

Extended Abstract

Serological Profile of Hepatitis B Virus Infection HIV Infected Adult Patients in Kano, North Western Nigeria

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Abstract:

Objective: To determine the serological profile of Hepatitis B virus infection among HIV infected adult patients in Kano. This was a hospital based retrospective observational study where subjects were screened and those who met the inclusion criteria and informed consented were consecutively recruited until required sample size was obtained. Data were collected using the pre-tested interviewer administered questionnaire with sections on socio-demographic information, medical history including risk factors, clinical and laboratory findings. All subjects were thoroughly examined and venous blood samples were taken for necessary investigations and subsequently analysed at the Aminu Kano Teaching Hospital central and PEPFAR laboratories. Data was analysed with SPSS Version 18. Hepatitis B virus has an enormous global impact. Despite the availability of a vaccine, two billion people have been acutely infected. Of these, 240 million remain chronically infected. The infection has different forms of presentation including acute infections, chronic infections, hidden infections, and reactivation when there is immunosuppression. Similarly, there are very sensitive markers such as anti-core, but a positive test can have different meanings. This recently described antigen which is related to the core antigen is an emerging marker that could replace viral DNA. In this review we discuss the laboratory tests necessary for diagnosing the various scenarios of the infection. The hepatitis B virus (HBV) is a health problem throughout the world. It is estimated that 2000 million people have been exposed to the virus and that 240 million are chronically infected making it the most frequent chronic viral infection of all. Between 15% an 40% of those with chronic infections progress to cirrhosis and its complications, including hepatocellular carcinoma. In 2013, HBV

Central America was less than 2% and in South America it was 2% to 4%, but in South America there are now 400,000 new cases each year. Despite recommendations for universal vaccination against HBV, this prophylaxis has not been widely implemented in the countries with the highest prevalences due to lack of economic and logistical resources. HBV is a hepatotropic virus with an external envelope and is a member of the Hepadnaviridae family of small deoxyribonucleic acid (DNA) viruses (3,200 base pairs). Its DNA is partially double-stranded and partially single-stranded, and it has a transcriptional template that is covalently closed circular DNA (cDNA) which is introduced very rapidly into the nucleus of the hepatocyte during acute infection. It belongs to the genus Orthohepadnavirus which infects mammals and the genus Avihepadnaviridae which affects birds. It is thought that this virus originated in Africa at least 40,000 years ago. It has 10 genotypes (A-J), A is frequent in North America, Northern Europe and Africa while B and C occur frequently in Asia. Some studies have found associations between the genotype, progression of the disease, and response to interferon. Genotypes C and F are more frequently associated with hepatocellular carcinoma as well as some subgenotypes of type A. On the other hand, genotype A is associated with risk of progression to chronic infection. Nevertheless, any acute infection regardless of genotype can progress to a chronic infection. HBV is primarily transmitted through sexual, perinatal, or mucosal routes or through percutaneous parenteral routes resulting from injuries with sharp elements contaminated with infected blood. This last form of transmission includes accidental punctures in hospital environments with contaminated surgical instruments, manicure procedures, pedicures, tattoos, intravenous drug abuse (sharing contaminated syringes) and piercings. Infection from these procedures has decreased as the risks inherent to them have become known, sterilization of medical instruments has been implemented, and reuse of needles has been banned. Sexual transmission has been reduced by education about the use of sexual protection measures. Ninety-five percent of cases of vertical transmission occur during vaginal deliveries and 5% occur through intrauterine transmission.

The clinical spectrum of HBV infection includes acute hepatitis, chronic hepatitis and occult infections. Similarly, HBV can cause cirrhosis, hepatocellular carcinoma and can compromise extrahepatic organs. Due to the impact and complexity of HBV infections, this review discuss the various tests used to diagnose the infection in scenarios found in daily practice.

Acute Hepatitis B: The diagnosis of acute Hepatitis B is confirmed by a positive blood test for HBV surface antigen (HBsAg) and IgM antibody to hepatitis B core antigen (anti-HBc IgM). HBsAg is the serological marker of HBV infections, 15 but there are cases in which HBsAg disappears rapidly without the appearance of HB surface antibodies. This is the immunological window period in which the only evidence of acute infection with HBV is the IgM antibody. HB surface antibodies appears two weeks after HBsAg and may persist for up to two years. HBsAg is detectable from one week to ten 10 weeks after contact. Detection of anti-HBc IgM coincides with development of general symptoms and increasing aminotransferases. The resolution of acute hepatitis is characterized by disappearance of HBsAg, appearance of anti-HBsAg antibodies, anti-HBc immunoglobulin G (IgG) and normalization of alanine-aminotransferase (ALT) levels. This profile indicates apparent cure and has been defined as functional healing. Nevertheless, it has been found that despite markers of disappearance of the infection, cDNA persists in the nucleus of the hepatocyte as an episome or minichromosome from which ribonucleic acid (RNA) and this DNA are generated to initiate replication viral. This cDNA remains in the host indefinitely after the first hours of infection. Replication from this reservoir of HBV can restart if immune defense mechanisms are blocked, as occurs with immunosuppression since host immunity controls those infected cells. Recently, the concept of a functional cure has been redefined as the loss of HBsAg with or without the appearance of anti-HBsAg antibody or any HBV DNA detectable in serum, but with the persistence of cDNA.^{6,13} In contrast, a total cure is functional healing plus elimination of cDNA. At present, it is impossible to cure HBV infections because the available drugs only suppress viral replication but cannot eliminate cDNA. The elimination of cDNA is the ideal goal of treatment of chronic HBV infections. Tests for IgM anti-HBc are positive in 10% to 15% of patients whose chronic HBV infections have reactivated and are indistinguishable

from acute infections.^{15,16,23,24} Nevertheless, other serological characteristics can help differentiate them. In acute infections, the IgM is pentameric and has a molecular weight of 19 S, but in chronic infections, the IGM is monomeric and has a molecular weight of 7 to 8 S. 16 Titers greater than 1:1,000 are seen in 80% of acute infections with a sensitivity of 96.2% and a specificity of 93.1% when determined by enzyme immunoassay. IgM titres less than 1:1,000 are seen in 70% of acutely exacerbated chronic hepatitis B cases.

Results: 431 HIV subjects were screened for HBV to obtain the required 100 HBV infected patients giving HBV seroprevalence of 23.2% among HIV infected patients. The results were presented as percentage of all patients with HBV/HIV co-infection below:

Table 1: Frequency of Hepatitis B serological makers among HBV/HIV cases N=100

	Frequency n	Percentage (%)
HBsAg	100	100
HBsAb	0	0
HBeAg	47	47
HBeAb	36	36
HBcAb	83	83

Conclusion: The frequency of Hepatitis B seromarkers shows that of all the co-infected patients 83% had HBcAb indicating chronic infection with HBV, out of which 47% are HBeAg positive and are actively replicating while 36% are HBeAb positive and seroconvert to inactive carriers, with zero HBsAb. This explains the increased HBV viral replication observed in HIV patients and supports the fact that Hepatitis Bclearance is more difficult among HBV/HIV co-infected adult patients.