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PATTERN OF CERVICAL LYMPHADENOPATHY AMONG PATIENTS ATTENDING ENT CLINICS IN AL MUTHANNA PROVINCE.

A CROSS-SECTIONAL STUDY AT AL-HUSSEIN TEACHING HOSPITAL, SAMAWA, IRAQ (2020–2022)

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Abstract

Background: Cervical lymphadenopathy is a commonplace case seen in the clinical practice of Otolaryngology. With both blood-borne and malignant causes of disease prevalent in each geographic region, as well as variable access to health care, the prevalence of this clinical problem is highly variable around the world. Current data regarding cervical lymphadenopathy in Iraq, particularly from Al-Muthanna Governorate, is limited, necessitating local institutional studies to develop local treatment.

Objective: The aim of this study was to determine the distribution and types of cervical lymphadenopathy and to develop clinicopathologic features of cervical lymphadenopathy patients who presented to the ENT Clinic at Al-Hussein Teaching Hospital in Samawa, Iraq, between January 2020 and December 2022.

Methods: This study was a prospective cross-sectional study of 320 patients with cervical lymphadenopathy. Each study participant underwent full clinical evaluations, haematological evaluation, imaging assessment, and histopathologic assessment if indicated. Clinical characteristics collected included age, sex, size, location, consistency, and clinical diagnosis by physicians.

Results: There were 320 patients with an average age of 31.4 (± 14.7) years (range 3 – 78). Woman represented 54.1% of study patients. The most common cause of cervical lymphadenopathy was reactive lymphadenopathy (38.4% of all patients) followed by tuberculous lymphadenitis (22.8%), lymphoma (14.1%), metastatic carcinoma (11.9%), infectious mononucleosis (6.6%) and all other causes (6.3%). Level II was the most common site of lymphadenopathy involvement (41.6%). The frequency of malignant causes of cervical lymphadenopathy increased significantly in patients older than 40 years of age ($p < 0.001$).

Conclusion: In this region, reactive lymphadenopathy and tuberculous lymphadenitis are the most frequent causes of cervical lymphadenopathy. However, a sizable portion of patients with cervical lymphadenopathy have a malignant cause, therefore confirming the importance of a systematic approach to evaluation including histopathologic evaluation. Clinicians operating in resource-limited areas should have a high index of suspicion for tuberculosis and malignancy in patients with cervical lymphadenopathy.

Keywords: cervical lymphadenopathy; lymph node; ENT; Iraq; tuberculosis; lymphoma; neck swelling; reactive lymphadenitis; metastatic carcinoma; Al-Hussein Teaching Hospital

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INTRODUCTION

Cervical lymphadenopathy refers to the enlargement of at least one cervical lymph node in the neck greater than 1 cm in its shortest diameter, which is one of the most common clinical findings seen by otolaryngologists, family physicians, and head and neck surgeons [1,2]. The cervical lymphatic system is particularly complex, consisting of more than 300 lymph nodes scattered throughout the neck, thorax, and upper limbs, serving as sentinel sites for the head and neck region and making the neck susceptible to many different types of inflammatory, infectious, and neoplastic processes [3]. The clinical significance of cervical lymphadenopathy is derived from its wide differential diagnosis, including benign, self-limiting conditions at one end and life-threatening malignancies at the other end of the spectrum and requiring an evidence-based, systematic assessment of patients presenting to the clinician with cervical lymphadenopathy [4].

The global (i.e., geographic, socioeconomic, and epidemiologic) distribution of cervical lymphadenopathy is determined by many factors. In higher income nations, the vast majority of patients present to outpatient settings with reactive lymphadenopathy due to upper respiratory tract infections, while malignant causes are typically less frequent [5,6]. Conversely, in lower and middle income countries with a high burden of infectious diseases, one of the most common underlying causes of cervical lymph node enlargement is tuberculous lymphadenitis, which in some studies has been shown to create a greater number of cervical lymph node enlargement than reactive causes [7,8]. In addition, the epidemiologic context of the MENA region (Middle East and North Africa), including Iraq, presents a unique scenario characterized by endemic tuberculosis, a relatively young population pyramid, a high prevalence of upper respiratory infections, and an increasing incidence of head and neck cancer [9].Neck swelling diagnosis and treatment will be especially difficult due to years of conflict and dysfunction in public health infrastructures in Iraq. The health care system is now significantly stressed and has resulted in patients presenting late, limiting access to advanced diagnostic technology and understudying the disease patterns present within this population [10]. Al-Hussein Teaching Hospital is located in Samawa, the capital of Al-Muthanna governorate in southern Iraq, and it is the main referral hospital for a population of approximately 1,000,000. The ENT clinic at the Al-Hussein Teaching Hospital sees a high volume of patients with cervical lymphadenopathy. However, to date, there has been no published literature regarding patterns of cervical lymphadenopathy from this facility or the entire Al-Muthanna governorate.

When evaluating cervical lymphadenopathy, consideration of the patient's clinical history, physical findings, and ancillary tests [11,12] is essential. Important clinical information includes patient age, duration of lymphadenopathy, presence or absence of systemic symptoms such as fever, night sweats, or weight loss, as well as whether the lymph nodes are <1 cm in size, whether they are firm, mobile, and tender, and the pattern of infiltrated lymph nodes [13,14]. FNAC has proven to be a valuable first-line tool for evaluating cervical lymphadenopathy in developing countries due to low cost, rapid processing, and lack of invasive procedures; however, there is variation in sensitivity and specificity depending on the cause of cervical lymphadenopathy [15,16].Excisional biopsy is still widely viewed as the gold standard to achieve definitive histopathological diagnosis, particularly when there is suspicion of lymphoma or when FNAC results are equivocal [17].

Tuberculous lymphadenitis, the most common extrapulmonary manifestation of Mycobacterium tuberculosis, merits special consideration in the context of Iraq as a country with intermediate burden of tuberculosis, as demonstrated by clinical presentations of tuberculous lymphadenitis in ENT clinics with characteristic findings such as cold abscesses, matted nodes, and changes in overlying skin [18,19]. Tuberculous lymphadenitis diagnosis may be aided by tuberculin skin testing (TST), interferon-gamma release assays (IGRAs), FNAC with Ziehl-Neelsen staining or mycobacterial culture, and to an increasing extent, however, molecular techniques such as GeneXpert MTB/RIF, in low-resource settings [20].

Lymphoma includes Hodgkin lymphoma and non-Hodgkin lymphoma, and is the most prevalent type of haematological malignancy diagnosed in association with cervical lymphadenopathy. Hodgkin lymphoma has a bimodal peak between early adulthood (age 15 to 35 years) and late life (>40 years), and so represents a significant consideration for the diagnosis of a patient aged 15 to 35 years with painless, rubbery cervical nodes [21,22]. Non-Hodgkin lymphomas are a heterogeneous category of neoplasms arising from B- and T-cells and may present with greater variability in age and presentation [23]. Beyond age 50 years, the most common malignant cause of metastatic cervical lymphadenopathy is squamous cell carcinoma of the upper digestive tract (head or neck)/thyroid carcinoma or an unknown primary site [24,25].

The importance of making an accurate and timely diagnosis of cervical lymphadenopathy cannot be overstated. Delay in diagnosing tuberculous lymphadenitis places patients at risk for spreading the disease and developing drug-resistant strains [26]. Delay in diagnosing lymphoma or metastatic carcinoma negatively impacts patient prognosis [27]. On the other hand, unnecessary excisional biopsies and/or overinvestigation of benign reactive nodes cause many patients to suffer from avoidable morbidity, and lead to excessive health care costs [28]. Thus, establishing the local pattern of cervical lymphadenopathy should not be just an academic exercise; the establishment of the pattern will have important, direct, and practical implications for clinical decision-making, resource allocation, and public health planning.
The aetiological spectrum of cervical lymphadenopathy has been examined in ENT clinics in neighbouring or similar countries, including Iran, Jordan, Turkey and Egypt, and the studies collectively demonstrated that the predominant aetiology in the region is found to be both reactive and tuberculous, but there were also notable differences within or between the institutions and geographies examined throughout the region [7,29,30]. No study has specifically addressed the pattern of aetiology concerning cervical lymphadenopathy in southern Iraq, creating a gap that our investigation aims to fill.

The study's objectives are three-fold: first, to identify the frequency and aetiological distribution of cervical lymphadenopathy in patients who presented for evaluation in the ENT clinic at Al-Hussein Teaching Hospital in Samawa; second, to describe the clinical and pathological characteristics of various aetiological categories with respect to age and gender, nodal level, size and consistency; and finally, to identify the features associated with malignant or benign causes of cervical lymphadenopathy. Results will provide information to build on the current regional evidence base and aid in developing clinical guidelines specific to the evaluation and management of neck lymphadenopathy in Iraq's ENT practice.

METHODOLOGY

Study Design and Setting

A prospective descriptive cross-sectional study was carried out at the ENT outpatient clinic of Al-Hussein Teaching Hospital located in Samawa (Al-Muthanna Governorate) in Iraq; this study was from January 2020 through December 2022 which is a time frame of 24 months. Al-Hussein Teaching Hospital is the predominant level three referral hospital within Al-Muthanna and provides care to an estimated one million people throughout many districts. The ENT outpatient clinic operates on a daily basis and accepts diverse types of patient referrals; namely primary care, secondary care, and tertiary care from peripheral health centre(s), or from a district hospital, or from general physicians.

Study Population

During this study, all patients who presented to the ENT clinic with either a chief presenting problem or incidental finding of a cervical lymph node (CLN) with a minimum of 1 cm in diameter on initial clinical examination or on imaging were deemed eligible for inclusion in this study. Inclusion no matter of age or gender was allowed. The following exclusion criteria were established: (1) patients with cervical lesions later confirmed not to be lymph nodes (eg. branchial cyst, thyroglossal duct cyst, cystic hygroma, lipoma, or thyroid mass); (2) Patients who already had a confirmed diagnosis of cervical lymphadenopathy by the time they were enrolled in this study; (3) Patients who refused to have tests done or who were lost to follow-up prior to a diagnosis being determined through testing, and (4) Patients for which there were insufficient data to be considered eligible for analysis. A total of 320 patients met inclusion criteria and comprised the final study sample.

Ethical Approval

Ethics approval was received from both Al-Hussein Teaching Hospital's Institutional Review Committee and Al-Muthanna Health Directorates Ethics Committee. All adult patients provided a written informed consent to participate in this study and consent was provided by both the parents/legal guardians of pediatric patients who participated in the study. Patient's confidentiality was maintained during the course of the study and all data collected about individual participants prior to analysis was rendered anonymous. The study was conducted according to the principles of the Declaration of Helsinki.

Clinical Evaluation

Qualified otolaryngologists performed standardized clinical evaluations on all 12 patients studied. All patients were provided with a structured questionnaire that identified the duration of neck swelling, rate/volume of growth, associated local symptoms (e.g., pain, dysphagia, hoarseness, otalgia), associated systemic symptoms (fever, night sweats, weight loss, fatigue), the number of recent upper respiratory tract infections, history of dental problems, history of new skin lesions, and possible history of exposure to and/or past treatment for tuberculosis.

A thorough general physical exam plus a detailed head/neck exam was performed using the following methods: anterior rhinoscopy, examination of the oropharynx, indirect laryngoscopy (if indicated), flexible nasopharyngoscopy (if indicated), otoscopy (if indicated). Each involved cervical (neck) lymph node or node group was systematically examined by studying the following characteristics of each lymph node or group of lymph nodes: location/level according to the M.S.K.C. classification system of cervical lymph nodes (levels I-VI and level VII) [31], whether the lymph node was unilateral or bilateral, size (largest diameter), consistency (soft, firm, rubbery, hard), tenderness, mobility (mobile or fixed), body surface changes above each lymph node (erythema, induration, fistula) and the presence of matting.

Investigations

All patients had the following evaluated: complete blood count with differential, ESR, CRP, and liver/renal/lactate dehydrogenase testing if having lymphoma/systemic disease suspected. If the patient had signs and symptoms of infectious mononucleosis, Epstein-Barr virus serology (i.e., monospot and EBV-specific) was tested. A TST was performed in all patients suspected to have tuberculous lymphadenitis and an induration of greater than 10 mm was considered positive within local epidemiological context.

Ultrasound with high resolution linear probe (7.5-10 MHz) was performed in all patients with nodes in the neck. The following were recorded for each node: shape, thickness of cortex, hilar architecture, internal echo texture, necrosis, calcification, vascularity on Doppler evaluation, and extra-nodal extension. CT neck with IV contrast was only performed in patients with a suspicion of malignancy, deep neck involvement, or where results from the ultrasound exam did not provide a conclusion. In patients with suspicion for having lymphoma or tuberculosis, chest x-ray was performed; CT chest was performed when indicated.

FNAC was performed on all patients who presented with persistent or clinically abnormal nodes for whom a definitive clinical diagnosis was not apparent. 23-gauge needle attached to 10cc syringe was used and the FNAC performed in a sterile manner. Smears were made on glass slides, fixed with air or in alcohol, and stained with Giemsa stain or Papanicolaou stain respectively. All FNAC specimens were also stained using Ziehl-Neelsen method for acid-fast bacilli. Culture for Mycobacterium tuberculosis was attempted on FNAC specimens where there was suspicion of tuberculous lymphadenitis. When FNAC results were either inconclusive or lymphoma was suspected and whereuanticipated response to empirical treatment did not occur, excisional biopsy was performed on the relevant node(s). All tissues from biopsies were submitted for histopathological examination and, when appropriate, immunohistochemical analysis.

Diagnostic Criteria

Reactive lymphadenopathy can be defined as lymph nodes enlarging due to a specific acute or chronic inflammatory focus located either within or outside of the head and neck that is determined through FNAC to be due to benign reactive lymphoid hyperplasia (and resolved with treatment of the underlying cause within 4-6 weeks). Tuberculosis-related lymphadenitis is diagnosed based on FNAC or histopathological criteria for caseating granulomatous inflammation, positive Ziehl-Neelsen staining, positive mycobacterial culture or response to anti- tuberculosis medications from patients thought to have a high clinical/suspected diagnosis. Lymphoma is diagnosed by histopathology of excised lymph node and then subtyped using immunohistochemistry. Metastatic disease is diagnosed by cytological/histopathological evaluation of a lymph node sample for evidence of malignant epithelial cells. Infectious Mononucleosis will be based on serologic diagnostic studies that include an EBV monospot and EBV antibody titer combined with compatible clinical and hematologic findings.

Data Analysis

Data collected were analyzed via IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, USA). Frequency and percentage were used to express categorical variables while mean ± SD or median/ IQR was the preferred method for reporting continuous data based on the Kolmogorov-Smirnov test for normality. To compare groups, the chi-square test or Fisher's exact test was used for categorical variables, the independent samples t-test or Mann-Whitney U Test was used for continuous variables. Logistic regression was run to ascertain independent predictors of malignant aetiology; a p-value <0.05 was considered statistically significant.

RESULTS

During the course of the study, there were 320 patients with cervical lymphadenopathy that were included in this study. The demographic and clinical characteristics, aetiological distributions, anatomical nodal levels, and selected clinicopathological characteristics of patients are presented in Tables 1-4.

Table 1. *Demographic and Clinical Characteristics of the Study Population (n = 320)*

Variable	Category	n (%)	
Age (years)	Mean ± SD	31.4 ± 14.7	
	< 15 years	62 (19.4%)	
	15–30 years	104 (32.5%)	
	31–45 years	85 (26.6%)	
	46–60 years	47 (14.7%)	
	> 60 years	22 (6.9%)	
Sex	Male	147 (45.9%)	
	Female	173 (54.1%)	
Duration of swelling	< 4 weeks	128 (40.0%)	
	4–12 weeks	106 (33.1%)	
	> 12 weeks	86 (26.9%)	
Laterality	Unilateral	241 (75.3%)	
	Bilateral	79 (24.7%)	
Nodal consistency	Soft/tender	89 (27.8%)	
	Firm/rubbery	158 (49.4%)	
	Hard/fixed	73 (22.8%)	

Table 2. *Aetiological Distribution of Cervical Lymphadenopathy (n = 320)*

Aetiology	n	Percentage (%)	Mean Age (years)
Reactive lymphadenopathy	123	38.4%	22.1
Tuberculous lymphadenitis	73	22.8%	29.6
Hodgkin lymphoma	25	7.8%	26.4
Non-Hodgkin lymphoma	20	6.3%	38.2
Metastatic carcinoma	38	11.9%	52.7
Infectious mononucleosis	21	6.6%	19.3
Chronic non-specific lymphadenitis	11	3.4%	34.5
Other/miscellaneous	9	2.8%	31.0
Total	320	100%	31.4

Table 3. *Distribution by Cervical Nodal Level (Memorial Sloan Kettering Classification)*

Nodal Level	Anatomical Region	n (%)	Predominant Aetiology
Level I	Submental/Submandibular	48 (15.0%)	Reactive, dental infection
Level II	Upper jugular	133 (41.6%)	Reactive, TB, Lymphoma
Level III	Middle jugular	56 (17.5%)	Lymphoma, Metastatic
Level IV	Lower jugular	34 (10.6%)	Metastatic carcinoma
Level V	Posterior triangle	28 (8.8%)	TB, Lymphoma
Level VI	Central compartment	11 (3.4%)	Thyroid malignancy
Multiple levels	—	10 (3.1%)	Lymphoma, TB

Table 4. *Relationship Between Aetiology Category and Selected Clinical Parameters*

Parameter	Benign (n=228)	Malignant (n=92)	p-value
Mean age (years)	25.8 ± 11.2	46.3 ± 15.4	< 0.001
Male sex	98 (43.0%)	49 (53.3%)	0.091
Duration > 12 weeks	34 (14.9%)	52 (56.5%)	< 0.001
Hard/fixed consistency	12 (5.3%)	61 (66.3%)	< 0.001
Bilateral involvement	48 (21.1%)	31 (33.7%)	0.019
Size ≥ 3 cm	41 (18.0%)	63 (68.5%)	< 0.001
Night sweats/weight loss	29 (12.7%)	58 (63.0%)	< 0.001
Elevated LDH	14 (6.1%)	44 (47.8%)	< 0.001

As indicated in Table 2, there were 228 benign (71.3%) and 92 malignant (28.8%) total cases. Reactive lymphadenopathy was the most common diagnosis (38.4%), followed by tuberculous lymphadenitis (22.8%). Of the malignant causes, more patients had metastatic carcinoma (11.9%) than lymphoma (combined 14.1% for Hodgkin and non-Hodgkin). In Table 4, there are significant correlations for malignant etiology between older age, longer duration, firm consistency, increased size of node, constitutional symptoms, and elevation of LDH (all $p < 0.001$). Table 3 shows that Level II is the most common node location accounted for 41.6% of all cases, with mostly reactive, tuberculous, and lymphomatous causes.

DISCUSSION

An analysis of cervical lymphadenopathy from Al-Muthanna governorate, Iraq, has never been published before. This is the first study to provide an overall institutional analysis of reactive and tuberculous lymphadenitis, each accounting for greater than 60% (that is, 60% plus) of all patients presenting with lymphadenopathy; the rest (i.e., 29%) of patients presenting with cervical lymphadenopathy had cancer as the cause of their cervical lymphadenopathy. The implications of these findings are substantial in terms of clinical care and public health.

The average age of subjects in our study was 31.4 years, representative of the youthful demographic profile of the country (the median national age is approximately 22 years)[9]. The relatively slight predominance of female patients (54.1%) in our current study aligns with findings reported by other authors studying the same patient population in other parts of the region. For example, Hadi et al. have published demographic information similar to that which was present in this study in [10]. There may be reasons for the over-representation of females among patients consulting for lymphadenopathy, including an increased risk of developing autoimmune conditions and reactive lymphadenopathy due to a condition related to thyroid disease, as well as gender-based differences in the willingness of patients to seek healthcare in Iraq's sociocultural framework.

In our study, reactive lymphadenopathy constituted the most common cause (38.4%) of lymphadenopathy. Additionally, the predominant cause of lymphadenopathy throughout the world is documented in the literature to be reactive (i.e., non-specific) inflammatory lymphadenopathy or reactive lymphadenopathy, according to studies published in outpatient settings [1,5,6].Most of the reactive cases within this study had identifiable foci of infection/inflammation in the head & neck (most of them were acute tonsillitis, peritonsillar abscesses, dental abscesses, acute otitis media, or upper respiratory tract infections). This finding is consistent with the drainage patterns of the cervical lymphatic system and emphasizes the relationship between ENT pathology and the reactivity of cervical lymph nodes [3, 12]. Further confirmation of reactivity as an aetiology for each case that met diagnostic criteria came from the resolution of lymphadenopathy following treatment of the underlying focus.

The second most common diagnosis was tuberculous lymphadenitis, which occurred in 73 patients (22.8%). The high prevalence of tuberculous lymphadenitis reflects Iraq's intermediate burden of tuberculosis and is consistent with regional data reported in other ENT series. For example, a study performed by Al-Jewari et al. in Baghdad showed that 19.3% of patients with cervical lymphadenopathy had tuberculous lymphadenitis, while Obaid et al. found 25% of patients in Mosul had the same diagnosis [18]. Worldwide, tuberculous cervical lymphadenitis remains the most frequent cause of chronic cervical lymphadenopathy found in countries wherein tuberculosis is endemic; therefore, continued emphasis should be placed on tuberculosis as a differential diagnosis in ENT practice within Iraq as shown by its prevalence within this study [7, 19, 20]. Some of the patients' clinical features, such as matted nodes or a fluctuant cold abscess with overlying changes to the skin provided a basis for clinical suspicion; however, a large number of cases presented without these findings, mimicking other chronic lymphadenopathies, necessitating FNAC and mycobacterial culture for definitive diagnosis.The response to anti-tuberculous treatment is a basis for confirming the diagnosis of TB in patients whose TB cultures are negative, as has been previously outlined through WHO diagnostic frameworks [20].

14.1% of the patients were diagnosed with lymphoma (7.8% Hodgkin lymphoma and 6.3% non-Hodgkin lymphoma), which is the most frequently diagnosed malignancy after metastatic carcinoma. The average age of Hodgkin lymphoma patients was found to be 26.4 years old, corresponding to the early adult peak incidence that has been documented in the literature [21, 22]. The most common clinical finding in Hodgkin lymphoma patients was painless, rubbery, nontender cervical lymphadenopathy at Level II and 64% of patients experienced at least one of the B-symptoms of fever, night sweats, and weight loss; these findings are similar to those reported in other published series [21, 23]. Elevated LDH and ESR were determined to be useful laboratory markers for differentiating lymphoma from the other diagnoses in this series. In general, non-Hodgkin lymphoma patients were older (38.2 years) and presented with more variable lymph node characteristics and a greater incidence of bilateral involvement. These clinical differences may be useful markers for guiding clinicians to refer suspicious cases for early histopathological diagnosis in ENT settings with limited resources.

Metastatic carcinoma was diagnosed in 11.9% of patients and accounted for the highest percentage of malignancies in patients 45 years old or older. This pattern of incidence conforms to the established epidemiologic data on squamous cell carcinoma of the upper aerodigestive tract, which is the most frequent primary malignant tumor to give rise to cervical lymph node metastases in the head and neck region [24, 25].The group with the highest prevalence of hard, non-moving, and only one-sided lympedema presented significantly later than expected (more than 16 weeks on average) and this is concerning evidence of patient- and system-initiated delays in accessing healthcare services. Predictably, late-stage presentations of head and neck cancers in developing countries are associated with relatively poor outcomes [27] compared to earlier diagnoses. Additionally, the large representation of Level IV lymph nodes in the metastatic cohorts is consistent with the anatomy of the drainage pathways for laryngeal, hypopharyngeal and thyroid cancers, which primarily drain through to the low jugular chain nodes [31].

There were 6.6% of cases represented by infectious mononucleosis, with predominately adolescent and young adult populations affected (the mean age of infected patients was 19.3 years old). In the majority of cases, clinical presentations of bilateral cervical lymphadenopathy associated with fever, pharyngitis, and fatigue, combined with a positive monospot result and increased levels of EBV-targeted antibodies, made diagnosis relatively straightforward. The occurrence of infectious mononucleosis in this study may also reflect the age of participants as this is generally when primary EBV infections are clinically apparent amongst adolescents and young adult patients in developing countries [5,11]. Clinicians should note that the clinical findings of infectious mononucleosis have overlapping characteristics with lymphoma; therefore serological tests should be performed on all young patients who presents with rubbery bilateral cervical lymphadenopathy, splenomegaly, orThe present study's findings for the anatomical

distribution of cervical lymphadenopathy (Table3) indicate that a predominant number of patients have level II lymphadenopathy (41.6%) followed by level III (17.5%) and level I (15.0%). The distribution suggests that the majority of head/neck mucosal surfaces drain through the jugular node chains of levels II and III. Our findings are consistent with these previous studies [14,29,30].

Tuberculous lymphadenitis frequently occurs in the posterior triangle (level V) as reported in the aforementioned papers. The posterior triangle drains lymph from the posterior scalp and nasopharynx, both areas where patients may have subclinical mycobacterial foci [7,19]. Using logistic regression analysis and using data shown in Table 4, we identified several independent clinical predictors of malignant disease etiology including age over 40, duration of cervical swelling greater than 12 weeks, firm or immobile consistency, lesion size greater than 3cm, bilateral lesions, presence of constitutional symptoms and elevated serum LDH. Our results support validated clinical prediction models for the evaluation of cervical lymphadenopathy published in the international literature [13,14,17]. Combined with these features, it is imperative that ENT clinicians refer patients urgently for detailed diagnosis of histopathology.If a patient is diagnosed with unilateral soft lymph node swelling (lymphadenopathy) on only one side of their neck/lower jaw area and there is a known source of infection located within the same area, the lack of high risk characteristics might indicate a wait and see approach along with antibiotic treatment before conducting any kind of invasive testing; this is endorsed in the current Ear, Nose & Throat (ENT) clinical practice guidelines at [11,12].

A separate discussion needs to occur relating to the utility of Fine Needle Aspiration Egypt (FNAC) compared to other testing methods used to diagnose cervical lymphadenopathy. This research has shown that FNAC almost always was the primary source to diagnose cases of tuberculous lymphadenitis or to identify suspected malignant (cancerous) involvement (metastatic carcinoma). The level of accuracy in making FNAC diagnoses associated with tuberculous lymphadenitis is well established with ranges as high as 90% (with the range of 60%) depending on the laboratory expertise making the diagnosis, and as defined by the published literature [15],[16]. The literature states that FNAC is not sufficient by itself to definitively subtype lymphomas, and that an excisional biopsy (with immunohistochemistry) must be obtained in all lymphoid cases, consistent with worldwide standards [17]. The findings support using a sequential test method in diagnosing cervical lymphadenopathy, beginning with FNAC as the first line testing method, followed by an excisional biopsy should the FNAC results be non-diagnostic, or if the FNAC results were suspicious of lymphoma.

Several limitations exist with this research. The first limitation is that all investigations occurred at a single site, within a University Hospital; therefore, the results may not represent the typical presentation of patients with cervical lymphadenopathy as observed through most primary care or community-based health centres across Iraq. Secondly, the COVID-19 pandemic affected the presentation of patients presenting with cervical lymphadenopathy as there were restrictions generally across Iraq and at times, patients presented with cervical lymphadenopathy much later when compared with previous presentations; therefore, there may exist a selection bias effecting the total number of patients evaluated late that have malignant lymphatic disease. Thirdly, mycobacterial cultures could not be obtained from all suspected tuberculosis patients, thus creating a risk of under-diagnosing cases if the sample did not develop enough mycobacteria to be detected in the laboratory. Fourthly, the use of some molecular diagnostic tests (e.g., GeneXpert MTB/RIF) is not universally available; thus, limiting their use across all study subjects. Even with the limitations previously stated, this research provides a basic description of lymphadenopathy for those patients who reside in Al-Muthanna Governorate, and will contribute to the limited scientific literature published regarding the diagnosis and treatment of lymphadenopathy within Southern Iraq.

From a public health perspective and, without rehashing previously provided content contained within the Discussion Section of the paper, these results provide an indication of various priorities developed from this research. The high occurrence of tuberculous lymphadenopathy supports the need for improvements in the currently employed tuberculosis control programs, the development of definitive diagnosis infrastructures (doctors who can refer to a hospital, community, etc.), and provide support as positive references within Southern Iraq. The high occurrence of malignant cervical lymphadenopathy (combined with the fact that some patients presented late to the hospital with advanced disease), illustrates the need for additional forms of public education regarding the awareness of any persistent swelling around the neck that could indicate malignancy. In addition, there is a clear requirement for the development of well defined diagnosis pathways within ENT facilities across Iraq, inclusive of the use of FNAC testing, imaging, and appropriate referral processes to allow for more standardised and efficient management of patients across the continuum of care provided within the health system.

CONCLUSION

The cervical lymphadenopathy patient group at the ENT clinic of the Al-Hussein Teaching Hospital in Samawa/Iraq is characterized by a wide range of causes of this pathology, with reactive lymphadenopathy and tuberculous lymphadenitis being the most common; malignant lymphadenopathy represent around 29% of cases. The Level II node is frequently involved as an anatomical site. Factors associated with malalignment of cervical lymph nodes are: older age, prolonged duration, hard consistency, larger node size, and the presence of constitutional symptoms. This data supports a systematic approach to addressing these patients that includes a clinical evaluation, fine-needle aspiration cytology (FNAC) and selective excisional biopsy, while being alert for tuberculosis and malignancy given the local epidemiology of cervical lymphadenopathy. Multicentre studies throughout the governorates of Iraq are needed to develop a national analysis of the distribution of this disease.

REFERENCES

1. Ferrer R. Lymphadenopathy: differential diagnosis and evaluation. Am Fam Physician. 1998;58(6):1313-1320.
2. Bazemore AW, Smucker DR. Lymphadenopathy and malignancy. Am Fam Physician. 2002;66(11):2103-2110.
3. Robbins KT, Clayman G, Levine PA, Medina J, Sessions R, Shaha A, et al. Neck dissection classification update: revisions proposed by the American Head and Neck Society and the American Academy of Otolaryngology–Head and Neck Surgery. Arch Otolaryngol Head Neck Surg. 2002;128(7):751-758.
4. Swartz MH. The lymph nodes. In: Textbook of Physical Diagnosis: History and Examination. 7th ed. Philadelphia: Elsevier Saunders; 2014. p. 248-260.
5. Twist CJ, Link MP. Assessment of lymphadenopathy in children. Pediatr Clin North Am. 2002;49(5):1009-1025.
6. Pangalis GA, Vassilakopoulos TP, Boussiotis VA, Fessas P. Clinical approach to lymphadenopathy. Semin Oncol. 1993;20(6):570-582.
7. Mohan A, Reddy MK, Phaneendra BV, Murthy A. Aetiology of peripheral lymphadenopathy in adults: analysis of 1724 cases seen at a tertiary care teaching hospital in southern India. Natl Med J India. 2007;20(2):78-80.
8. Moore SW, Schneider JW, Schaaf HS. Diagnostic aspects of cervical lymphadenopathy in children in the developing world: a study of 1877 surgical specimens. Pediatr Surg Int. 2003;19(4):240-244.
9. United Nations Population Fund (UNFPA). Iraq Population Situation Analysis. Baghdad: UNFPA Iraq; 2019.
10. Hadi NI, Sultan MH, Al-Khafaji JA. Pattern of cervical lymphadenopathy in ENT department at Al-Kindy Teaching Hospital, Baghdad, Iraq. Iraqi Postgrad Med J. 2015;14(2):178-183.
11. NICE Guideline NG12. Suspected cancer: recognition and referral. London: National Institute for Health and Care Excellence; 2015. Updated 2021.
12. Gaddey HL, Riegel AM. Unexplained lymphadenopathy: evaluation and differential diagnosis. Am Fam Physician. 2016;94(11):896-903.
13. Patel SG, Shah JP. TNM staging of cancers of the head and neck: striving for uniformity among diversity. CA Cancer J Clin. 2005;55(4):242-258.
14. Leung AK, Davies HD. Cervical lymphadenitis: etiology, diagnosis, and management. Curr Infect Dis Rep. 2009;11(3):183-189.
15. Das DK. Fine needle aspiration cytology in diagnosis of tuberculous lesions. Lab Med. 2000;31(11):625-632.
16. Naik LP, Sarode DR, Soni NC, Jadhav MV. Fine needle aspiration cytology of cervical lymph nodes: a study of 200 cases. Indian J Otolaryngol Head Neck Surg. 2004;56(3):200-203.
17. Maitra A, Kumar V. Diseases of white blood cells, lymph nodes, spleen and thymus. In: Kumar V, Abbas AK, Fausto N, Mitchell RN, editors. Robbins Basic Pathology. 8th ed. Philadelphia: Saunders Elsevier; 2007. p. 455-500.
18. Al-Jewari AA, Al-Saffar MQ. Clinicopathological pattern of tuberculous lymphadenitis in Baghdad: a study of 64 cases. J Fac Med Baghdad. 2013;55(1):33-36.
19. World Health Organization. Global Tuberculosis Report 2021. Geneva: World Health Organization; 2021.
20. World Health Organization. Definitions and Reporting Framework for Tuberculosis – 2013 Revision (Updated December 2014). Geneva: WHO; 2013.
21. Kuppers R, Engert A, Hansmann ML. Hodgkin lymphoma. J Clin Invest. 2012;122(10):3439-3447.
22. Armitage JO. Early-stage Hodgkin's lymphoma. N Engl J Med. 2010;363(7):653-662.
23. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al., editors. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: International Agency for Research on Cancer; 2017.
24. Shah JP, Candela FC, Poddar AK. The patterns of cervical lymph node metastases from squamous carcinoma of the oral cavity. Cancer. 1990;66(1):109-113.
25. Robbins KT, Medina JE, Wolfe GT, Levine PA, Sessions RB, Pruet CW. Standardizing neck dissection terminology: official report of the Academy's Committee for Head and Neck Surgery and Oncology. Arch Otolaryngol Head Neck Surg. 1991;117(6):601-605.

26. Raviglione MC, Smith IM. XDR tuberculosis—implications for global public health. N Engl J Med. 2007;356(7):656-659.
27. Pulte D, Brenner H. Changes in survival in head and neck cancers in the late 20th and early 21st century: a period analysis. Oncologist. 2010;15(9):994-1001.
28. Tower RL, Camitta BM. Lymphadenopathy. In: Kliegman RM, Stanton BF, St Geme JW, Schor NF, editors. Nelson Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier; 2016. p. 1721-1726.
29. Salam MA, Siddiqui AH, Das S. Lymph node biopsy in neck swellings—an analysis of 200 cases. Mymensingh Med J. 2001;10(1):11-14.
30. Zidan AS, El-Gharib AM, Abu El-Makarem MA. Study of cervical lymphadenopathy in ENT outpatient clinic at El-Minia University Hospital, Egypt. Al-Minia Med Bull. 2014;25(1):55-63.
31. Som PM, Curtin HD, Mancuso AA. An imaging-based classification for the cervical nodes designed as an adjunct to recent clinically based nodal classifications. Arch Otolaryngol Head Neck Surg. 1999;125(4):388-396.
32. Obaid HO, Saad AA. Cervical lymphadenopathy in Mosul: a clinicopathological study. Ann Coll Med Mosul. 2009;35(2):139-145.
33. Ifeacho S, Pritchard D, MacFarlane PL. Cervical lymphadenopathy in children at a district general hospital in UK: experience and challenges of management. J Laryngol Otol. 2009;123(8):900-904.
34. Soldes OS, Younger JG, Hirschl RB. Predictors of malignancy in childhood peripheral lymphadenopathy. J Pediatr Surg. 1999;34(10):1447-1452.
35. Steel BL, Schwartz MR, Ramzy I. Fine needle aspiration biopsy in the diagnosis of lymphadenopathy in 1103 patients: role, limitations and analysis of diagnostic pitfalls. Acta Cytol. 1995;39(1):76-81.
36. van den Brekel MW, Stel HV, Castelijns JA, Snow GB. Lymph node staging in patients with clinically negative neck examinations by ultrasound and ultrasound-guided aspiration cytology. Am J Surg. 1991;162(4):362-366.
37. Torabi M, Aquino SL, Harisinghani MG. Current concepts in lymph node imaging. J Nucl Med. 2004;45(9):1509-1518.
38. Rajasekaran K, Krakovitz P. Enlarged neck lymph nodes in children. Pediatr Clin North Am. 2013;60(4):923-936.
39. Vassilakopoulos TP, Pangalis GA. Application of a prediction rule to select which patients presenting with lymphadenopathy should undergo a lymph node biopsy. Medicine (Baltimore). 2000;79(5):338-347.
40. Kelly CS, Kelly RE Jr. Lymphadenopathy in children. Pediatr Clin North Am. 1998;45(4):875-888.