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ORIGINAL ARTICLE

Evaluation of Children Diagnosed with Mesenteric Lymphadenitis by Ultrasonography

ABSTRACT

Objectives: Mesenteric lymphadenitis (ML) is commonly encountered in the pediatric population. Despite its prevalence, its etiology, clinical course, and management remain under-researched. This study aimed to evaluate the etiology, clinical, and laboratory findings of ML and its correlation with lymph node size among pediatric patients.

Methods: Patients diagnosed with ML via ultrasonography between August 2017 and July 2018 were retrospectively reviewed for inclusion in the study. Enlarged mesenteric lymph nodes were identified as those with a short axis measuring ≥5 mm. The study analyzed patients> clinical characteristics, along with laboratory and ultrasonographic findings.

Results: A total of 865 pediatric patients received an ML diagnosis. Among these, 9.8% were asymptomatic. The most frequently reported symptoms included abdominal pain (82.7%), vomiting (45.3%), and diarrhea (26.2%). Leading etiologies encompassed infections (28.3%), appendicitis (7.1%), and malignancy (2.3%). In 73.7% of symptomatic patients, the short axis of the mesenteric lymph node ranged between 5-8 mm. The symptomatic group exhibited a statistically significant longer mean length of the mesenteric lymph node³s long axis (p<0.05). Every clinical symptom was associated with a longer mean mesenteric lymph node³s long axis. Furthermore, the presence of feeding difficulties (OR1=8.9[6.3-15.4]) and the long axis diameter of the mesenteric lymph node (OR2=2.7[1.5-3.1]) were statistically significant independent predictors of hospitalization.

Conclusion: Given that the majority of symptomatic patients have a mesenteric lymph node short axis size between 5-8 mm, we recommend adopting a short-axis threshold exceeding 5 mm when identifying enlarged mesenteric lymph nodes to minimize false negatives. The study further indicates that the long axis diameter corresponds more closely with clinical findings compared to the short axis diameter. Significantly, the long axis diameter of the mesenteric lymph node emerged as an independent predictor of hospitalization.

Keywords: Abdominal pain, appendicitis, gastroenteritis, lymph nodes, malignancies

esenteric lymphadenitis (ML) is an inflammatory condition of the mesenteric lymph nodes and often presents with acute or chronic abdominal pain. Apart from asymptomatic healthy children, ML can also be observed in children with infections, malignant diseases, or inflammatory lesions of the gastrointestinal tract. ML predominantly affects younger children (1). Although ML is common, there is still no consensus on its diagnosis, follow-up, or treatment. Few studies exist on this topic; while the majority focus on the radiological definition of ML, others have concentrated on its clinical and laboratory characteristics. Primary (nonspecific) ML is typically defined as self-limiting right-sided lymphadenopathy without an identifiable inflammatory cause (2). Conversely, secondary ML refers to lymphadenitis associated with an inflammatory process that has a known cause. Etiologies of secondary ML include inflammatory bowel diseases, systemic chronic inflammatory diseases, malignancies, and infections. The primary goals in managing ML patients are to recognize those requiring immediate surgical intervention and to ensure that these nodes are not misdiagnosed as an early manifestation of a lymphoproliferative disorder (3). Surprisingly, no consensus exists among clinicians regarding the radiological definition and clinical semiology of this prevalent disease. While some consider the minimum limit of the lymph node>s short axis to be 5 mm, others argue for limits of 8 mm or 10 mm (4-6).

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This study aims to determine and evaluate the correlation between clinical findings and lymph node size in patients diagnosed with ML. We assessed the etiology, clinical, and laboratory findings of ML in the pediatric population.

METHODS

This was a retrospective descriptive study conducted in a tertiary children's hospital. Between August 2017 and July 2018, we reviewed consecutive pediatric patients diagnosed with ML using graded compression real-time Ultrasonography (US).

US examinations were carried out by a radiologist using a linear array, high-frequency (6-MHz) probe transducer (Toshiba Aplio 500, Toshiba Medical Systems Corporation, Tokyo, Japan). Oblique, transverse, and longitudinal scans of the lower abdomen were obtained using the graded compression US technique described by Puylaert (7). Each ultrasonographic examination not only investigated ML but also performed a full abdominal examination. US findings were documented at the time of examination. Enlarged mesenteric lymph nodes were characterized as those with a short axis greater than 5 mm in diameter in the anteroposterior plane (8). For each patient in the study, the largest mesenteric lymph node sizes were recorded for both long and short axes.

Patients were categorized into two main groups:

Symptomatic ML: This group included patients who underwent abdominal US due to acute (generalized or localized) symptoms like acute abdominal pain, vomiting, and/or diarrhea. Symptomatic patients were further divided based on their etiology. Primary (nonspecific) ML is defined as self-limiting right-sided lymphadenopathy without any identifiable inflammatory cause in etiological studies (9). Secondary ML is defined as lymphadenitis linked to an inflammatory process with a specific cause. Inflammatory bowel diseases, systemic chronic inflammatory diseases, malignancies, and infections all contribute to secondary ML etiology.

Asymptomatic ML (Control Group): This group comprised patients with incidentally enlarged mesenteric lymphadenopathy who showed no symptoms like acute abdominal pain, vomiting, or diarrhea during the abdominal US. Reasons for the US examination in this cohort were obesity, recurrent urinary tract infections, malnutrition, congenital anomalies, hematuria, proteinuria, and previous nephrolithiasis. All children with a prior lower urinary tract infection completed an antibiotic course at least a month before the US examination and had negative urine cultures. All had standard kidney function and underwent successful medical treatment.

Data analyzed in the study population included: age, sex, clinical signs and symptoms upon presentation, detailed physical examination outcomes, C-reactive protein (CRP), and other laboratory findings, such as complete blood counts with differential (concentrations of hemoglobin (Hb), white blood cells (WBC), neutrophils, lymphocytes, and platelet counts).

Causes of mesenteric lymph nodes enlargement in the symptomatic group were noted. S. pyogenes pharyngitis was diagnosed via backup culture. Epstein-Barr virus (EBV) and adenovirus were identified through immunoglobulin M antibodies or genomic DNA copy numbers using polymerase chain reaction (PCR). Influenza was detected either by the rapid antigen-based test or real-time quantitative PCR. H. pylori was identified through histologic examination of gastric biopsy specimens. Serological tests for pathogens like E. granulosus, Salmonella, Brucella, Mycoplasma, Parvovirus, Hepatitis A, Leishmania, and Toxoplasma were documented. Diagnosis of Amebiasis was confirmed through the detection of E. Histolytica antigen in stool samples. Intestinal tuberculosis was diagnosed using tissue PCR.

Patients' antibiotic usage, hospitalization, and surgical statuses were ascertained through a retrospective review of their electronic health records.

Differences and correlations between clinical and laboratory findings and the lymph node sizes (short and long axis) were determined. The groups were statistically compared concerning symptoms, laboratory features, antibiotic use, and the presence and duration of hospitalization.

Statistical analyses were conducted using SPSS v21 statistical software (SPSS Inc., Chicago, IL, USA). Descriptive statistics are presented as numbers, percentages, arithmetic means±standard deviation (S.D.), and median values (minimum and maximum). The normality of distributions was ascertained using the Kolmogorov–Smirnov test, histograms, and P–P plots. Depending on data normality, variables were compared either with an independent samples t-test or the Mann–Whitney U-test. Categorical variables were contrasted using the Pearson χ^2 test, Yate's correction χ^2 test, and Fisher's exact test. Continuous and ordinal variables' relationships were analyzed through Kendall's τ and Spearman's ' ρ ' correlations. Multiple logistic regressions identified risk factors for hospitalization. A p-value less than 0.05 was deemed statistically significant.

The study protocol was approved by the Health Sciences University Ankara Child Health and Diseases Hematology Oncology SUAM Clinical Research Ethics Committee on December 10, 2018 (protocol no: 2018-176), and it was conducted in accordance with the principles of the Helsinki Declaration.

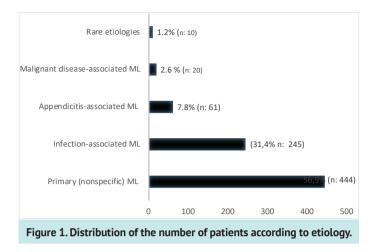
RESULTS

The total number of patients diagnosed with ML during the study period was 865. The mean age of these patients was 7.76 ± 4.2 years, with 56.9% being male. Out of these patients, 90.2% (n=780) were categorized into the symptomatic ML group, while 9.8% (n=85) were part of the asymptomatic ML group (control group). No significant differences in terms of gender and age were observed between the symptomatic and asymptomatic groups.

The underlying cause of lymphadenitis was identified in 336 of the symptomatic patients, distributed as follows: infection (n=245), acute appendicitis (n=61), and malignancy (n=20). For 444 patients exhibiting acute symptoms related to ML, the etiology remained undetermined. Figure 1 displays the distribution of symptomatic ML patients by their respective etiologies.

Among patients with infection-associated ML, the most common etiologies were: acute gastroenteritis [n=167; rotavirus-associated gastroenteritis (n=59), E. Histolytica-associated gastroenteritis (n=23), salmonella-associated gastroenteritis (n=5)], EBV infection (n=26), S. pyogenes (n=20), and influenza virus (n=14). Less frequently detected infectious agents included: adenovirus (n=7), H. pylori (n=4), E. granulosus (n=2), M. pneumoniae (n=2), hepatitis A virus (n=1), M. tuberculosis (n=1), and parvovirus B19 (n=1).

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In 20 cases, mesenteric lymphadenitis was linked to malignancy. These cases were diagnosed as follows: non-Hodgkin lymphoma (n=6), Hodgkin lymphoma (n=3), acute lymphoblastic leukemia (n=3), acute myeloid leukemia (AML) (n=2), neuroblastoma (n=2), Sertoli-Leydig cell tumor (n=1), rhabdomyosarcoma (n=1), sacrococcygeal teratoma (n=1), and carcinoid tumor (n=1).

The less common etiologies included: celiac disease (n=3), acute pancreatitis (n=2), familial Mediterranean fever attack (n=2), immunoglobulin A vasculitis (n=2), and Crohn's disease (n=1).

The mean mesenteric lymph node short and long axis diameters for the asymptomatic ML group (control group) were 5.9 ± 1.5 mm (short axis) and 11.2 ± 3.5 mm (long axis), respectively. For the symptomatic group, the measurements were 6.5 ± 1.8 mm (short axis) and 17.5 ± 3.2 mm (long axis), respectively. The mean long axis diameter for symptomatic ML patients was statistically longer than that of asymptomatic ML patients (p<0.01). Patients with malignancy-associated ML exhibited the highest mean short-axis (7.2 ± 2 mm) and long axis (17.9 ± 1.8 mm) mesenteric lymph node dimensions. Long axis diameters of mesenteric lymph nodes were significantly longer in patient groups with Primary ML, Appendicitis-associated ML, Infection-associated ML, and Malignancy-associated ML compared to the control group. However, the short axis diameters weren't statistically longer in the Primary ML and Appendicitis-related ML groups compared to the control group (Table 1).

Table 1. The Demographic, Clinical, and Laboratory Outcome Parameters of the Symptomatic ML Patients. The Comparative Mean of Mesenteric Lymph Node Sizes of the Symptomatic ML, Primary ML, Appendicitis-associated ML, Infection-associated ML, Malignant Disease-associated ML, and Asymptomatic Control ML Groups.

		Asymptomatic ML n=85	Symptomatic ML n=780	Primary (nonspecific) ML n=444	Appendicitis- associated ML n=61	Infection- associated ML n=245	Malignant disease associated ML n=20
Age (years)		7.7±4.7	7.7±4.1	8.0±4.1	10.2±3.3	6.7±4.0	9.4±4.2
Gender(Male/Female)		1.3	1.3	1.4	1.9	1.1	1.0
The mean of mesenteric lymph node size±SD (mm)	Short axis	5.9±1.5	6.5±1.8	6.4±1.8	6.4±1.7	6.8±2.0	7.2±2.0
	Long axis	11.2±3.5	17.5±3.2	17.1±3.1	16.9±3.6	17.6±3.3	17.9±1.8
	P1		0.25	0.82	0.72	<0.01	<0.01
	P2		<0.01	<0.01	<0.01	<0.01	<0.01
Presence of syn	nptoms (%)						
/omiting		-	45.3	46.6	42.6	45.3	35
Abdominal Pain		-	82.7	88.1	100	71.8	45
Feeding Difficulties		-	21.9	19.8	42.6	22.9	10
Diarrhea		-	26.2	0.9	8.2	78.8	15
Fever (two consecutive measurements are >38 °C.)		-	22.1	18	16.4	30.2	30
Ouration of feve Days)	er (M, SD in	-	0.61±1.8	0.5±1.9	0.28±0.9	0.9±1.8	0.3±0.5
ntibiotic usage	e Rate (%)	-	45.5	40.8	100	42.4	25
lospitalization	Rate (%)	-	38.5	32.4	100	35.1	20
Ouration of Hos Days)	pitalization	-	1.2±2.1	1.0±2.0	3.1±1.3	1.0±2.0	1.1±2.6
aboratory Resu	ults						
CRP (mg/L)		-	25.8±45.4	24.7±44.2	28.6±32.8	31.3±51.8	7.4±16.8
VBC (x10 ³ /µL)		-	10.8±5.6	10.3±6.2	10.1±4.7	10.0±4.9	7.9±4.7
lb (g/dL)		-	12.6±1.4	12.7±1.4	12.8±1.3	12.4±1.4	11.7±2.0
PLT (x10 ³ /µL)		-	320.6±5.6	323.0±103.6	322.0±94.6	316.7±88.6	316.3±188.0

ML: Mesenteric Lymphadenitis, CRP: C-reactive protein, WBC: White blood cell count, HB: Hemoglobin concentration, PLT: Platelet count.

 p_1 = Comparative mean of MLN short axis length of groups with asymptomatic ML (control) group.

 p_2^2 = Comparative mean of MLN long axis length of groups with asymptomatic ML (control) group.

p<0.05 was considered statistically significant.

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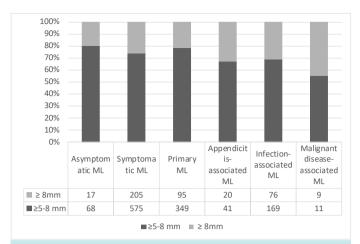


Figure 2. Distribution of the number of patients in the asymptomatic and symptomatic ML groups according to threshold of short-axis \geq 5-8 mm, and \geq 8 mm.

Within the symptomatic ML group, 205 patients had a short axis diameter ≥ 8 mm, while 570 patients ranged between 5 and 8 mm. The proportion of patients with mesenteric lymph node short axis diameter less than 8 mm in the symptomatic ML group was 73.7% (Figure 2). For those with a mesenteric lymph node short axis diameter ≥ 8 mm, the negative predicted value for acute symptom development stood at 11.7%.

Among the symptomatic ML group, prevalent symptoms were abdominal pain (82.7%), vomiting (45.3%), diarrhea (26.2%), fever (22.1%), and feeding difficulties (21.9%). Clinical findings of patients were juxtaposed based on the lengths of the short and

Table 2 Relationship Retween Lymph Node Sizes and Clinical Findings

long axes of the mesenteric lymph node as seen on the US, with results detailed in Table 2. The mean mesenteric lymph node long axis length was associated with symptoms such as abdominal pain, feeding difficulties, diarrhea, fever, antibiotic usage, and hospitalization (p1; abdominal pain=0.04, p1; feeding difficulties=<0.01, p1; diarrhea=<0.01, p2; fever=<0.01, p1; antibiotic usage=0.02, p1; hospitalization=0.02). Yet, no significant difference was observed with the presence of vomiting (p1; vomiting=0.15). The mean mesenteric lymph node short axis was longer in patients who had fever and took antibiotics (p2; fever=0.04, p2; antibiotic usage=0.04).

Within the symptomatic ML group, 45.5% of patients were treated with antibiotics, and 38.5% were hospitalized. The average hospital stay lasted 1.2±2.1 days. Every patient with appendicitis-associated ML received antibiotics and required hospitalization. When omitting appendicitis and bacterial-parasitic infection-associated ML patients, antibiotics were administered to 21.8% of the symptomatic patients.

Based on the logistic regression analysis, factors such as the presence of feeding difficulties (OR1=8.9[6.3-15.4]) and the long axis length of the mesenteric lymph node (OR2=2.7[1.5-3.1]) were identified as risk factors for hospitalization in symptomatic ML groups, excluding those associated with appendicitis (Table 3).

Laboratory findings for symptomatic patients were as follows: Hb: 12.6±1.4g/dl, WBC: 10.8±5.6×10⁹/L, PLT: 320.6±5.6×10⁹/L, and CRP: 25.8±45.4 mg/L. Table 1 displays the demographic, clinical, and laboratory outcome parameters of the symptomatic ML patients.

Correlation analysis revealed no statistically significant association between the patients' mesenteric lymph node long (p1) and short (p2) axis diameters and their laboratory results. Specifically, the values were: (p1; CRP=0.57, p1; WBC=0.66, p1; Hb=0.14, p1; PLT=0.34; p2; CRP=0.46, p2; WBC=0.19, p2; Hb=0.57, p2; PLT=0.50).

Symptoms and treatment	Status	The mean of mesenteric lymph node size±SD (mm)		p1	p2
		Long axis	Short axis		
Vomiting	present	16.9±3.3	6.5±1.8	0.15	0.64
	absent	16.7±3.2	6.5±1.8		
Abdominal pain	present	17.0±3.3	6.5±1.9	0.04	0.94
	absent	16.4±3.3	6.4±1.6		
Feeding difficulties	present	17.3±3.2	6.6±1.8	<0.01	0.55
	absent	16.7±3.3	6.5±1.8		
Diarrhea	present	17.8±3.2	6.7±2.1	<0.01	0.05
	absent	16.5±3.2	6.4±1.8		
Fever	present	17.6±3.6	6.8±2.1	<0.01	0.04
	absent	16.6±3.2	6.4±1.8		
Antibiotic usage	present	17.1±3.4	6.6±1.8	0.02	0.04
	absent	16.5±3.2	6.4±1.8		
Hospitalization	present	17.1±3.2	6.6±1.9	0.02	0.22
	absent	16.6±3.3	6.4±1.8		

 p_1 = Comparative mean of MLN long axis length with the presence and absence of the symptoms and treatment. p_2 = Comparative mean of MLN short axis length with the presence and absence of the symptoms and treatment. p<0.05 was considered statistically significant.

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Risk Factors	Adjusted OR	95% CI	р
Age (year)	0.8	[0.3-1.6]	0.23
Feeding Difficulties	8.9	[6.3-15.4]	0.01
Vomiting	3,2	[0.9-4.2]	0.32
Fever (two consecutive measurements are >38 °C.)	0.9	[0.8-1.2]	0.54
CRP Level	0.8	[0.4-1.5]	0.83
WBC Level	0.7	[0.5-1.3]	0.92
Long axis length of mesenteric lymph node	2.7	[1.5-3.1]	0.01
Short axis length of mesenteric lymph node	1.1	[0.9-1.9]	0.13
p<0.05 was considered statistically significant.			

Table 3: Logistic Regression Analysis of Risk Factors of Hospitalization

DISCUSSION

While ML is frequently observed in pediatric practice due to the prevalent use of US, a consensus regarding its clinical significance, causes, and approach remains undefined (10). In light of this, we examined 865 consecutive patients whose US scans indicated ML. Our study delved into the etiology of ML and the relationship between clinical findings and mesenteric lymph node size. Data from our research indicates that 9.8% of the patients were asymptomatic. Infections emerged as the predominant etiology. Only the mean long axis length of the mesenteric lymph node was statistically longer in the symptomatic ML group. Patients with malignancy-associated ML presented the greatest mean measurements for both the short and long axes. Notably, this study identified the presence of feeding difficulties and the long axis diameter of the mesenteric lymph node as statistically significant independent predictors for hospitalization.

The clinical community has yet to reach a consensus on the radiological definition and clinical semiology of this prevalent condition. US determinations of enlarged mesenteric lymph nodes have been inconsistently defined—sometimes denoted as larger than 4 mm in the short axis and over 10 mm in the long axis (11). Wang et al. (12) posited that many healthy children have enlarged mesenteric lymph nodes, which doesn't necessarily indicate any abnormalities. In contrast, Karmazyn et al. found that 54% of asymptomatic children had enlarged mesenteric lymph nodes with a short axis ≥ 5 mm. They proposed that a short-axis diameter of 8 mm might more accurately define the upper limit of a standard mesenteric lymph node size in children (9). However, our findings suggest that employing a threshold of short-axis ≥ 8 mm for determining enlarged mesenteric lymph nodes could result in a notably low negative predictive index of 11.7%.

Very few studies have explored the differences between clinical and laboratory findings in relation to mesenteric lymph node size. In our study, we found a statistically significant correlation: the long axis was longer in the presence of nearly all clinical symptoms, with the exception of vomiting. We also determined that the presence of antibiotic use and hospitalization was statistically associated with the long axis of the mesenteric lymph node. While much of the literature focuses on the short axis diameter of the lymph node, our study highlighted the long axis diameter of the mesenteric lymph node as a statistically significant independent predictor of hospitalization. In our findings, the long axis diameter more closely aligned with clinical observations compared to the short axis diameter.

A study by Cai et al. (13) on asymptomatic children with ML revealed significant correlations between the short-axis diameter of the mesenteric lymph node and lymphocyte count across all age groups. In our study, we didn't identify any correlation between mesenteric lymph node size and the laboratory outcome parameters for symptomatic ML patients. Moreover, we lacked laboratory data from the asymptomatic patient group.

In our symptomatic ML cohort, the antibiotic usage rate stood at 45.5%. When we set aside cases of appendicitis and bacterial-parasitic infection-associated ML, we observed an unnecessary antibiotic prescription rate of 21.8% among the symptomatic patients. Antibiotics should ideally be reserved for patients with confirmed bacterial infections or those necessitating surgical intervention. This emphasizes the need for a more discerning approach when prescribing antibiotics for patients diagnosed with mesenteric lymphadenitis.

An identifiable cause was found in 38.8% of the patients. The predominant etiology was infection, with the most common infectious agents being rotavirus, E. Histolytica, and EBV, in that order. A study examining the anatomical changes in young children with natural rotavirus infection showed that this infection can enlarge the mesenteric lymph node size. In fact, ML was observed in 92% of patients with rotavirus infection during their examination (14). Mononucleosis can affect various organ systems, and within the abdomen, manifestations may include splenic involvement, hepatitis, ML, and hyperplasia of gut-associated lymphoid tissue. Consequently, EBV and adenovirus-associated ML is an anticipated complication, as reported in our study (15). Prior research has highlighted the association between viral infections, including adenovirus and influenza B virus, and mesenteric adenitis. However, the exact incidence of viral infection in ML remains undetermined (6). In our study, aside from bacterial etiologies, viral causes accounted for 77.9% of infection-associated ML cases. Acute ML can also manifest due to infections from various enteric and systemic pathogens, such as Y. enterocolitica and Y. pseudotuberculosis. Yet, in this study, only four patients with ML secondary to gastroenteritis were tested for Y. enterocolitica, and all stool cultures came back negative. History of consuming raw or undercooked pork products, unpasteurized milk, or exposure

to domestic and/or wild animals are significant risk factors for Y. enterocolitica infection (16). The absence of Y. enterocolitica infection in this study could be attributed to the minimal pork consumption in our country. Salmonella spp. is recognized for its association with acute enterocolitis, causing acute abdominal pain and has thus been implicated as a causative agent for ML. In our study, non-typhoid Salmonella was identified as the cause in five ML cases.

Historically, tuberculosis was regarded as the primary cause of ML. However, in our study, we diagnosed only one case with tuberculosis lymphadenitis. Tuberculous lymphadenitis represents an extrapulmonary manifestation of mycobacterium tuberculosis infection, characterized by a necrotizing mycobacterial infection within the lymph nodes (17).

In our study, two patients were diagnosed with ML due to H. pylori infection. Cakmaci et al. (18) found that antral gastritis, caused by H. pylori infection in the pediatric age group, was associated with an increased mesenteric lymph node dimension observed by US.

ML can be attributed to malignancy, and while any malignancy might lead to mesenteric lymphadenopathy, lymphoma is most commonly associated (19). In this study, 2.3% (n=20) of patients had malignant disease-related ML, with lymphoma identified in 9 patients. Both the short and long axes of the mesenteric lymph node diameter were statistically longer in the malignancy-associated ML group compared to the control group (Table 1). Nevertheless, relying solely on the mesenteric lymph node diameter for differentiation between benign and malignant conditions has been reported as inefficient. Parameters such as cortical echotexture, spherical shape, capsular irregularity, and absence of a fatty hilum in lymph nodes can be reliably investigated using US, helping to distinguish between benign and malignant lymph nodes (20). Conversely, Corwin et al., in a prospective adult study, highlighted that patients with misty mesentery and large mesenteric lymph nodes smaller than 10 mm typically followed a benign course. In our study, 75% (n=15) of the patients with malignancy-associated ML had a short axis lymph node diameter between 5-10 mm (Figure 2). However, 12 patients in remission and 8 newly diagnosed did not undergo mesenteric lymph node biopsies. Hence, we can't definitively associate these patients with malignancy. Relying solely on size as a diagnostic criterion for ML seems imprudent. To ascertain the natural course of an incidentally detected misty mesenteric lymph node on US, prospective cohort studies of patients with no known malignancy at the time of the initial US are essential.

ML is frequently considered an alternative diagnosis in children suspected of having acute appendicitis. Furthermore, appendicitis often presents alongside lymphadenopathy. In this study, 10% of the patients with ML had acute appendicitis. Clinically differentiating between acute appendicitis and acute mesenteric lymphadenitis in children is typically challenging (10). In our findings, the incidence of feeding difficulties was higher in the appendicitis-associated ML group compared to others (Table 1). However, the distribution of other symptoms did not show any significant difference. Gross et al.'s (21) study revealed a higher mean CRP level in the appendicitis-associated ML group compared to primary ML. Similarly, our study found a higher CRP level in the appendicitis-associated mesenteric lymphadenitis group, but no statistically significant difference was observed. The most elevated CRP level appeared in the infection-related ML group.

This study has its limitations. Firstly, it is retrospective, which limited our ability to monitor the disease's progression. Secondly, more in-depth analyses could have been performed on patients classified as primary ML; they might have been reclassified into the secondary ML group if the etiology had been determined.

CONCLUSION

Our study indicates that a considerable number of symptomatic patients present mesenteric lymph node short axis sizes ranging between 5-8 mm. To reduce the risk of false negatives when identifying enlarged mesenteric lymph nodes, we advocate for a short-axis threshold exceeding 5 mm. Notably, the long axis diameter aligns more closely with clinical observations than the short axis diameter in our findings.

The long axis diameter of mesenteric lymph nodes emerged as an independent predictor of hospitalization, underscoring its potential significance in clinical evaluations. Thus, we recommend that clinicians consider the long axis diameter during their assessments. The emphasis on the long axis diameter in our results suggests it might be a crucial parameter in evaluating clinical presentations. This highlights the imperative for further research to provide a deeper understanding of this aspect.

Ethics Committee Approval: The study protocol was approved by the Health Sciences University Ankara Child Health and Diseases Hematology Oncology SUAM Clinical Research Ethics Committee on December 10, 2018 (protocol no: 2018-176).

Informed Consent: Informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – O.D., M.M.O., A.S.Y., C.U., H.G.Ç.; Design – O.D., M.M.O., A.S.Y., C.U., H.G.Ç.; Supervision – O.D., M.M.O., A.S.Y., C.U., H.G.Ç.; Resources – O.D., M.M.O., A.S.Y.; Materials – O.D., M.M.O., A.S.Y., C.U., H.G.Ç.; Data Collection and/or Processing – O.D., M.M.O., A.S.Y., C.U., H.G.Ç.; Analysis and/or Interpretation – O.D., M.M.O.; Literature Search – O.D., M.M.O., A.S.Y.; Writing – O.D., M.M.O.; Critical Review – O.D., M.M.O., A.S.Y., C.U., H.G.Ç.

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REFERENCES

- 1. Carty HM. Paediatric emergencies: non-traumatic abdominal emergencies. Eur Radiol 2002;12(12):2835-48. [CrossRef]
- Helbling R, Conficconi E, Wyttenbach M, Benetti C, Simonetti GD, Bianchetti MG, et al. Acute nonspecific mesenteric lymphadenitis: more than "no need for surgery". Biomed Res Int 2017;2017:9784565. [CrossRef]
- Lucey BC, Stuhlfaut JW, Soto JA. Mesenteric lymph nodes: detection and significance on MDCT. AJR Am J Roentgenol. 2005;184(1):41-4. [CrossRef]
- Sivit CJ, Newman KD, Chandra RS. Visualization of enlarged mesenteric lymph nodes at US examination clinical significance. Pediatr Radiol 1993;23(6):471-5. [CrossRef]
- Rathaus V, Shapiro M, Grunebaum M, Zissin R. Enlarged mesenteric lymph nodes in asymptomatic children: the value of the finding in various imaging modalities. Br J Radiol 2005;78(925):30-3. [CrossRef]
- Sikorska-Wiśniewska G, Liberek A, Góra-Gebka M, Bako W, Marek A, Szlagatys-Sidorkiewicz A, et al. Mesenteric lymphadenopathy - a valid health problem in children. Med Wieku Rozwoj [Article in Polish] 2006;10(2):453-62.

- Puylaert JB. Mesenteric adenitis and acute terminal ileitis: US evaluation using graded compression. Radiology 1986;161(3):691-5. [CrossRef]
- Maconi G. Mesenteric lymphadenopathy. In: Maconi G, Porro GB, editors. Ultrasound of the gastrointestinal tract. 2nd ed. Springer;2013. p. 29-36. [CrossRef]
- 9. Karmazyn B, Werner EA, Rejaie B, Applegate KE. Mesenteric lymph nodes in children: what is normal? Pediatr Radiol 2005;35(8):774-7. [CrossRef]
- Toorenvliet B, Vellekoop A, Bakker R, Wiersma F, Mertens B, Merkus J, et al. Clinical differentiation between acute appendicitis and acute mesenteric lymphadenitis in children. Eur J Pediatr Surg 2011;21(2):120-3. [CrossRef]
- 11. Vayner N, Coret A, Polliack G, Weiss B, Hertz M. Mesenteric lymphadenopathy in children examined by US for chronic and/or recurrent abdominal pain. Pediatr Radiol 2003;33(12):864-7. [CrossRef]
- Wang WG, Tian H, Yan JY, Li T, Zhang TD, Zhao YP, et al. Enlarged mesenteric lymph nodes in children: a clinical analysis with ultrasonography and the implications. J South Med [Article in Chinese] 2011;31(3):522-4.
- Cai B, Yi H, Zhang W. Reference intervals of mesenteric lymph node size according to lymphocyte counts in asymptomatic children. PLoS One 2020;15(2):e0228734. [CrossRef]
- Robinson CG, Hernanz-Schulman M, Zhu Y, Griffin MR, Gruber W, Edwards KM. Evaluation of anatomic changes in young children with natural rotavirus infection: is intussusception biologically plausible? J Infect Dis 2004;189(8):1382-7. [CrossRef]

- 15. Gisserot O, Landais C, Cremades S, Bernard P, de Jaureguiberry JP. Acute abdominal pain in a 8-year-old girl with Epstein-Barr infection. Arch Pediatr [Article in French] 2005;12(3):288-90. [CrossRef]
- Zińczuk J, Wojskowicz P, Kiśluk J, Fil D, Kemona A, Dadan J. Mesenteric lymphadenitis caused by yersinia enterocolitica. Prz Gastroenterol 2015;10(2):118-21. [CrossRef]
- 17. Mehmood A, Ehsan A, Mukhtar M, Inayat F, Ullah W. Acute mesenteric tuberculous lymphadenitis: a comparative analysis of twenty-one cases. Cureus 2019;11(4):e4454. [CrossRef]
- Cakmakci E, Sahin GE, Hosnut FO, Cinar HG, Ucan B, Pala M, et al Antral gastritis caused by helicobacter pylori infection in the pediatric age group is associated with increased mesenteric lymph node dimension observed by ultrasonography. QIMS 2015;5(6):829-34.
- Lucey BC, Stuhlfaut JW, Soto JA. Mesenteric lymph nodes seen at imaging: causes and significance. Radiographics 2005;25(2):351-65. [CrossRef]
- 20. Bayramoglu Z, Caliskan E, Karakas Z, Karaman S, Tugcu D, Somer A, et al. Diagnostic performances of superb microvascular imaging, shear wave elastography and shape index in pediatric lymph nodes categorization: a comparative study. Br J Radiol 2018;91(1087):20180129. [CrossRef]
- Gross I, Siedner-Weintraub Y, Stibbe S, Rekhtman D, Weiss D, Simanovsky N, et al. Characteristics of mesenteric lymphadenitis in comparison with those of acute appendicitis in children. Eur J Pediatr 2017;176(2):199-205. [CrossRef]