

Abdominal ultrasound findings in HIV and tuberculosis

It is estimated that almost 34 million people worldwide live with HIV/AIDS. The clinical and imaging features of HIV/AIDS are varied depending on the patient's immune status. Currently with wide application of highly active antiretroviral therapy, the disease pattern has furthermore changed. Ultrasound is often the most available, most accessible and often the initial imaging modality for HIV patients with abdominal symptoms. It is important that those managing these patients are updated with the ultrasound appearances to facilitate rapid and accurate diagnosis of HIV and its comorbidities. This review paper, illustrated with relevant images, outlines ultrasound appearances in HIV/AIDS-related tumors, tuberculosis, hepatitis, cholangiopathy, pancreatitis, immune reconstruction syndrome, nephropathy and the vascular system. This review is intended to be a resourceful update and an aid to more accurate diagnosis of abdominal complications of HIV/AIDS.

KEYWORDS: HIV/AIDS • tuberculosis • ultrasound

Michael Grace Kawooya

Ernest Cook Ultrasound Research
& Education Institute (ECUREI),
Kampala, Uganda
kawooyagm@yahoo.co.uk

AIDS was first recognized in the early 1980s as a disease entity caused by a virus (HIV) and manifesting as a complex collection of clinical features due to the primary HIV infection plus related comorbidities. Currently with wide application of highly active antiretroviral therapy (HAART), the disease pattern has furthermore changed. Ultrasound (US) is often the most available, most accessible and often the initial imaging modality for HIV patients with abdominal symptoms. Over the past two decades, numerous studies, in various parts of the world, have documented the complex, yet informative and clinically useful abdominal US findings in HIV/AIDS. The comorbidities for which US is useful include tumors, infections and vascular pathology resulting from abnormal fat metabolism and inflammatory and degenerative changes. US has proven useful for diagnosis, image-guided interventional procedures, follow-up of patients on specific treatment regimens and screening for early detection of comorbidities. This review article outlines these applications.

Tumors

Tumors affecting HIV patients are divided into AIDS-defining cancers (ADC) and non-ADC. ADC are: non-Hodgkin's lymphoma (NHL), Kaposi sarcoma (KS) and cervical cancer. Non-ADC include several cancers such as lung and breast cancer. Benign neoplasms also manifest as comorbidities in HIV/AIDS. Common benign neoplasms include liver hemangiomas, and

lipomas in different parts of the body. In the USA, the incidence of ADC (NHL and KS) stood at 3.5/1000 person-years in 2005, and the proportion of cancers in HIV/AIDS contributed to by ADC was 25.9% in the same year [1].

■ NHL & Hodgkin's lymphoma

NHL is the most prevalent comorbid tumor in HIV/AIDS. In the USA, there has been a decrease in NHL between 1996 and 2005 from >5/1000 to 1/1000 person-years [1,2].

HIV/AIDS-associated NHL is often of a high grade and with a poor prognosis. Common histological types are lymphoblastic, immunoblastic and Burkitt's. NHL is often multifocal, involving several organs in the abdomen. In the liver, it may be solitary or multiple and is usually hypoechoic or anechoic, but may also be hyperechoic and, at times, with a target sign [3].

In the spleen, NHL may manifest as splenomegaly with or without focal masses. The masses are usually hypoechoic or anechoic [3,4].

In the kidney, NHL takes on different appearances depending on its location and multiplicity. It may manifest as generalized kidney enlargement or as solitary or multiple parenchymal masses, displacing vessels. The masses may be hypoechoic or anechoic and may not show a malignant pattern of vascularity with Doppler testing. This malignant pattern is characterized by an increase in the number of vessels. These numerous vessels also appear abnormally tortuous and haphazardly distributed. NHL may show subcapsular, perirenal

and pararenal extensions [5]. Bowel involvement may be seen as thickening, loss of the normal five-layer structure or hypervascularity on a color Doppler [3,6]. Ovarian involvement in NHL may show as hyperechogenic masses, which may be bilateral [7]. In the testis, NHL may manifest as mixed echogenicity, predominantly hypoechoic mass, with increased flow at Doppler [8].

Lymph node involvement in NHL is common. Retroperitoneal and intraperitoneal nodes may be involved. They may be isoechoic or hypoechoic with the surrounding structures. Rarely the lymph nodes may show areas of calcification [3]. Uniform thickening of major abdominal and hepatic vessels due to NHL infiltration has been observed [3]. NHL may extensively extend into the pararenal and perirenal spaces of the abdomen and retroperitoneum, surrounding the major arteries, pancreas and kidney (FIGURE 1).

The incidence of Hodgkin's lymphoma in HIV patients on HAART in one study in the USA was 0.65%. This may manifest as multiple abdominal lymphadenopathy [9].

■ **Kaposi sarcoma**

KS is one of the most common malignancies of the abdomen in HIV/AIDS patients. In the USA, there has been a decrease in KS between 1996 and 2005 from 5/1000 to 1/1000 person-years [1,2]. KS may involve the GI tract and other abdominal and retroperitoneal structures. The most common gastrointestinal sites are the small intestines, colon and stomach [10,11]. In the liver, KS may manifest as hepatomegaly or focal hyperechoic masses, which may be adjacent to the portal triad [12]. In the genitourinary system, there may be hydronephrosis, with or without hydro-ureter. Retroperitoneal masses encasing the aorta and ureters leading to hydronephrosis have been observed. The lymph node enlargement in KS cannot be distinguished from tuberculosis (TB) just by US (FIGURE 2) [3].

■ **Hepatocellular carcinoma**

Hepatocellular carcinoma has been noted as a comorbidity in HIV/AIDS and its incidence is rising, especially in the context of hepatitis C and B virus coinfections. The reason for the

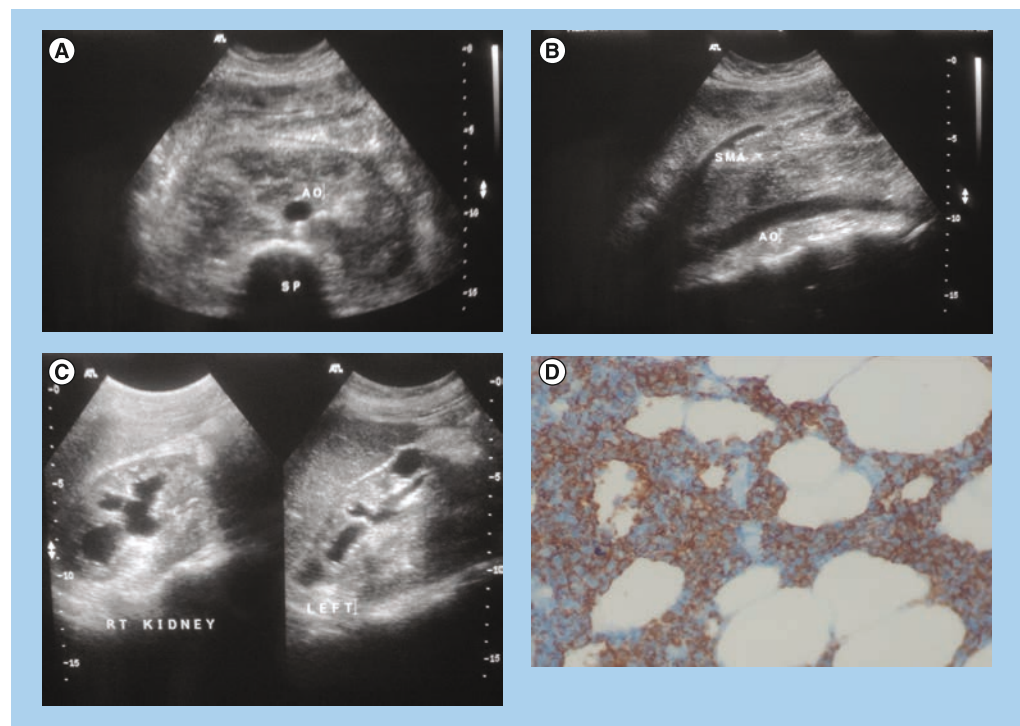


Figure 1. A 48-year-old female with marginal zone B-cell lymphoma. (A) This transverse scan through the pancreas shows retroperitoneal and intraperitoneal extension of lymphoma masses. The retroperitoneal masses involve the anterior pararenal space, which contains the pancreas. They also involve the perirenal space that surrounds the kidneys, the aorta and its branches and the inferior vena cava. **(B)** This sagittal section shows lifting up of the aorta and the superior mesenteric artery due to the tumor masses that surround them. **(C)** This sagittal scan of the kidneys shows lifting up of the kidneys because of the mass effect resulting from the tumor in the retroperitoneal space. **(D)** The tissue biopsy specimen of the retroperitoneal masses, obtained using ultrasound guidance and stained with immunoperoxidase, shows tumor cells consistent with marginal zone B-cell lymphoma.

increase is postulated to be either acceleration of hepatocellular carcinoma pathogenesis by the HIV virus or the increased longevity of HIV/AIDS patients due to HAART, but there is no proof for either. Hepatocellular carcinoma may be solitary or multiple and with varying grades of echogenicity [3,4,13].

■ Cholangiocarcinoma

Cholangiocarcinoma has also been documented in HIV/AIDS patients, and at times in association with AIDS-related cholangitis, but it is not yet proven if its incidence is more than in the seronegative population [14].

■ Hemangiomas

The most frequent histopathological diagnosis for solitary echogenic liver masses in HIV/AIDS patients in Uganda is cavernous hemangioma. In one patient, a coexistence of hemangioma and *Cryptococcus* microorganisms was documented (FIGURE 3) [3].

Lipomas have been described, especially in patients on HAART treatment. These lipomas may be in subcutaneous tissues of the abdomen. The lipomas usually appear as echogenic masses [15].

Tuberculosis

AIDS remains the strongest risk factor for developing abdominal TB. The incidence of TB among patients varies with CD4 count or WHO stage, and with HAART treatment. In South Africa in 2005, the risk of TB in patients with CD4 of <100 ml and with WHO stages 3–4 was 5.7 and 3.88/100 person-years, respectively [16]. The impaired Th1-type immune response makes HIV/AIDS patients more susceptible to abdominal TB. Abdominal TB prevalence in HIV/AIDS varies depending

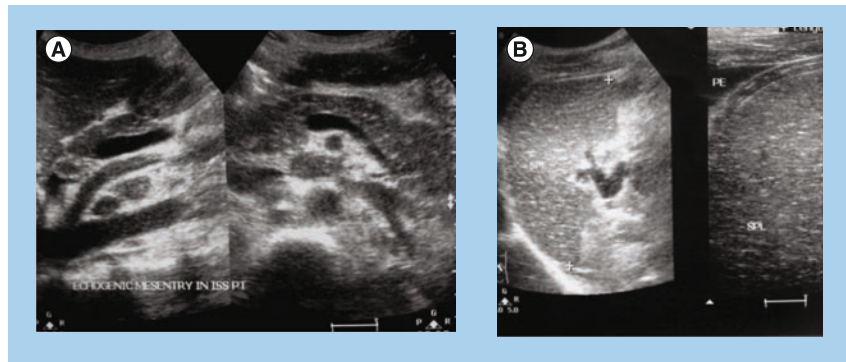


Figure 2. Retroperitoneal lymph nodes and stippled spleen in epidemic Kaposi sarcoma. (A) Retroperitoneal and mesenteric lymphadenopathy in a patient with epidemic Kaposi sarcoma. Enlarged, ovoid hypoechoic lymph nodes are seen surrounding the aorta and superior mesenteric artery. **(B)** Spleen showing fine echogenic stippling in a patient with epidemic Kaposi sarcoma. There are fine, thin, short, linear echogenic shadows scattered uniformly throughout the spleen. In addition, the patient has a small pleural effusion. A biopsy of skin nodules had shown Kaposi sarcoma. Scale bars represent 1 cm.

on the geographical location and the patient's immunity as per CD4 count [17].

The sonographic appearance of abdominal TB is not pathognomonic, and biopsy with histology and/or staining for acid-fast bacilli is the only method of proof [3,18].

In most studies, the most common sonographic observation in 55.3–96.7% of patients is lymphadenopathy. This may be retroperitoneal and/or mesenteric. The size of lymph nodes varies, but they are commonly hypoechoic or anechoic and avascular, at times with loss of central hilar echogenicity. Sometimes the nodes may coalesce. Aspiration of nodes commonly shows caseation, granulomas and plenty of acid-fast bacilli (FIGURE 4) [3,18–24].

In one study in India, among non-AIDS patients with abdominal TB, ascites were more common (79%) compared with lymphadenopathy (39%) and in this study, US proved to be more useful in

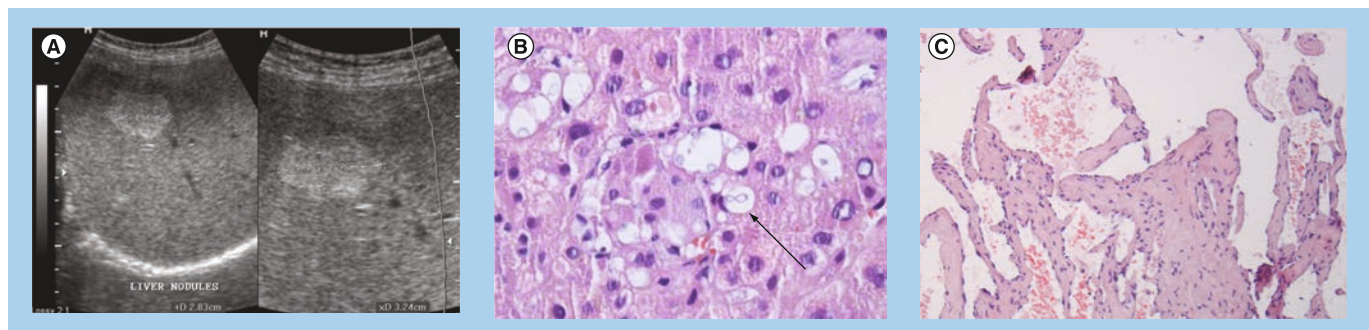


Figure 3. A 45-year-old female with cavernous hemangioma coexisting with *Cryptococcus*. (A) There is a well-defined ovoid uniformly hyperechoic nodule in the right liver lobe. **(B)** The tissue biopsy specimen, obtained from the liver using ultrasound guidance, shows budding yeast cells (arrow) with a narrow base and thick capsule consistent with *Cryptococcus* microorganisms. **(C)** The tissue biopsy specimen of the liver, obtained using ultrasound guidance, in the same patient with *Cryptococcus* microorganisms also shows anastomosing vascular channels lined by bland epithelium, consistent with cavernous hemangioma.

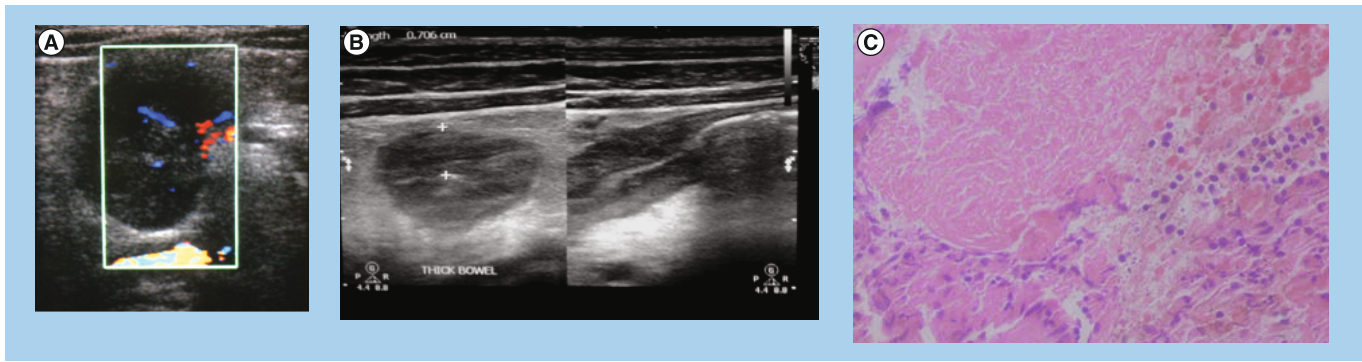


Figure 4. Lymphadenopathy and thick bowel loops in tuberculosis in a 14-year-old female. (A) This sonogram shows a large ovoid hypoechoic mesenteric lymph node with no increase in vascularity. (B) The small bowel loop is 7 mm thick and hypoechoic. The central echogenic stripe represents the bowel lumen. The surrounding mesentery is echogenic. (C) The tissue biopsy specimen of the lymph node obtained using ultrasound guidance shows a well-formed granuloma with central caseous necrosis indicating tuberculosis.

comparison with other imaging modalities for the investigation of TB abdomen [25].

Apart from *Mycobacteria tuberculosis*, other mycobacteria have been documented in some cases of lymphadenopathy.

The commonest splenic appearance in abdominal TB is multiple small hypoechoic splenic nodules of size 0.1–1 cm (FIGURE 5). These are seen in 7.1–89.7% of patients with TB abdomen, and thus high-resolution US is

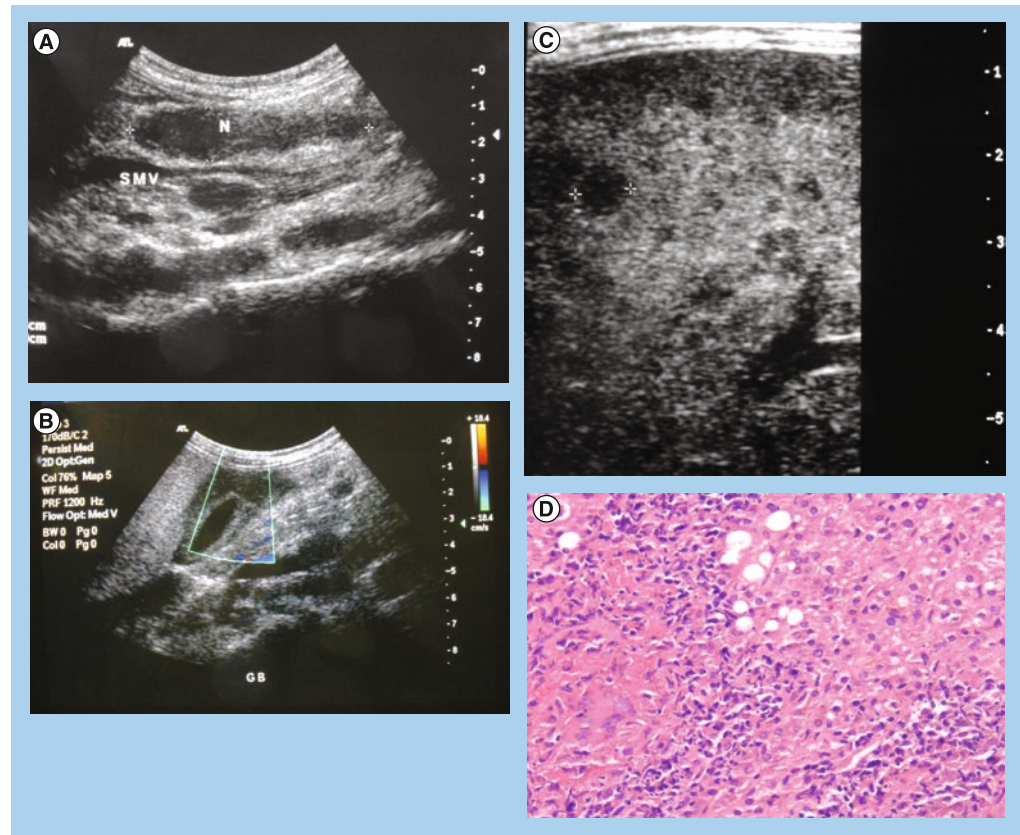


Figure 5. Tuberculous adenitis, hepatitis and splenic nodules in a 23-year-old female. (A) This sagittal scan of the upper abdomen shows a large hypoechoic lymph node anterior to the superior mesenteric vein and a smaller node posterior to the superior mesenteric vein. The nodes are surrounded by echogenic mesentery. (B) This scan of the gall bladder and the liver shows a focal hypoechoic lesion within the liver, adjacent to the gall bladder. (C) This scan of the spleen shows multiple widespread hypoechoic splenic nodules of varying size, with the largest measuring 5 mm. (D) A tissue biopsy specimen of the liver obtained using ultrasound guidance shows necrotizing granulomatous inflammation consistent with tuberculosis hepatitis. Abdominal lymph node biopsy of the same patient showed histology consistent with tuberculosis lymphadenitis.

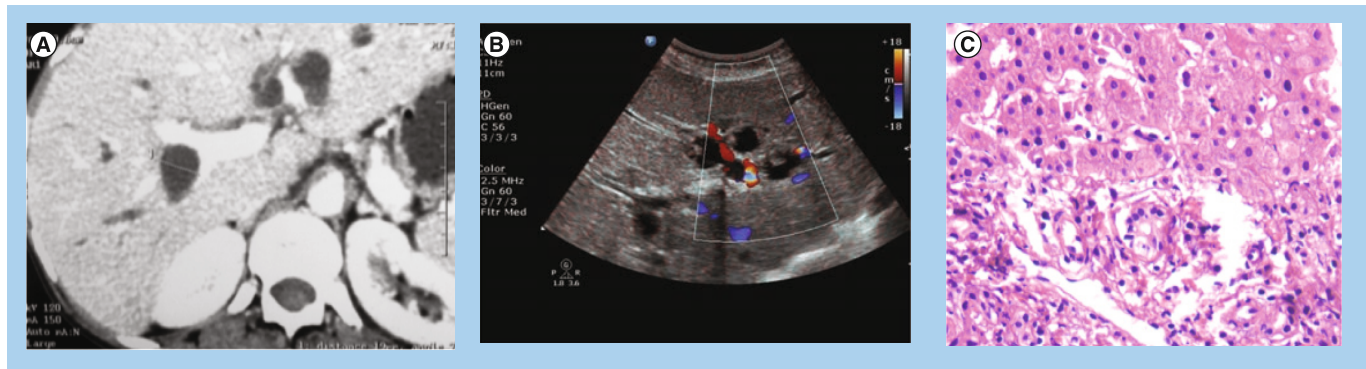


Figure 6. Hepatitis and periportal inflammation with cystic formation. (A) This enhanced CT scan shows nonenhancing periportal masses. **(B)** This ultrasound scan of the liver shows that the hypodense masses seen in the CT scan are cystic. **(C)** This tissue biopsy specimen of the liver and wall of the cyst, obtained using ultrasound guidance, shows hepatitis and periportal inflammation.

necessary to clearly show these small nodules. Splenomegaly is encountered in 12.9–27.6% of patients with abdominal TB. The spleen may also show small hypoechoic nodules or areas of necrosis [3,20,26,27]. Mycobacteria other than *M. tuberculosis* may also give small hypoechoic splenic nodules.

The most common liver finding in abdominal TB is hepatomegaly (18.8–20.08%). Other findings are increases in liver echogenicity and hyperechoic nodules, larger hepatic masses or granulomas, and periportal hypoechoic masses coexisting with scattered foci of calcifications (FIGURE 5) [3,4,20,28].

Ascites are a common manifestation of abdominal TB, and may be seen in 2.9–76% of TB patients. The ascites may be free or loculated, and may have septations. Ascites may also give a lattice-like pattern, and may show small particles or incomplete septa resembling violin strings [3,17,19,20,22,29,30].

Renal involvement in abdominal TB may manifest as multiple hypoechoic lesions, small cortical thick-walled abscesses or small calcified foci in longstanding infections. Hydronephrosis due to obstruction by retroperitoneal masses has been observed and this may resolve with TB therapy. The adrenal glands and urinary bladder wall may also show small hypoechoic nodules [5,26].

Bowel involvement is frequently observed in abdominal TB. The small bowel is most commonly involved, but the stomach, duodenum, jejunum and colon are also involved. The most common portion of the small bowel to be involved is the ileal–cecal junction. The involved bowel is often thickened and the thickening is often uniform, and the wall hypoechoic, with loss of the normal five-layer wall structure, and with no increase in vascularity (FIGURE 4). The bowel is sometimes matted, and may be associated with intestinal obstruction [3,18,26,31].

Pelvic TB may present with ascites, tubo-ovarian masses or omental nodules or masses. The sonographic appearance of an ovarian or pelvic mass and ascites may mimic ovarian carcinoma and, furthermore, the carcino–embryonic antigen may also be positive in women with TB pelvis. Laparoscopy and biopsy are necessary for differentiating TB pelvis from ovarian carcinoma [29,32]. The mesentery may be involved in TB abdomen and this may be seen as thickening and hyperechogenicity [23].

Nonspecific adenitis

Nonspecific lymphadenitis is not infrequent in HIV. Some patients may present with significantly large mesenteric or retroperitoneal lymphadenopathy but with no specific histological finding. In some of these patients, the histology report is nonspecific inflammation, nonspecific lymphocyte infiltration with or without background necrosis and cellular debris. US is not able to differentiate nonspecific adenitis from other types of lymphadenopathy which have a specific cause. Special histology stains are necessary to exclude TB and the clinical picture or

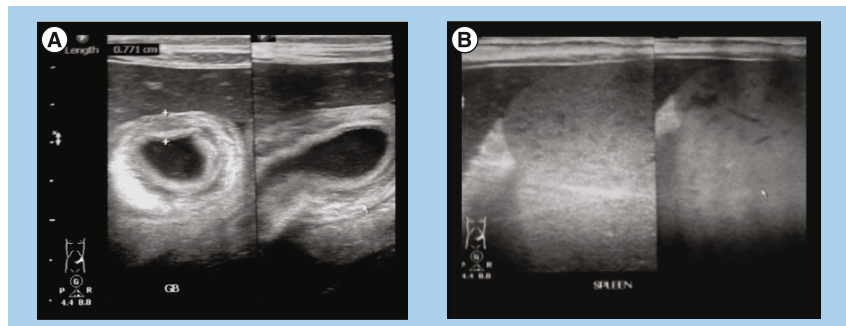


Figure 7. Gall bladder thickening and enlarged echogenic spleen in a 45-year-old female. (A) This transverse and longitudinal scan of the gall bladder shows a wall thickening of 7 mm. **(B)** This transverse scan of the spleen shows an enlarged and echogenic spleen that touches the relatively hypoechoic liver in the midline, giving the ‘kissing sign’ of the liver and spleen.

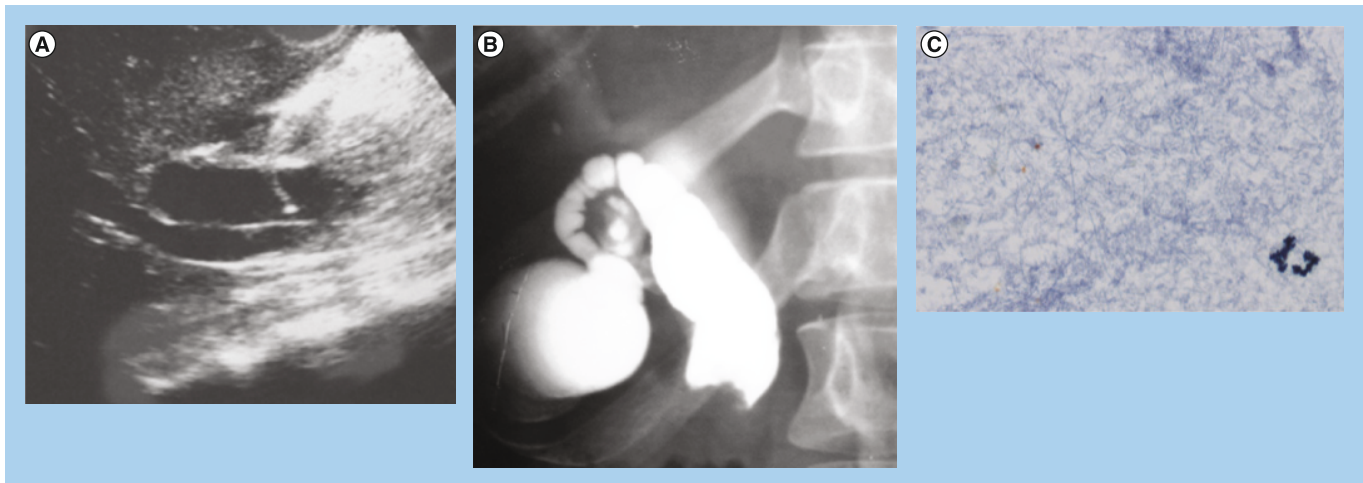


Figure 8. Cholangiopathy in a 24-year-old female presenting with jaundice. (A) Dilated common bile duct. An oblique scan of the right upper abdomen shows a dilated common bile duct. A Chiba needle (bright echo in duct) was inserted under ultrasound guidance into the common bile duct to obtain a sample for analysis and to opacify the duct with iodinated x-ray contrast medium. **(B)** A film taken after opacifying the common bile duct shows gross dilatation and beading of the duct with a distal obstruction depicting a sharp cutoff at the point of the obstruction. **(C)** The smear from the bile aspirate reveals branching bacilli indicative of *Nocardia*.

evidence of TB elsewhere in the body are useful in excluding TB adenitis.

Immune reconstitution inflammatory syndrome

Immune reconstitution inflammatory syndrome (IRIS) is characterized by the flaring up of already existing comorbid conditions at the onset of HAART treatment. IRIS is due to unregulated restitution of a pathogen-specific immune response. It is observed in 10–25% of patients on HAART [33]. It may occur for a variety of comorbidities, such as *M. tuberculosis*, atypical mycobacterium, fungi, herpes viruses, cholangiopathy and even tumors. For TB, this may be seen as lymphadenopathy, ascites, splenic nodules and abscesses in different organs. Patients with extrapulmonary TB at initial diagnosis and low lymphocyte counts are more at risk. IRIS may

occur from a few weeks to 2 years after initiation of HAART [16,34–38].

Hepatitis

Hepatitis has been documented as one of the HIV/AIDS comorbidities. The liver may appear normal in size and often shows increased echogenicity. Hepatitis may be viral or TB-related (FIGURE 5) [3,4]. Irregular thick-walled cystic spaces may accompany the hepatitis (FIGURE 6).

Gall bladder wall thickening & cholangiopathy

Gall bladder wall thickening and HIV-associated cholangiopathy are comorbidities in HIV/AIDS. Gall bladder wall thickening and cholangiopathy often coexist and their pathogenesis is thought to be similar (FIGURE 7) [3].

Bile duct abnormalities in HIV/AIDS are observed in 20–49% of patients and the most common is cholangiopathy [3,4,39–41]. Cholangiopathy is seen using US as bile duct thickening, obstruction and dilatation. Various infective agents have been associated with HIV cholangiopathy, namely cryptosporidia, microsporidia, cytomegalo-inclusion virus, mycobacteria avium intracellulare and other mycobacteria (FIGURE 8). Other associated infections are fungus-like *Histoplasma capsulatum* and viruses. All these have been isolated in the specimens of these patients, but none are yet proven to be the actual causative agent. KS of the biliary ducts may also have been associated with cholangitis [3,42–47]. Patients with cholangiopathy are known to have a poor prognosis, but antiretroviral treatment

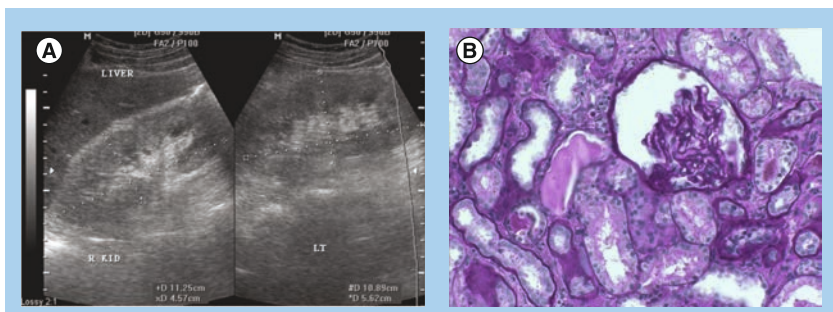


Figure 9. HIV-associated nephropathy in a 43-year-old female. (A) The kidneys are normal in size but moderately echogenic with loss of cortical medullary differentiation. **(B)** The histology demonstrates collapsing glomerulosclerosis evidenced by wrinkling and collapse of the glomerular basement membrane, constricted glomerular capillaries and microcystic dilatation of the tubules. The dilated tubules show eosinophilic proteinaceous casts.

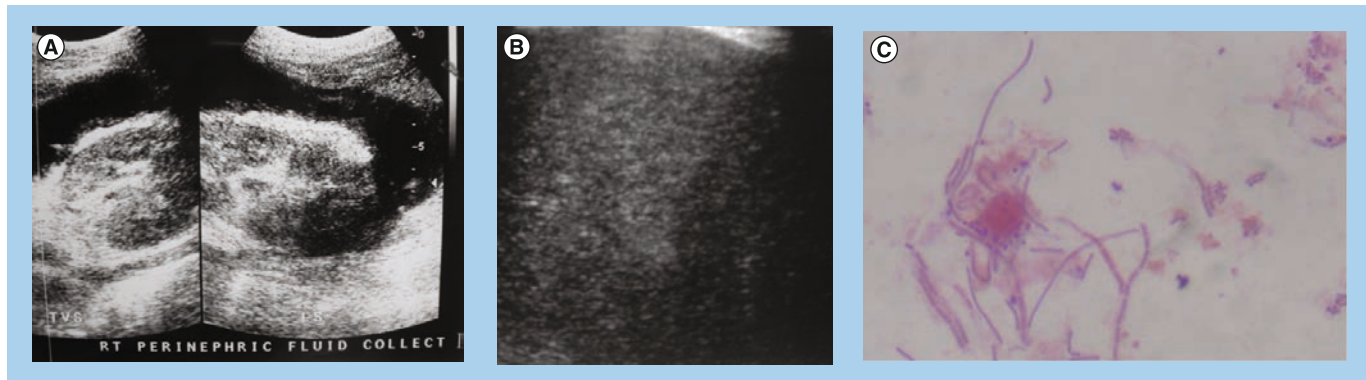


Figure 10. Perinephric fluid collection due to fungal infection in a 43-year-old male. (A) This scan of the right kidney shows perinephric fluid with strands. The strands give the kidneys a shaggy contour. **(B)** This scan of the spleen shows a markedly heterogeneous echotexture. **(C)** This aspirate of perinephric fluid obtained under ultrasound guidance shows budding yeast cells.

has improved the prognosis of these patients. Antiparasitic agents against cryptosporidia do not appear to improve prognosis [46,48].

Pancreatitis

The incidence rate of pancreatitis among HIV-1-infected patients as per one study in the USA in 2006 was 0.61/1000 person-years [49]. Acute and chronic pancreatitis may occur at times with pseudocyst formation. Giant pseudocysts in the pancreas have been documented [3,50]. Some studies have reported an increased incidence of acute pancreatitis for patients in whom hydroxyureas are used to potentiate antiretroviral treatment. The proportion of pancreatitis attributed to antiretroviral treatment in HIV/AIDS patients is uncertain [51]. Pancreatic TB has been documented in patients with immunodeficiency syndrome. It may manifest as well-defined cystic masses, solid masses or pancreatitis. Aspirate of cystic masses is often positive for acid-fast bacilli with Ziehl–Neelsen stain [52,53].

HIV-associated nephropathy & other renal pathologies

The incidence of HIV-associated nephropathy (HIVAN) among the black population in the USA is 3.5–12% [54]. The most common renal pathology is HIVAN. In the USA, HIVAN has been found to be more prevalent in American men of African origin. This higher prevalence is thought to be genetic and a gene *MYH9* is now considered to be a major-effect risk gene for the histopathological changes in HIVAN. HIVAN may present as reduced renal function or renal failure characterized by proteinuria and high creatinine levels. The most common histopathological diagnosis in HIVAN is collapsing focal segmental glomerulosclerosis. Increased renal echogenicity, equal to or approaching that

of the renal sinus fat, has been demonstrated to be statistically significant for HIVAN, occurring in up to 89% of patients. The echogenicity is often associated with loss of corticomedullary differentiation and there may be thick pelvicalyceal system walls. The kidneys in HIVAN are often normal in size but may be enlarged and enlargement is usually globular in the initial stages. HIVAN can only be confirmed by biopsy and histology (FIGURE 9) [5,55–57]. The perinephric space may be infiltrated by tumor, bacterial or fungal infections (FIGURE 10).

Apart from HIVAN, other pathologies include nephrolithiasis, chronic pyelonephritis, fungal infections (*Pneumocystis jiroveci* and *Candida albicans*) and HAART-related nephropathy.

Other HIV/AIDS comorbid infections

Other infectious HIV comorbidities include pyogenic, fungal and bacterial infections and these may involve all abdominal organs, but more commonly the liver, spleen and kidneys. Candida of the spleen shows as multiple small nodules typically with a target sign (FIGURE 11) [3,4]. The psoas

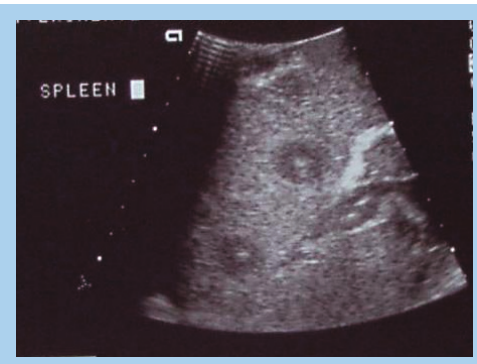


Figure 11. Target lesions in spleen suggesting candida. A scan of the spleen shows scattered focal nodules with a 'target' sign suggestive of candidiasis.

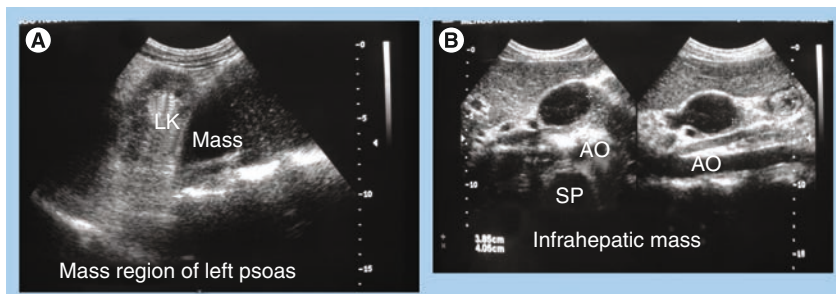


Figure 12. Large left psoas abscess in a 45-year-old male. (A) This longitudinal scan of the left renal fossa shows a large hypoechoic mass (psoas abscess), located in the region of the psoas, lifting up the LK. **(B)** These transverse and sagittal scans of the pancreas shows a thick-walled cystic mass within the neck and body of the pancreas. AO: Aorta; LK: Left kidney; SP: Spine.

is the most commonly involved abdominal wall muscle and psoas abscesses have been described (FIGURE 12) [3].

Vascular manifestations

Premature atherosclerosis may occur due to inflammatory action of the HIV virus on the endothelial wall and abnormal fat metabolism. Abnormal fat metabolism is a physiological complication of HIV/AIDS and manifests as high levels of low-density lipoprotein cholesterol, especially in patients on HAART. Other vascular complications may be aneurysms and pseudoaneurysms, aortitis, thrombosis and thromboembolism. For patients with pseudoaneurysms, a defect may be visualized in a thickened part of the vessel associated with hyperechoic spotting [58–62].

Conclusion

US is valuable in the assessment of abdominal pathology in HIV/AIDS patients. It is applicable in the evaluation of HIV/AIDS-related tumors, TB, hepatitis, cholangiopathy, pancreatitis, IRIS, nephropathy and vascular system changes. The findings, though not pathognomonic, help in characterizing some of the diseases and in image-guided biopsy procedures. Physicians

should exploit this widely available and relatively affordable technology in the management of HIV/AIDS patients with abdominal symptoms.

Future perspective

■ Applying results to routine screening before institution of ARVs

It is hoped that nurses, assistant physicians and physicians can be taught basic abdominal US and with the rapidly evolving technology in handheld US scanners they will be able to quickly screen and triage patients with or without pathology, such as TB, which can lead to IRIS.

■ Applying tele-US for remote diagnosis of HIV abdominal morbidity

These portable or handheld devices can also be used for tele-US for diagnostic or consultation purposes in cases where US interpretation expertise is lacking.

■ Better disease characterization using advances in US technology

With recent advances in US tissue elastography, it is possible that this can be applied to non-invasively distinguish tumors, such as KS and lymphoma, from other masses, such as TB and pyogenic abscesses. This would reduce the number of unnecessary biopsies and increase the yield for positive histology.

Contrast-enhanced US may also aid in localization and characterization, but it is still expensive for developing countries.

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Executive summary

- Ultrasound can detect abdominal pathology, such as AIDS-defining cancers, non-AIDS-defining cancers, tuberculosis and other AIDS-related changes in the biliary system, alimentary tract, pancreas, kidneys, lymph nodes and vessels.
- High-resolution transducers may be required to better visualize fine pathology especially in the liver, spleen and intestines.
- Abdominal pathology commonly manifests as diffuse organ involvement with enlargement, change in echogenicity and echotexture or as a focal lesion in the organ.
- Abdominal lymphadenopathy, splenic nodules, thick bowel loops and ascites alone or in combination should indicate abdominal tuberculosis, but the findings are not pathognomonic. Flaring of these changes with highly active antiretroviral therapy should indicate immune reconstruction syndrome.
- Ultrasound findings are not pathognomonic and one should consider tissue diagnosis using ultrasound or other modalities for needle guidance.

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