

Epidemiology of viral hepatitis in Sudan

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Abstract: Hepatitis virus infections are the most common cause of liver disease worldwide. Sudan is classified among the countries with high hepatitis B virus seroprevalence. Exposure to the virus varied from 47%–78%, with a hepatitis B surface antigen prevalence ranging from 6.8% in central Sudan to 26% in southern Sudan. Studies pointed to infection in early childhood in southern Sudan while there was a trend of increasing infection rate with increasing age in northern Sudan. Hepatitis B virus was the commonest cause of chronic liver disease and hepatocellular carcinoma and was the second commonest cause of acute liver failure in the Sudan. Studies of hepatitis C virus showed a low seroprevalence of 2.2%–4.8% and there was no association with schistosomiasis or with parenteral antischistosomal therapy. Hepatitis E virus was the commonest cause of acute hepatitis among pediatric, adult, and displaced populations. Recent introduction of screening of blood and blood products for hepatitis B virus and hepatitis C virus infections and the introduction of hepatitis B virus vaccine as part of the extended program of immunization is expected to reduce the infection rate of these viruses in the Sudan.

Keywords: hepatitis, Sudan, liver disease

Introduction

Viral hepatitis is a major public health problem affecting several hundred million people worldwide. It causes considerable morbidity and mortality from both acute infection and chronic sequelae including chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). This article aims to summarize most of the studies on viral hepatitis in Sudan and try to highlight the burden of the disease and the challenge facing health care workers in the country in combating this serious health problem.

Methodology

A comprehensive literature search was performed using electronic databases, primarily Medline. All relevant articles examining the epidemiology of viral hepatitis in Sudan since 1981 were carefully analyzed. More than 40 articles were identified and unpublished data was also analyzed when necessary.

Results

Hepatitis B virus

Over two billion people worldwide have evidence of previous or current hepatitis B virus (HBV) infection. Three quarters of the world population live in areas with high levels of infection; risk factors for infection include blood transfusion, sexual intercourse, intravenous drug abuse, vertical and horizontal transmission of the virus. Sudan is classified among countries with a high hepatitis B surface antigen (HBsAg) endemicity of more than 8%.¹ Exposure to HBV infection ranges from 47%² to 78%³ with a hepatitis B surface antigen (HBsAg) seroprevalence ranging from as low as 6.8%² in central Sudan to as high as 26%⁴ in southern Sudan. Identified risk factors for HBV infection in Sudan include living in southern Sudan, parenteral antischistosomal therapy,² sexual promiscuity,³ and scarification⁴ which is a common ritual in

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southern Sudan. There was no association with schistosomal infection or blood transfusion^{2,5} These rates are comparable to some African countries where seroprevalence of HBsAg was reported at rates of 15.6% in Burundi,⁶ 14% in Central African Republic,⁷ and 10% in Uganda.⁶ Lower rates were however found in other countries such as Tanzania (4.4%),⁸ Nigeria (4.98%),⁹ and Ethiopia (7%).¹⁰ Seroprevalence of HBsAg among asymptomatic blood donors ranged from 12.3%¹¹ in southern Sudan to 17.5%¹² in central Sudan. These studies were carried out in the eighties and nineties when screening of blood and blood products was only done in a few blood banks in the capital, Khartoum. In 2002, a national program for screening blood and blood products for HBV and HCV infection was introduced throughout the whole country.

A high seroprevalence of HBsAg was detected in patients with liver cirrhosis ranging from 31%–61%^{13,14} and similar carrier rates of 43%–60%^{14,15} were found in patients with HCC, indicating that HBV infection is perhaps the commonest risk factor for developing HCC besides hepatitis C virus (HCV) infection at a rate of 11%.¹⁵ Peanut butter, a rich source of Aflatoxin B1 has also been identified as a strong risk factor for HCC in western Sudan; this was well documented in a study by Omer and colleagues where 80% of cases in a case control study were attributed to a combined effect of HBV infection and Aflatoxin exposure.¹⁶ HBV was also the second commonest cause of acute liver failure in Sudanese subjects at a rate of 22%, seronegative hepatitis being the commonest cause at 38%, other causes included severe *Plasmodium falciparum* malaria, hepatitis E virus (HEV) and idiosyncratic drug reactions.¹⁷ Common risk factors for acute liver failure worldwide include paracetamol over dose, idiosyncratic drug reactions, HBV infection, and seronegative hepatitis.¹⁸ Among patients with end-stage renal disease undergoing hemodialysis, studies have revealed an HBsAg seroprevalence of 7.6%.¹⁹ Currently all patients planned for hemodialysis who are negative for HBV antibodies are vaccinated prior to undergoing hemodialysis.

Age pattern of HBV infection

Age pattern of exposure to HBV infection differed between various geographic locations in Sudan; this was noted in a study on the prevalence of HBV exposure in soldiers from five urban locations in Sudan. In soldiers from northern Sudan, exposure to HBV infection increased from 47.5% in those <20 years of age to 80% in those >39 years of age, in contrast, HBV infection was not found to increase after the age of 20 years among soldiers raised in the south Sudan

as 94% of soldiers under the age of 20 years had serologic evidence of HBV infection pointing to infection in childhood in south Sudan while there was a trend of increasing infection rate with increasing age in north Sudan.³

HBV infection in children and pregnant ladies

A recent study in Khartoum state on pregnant women showed an HBsAg carrier rate of 5.6% with a very low prevalence of HCV infection of 0.6%.²⁰ An earlier study in the Gezira state in central Sudan showed that 70% of HBsAg positive women of child bearing age were also HBeAg-positive,²¹ an important risk factor for vertical transmission of the infection. Mother to child transmission of HBV infection was studied in Juba, southern Sudan on eighty eight mother and child pairs. In nine HBsAg positive mothers, five of their children were infected (55.5%), where as in seventy-nine HBsAg-negative mothers only nine children were HBsAg-positive (11.4%), again pointing towards infection in early childhood in southern Sudan. It was however difficult to conclude that the infection was vertical in these cases as the mean age of children studied was 15.5 months.²²

Hepatitis D virus

The few studies on HBV infection which conducted Hepatitis D virus seroprevalence, found this to be between 9% in eastern Sudan²³ and 27.8% in central Sudan.²¹ Studies from neighboring Uganda demonstrated seroprevalence of anti-D antibodies in up to 30.6% of those who are HBsAg-positive.⁶

Hepatitis C virus

Hepatitis C virus (HCV) is a major cause of end stage liver disease in many parts of the world. One hundred and seventy million people are estimated to be infected worldwide.²⁴ Studies on the epidemiology of HCV have suggested that the Nile delta region of Egypt has one of the highest prevalence rates of HCV infection in the world with seroprevalence rates approaching 20% in villagers over the age of 30 years.²⁵ This was largely attributed to infection with schistosomiasis²⁶ and to mass treatment with parenteral antischistosomal therapy.²⁷ The few studies on HCV infection in Sudan demonstrated a low seroprevalence ranging from 2.2% in the Gezira state,²⁸ an area endemic with schistosomiasis to 4.8% in patients with schistosomal periportal fibroses. Genotype 4 was the commonest isolated genotype.²⁹ No association was found between HCV infection and schistosomiasis or with parenteral antischistosomal therapy.^{28,29}

Similar HCV seroprevalence was noted in other African countries such as Ethiopia (2%),³⁰ Central African Republic (5%),⁷ and Libya (7.9%).³¹ Genotype 4 was also the commonest genotype isolated in Cameroon,³² Nigeria,³³ Egypt,³⁴ and the Central African Republic.³⁵

Prevalence of HCV infection amongst asymptomatic blood donors was found to be 4.4% (Alfadil, Unpublished data), currently screening of blood and blood products for HCV infection is carried out in most blood banks round the country.

The difference between the low seroprevalence of HCV infection between Sudan and neighboring Egypt which has one of the highest HCV seroprevalence worldwide, may be due to the fact that parenteral antischistosomal therapy was only offered to those over the age of 12 years in Sudan whereas in Egypt it was offered to those over the age of 6 years, equipment sterilization was more strictly observed in Sudan due to low volume of patients treated per session when compared to Egypt,^{27,28} other factors thought to contribute to the high seroprevalence in Egypt include intravenous drug abuse³⁶ and interfamilial transmission between parents and children.³⁷ The highest prevalence of HCV infection in Sudan was noted in patients with end stage renal disease on regular hemodialysis with a seroprevalence of 23.7%.¹⁹ Major risk factors for infection were longer duration of dialysis, dialysis in multiple centers, and an age over 30 years.

HBV/HCV and human immunodeficiency virus co-infection

The only study on HBV and human immunodeficiency virus (HIV) co-infection was carried out in 1987 on 593 subjects who practiced high risk behavior, including sexual promiscuity. Although the study showed a high prevalence of HBV markers (80%), none of the subjects was HIV-positive.³⁸ There are as yet no published studies on HCV/HIV co-infection. Recent studies from neighboring African countries reported HBV/HIV co-infection in 6% of a studied population in Kenya,³⁹ 9.2% in Nigeria,⁴⁰ and 20.4% in Malawi.⁴¹ HCV/HIV co-infection was found in 1% in Kenya,³⁹ 5.8% in Nigeria,³⁰ and 5% in Malawi.⁴¹ With the spread of HIV infection in the African continent, urgent studies are needed in Sudan to assess the current prevalence of HBV/HCV/HIV co-infection specially as the components of the most common antiretroviral drug therapy used in Africa can cause hepatic problems, and lamivudine-resistant HBV is known to emerge after HBV monotherapy in co-infected patients.

Enterically transmitted viruses

It is thought that more than 50% of hepatitis cases occurring in developing countries are unrelated to hepatitis A virus (HAV) or HBV infection, and a high proportion of these cases appear to be enterically transmitted.⁴² Studies on patients with acute hepatitis during the floods of 1988 in Khartoum demonstrated that infection was mainly due to HEV (58%) with low incidence of HAV infection at (5.45%).⁴³ Another study amongst children with acute hepatitis in Khartoum state concluded that HEV was also the commonest cause of acute clinical hepatitis among that pediatric population with HEV infection at 59%, HAV at 33.3%, and HBV at 2.6%.⁴⁴ The largest documented outbreak of HEV infection in displaced populations was reported from Mornay camp in western Darfur in 2004, when, out of a total population of 78,800 people, 2621 were infected with HEV, with an attack rate of 3.3% and an overall case-fatality rate of 1.7%. Death was highest amongst pregnant women with a mortality rate of 31%. The most important risk factor for HEV infection was drinking chlorinated surface water. It was thought that although the levels of free chlorine residual were sufficient to reduce fecal *coliform* load in tap water it may not have been enough to inactivate HEV.^{45,46} This outbreak highlights the importance of further laboratory studies on inactivation of HEV. Currently HEV is thought to be the commonest cause of symptomatic hepatitis in both adults and children. As both these viral infections are spread via oral – fecal routes, public health measures, such as provision of clean water and adequate disposal of sewage should be taken.

Viral hemorrhagic fevers

These are a group of illnesses resulting from infection with one of several viral families; these include Rift Valley fever, yellow fever, and the Ebola virus. Patients commonly present with hepatitis among other clinical manifestations. Recently an outbreak of Rift Valley fever occurred in the Gezira state of central Sudan in November 2007, with over 436 human cases reported including 161 deaths, a mortality rate of 37%.⁴⁷ Similar outbreaks caused by Ebola virus and yellow fever were reported from Sudan in the past.^{48,49}

Conclusion

HBV infection is a major cause of chronic liver disease, acute liver failure and HCC in Sudan. Introduction of blood and blood products screening for HBV and HCV in all blood banks in the country and the inclusion of HBV vaccination as part of the extended program of immunization are two

major achievements in the battle against viral hepatitis in this country. This is expected to reduce the carrier pool and eventually reduce infection rates in both adults and children in the coming few years.

Disclosure

The authors report no conflicts of interest in this work.

References

- Expanded program on immunization, hepatitis B vaccine, making global progress: EPI update. Geneva, Switzerland: World Health Organization; October, 1996.
- Mudawi HM, Smith HM, Rahoud SA, Fletcher IA, Saeed OK, Fedail SS. Prevalence of hepatitis B virus infection in the Gezira state of central Sudan. *Saudi J Gastroenterol.* 2007;13:81–3.
- McCarthy MC, Hyams KC, el-Tigani el-Hag A, et al. HIV-1 and hepatitis B transmission in Sudan. *AIDS.* 1989;3:725–9.
- McCarthy MC, el-Tigani A, Khalid IO, Hyams KC. Hepatitis B and C in Juba, southern Sudan: results of a serosurvey. *Trans R Soc Trop Med Hyg.* 1994;88:534–6.
- Eltoum IA, Ghalib HW, Abdel Gadir AF, Suliaman SM, Homeida MM. Lack of association between schistosomiasis and hepatitis B virus infection in Gezira-Managil area, Sudan. *Trans R Soc Trop Med Hyg.* 1991;85:81–2.
- de Lalla F, Rizzardini G, Rinaldi E, Santoro D, Zeli PL, Verga G. HIV, HBV, delta-agent and *Treponema pallidum* infections in two rural African areas. *Trans R Soc Trop Med Hyg.* 1990;84:144–7.
- Pawlotsky JM, Bélec L, Grésenguet G, et al. High prevalence of hepatitis B, C, and E markers in young sexually active adults from the Central African Republic. *J Med Virol.* 1995;46:269–72.
- Pellizzer G, Blè C, Zamperetti N, et al. Serological survey of hepatitis B infection in Tanzania. *Public Health.* 1994;108:427–31.
- Ejele OA, Ojule AC. The prevalence of hepatitis B surface antigen (HBsAg) among prospective blood donors and patients in Port Harcourt, Nigeria. *Niger J Med.* 2004;13:336–8.
- Abebe A, Nokes DJ, Dejene A, Enquesslassie F, Messele T, Cutts FT. Seroepidemiology of hepatitis B virus in Addis Ababa, Ethiopia: transmission patterns and vaccine control. *Epidemiol Infect.* 2003;131:757–70.
- Ahmed SA, Sanyal RK, Scedrou P, Ahmed MG. Hepatitis B surface antigen in South Sudan. *J Commun Dis.* 1984;16:330–1.
- Elshafie SS. The prevalence of hepatitis B surface antigen in the Gezira (Sudan). *Afr J Med Med Sci.* 1992;21:61–3.
- Itoshima T, Fedail SS, Suliman I, Ali AK, Higashi T, Tsuji T. Hepatitis B virus markers in patients with schistosomiasis, liver cirrhosis and hepatocellular carcinoma in Khartoum, Sudan. *Acta Med Okayama.* 1989;43:241–4.
- Yousif-Kadaru AGM, Mohamedein A, Ahmed SAM, et al. Hepatitis B virus markers in Sudanese patients with hepatocellular carcinoma and other liver diseases. *Yemeni Med J.* 1998;2:17–22.
- Omer RE, Van't Veer P, Kadaru AM, et al. The role of hepatitis B and hepatitis C viral infections in the incidence of hepatocellular carcinoma in Sudan. *Trans R Soc Trop Med Hyg.* 2001;95:487–91.
- Omer RE, Kuijsten A, Kadaru AM, et al. Population-attributable risk of dietary aflatoxins and hepatitis B virus infection with respect to hepatocellular carcinoma. *Nutr Cancer.* 2004;48:15–21.
- Mudawi HM, Yousif BA. Fulminant hepatic failure in an African setting: etiology, clinical course, and predictors of mortality. *Dig Dis Sci.* 2007;52:3266–9.
- O'Grady JG. Acute liver failure. *Postgrad Med J.* 2005;81:148–54.
- El-Amin HH, Osman EM, Mekki MO, et al. Hepatitis C virus infection in hemodialysis patients in Sudan: two centers' report. *Saudi J Kidney Dis Transpl.* 2007;18:101–6.
- Elsheikh RM, Daak AA, Elsheikh MA, Karsany MS, Adam I. Hepatitis B virus and hepatitis C virus in pregnant Sudanese women. *Virology.* 2007;4:104.
- Hyams KC, al-Arabi MA, al-Tagani AA, Messiter JF, al-Gaali AA, George JF. Epidemiology of hepatitis B in the Gezira region of Sudan. *Am J Trop Med Hyg.* 1989;40:200–6.
- Woodruff AW, Adamson EA, el Suni A, Maughan TS, Kaku M, Bundru W. Children in Juba, southern Sudan: the second and third years of life. *Lancet.* 1986;2:615–8.
- McCarthy MC, Burans JP, Constantine NT, et al. Hepatitis B and HIV in Sudan: a serosurvey for hepatitis B and human immunodeficiency virus antibodies among sexually active heterosexuals. *Am J Trop Med Hyg.* 1989;41:726–31.
- Lauer GM, Walker BD. Hepatitis C virus infection. *N Engl J Med.* 2001;345:41–52.
- Nafeh MA, Medhat A, Shehata M, et al. Hepatitis C in a community in Upper Egypt: I. cross-sectional survey. *Am J Trop Med Hyg.* 2000;63:236–41.
- Darwish MA, Raouf TA, Rushdy P, Constantine NT, Rao MR, Edelman R. Risk factors associated with a high seroprevalence of Hepatitis C virus infection in Egyptian blood donors. *Am J Trop Med Hyg.* 1993;49:440–47.
- Frank C, Mohamed MK, Strickland GT, et al. The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. *Lancet.* 2000;11;355:887–91.
- Mudawi HM, Smith HM, Rahoud SA, et al. Epidemiology of HCV infection in Gezira state of central Sudan. *J Med Virol.* 2007;79:383–5.
- Mudawi HM, Smith HM, Fletcher IA, Fedail SS. Prevalence and common genotypes of HCV infection in Sudanese patients with hepatosplenic schistosomiasis. *J Med Virol.* 2007;79:1322–4.
- Frommel D, Tekle-Haimanot R, Berhe N, et al. A survey of antibodies to hepatitis C virus in Ethiopia. *Am J Trop Med Hyg.* 1993;49:435–9.
- Saleh MG, Pereira LM, Tibbs CJ, et al. High prevalence of hepatitis C virus in the normal Libyan population. *Trans R Soc Trop Med Hyg.* 1994;88:292–4.
- Njouom R, Pasquier C, Ayoub A, et al. High rate of hepatitis C virus infection and predominance of genotype 4 among elderly inhabitants of a remote village of the rain forest of South Cameroon. *J Med Virol.* 2003;71:219–25.
- Oni AO, Harrison TJ. Genotypes of hepatitis C virus in Nigeria. *J Med Virol.* 1996;49:178–86.
- Ray SC, Arthur RR, Carella A, Bukh J, Thomas DL. Genetic epidemiology of hepatitis C virus throughout Egypt. *J Infect Dis.* 2000;182:698–707.
- Fretz C, Jeannel D, Stuyver L, et al. HCV infection in a rural population of the Central African Republic (CAR): evidence for three additional subtypes of genotype 4. *J Med Virol.* 1995;47:435–7.
- Bassily S, Hyams KC, Fouad RA, Samaan MD, Hibbs RG. A high risk of hepatitis C infection among Egyptian blood donors: the role of parenteral drug abuse. *Am J Trop Med Hyg.* 1995;52:503–5.
- Mohamed MK, Magder LS, Abdel-Hamid M, et al. Transmission of hepatitis C virus between parents and children. *Am J Trop Med Hyg.* 2006;75:16–20.
- Burans JP, McCarthy M, el Tayeb SM, et al. Serosurvey of prevalence of human immunodeficiency virus amongst high risk groups in Port Sudan, Sudan. *East Afr Med J.* 1990;67:650–5.
- Harania RS, Karuru J, Nelson M, Stebbing J. HIV, hepatitis B and hepatitis C co-infection in Kenya. *AIDS.* 2008;22:1221–2.
- Lesi OA, Kehinde MO, Oguh DN, Amira CO. Hepatitis B and C virus infection in Nigerian patients with HIV/AIDS. *Niger Postgrad Med J.* 2007;14:129–33.
- Nyirenda M, Beadsworth MB, Stephany P, et al. Prevalence of infection with hepatitis B and C virus and co-infection with HIV in medical inpatients in Malawi. *J Infect.* 2008;57:72–7.
- Bradley DW. Enterically-transmitted non-A, non-B hepatitis. *Br Med Bull.* 1990;46:442–61.

43. McCarthy MC, He J, Hyams KC, el-Tigani A, Khalid IO, Carl M. Acute hepatitis E infection during the 1988 floods in Khartoum, Sudan. *Trans R Soc Trop Med Hyg.* 1994;88:177.
44. Hyams KC, Purdy MA, Kaur M, et al. Acute sporadic hepatitis E in Sudanese children: analysis based on a new western blot assay. *J Infect Dis.* 1992;165:1001–5.
45. Guthmann JP, Klovstad H, Boccia D, et al. A large outbreak of hepatitis E among a displaced population in Darfur, Sudan, 2004: the role of water treatment methods. *Clin Infect Dis.* 2006;42:1685–91.
46. Boccia D, Guthmann JP, Klovstad H, et al. High mortality associated with an outbreak of hepatitis E among displaced persons in Darfur, Sudan. *Clin Infect Dis.* 2006;42:1679–84.
47. Outbreak news. Rift Valley fever, Sudan – update. *Wkly Epidemiol Rec.* 2007;82:417–8.
48. Ebola haemorrhagic fever in Sudan, 1976. Report of a WHO/International Study Team. *Bull World Health Organ.* 1978;56:247–70.
49. Onyango CO, Grobbelaar AA, Gibson GV, et al. Yellow fever outbreak, southern Sudan, 2003. *Emerg Infect Dis.* 2004;10:1668–70.

