Checklist item description	Page Number
Title	1	The Tuberculous lymphadenitis in Baghdad city: a review of 188 cases.	1
Key Words	2	Extrapulmonary tuberculosis, tuberculous lymphadenitis, fine needle aspiration cytology, excisional biopsy.	1
Abstract	3a	Tuberculosis is still a major health problem in the world, Iraq still one of the endemic country with tuberculosis with incidence 43/100000 population. Tuberculous lymphadenopathy considers the most common extrapulmonary manifestation of tuberculosis. The role of surgery is well established in diagnosis but still not clear in therapy.	1
	3b	Tuberculous lymphadenitis w usually present as non-tender chronic LN enlargement of single or multiple groups of LN either discrete or matted together, bilateral involvement not uncommon.Tuberculous lymphadenitis can present as abdominal or mediastinal mass which raise diagnostic difficulty to clinician.	
	3c	Diagnosis achieved mainly by clinical with support from results of histopathology after biopsy or FNAC {excisional biopsy in (74.47%) followed by FNAC in (11.17%)}.surgery also rapid symptomatic relief from the mass effect of enlarging LN and control of TLN local complications like an abscess or sinus formation.	
	3d	**Conclusion** — Tuberculous lymphadenopathy is a common disease, especially in the endemic area and should put in the differential diagnosis in the aetiology of LAD in different body regions. Its effect female more than male at age of thirty. Diagnosis mainly achieved by the different tissue sampling technique. Surgery role well-established in the diagnosis and treatment of complications, assisting in rapid relief of mass symptoms, but the role in the treatment of TLN with chemotherapy not yet well-known.	
Introduction	4	Tuberculosis (TB) is still a major health problem, especially in developing countries with 10 million people infected each year, it is considered one of ten major causes of death worldwide 1. Extrapulmonary disease (ET) seen in 20% of patients of TB in the United States, tuberculous lymphadenitis (TLN) represents a major form of ET was seen in 30–40% of all cases of ET 2, 3, 4. The pathogenesis of TLN due to reactivation of previously latent diseases in a previously infected lymph node (LN) or reinfection 5, 6, 7. The infection reach LN in cervical region hematogenously and to the intraabdominal LN by ingestion of sputum or infected milk. Definitive diagnosis of TLN done by culture or by polymerase chain reaction PCR showing M. Tuberculosis in involved LN. However, culture need 2–4 weeks to show the results. Specimen for histopathology and acid-fast bacilli (AFB) smear can establish the diagnosis, especially in the endemic area with TB.	2
Patient Information	5a	**Demographic details** – 188 patients in the study, 135 (71.8%) female 53 (28.2%) male patients. All patients are Iraqi ethnicity except one who is worker from Bangladesh	**3**
	5b	**Presentation** - TLN usually present as non-tender chronic LN enlargement of single or multiple groups of LN either discrete or matted together, bilateral involvement not uncommon.LN usually up to 3 cm in size, but it can present as a large mass up to 8–10 cm, TLN can complicate by abscess formation (cold abscess) and draining sinus (patient usually referred by family physician, except for abscess came walked into Emergency room).	
	5c	Any Past medical or surgical history obtained, and relevant outcomes from interventions.	
	5d	Any patient's pharmacological history including allergies, psychosocial history (Drug, smoking, family history were obtained.	
Clinical Findings	6	Site of involvement of the affected LN, size of LN, characteristic, whether discrete, matted together, mass-like more than 5 cms presentation, abscess, and sinus formation.	4
Timeline	7	patients who present with TLN in Baghdad city are collected from the period between 1/1/2016 to 31/12/2016	3
Diagnostic Assessment	8a	**Diagnostic methods** – Final diagnosis based on histopathological tests (excisional biopsy, incisional biopsy, FNAC), TST, and clinical based diagnosis, other ancillary investigations also recorded like HIV test or CXR and use of AFB stain on the pathological specimen.	4
	8b		

(*continued*)

SCARE 2018 Checklist			
Topic	Item	Checklist item description	Page Number
		Diagnostic challenges – Ideally the definitive diagnosis of TLN by the identification of Mycobacterium tuberculosis, by culture or PCR. But because culture takes longer time and high cost and limited used of the PCR, The diagnosis has been mainly clinical with support from the results of histopathology after biopsy or FNAC.	
	8c	**Diagnostic reasoning** – TLN should put in the differential diagnosis in the aetiology of LAD in different body regions and it can represent diagnostic challenge to clinician to differentiate it from malignant mass in different site in the body,	
	8d	Prognostic characteristics when applicable: Nil.	
Therapeutic Intervention	9a	It was retrospective study were the patients optimized by their surgeon and doctors in the National specialized Centre for respiratory and chest diseases in Baghdad before intervention.	4–5
	9b	**Interventions** – surgery used to obtained histopathological material by either excisional biopsy, incisional biopsy. Or by used of FNAC and TRU-cut biopsy. or surgery may use for treatment of TLN complications e.g. abscess formation	
	9c	**Intervention details** – Surgical options used in diagnosis and adjuvant to therapy of TLN were complete surgical excision where all the affected LN was excised, Incomplete surgical excision used When TLN involve different LN groups which remote from each other or bilateral or generalized involvement, it's not feasible to excised all LN in different groups so the excised only one or more LN in the accessible LN group, partial excision (Incisional biopsy) in a patient where LN was large and adherent to surrounding structures and difficult to excised completely, Surgical drainage and biopsy inpatient present with abscess and Aspiration of pus from affected LN. Treatment regimens used in each patient reported. The treatment policy was based on DOTS course, as recommended by the WHO. Treatment regime was antituberculous drugs for 6 months duration (2 moths Isoniazid (H) + Rifampicin (R) + Pyrazinamide (Z) + Ethambutol (E) than 4 months H + R) for patients present for the 1st time, while the treatment regimen in patients who relapse (patient's disease reoccur after a complete course of treatment and patient become disease-free) or defaulter (patients did not complete their treatment course) was 2 months HRZES (streptomycin = S) +1 month HRZE+ 5 months HRE.	
	9d	Who performed the procedure – the procedures performed by authorized well trained surgeon from Baghdad city.(All of them have at least 5 years period of surgical training)	
	9e	nil	
Follow-up and Outcomes	10a	**Follow-up** – 18 months period of follow up (study from 1/1/2016 to 31/12/2016 and data collected at august 2018) the size of LN and imaging technique used in the follow up.	4–5
	10b	**Outcomes** - Treatment program completed in 184 patients (97.87%), 4 patients defaulter (not complete their treatment)(2.13%), 13 patients relapse after treatment (4.79%) and only 1 patient died (the cause of death unknown).during 18 months follow up period	
	10c	**Intervention adherence/compliance** - Treatment program completed in 184 patients (97.87%), 4 patients defaulter (2.13%)(not complete their treatment)	
	10d	**Complications and adverse events** – all complications and adverse or unanticipated events were reported.	
Discussion	11a	**Strengths** – we include 188 case of TLN in the study giving evaluation to the patients with tuberculous lymphadenitis and defined their incidence, demography, presentation, approach to diagnosis, and the role of surgery in the diagnosis, treatment and outcome in Iraq. And it can part of feature meta-analysis.	6–8
	11b	**Weaknesses and limitations in your approach to this case**. Ideally the definitive diagnosis of TLN by the identification of Mycobacterium tuberculosis, by culture or PCR. But because culture takes longer time and high cost and limited used of the PCR, The diagnosis has been mainly clinical with support from the results of histopathology after biopsy or FNAC.	
	11c	TB is a leading cause of death from a single infectious agent in the world. TLN is the most common form of non-pulmonary TB, it constitutes an important cause of LAD especially in developing world where the tuberculous LN origin present in 22–43%24,25 of all cases of lymphadenopathy, variation in this figure depending on the prevalence of TB in different countries. It can raise a diagnostic and therapeutic difficulty for the clinician as it may confuse with other serious causes of lymphadenopathy. In Iraq at 2016 TLN reported in 903 patients (12.34%) of all cases of TB notified in Iraq, representing 31.87% of all ET cases, while in the United States In 2016 a total of 9272 TB cases was reported, TLN disease accounts 710 patients (35.8% of ET and 7.66% of all notified TB cases) 26 and in Germany approximately 800 new TLN case per year and accounts for about 7.5% of TB cases 17. In India TLN constitutes 35% of extrapulmonary TB, which comprises 15–20% of all cases of TB27, we notice from all these series that TLN remains the main form of ET disease, but in western developed country's percentage of TLN from total TB cases is less, this difference because of higher prevalence of ET in Iraq (38.7% of all TB cases) 23 and other developing country in comparison to western developed countries like USA (about 20% of TB cases were ET) 3 but there is a gradual increase in ET and TLN cases in these countries. The difference in the extent of TLN disease in different geographic settings explained by different genetic groups of *M. tuberculosis* strains 28, 29..	
	11d	Tuberculous lymphadenopathy is a common disease, especially in the endemic area and should put in the differential diagnosis in the aetiology of LAD in different body regions. Its effect female more than male at age of thirty. Diagnosis mainly achieved by the different tissue sampling technique. Surgery role well-established in the diagnosis and treatment of complications, assisting in rapid relief of mass Its effect female more than male with the mean age of incidence of TLN was 32.09 ± 18.8 years, but it can affect any age group from infancy to elderly patients.	
	11e	**The primary "take-away"** The TLN is still a common problems and should be it in mind in differential diagnosis of LAD in different body regions.	
Patient Perspective	12	Nil, it was retrospective study performed on the data of the patients from National specialized Centre for respiratory and chest diseases. There was no direct patient interview.	
Informed Consent	13	Nil, it was retrospective non interventional study done on the data from National specialized Centre for respiratory and chest diseases where the patients already had intervention previously	
Additional Information	14	Conflicts of Interest = nil.	

5. Conclusion

TLN is still the most common form of ET, with cervical involvement representing the most common site of involvement. TLN is a common disease, especially in the endemic area with TB and should put in the differential diagnosis in the aetiology of LAD and masses in different body regions.

Its effect female more than male with the mean age of incidence of TLN was 32.09 ± 18.8 years, but it can affect any age group from infancy to elderly patients.

TLN most commonly presents as discrete LAD unilateral or bilateral or may present LAD matted together or as mass more than 5 cm in different body regions representing a diagnostic problem for the clinician.

Diagnosis mainly based on histopathology by using the different tissue sampling technique. Surgery role well established in the diagnosis and treatment of complications, assisting in rapid relief of mass symptoms, but the role in the treatment of TLN with chemotherapy not yet well known.

Learning points

- TLN is still a common disease, especially in the developing world and should be put in mind in the differential diagnosis of the LAD and masses in different body region.
- TLN affects female more than male with an incidence at age of thirty (previously disease of childhood).
- Still histopathology play a crucial role in diagnosis of TLN in developing countries and there is need to increase the use of more advance technique in diagnosis.
- Surgery role well established in the diagnosis and treatment of complications, assisting in rapid relief of mass symptoms, but the role in the treatment of TLN with chemotherapy not yet well known. And need further study to clarify the role of surgery in the treatment of TLN.

Ethical approval

Ethical approval was given by the ethical committee of Department of surgery/College of Medicine/Almustansiriyah University.

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Nil.

Author contribution

The study was designed and the data collected and analyzed by the all 3 authors, all of us contribute evenly to all parts of this paper.

Conflict of interest statement

Nil.

Guarantor

Dr hasanain abdulameer jasim as the contributing author.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijso.2018.12.001.

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