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Concurrent Parasitosis in the Liver of Seropositive Hiv Patients

[1]Obi, R.K, [1]Nwanebu, F.C, [1]Chikwendu C.I, [2]Ndubuisi-Nnaji, U.U, [3]Okangba, C.C, [4]Orji, N.M.

[1]Department of Microbiology, Federal University of Technology, Owerri, PMB 1526, Owerri, Imo State, Nigeria.
[2]Department of Microbiology, University of Uyo, P.M.B. 1017, Uyo, Akwa Ibom State, Nigeria.
[3]WHO/TDR Malaria Specimen Bank Collection Site, Department of Medical Microbiology and Parasitology, College of Medicine, University of Lagos, Nigeria.
[4]Department of Biological Sciences, Anambra State University, Uli, P.O.Box 02, Uli, Anambra State, Nigeria.

Abstract: The liver is the initial site of filtration of absorbed intestinal luminal contents and is particularly susceptible to contact with microbial antigens of all varieties. In addition to infection by viruses, the liver can be affected by spread of bacterial or parasitic infections from outside the liver. Well-documented cases have shown that HIV attacks liver cells directly producing liver inflammation and the initial flu-like syndrome that precedes seroconversion. Both protozoa and helminthic opportunistic and invasive parasites afflict the liver of patients infected by HIV. Whereas HIV infection may alter the natural history of parasitic diseases, impede rapid diagnosis or reduce the efficacy of antiparasitic treatments, parasitoses may facilitate infection with HIV as well as progression from asymptomatic infection to AIDS. Some of the protozoans involved include Cryptosporidium parvum, Leishmania species, Entamoeba histolytica, Plasmodium species etc, while the representative helminthes include Echinococcus sp, Schistosoma sp, Fasciola sp, Ascaris sp etc. The symptoms of diseases caused by these parasites could manifest in the form of any of those associated with liver damage especially hepatitis, fibrosis, hepatomegaly and cirrhosis. It is therefore recommended that efforts currently made to control parasitic diseases should be stepped up and modified to complement the tools currently used in combating the HIV pandemic.

Key words: HIV, Protozoa, Helminth, Liver, Coinfection.

INTRODUCTION

The word liver was derived from the Greek word *hepato / hepatic.* It is a, large, dark reddish brown, glandular organ, divided into two main lobes: the much larger right and the smaller left, both of which are further subdivided into approximately 100,000 small lobes, or lobules. About 60% of the liver is made up of cells called hepatocytes which absorb nutrients and detoxify and remove harmful substances from the blood. Two-thirds of the body of the liver is made up of the cells known as the parenchyma, which contains the hepatocytes, while the remainder is made up of ducts called the biliary tract (Norman, 1999).

The liver lies on the right side of the abdominal cavity beneath the diaphragm and weighs about 1.5kg. Blood is carried to the organ via two large vessels called the hepatic artery and another known as the portal vein. The hepatic artery carries oxygen-rich blood from the aorta while the portal vein carries blood containing digested food from the small intestine. These blood vessels subdivide in the liver repeatedly, terminating in very small capillaries, each of which leads into a lobule (Bramstedt, 2006).

The liver performs many critical functions which include filtration of blood, elimination of toxins, secretion of bile, and production of clotting factors.

It also converts sugar into triglycerides and glycogen to be stored for energy, and, between meals, converts triglycerides, glycogen and amino acids into blood sugar to meet the body's immediate energy needs (Richardson *et al.,* 1994).

Corresponding Author: Obi, R.K, Department of Microbiology, Federal University of Technology, Owerri, PMB 1526, Owerri, Imo State, Nigeria.
E-mail: robertobi_2003@yahoo.ca

The various metabolic activities in the liver leads to the generation of a large quantity of nutrients which serve as nutrient sources for a large number of pathogenic microorganisms, making it one of the most parasitized organs in the body. Consequently both protozoa and helminthic opportunistic and invasive parasites afflict the liver. Some of the protozoa involved include *Cryptosporidium parvum*, *Leishmania* species, *Entamoeba histolytica*, *Plasmodium* species etc, while the representative helminthes include *Echinococcus* sp, *Schistosoma* sp, *Fasciola* sp, *Ascaris suum*, etc (Ocama *et al*., 2008).

The symptoms of the diseases caused by these parasites could manifest in the form of any of those associated with liver damage especially hepatitis, fibrosis, hepatomegaly and cirrhosis. These symptoms are however made severe if the liver is infected by the human immunodeficiency virus (HIV), since well-documented cases have shown that various parasitic opportunistic infections in AIDS often involve the liver, sometimes leading to unusual clinical presentations. In addition, AIDS-related tumors as well as drugs used in the treatment of HIV and the various parasitic opportunistic infections, may further lead to adverse reactions and a greater risk of liver damage. Finally, whereas HIV infection may alter the natural history of parasitic diseases, impede rapid diagnosis or reduce the efficacy of antiparasitic treatments, parasitoses may facilitate infection with HIV as well as the progression from asymptomatic infection to AIDS (Gundel and Herman, 2002).

Given the danger posed by coinfection of the liver by parasitic pathogens and HIV, it has become imperative to carry out a study on Liver parasitosis to highlight the impact of HIV on the increased prevalence of parasitic infections of the liver.

Symptoms of a Diseased Liver in HIV/parasitic Coinfections:

HIV infection leads to more aggressive parasitic infections and a higher risk of liver damage. Symptoms of diseases caused by the co-invasion of the liver could manifest in the form of any of those associated with liver damage especially hepatitis, fibrosis, hepatomegaly and cirrhosis (Housset, 1990). Table 1 represents parasites involved in liver disease.

Cirrhosis:

This occurs when more and more normal liver tissue become replaced by hardened scar tissues that can obstruct the normal flow of blood through the liver and seriously affect its structure and ability to function properly. If the liver is severely damaged, blood can back up into the spleen and the intestines, and these can result in high pressure in these organs. Consequences of this condition, called portal hypertension include bleeding (variceal bleeding) and fluid in the abdomen (ascites). One helminth implicated in this condition is *S mansoni* (Housset, 1990).

Hepatitis:

Some parasites such as *E. histolytica* and *L. donovani* attack liver cells (hepatocytes) that provide the best conditions for them to reproduce. In response to the infection, the body's immune system targets the liver, causing inflammation (amoebic and leishmania hepatitis). In severe cases, hardened fibers can develop in the liver, a condition called fibrosis. Amoebic and leishmania hepatitis are extremely serious diseases that can lead to death from liver failure (Housset, 1990).

Enlarged Liver or Hepatomegaly:

Can occur even though on itself is not life threatening, but could be a sign of some other liver-related problems. The liver responds to the presence of most parasitic infections by becoming enlarged. Malaria, leishmaniasis, and amoebiasis cause hepatomegaly in their acute phases (Bierhoff *et al*., 1993).

Functional abnormalities caused by a diseased liver could manifest in a variety of symptoms related to digestive problems, blood sugar problems, immune disorders, abnormal absorption of fats, and metabolism problems. The malabsorption of fats could lead to symptoms that include indigestion, reflux, hemorrhoids, gall stones, intolerance to fatty foods, and intolerance to alcohol, nausea and vomiting attacks, abdominal bloating, and constipation (Richardson *et al*., 1994).

Nervous system disorders associated with liver disorders also occurs and this may include depression, mood changes, especially anger and irritability, poor concentration and foggy brain, overheating of the body, especially the face and torso, and recurrent headaches (including migraine) associated with nausea (Dieterich *et al*., 2004).

Coinfection of the Liver by HIV and Parasites:

Co-infection refers to infection with two or more different disease-causing organisms. Parasitic pathogens that on their own, will not cause disease but rely on the lowered host resistance generated by infection with HIV to launch their attack are referred to as opportunistic parasites (American Lung Association on tuberculosis and AIDS, 2007). The common immunopathogenetic basis for the deleterious effects parasitic diseases may have on the natural history of HIV infection seems to be a particular type of chronic immune activation and a preferential activation of the T helper 2 (Th 2) type and not T helper 1 (Th 1) (Gundel and Herman, 2002).

Protozoa:

Protozoa are among the most important pathogens that can cause infection in immunocompromised patients. They infect particularly individuals with impaired cellular immunity, such as those with hematologic neoplasias, those submitted to transplant of solid organs, those under high-dose corticosteroid therapy and carriers of the human immunodeficiency virus (Ferreira, 2000). Some representative species include:

***Leishmaniasis*:**

Leishmaniasis is one of several names for various tropical diseases, which are caused by flagellates of the genus *Leishmania*. The parasites are transmitted by sandflies, blood-sucking insects of the tropical and subtropical zones. The manifestation of the disease may be visceral (kala-azar), mucocutaneous (American Leishmaniasis) or cutaneous (Aleppo boil) (Bükte *et al*., 2004).

Of all the leishmania diseases, the most dangerous and often fatal form is the visceral, which is caused by the pathogen *Leishmania donovani*. The parasites live in the liver, spleen and bone marrow and reproduce rapidly, but are kept under control by the immune system. On occasions when the immune system is weakened, however, especially on infection with HIV, leishmaniasis parasites reproduce in an explosive way, entering the blood stream and attacking the liver, spleen and skin, which without treatment, results in death. Visceral leishmaniasis causes morphological and functional disturbance in the liver leading to focal fibrosis, hepatomegaly, splenomegaly and petechial haemorrage accompanied by leishmanial pyrexia (el Hag *et al*., 1994; Koshy *et al*., 2001).

To date, most Leishmania and human immunodeficiency virus (HIV) coinfection cases reported to WHO came from Southern Europe. Up to the year 2001, nearly 2,000 cases of coinfection were identified, of which 90% were from Spain, Italy, France, and Portugal. Most cases of coinfection in the Americas are reported in Brazil, where the incidence of leishmaniasis has spread in recent years due to overlap with major areas of HIV transmission. In some areas of Africa, the number of coinfection cases has increased dramatically due to social phenomena such as mass migration and wars (Alvar *et al.*, 2008).

Table 2 below represents a summary of the epidemiological information on coinfection of HIV and Leishmaniasis. India is reported to have the highest global burden of leishmaniasis and a high rate of resistance to antimonial drugs (Alvar *et al*., 2008).

HIV/AIDS pandemic has indeed modified the natural history of leishmaniasis. HIV infection increases the risk of developing visceral leishmaniasis (VL) by 100 to 2,320 times in areas of endemicity, reduces the likelihood of a therapeutic response, and greatly increases the probability of a relapse. At the same time, VL promotes clinical progression of HIV disease and the development of AIDS-defining conditions. Both diseases exert a synergistic detrimental effect on the cellular immune response because they target similar immune cells (Gradoni *et al*., 1993; Alvar *et al*., 1997; Nigro *et al*., 2007).

Leishmania-HIV coinfection is currently reported for 2 to 9% of all VL cases in given countries of endemicity. Generally, it is accepted that the reported global incidence of coinfection is underestimated, partly because VL occurs among neglected populations and is not on the CDC list of opportunistic infections. It is rarely therefore reported in AIDS notification systems (Vilaplana *et al*., 2004; Lopez-Velez *et al*., 2004).

A clear decrease in the incidence of *Leishmania*-HIV coinfection was observed by the end of the 1990s and this could be attributed to the routine use of HAART since 1997 in most of southern Europe. In the Leishmaniasis Reference Centers of Madrid, Montpellier, and Rome, which are members of the WHO network for monitoring *Leishmania*-HIV coinfection, an average of 35 cases (95% confidence interval [CI], which represented the incidence peak, were diagnosed in 1997). Cases began to steadily decrease during the period 1998-2001, and thereafter a low-incidence plateau was shown through 2006 (average of 12 cases; 95% CI) (Fig. 1). An additional 241 new (n), cases of primary infections from Spain (n = 95), Portugal (n = 64), Italy (n = 52), France (n = 30) and some persistent cases were reported to WHO during the period 2001-2006. Other countries, such as Switzerland, Germany, United Kingdom, and Greece, reported sporadic, imported cases (Albrecht *et al*., 1996; Delgado *et al*., 1999).

Different clinical studies performed recently illustrate the complexity of the interplay between HIV and Leishmania. It has been observed that *Leishmania* infection may affect the life cycle of the virus through increased expression of specific chemokine receptors.

Leishmania-HIV-coinfected patients have a significantly higher level of $CCR5^+$ $CD3^+$ T cells than do HIV-negative patients with VL or HIV-positive patients without VL (Nigro *et al*., 2003). CCR5 is a major coreceptor for HIV entry into target cells and its high expression in subjects is related to a high virus load and accelerated progression to HIV disease (Reus *et al*., 1999). Another study with coinfected patients showed a marked increase in circulating levels of the soluble form of the human leukocyte antigen G (HLA-G), a non classical histocompatibility complex class I molecule with immunosuppressive properties (Di Giorgio *et al*., 1999).

As a matter of fact, interactions between HIV and *Leishmania* are not only restricted to the replication of the virus. Clinical studies on the other hand, have demonstrated that the high incidence of disseminated leishmaniasis in AIDS patients and the high peripheral parasitemia (Bossolasco *et al*., 2003) are indicative of uncontrolled parasite growth. In concordance with this condition, experimental in vitro coinfection of monocyte-derived macrophages with HIV-1 and *L. donovani* or *L. infantum* promastigotes showed a significant enhancement of intracellular parasite growth compared with parasite infection alone. The lack of control of intracellular multiplication is probably related to the HIV-1-mediated impairment of an effector function carried out by macrophages, such as phagocytosis, intracellular killing, chemotaxis, and cytokine production. Despite the fact that HIV-1-infected monocyte-derived macrophages display an impaired capacity to phagocytose numerous pathogens, *Leishmania* uptake is increased following virus infection (WHO, 1995; Wolday *et al*., 2000).

In immunocompetent individuals, the protective *Leishmania*-specific immune response is associated with a Th1 cytokine profile, while susceptibility to *Leishmania* infection and disease progression are related to a Th2 cytokine response (Kedzierska and Crowe, 2002). It has been confirmed that HIV-1 inhibits the proliferative response to *L. donovani* (WHO, 2000). The reduced cellular response might be because the known inductive signal for gamma interferon (IFN-) is lacking or could be due to the direct influence of anti-inflammatory Th2 cytokines (Alvar *et al.*, 2008).

Clinical manifestations of VL caused by *L. infantum* and *L. donovani* in HIV-infected people are not significantly different from those in non-HIV-infected people (UNICEF/UNAIDS/WHO/MSF, 2005). Classical features are fever, weight loss, hepatosplenomegaly, and pancytopenia. Localization of parasites in VL-HIV coinfection is broadly similar to that described for immunocompetent subjects (Pineda *et al*., 2002), although whether the frequency of leishmaniasis found in atypical locations is higher for VL-HIV-coinfected patients has not yet been confirmed with large comparative studies (Rosatelli *et al*., 1998). In contrast to the clinical manifestations, the clinical course and prognosis of VL in HIV-infected individuals differ importantly from those in non-HIV-infected individuals. VL-HIV coinfection is characterized by significantly lower cure rates, higher drug toxicity, higher relapse rates, and higher mortality rates than those for VL in non-HIV-infected individuals (Ritmeijer and Davidson, 2003; Ritmeijer *et al*., 2006).

Amoebic Liver Abscess:

Amoebic liver abscess (ALA) which affects the right lobe in about 80% of cases is the most common extraintestinal manifestation of Entamoeba histolytica infection. E. histolytica transmission is associated with the oral-fecal pathway and is facilitated by poor sanitary conditions (Meng-Shuian *et al*., 2008). ALA or hepatic amoebiasis occurs when *E. histolytica* trophozoites penetrate the portal vessels and embolize to the liver causing patients to have single or multiple liver abscesses which may be indolent or acute (Kapoor and Joshi, 1972).

The abscess may have a cavity which may sometimes be filled with chocolate coloured pasty material (anchovy sauce-like) with the wall containing abundant fibrin and trophozoites clustered in the fibrin at the junction of viable and necrotic tissues. In addition, peritonitis and intra-abdominal abscesses may be caused by intestinal perforation or by rupture of the abscess. Furthermore, involvement of the pericardium may result in pericardial effusion, amoebic pericarditis, cardiac tamponade and cardiac failure. Liver abscess may also penetrate the diaphragm to involve the pleura, the lung, and the skin. If fistulisation to the skin occurs, there may be swift progression of a painful skin ulcer which may lead to death if left untreated. (www.surgical-pathology.com).

Other presentations of the disease include right upper quadrant pain (a prominent feature of the disease), tenderness, hepatomegaly, possible palpable mass, swinging fever, night sweats, nausea and vomiting, anorexia and weight loss, cough and dyspnoea due to diaphragmatic irritation, referred pain to the right shoulder and jaundice (Wan *et al*., 2007).

Immune suppression is an important risk factor for ALA. Evidence has shown that suppressed cellular immunity caused by use of steroids and malnourishment predispose to fatal amebiasis. Similarly, patients with CD4 cell counts <350/mm^3, comes down easily with infection suggesting that immune suppression by HIV infection may be another risk factor for ALA (Ghadirian and Meerovitch, 1981).

Consequently, Wan *et al*., (2007) reported the endemicity of amebiasis in the Republic of Korea. According to the report, amebiasis was previously an endemic disease in the Republic with positive rates for cysts of *E. histolytica / E. dispar* in the general population 10% in the 1960s. The report further showed that with improvements in sanitation, this rate decreased to 0.5% in 1993 and to nearly 0% in 2004, while it further revealed that cases of ALA in association with HIV infection are reemerging in the Republic on an increasing scale, while cases are on the decline in HIV-negative patients (Fig 2).

In a similar study in the United States, it was reported that 38% of patients with ALA who had no history of travel to any disease-endemic area were all observed to be HIV positive (Seeto *et al*., 1999), further supporting the view that ALA could be an emerging parasitic infection in HIV-infected patients in non–disease-endemic areas, as well as in disease-endemic areas. Furthermore, several other workers (Hung *et al*., 1999; Oh *et al*., 2000; Meng-Shuan *et al*., 2008) have also reported increasing cases and fatal consequences of ALA in patients diagnosed of the human immunodeficiency virus.

The clinical course and prognosis of ALA in HIV-infected individuals differ importantly from those in non-HIV-infected individuals. ALA-HIV coinfection is characterized by significantly lower cure rates, higher drug toxicity, higher relapse rates, and higher mortality rates than those for ALA in non-HIV-infected individuals (Seeto *et al*., 1999).

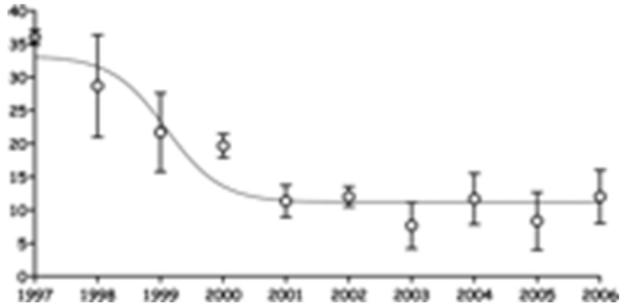

Fig. 1: Incidence trend of *Leishmania*-HIV coinfections recorded by three referral diagnosis centers, in France (1997-2005), Italy, and Spain (1997-2006). In these countries, HAART therapy for HIV treatment has been in routine use since 1997. Circles, means; bars, 95% confidence intervals (Source: Alvar *et al*., 2008).

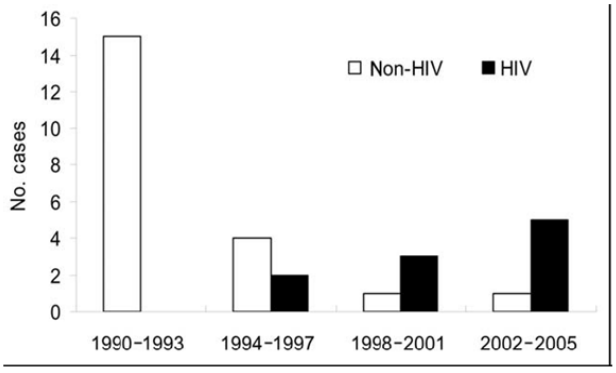

Fig. 2: Number of cases of amebic liver abscess in patients with and without HIV infection at Seoul National University Hospital, Republic of Korea, 1990–2005 (Source: Wan *et al*., 2007).

Table 1: Some Parasites of the liver.

Parasite	Disease	Symptom
Entamoeba histolytica	Amoebiasis amoebic hepatitis,	Hepatomegaly, Amoebic liver abscess (ALA)
Echinococcus granulosus	Echinococcosis	Hydatid cyst
Schistosoma mansoni	Schistosomiasis	Periportal fibrosis, Portal hypertension, hepaticgranuloma, Schistosomal hepatitis, Hepatomegaly.
Leishmania donovani	Visceral leishmaniasis,	Leishmanial hepatitis Acute hepatomegaly Plasmodium
sp		Malaria Hepatomegaly, portal hypertension, splenomegaly

(Sources: Macpherson *et al*., 1986; Radin *et al*., 1988; Stelma *et al*., 1994; Marty *et al*., 1994; Sowunmi, 1996).

Table 2: Epidemilogical Information on HIV/Leishmania Coinfection.

Country	Percentage rate of occurrence	Year
Southern Europe	23	2006
India	2.18	2006
Nepal	5.7	2004
Brazil	0.5	2005
B/Faso	14.3	2000
Ethiopia	40	2006
Kenya	15	2006
Uganda	8	2006
Sudan	3.6	2003

(Source: Alvar *et al.*, 2008).

Table 3: Epidemiological Analysis of *S. mansoni*/HIV coinfection.

Country	Percentage rate of occurrence	Year
Zimbabwe	26.3	2005
Kenya	14.5	2007
Uganda	13.2	2005

(Sources: Kallestrup *et al*., 2005; McElroy *et al*., 2005; Wanatabe *et al*., 2007).

Malaria:

Malaria and HIV are leading causes of morbidity and mortality, particularly in sub Saharan Africa. Both diseases are highly endemic and have a wide geographic overlap (Oyibo and Agomo, 2009).

Human immunodeficiency virus (HIV) and Plasmodium parasites are pathogens that induce significant perturbation and activation of the immune system. Due to their geographical overlap, there have been concerns that co-infection with the two pathogens may be a factor in the modification of their developments and in the severity and rate of disease progression they induce (Rénia and Potter, 2006).

Research has shown that malaria parasites kill the liver cells they occupy and make it detach from its neighbours. The apoptotic cells then squeeze through tiny gaps in the walls of blood vessels in the liver and as they do this, the cells break up into smaller cell-like structures called merosomes, each full of malaria parasites (Heussler *et al*., 2006; Jia, 2006).

Liver destruction is facilitated by large number of Kupffer cells which increase sporozoite infection by opening portals and providing direct access of the parasite to hepatocytes. This means that Kupffer cells are the portal for sporozoites to hepatocytes and is therefore critical for the onset of a malaria infection. Similarly, Kupffer cells are also target for HIV invasion of the liver (Fervert, 2008). Consequently, interaction of HIV/*Plasmodium falciparum* in the liver lead to CD4+ T cell loss, increased viral load, increased immunosuppression, and increased episodes of clinical malaria (Koehler *et al*., 2009). Malaria on the other hand has potent immunosuppressive effects on patients with HIV infection who contact the disease. Such patients tend to deteriorate rapidly into AIDS Related Complex (ARC) or AIDS. It has been confirmed that malarial infection supposedly accelerates replication of HIV and leads to higher plasma viral loads (Weinke *et al*., 1990). Some other protozoal diseases of the liver made worse by coinfection of the organ by HIV include hepatomegaly, granulomatous hepatitis, and reactive hepatitis caused by *Toxoplasma gondii* (Tiwari *et al*., 1982); cholangitis, cholestasis, and myositis hepatitis caused by species of Microsporidia (Minnaganti, 2008); malaise, anorexia, weight loss, and low-grade fever caused by *Isospora belli* and *Cyclospora cayatensis* (Tolan, 2009).

Helminths:

Human helminthic infestation is exceedingly common on a global scale, with as many as 1.5 to 2 billion people affected worldwide. Helminths (parasitic worms) that infect the liver and hepatobiliary system include nematodes (*Ascaris suum*, *Strongyloides stercolaris*), cestodes (*Echinococcus* sp), and trematodes (*Schistosoma* sp, *Fasciola* sp).

The majority of morbidity and mortality from these infestations is caused by the host immune response to the larvae or adult worm. Helminthic disease manifestations vary from the extremes of asymptomatic carriage to cirrhosis and decompensated liver disease (Pockros and Capozza, 2004).

Schistosomiasis:

Schistosomiasis, caused by species of Schistosoma, is an infectious disease affecting up to 300 million people worldwide. Of the three main species of the parasite, S. mansoni has the broadest geographical distribution. It is endemic to portions of South America, sub-Saharan Africa, the Middle East, and the Caribbean. S. haematobium is found mostly in North Africa, parts of sub-Saharan Africa, and the Middle East whiless S. japonicum is endemic to Asia (Greenwald, 2005).

Schistosomiasis presents with different manifestations depending on the offending organism. S. mansoni and japonicum affects the intestines and the liver, while S. haemotobium affects the kidneys and bladder (Krogstad *et al*., 1998). Patients afflicted with schistosomiasis, particularly those from endemic regions, are asymptomatic and symptoms could only be reactivated in the liver as a result of immune impairment, especially, on coinfection of the parasite with HIV (Bierman *et al*., 2005).

Schistosomiasis may involve the liver early in the disease in about 30% of the patients (schistosomal hepatitis) or more commonly, 5-10 years after initial infection when eggs of *S. mansoni*, either excreted in feces or impacted in the liver, induce granuloma formation that may lead to periportal fibrosis and portal hypertension due to ova migration, and development of hepatic granulomas followed by fibrosis. This may result in increase of portal pressure and development of esophageal or gastric varices and portal hypertensive gastropathy that may lead to severe morbidity (Gryseels *et al*., 2006).

In schistosomiasis, cirrhosis may occur as a result of anoxia following massive gastrointestinal bleeding. Hepatocellular carcinoma or other malignancies have not been reported with *S. mansoni* but reported with *S. japonicum*. The main cause of death is gastrointestinal bleeding from esophageal or gastric varices and sclerotherapy may be effective in these patients (Kallestrup *et al*., 2005).

S. mansoni coinfection leads to distinct dysregulation of HIV-specific responses that may contribute to the pathogenesis of HIV infection (McElroy *et al.*, 2005). Postulated mechanisms by which *S. mansoni* could accelerate HIV disease include enhanced rates of HIV replication in Th2 cells (Maggi *et al.*, 1994), increased immune activation (Gryseels *et al.*, 2006), or enhanced selective pressure to evolve to virulent variant strains (Bierman *et al*., 2005).

Expression of CD107, a marker for cytolytic activity, has been observed to be significantly lower in patients with *S. mansoni*/HIV coinfection compared to those with HIV-1 infection alone. In addition frequency of IL-10-positive Gag-specific $CD8^+$ T cell responses has also been reported to be higher in patients with *S.* mansoni/HIV coinfection (McElroy *et al.*, 2005) since *S. mansoni* has previously been reported to dysregulate the cellular immune responses in HIV infection by enhancing the activity of IL-10-producing $CD8^+$ T cells (Karanja *et al*., 1997). Furthermore *S. mansoni* coinfection has been reported to be associated with decreased Gag-specific $CD8^+$ cytolytic T cell responses and increased number of Gag-specific IL-10 positive $CD8^+$ T cells. Finally, decreased *Schistosoma* egg excretion in HIV-positive patients has also been reported among coinfected patients (McElroy *et al.*, 2005). Other helminthic infections of the liver aggravated by coinfection of the organ with HIV include granulomatous inflammatory reaction with dense eosinophilic infiltration and necrosis caused by *Angiostrongylus costaricensis* (Morera *et al*., 1982); hepatic nodules due to visceral larva migrans of *Ascaris suum* (Kakihara *et al*., 2004); septal fibrosis caused by *Capillaria hepatica* (Oliveira and Andrade, 2001); anaemia, weight loss and sub-mandibular oedema caused by *Fasciola hepatica* (Overend and Bowen, 1995); jaundice, abdominal pain, gastrointestinal discomfort of the upper abdomen, acute pancreatitis and portal hypertension caused by *Echinococcus granulosus* (Avgerinos *et al*., 2005) and liver pseudotumor which is a rare manifestation of hepatic granulomata, caused by *Ascaris lumbricoides ova (Fogaça et al*., 1999).

Conclusion:

HIV and parasitic infections interact and affect each other mutually in the liver. Whereas HIV infection may alter the natural history of parasitic diseases, impede rapid diagnosis or reduce the efficacy of antiparasitic treatments, parasitoses may facilitate infection with HIV as well as the progression from asymptomatic infection to AIDS. In addition, parasites found concurrently with HIV in the liver induce chronic immune activation, and therefore an increased HIV load with accelerated progression to AIDS, whereas immunological disturbances caused by HIV are particularly favourable for uncontrolled multiplication of the parasites. Furthermore, HIV/parasite coinfection of the liver leads to chronicity of parasitic infections, lower cure rates, and reduction in life expectancy.

Since this review has been able to establish that parasitic infections in the liver of patients seropositive for HIV speeds up the rate of liver damage, it is recommended that efforts currently made to control parasitic diseases should be stepped up and modified to complement the tools currently used in combating the HIV pandemic. There should also be public enlightenment, adequate health education, and measures put in place to enforce good sanitary practices to reduce the incidence of transmission of parasitic infections, especially among patients positive for HIV. Finally, since no cases were found reported in Nigeria in the course of this study, survey should be carried out in this direction, to complement one currently undertaken to determine the rate of hepatotoxicity of the liver by antiretroviral drugs and drugs used in treating opportunistic HIV infections.

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