

# Abdominal Ultrasound Findings in HIV Infected Patients and its Correlation with CD4+ Counts

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**Abstract:** ***Background & Objective:** Though the major target of the HIV-virus is the immune system, the frequency of abdominal disorders in HIV/AIDS patients has been reported to be second only to pulmonary disease. These abdominal manifestations may be on the increase as the use of antiretroviral therapy has increased life expectancy and improved quality of life. Ultrasonography is an easy to perform, non invasive, inexpensive and safe imaging technique that is invaluable in India. The objective of the study was to describe the finding of ultrasound findings in HIV-infected patients and compare of this findings with their CD4+ counts. **Patients and methods:** Total 80 confirmed HIV-positive patients underwent abdominal ultrasonography at SMIMER Hospital Surat during period of six month. A Prospective evaluation of the abdominal ultrasonography of 80 HIV positive patients was carried out at SMIMER Hospital Surat. Each patient's sonographic findings were correlated with their CD4+ counts using the World Health Organization's HIV classification index. **Results & Conclusion:** The HIV infected patients had a significantly higher proportion of lymphadenopathy, splenomegaly, hepatomegaly, fatty liver, splenic infiltration, and renal & Gall bladder abnormalities. The use of ultrasound as a baseline imaging modality in HIVinfected patients should be promoted. Its use is invaluable in the assessment of the disease state and in the monitoring of therapy and management of these immunocompromised individuals. However, few of the ultrasound findings correlated statistically with the CD4+ counts.*

**Keywords:** Hepatomegaly, Splenomegaly, Lymphadenopathy, fatty liver, renal echogenicity, HIV, CD4+ count

## 1. Introduction

The Acquired Immune-Deficiency Syndrome (AIDS), the clinical entity resulting from HIV infection is an increasingly important disease that has become a social phenomenon.

HIV infection is a major public health concern worldwide, the prevalence of AIDS in India in 2013 was 0.27, and about 2.39 million people are living with HIV/AIDS in India according to National AIDS Control Organization of India<sup>1</sup>. In India first case of human immune deficiency virus (HIV), infection was reported in Chennai in 1986<sup>2</sup>. Since then the incidence of HIV infection is increasing in Asia, particularly in the Indian subcontinent. India is in the epicenter of HIV pandemic<sup>3</sup>. Though the major target of this deadly virus is the immune system, the frequency of abdominal disorders in patients with AIDS has been reported to be second only to pulmonary disease<sup>4,5</sup>. These abdominal manifestations may now be on the increase as the discovery and use of antiretroviral therapy has prolonged life expectancy and improved quality of life<sup>6</sup>. HIV/AIDS is known to have a wide variety of clinical manifestations from involvement of various organs. Ultrasonography (US) is a versatile imaging tool, which can evaluate most of the abdominal organs affected by the disease; furthermore, it can guide biopsies allowing the cytohistological and microbiological investigations needed to obtain a definitive diagnosis and assist in directing appropriate therapy. Other imaging methods particularly Computed Tomography (CT) can explore these organs in more detail than US. However, CT may often be considered a second choice in abdominal imaging for the following reasons; it utilizes radiation, it is more expensive, less readily available and often yields

results comparable to US<sup>4,6</sup>. This is particularly true in developing countries where the absence or the high cost of the procedure makes abdominal US a suitable alternative diagnostic tool in the radiological investigation of HIV infected individuals. Radiology plays an important role in the management. CD4+ count is a good index for monitoring progression of the disease as the degree of immunodeficiency is related to the level of the CD4+ count<sup>7</sup>. It is expected that with the declining immune status, susceptibility to infection and consequently abnormal sonographic findings should increase<sup>8</sup>. It is expected that, as immune status decreases, susceptibility to infection and consequently abnormal sonographic findings should increase.

### Aims and objective

- To describe the abdominal findings in HIV/AIDS Patients on ultrasonography and evaluate the clinical utility of abdominal US in HIV/AIDS patients
- To compare its findings with CD4+ count

## 2. Material & Method

This is an observational study. Abdominal ultrasound scans were prospectively performed over a six month period (July 2014–Dec 2014) on 80 eligible HIV positive adults patients (aged 21– 71 years) referred from the wards and OPD at the SMIMER Hospital, Surat to the Department of Radiology for routine diagnostic imaging.

The patients were defined HIV seropositive if they tested positive for HIV infection by ELISA test (Micro Lisa – HIV) and a rapid test (HIV-Comb).

**Inclusion Criteria** include all patients which were found positive on serological testing and were referred to our department. Patients who were provided CD4+ count.

**Exclusion criteria** include non-fasting patients, children, and patients with incomplete ultrasound examinations. Patients who were not provided CD4+ count.

**Consent** Each patient gave an informed consent.

HIV-positive patients were subjected to routine chest X-ray and an abdominal Ultrasonography for early detection of abnormality and achievement of a base line. To examine the various abdominal organs, patients lay on the examination couch in different postures which included supine, prone, lateral and oblique positions. The abdominal organs were scanned in longitudinal, transverse and oblique planes. The ultrasound scans were performed after overnight fasting of at least 12 hours. It was done by using a 3.5–5.0 MHz frequency curvilinear probe on ESAOTE MY LAB 60 ultrasound. The high-frequency LINEAR (6.5 MHz) probe of the machine was used to evaluate the gallbladder, bowels, anterior abdominal wall and other superficial structures. The presence of the abnormalities such as lymphadenopathy, splenomegaly (with or without hypo or hyperechoic lesions), hepatomegaly (with or without single or multiple focal lesions), gallbladder and bile duct abnormality, ascites, renal abnormalities with diffusely increased echogenicity, bowel wall thickening were noted. In order to confirm the identification of vascular and ductal anatomy, Color Doppler sonography was used. Electronic calipers were used for all measurements on the ultrasound machine.

**The following criteria were utilised to assess the abdominal organs:**

lymphadenopathy – visualised lymph nodes with the short axis measured; The condition in which the nodes are larger than 1 cm in diameter is considered as lymphadenopathy. Hepatomegaly – longitudinal dimension at mid-clavicular line >15 cm; splenomegaly – longitudinal dimension >12 cm; thickened gallbladder wall – dimension >3 mm at the anterior wall; pancreatic enlargement – dimensions >2.5 cm, 1.5 cm or 2.0 cm for the head, body or tail respectively; renomegaly – longitudinal renal dimension >12 cm; thickened bowel wall – wall thickness >4 mm; biliary dilatation – intrahepatic biliary ducts luminal diameter >2 mm (or if >40% of the diameter of the adjacent portal vein) or extrahepatic biliary duct luminal diameter at the porta hepatis >5 mm for patients <50 years of age (or additional 1 mm per additional decade of life).

Finally results were correlated with CD4 count. The CD4 cell count estimations were done by FACS Count . Each time the patients provided their most recent CD4 count was recorded for analysis. The CD4 cell counts were taken post therapy also in order to assess the immune restoration for case management.

**Data Management and statistical analysis**

Demographic data of the patients were obtained from patients' record file. Data were recorded in paper and thereafter in computer. All collected data from the patients included within the study was done in Microsoft excel. Data

analysis would done by appropriate statistical test. Descriptive analysis were applied when needed. Various statistical characteristic of the test were calculated whenever applicable. Data is classified accordingly and frequencies described in number and their respective percentage.

**3. Results**

Of the 80 cases, 48 (60%) were males and 32(40%) were females. Of 80 patients, majority of patients belong to age group 31-40 accounting for 37 patients (46.25%) followed by 18 patients of age group 21-30 (22.5%). 14 patients were from age group 41-50 (17.5%). 07 (8.75%) and 04 patients (5%) were from age group 51-60 and more than 60 years respectively. The modal age group was the 3th decade with a frequency of 46.25% (Table 1).

**Table 1:** Age group distribution in HIV+ Patients

Age Group	Male	Female	Total
21-30 Years	11	07	18
31-40 Years	22	15	37
41-50 Years	08	06	14
51-60 Ears	05	02	07
>60 Years	02	02	04

**CD4 classification**

Grouping into CD4+ classes was done according to the World Health Organization's (WHO's) classification of CD4+ immunological profile in adult HIV-infected patients, with CD4+ counts >500/microlitre categorised into the **Not significant** class; 350 - 499 as **Mild**; 200 -349 as **Advanced**; and a CD4+ count <200 in the **Severe** category<sup>9</sup>. There were 10 (12.5%) patients in the **Not significant** category, 19 (23.75%) in the **Mild**, 16 (20%) in the **Advanced**, and 35 (44.75%) in the **Severe** CD4+ class.( Table 3)

**Sonographic Findings**

The significant abdominal US findings seen are shown in Table 2.

The Severe CD4+ class had the highest proportion of patients with abnormal abdominal sonographic findings.

**Table 2:** Abdominal findings on ultrasonography in HIV+ patients

Ultrasound Finding	HIV + Patients	% of Patients
Normal	17	21.25
Lymphadenopathy	36	45
Splenomegaly	27	33.75
Hepatomegaly	20	25
Fatty Liver	11	13.75
Reanal Echogenicity	18	22.5
GB Wall Oedema & Stone	06	7.5
Bowel Wall Thickening	06	7.5
Ascites	05	6.25
Hypoechoic Area In Liver	03	3.75

**Table 3:** Normal & abnormal abdominal ultrasound findings vs. CD4+ classification

CD4+ COUNT	Normal	Abnormal	Total
Not Significant (>500/microlitre)	06	04	10
Mild (350-499/microlitre)	04	15	19
Advanced (200-349/microlitre)	03	13	16
SEVER (< 200/microlitre)	04	31	35

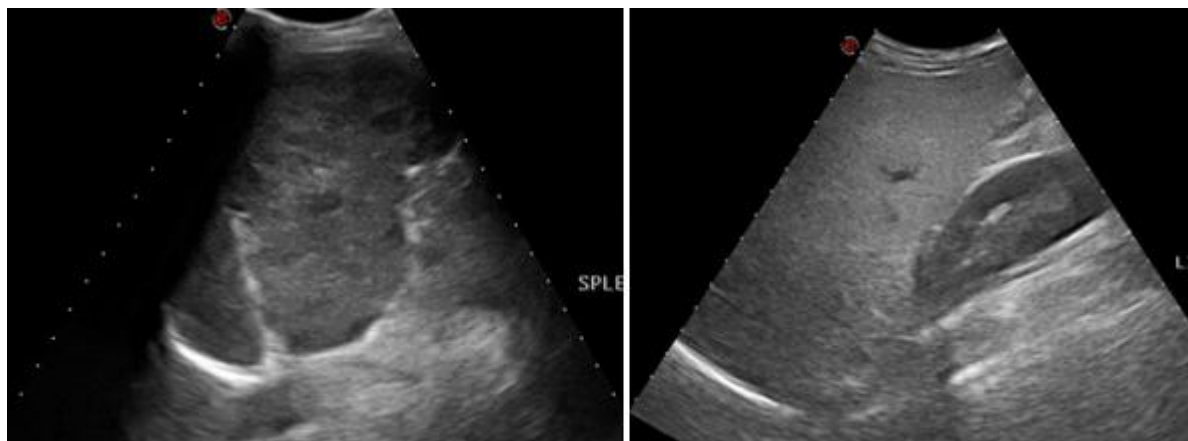
**Table 4:** Abdominal abnormal Sonographic findings and correlation with CD4+ classification

Sonographic Findings	Frequency		CD4+ CLASSIFICATION							
			Non Significant		Mild		Advanced		Severe	
	NO	%	NO	%	NO	%	NO	%	NO	%
Lymphadenopathy	36	45	02	20	05	26.3	09	56.3	20	57.1
Splenomegaly	27	33.75	03	30	05	26.3	07	43.8	12	34.3
Hepatomegaly	20	25	04	40	03	15.8	05	31.2	08	22.9
Fatty Liver	11	13.75	01	10	03	15.8	02	12.5	05	14.3
Increased Renal Echogenicity	18	22.5	02	20	02	10.5	05	31.2	09	25.7
GB Stone & Wall Oedema	06	7.5	00	00	01	5.3	00	00	05	14.3
Bowel Wall Thickning	06	7.5	00	00	01	5.3	01	6.3	04	11.4
Ascites	05	6.25	01	10	00	00	01	6.3	03	8.6
Hypoechoic Area In Liver	03	3.75	00	00	00	00	00	00	03	8.6

**Spleen**

Splenomegaly was found in 27 (33.75%) patients. Splenomegaly noted in Not significant, Mild, Advanced and a Severe category in 30%, 26.3%, 43.8% and 34.3% patients respectively. So there was no significant correlation with their CD4+ counts. But significant number of patients with severe category showed numerous hypoechoic lesions

spread throughout the splenic parenchyma and showed area of necrosis. So there were correlation between granuloma formation and CD4+ count. Two cases of wedge shaped hypoechoic splenic infarct noted which were sickle cell disease patients.



**Image 1:** Enlarged spleen with granulomatous changes and hepatomegaly with fatty changes

**Liver**

Hepatomegaly was the most common liver finding; it was demonstrated in 20 (25%) patients. Hepatomegaly was noted in Not significant, Mild, Advanced and a Severe category CD4+ patients in 40%, 15.8%, 31.2% and 22.9% patients respectively so did not correlate with their CD4+ counts. Most (82.5%) of the patients had normal hepatic echogenicity, whereas 11 (13.75%) patients had fatty liver showed hyperechoic parenchyma and 3 (3.75%) patients had a focal hypoechoic area within liver. However, there was no correlation between hepatic echogenicity and CD4+ count (Table 4).

**Kidney**

Renal US findings were diverse, renal parenchymal changes as evidenced by increased echo texture of both cortex and medulla were recorded in normal sized kidneys and also in enlarged kidneys. Renomegaly was seen in 6 (7.5 %) patients, without significant correlation with their CD4+ counts. Left renomegaly occurred more commonly than right-sided renomegaly, which may be because, anatomically, the left kidney generally is larger than the right. Normal renal echogenicity was seen in 62 (77.5%)

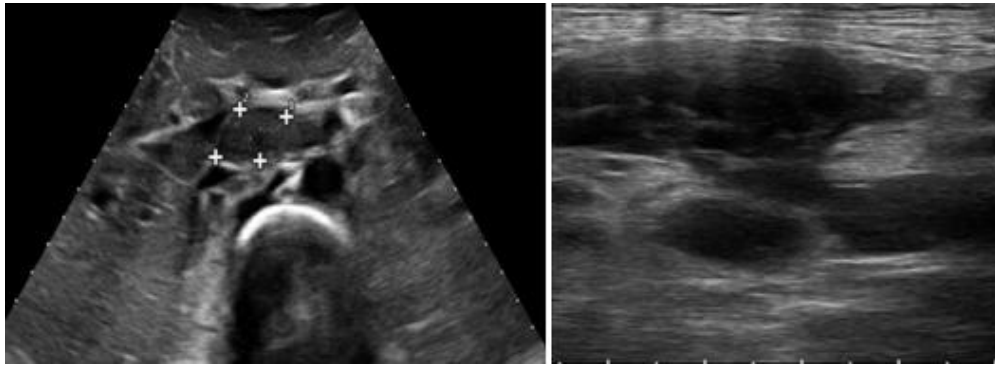
patients, while 18 (22.5%) patients had varying degree of increased renal echogenicity. Patients with depleted CD4+ had a higher proportion of increased cortical echogenicity. Other renal findings include hydronephrosis, nephrolithiasis and simple renal cysts noted in few patients and not correlate with CD4+ counts. Biochemical tests confirmed increased Urea level and Creatinine level in patients who showed increased renal echogenicity.

**Lymph node**

Enlarged lymph nodes was the most observed abnormal ultrasound finding found in 36 (45%) of the patients. Mesentric and retroperitoneal lymphnodes were most commonly involved. The other sites were lymph nodes seen in the hepatic hilum, peri-pancreatic, pre & para-aortic, coeliac, splenic hilum and in pelvic regions. Enlarged lymphnodes were noted in Not significant, Mild, Advanced and a Severe category CD4+ patients in 20%, 26.3%, 56.3% and 57.1% patients respectively and thus correlated with their CD4+ count (Table 4)

Many of these lymph nodes were seen at multiple sites. Enlarged Lymph nodes showed hypoechoic echotexture, with most of them loss of central hilar echogenicity. Many

of them showed area of necrosis. In few cases, multiple enlarged lymph nodes formed a large conglomerate mass.



**Image 2:** Periportal and mesenteric lymphnode enlargement

### Gallbladder and biliary system

The gallbladder wall and gall stone was noted in 6 (7.5%) patients both findings correlate with CD4+ count because 5 out of 6 cases noted in severe category CD4+ patients. Biliary duct abnormalities were also not commonly seen. There were 2 cases of biliary duct dilatation (both in the

Severe CD4+ class). These patients with gallbladder and biliary duct abnormalities were clinically asymptomatic. The width of the common bile duct ranged from 2.0 to 8.0 mm among HIV+ cases. No extrahepatic bile duct dilatation was recorded.



**Image 3:** GB wall oedema and gall bladder stone in two different HIV positive patients.

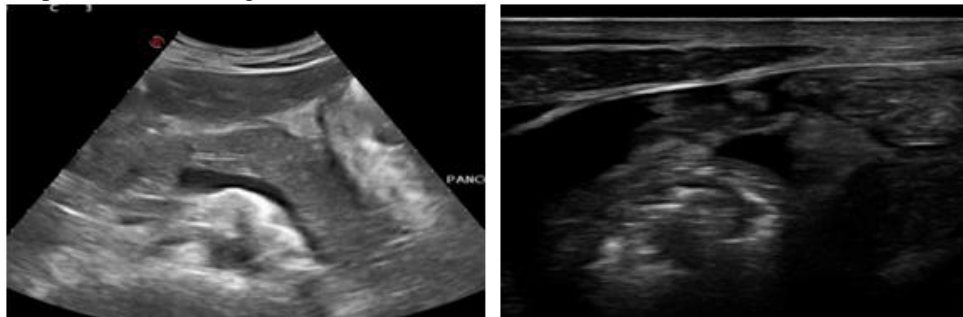
### Gastrointestinal tract

Small intestinal wall thickening was seen in 6 (7.5 %) patients showing uniform thickening mostly in the ileocecal region. There were few patients with fluid-filled bowel loops noted. Bowel wall thickening noted with the Severe class of patients having the highest proportion, but without significant correlation with their CD4+ count (Table 4).

with their CD4+ count. Pancreatic enlargement was seen in 3 patients without correlation with their CD4+ count. Other findings in this study included 3 cases of pleural effusions and 1 case of anterior abdominal wall abscess. Other notable incidental sonographic findings in this study were 2 cases of uterine fibroids and a case each of ovarian complex mass, midline infra-umbilical incisional hernia, and a markedly enlarged prostate gland.

### Others

Free fluid (ascites) within the abdomen was seen in five of 80 (6.5 %) in HIV+ patients without significant correlation



**Image 4:** Showing pancreatic enlargement and acites with bowel wall thickening & omental thickening in two different HIV+ patients

#### 4. Discussion

Imaging plays an important role in the detection of various pathologies associated with AIDS. The HIV virus causes a progressive reduction of cell-mediated immunity, leading to opportunistic infections, neoplasia and even local infection by the virus itself. In many cases, the radiologist provides to clinicians the first clue in suspecting the possibility of an underlying HIV infection<sup>10</sup>. Over 85% of the patients were within the age range of 20 - 50 years in our study, there by constituting the majority of the patients in this study population. However, with the present availability of free/subsidised drugs and therapy, many more elderly HIV-infected patients may be seen in the future, from the HIV-infected youths that survived. Abdominal symptoms are among the most frequent complaints of patients with AIDS. Since precise diagnosis based on symptoms alone is very difficult in these patients, the contribution of radiology is important to reaching the diagnosis<sup>11</sup>. Ultrasound offers a cheap avenue of diagnosing opportunistic infections in HIV. Evaluation of the abdomen by ultrasound is the alternative tool to CT scan, producing cross-sectional images of high diagnostic quality. Although US does not provide a definitive diagnosis, it may show areas of abnormal anatomy and pathology that may facilitate achieving a tissue diagnosis or add further support to the decisions on commencing empirical treatment.

The common and uncommon abdominal sonographic abnormalities found in this study are comparable with those documented by other authors<sup>4,6,7</sup>. These sonographic abnormalities are non-specific to a particular pathogen or disease entity<sup>4,6,7</sup>. However, such findings in the right clinical context and laboratory evaluation will help clinicians to arrive at a diagnosis, leading to better patient care and management. In 2003, Uygur-Bayramicli *et al.* showed that the most common abdominal US findings in HIV patients were ascites and hepatomegaly<sup>12</sup>. Findings in our study confirm previous documentation of the wide range of abdominal manifestations of HIV/AIDS and reveal that while abdominal abnormalities occur frequently, they are usually nonspecific, with splenomegaly, lymphadenopathy, biliary tract abnormalities, and hepatomegaly occurring most commonly. In our study the most common abdominal ultrasound finding was lymphadenopathy followed by splenomegaly. Lymph nodes are important components of the immune system that filter and remove foreign particles. In HIV/AIDS patients, lymph nodes are expected to be more active owing to the increased occurrence of infections (and neoplasia). In this study, the frequency of occurrence of visualised lymph nodes correlated with patients' CD4+ counts, which Erdozain *et al.*<sup>19</sup> ascribed to the fact that as patients become more immune-compromised, the probability of factors (such as infection and neoplasia) causing lymph node enlargement increases. Ultrasound allows assessment of location, number and sizes of pathological lymph nodes. It also permits evaluation of their shape, presence or absence of hilum/mediastinum. Splenomegaly without focal masses is relatively common in the tropics and can have myriads of causes including malaria, septicaemia, typhoid, schistosomiasis, portal hypertension, haemolytic anaemia and tropical splenomegaly. Porcel-Martin *et al.* documented the utility of abdominal US in detecting focal splenic lesions

in patients with AIDS<sup>13</sup>. Hepatomegaly is commonly attributed to either a non-specific response to infection, hepatitis, fatty change, or neoplastic infiltration from lymphoma or Kaposi's sarcoma<sup>17</sup>. However, hepatosplenomegaly in AIDS patients in the absence of hepatic focal lesions may suggest infection (*M. avium intracellulare*, malaria or histoplasmosis) rather than lymphoma<sup>18</sup>. We found pancreatic or biliary pathology in three and six patients respectively. Pancreas and biliary tract are reported to be the frequent sites of infectious, inflammatory and neoplastic diseases in patients with HIV infection. However, the symptoms of pancreaticobiliary involvement may be relatively mild so thus their prevalence is probably underestimated. Imaging findings of HIV associated pancreaticobiliary disorders is important, because at times, involvement of these organs may be the only suggestion for establishing the diagnosis of AIDS<sup>14</sup>. Renal disease may be caused by the HIV virus itself, secondary infections or the administered drugs. The statistically significant finding of more patients with renomegaly and associated increased cortical echogenicity may be ascribed to HIV nephropathy, which usually causes diffuse renal cortical echogenicity as well as renal enlargement<sup>18</sup>. The pattern of increased renal cortical echogenicity seen in this study is similar to that described by some authors as AIDS nephropathy which is shown to occur primarily in black patients. Although the utility of US has been tried to be highlighted for the evaluation of visceral involvement and lymphadenopathy, it is prudent to remember that the use of US often needs to be supported by other appropriate diagnostic tools<sup>15</sup>. The gastrointestinal findings in this study (thickened bowel walls, fluid-filled bowels, ascites) were mainly demonstrated in the small intestine, and their high incidence in the Severe CD4+ class of patients may be attributed to the increased frequency of opportunistic gastrointestinal infections with depressed immunity since immunosuppression impairs gastric acid secretion and peristalsis, which are non-specific host defence mechanisms. Hence, HIV-infected patients have gastric secretory failure, altered intestinal motility, impaired local immunoglobulin A and cellular immune responses which predisposes the gastrointestinal tract to increased bacterial colonisation, leading to malabsorption, diarrhoea and opportunistic infections.

In our setting, US is provided of minimal charge where as an abdominal computed tomography (CT) cost is high. The patients who could afford it were advised to undergo CT, and the findings correlated well with the US interpretation. As prevalence of HIV is rising in India, it is important to develop cost-effective and affordable protocols for the management of it. Moreover, with long-term survival of HIV patients becoming the rule rather than the exception, patients need to be followed up with feasible options and guidelines. Tissue diagnosis and sophisticated imaging are difficult to access in our country. Ultrasound assumes an even greater importance in the setting of worsening immune status<sup>16</sup>.

#### 5. Conclusion

The findings in our study demonstrate that variables abnormal sonographic findings can appear in various organs

of the abdomens of HIV/AIDS patients like Splenomegaly, hepatomegaly, fatty liver, increased renal cortical echogenicity, lymphadenopathy, thickened bowel walls and fluid-filled bowels. Most of the sonographic abnormalities did not correlate with CD4+ counts, indicating that there is no direct association between the infection stage, the CD4+ count and ultrasound findings. However lymphadenopathy, GB abnormality and granuloma formation correlate with depleted CD4+ count. We conclude that ultrasonography is a versatile tool for evaluating abdominal organs affected by HIV/AIDS. Ultrasound should be used as an affordable diagnostic tool for HIV patients in resource-poor settings, and it is particularly cost-effective in those patients with low CD4 counts. Ultrasound scans should be used as a routine baseline investigation as well as in the follow-up of HIV-infected patients.

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