International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Frequency and Risk Factors of Hepatitis B and C in Hemodialysis Patients in Khartoum

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Abstract: ***Background**: Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections are considered to be a global health concern. Patients on maintenance hemodialysis (HD) are at increased risk of acquiring such infections. The aim of this study is to investigate the frequency of HBV and HCV seropositivity in HD patients, rate of conversion of patients and risk factors for acquiring these infections. **Methodology**: It is across sectional study conducted among 446 patients from 6 HD: (Bashair Hospital, Bahri Alsafia, Alnaw Hospital, Jabal awliya Hospital, Hospital of dermatology and Sexually transmitted diseases "STI"and Ali bin Jabr HD centers) in Khartoum, Sudan. Interviewer administered questionnaire was used to collect data about current HBV and HCV serology status and at initiation of HD, history of blood transfusion, HBV vaccination status, history of dialysis in multiple centers and history of renal transplantation. **Results**: A) for HBV, a total of 356 patients from 4 centers dialyzing HBV (Bashair hospital, Bahri alsafia, Alnaw, Hospital of dermatology & STI HD centers) were included. Frequency of HBV seropositivity among patients was 10.4 % (37 patients). Of those, 13 converted after initiation of HD. Six out of the 13 patients who converted to be HBV positive did that in the first year giving a rate of 1.8% per year. Analysis of possible risk factors showed that number of centers in which patient received HD and HBV vaccination were significantly associated with HBV new infections. (B) For HCV, a total of 372 patients from 5 centers (Bahri alsafia, Alnaw, Hospital of dermatology and Sexually transmitted diseases, Ali bin Jabr, Jabal Awliya HD centers) dialyzing seronegative patients and HCV positive patients were included. Frequency of HCV seropositivity was 5.9 % (22 patients). Twenty out of the 22 seropositive patients converted after initiation of HD. Rate of conversion during the first year of HD was found to be between 0.54% to 0.81% per year. Analysis of possible risk factors revealed that number of centers in which patient received HD, number of blood transfusions and duration of dialysis were significantly associated with HCV new infections. **Conclusion**: patients on HD in Khartoum have high frequency of HBV and HCV seropositivity. The incidence of new positive cases of HBV during the first year of HD is about 1.8 case per year and for HCV is 0.54 to 0.81. Number of centers in which patient received HD and HBV vaccination status were found to have significant statistical relation to new positive cases of HBV while number of centers in which patient received HD, number of blood transfusions and duration of HD were shown to be significantly related to new cases of HCV.*

Keywords: Hepatitis B virus (HBV); Hepatitis C virus (HCV); hemodialysis patients; risk factors; Khartoum; Sudan

1. Introduction

Viral hepatitis has been a global health concern and economic burden for over the past century. Hepatitis B virus (**HBV)** and hepatitis C virus (**HCV)** are the most common causes of chronic viral hepatitis worldwide [1].

The overall prevalence of HBV is reported to be 3.6 percent and for HCV is 1 percent with great variations depending upon the geographic area [2, 3].

Patients receiving maintenance haemodialysis (**HD)** therapy are at increased risk for acquiring these infections and have a higher prevalence of HBV and HCV than the general population [4].

Hepatitis B virus, is a hepadnavirus that can cause both acute and chronic hepatitis. Identified methods of transmission of Hepatitis B include:

1) Contaminated needles (e. g. sharing needles or syringes for injecting drugs, tattooing, acupuncture, or body piercing if these procedures are done with contaminated instruments), 2 - Sexual contact with someone who is infected,
2) passage from mother to infant during or shortly after delivery and
3) Blood transfusion and organ transplantation (although Nowadays, it is rare due to Blood and organ donors screening for markers of hepatitis infection.)

After initial infection with hepatitis B, patients develop acute hepatitis. Most people with acute hepatitis B recover uneventfully. However, in about 5 percent of adults the virus settles in the body for many years and continue multiplication. If liver damage develops because of longstanding infection, the patient is said to have chronic hepatitis. There are a number of tests that can be used to diagnose and monitor hepatitis B infection. Most of them are blood tests and include Hepatitis B surface antigen (**HBsAg**), Hepatitis B surface antibody (**anti - HBs**), Hepatitis B core antibody (**anti - HBc**), Hepatitis B e antigen (**HBeAg**), Hepatitis B e antibody (**anti - HBe**) and Hepatitis B DNA (**HBV DNA**)

Specific treatment for acute hepatitis B is usually not needed. In people who develop chronic hepatitis, an antiviral medication might be recommended to reduce or reverse liver damage and to prevent long - term complications. there are two types of antiviral medications that can be used, nucleos (t) ide analogues (e. g. Entecavir and tenofovir are the most commonly used) and interferon (an injectable medication). [5]

Hepatitis C is caused by hepatitis C virus, an RNA virus of the family Flaviviridae. HCV can be transmitted through 1 - Sharing needles, syringes, or other methods used for injection drug use, 2 - Receiving a blood transfusion

specially when blood was not routinely tested for hepatitis C and through 3 - sexual intercourse with an infected person.

Hepatitis C usually leads to chronic hepatitis, culminating in cirrhosis in some people. It usually remains asymptomatic for decades.

Checking the blood for hepatitis antibodies or the viral RNA are the main methods for diagnosing hepatitis C infection. HCV viral levels can be reduced to undetectable levels by a combination of antiviral medications. In general, treatment is safe and effective, and anyone with hepatitis C should be considered for starting antiviral treatment. Antiviral regimen selection varies by genotype and other patient factors [6].

2. Materials and Methods

A cross - sectional study was conducted among 446 Sudanese patients on maintenance HD (n=446) from six HD centers in Khartoum (namely: Bashair Hospital HD center, Bahri Alsafia HD center, Alnaw Hospital HD center, Jabal awliya Hospital HD center, Hospital of dermatology and Sexually transmitted diseases **''STI''** HD center and Ali bin Jabr HD center), from July 2019 to April 2020.

All patients on regular HD who fulfilled the inclusion criteria of the study as being Sudanese patients, from one of the above mentioned HD centers in Khartoum during study period from July 2019 to April 2020 and accepted to participate in the study, were included.

Interviewer - administered structured questionnaire about HBV and HCV status (currently and at initiation of HD) and risk factors of contracting these infections were used to collect the information from patients and their records. Informed consent was obtained from all participants.

3. Results

A total of 446 patients on regular HD from the above mentioned HD centers in Khartoum were included in the analysis. All the 6 HD centers were dialyzing seronegative patients. In addition, 3 centers (Bahri alsafia, Alnaw, hospital of dermatology and STI "Aljildia") were dialyzing both HBV and HCV seropositive patients, 2 centers (Ali bin jabr and Jabal awliya) were dialyzing HCV seropositive patients and 1 center - which is Bashaier HD center - was dialyzing HBV seropositive patients.

HBV frequency in HD

For calculating HBV frequency, a total of 356 patients from the 4 centers dialyzing HBV seropositive patients (Bashair hospital, Bahri alsafia, Alnaw hospital, Hospital of dermatology and STI"Aljildia" HD centers) were included. Two hundred and twelve patients (59.6%) were males and 114 were females (40.4%)

Most of the patients (41%) were over 50 years of age, while 28% were in between 31 to 50 years, 26% were between 16 to 30 years and only 4.2% patients were under 16. Age distribution of patients is shown in figure 1.

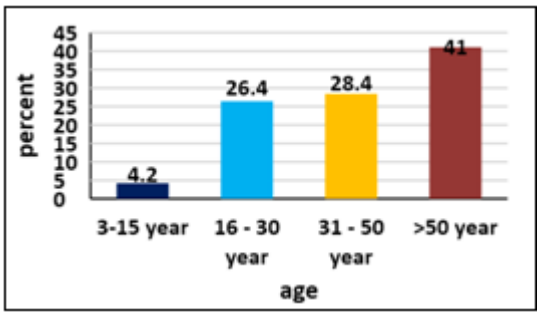

Figure 1: Distribution of patients according to age. (centres dialyzing HBV seropositive patients)

Regarding time since the initiation of HD, most patients (29.8%) were in between 1 to 3 years since initiation of HD, 23% of patients were > 3 years to less than 6 years and 21.3% were receiving HD for more than 6 years.

Only 9% of patients were found to be on regular HD for 6 month or less and 14% were > 6 month to 1 year.

2.8% were not sure about the exact time of initiation of HD as displayed in figure 2.

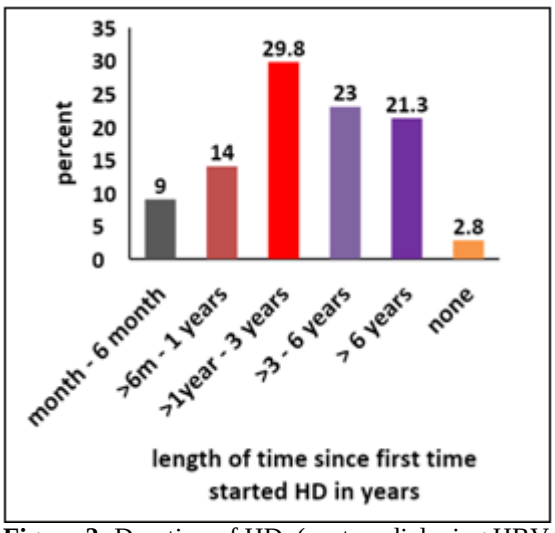

Figure 2: Duration of HD. (centres dialyzing HBV seropositive patients)

Concerning HBV serology status of patients, 37 patients (10.4 %) were found to be positive for HBV (frequency of 10.4%). Of those 24 patients were positive before initiation of HD and 13 patients converted after initiation of HD.

Six out of the 13 patients who seroconverted did that in the first year of HD while another 5 patients turned to be HBV positive in between 1 - 4 years of HD and only 2 patients converted positive after 4 years of HD.

Analysis of possible risk factors for new HBV infections using Chi - Square test of independence we found that there is significant difference in number of centers in which patient received HD (**P value = 0.000**) and HBV vaccination status (**P value = 0.033**) between those who seroconverted and those who remained seronegative . With no significant difference found in other factors (duration of HD, history of previous blood transfusion, previous renal transplant and history of dialysis in multiple centers) between the two

groups.

Regarding vaccination history 185 patients (51.7 %) were not vaccinated against HBV while 170 patients (47.8%) gave a history of vaccination.2 patients (0.6%) were not aware of their vaccination status.

HCV frequency in HD

For calculating frequency of HCV a total of 372 patients from 5 centers (Bahri alsafia, Alnaw hospital, Hospital of dermatology and Sexually transmitted diseases, Ali bin Jabr HD center, Jabal Awliya HD center) dialyzing seronegative patients and HCV positive patients were included.227 (61.0%) of patients were males and 145 (39.0%) were females.

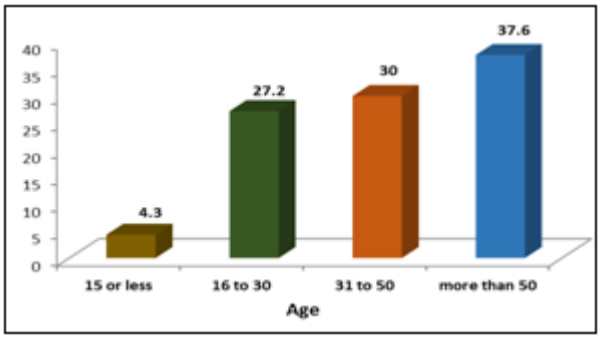

Figure 3: Distribution of patients according to age. (centers dialyzing HCV seropositive patients)

The length of time since start of HD is shown in table (3) with most of patients falling in the range of 1 to 3 years.

Table 3: Duration of dialysis (centres dialyzing HCV seropositive patients)

	Frequency	Percent
month - 6 month	34	9.1
>6m - 1 years	53	14.2
>1year - 3 years	107	28.8
3 - 6 years	96	25.8
> 6 years	80	21.5
Not sure	2	0.5
Total	372	100

Our result showed that 22 patients were found to be positive for HCV representing a frequency of (5.9 %). Two out of them were known to be infected before the initiation of HD, while 20 patients became positive after that.

Most of the patient (9 patients) converted positive within 1 to 4 years of HD, 8 patients converted after 4 years and only 2 patients converted during the first year of HD. Duration of HD before seroconversion is undetermined for 1 patient.

Analysis of possible risk factors for new HCV infections showed that there is significant difference in duration of dialysis (table4), number of blood transfusions (table5) and number of dialysis centers in which patient received HD (table6) between those who seroconverted and those who remained seronegative. With no significant difference found in other factors (history of previous blood transfusion, previous renal transplant and history of dialysis in multiple centers) between the two group.

Table 4: Correlation between duration of HD and HCV status

HD starting time	HCV status		Total
	Sero converted	Remained seronegative	
1 - 6m.	0	34	34
6m - 1yr	1	52	53
1 - 3 yr	2	105	107
3 - 6 yr	2	93	95
> 6 yr	15	64	79
None	0	2	2
Total	20	350	370

P value = 0.000

Table 5: Correlation between No. of blood transfusions and HCV status

No. blood transfusion	HCV status		Total
	+v e	- ve	
1 - 3	9	148	157
>3 – 5	0	42	42
>5 – 10	5	53	58
>10	2	9	11
None	3	95	98
Unknown	1	3	4
Total	20	350	370

P value = 0.048

Table 6: Correlation between Number of centers and HCV status

Number of centres	HCV status		Total
	Positive	Negative	
1 – 3	12	220	232
>3 – 5	7	43	50
>5 – 7	0	3	3
>7	0	4	4
None	1	80	81
Total	20	350	370

P value = 0.034

4. Discussion

This study was conducted to determine the degree of spread of HBV and HCV in patients on regular HD in Khartoum by measuring the proportion of patients who are currently positive for HBV or HCV and also by estimating the rate of new positive cases. Furthermore, the study investigated the relationship between some proposed risk factors and the occurrence of new positive cases.

Our results revealed that the frequency of HBV seropositivity among HD patients is 10.4 % which is higher than the overall global prevalence of HBV among general population (3.6%) but is slightly lower than a pooled prevalence of general population in sudan which is 12.07% [2, 7]. Also the frequency is higher than that found by Gasim et al.2011, cross sectional study conducted at Ahmed Gasim HD unit, Khartoum - Sudan which found that the prevalence of HBsAg was 4.5% among HD patients. [8].

This relatively high prevalence rate is consistent with the high prevalence of HBV in the general population in Sudan and the increased susceptibility of patients on HD to viral infections.

Similar to HBV seropositivity in HD patients, the study showed a high prevalence of HCV seropositivity at 5.9% when compared to prevalence of 1% of the global general population estimated by the WHO and to a prevalence of 2.74 % found by systematic review and meta - analysis of HCV infection prevalence in Sudan conducted in 2017 [3, 7].

Although this result is consistent with a prevalence of 8.5% of HCV among HD patients in Khartoum demonstrated by Gasim et al.2011 cross sectional study, it is remarkably lower than that shown by another cross sectional study which showed a prevalence of 34% among HD patients in Khartoum, Sudan 2005 [8, 9].

Retrospective follow up of patients revealed that 13 patients out of 332 seronegative patients - when started HD - had converted to be HBV positive.6 of them converted during the first year giving an incidence of 1.8% per year. However, the incidence of new cases decreased remarkably during the next years where a total of 5 patients has converted during the next 3 years giving a conversion rate of approximately 0.5 % per year, and the incidence decreased further to only 2 new cases after 4 years on HD. This reduction in new cases over years may be explained by the fact that many patients face problems during initiation of HD due to the limited resources and the delay in distribution of new patients to HD centers. In turn, several patients might receive HD in several centers before distribution to specific center. In addition, many patients do not receive HBV until after the initiation of HD and both factors, number of centers in which patient received HD and vaccination status were found to be significantly related to HBV infection.

Conversely, HCV seroconversion rate seems to follow a relatively more static rate during successive years of HD where only 2 out of 370 patients converted during the first year of HD (rate of 0.54% to 0.81% per year) and 9 patients during the next 3 years (rate of 0.81 % to1.08 % per year).

Concerning possible risk factors, the study revealed that number of centers in which patient received HD is strongly associated with both HBV and HCV new infections while HBV vaccination status was found to be strongly associated with new HBV infection. On the other hand, HCV new infection was found to be strongly associated with duration of HD and number of blood transfusions. The latter two associations with new HCV infection might explain the relatively static rate of seroconversion - with very slight increase - of HCV over years of HD.

This study, however, is subject to some limitations. First, much Information like duration of dialysis, vaccination status and` number of previous HD centers was frequently obtained from the patients or their caregivers because of incomplete medical records of patient. Second point, is the fact that only the current HBV and HCV serology status and at the time of initiation of HD were taken into account. Although, majority of patients once tested positive will remain positive for a long period but there are some patients who managed to clear the infection either spontaneously or after treatment and those patients positivity status were not included in the analysis of results.

5. Conclusion

In conclusion, patients on maintenance HD in Khartoum have high frequency of HBV and HCV seropositivity measured at 10.4% and 5.9% respectively. The incidence of new positive cases of HBV during the first year of HD is about 1.8 case per year and for HCV is 0.54 to 0.81 case per year. Incidence of new HBV is at maximum during the first year of dialysis and decreases afterwards. However, HCV new cases seem to increase slightly after the first year of HD. Number of dialysis centers and HBV vaccination status were found to have significant statistical relation to new positive cases of HBV while number of centers in which patient received HD, number of blood transfusions and duration of HD were shown to be significantly related to new cases of HCV.

6. Recommendations

Based on these conclusions, health authorities should consider improving delivery of HD service by developing early detection and referral system for the patients who meet the criteria for renal replacement therapy. As a result, early preparation of patients through vaccination, counseling and avoidance of the unnecessary exposure to multiple HD centers will be possible.

Further research is needed to study the relation between these high prevalence rates of viral hepatitis in HD patients and other important risk factors specially those associated with infection control (e. g. isolation of positive patients, hygiene. . etc)

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