Seroprevalence occurrence of viral hepatitis and HIV among hemodialysis patients

Inass Mahmood Kamal¹, Batool Mutar Mahdi²

¹Al-Kindy Teaching Hospital
²Al-Kindy College of Medicine University of Baghdad
E-mail: abas_susan@yahoo.com

ABSTRACT. Background: Patients with chronic renal failure (CRF) were on maintenance invasive haemodialysis (HD) procedure. This procedure by itself affects immunity of the patients and became more susceptible to viral infections.

Aim of the study: to investigate the occurrence of HBV, HCV and HIV infections in patients with hemodialysis.

Patients and methods: A retrospective study of 430 end-stage renal failure patients, referred to hemodialysis department at Al-Kindy Teaching Hospital, Baghdad-Iraq from January-2015 to January-2017. Patients were investigated for HBs-Ag using enzyme-labeled antigen test (Foresight-EIA-USA), HCV- Abs (IgG) specific immunoglobulin using a HCV enzyme-labeled anti- gen test (Foresight-EIA-USA) and anti HIV Abs (IgG) using enzyme-labeled antigen test (Foresight-EIA-USA).

Results: The frequency of HBV infection in the first year was not significant between males (1.11%) and females (0.00%)(P= 0.295). About HCV also there are no significant differences between males (12.63%) and females (9.31%)(P=0.347). After one year of follow up the frequencies of HBV and HCV were not significant between two sexes. Additionally, no any one of the patients had HIV infection.
Conclusions: This study brings a light on that HBV and HCV were having the same frequencies in both genders and lower occurrence with time. Furthermore, HIV was not detected in those patients.

Key words: virus, haemodialysis, infection.

1. Introduction
One of the treatments of chronic renal failure (CRF) is maintenance invasive hemodialysis (HD) procedure. This procedure by itself affects innate immunity like changes in chemotactic factor for leukocytes, phagocytic function of neutrophils and monocytes and natural killer cell (1, 2, and 3). Moreover, adaptive immunity is affected for example defect in proliferation of T lymphocytes and down regulation of phosphorylation pathways of lymphocytes (4, 5 and 6). Therefore, HD patients are more susceptible to blood born viral infection like hepatitis B virus (HBV), hepatitis C virus (HCV) and Human immunodeficiency virus (HIV) due to disturbance in immune system (7).

Infection with these viruses is the main reason of morbidity in HD patients. However, precautions’ must be taken to prevent disseminations of viruses in the unit like available treatments and vaccines (8). In USA, after acquiring viruses like HBV in HD patients, 60% of them become chronic carriers, while in the general population was 5% of them became chronic carrier (9). A study showed that chronic HBV infection had a relation with mortality (10). Additionally, there are 170 million hepatitis C virus carriers worldwide and one of the risk group is HD patients and the risk of death was 1.57 times more than others in association with liver cirrhosis and hepatocellular carcinoma (11,12).

Subsequently infection of liver with viruses was fatal for patients on HD and constitutes 1.9% of all deaths (13). Additional virus that is important in HD patients is HIV. The prognosis of this virus was changed significantly due to administration of Highly Active Anti-Retroviral Therapy (HAART), stage of HIV disease at time of dialysis start and T helper (CD4+) lymphocyte count (14, 15 and 16).

The goal of the present study is to investigate the occurrence of viral infection like HBV, HCV and HIV in patients with the end-stage renal failure on hemodialysis.

2. Patients and methods:
A retrospective study of 430 end-stage renal failure patients, referred to hemodialysis unit of Al-Kindy Teaching Hospital, Baghdad-Iraq from January-2015 to January-2017. All patients were subject to the process of hemodialysis.

Hemodialysis patients’ were a case for the study if their serum tested positive for HBV, HCV and HIV. In contrast, the patients receiving hemodialysis were considered as a “control” if their serum tested negative for those three viruses. For every case, one age- and gender-matched control receiving haemodialysis was selected.

The Broad of Medical Ethics has been approved for these patients and accepted their review of Al-Kindy College of Medicine and Al-Kindy Teaching Hospital. The knowledgeable permission was obtained from patients. Data collected from both groups including demographic information age, sex, marital status, occupation, residential status, onset of renal failure and hemodialysis history.

2.1 Serological testing
A 430 patients were investigated for HBs-Ag using enzyme-labeled antigen test (Foresight-EIA-USA), HCV- Abs (IgG) specific immunoglobulin using a HCV enzyme-labeled antigen test (Foresight-EIA-USA) and anti HIV Abs (IgG) using enzyme-labeled antigen test (Foresight-EIA-USA).
The principle for detection antibodies in the serum are illustrated as follows using leaflet kit:

The micro-wells are coated with Ags then the serum will be added that contains Abs lead to formation a complex. After incubation, washing was done and enzyme conjugated with Abs was added. After incubation and washing were done; substrate A and B were added. The color was formed and the reaction was stopped by sulfuric acid. The results were interpreted after reading with micro plate reader at 450nm within 30 minutes. Samples with optical density below the cutoff were recorded as negative, those with optical densities (< 10% - > 10%) of the cutoff were equivocal, and all others were positive. The sample was retested when the absorbance was within 10% of the cutoff level.

2.2 Statistical analysis:
Data were analyzed statistically using:
- Descriptive statistics: frequencies, mean and standard deviation.
- Inferential statistics: Chi-square tests and fisher exact test.

All of these were done using MiniTab statistical software program 13.20. A P-value ≤ 0.05 was considered to be significant.

3. Results:
A total of 430 patients with chronic kidney disease (renal failure) were on hemodialysis during the study period. The proportion of males 269 (62.55%) was more than that of females 161 (37.44%). Their ages ranged from 16 to 76 years, (median=35), (31.2 ±0.80). The frequency of HBV infection in the first year was not significant between males (1.11%) and females (0.00%)(P= 295) as shown in table - 1- About HCV also there is no a significant difference between males (12.63%) and females (9.31%)(P=0.347). After one year of follow up the frequency of HBV and HCV was also not significant between two sexes as was reported in (table-2). HIV was not affecting any of HD patients. There was a significant reduce in the frequency of infection with HCV while occurrence of HBV was not changed (table-3-).

Table-1- Frequency of viral infection in patients in the first year of hemodialysis.

| Viral markers      | HD Patients positive for the viruses males | HD Patients negative for the viruses Males | HD Patients positive for the viruses females | HD Patients negative for the viruses Females | P -value |
|--------------------|------------------------------------------|------------------------------------------|-------------------------------------------|-------------------------------------------|----------|
| HBs-Ag             | 3 1.11                                   | 266 98.88                                | 0 0                                       | 161 100                                   | 0.295*   |
| Anti HCV Abs       | 34 12.63                                 | 235 87.36                                | 15 9.31                                   | 146 90.68                                 | 0.347*   |
| Anti HIV Abs       | 0 0                                     | 0 0                                      | 0 0                                       | 0 0                                       | --------  |

* Not significant.
Table-2: Frequency of viral infection in patients in the second year of haemodialysis.

| Viral markers | HD Patients positive for the viruses males | HD Patients negative for the viruses Males | HD Patients positive for the viruses females | HD Patients negative for the viruses Females | P -value |
|---------------|------------------------------------------|------------------------------------------|-------------------------------------------|-------------------------------------------|---------|
|               | No. | %  | No. | %  | No. | %  | No. | %  |             |
| HBs-Ag        | 0   | 0  | 269 | 100| 0   | 0  | 161 | 100| 1.00*       |
| Anti HCV Abs  | 15  | 5.57| 254 | 94.42| 9  | 5.59| 152 | 94.4| 1.00*       |
| Anti HIV Abs  | 0   | 0  | 0   | 0  | 0   | 0  | 0   | 0  | -----       |

* Not significant.

Table-3: Comparison of viral infection in hemodialysis patients in two years of follow-up.

| Viral markers | HD Patients positive for the viruses 2015 | HD Patients positive for the viruses 2016 | P -value |
|---------------|------------------------------------------|-------------------------------------------|---------|
|               | No. | %  | No. | %  |             |
| HBs-Ag        | 3   | 0.697| 0   | 0  | 0.248*       |
| Anti HCV Abs  | 49  | 11.39| 24  | 5.58| 0.002        |
| Anti HIV Abs  | 0   | 0  | 0   | 0  | -----        |

* Not significant.

4. Discussion:
Chronic renal failure patients receiving hemodialysis are often acquiring blood-borne viral infection over their long treatment period like HBV, HCV and HIV. In our study, HD patients had HBV and HCV infection and after follow them the percentage of HBV decreased. Additionally, HCV still in the same percentage. There was no significant difference regarding gender in the frequency of these viruses. There was a significant reduce in the frequency of infection with HCV table-3 with time. A study done in Canada demonstrated that two patients (0.8%) were positive for HBs-Ag and 9 (3.8%) had viral HB DNA by PCR(17). This is in agreement with our study (1.1%) in 2015 and then (0.0%) in 2016. Therefore the molecular investigation that detects HBV-DNA using nested PCR is helpful for patients with anti-HB core Ab positive, negative for HBs-Ag and anti-HBs Abs (18). It is recommended to analyze HBV-DNA annually and biopsy from liver (19). Additional study done in Madhav Nagar city reported that the frequency of HBV and HCV infections in HD patients was 1.52% and 1.11%, respectively (20, 21). In India, the occurrences of HBV were 3.4% to 42%, which is higher than found in our study (22, 23). The lower occurrence of HBV in this study may be caused by sample size, method used for detection the virus, less blood transfusion and blood products for the patients and screening of
blood for blood-borne viral infections before transfusion. The availability of erythropoietin leads to lowering blood transfusion times to the patients. The only three patients with HBs-Ag positive were treated and recover from the disease. Consequently, HBV did not detect after one year of follow. Management patients with HBV vaccine, separation of infected patient on separate machine, and habitual surveillance for HBV infected patients in the hospitals leads to lower rates of infection with HBV.

Regarding the frequency of HCV infection was higher than HBV in our study while, other studies reported less prevalence of HCV infection in HD patients like Spain (24) and Brazil (25). This may be due to sample size, method of detection and screening blood for antibodies against HCV with control measures in hospitals. Double infection with two viruses (HBV and HCV) in same patient were not detected in our study while in other studies were 4.4% (26, 27). The lower number of the patients who were positive for anti-HCV after one year of follow-up was due to their deaths.

About HIV infection; there was no cases of this virus in HD patients in our study due to control measures of this disease. The prevalence of this virus varies in different countries depending on district of the countries (28, 29). Within USA about 1% of HD patients had HIV due to HIV associated nephropathy (30). HD patients should be investigated by ELISA, Western blot and serum HIV-RNA for positive cases. The prognosis of HIV infected HD patients has considerably better by using Highly Active Anti-Retroviral Therapy (HAART) (31), stage of HIV disease at initiation of dialysis (32) and Th CD4+ T helper count (33).

Infections with these viruses are important cause of death following cardiovascular diseases in HD patients. Thus, many safety measures must do to limit the dissemination of these viruses (34). There is a need for treatment of HCV end-stage renal disease patients and sustained systematic immunization campaigns for HBV infection (35). Investigating hemodialysis patients for anti-HBc is important to show latent HBV infection (36). Thus, early vaccination and better nutritional conditions, improves anti-HBV response (37).

4. Conclusions:
This study brings a light on that HBV and HCV infections were in the same in both genders, though less common with time. HIV was not detected in HD patients.

References:
[1] Lewis SL, Van Epps DE, Chenoweth DE. Alterations in chemotactic factor-induced responses of neutrophils and monocytes from chronic dialysis patients. Clin Nephrol. 1988; 30: 63-72.
[2] Muniz-Junqueira MI, Braga Lopes C, Magalhaes CA, Schleicher CC, Veiga JP. Acute and chronic influence of hemodialysis according to the membrane used on phagocytic function of neutrophils and monocytes and pro-inflammatory cytokines production in chronic renal failure patients. Life Sci. 2005; 77: 3141-3155.
[3] Eleftheriadis T, Kartsios C, Yiannaki E, Kazila P, Antoniadi G, Liakopoulos V, et al. Chronic inflammation and CD16+ natural killer cell zeta-chain down regulation in hemodialysis patients. Blood Purif. 2008; 26: 317-321.
[4] Eleftheriadis T, Papazisis K, Kortsaris A, Vayonas G, Voyatzis S, Vargemezis V. Impaired T cell proliferation and zeta chain phosphorylation after stimulation with staphylococcal enterotoxin-B in hemodialysis patients. Nephron Clin Pract. 2004; 96: c15-20.
[5] Eleftheriadis T, Antoniadi G, Liakopoulos V, Kartsios C, Stefanidis I. Disturbances of acquired immunity in hemodialysis patients. Semin Dial. 2007; 20: 440-451.
[6] Eleftheriadis T, Kartsios C, Yiannaki E, Kazila P, Antoniadi G, Liakopoulos V, et al. Chronic inflammation and T cell zeta-chain downregulation in hemodialysis patients. Am J Nephrol. 2008;28: 152-157.

[7] Abumwais JQ and Idris OF, “Prevalence of hepatitis C, hepatitis B, and HIV infection among haemodialysis patients in Jenin District (Palestine),” Iranian Journal of Virology.2010; 4: 38–44.

[8] Kausz A, Pahari D. The value of vaccination in chronic kidney disease. Semin Dial. 2004; 17: 9-11.

[9] Szmuness W, Prince AM, Grady GF, Mann MK, Levine RW, Friedman EA, et al. Hepatitis B infection. A point-prevalence study in 15 US hemodialysis centers. JAMA. 1974; 227: 901-906.

[10] Fabrizi F, Martin P, Dixit V, Kanwal F, Dulai G. HBs-Ag seropositive status and survival after renal transplantation: meta-analysis of observational studies. Am J Transplant. 2005; 5: 2913-2921.

[11] Yen T, Keefe EB, Ahmed A. The epidemiology of hepatitis C virus infection. J Clin Gastroenterol. 2003; 36: 47-53.

[12] Fabrizi F, Martin P, Dixit V, Bunnapradist S, Dulai G. Metaanalysis: Effect of hepatitis C virus infection on mortality in dialysis. Aliment Pharmacol Ther. 2004; 20: 1271-1277.

[13] Aghakhani A, Banifazl M, Eslamifar A, Ahmadi F, and Ramezani A, “Viral hepatitis and HIV infection in hemodialysis patients,” Hepatitis Monthly, 2012; 12: 463-464.

[14] Ahuja TS, Borucki M, Grady J. Highly active antiretroviral therapy improves survival of HIV-infected hemodialysis patients. Am J Kidney Dis. 2000; 36: 574-580.

[15] Ortiz C, Meneses R, Jaffe D, Fernandez JA, Perez G, Bourgoignie JJ. Outcome of patients with human immunodeficiency virus on maintenance hemodialysis. Kidney Int. 1988; 34: 248-253.

[16] Perinbasekar S, Brod-Miller C, Pal S, Mattana J. Predictors of survival in HIV-infected patients on hemodialysis. Am J Nephrol.1996; 16: 280-286.

[17] Minuk GY, Sun DF, Greenberg R, Zhang M, Hawkins K, Uhanova J, et al. Occult hepatitis B virus infection in a North American adult hemodialysis patient population. Hepatology. 2004;40: 1072-1077.

[18] Hui CK, Sun J, Au WY, Lie AK, Yueng YH, Zhang HY, et al. Occult hepatitis B virus infection in hematopoietic stem cell donors in a hepatitis B virus endemic area. J Hepatol. 2005; 42:813-819.

[19] Ozdogan M, Ozgur O, Gur G, Boyacioglu S, Ozderin Y, Demirhan B, et al. Histopathological impacts of hepatitis virus infection in hemodialysis patients: should liver biopsy be performed before renal transplantation? Artif Organs. 1997; 21: 355-358.

[20] Otedo AEO, Mc’Ligeyo SO, Okoth FA, and Kayima JK,“Seroprevalence of hepatitis B and C in maintenance dialysis in a public hospital in a developing country,” South African Medical Journal,2003; 93: 380–384.

[21] Busek SU, Bab’a EH, Tavares Filho HA et al., “Hepatitis C and hepatitis B virus infection in different hemodialysis units in Belo Horizonte, Minas Gerais, Brazil,” Memorias do Instituto Oswaldo Cruz. 2002; 97: 775–778.

[22] Agarwal SK, Dash SC, and Irshad M, “Hepatitis C virus infection during haemodialysis in India,” Journal of Association of Physicians of India. 1999; 47: 1139–1143.

[23] Saha D and Agarwal SK, “Hepatitis and HIV infection during haemodialysis,” Journal of the Indian Medical Association2001;99; 194–199.

[24] Espinosa M, Mart’in-Malo A, Ojeda R et al., “Marked reduction in the prevalence of hepatitis C virus infection in hemodialysis patients: causes and consequences,” American Journal of Kidney Diseases. 2004; 43; 685–689.

[25] Carneiro MAS, Teles SA, Dias MA et al., “Decline of hepatitis C infection in hemodialysis patients in Central Brazil: a ten years of surveillance,”Memorias do InstitutoOswaldoCruz.2005;100; 345–349.
[26] Kosaraju K, Faujdar SS, Singh A, and Prabhu R. Hepatitis Viruses in Hemodialysis Patients: An Added Insult to Injury? Hepatitis Research and Treatment. 2013;1-4.

[27] Reddy GA, Dakshinamurthy KV, Neelaprasad P, Gangadhar T, and Lakshmi V, “Prevalence of HBV and HCV dual infection in patients on haemodialysis,” Indian Journal of Medical Microbiology. 2005; 23: 41-43.

[28] Perez G, Ortiz-Interian C, Lee H, de Medina M, Cerney M, Allain JP, et al. Human immunodeficiency virus and human T-cell leukemia virus type I in patients undergoing maintenance hemodialysis in Miami. Am J Kidney Dis. 1989; 14: 39-43.

[29] Vigneau C, Guiard-Schmid JB, Tourret J, Flahault A, Rozenbaum W, Pialoux G, et al. The clinical characteristics of HIV-infected patients receiving dialysis in France between 1997 and 2002. Kidney Int. 2005; 67: 1509-1514.

[30] Eggers PW, Kimmel PL. Is there an epidemic of HIV Infection in the US ESRD program? J Am Soc Nephrol. 2004; 15: 2477-2485.

[31] Ahuja TS, Borucki M, Grady J. Highly active antiretroviral therapy improves survival of HIV-infected hemodialysis patients. Am J Kidney Dis. 2000; 36: 574-580.

[32] Ortiz C, Meneses R, Jaffe D, Fernandez JA, Perez G, Bourgoignie JJ. Outcome of patients with human immunodeficiency virus on maintenance hemodialysis. Kidney Int. 1988; 34: 248-253.

[33] Perinbasekar S, Brod-Miller C, Pal S, Mattana J. Predictors of survival in HIV-infected patients on hemodialysis. Am J Nephrol. 1996; 16: 280-286.

[34] Eleftheriadis T, Liakopoulos V, Leviditis K, Antoniadi G, Stefanidis I. Infections in hemodialysis: a concise review. Part II: blood transmitted viral infections. Hippokratia. 2011; 15: 120-126.

[35] Isnard Bagnis C, Couchoud C, Bowens M, Sarraj A, Deray G, Tourret J, Cacoub P, Tezenas du Montcel S. Epidemiology update for hepatitis C virus and hepatitis B virus in end-stage renal disease in France. Liver Int. 2017 37:820-826.

[36] Ayatollahi J, Jahanabadi S, Sharifyazdi M, Hemavati R, Yakili M, Shahcheraghi SH. The Prevalence of Occult Hepatitis B Virus in the Hemodialysis Patients in Yazd, Iran. Acta Med Iran. 2016 ;54:784-787.

[37] Cordova E, Miglia I, Festuccia F, Sarlo MG, Scornavacca G, Punzo G, Menè P, Fofi C. Hepatitis B vaccination in haemodialysis patients: an underestimated problem. Factors influencing immune responses in ten years of observation in an Italian haemodialysis centre and literature review. Ann Ig. 2017;29:27-37.