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HCV Seroconversion in two Egyptian Hemodialysis Units: Role of Detection Method and Patients Isolation

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Abstract

Background: Hepatitis C virus (HCV) infection is a significant cause of morbidity and mortality in end stage renal disease (ESRD) patients on hemodialysis (HD). Routine HCV viremia screening is recommended in those patients but it is not applied.

Aim: To evaluate the seroconversion rate in HD patients based on viremia detection compared to antibody (Ab), and to assess the role of isolation on the rate of seroconversion in those patients.

Materials and Methods: One hundred ESRD patients from two HD units using same infection control criteria were enrolled in the study; only one unit was applying isolation for HCV patients. Patients were followed up for 12 month; HCV positivity was tested at the begining of the study and after 12 month of HD. HCV Ab and viremia were detected by third generation ELISA and PCR respectively.

Results: The seroconversion rate was 0% based on HCV Ab detection by ELISA, compared with the 16 % seroconversion rate based on viremia detection by PCR. Notably, viremia seroconversion was seen only in the HD unit lacking the isolation system.

Conclusion: HCV screening in HD units should be based on viremia detection; isolation in HD units prevents HCV spreading.

Introduction

Worldwide, 130–170 million persons are living with chronic hepatitis C virus (HCV) infection [1], which, if left untreated, can result in cirrhosis and liver cancer. Egypt has the largest burden of HCV infection in the world, with a 14% prevalence of chronic HCV infection among persons aged 15–59 years [2]. HCV transmission in Egypt is associated primarily with inadequate infection control during medical and dental care procedures [3, 4].

Hepatitis C virus (HCV) infection is a severe problem in maintenance hemodialysis patients whom are at particular high risk for blood-borne infections because of prolonged vascular access and potential for exposure to contaminated equipment [5]

The prevalence of HCV infection among dialysis patients is generally much higher than healthy blood donors and general population. Studies held in dialysis centers from different countries revealed that prevalence ranges form 1-84.6% and there is a particular concern because HCV chronic infection causes significant morbidity and mortality among patients undergoing hemodialysis (HD) [6]. In Egypt the prevalence of HCV infection was variable ranging from 49% to 64% [7].

Risk factors for HCV infection in dialysis patients include number of blood transfusions, duration of HD, and mode of dialysis, prevalence of HCV infection in the dialysis unit, previous organ transplantation, intravenous drug use, male gender, older age, and nosocomial transmission of HCV in HD units [8-11].

The spread of HCV infection in HD units is mainly due to nosocomial transmission between patients [12, 13]. In order to control the diffusion of

HCV in hemodialysis units some authors recommended using a separate section to dialyze HCV+ patients [14], especially in hemodialysis units with a high HCV prevalence or in which there is no fulltime infection control personnel dedicated to the infected patients during the hemodialysis sessions, could have a greater risk of sero-conversion [15].

Prompt detection of de novo HCV among dialysis patients is required to limit nosocomial spread of HCV. Enzyme immunoassay (EIA) provided excellent accuracy, with 0–0.23% false-negative rates. Thus, EIA-3 is an effective screening tool for HCV infection in patients with ESRD [16]. But, similar to other viral infections, the window period in HCV infection is still a major problem. During the window period, specific antibodies are not detectable, but the virus is present in the blood. For this reason, anti-HCV tests are unable to identify the subjects in this early stage of infection. The stage prior to seroconversion may last up to 2 months in immunocompetent subjects and as long as 6–12 months in immunodeficient patients [17]. Consequently, implementation of high sensitivity techniques for screening of HCV viremia in HD units should be applied.

The aim of this study was to evaluate the rate of seroconversion in anti HCV Ab negative and viremia negative patients after 12 month HD by PCR and to assess the role of isolation on the rate of seroconversion in those patients.

Materials and Methods

Study population

The prospective study included 100 end stage Renal disease (ESRD) Egyptian patients who underwent regular HD, fifty of them (Group A) recruited from a University hospital HD unit and the other fifty patients (Group B) were selected from a private HD unit. These two HD units are using the same infection control guidelines. Patient selection criteria was to be seronegative on three successive testing and to be confirmed in our lab as HCV RNA negative, those who proved HCV Ab negative but HCV RNA positive were excluded from the study. This study was approved by the local research ethics committee of National Research Center and a written informed consent was obtained from all participants in this study.

Virological testing

The detection of HCV antibodies (Ab) was determined every three month of the study by third generation ELISA (Dia Sorin, Torino, Italy) according to the manufacturer protocol. Serum RNA was extracted using Biozol reagent according to manufacturer protocol, HCV was detected using the conventional reverse transcription-polymerase chain reaction (RT- PCR) as described previously [18].

Statistical analysis

Statistical analysis was performed using version 16 of the SPSS computer program. Data of different variables were expressed as means ± SD. T-test was used to compare means for continuous variables and for non-normally distributed continuous variables. Comparison between distributions of categorical variables was performed using Chi-square (χ^2) test. In addition, variables were described as odds ratio (OR) with 95% confidence interval (95% CI) where appropriate. The data were considered significant if p values was < 0.05 and highly significant if $p < 0.01$.

Results

Demographic data, clinical and laboratory investigations of the study population

The demographic data and clinical procedures for patients included in the current study were outlined as shown in Table 1; the laboratory investigations of the two groups of patients before and after HD are summarized in Table 2.

Table 1: Demographic and clinical procedures for patient's groups.

Variable	Group A	Group B	P value
Age	53 ± 9.07	47 ± 13.51	0.015
Gender M/F	33/17	29/21	0.679
No of blood transfusion mean ± SD	5.04 ± 3.67	1.4 ± 1.12	0.0001
Dialysis duration / months mean ± SD	79.78 ± 56.42	46.28 ± 38.68	0.001
No of operations mean ± SD			
Shifting between dialysis units +ve/-ve	31/19	21/29	0.045
Antibilharzial treatment +ve/-ve	12/38	0/50	0.0001
DM +ve/-ve	6/44	7/43	0.766

+ve/-ve: positive, negative; DM: Diabetes Mellitus.

In brief, except gender all seroconversion risk factors were significantly higher in group A compared to group B. Notably, ALT level was significantly higher in group A before HD, and this difference was lost after HD due to elevation of its level in group B after HD.

Results of detection of HCV RNA after HD

After one year of HD, all patients were HCV Ab negative by ELISA. While HCV RNA was detected in 16% of group B patients, but none of group A patients had detectable HCV RNA Table 3.

Table 2: Laboratory investigations of patients before and after HD.

Variable	Before HD		*P* value	After HD		*P* value
	GA	GB		GA	GB	
ALT U/l mean ± SD	22.2±6.77	15.6±5.55	0.0001	26.88±17.12	28.58±24.27	0.68
AST U/l mean ± SD	25.92±7.01	23.26±7.45	0.069	27.6±12.99	29.3±13.15	0.512
BIL gm/dl mean ± SD	0.649±0.428	0.834±.649	0.096	0.692±0.395	0.764±0.573	0.47
ALB gm/dl mean ± SD	3.47±0.481	3.646±0.467	0.076	3.506±0.539	3.604±0.6	0.393
ALP U/l mean ± SD	144.0±81.01	142.4±79.1	0.921	133.5±85.6	125.6±79	0.632
PT/SEC mean ± SD	15.4±5.32	11.66±1.319	0.0001	16.9±8.65	12.64±1.509	0.001
Crm gm/dl mean ± SD	8.722±3.09	8.612±2.07	0.209	8.732±2.6	9.198±2.594	0.372
Hb gm/dl mean ± SD	10.67±1.42	10.3±1.55	0.23	10.5±11.58	10.09±1.64	0.197
Urea mg/dl mean ± SD	163.8±61.00	180.4±51.34	0.143	155.62±62.9	161.66±63.3	0.633

Discussion

HCV chronic infection causes significant morbidity and mortality among patients undergoing hemodialysis (HD) [19]. Prompt diagnosis of HCV infection in patients on chronic hemodialysis is important not only to offer the appropriate treatment for those who require it, but also to decrease the rate of infection transmission in hemodialysis units. In patients with ESRD the prolonged window period and the risk of infection spread through hemodialysis devices are among other reasons to look for a simple, reliable diagnostic method for HCV infection even before anti-HCV Ab production, in this population of patients, as a critical step for the control of infection spread in hemodialysis units [20].

Table 3: HCV RNA Seroconversion results after HD.

HCV RNA	After HD		P value
	GA	GB	
positive	0	42	
negative	50	8	0.001

G:group.

This study was conducted to assess the rate of seroconversion in HCV Ab and viremia negative HD patients using a sensitive PCR technique and to evaluate the role of isolation in HD units on the rate of seroconversion in this patient's category. Results in this study revealed a statistically significant difference in the rate of seroconversion based on ELISA results (0%) compared to that based on PCR (16%). As they were HCV RNA negative at initiation of the study, this ensures either a false negative ELISA results or they may be at the window period and both explanations are satisfactory and are concordant with previous studies who showed that the rate of HCV ab negative viremia detected by PCR in hemodialysis patients was reported to be 0-12% globally and that a false negative rate of 17.9% has been detected for HCV Ab among Egyptian hemodialysis patients [21, 22]. Consequently, the rate of seroconversion calculated based on ELISA results only is underestimated and it is highly recommended to depend on PCR in HCV surveillance in Egyptian HD units, a conclusion that matches with previously described by Schneeberger et al, [23]. Nonetheless, this criterion is not yet applicable in most HD units in Egypt.

As this study was designed to assess the role of isolation in HD units on seroconversion, the two HD units were chosen to be applying exactly the same infection control criteria, but isolation of HCV patients was applied in only one of them. Notably, the seroconversion was detected in patients of GB only but not in patients of GA, in other words seroconversion was not seen in patients from the HD unit applying the isolation strategy but was evident in patients from the HD unit not using the isolation policy.

To ensure that the seroconversion was due to experiencing the isolation in the HD unit, we studied all other risk factors which may be responsible for it. As the infection control criteria were exactly the same, we compared seroconversion risk factors in the two groups including age, duration of HD, shifting between dialysis units, antibilharzial treatment, and presence of Diabetes Mellitus (DM). Strikingly, all of them were significantly higher in GA than GB patients; nonetheless GA patients maintained 0% seroconversion versus 16% seroconversion in GB, bringing a strong evidence of the isolation role in seroconversion in this study.

The role of isolation in control of HCV spreading in HD units is controversial, Although some studies found that nosocomial spread of HCV declined when HCV-infected patients were treated in dedicated HD units [24, 25], other investigators could control nosocomial spread of HCV by strict application of hygienic precautions without isolation of HCV-infected subjects or machine segregation [26, 27]. Similarly in Egypt, results are controversial, while Shebeb et al., [28] showed that strict adherence to universal precautions was more effective than anti HCV seropositive patients isolation in limiting the spread of HCV infection among hemodialysis patients, two recent studies [29, 30] confirmed that strict isolation of HCV+ patients in combination with implementation of

universal prevention measures can limit the spread of HCV infection in HD patients. Notably all these studies evaluated seroconvertion by third generation ELISA only. In this study we emphasize the role of isolation of HCV positive patients on control of HCV infection spread in HD units in Egypt.

In conclusion, surveillance of HCV in HD units should be done using PCR technique not only ELISA. Isolation of HCV positive patients in HD units protects from dissemination of HCV infection.

References

1. The Global Burden of Hepatitis C Working Group. Global burden of disease (GBD) for hepatitis C. J Clin Pharmacol. 2004; 44:20–9.
2. El-Zanaty F, Way A: Egypt Demographic and Health Survey 2008. Egyptian:Ministry of Health. Cairo: El-Zanaty and Associates, and Macro International, 2009.
3. Paez Jimenez A, Mohamed MK, Sharaf Eldin N, et al. Injection drug use is a risk factor for HCV infection in urban Egypt. PloS One. 2009; 4:e7193.
4. Paez Jimenez A, Sharaf Eldin N, Rimlinger F, et al. HCV iatrogenic and intrafamilial transmission in greater Cairo, Egypt. Gut. 2010; 59:1554–60.
5. Yuqiang, C.; Wang, N.; Sheng, X., et al.: Hepatitis C virus infection in uremic patients on maintenance hemodialysis. Afric J Microb Res. 2011; 22: 3677-83.
6. Khan, S., Attaullah, A., Ijaz, A., et al. Rising burden of Hepatitis C Virus in hemodialysis patients. J Virol. 2011;8: 438.
7. Egyptian Renal Registry**:** 2008 report, ESNT congress, Hurghada Egypt, February, 2009.
8. Nicolardi E, Grieco A, Rapaccini GL, Pompili M: [Natural history, diagnosis and treatment of chronic hepatitis B and C in hemodialysis patients]. G Ital Nefrol. 2010; 27(3):262-73.
9. Tu AW, Buxton JA, Whitlock M.: Prevalence and incidence of hepatitis C virus in hemodialysis patients in British Columbia: Follow-up after a possible breach in hemodialysis machines. Can J Infect Dis Med Microbiol. 2009; 20(2):e19-23.
10. Sun J, Yu R, Zhu B, Wu J, Larsen S, Zhao W: Hepatitis C infection and related factors in hemodialysis patients in China: systematic review and meta-analysis. Ren Fail. 2009; 31(7):610-20.
11. Natov SN, Pereira BJ: Hepatitis C virus in chronic dialysis patients. Minerva Urol Nefrol. 2005; 57(3):175-97.
12. Izopet J, Sandres-Sauné K, Kamar N, Salama G, Dubois M, Pasquier C, Rostaing L. Incidence of HCV infection in French hemodialysis units: a prospective study. J Med Virol. 2005; 77: 70-76.
13. Taskapan H, Oymak O, Dogukan A, Utas C. Patient to patient transmission of hepatitis C virus in hemodialysis units. Clin Nephrol. 2001; 55: 477-48.
14. Marchesi D, Aric I, and Poletti E. Outbreak of HCV infection in hemodialysis patients. Nephrology Dialysis Transplantation. 1998; 13, 795–799.
15. Yang CS, Chang HH, Chou CC, Peng SJ.: Isolation effectively prevents the transmission of HCV in the hemodialysis units. J Formos Med. Assoc. 2003; 102:79-85.
16. Liu CH. and Kao JH. Treatment of hepatitis C virus infection in patients with end-stage renal disease. J Gastroent. and Hepat. 2011; 26: 228–239.
17. Muerhoff AS, Jiang L, Shah DO, Gutierrez RA, Patel J, Garolis C, Kyrk CR, Leckie G, Frank A, Stewart JL, Dawson GJ. Detection of HCV core antigen in human serum and plasma with an automated chemiluminescent immunoassay. Transfusion. 2002; 42: 349-356.
18. Youssef SS, Nasr AS, El Zanaty T, El Rawi RS, Mattar MM. Prevalence of occult hepatitis C virus in egyptian patients with chronic lymphoproliferative disorders.Hepat Res Treat. 2012; 2012:429784.
19. Alter, MJ. Prevention of spread of hepatitis C. Hepatology. 2002; 36(5 Suppl l):S93-8.
20. Moini M, Ziyaeyan M, Aghaei S, Sagheb MM, Taghavi SA, Moeini M, Jamalidoust M, Hamidpour L. Hepatitis C virus (HCV) Infection Rate among Seronegative Hemodialysis Patients Screened by Two Methods; HCV Core Antigen and Polymerase Chain Reaction. Hepat Mon. 2013;13(6):e9147.
21. Rahnavardi M, Hosseini Moghaddam SM, Alavian SM. Hepatitis C in hemodialysis patients: current global magnitude, natural history, diagnostic difficulties, and preventive measures. Am J Nephrol. 2008;28(4):628-40.
22. El-Sherif A, Elbahrawy A, Aboelfotoh A, Abdelkarim M, Saied Mohammad AG, Abdallah AM, et al. High false-negative rate of anti-HCV among Egyptian patients on regular hemodialysis. Hemodial Int. 2012;16(3):420-7.
23. Schneeberger PM, Keur I, Van der Vliet W, et al. Hepatitis C virus infection in dialysis centers in The Netherlands: a national survey by serological and molecular methods. J Clin Microbiol. 1998; 36:1171-1175.
24. Gallego E, Lopez A, Perez J et al., Effect of isolation measures on the incidence and prevalence of hepatitis C virus infection in hemodialysis. Nephron Clinical Practice. 2006; 104: c1–c6.
25. Yang C S, Chang H H, Chou C C, and Peng S J. Isolation effectively prevents the transmission of hepatitis C virus in the hemodialysis unit. Journal of the Formosan Medical Association. 2003; 102: 79–85.
26. Gilli P, Soffritti S, De Paoli Vitali E, Bedani PL. Prevention of hepatitis C virus in dialysis units. Nephron. 1995; 70: 301–306.
27. Shaheen F A, Huraib S O, Al-Rashed R et al. Prevalence of hepatitis C antibodies among hemodialysis patients in Jeddah area, Saudi Arabia. Saudi Medical Journals. 2003; 2: S125–S126.
28. Shebeb AM, Kotkat AM, Abd El Reheim SM, Farghaly AG, Fetohy EM. An intervention study for prevention of HCV infection in some hemodialysis units in alexandria. J Egypt Public Health Assoc. 2006; 81(1-2):119-41.
29. Soliman AR, Abd Elaziz M M, and El lawindi M I. Evaluation of an Isolation Program of Hepatitis C Virus Infected Hemodialysis Patients in Some Hemodialysis Centers in Egypt. ISRN Nephrology. 2013, Article ID 395467.
30. Yassin S, El Dib M and Roshd D. Nurses' Performance, isolation policy and HCV Sero-conversion among Hemodialysis Patients in Egyptian Hospitals. Life Science Journal. 2012;9(1):740-749.