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Antigen Detection of Hepatitis D Virus Infection among Renal Failure Patients with Hepatitis B Viruses on Hemodialysis in Khartoum State

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Abstract

Background: Delta virus or hepatitis D virus (HDV) is a small RNA-containing virus requiring the concomitant presence of hepatitis B virus (HBV) for its survival and pathogenicity. Within a few years of its discovery, it was linked to cases of progressive chronic hepatitis B. Approximately, 5% of the patients with chronic hepatitis B infection worldwide are infected with HDV. Development of chronic kidney disease (CKD) has become a serious problem worldwide. CKD is characterized by a slow and progressive decline in the kidney function. Some of the manifestations of CKD include atherosclerosis, increased hemolysis, platelet dysfunction, and neuropathy. Carriers of HBV are at increased risk of developing cirrhosis, hepatic decompensation, and hepatocellular carcinoma. This study aimed to assess the prevalence of HDV among HBV on hemodialysis and correlating its relationship with age, gender.

Materials and methods: This was an active surveillance cross sectional study conducted to detect the prevalence of HDV among HBV on hemodialysis. Ninety (90) HBV on hemodialysis patients were recruited in this study. It conducted at AL-shaheda Salma center for hemodialysis and hemodialysis center of Unmada hospital in Khartoum, Sudan from April to June 2017. All statistical analyses were performed by SPSS software version (20). Continuous variables were expressed as mean and standard deviation. Comparison between groups was performed with Pearson correlation. P-value<0.05 was considered significant.

Results: In this study, increase prevalence of HDV among hepatitis B patients on hemodialysis was the most important findings. 13.3% of cases showed positive HDV, 61% of participants were males with mean age 44.8 ± 8. HDV had positive correlation with age when (R=0.249, P=0.018).

Conclusion: This study ensures that; increase possibility of HDV infection among hepatitis B patients on hemodialysis.

Keywords: Hepatitis D virus; Hepatitis B virus; Hemodialysis

Introduction and Literature Review

Viral hepatitis delta (D) is caused by hepatitis D virus (HDV), which is a defective RNA viral agent that usually exists in association with the presences of hepatitis B virus (HBV) [1]. Hepatitis D infection varies from a mild disease to chronic hepatitis or even fulminant hepatic failure (FHF) [2]. Epidemiological studies have shown that the prevalence of HDV infection among hepatitis B surface antigen (HBsAg) carriers is approximately 5% all over the world [3] however; the prevalence of hepatitis D infection in HBV carriers is different in various clinical settings and in different parts of the world [4-6]. Two forms of infection of HDV and HBV have been described, co-infection and Super-infection, that despite an evidence reflecting different pathophysiologic mechanisms of these two types of infection, both can potentially lead to severe and irreversible hepatic damage. Super infection with HDV is the most important reason for chronic hepatic failure which may yet to co-infection that may seldom lead to FHF [7]. The risk of HBV/HDV transmission is a major problem in Hemodialysis (HDi) patients, different rates of HDV transmission in HDi patients were reported in previous studies, but these studies are too limited to provide a paradigm of the importance of HDV in HDi patients [8], wail the high risk of HDV/HBV transmission in HDi stems from the possible contamination of the HDi machinery with infected blood and from the many transfusions that these patients often received, as well as from lack of adherence to universal precautions [9]. Two other problems make the control of HDV infection a serious problem in HDi patients, the physicians usually do not bear in mind that HDV infection should be checked in the initial evaluation of HBV infected patients as well as in surveillance protocol, the second one is the diagnosis of HDV in HDi patients that always shows many problems. The issue is complicated by the significant mortality and morbidity of hepatitis D related to complications such as hepatic cirrhosis or hepatocellular carcinoma (HCC) [10-12], furthermore; treatment protocols are controversial and there is no specific guideline to prevent, diagnose and controlling HDV infection in HDi patients. As HDV infection in HDi seems to be a relatively neglected issue, we gathered on the midline all the findings of published reports on hepatitis D in HDi patients. In this paper, we review all aspects of HDV infection in HDi in order to assess the world-wide impact of the infection and the best way to manage hepatitis D in HDi. European reports have suggested that HDV infection is rare or absent in HDi patients, however; other studies have shown that even of HDV in Europe remains a major problem in HDi patients. HDV seems to be a serious problem in western Asian countries. A study in Turkey in 1993 reported that the frequency rate of HDV in HDi patients was higher than 8% [13]. research in Oman in 1994 demonstrated that the 7.7% of HDi patients were HDV infected [14,15] and a case control study in Saudi Arabia in 1992 revealed that 11.4% of patients in control

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	Mean	Std. Deviation	R	Sig.
Age	44.86	8.5	0.249*	0.018

*Correlation is significant at the 0.05 level (2-tailed).

Table 1: Mean ± SD and its correlation with HIDV.

		HDV		Total	R	Sig.
		Positive	Negative			
Gender	Male	6	49	55	-0.089	0.402
	Female	6	29	35		
Total		12	78	90		

Table 2: Distributor and correlation of HDV with gender.

group and 12.5% of patients in case group (HDi patients) had evidence of HDV infection. Despite the concern raised by these studies which suggested that the prevalence of HDV in HDi was higher than the average global prevalence (5%), no other specific research has been carried out since 1994 in HDi patients in Middle East. Previous studies indicate that there is no age limit for HDV infection among HBsAg positive subjects [16].

Overall, two forms of acute HDV infection may occur: Co-infection (simultaneous acquisition of HBV and HDV infection) and super-infection (acute HDV infection in a chronic HBsAg carrier). In patients with co-infection, the rate of progression to chronic hepatitis seems similar to acute HBV infection, but these subjects are at a significant risk of FHF. In contrast, patients with super-infection almost always progress to chronic hepatitis D virus, thus; in this setting cirrhosis due to chronic progressive liver disease is a major concern. Early diagnosis of cirrhosis should alarm physicians to complications such as esophageal varies or hepatic encephalopathy. In spite of this laboratory diagnosis algorithm, the diagnosis of HDV infection in HDi patients remains difficult, firstly the clinical presentations of HDV infection are remarkably variable and nonspecific; there is no specific sign or symptom alerting to a diagnosis of the HDV superimposition on HBV infection., considering that all patients with HDV infection are HBV infected, physicians are not able to differentiate super infection or co-infection of HDV from exacerbation of hepatitis B based on clinical findings and no sign or symptom of hepatitis delta is distinctive to allow an early diagnosis of HDV infection among HBV carriers.

Rationale

Probably at least 5% of the HBV carriers have HDV infection. HBV/HDV co infection may lead to more severe acute disease and higher risks of fulminant hepatitis, cirrhosis and hepatocellular carcinoma than those having HBV infection alone. As we know patients on Hemodialysis are prescreened to very limited viruses includes HBV, HCV and HIV that lead to missing many other clinically impotent agent such as HDV, which may lead to progressive transmission of HDV among HBV on Hemodialysis receiving patients due to the same clinical presentation of both infection. In Sudan there is no a well-recognized data concerning these dangers situation. This study will aim to detect the sero prevalence of hepatitis d virus infection among renal failure patients with hepatitis b viruses on hemodialysis in Khartoum state to evaluate the running hemodialysis screening protocol's.

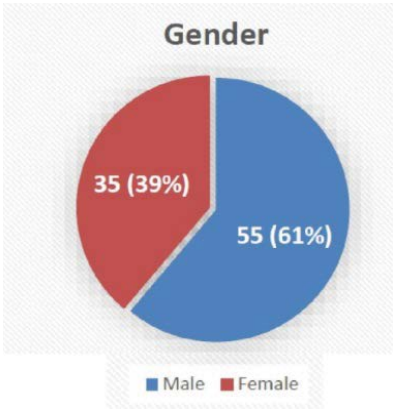
Materials and Methods

This was an active surveillance cross sectional study conducted to detect the prevalence of HDV among HBV on hemodialysis. Ninety (90) HBV on hemodialysis patients were recruited in this study. It conducted at AL-shaheda Salma center for hemodialysis and hemodialysis center of Unmada hospital in Khartoum, Sudan from April to June 2017. This study was approved by ethical committee of the faculty of medical laboratory sciences, Alneelain University, and informed consent was obtained from each participant before sample collection and Ethical conduct was maintained during data collection and throughout the research process.

Results

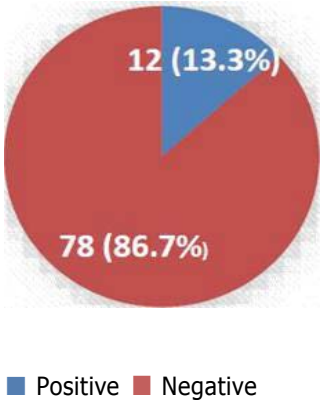
All statistical analyses were performed by SPSS software version (20). Continuous variables were expressed as mean and standard deviation. Comparison between groups was performed with Pearson correlation. P-value<0.05 was considered significant. Present study included 90 HBV participant, more than half 55 (61%) were males, while 35 (39%) were females (Figure 1)

Figure 2 represent the prevalence of HDV among HBV, 12 (13.3%) of participants showed positive HDV, when the majority 78 (86.7%) were negative HDV. Table 1 illustrate the mean of participants age which revealed that; mean age of participants was 44.86 ± 8.5, there was median positive correlation when *R*=(0.249) and *P*=(0.018). Table 2 shows the distribution of HDV according to gender and their relationship; 6 positive HDV was males similarly to 6 females showed



	Frequency	Percent
Male	55	61%
Female	35	39%

Figure 1: Prevalence of gender.



HDV	Frequency	Percent
Positive	12	13.3%
Negative	78	86.7%

Figure 2: Prevalence of HDV.

positive HDV, on the other hand, 49 negative HDV were males, while, 29 negative HDV were females. There was no significant correlation revealed with gender when *R*=(-0.089) and *P*=(0.402).

Discussion

Previous epidemiological studies had shown that the prevalence of HDV infection among hepatitis B surface antigen (HBsAg) carriers was approximately 5% all over the world. In addition, as we know patients on Hemodialysis are prescreened to very limited viruses includes HBV, HCV and HIV that lead to missing many other clinically impotent agent such as HDV, which may lead to progressive transmission of HDV among HBV on Hemodialysis receiving patients due to the same clinical presentation of both infection, From this, The risk of HBV/HDV transmission is a major problem in Hemodialysis (HDi) patients, different rates of HDV transmission in HDi patients were reported in previous studies, but that studies were too limited to provide a paradigm of the importance of HDV in HDi patients. In this study which included 90 HBV patients on hemodialysis, 55% of them were males with mean age (44.86 ± 8.5). According to our findings, 13.3% of HBV on hemodialysis were having HDV. In addition, there was a significant positive correlation between HDV and age when (*R*=0.249, *P*=0.018).This findings were in consist with a study conducted in Saudi Arabia in 1992 which revealed that 12.5% of patients on hemodialysis revealed HDV infection, similarly with study done in Turkey in 1993 which reported that the frequency rate of HDV in HDi patients was higher than 8%, research done in Oman in 1994 demonstrated that 7.7% of HDi patients were HDV positive. On the opposite, European reports had suggested rare or absent HDV infection among HDi patients. Increase frequency of HDV among hemodialysis patients especially in developing countries may be because the prescreening on Hemodialysis is only limited to HBV, HCV and HIV without HDV prescreening, this may increase the possibility to occurrence of acute HDV infection either by Co-infection (simultaneous acquisition of HBV and HDV infection) or super-infection (acute HDV infection in a chronic HBsAg carrier). From this, we ring the alarm on the probability of transmission prevalence of HDV during hemodialysis and we recommend periodic testing for HDV infection by anti-HDV antibody in HBsAg positive carriers on chronic hemodialysis treatment.

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