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SEROPREVALENCE OF HAV, HBV, HCV, AND HEV AMONG ACUTE HEPATITIS PATIENTS AT KENYATTA NATIONAL HOSPITAL IN NAIROBI, KENYA

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SEROPREVALENCE OF HAV, HBV, HCV, AND HEV AMONG ACUTE HEPATITIS PATIENTS AT KENYATTA NATIONAL HOSPITAL IN NAIROBI, KENYA

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ABSTRACT

Background: **Acute viral hepatitis is most frequently caused by the hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E virus (HEV).**
Objectives: **To determine seroprevalence of HAV, HBV, HCV and HEV among patients with acute hepatitis in Nairobi, Kenya, elucidate various risk factors for hepatitis viral infection and determine the co-infection rates with these viruses in the acute hepatitis patients.**
Design: **Across sectional descriptive study.**
Setting: **Kenyatta National Hospital, from November 2007 to April 2008.**
Subjects: **One hundred patients were recruited by purposive sampling method and comprised of 57 males and 43 females.**
Results: **Among the enrolled patients, twenty three tested positive for one or more markers of acute viral hepatitis, that is, HAV, HBV, HCV and HEV. No markers were detected in 77 patients, 2% tested positive for IgM anti-HAV; 11% for IgM anti-HBc; 3% for HBsAg; 5% for HCV RNA and 7% for IgM anti-HEV. Various risk factors associated with acute viral hepatitis were identified; poor sanitation, source of water, occupation, place of residence, level of education, household size, drug abuse and sexual behaviours. Co-infection rate with hepatitis Viruses was at 4%, IgM anti-HAV and IgM anti-HEV 1 % (n=1); IgM anti-HBc and IgM anti-HEV 1% (n=1); IgM anti-HBc and anti-HCV 2% (n=2). Three patients were positive for HBsAg; among this two were negative for IgM anti-HBc and this accounted for HBV carriage (2 %).**
Conclusion: **Hepatitis viruses' infections are common cause of hepatitis among patients with acute hepatitis at Kenyatta National Hospital. Co-infection with these viruses was also identified among these patients.**

INTRODUCTION

Viral hepatitis is a recognised major public health problem worldwide, but more prevalent in developing countries. Hepatitis B virus (HBV) and Hepatitis C virus (HCV) have received more attention due to their wide distribution and high prevalence, and also to the severe long-term sequelae of chronic infections with these agents, liver cirrhosis and hepatocellular carcinoma (3).

The global distribution of hepatitis B infection varies greatly. It is estimated that 350 million people globally are chronic carriers of the hepatitis B virus of who 170 million reside in Africa. The prevalence of HBV carriers varies substantially between regions, from 7 to 35 % (22). The wide range is largely related to differences in age at the time of infection, a factor that is inversely related to the risk of chronic infection. In areas where the prevalence is high, such as Africa, Southeast Asia and China more than half the

population is infected at some time in their lives, and more than eight percent are chronic carriers of HBV, the result of either neonatal transmission (vertical) or transmission from one child to another (horizontal) (3). Areas with low levels of endemicity include North America, Western Europe, and Australia, where only a minority of people comes into contact with the virus, as a result of horizontal transmission among young adults (3).

The prevalence of serological markers of exposure to HBV in sub-Saharan Africa is high, up to 90% in many areas (1). In Kenya carrier rate for Hepatitis B surface Antigen is between 10 and 15 % (8). The prevalence of HBsAg in Nairobi and rural Kenya range between 3 to 30 %(16) and at the Kenyan coast, 11.4% of the population are positive for HBsAg (16). A study on the seroprevalence of hepatitis B virus and hepatitis C virus in the regional blood transfusion centres of Kenya showed prevalence of HBV and HCV to be 3.0 and 0.75% respectively (23).

Hepatitis C virus (HCV) infects an estimated 170 million persons worldwide and thus represents a global viral pandemic. Egypt has the highest HCV prevalence (7, 8, 19, and 23). The use of parenteral antischistosomal therapy in Egypt is thought to have contributed to thehighprevalence of antibodies against HCV in various regions ranging from 6 to 28 percent (mean, 22 percent) (7). In Kenya, less than one percent of the population is positive for HCV antibodies (23).In the United States, 1.8 percent of the population is positive for HCV antibodies. HCV is responsible for 75 to 95% of all post-transfusion hepatitis (8, 19, and 23). High prevalence of HCV has also been documented in patients with hepatocellular carcinoma in Kenya's Provincial Hospitals (17).

HAV is present worldwide, and the risk of infection is inversely proportional to levels of sanitation and personal hygiene (11). Worldwide, an estimated 1.4 million cases of acute hepatitis A occur annually. Geographic areas can be characterised by high (incidence may reach 150 per 100 000 per year.), intermediate or low levels of endemicity patterns of HAV infection. The levels of endemicity correlate with hygienic and sanitary conditions of each geographic area (13).

Hepatitis E virus (HEV) causes epidemics and sporadic viral hepatitis, often involving very large numbers of patients. Such epidemics have occurred in several countries on all continents, although most are in tropical and subtropical areas of the world (18). Hepatitis E virus is the leading cause of acute viral hepatitis in young to middle-aged adults in Asia (18). In a study carried out in Cairo, Egypt; HEV was found to be a common cause of acute hepatitis in a paediatric population occurring in 12% of the patients (10). HEV has also been implicated as cause of fulminant hepatic failure in India (1).The highest prevalence of infection occurs in regions where low standards of sanitation promote the transmission of the virus. The prevalence of antibody to HEV in suspected or documented endemic regions has been much lower than expected (3-26%). Screening of blood donors in central Europe and North America has shown a prevalence of anti-HEV antibodies of 1.4 - 2.5%, in South Africa of 1.4%, in Thailand of 2.8%, in Saudi Arabia of 9.5%, and in Egypt of 24.0% (18). The prevalence of antibody to HEV in non-endemic regions (like the US) has been much higher than anticipated (1 - 3%) (18),in Western Europe it is at 5.3 % (5). In the Asian subcontinent, Hepatitis E is more severe than hepatitis A, with mortality rates in the range of 1–2%, compared with 0.2% for hepatitis A (18).

Previous prevalence studies of acute viral hepatitis in Kenya were carried out by Bagshawe *et al*., in 1972, Greenfield in 1982 and Atina *et al*., in 2004. In The first study, HBsAg was found in 54% of acute hepatitis cases at the Kenyatta National Hospital. The second study looked at adults with acute sporadic hepatitis at KNH; Hepatitis B virus was responsible for 70% of cases, HNANB for 18%, and HAV for only 12%. The third study looked at patients at least six months old with a history of jaundice not exceeding six months and Hepatitis A, B, and C accounted for 41.7, 26.2 and 7.1% of the patients respectively, 13.1% of all patients were HBsAg carriers.

HEV had not yet been discovered during the first studies hence its involvement in acute hepatitis was not assessed. HEV has been shown to be a significant cause of epidemics and acute sporadic hepatitis in the developing countries. HEV has been identified as a cause of acute sporadic hepatitis in refugee camps in northern Kenya (13); these refugees originate from the neighbouring countries like Somalia, Southern Sudan and Ethiopia where HEV epidemics have been reported (13).

MATERIALS AND METHODS

Study site: This study was carried out at Kenyatta National Hospital, a referral hospital in Nairobi after approval by the hospital's Ethical Review Committee and the Kenya medical Research Institute/National Ethical Review Committee (KEMRI/NERC). After collecting specimens from patients in this site, the main laboratory work was carried out at the Center for Virus Research (CVR), Kenya Medical Research Institute, Nairobi.

Study Population: A total of a hundred patients (both inpatients and outpatients) were recruited for this study by purposive sampling at Kenyatta National Hospital's Medical wards and the Liver clinic between November 2007 and April 2008. The patients who visit this section of the hospital normally have liver diseases of various forms and are normally refered

here for specialised treatment and care. Subjects whose main complaint was consistent with WHO recommended case definition of acute hepatitis were enrolled into the study (25).

Questionnaire: Health history and lifestyle/ demographic questionnaires were administered to all subjects by the clinician attending to the patient at the study sites. All the patients were interviewed to identify risk factors for hepatitis during the six months preceding the onset of illness.The questionnaires included: a detailed assessment of the patient health history; patient demographics; age, sex; social and economic lifestyle; occupation and place of residence.

Specimen collection: The attending clinician or a phlebotomist drew five millilitres of blood from all enrolled patients which was transported to the laboratory immediately. The specimens were kept at temperature of 0ºC to 4ºC in ice packs until they got to the laboratory where the serum was separated from the red blood cells by centrifugation at 10000 rpm for ten minutes (KUBOTA KS-5000) and stored at -20°C in a freezer until processed.

Specimen processing: The blood was screened for HAVIgM antibody by ELISA method; hepatitis B surface antigen by an inhouse method,HBsAg reverse passive haemagglunation test and hepatitis B core antigenIgM antibody by ELISA method; total antibody against HCV (anti-HCV) by ELISA method and HCV-RNA by RT-PCR method; HEVIgM antibody by ELISA method. The laboratory tests were aimed at detecting these viral markers in the collected specimens.

Data management and Statistical analysis: All questionnaire data and laboratory serological tests results data were entered into a computer using Microsoft Accessand Microsoft excel programmes respectively. Prevalence and 95% confidence intervals (C.Is) were calculated using standard equations.

Frequency distributions and risk factors association were compared by the use of the Pearson chi-square test. P-values of less than 0.05 were considered to be statisticallysignificant. Data analysis was carried out using SPSS 11.5 computer software.

Ethical considerations: Authorisation to carry out this study was obtained from the Board of Postgraduate studies of Jomo Kenyatta University of Agriculture and Technology (JKUAT) and Kenya Medical Research Institute/NationalEthical Review Committee (KEMRI/NERC), the study Protocol was approved by the Ethical Review Committees of KNH. Informed consent and incase of minors assent were obtained from the patients before they were enrolled into the study.

RESULTS

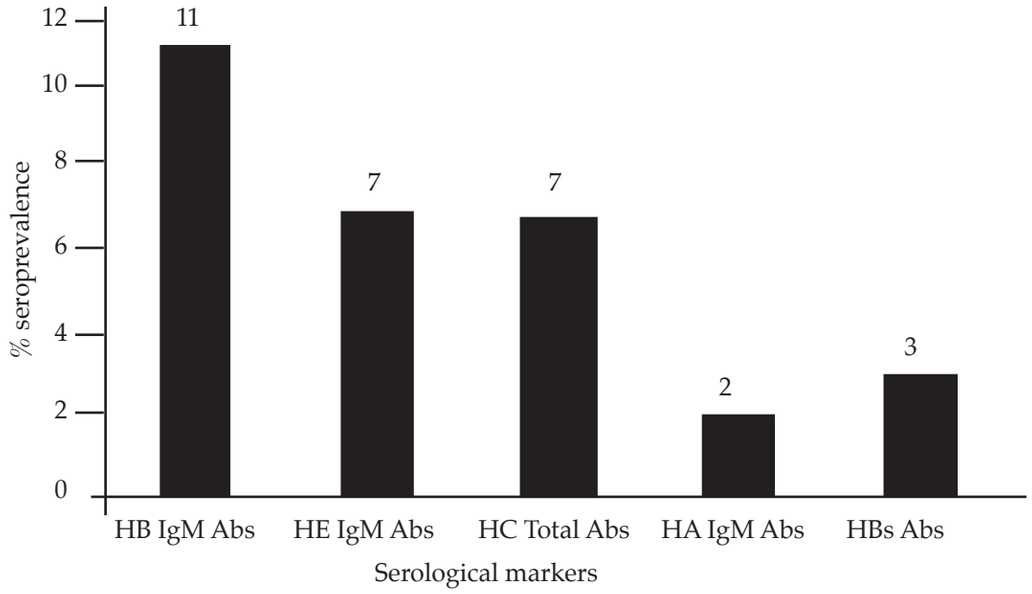
Prevalenceof Hepatitis Viruses: A total of 100 patients, 57 males and 43 females were recruited into the study. The age range was 16 years to 83 years; 19 to 83 years in males and 16 to 78 years in females, with a mean of 38.95 years and 36.40 years, standard deviation of 13.87 and 14.68, and median of 34 and 31 respectively (Table 1).

Among the enrolled patients, twenty-three tested positive for one or more markers of acute viral hepatitis, that is, HAV, HBV, HCV and HEV. No markers were detected in 77 patients. Two patients (2%) tested positive for IgM anti-HAV; Three patients (3 %) tested positive for HBsAg; 11 (11%) tested positive for IgM anti-HBc; Five patients(5%) tested positive for HCV RNA (seven tested positive for anti-HCV antibody(this were confirmed using RT-PCR for HCV but only five tested positive for HCV RNA) and seven patients (7%) tested positive for IgM anti-HEV (Figure 1).

Table 1
Demorgraphic Characteristics of Recruited Patients

Gender	N (%)	Age range(years)	Mean age	Standard deviation	Median
Male	57	19-83	38.95	13.87	34
Female	43	16-78	36.40	14.68	31

Figure 1
Seroprevalence of viral markers in acute hepatitis



The seven samples positive for HCV total antibodies were ran through a confirmatory test using a molecular diagnostic test. Five among them turned positive for HCV RNA (Table 2).

Table 2
Prevalence of viral hepatitis in acute hepatitis

Virus markers	Positive N (%)	Negative N (%)
HBV	13 (13)	87 (87)
HEV	7 (7)	93 (93)
HCV RNA	5 (5)	95 (95)
HAV	2 (2)	98 (98)

Co-infection rate of hepatitis viruses: Four patients tested positive for more than one marker of acute infection of hepatitis virus (Table 3). One had IgM anti-HAV and IgM anti-HEV; one had IgM anti-HBc and IgM anti-HEV; and two had IgM anti-HBc and anti-HCV; two patients had the HBsAg with negative IgM anti-HBc.Out of the three patients positive for HBsAg, two were negative for IgM anti-HBc antibody and this accounted for HBV carriage, which is 2% carriage.

Table 3
Co-infection rate with hepatitis viruses

Co-infection	Frequency(n)	Percent (%)
HAV + HEV	1	1
HBV + HEV	1	1
HBV+ HCV	2	2
HAV	1	1
HBV	10	10
HCV	3	3
HEV	5	5
TOTAL	23	77 (Non Reactive)

Risk Factors

Source of water: the source of household water had an influence on the infectivity with HAV; those without tap water inside the house n=33 (42.9%)had a greater probability of being infected than those that had tap water inside the house n=17 (22.1 %). This difference was statistically significant (p=0.024).

Type of toilet: the type of toilet used by the study participants influenced the infectivity, although the association is not statistically significant. Those positive for IgM anti-HAV and IgM anti-HEV all used pit latrines in their homes (p=0.055), only n=7 (63.6%), (p=0.065)and n=3(60%), (p>0.05)of those positive for IgM anti-HBc and HCV RNA respectively used pit latrines.

Blood and blood product transfusion: Among those positive for IgM ant-HBc, n=6 (54.5 %) (p=0.054) had had blood/blood product transfusion during the six months preceeding the infection.

Sexual behaviours: Some of those positive for IgM anti-HBc and HCV-RNA had same sex partners, however the association is not statistically significant, n=1(9.1%), p=0.067 and n=1 (25%) p>0.05 respectively and also multiple sex patners, n=1 (9.1 %) and n=1 (25%) respectively.

Intravenous drug use (IVDU): One of the patients positive for IgM anti-HBc admitted to have abused IV drugs, the association is however not statistically significant (p>0.05).

Occupation: most of the patients enrolled into the study were non-skilled or semi-skilled however there was no statistically significant relation between infectivity and the occupation of the patient (p=0.069).

HIV co-infection: In the questionnaires the participants had been asked if they had been tested for HIV, only 57 responded and n=18 (31.5%) p>0.05were positive. Among those positive for HIV, n=1 (6.7%) p>0.05were positive for HBV, n=3 (5.6%) p>0.05 were positive for HBsAg, n=2 (5.6%) p>0.05 were positive for HCV and n=2 (11.1%) p>0.05 were positive for HEV.

DISCUSSION

Prevalence of Hepatitis viruses: Hepatitis B was the leading cause of acute hepatitis overall, accounting for 13% of all patients enrolled in the study. This is comparable to rates reported from other parts of the developing world (6, 19). There was a marked decrease in prevalence of acute hepatitis B from the 29.9% Atina, *et al*; found in 2004 among patients above 15 years of age. With onlya few variable set collected and a small patient sample size, it is not possible to hypothesise with certainity that various interventions, such as past vaccination or health promotion campaigns, had an impact on the hepatitis B. Vaccination programme has been implemented for infants; assessment of such interventions would require an additional set of variables to be collected over a period that include the pre-intervention period.

Acute hepatitis E was the second most common type of hepatitis affecting 7 % (n=7) of all patients. This is proportionate to rates reported from other parts of the developing world like Taiwan and China at 3 to 26% (1), but slightly lower than other studies, 12 % in Egypt (10). The reason for this variations could be that the subjects in this study were 12 years and above whereas the other studies included all ages. The prevalence of antibody to HEV in suspected or documented endemic regions has been found to be 3 - 26% (1, 5) and in non-endemic region it was found to be between 1-36% (21). Acute hepatitis E is a childhood illness in the developing world because it is mainly spread via the oral faecal route and this age group may be unable to maintain good hygiene standards.In Cairo, Egypt HEV has been found to be a common cause of acute hepatitis in a paediatric population occurring in 12% of the patients (10).

The prevalence of hepatitis C was 5%(n=5) which is less than what Atina *et al*., reported in 2004, they found the seroprevalence of HCV to be 7.1%. The reason for the difference could be that a more specific analytical methods were used in this study, that is, a fourth generation Elisa kit for HCV and a molecular technique(RT-PCR) for HCV. However, these findings are comparable with figures reported from other part of the world, 4.4% in the USA (3), 5.4% in Malaysia (19), 9.9% reported in China (24) and 10.3% in Japan (25). Ethiopia and Egypt have much higher hepatitis C prevalence of 19 and 22% respectively, this is attributed to the use of parentral anti-schistosomiasis drugs in Egypt (7).

The prevalence of hepatitis A was found to be 2%. Studies from other parts of the world have found hepatitis A to account for between 3.6 and 66.4% of overall acute sporadic hepatitis (3, 6, 19, 24, 25). However, these results differ from that found by Atina *et al.*, 2004 (7), where hepatitis A was the leading cause of acute icteric hepatitis accounting for 41.7% of all the acute hepatitis patients. The reason for the difference is probably because the participant enrolled in this study were aged 12 years and above whereas in the previous study children below 12 years were included. Hepatitis A is more of a childhood illness than adult where in most cases it is as symptomatic, hence a number of young (<12 years) probable subjects were excluded from this study. HAV is spread oral faecally and the young are less likely to maintain good personal hygiene standards. Increasing awareness of the infectious diseases and improved

hygiene standards may also have resulted in the decreased prevalence. These results vary from those of the developed countries where its been found that hepatitis A is an adulthood illness (11), the patients are also more affluent and in some cases having just returned from holiday in endemic regions.

Risk factors: Although the prevalence of the hepatitis viral markers did not vary with the age of the participants and also between the genders of the participants in this study, other studies have demonstrated variations (14). Young adults (18 to 39 years of age) are at increased risk for HBV infection; this increase is attributed to the greater likelihood of multiple sex partners, illicit injection of drugs, and other high-risk behaviours in this age group than in others (14).

Blood and blood product transfusion; this study demonstrated an association between HBV and blood transfusion although not statistically significant, p=0.054. HBV and HCV are both transmitted through the blood and by sexual contact. Infection with both viruses is frequent, particularly in areas where the two viruses are endemic and among people at high risk for parenteral infections (2).

There was a difference in infectivity with HEV between those without tap water inside the house and those that had tap water inside the house. This difference was statistically significant (p=0.024). Hepatitis E virus (HEV) has been identified as responsible for massive waterborne epidemics of acute hepatitis in Asia, and also in Sudan and Iraq (11).

The type of toilet used by the study participants influenced the infectivity although not statistically significant. Those positive for IgM anti-HAV and IgM anti-HEV all used pit latrines in their homes. Infections with HAV and HEV occur early in life in areas where sanitation is poor and living conditions are crowded (11), since transmission of the viruses is through the faecal oral route.

Co-Infection rates with Hepatiti Viruses: The prevalence of HbsAg was 3%(2), and 2% were positive for HbsAg but negative for IgM ant-HBc. This indicates persistent HBV infection and which accounted for HBV carriage, this is lower than what was reported by Okoth and others, it was reported at between 5-15% in Nairobi province of Kenya (17) and at 13.1% reported by Atina and others (4). Globally,Carriage vary from 8 to 53% (6, 9, 19).

Co-infection rate with hepatitis virus among acute hepatitis patients was 4%,Four patients tested positive for more than one marker of acute infection with hepatitis viruses. One had IgM anti-HAV and IgM anti-HEV (1%); one had IgM anti-HBc and IgM anti-HEV (1%); and two had IgM anti-HBc and anti-HCV antibodies (andHCV-RNA) (2%). Co-infection with Hepatitis viruses causes a more severe acute hepatitis than that caused by either of these viruses alone and may develop to fulminant infection that is more severe and deadly (2). Co-infection with Hepatitis B virus and Hepatitis C virus is possible because of the shared transmission route; co-infection in intravenous drug users accelerates the clinical progression of both hepatitis B and hepatitis C (2). Co-infection of children with HAV andHEV is high because both viruses are transmitted mainly through the faecal oral route (11).

Co-infection of Hepatitis viruses with HIV, among those positive for HIV; 0% was positive for HAV, 6.7 %(n=1) were positive for HBVIgM, 5.6 % (n=3) were positive for HBsAg, 5.6% (n=2) were positive for HCV and 11.1% (n=2) were positive for HEVIgM. These infection rates among the HIV patients are high compared to the HIV negative patients and demonstrate a higher susceptibility of the HIV positive persons to hepatitis virus infection than the general population. There was an association between HIV and hepatitis virus infection however it is not statistically significant (p>0.05). An earlier study at Kenyatta National Hospital had shown HIV/HAV, HIV/HBV and HIV/HCV co-infection rates at 19.2, 22.7 and 0 % respectively (4). A South African study found HIV/HBV and HIV/HCV co-infection rates of 41% and 1% respectively (15). In Tanzania co-infection rate of HIV/HBV and HIV/HCV was found to be 1.2 and 13.8% respectively (20).

In conclusion, in this study, Hepatitis viruses were identified as important aetiological agents of acute hepatitis with a prevalence rate of 2, 11, 5 and 7% for HAV, HBV, HCV and HEV respectively, 77% were non-reactive for any of the hepatitis viruses.
Various risk factors associated with acute viral hepatitis were identified, for example;sanitation, source of water, drug abuse and sexual behaviours. Co-infection rate with hepatitis virus was at 4%; IgM anti-HAV and IgM anti-HEV 1 % (n=1); IgM anti-HBc and IgM anti-HEV 1% (n=1); IgM anti-HBc and anti-HCV 2% (n=2), and HbsAg carriage rate was at 2%.

Recommendations: the findings in this study may be an underestimate of the true prevalence of hepatitis viruses since not all infected persons have persistent serological evidence of infection. HAV, HBV and HEV IgM antibodies levels in infected patients' blood decreases gradually overtime. Hence timing of blood specimen collection at clinical symptoms onset is paramount, this can be achieved by conducting senitel surveillance studies at various health facilities.
HIV positive patients may have a higher rate of infection with the Hepatitis viruses as shown in this study and other studies carried out elsewhere, hence a further study is important to determine the

prevalence of hepatitis viruses among HIV positive patients.

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