

## Risk Factors for Hepatitis C Virus Infection among Patients with End Stage Renal Disease in Hemodialysis Unit -Al Kindy Teaching Hospital, Baghdad.

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### Abstract

**Background:** Hepatitis C virus (HCV) infection is a common global public health problem, and it is a significant problem among patients with end stage renal disease on hemodialysis (HD).

**Aim:** To determine the risk factors of HCV infection among patients with end stage renal disease on HD.

**Patients and methods:** A case control study was performed in HD units of Al-kindy teaching hospital in the period between October 2011- August 2012. A total of ninety patients with Positive Anti HCV and ninety patients with Negative anti-HCV were enrolled in this study.

Anti-HCV antibody was detected by the third generation enzyme immunoassay (ELISA). Direct interview was done with each patient, odds ratio and 95% CI were used to test significant differences.

**Results:** The results showed that 40 males and 50 females with positive antiHCV test didn't show any significant difference in comparison with 38 Males 52 females with negative HCV test regarding gender or age. It was found that as the number of dialysis passed 50 times the chance of getting HCV infection would be significantly high but as the frequency passed 100 times, the probability of getting infection would be significantly less. History of blood transfusion made prediction of having HCV infection significantly high. Absence of history of jaundice did not affect significantly probability of having hepatitis C infection among patients on HD. There was no association between history of diabetes mellitus and/or hypertension and probability of getting HCV infection.

**Conclusion** The blood transfusion was significantly associated with HCV infection. Frequent HD increase probability of getting HCV but not when the number passed 100 times.

**Key Words:** Hepatitis C virus, Hemodialysis, Al-kindy teaching hospital

### خلاصة

يشكل التهاب الكبد الفيروسي نمط سي مشكلة صحية عالمية خصوصا بين مرضى عجز الكلى المزمن الخاضعين للديليزة الدموية، وتهدف هذه الدراسة الى تحديد عوامل الخطورة لالتهاب الكبد الفيروسي لدى مرضى عجز الكلى المزمن الخاضعين للديليزة الدموية.

لقد تم اجراء دراسة مقارنة في وحدة الديليزة الدموية في مستشفى الكندي التعليمي خلال الفترة من تشرين الاول 2011 وحتى اب 2012، وقد شملت الدراسة 180 مريضا مصابا بعجز الكلى المزمن ويخضع للديليزة الدموية بصورة منتظمة نصفهم كان مصابا بالنمط سي من التهاب الكبد الفيروسي مثبتة مختبريا

لم تظهر نتائج الدراسة اي فروقات ذات دلالة احصائية فيما يتعلق بمتغيري الجنس والعمر واحتمال الاصابة بالتهاب الكبد الفيروسي نمط سي في حين ان الفرق الاحصائي كان واضحا في احتمال اصابة مرضى الديليزة بالتهاب الكبد اذا كان المريض قد اعطى تاريخا مرضيا لعمليات نقل دم كما ان تكرار اجراء الديليزة لاكثر من 50 مرة يزيد من احتمال الاصابة بالتهاب الكبد الفيروسي ولكن اذا تجاوزت عدد مرات الغسل الكلوي 100 مرة دون ان يكتسب المريض الاصابة فان احتماليته تقل بعد ذلك. ان احتمال اصابة المريض بالتهاب الكبد الفيروسي لا تتاثر اذا كان المريض مصابا بداء السكر او ارتفاع ضغط الدم.

## Introduction

Hepatitis C virus (HCV) infection is a common global public health problem<sup>(1, 2)</sup>. Approximately 200 million individuals are infected with HCV worldwide<sup>(3)</sup>. Although the prevalence of HCV infections has reduced in developed countries because of effective prevention plans<sup>(4)</sup>, it is still high in developing countries<sup>(5)</sup>. HCV is considered as the main cause of liver diseases in both developed and developing countries and contributes to the increasing risk of liver failure and hepatocellular carcinoma (HCC)<sup>(3, 4, 6, 7)</sup>. In addition, HCV is responsible for 20% of all acute hepatitis cases, 70% of all chronic hepatitis cases, 40% of all liver cirrhosis cases, 60% of HCCs, and 30% of infections in liver transplants in Europe<sup>(8, 9)</sup>. Moreover, most of the recently admitted HCC patients had viral hepatitis C<sup>(10)</sup>. The HCV prevalence in the Eastern Mediterranean Region is variable and ranges from 1% to 2.5% in most countries, with higher prevalence reported in Egypt (>10%), and in Libyan Arab Jamahiriya, Sudan and Yemen (2.5%–10%)<sup>(13, 14)</sup>. In Iraq, Based on the World Health Organization – supported study in 2006, Hepatitis C has endemicity 0.4%<sup>(15)</sup>

Hepatitis C virus (HCV) infection is a significant problem in HD patients with high prevalence has been reported. Prevalence rates of HCV infection in HD patients ranging between 2.9 and 68%, it is higher in the Middle East and Far East compared to the Western countries<sup>(11, 12, 13, 14)</sup>. Reports have shown prevalence from 17-51% in Asia, 8-36% in North America, and 1-54% in Europe<sup>(16)</sup>. In Iraq, a study done in 2008, the prevalence of Hepatitis C in hemodialytic patient was 7.1%<sup>(17)</sup> Risk factors such as the number of blood transfusions or duration on HD has been identified<sup>(18)</sup>. The natural course of hepatitis C in HD patients is not well understood, It seems to differ from that in

other HCV patients.<sup>(19)</sup> Liver function tests are close to or near normal in many cases.<sup>(20, 21)</sup> But the mortality of HCV infected HD patients seems to be enhanced compared with HCV negative HD patients in preliminary studies.<sup>(22)</sup> Thus patients with HCV on chronic HD are at increased risk of death, which suggests that the focus should be directed more to identification and prevention of hepatitis C infection in HD patients.

Because of this risk of death, this study is designed to determine the risk factors of HCV transmission among hemodialysed patients and the suggestions to reduce these risk factors.

## Material and Methods

The study was performed in HD units of Al-Kindy teaching hospital in the period between October 2011 - August 2012. A total of ninety patients with Positive Anti HCV and ninety patients with Negative anti-HCV were enrolled in this case control study. All patients (Negative and positive HCV test) underwent chronic HD treatment for end stage renal disease during the study period. None of these patients was known to be an intravenous drug abuser.

A direct interview was done with each patient inquiring about age, sex, history of hypertension, diabetes mellitus, jaundice, blood transfusion and number of dialysis and period passed since starting HD was checked.

Routine HD techniques were done for all patients, with 3-4 hours of dialysis performed 1-3 times weekly using polysulfone dialyzers with acetate solution of standard composition. Patients who were hepatitis B surface antigen (Hbs Ag) positive, as well as those with anti- HCV antibody-positivity were dialyzed in separate rooms using separate machines. Disposable kits and needles were used, and universal precautions such as use of

gloves, disinfection of surfaces were followed.

**Laboratory test**

Blood samples (5mL) were drawn into plain vacutainer from the antecubital vein of patients. The blood was allowed to clot for 30 minutes and centrifuged at 2000 g for 15 minutes for clear separation of serum. Serums were stored at -20 C until analyzed. The tests were performed at the virological laboratory department of Al-kindy teaching hospital. Anti-HCV antibody was detected by the third generation enzyme immunoassay (ELISA) (bioelisa HCVthis test use three recombinant antigen: Core, NS3, NS4, and NS5. Spain), and the result was interrupted according to the manufacturer instructions. The interpretation of the results of ELISA is as the following: If ELISA is negative for Anti-HCV, the result is that Anti HCV is negative while Positive result should be repeated by the same kit company and by Another kit company, then positive test is considered as a Positive result by

screening method and these positive results will confirmed by Recombinant ImmunoBlot Assay (RIBA) test which if it is positive then the result status of the patient is positive for Anti HCV test <sup>(23)</sup>.

**Statistical Analysis**

Data were analyzed using Mini Tab version 16. Descriptive statistics were used as frequencies and percentages. Odds ratio (OR) with 95% confidence interval (CI) was used as inferential statistics to evaluate the association between the presumptive risk factors and HCV infections

**Results**

Males formed Forty (51.2%) of HCV patients and 38(48.7%) of non HCV patients corresponding to 50(49%) and 52(51%) female respectively which showed no significant association between patient gender and getting HCV infection in hemodialytic patients (OR=1.094 , CI=0.607-1.974 ). See table 1.

Table 1. Gender distribution of the studied group on HD .

|        | ANTI –HCV  |           | TOTAL | OR with CI                    |
|--------|------------|-----------|-------|-------------------------------|
|        | POSITIVE   | NEGATIVE  |       |                               |
| Male   | 40 (51.2%) | 38(48.7%) | 78    | OR=1.094<br>95%CI=0.607-1.974 |
| Female | 50(49%)    | 52(51%)   | 102   |                               |
| Total  | 90         | 90        | 180   |                               |

Regarding age distribution this study showed no significant effect of age on acquiring HCV infection as shown in table 2 (OR=1.217, CI=0.657-2.254)

Table 2. Age distribution of the studied group on HD.

| AGE (YEARS) | ANTI –HCV |           | TOTAL | SIGNIFICANY                |
|-------------|-----------|-----------|-------|----------------------------|
|             | POSITIVE  | NEGATIVE  |       |                            |
| ≤ 40        | 33(53.2%) | 29(46.8%) | 62    | OR=1.217<br>CI=0.657-2.254 |
| >40         | 57(48.3%) | 61(51.7%) | 118   |                            |
| total       | 90        | 90        | 180   |                            |

When number of dialysis passed 51 times the chance of getting HCV infection was significantly high (OR=0.43, CI=0.18-0.99),but when number of dialysis passed 100 times the chance of getting HCV infection was significantly less, table 3.

Table .3a. Association between No. of dialysis and positive HCV antibody.

| DIALYSIS NO | ANTI –HCV |           | TOTAL | SIGNIFICANY             |
|-------------|-----------|-----------|-------|-------------------------|
|             | POSITIVE  | NEGATIVE  |       |                         |
| <50         | 14(46.6%) | 16(53.4%) | 30    | OR=0.43<br>CI=0.18-0.99 |
| 51-100      | 61 (67%)  | 30(33%)   | 91    |                         |
| Total       | 75        | 46        | 121   |                         |

Table .3b. relation between No. of dialysis and getting HCV infection ( comparison between those who exposed to HD from 51-100 and more than 100 times)

| DIALYSIS NO | ANTI –HCV |           | TOTAL | SIGNIFICANY              |
|-------------|-----------|-----------|-------|--------------------------|
|             | POSITIVE  | NEGATIVE  |       |                          |
| 51-100      | 61 (67%)  | 30 (33%)  | 91    | OR=5.96<br>CI=2.87-12.38 |
| >100        | 15(25.4%) | 44 (74.6) | 59    |                          |
| Total       | 76        | 74        | 150   |                          |

Table 4 showed that if the patient gave history of blood transfusion the prediction of having HCV infection would be significantly higher than those who were not taken blood(OR=2.66, CI=1.44-4.91)

Table .4. Relation between history of blood transfusion and getting HCV infection

|                   |          | ANTI –HCV |          | TOTAL | SIGNIFICANY                |
|-------------------|----------|-----------|----------|-------|----------------------------|
|                   |          | POSITIVE  | NEGATIVE |       |                            |
| blood transfusion | Positive | 48(64%)   | 27(36%)  | 75    | OR=2.666<br>CI=1.445-4.916 |
|                   | Negative | 42 (40%)  | 63(60%)  | 105   |                            |
| Total             |          | 90        | 90       | 180   |                            |

As shown in table 5 absence of history of jaundice did not affect significantly probability of having hepatitis C infection.(OR=0.812, CI=0.331-1.989)

Table .5.History of jaundice and HCV infection in HD patients

|             | ANTI –HCV  |           | TOTAL | SIGNIFICANY                |
|-------------|------------|-----------|-------|----------------------------|
|             | POSATIVE   | NEGATIVE  |       |                            |
| Jaundice    | 10(45.4%)  | 12(54.5%) | 22    | OR=0.812<br>CI=0.331-1.989 |
| No jaundice | 80 (50.6%) | 78(49.4%) | 158   |                            |
|             | 90         | 90        |       |                            |

In this study no association had been found between hypertension and HCV infection (OR=1.188, CI=0.610-2.314),and no significant association with diabetes mellitus( OR=1.37, %C1=0.62-3.09) , see table 6

Table .6.History of chronic disease and HCV infection in HD patients

|                  | Anti-HCV   |           |                               |
|------------------|------------|-----------|-------------------------------|
|                  | Positive   | Negative  |                               |
| Diabetic         | 17(57%)    | 13(43%)   | OR=1.37<br>95%CI=0.62-3.09    |
| Non diabetic     | 73 (48.7%) | 77(51.3%) |                               |
| Hypertensive     | 25(53.2%)  | 22(46.8%) | OR=1.188<br>95%CI=0.610-2.314 |
| Non hypertensive | 65(48.9%)  | 68(51.1%) |                               |

## Discussion

One important risk factor for HCV infection is blood transfusion, in this study 64% of patients with HCV infection gave history of blood transfusion before acquiring the infection with a risk of 2.66% higher than those without a history of blood transfusion and this supports the fact that blood and blood products are considered as the primary source for HCV transmission<sup>(24)</sup>. On the other side, 40% of patients with HCV infection had no history of blood transfusion indicating that there are other risk factors contributing to HCV infection. Some authors found no correlation between HCV and blood transfusion<sup>(25, 26)</sup>.

Another important risk factor is the number and the period of HD. In this study, high risk of getting HCV infection was found among patients undergoing HD for 50-100 times which was usually done during 6-12 months of putting patients on HD, and the risk may decrease after the first year, this can be explained by the fact that the prevalence of anti-HCV decreased significantly after 12 months on dialysis; this reduction could be due to reduction of titer of anti-HCV with time, as was noted by others<sup>(27, 28)</sup>. Another explanation is that in our study, because the patients have two- three sessions/week of HD and this can be explained that the HD procedure per se can preserve patients from an aggressive course of HCV by reducing the viral load (HCV RNA). Dialysis patients have immune compromise due to uremia; in spite of this, HCV viral load is not high and does not increase over time<sup>(29)</sup>. A number of studies support the notion that this dynamics of HCV viral load may be related to lowering of HCV RNA titers during the HD procedure<sup>(29, 30)</sup>. It has been suggested that the intradialytic reduction of HCV is membrane-dependent; polysulphone (PS) and hemophan membranes appear more effective<sup>(31)</sup>. Various mechanisms have been mentioned to explain the reduction of

HCV RNA during HD (HD): adsorption of HCV onto dialysis membrane, HCV escape into spent dialysate, destruction of HCV particles or increased interferon (IFN) activity<sup>(32)</sup>.

For the history of jaundice, 89% of the patients have no history of jaundice when Anti HCV has been detected, and this is consistent with the natural history of the disease<sup>(33)</sup>.

This study concluded that blood transfusion is significantly associated with HCV infection, but age and gender are not proved to be risk factors for HCV infection. Frequent HD increases probability of getting HCV but not when the number passed 100 times, chronic diseases mainly diabetes and hypertension were not found to be risk factors of HCV infection in HD.

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