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ORIGINAL ARTICLE

PATTERNS OF ULTRASOUND FINDINGS IN ABDOMINAL LYMPHOMA PATIENTS AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

Asfaw Atnafu Kebede, MD[1], Frehiwot Bekele Getaneh, MD[1]

ABSTRACT

Background: *Malignant lymphoma is a common primary hematopoietic malignancy. Cross sectional imaging is used commonly. The wide spread availability and diagnostic potential of ultrasound (US) place it at the forefront in the setting of resource limited countries that do not have access to the full range of imaging modalities and in which patients frequently present in the late stages of diseases.*

Objective: *Assess the patterns of abdominal organ involvement and ultrasound findings in patients with abdominal lymphoma.*

Material and Methods: *69 consecutive patients who came to the US unit of Tikur Anbessa Specialized Hospital (TASH) with the diagnosis of lymphoma were scanned. All examinations were performed by the authors based on standard scanning techniques. Cine and spot images were stored for analysis and finding recorded on a prepre-prepared and pretested format.*

Results: *Eighty nine percent of the patients were below the age of 60 and 75% were males. Chest x-ray and US were the modalities commonly used, while only 6 of 69 had computed tomography (CT) scans. Non-Hodgkin's lymphoma account for 81% of the cases. Lymph nodes were the most common organ involved and abdominal nodes accounted for 61% of the cases. Homogenous and hypoechoic echo appearances were seen in 52% and their pattern of involvement comprised multiple discrete nodes. Comparable overall patterns of involvement were seen in both pathologically confirmed and unconfirmed lymphoma cases. Liver followed by spleen was the most common abdominal organ involved, and organ enlargement and/or multiple variable sized hypoechoic lesions were the most common US findings.*

Conclusion: *Our study emphasizes the continued role of US for lymphoma patients. The US findings and pattern of organ involvement was found to be comparable with previous studies.*

Key words: US- ultrasound, CT- Computed tomography, Lymphoma

INTRODUCTION

Malignant lymphoma is a heterogeneous but potentially curable group of neoplasms, and is the most common primary hematopoietic malignancy. Its overall incidence is increasing globally, with age-adjusted incidence rates for Non-Hodgkin lymphoma (NHL) being highest in more developed countries. The incidence is also rising in sub-Saharan Africa where the prevalence of HIV is the highest in this part of the world, (1) and with HIV infection significantly increasing the risk for NHL.

Relatively older African studies showed that anemia accounted for the most common hematological disorder while malignancy accounted for only 3.5% hospital admissions.(2) However, Shamebo in 1987 analyzed the pattern of hospital admissions at Tikur Anbessa hospital and found out that, out of 450 hematologic pathologies, hematologic malignancies, i.e. leukemia and lymphoma, accounted for 56% of hospital admissions. (3)

Criteria for precise diagnosis of lymphoma depends on clinical, laboratory and imaging findings. Traditionally, clinical findings together with imaging including US contributed to diagnosis and staging which usually depended additionally on a surgical

[1]Department of Radiology, Addis Ababa University, College of Health Sciences, Addis Ababa, Ethiopia

biopsy specimen to obtain adequate tissue for pathological evaluation. However, currently cross-sectional imaging is primarily used to detect lymphadenopathy and the pattern of nodal involvement. Functional imaging, such as positron emission tomography (PET) with fluorodeoxyglucose (FDG), has shown promising results in the diagnosis, follow up and complete assessment of disease extent. (4, 5)

In Ethiopia, like other developing countries, radiological services are poorly developed. Plain radiographs and US are the most commonly available imaging modalities. CT is available in only in few centers. (6)

Sonography is a straightforward and convenient technique to investigate lymphadenopathy.(7) Superficial lymphadenopathy like the region of the neck is a common manifestation of lymphoma and detailed analysis of these nodes help in suggesting the cause of enlargement. Most lymphnodes in the abdomen are accessible and can be assessed transabdominally. This helps to determine which lymph node groups are involved and the different US appearance. Features like size, shape, echo texture, internal architecture, presence of calcification, and color Doppler flow studies help in suggesting whether a lymphvnode is lymphomatous or metastatic. (8)

Moreover, US is also a quick and noninvasive method for detecting lymphomatous involvement of abdominal organs such as liver, spleen, and gastrointestinal tract which are common organs involved in lymphoma. Different diseases can mimic lymphoma in ultrasound appearance, indicating the need for clinical correlation. Moreover, in countries like Ethiopia, patients frequently present at later disease stages and after using traditional medications which have potential to modify the US findings.

Therefore, identifying possible specific patterns related to delayed patient presentation, after local interventions, and in those patients related with HIV/ AIDS would aid interpretation of US findings for diagnosis and follow up. Few studies have been performed in Ethiopia to address these issues. Therefore, our objective in the present study was to assess the frequency of organ involvement and the patterns of ultrasound findings of patients with lymphoma, especially abdominal lymphoma.

MATERIALS AND METHODS

Consecutive patients who came to the US unit of Tikur Anbessa hospital from July 2013 to June 2014 with the clinical diagnosis of suspected or proven lymphoma were evaluated by US by the authors based on agreed standard protocols, and if compatible evidence of lymphoma was obtained by US were selected for review. Sixty-nine patients met these criteria. All examinations, including Doppler, were performed by a Toshiba US machine using a 5 MHz sector and a 7.5 MHz linear probe. Most patients were examined by both authors together and were recorded in both cine and spot film. The US findings were reviewed and documented based on the authors' consensus.

The patient record cards were reviewed after formal request of the hospital administration, and all relevant information was extracted. A prepared and pretested format was used to capture data, which was later entered into a spread sheet for analysis.

RESULTS

US findings of sixty nine consecutive lymphoma patients who came to the US unit of radiology department of Tikur Anbessa hospital from July, 2013 to the end of June, 2014 were reviewed. Fifty eight (84%) patients were below the age of 60. About forty one percent (28/69) were below thirty years of age. Females account for only twenty five percentage (17/69) of the total study population.

81% (56/69) of our patients had a chest x-ray (CXR) performed, while only about 9% (6/69) had a CT scan. No magnetic resonant imaging (MRI) or nuclear medicine examinations were performed for these patients. Forty five percent of patients had not started treatment and the rest had taken varying cycles of anti-lymphoma regimens. Review of their pathology reports revealed that the majority of patients, 52% (20/38), were reported to have high grade NHL, while 11% had low grade lymphoma. Among the pathologically proved patients, only 19% of patients had Hodgkin's lymphoma, while the rest (81%) had NHL with Burkitt, large cell and small cell lymphoma account for 5% (2/38), 8% (3/38) and 5% (2/38), respectively. (Table 1)

Table 1.Pathological Types of Lymphoma

Type of Lymphoma	*Frequency*	*Percentage*
High Grade NHL	20	52.6
Low Grade NHL	4	10.5
Large Cell NHL	3	7.9
Small Cell NHL	2	5.3
Burkittlymphoma	2	5.3
Hodgkin lymphoma	7	18.4

The abdominal nodes were involved in about 61%, and neck and other superficial nodes in 46 % of the sixty nine patients. The percentage of abdominal nodes was comparable among those cases which were pathologically confirmed (63%) and unconfirmed (58%), respectively. These lymph node regions were involved individually or in combination. Higher percentages of isolated neck and superficial nodes were seen in pathologically confirmed cases compared to those diagnosed clinically and by imaging, probably related to ease accessibility of these nodes. Isolated abdominal node involvement was noted in 13%. However, abdominal organ and node involvement was seen in 30% (Table 2). Isolated abdominal regional involvement was seen in 46% of cases, isolated abdominal node (13%)+ isolated abdominal organ (3%)+combined abdominal organ and node (30%). The common lymph node region involved in the abdomen were mesenteric node followed by retroperitoneal 43 vs. 23 %, which is also comparable irrespective of how the diagnosis of lymphoma was made. (Table 2)

The US echo appearance (Table 3) of the lymph nodes was found to be homogenous and hypoechoic in 52%, and heterogeneous with irregular and thickened hilum in 20%. (Table 3, Fig 1) Fifty four percent of the nodes were multiple, discrete and hypovascular in pattern. (Table 3) The classical sandwich sign, conglomerate and matted nodal involvement, was seen in 25% of cases. (Table 3, Fig 1) The general trend on the echo appearance, nodal pattern and vascularity of lymph nodes was found to be similar in both pathologically confirmed and unconfirmed. (Table 3) Abdominal organs were involved in 37 cases and isolated solid abdominal organ involvement was seen in only 2 cases. (Table 2) Patients who had a prior proven diagnosis of lymphoma by pathology and who were observed to have positive abdominal US findings were assumed to have lymphomatous spread of lymphoma within the abdomen.

Table 2. Comparative Pattern of Regional & lymphnode Involvement of the Lymphoma patients

Involvement pattern	Nodal region	Number among all 69 cases	% of total	Number among 38 confirmed cases	% of total confirmed	Number among 31 un-confirmed cases	% of total un- con-firmed
Site involved	Neck or other Superficial Nodes	32	46	22	58	10	32
	Abdominal Nodes	42	61	24	63	18	58
	Abdominal Or-gans	37	54	19	50	18	58
Mode of in-volvement	Neck and other superficial nodes only	9	13	8	21	1	3
	Abdominal Nodes Only	9	13	3	8	6	19
	Abdominal Or-gan Only	2	3	1	3	1	3
	Abdominal Or-gan and Nodes*	21	30	12	32	9	29
	Combined In-volvement**	28	41	15	39	13	42
LN site in-volvement in the abdomen	Retro-peritoneal	16	23	9	24	7	23
	Mesenteric	30	43	15	39	15	48
	Para solid organ	16	23	8	21	8	26
	Para aortic	14	20	6	16	8	26

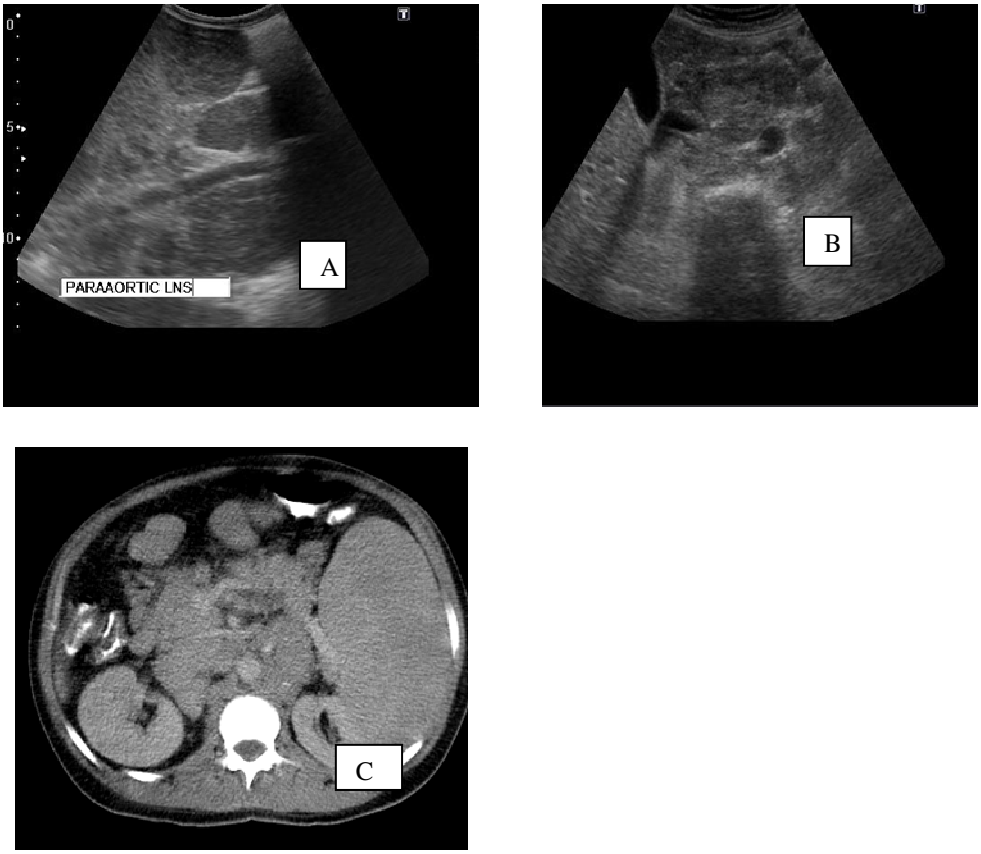
* A patient can have a combination of findings
**Combined Involvement: Patients with a combination of two or more findings from among the other categories: Neck and other superficial nodes only, Abdominal Nodes only, and/or Abdominal organ only

Table 3. Ultra Sound Appearance of Involved Lymph Nodes

US pattern and appearance of in-volved node		Number among all 69 cases	% of total	Number among 38 confirmed cases	% of total con-firmed	Number among 31 un confirm-ed cases	% of total un-confirmed
Nodal pattern	Discrete Multi-ple Node	37	54	23	61	14	45
	Conglomerate and Matted Node	17	25	11	29	6	19
	Discrete few Node	4	6	2	5	2	6
Echo Appear-ance	Homogenously hypoechoic	36	52	16	42	20	65
	Heterogeneous	14	20	8	21	6	19
Nodal Vascu-larity	Hypo vascular	28	41	12	32	16	52
	Hyper vascular	19	28	9	24	10	32

*****Includes patients whose US patterns can be determined in each category

Fig 1. A, B, & C. Retroperitoneal and mesenteric nodes (A,B), and CT scan (C) of a different patient with vascular elevation and encasement "Sandwich sign" (star in A, B & C)



Gastrointestinal and renal findings were seen in only 6 % of cases each (Figs 3 and 4). No pancreas, gallbladder, and pelvic organs findings were seen in our series. The most commonly involved abdominal organs were the liver and spleen which accounted for 35% and 29%, respectively. For both organs the most common US finding was non-specific hepatomegaly in 53% and splenomegally in 56% of patients. The other finding observed in the liver was few or multiple variable sized hypoechoic lesions (Fig 2A) in 25 % of cases. Multiple small hypoechoic lesions were observed in 30% of patients with splenic involvement. (Fig 2B)

Renal US abnormalities were was seen in two cases. The findings were multiple well defined hypoechoic lesions (Fig. 4A) and one case revealed an infiltrative perirenal mass. (Fig. 4B) One patient had bilateral hypoechoic adrenal lesions. (Fig 5A&B)

Positive bowel finding was seen in 4 cases (6 %), and the findings observed were a polypoid thickening of the bowel wall with associated dilatation of it's lumen and lymphadenopathy. One of these patients had CT scan and the findings were comparable to that of US. (Fig 3)

Fig 2.Multiplehypo echoic splenic and hepatic hypovascularlesions in a confirmed lymphoma patient (A& B stars).

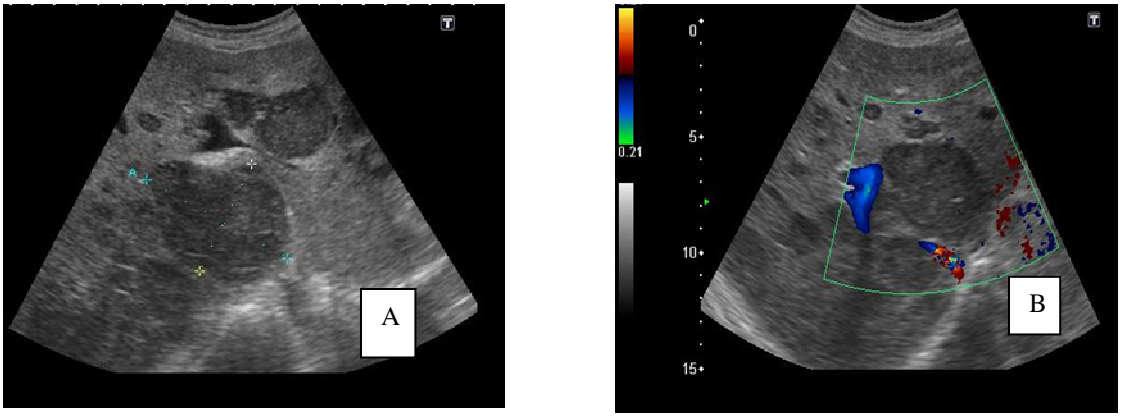


Fig 3 A. US showed uniformly thickened bowel wall (star), hypoechoic appearance with echogenic mucosa and air shadow (arrow). The corresponding CT image (B) in the same patient showed thickened wall (star) with dilated bowel loop (arrow).

Fig. 4. Transverse (A) and longitudinal (B) US images of two patient with proven lymphoma illustrating renal involvement, focal hypoechoic shadow (arrow in A) and a perirenal infiltrative lesion (arrows in B).

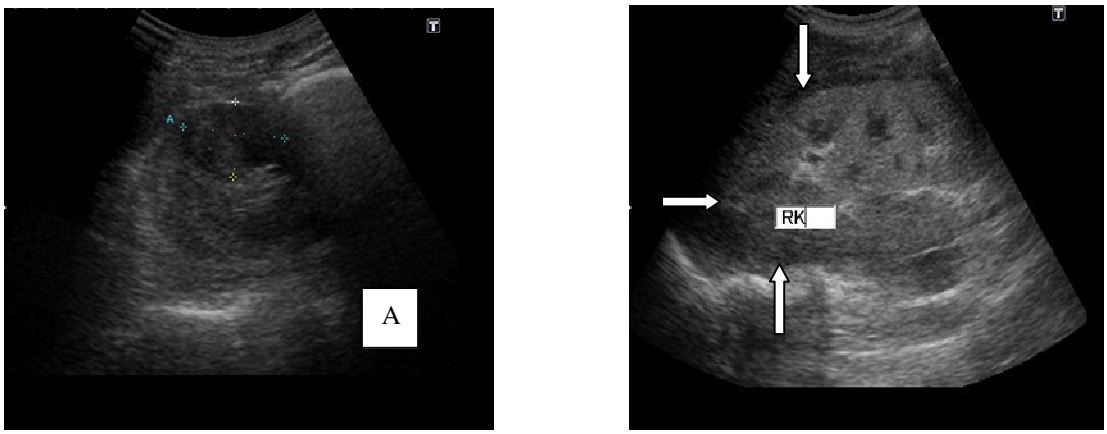
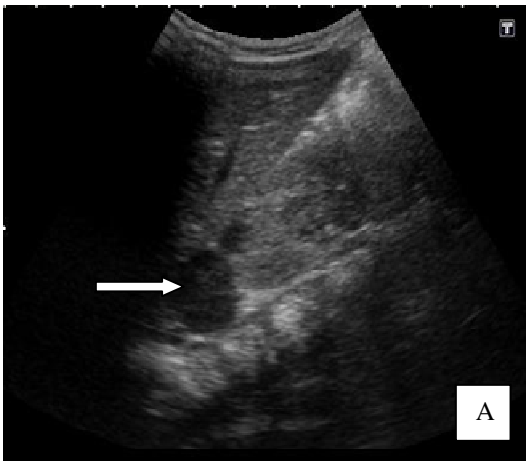
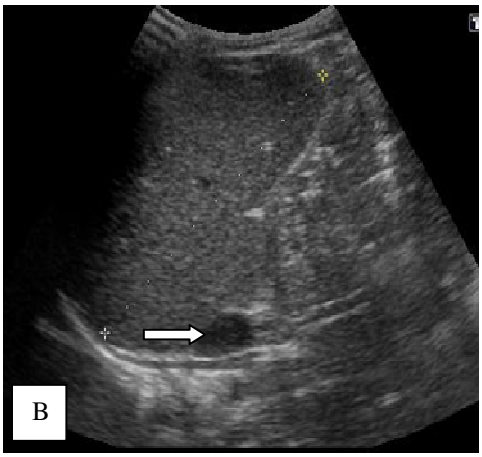


Fig.5A & B. US of the adrenal gland in confirmed lymphoma patients showed hypoechoic adrenal lesion (arrows in A and B)





DISCUSSION

Lymphoma, solid tumors of the immune system, commonly involve organs which contain lymphoid cells, especially at the onset of disease; nodal and splenic involvements are more common in Hodgkin disease, whereas extranodal involvement is more frequent in non-Hodgkin lymphomas. (9)

About 45% (31/69) of our patients were not pathologically confirmed and their diagnosis was made on the basis of clinical and imaging criteria. However, studies have shown that diagnosis of lymphoma can be made with a high degree of certainty based on clinical, laboratory and imaging findings. Precise staging has previously requires surgical biopsy, but recently cross-sectional imaging replaced the need for biopsy. (4,5) The relatively comparable US findings we observed in both confirmed and unconfirmed lymphoma patients illustrates the strength of imaging studies in the diagnosis of lymphoma in the appropriate clinical setting.

Nodal involvement by lymphoma is confirmed based on change in size in relation to the specific site involved. (10) Based on change in nodal size, our series showed nodal involvement to be the most involvement. Castellino and Goffinet et al reported similar findings where lymph node involvement was the most common involvement. (11, 12) Mesenteric nodes are commonly involved in the current study followed by retroperitoneal and para-solid organs involvement. These observations are in agreement with the previously stated study, where retroperitoneal nodes were involved in 25–35% of patients with HD and 45–55% of patients with NHL, while mesenteric lymph nodes were involved in more than half the patients with NHL and less than 5% of patients with HD. Usually patients develop retroperitoneal or mesenteric nodal involvement which gradually extends to other lymphnodes. Combinations of lymph node involvement in distant anatomic regions was a common finding in our cases, which could be due to presentation of our patients at later stages of disease.

Various studies showed that abdominal nodal involvement on US and CT imaging is seen as homogenous discrete masses that often surround mesenteric arteries and veins. They can grow so large that it encases the mesenteric vasculature and displace abdominal organs.(13-16) The present study also showed frequent homogenous discrete hypoechoic US findings(54%). Those cases involving the mesentery showed conglomerate multiple nodes surrounding the vessels, most were hypovascular.

Spleen, like nodal lymphoma, is a common site involved by lymphoma. Munazza et al and Goerg et al observed that spleen, more than the liver, is involved in 30–40% of patients with HD and NHL at the time of presentation.(4,13,14) Unlike their studies, splenic involvement in our series occurred in only about 29% of the cases, and less than that of the liver involvement. There is no explanation for this discrepancy. However, in agreement with these studies, nonspecific splenic enlargement and multiple hypoechoic small deposits were common findings. Even though splenomegally is often assumed to arise

secondary to microscopic and diffuse lymphomatous involvement, studies have shown that it does not necessarily indicate lymphoma involvement; 33% of patients have splenomegaly without infiltration and, conversely, 33% of normal-sized spleens are found to contain tumor following splenectomy. (4,13,14) Thus clinicians should be cautious in staging these patients in light of these observations.

Hepatic lymphoma usually occurs in the setting of systemic lymphoma in both HL and in NHL. Rarely, it may be a primary lesion and almost always of the NHL large cell type. In our series, liver (35%) was the most frequently involved abdominal organ, even higher than the spleen. Several patterns of hepatic involvement have been previously reported, including hepatomegaly, suggestive of diffuse liver infiltration, and multifocal hepatic masses resembling metastatic disease. (13,14,17) Except for a relatively higher percentage of liver involvement, our US findings here are in agreement with others' findings; 53% of patients had non-specific hepatomegaly while 25% showed few or multiple variable sized hypoechoic lesions. The uniform cellularity of lymphoma without significant background stroma is thought to be related to the hypoechoic appearance. (17)

The Gastrointestinal (GI) tract can be involved in both secondary and primary lymphoma. Secondary gastrointestinal involvement is common because of the frequent origin of lymphomas in the mesenteric or retroperitoneal nodes and the abundance of lymphoid tissue in the gastrointestinal tract. Unlike our series, in which 6% of cases showed GI involvement, reports of GI involvement in up to 50% of lymphoma cases. The stomach, followed by duodenum, small and large bowel have shown involvement in that order of incidence. (14) The relatively low GI involvement seen in our study is likely because Ultrasound is relatively insensitive to subtle gastrointestinal wall changes compared to CT.(18, 19)

Patterns of GI involvement in lymphoma include infiltrative, radiologically seen as circumferential wall thickening, and polypoid, appearing as a submucosal mass or as multiple discrete submucosal nodules which may have central ulceration or cavitation. (4,19) Our cases showed the former two appearances.

According to Dawson et al (20) diagnosis of primary GI lymphoma requires a normal chest x-ray, normal white blood cell count and absence of other organ involvement at laparotomy; nonetheless, we suspected one of our patients had primary lymphoma.

The genitourinary system, in particular the kidney is often affected by extranodal spread of lymphoma, and is reportedly the second most commonly affected anatomic site after the hematopoietic and reticuloendothelial systems. Reports from autopsy series describe foci of lymphoma in the kidneys in approximately one-third of cases. Unlike the autopsy series, only 3–8% of patients undergoing routine evaluation for staging or during the course of therapy show renal involvement. (21,22) The observation in our series (6% of cases with renal involvement) is in agreement with the literature. Our US findings here of focal solitary and multiple hypoechoic cortical lesions in two patients and one patient with perirenal infiltrates encasing the kidney are also compatible with the aforementioned reports. None of our patients underwent biopsy to prove lymphoma; however, the literature recommends that in the setting of disseminated disease, positive renal US findings can be considered as renal involvement. (21, 22)

Adrenal glands are unusual sites for primary lymphoma but are involved in 4% of patients with NHL. In our study, there was only one patient with bilateral adrenal involvement which appeared as hypoechoic adrenal masses.

In conclusion, the current study confirmed the continued role of US in lymphoma patients. Even though our study was limited by lack of confirmatory pathology in a minority of cases and the inability to scan all patients prior to therapy, our US findings and pattern of organ involvement was comparable with other studies. While US is being replaced by other imaging modalities in developed nations, given it's widespread availability and potential value in revealing abdominal pathology as demonstrated in this series, US should remain as the main diagnostic modality in abdominal lymphoma.

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