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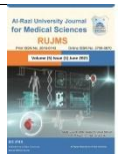

Epidemiology of Hepatitis B & C virus infections among hemodialysis patients: A cross-sectional survey in five hemodialysis centers in Yemen

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Abstract:

Background: *Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections represent significant public health issues globally. They are important causes of morbidity and mortality in hemodialysis patients. Patients with HBV/HCV co-infection have a higher risk of progression to cirrhosis and decompensated liver disease and have an increased risk of hepatocellular cancer (HCC).* ***Aim:*** to assess epidemiology of hepatitis B and C virus infections in patients undergoing hemodialysis in five hemodialysis centers in Yemen. **Methods**: A cross-sectional survey was applied*; a five hemodialysis centers study was carried out in Yemen. All the patients who underwent hemodialysis from January 2019 to December 2019 were included in the study. Patients of all age groups were tested for anti-HCV antibodies by* a third generation enzyme linked immunoassay (ELISA). ELISA tests were performed in local laboratories. These tests obtained annually or every six months, different from center to other and between the patients. **Results:** *Of the total 521 patients on hemodialysis, 34 (6.53%) were found to be having HBsAg infection, 54 (10.36%) were found to be positive for HCV. Co-infection with HBV/HCV was observed in 3 (0.58%) patients, 351 (67.4%) were males and 170 (33%) were females. The majority of the patients were found to be of 41-65 years of age (46.0%), followed by 18-40 years (32.0%) and thereafter in ≥ 65 years (22.0%) and lowest prevalence was observed in the age group of <18 years (1.34%). Percentage of hepatitis in various hemodialysis center was higher in males compared to females and was statistically significant (P = 0.028). Duration since initiation of dialysis was associated with hepatitis in various hemodialysis center (P = 0.0006).* **Conclusion:** Patients on maintenance hemodialysis in five centers, included in our study, have a high prevalence of HCV infection more than rates of HBV infection. The factors associated with HBV and HCV infection are highly suggestive of nosocomial transmission within HD units. Urgent action is required to improve infection control measures in hemodialysis centers and to reduce dependence on blood transfusions for the treatment of anemia associated with End-Stage Renal Disease (ESRD). We need to increase the capacity of each center and isolate HBV & HCV seropositive patients.

Keywords: Hemodialysis; Hepatitis C; Hepatitis B; Prevalence; Yemen

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Introduction

Hepatitis is an inflammation of the liver that is caused by a variety of infectious viruses and noninfectious agents leading to a range of health problems, some of which can be fatal.

World health organization estimated that 354 million people globally live with a hepatitis B or C infection and almost 3000 people die from hepatitis B and C every day [1]. As of 2019, an estimated 116 million people in the Western Pacific are living with hepatitis B and 10 million with hepatitis C [2].

HBV and HCV are highly infectious and transmitted from person to person by blood transfusions, sexual, and vertical routes. Recently, these types of viruses are common nosocomial problems and the cause of morbidity and mortality among hemodialysis (HD) patients because of the complications in the management of patients in the dialysis units [4 ،3] .

The prevalence and incidence of hepatitis C infection in dialysis patients varies from country to country and ranges from 1 to 84.6%3. Due to the common transmission methods, infection with HBV/HCV is not common in severely infested areas and among people at high risk of parenteral transmission. Patients with dual HBV/HCV infection have a higher risk of progressing to cirrhosis [5], as well as an increased risk of hepatocellular carcinoma (HCC) [6].

Long-term exposure to blood vessels and multiple blood transfusions increase the risk of these blood-borne diseases in dialysis patients. Contaminated devices, equipment and supplies, environmental surfaces and staff involved may play an important role in the transmission of this infection.[7]. Infections of hepatitis viruses in dialysis patients are enhanced by a significant dysfunction of the immune state that develops due to irreversible renal settlement [8].

HBV infection is less prevalent than HCV in dialysis units due to the introduction of HBV vaccine, isolation of HBV-positive patients, use of dedicated dialysis machines and regular monitoring of HBV infection have significantly reduced HBV prevalence in this situation [9].

Yemen has been under war and siege for eight years since 2015, which has destroyed the country's infrastructure, resulting in disasters such as the modern HD crisis. But the damage to Yemen's healthcare sector is so great that individuals with chronic illnesses do not have access to life-saving treatment. Of the 32 dialysis centers in Yemen before the war, four were closed. The others are struggling to provide services, with broken machines, lack of basic supplies and unpaid staff [10]. Patients usually need three sessions of four hours per week. In Yemen, the fragile situation has forced patients to reduce two cycles. The United Nations considers the situation in Yemen to be the worst humanitarian crisis in the world.

Aim of the study

To assess epidemiology of hepatitis B and C virus infections in patients undergoing hemodialysis in five hemodialysis centers in Yemen. .

Material and Methods

A cross-sectional survey was applied. Data extracted and collected from the medical reports of 521 patients of Ministry of public health and population of Yemen presented to Zabid, Al Qanawes, Al Mahweet, 22 May Sana'a governorate and Amran governorate hemodialysis centers (**Figure** 1). in the period from 1 January 2019 to 31 September 2019.

Clinical, demographic and geographical data of the renal disease patients admitted to five hemodialysis centers were collected for a period of 1 years (January 2020-December 2020).

Patient records were used to obtain patients' age, gender, time on HD, number of blood transfusion, period of hemodialysis and sero-positivity to HBV and HCV. Sero-positivity to HBV was defined by detection of hepatitis B surface antigen (HBsAg) and sero-positivity to HCV by detection of anti-HCV antibodies by a third generation enzyme linked immunoassay (ELISA). ELISA tests were performed in local laboratories. These tests obtained annually or every six months, different from center to other and between the patients. Reprocessing of the dialyzers of the HBV/HCV positive patients are done in a separate room, away from the rest of the patients. Dedicated nursing staff looks after each patient during the dialysis session.

All respondents presented to one of 5 HD centers collected, samples taken from patient's records. As 223 from Zabid HD center, 74 from 22nd of May HD center, 96 from Al Mahweet HD center, 67 from Amran HD center, 61 from Al Qanawes HD center.

Data was entered in excel sheet initial and described by using SPSS Software (SPSS Inc. Chicago. II.USA, version 25.0) prior to beginning of the analysis. The data was started computed to state descriptive statistics (frequency, percentage, mean, SD).

The Independence Chi-square test was used to see the association between localization of hemodialysis center and independent variables. Percentages and frequency were used. The result at p-value ≤ 0.05 was considered as statistically significant.

The study was approved by the Ethics committee of the Faculty of Medicine and Health Sciences, Al-Razi University, Yemen.

Results

Profile of the study

The sample in our study obtained retrospectively, containing 521 patients presented regularly for hemodialysis in the period between the 1 January 2019 and the 31 December 2019, in five dialysis centers

including (Zabid, 22nd of May-Hamdan, Amran, Al Mahweet, Al Qanawes).
Table 1 shows the prevalence of different types of viral infections hepatitis among HD patients one year after dialysis. The prevalence rate of single hepatitis B virus was 6.53%, the rate of single hepatitis C virus infection was 10.36%, and 0.58% of HD patients found to have CoHBV/HCV infection.

Table 1: The prevalence rate of different types of Hepatitis viral Infections among HD patients after 1 year of dialysis.

Types of Hepatitis viral Infections	Number	Percentage
HBV-single infection	34	6.53%
HCV-single infection	54	10.36%
Both HBV and HCV-infection	3	0.58%
Total infection	**91**	**17.5%**

In the present study, out of the total 521 patients, 351 (67.4%) were males and 170 (33.0%) were females.

Table 2: Distribution of respondents according to place of residence sorted by gender

Dialysis Centers	Male n (%)	Female n (%)	Total n (%)
Zabid dialysis center	159 (71.30)	64 (28.70)	223 (42.8)
22nd of May dialysis center	42 (56.75)	32 (43.25)	74 (14.2)
Aljumhori/Almahweet dialysis center	63 (65.62)	33 (34.37)	96 (18.4)
Amran dialysis center	47 (70.14)	20 (29.86)	67 (12.9)
Al-Qanawes dialysis center	40 (65.57)	21 (34.43)	61 (11.7)
Total	**351 (67.4)**	**170 (33.0)**	**521 (100.0)**

Most of the patients were in the 41-60 years of age group (46.0%) followed by 18-40 years (32.0%), thereafter in 41-65 years (22.0%) and lowest prevalence was observed in the age group of <18 years (1.34%) **(Figure 2)**.

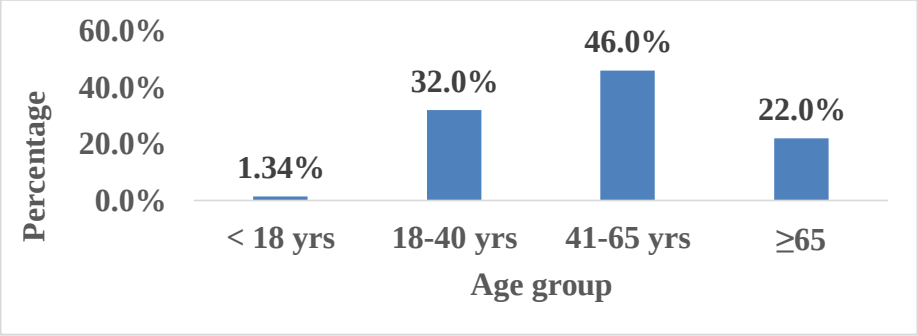

Figure 2: Distribution of hemodialysis patients according to age group

Figure 3 presents that among the dialysis Centers, the highest frequency distribution of positivity was found in Zabid (30.8%) followed by Al Qanawes (27.5%), thereafter Amran (18.7%) and lowest was observed in 22 may dialysis Centers (8.8%).

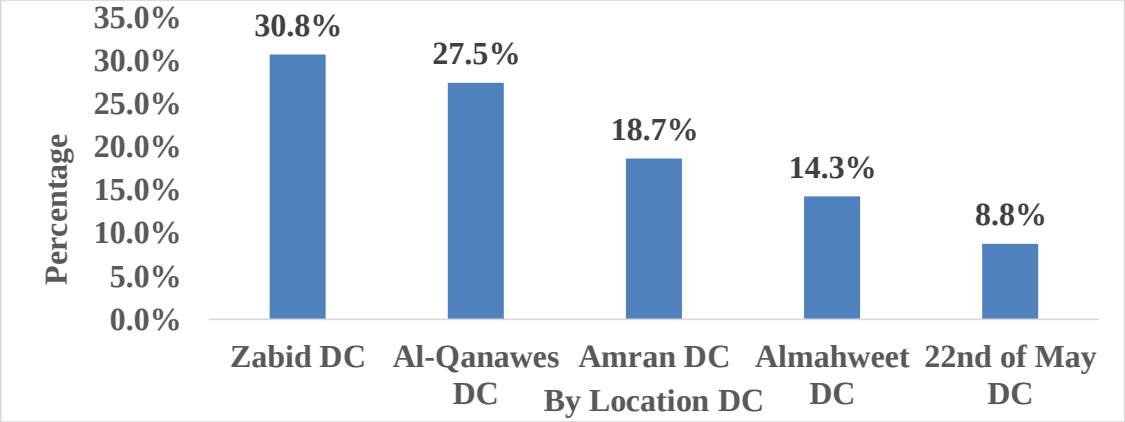

Figure 3: distribution of positive hemodialysis patients according to location of hemodialysis center

Table 3 shows that duration of hemodialysis varying from 4 months to 11 years (mean= 47 months, SD = 39 months). Patients presented for less than 1 year were 146/521 (28.02%), ranging from 20.17% to 40.54% for each center (mean=31.37, SD=7.6). One to 5 years' dialysis duration group patients were 269/521 (51.63%) (mean=48.51, SD=8.53. More than 5 years' dialysis duration patients were 106/521 (20.34%) (mean= 20.11, SD=9.20).

Table 3: Distribution of respondents according to duration of hemodialysis

Dialysis Centers	Duration of hemodialysis			Total n (%)
	<1 year n (%)	1-5 years n (%)	>5 years n (%)	
Zabid dialysis center	45(20.17)	133(59.64)	45(20.18)	223 (42.8)
22nd of May dialysis center	30(40.54)	33(44.59)	11(14.86)	74 (14.2)
Al Mahweet dialysis center	28(29.17)	42(43.75)	26(27.08)	96 (18.4)
Amran dialysis center	24(35.82)	37(55.22)	6(8.95)	67 (12.9)
Al-Qanawes dialysis center	19(31.14)	24(39.34)	18(29.51)	61 (11.7)
Total	**146(28.02)**	**269(51.63)**	**106(20.34)**	**521 (100.0)**

Among seropositive viral hepatitis (either B or C or B&C), 58/91 (63.74%) were diagnosed prior to the onset of the dialysis sets. While 33/91 (36.26%) were diagnosed in post dialysis routine viral hepatitis serology tests annually in some centers or every six months in others **(Table 4).**

Table 4: Distribution of respondents according to Diagnosis of HBV & HCV related to dialysis

Dialysis Centers	Diagnosis of HBV & HCV related to dialysis	
	Before n (%)	**After n (%)**
Zabid dialysis center	20 (34.5)	8 (24.2)
22nd of May dialysis center	5 (8.6)	3 (9.1)
Al Mahweet dialysis center	9 (15.5)	4 (12.1)
Amran dialysis center	10 (17.2)	7 (21.2)
Al Qanawes dialysis center	14 (24.1)	11 (33.3)
Total	**58 (63.74)**	**33 (36.26)**

Association between characteristics of participants and location of Hemodialysis center

A Chi-square test of independence was performed to examine the relation between gender and the admitted to hemodialysis center. The relation between these variables was significant, $X^2 = 10.9$, $p = 0.029$. Male were more likely than female to be admitted to the hemodialysis center

The percentage of participants that were age groups did not differ number participants who admitted to the hemodialysis center, $X^2 = 9.02$, $p > .05$.

As can be seen by the frequencies cross tabulated in Table 5, there is a significant relationship between duration of hemodialysis and location of hemodialysis center, $X^2 = 27.36$, $p < 0.0006$. Finally, the units' blood transmission was a significant associated with location of hemodialysis center, $X^2 = 31,53$, $p < 0.0001$.

Table 5: Association between characteristics of participants and location of Hemodialysis center

Dialysis Centers	Zabid dialysis center n (%)	22nd of May dialysis center n (%)	Al Mahweet dialysis center n (%)	Amran dialysis center n (%)	Al Qanawes dialysis center n (%)	**Total n (%)**	**X^2**	**P - Value**
Gender							10.9	**0.028**
Male	159 (71.3)	42 (56.8)	63 (65.6)	47 (70.1)	40 (65.6)	351 (67.4)		
Female	64 (28.7)	32 (43.3)	33 (34.4)	20 (29.9)	21 (34.4)	170 (32.6)		
Total	**223 (42.8)**	**74 (14.2)**	**96 (18.4)**	**67 (12.9)**	**61 (11.7)**	**521 (100.0)**		
Age group							9.023	**0.34**
< 18	81 (36.3)	23 (31.1)	37 (38.5)	16 (23.9)	25 (40.1)	165 (31.7)		
18-40	103 (46.2)	31 (41.9)	44 (45.8)	33 (49.3)	26 (42.6)	237 (45.5)		
>40	49 (22.0)	20 (27.0)	15 (15.7)	18 (26.9)	10 (16.4)	112 (21.5)		

Total	**223 (42.8)**	**74 (14.2)**	**96 (18.4)**	**67 (12.9)**	**61 (11.7).**	521 (100.0)		
Duration of hemodialysis							27.36	**0.0006**
<1 year	45(20.2)	30(40.5)	28(29.2)	24(35.8)	19(31.1)	146(28.0)		
1-5 years	133(59.6)	33(44.6)	42(43.8)	37(55.2)	24(39.3)	269(51.6)		
>5 years	45(20.2)	11(14.9)	26(27.1)	6 (9.0)	18(29.5)	106(20.3)		
Total	**223 (42.8)**	**74 (14.2)**	**96 (18.4)**	**67 (12.9)**	**61 (11.7).**	521 (100.0)		
Blood Transfusion							31.53	**0.0001**
1-5units	72 (54.1)	10 (32.3)	16 (25.8)	8 (20.0))	13 (32.5)	119 (37.7)		
5-10units	25 (18.8)	14 (45.2)	22 (35.5)	19 (47.5)	11 (27.5)	94 (29.8)		
>10units	36 (27.1)	7 (22.6)	24 (38.7)	13 (32.5)	16 (40.0)	103 (32.6)		
Total	**133 (42.1)**	**31 (9.8)**	**62 (19.6)**	**40 (12.7)**	**40 (12.7)**	**316 (100.0)**		

X^2 - Chi-Square53, P – Value : P <0.05, statistically significant

Discussion

Since dialysis requires access to the circulatory system, patients undergoing dialysis may expose the microbial circulatory system, which may lead to bacteremia, or viral infections as HBV, HCV, and HIV.

The results of the current study showed that the prevalence of HBV and HCV infection in HD patients is 6.53% and 10.36%, respectively, with the combined infection rate of HBV-HCV equal to 0.58% and the overall infection rate was 17.5%. These findings were remarkably high and is approximately 5 to 10 times higher than in the general population [11]

The findings from Omar Ayedh Abdullah Amran's 2018 study, which indicated a prevalence of 9.9% in a sample of 202 HD responders in the Dhamar HD center, are fairly close to this one [12]. However, it is also lower than the 21% prevalence noted in Ibb City [13]. Actually the prevalence varying from center to other, it is 30.08% in Zabid HD center to 8.8% in 22nd of May center. Globally the prevalence of HCV among patients receiving HD varies from as low as 6.1% in Germany [14], to as high as 76% in Casablanca [15]. In general, North Africa and the Middle East are high prevalence areas both in the general population and in HD patients [16]. Previous studies from the region have reported a prevalence of anti-HCV antibodies in HD patients of 50% in Saudi Arabia [17]. 42% in Tunisia [18], 20.2% in Turkey [19], and 21% in Jordan [20]. In contrast, the prevalence of HBV infection in current study was (6.53%) is close to the study conducted in Aden among general population (5.1%) [21]. Also, It is close to prevalence reported in Omar Ayedh Abdullah Amran 8.9%[12].

Studies from low-developed countries estimated that the proportion of HBsAg carriers in the HD population varies from 2% to 20% [22-24]. According to the study conducted in Saudi Centre for Organ Transplantation (SCOT) reported, HBV sero-positivity was 4.6% in the Saudi HD in the population [25]. while among Jordanian HD patients it was 5.9% [26].

In general, the prevalence and incidence of HBV and HCV infections in HD patients reflects the prevalence of these infections in the general population, the quality of healthcare services in a community and the standards of infection control practices in HD units.

The prevalence of HBV or HCV sero-positivity was significantly related to the length of time on HD. This is consistent with study conducted in Pakistan indicated that duration since initiation of dialysis was associated with hepatitis (p<0.001) as well as. Percentage of hepatitis was higher in males compared to females [27].

This is may be due to a nosocomial transmission related to dialysis since longer duration of dialysis represents a longer period at risk of acquiring an infection. Prevention of nosocomial transmission is of vital importance in Yemen as HCV antiviral treatment is expensive and its availability is limited to only a few centers.

A positive history of blood transfusions as well as the number of blood transfusions was strongly associated with HBV or HCV infection in various hemodialysis center in recent study. Similarly with study conducted in Zabid in 2015 revealed that the history of blood transfusion was found to be a statistically significant [28]. Prior to the introduction of effective screening of blood donors, blood transfusions were recognized as the leading source of HCV infection and some of these

infections may have been acquired before adequate screening was introduced. In addition, it is possible that some blood donors with HCV infection are being missed by current screening procedures and these may need to be reassessed.

Interestingly most of new infections were in more than one-year dialysis (72%) as well as all cases diagnosed with both HBV & HCV infections diagnosed after they started HD. This increases the possibility of transmission from a carrier that was not detected by current screening procedures.

A striking observation from this study is the wide variation in incidence and prevalence of HBV and HCV infections among different HD units. On the other hand, we observed variations in other practices that may be relevant. All the facilities faced a problem of increasing number of patients and most of them responded by adding more HD stations at expense of space and staff. Infection control precautions also varied widely between centers. They were strictly enforced in some places but frequently breached in others. This seemed to depend on staff initiative and the capacity and the utilities rather than national guidelines.

On the other hand, dialyzer reuse was not permitted and all bloodlines as well as other consumables were disposed after a single use. Some brands of HD machines were equipped with a sphygmomanometer. Otherwise, most non- disposable instruments used in HD environment were shared between sero-positive and sero-negative patients. In particular infection control procedures should be investigated in centers with high infection rates and the use of multidose heparin vials must be stopped urgently

Several limitations of this study. First, the medical records were often incomplete and additional clinical information was not included, the variable numbers of patients between selected HD centers. It needed to follow patients prospectively to recording new seroconverted cases and documenting them and there was no visiting to centers by the researchers to get more valuable information about each center instead of making calls with some of stuff. Numbers of HD patients have emerged between cities, i.e. from Zabid to Al Hodaidah, so we missing out the opportunity to include them in our study. Accumulatively, we noticed that serological testing was done in local laboratories and it is likely that there was some variation in the quality of testing. Data regarding hepatitis B core antibodies (HBcAb) or hepatitis B DNA were not available.

Conclusion and Recommendations

in our study, have a high prevalence of HCV infection more than rates of HBV infection, which is still high. The factors associated with HBV and HCV infection are highly suggestive of nosocomial transmission within HD units. Urgent action is required to improve infection control measures in HD centers and to reduce dependence on blood transfusions for the treatment of anemia associated with ESRD. It need to increase the capacity of each center and isolate HBV & HCV seropositive with specific HD units. Training sessions is needed to educate the staff about infection control methods and increases the stuff to maintain different stuff dealing with seropositive and others dealing with seronegative, to avoid mixing these two groups of patients.

This study is recommending to conduct new prospective studies about the incidence of viral hepatitis in HD centers, and studies depending in blood testing.

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وبائيات عدوى فيروس التهاب الكبد B وC بين مرضى الغسيل الكلوي: مسح مقطعي في خمسة مراكز غسيل كلوي في اليمن

الملخص

الخلفية: تمثل عدوى فيروس التهاب الكبد B (HBV) وفيروس التهاب الكبد C (HCV) قضايا صحية عامة هامة على مستوى العالم. تعد هذه العدوى من الأسباب الرئيسية للمراضة والوفيات بين مرضى الغسيل الكلوي. المرضى المصابون بالعدوى المشتركة بـ HBV/HCV لديهم خطر أعلى للتطور إلى تليف الكبد وأمراض الكبد المعاوضة، ولديهم خطر متزايد للإصابة بسرطان الكبد (HCC). **الهدف**: تقييم وبائيات عدوى فيروس التهاب الكبد B وC في المرضى الذين يخضعون لغسيل الكلى في خمسة مراكز غسيل كلوي في اليمن. **الطريقة**: تم تطبيق مسح مقطعي؛ وأجريت الدراسة في خمسة مراكز غسيل كلوي في اليمن. شمل الدراسة جميع المرضى الذين خضعوا لغسيل الكلى من يناير 2019 إلى ديسمبر 2019. تم اختبار المرضى من جميع الفئات العمرية للكشف عن الأجسام المضادة لـ HCV بواسطة اختبار مرتبط بالإنزيم من الجيل الثالث (ELISA). تم إجراء اختبارات ELISA في المختبرات المحلية. تم إجراء هذه الاختبارات سنويًا أو كل ستة أشهر، وتختلف من مركز لآخر وبين المرضى. **النتائج**: من بين إجمالي 521 مريضًا على الغسيل الكلوي، تم العثور على 34 (6.53%) منهم مصابين بعدوى HBsAg، و54 (10.36%) تم العثور عليهم إيجابيين لـ HCV. لوحظت العدوى المشتركة بـ HBV/HCV في 3 (0.58%) من المرضى، وكان 351 (67.4%) من الذكور و170 (33%) من الإناث. تم العثور على أن غالبية المرضى كانوا في الفئة العمرية من 41-65 عامًا (46.0%)، تليها الفئة العمرية من 18-40 عامًا (32.0%)، ومن ثم الفئة العمرية ≤ 65 عامًا (22.0%)، وكانت أقل نسبة انتشار في الفئة العمرية <18 عامًا (1.34%). كانت نسبة الإصابة بالتهاب الكبد في مراكز الغسيل الكلوي المختلفة أعلى بين الذكور مقارنة بالإناث وكانت ذات دلالة إحصائية (P = 0.028). ارتبطت مدة بدء الغسيل الكلوي بالإصابة بالتهاب الكبد في مراكز الغسيل الكلوي المختلفة (P = 0.0006). **الاستنتاج**: المرضى الذين يخضعون لغسيل الكلى في المراكز الخمسة المشمولة في دراستنا لديهم انتشار مرتفع لعدوى HCV أكثر من معدلات عدوى HBV. تشير العوامل المرتبطة بعدوى HBV وHCV بقوة إلى انتقال العدوى داخل وحدات الغسيل الكلوي. هناك حاجة ملحة لاتخاذ إجراءات لتحسين تدابير مكافحة العدوى في مراكز الغسيل الكلوي وتقليل الاعتماد على نقل الدم لعلاج فقر الدم المرتبط بمرض الكلى في المرحلة النهائية (ESRD). نحن بحاجة إلى زيادة قدرة كل مركز وعزل المرضى الإيجابيين لـ HBV وHCV.