

Evaluation Study of Patients Infected with Chronic Hepatitis C in Iraq

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ABSTRACT

Background: Hepatitis C virus (HCV) is a major cause of chronic liver disease. Approximately 85% of patients acutely infected with HCV progress to chronic liver disease with persistence of HCV-RNA for more than 6 months. Among patients with chronic HCV infection, 15-20% progress to end-stage liver disease. Main transmission methods of the virus is by: blood and blood products; sharing needles and acupuncture.

Objective: To evaluate Iraqi patients infected with chronic HCV, including their treatment, and factors that affect their response to treatment.

Methods: This study was performed at Gastroenterology and Hepatology hospital in Baghdad from January 2011 to March 2012. The study enrolled 90 patients with HCV Antibody positive (Ab +ve), every patient subjected to thorough history taking and clinical examination, and complete investigations, some of the patients subjected to liver biopsy which is analyzed by Ishak classification, the data analyzed by chi square and P value <0.05 considered statistically significant. All these patients were treated with peg interferon alpha2a given once weekly and ribavirin given in two doses daily and follow up the patients during treatment regimen.

Results: Ninety patients were enrolled, 66(73.3%) patients were male, 24(26.7%) patients were female, patient age range from 18-63, mean age 41.4 year. The predominant genotype is genotype 1:45 (50%) patients, genotype 4:33(36.7%) patients. Only 27(30%) patients have viral load more than 600,000U/ml while 63(70%) patients have viral load less than 600,000U/ml. 34(37.7%) patients showed End treatment virological response. 39 (42.2%) patients had been subjected to liver biopsy including those genotype 1 and 4. There was a significant association between viral load and liver enzymes.

Conclusion: There is a relatively low complete response to the treatment regimen for hepatitis C. Most of our patients with hepatitis C are discovered accidentally, Most of them are male, young or middle age, asymptomatic or have minimal symptoms, have low viral load. The commonest genotype is 1(50%) followed by genotype 4(36.7%). Early virologic response were seen in most of the patients while end treatment response were seen in only 37.78%.

Key Words: Hepatitis, liver, ribavirin.

Al-Kindy College Medical Journal Vol. 11 No.2. Page:35-38

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Received at 8th Dec. 2014. Accepted at 24th June 2015.

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Hepatitis C virus (HCV) infects 170 million people worldwide. HCV successfully evades the host immune response in 55% to 85% of acutely infected persons, thus leading to chronic infection. The natural history of hepatitis C varies greatly; reasons for this heterogeneity remain incompletely understood but are related to both viral, host, and environmental factors⁽¹⁾.

Epidemiology: Initially referred to as non-A, non-B hepatitis Choo and colleagues⁽²⁾, first characterized the HCV in 1989 in the past it was responsible for more than 90% cases of post-transfusion hepatitis⁽³⁾.

Chronic hepatitis C represents one of the biggest healthcare problems worldwide. Although symptoms may be mild for decades, 20% of persistently infected individuals may eventually develop serious liver disease including cirrhosis and liver cancer⁽⁴⁾.

TRANSMISSION: No identified risk factors for HCV infection during the previous six months can be identified in up to 44 percent of cases with new infections⁽⁵⁾. However, after careful questioning, most of these patients give a past history of high-risk behavior (such as injection drug use⁽⁶⁾. Blood transfusion, before the introduction of screening, and

injection drug use are the most clearly documented risk factors for HCV infection. Following the introduction of anti-HCV screening of blood donors between 1990 and 1992. The number of transfusion-related cases of HCV infection declined sharply, and currently less than 1 case occurs per 2,000,000 units transfused^(7,8).

Chronic hemodialysis is also associated with increased rates of HCV infection. The frequency of anti-HCV in patients on hemodialysis ranges from 11.6% in the United States to 55% to 85% in Jordan, Saudi Arabia, and Iran⁽⁹⁾. Although monogamous sexual relationship carries a low risk of transmission of HCV infection, the risk is higher in persons involved with multiple sexual partners, and the degree of HCV viremia HCV antibodies occur in approximately 2% of the spouses⁽¹⁰⁾. There is no need to curtail ordinary household activities except those that might result in blood exposure, such as sharing a razor or toothbrush. Other situations that have been suggested to carry a risk for HCV transmission include certain folk medicine practices (acupuncture, ritual scarification), body piercing, tattooing, and even commercial barbering^(11,12). The risk of perinatal transmission of HCV infection is low,

averaging 5.1% to 6.7% for HCV-monoinfected patients and two to three times higher for HIV-HCV-coinfected patients⁽¹³⁾.

Surprisingly high rates of HCV infection (approximately 30 percent) have been found in patients with alcohol abuse, even in the absence of other risk factors for infection^(14,15). HCV may accelerate the liver injury in patients who drink heavily⁽¹⁶⁾, alcohol use appears to decrease the efficacy of interferon therapy for HCV⁽¹⁷⁾, and patients with alcohol and HCV-induced liver injury have a greater risk for hepatocellular carcinoma⁽¹⁸⁾

LIVER BIOPSY : Liver histology is useful for determining the stage of disease, excluding other causes of liver test elevation, and guiding decisions regarding treatment and surveillance.

Treatment :The current standard of care for the treatment of HCV infection is the combination of a pegylated interferon2a administered subcutaneously once per week and ribavirin taken orally every day. *Interferons* are naturally occurring proteins that exert a wide array of antiviral, antiproliferative, and immunomodulatory effects *Ribavirin* has no direct antiviral activity, but it has synergistic effect when administered in combination.

Aim of Antiviral Therapy for CHC :Despite the importance of these clinical end points, in practice virological endpoints are used to define the success of anti-viral therapy . In particular, the definition of treatment success is a *sustained virological* response(SVR) that is defined by having undetectable HCVRNA 24 weeks after the cessation of treatment. This is invariably associated with an *end* of treatment response (ETR) that refers to having undetectable HCV RNA at the cessation of therapy. SVR is durable end point with over98% sustained responders remaining PCR negative at 5 year.

Patients and Methods: Between January 2011 & March 2012, there are 553 patients with HCV Ab positive test visited the outpatient clinic in the gastroenterology & teaching hospital, had been taken into our study. Every patient has been subjected to thorough history taking and clinical Examination ,the history was concentrating on the following points :

- Risk factors for infection (blood transfusion,surgery,etc) .
- House hold contact with the same disease .
- Any symptom of liver disease (jaundice, subcostal discomfort , fatigue , etc) .
- Full clinical examination was done for every patient .
- Liver function test data;total serum bilirubin(TSB),aspartate aminotransferase (AST) , alanin aminotransferase (ALT) were measured .
- PT, INR .
- Serum protein,serum Albumin .
- HCVAb positive assayed by third generation enzyme linked immune sorbant assay ELISA type III .
- Investigations to exclude other causes of liver disease (HBsAg , immune screen , etc) .
- Abdomen ultrasound was performed for all patients by experienced sonographist , the liver size , texture , the size of spleen and presence or absence of ascites was recorded .

Alpha fetoprotein in patients with evidence of liver cirrhosis .
Viral load using branched-DNA-technology assay(bayer system 340b-DNA analyzer 3.0)with detection limit 625-17857100 iu/ml .

All patients assessed for Genotype using PCR & depend on two private laboratories.

Liver biopsy was done in indicated cases those genotype 1or4 and those who has normal liver function tests and normal U/S after taking signed patient consent and there is no contraindication to procedure .

With prior approval of the local Institutional Committee for Human Investigation,

And among those patients only 90 patients where completed their work up and entered their treatment phase according to schedule .

Statistical analysis: All data were coded and enter to the computer by using statistical Package for Social Science (SPSS 14) association between variables. Measured by using Chi-Square test P<0.05 consider as level of significancy.

Results:_During the duration of study 553 patients with HCV Ab positive test visiting the outpatient clinic in Gastroenterologyand hepatology hospital _Most of our patients discovered accidentally during blood donation , testing before intervention , testing for life health insurance , high risk group ; medical staff ,and household contact . **table 1** .90 patients have completed treatment , 66 (73.3%) patients were male,24(26.7%) patients were female were included in study. Age range was between 18-63years, mean age of patients is 41.4year , most of the patients lie in the young and middle age group range. Abnormal liver enzymes were seen in 20 patients(22.2%) of 90 patients .

table2 According to viral load patients divided into two groups, Only 27(30%)patients have viral load >600000U\ml while 63(70%)Patients have viral load<600000U\ml.39(42.2%) patients have been subjected to liver biopsy including those genotype 1or4 and those with normal liver function tests and normal U/S .**Table 3** 80(88.9%) patients have early virological response (EVR) 11(13.75%of_EVR patients) have partial early virological response (p EVR),69(76.2%) patients have complete early virological response (c EVR) .10 patients have no early virological response (<2log decrease in viral load) but we choosed to continue treatment as they have high viral load,increase in liver enzymes , 2 of them have progressive liver disease in histopathology .Only 34(37.7%)patients who completed treatment achieved end treatment response (ETVR) .

Table 1:Methods of HCV diagnosis.

| Methods of diagnosis | NO. (%) |
|------------------------------------|-----------|
| Blood donation | 37(41.1%) |
| Accidental & health life insurance | 22(24.5%) |
| Screening before surgery | 16(17.8%) |
| Symptomatic | 7(7.8%) |
| House hold contact | 4(4.4%) |
| Before cardiac catheter | 4(4.4%) |

Table 2: Distribution of liver enzymes in patients with HCV

| Liver enzymes(sGOT,sGPT) | NO.(%) |
|--------------------------|----------|
| ≥40 IU/ml | 20(22.2) |
| <40 IU/ml | 70(77.8) |

Normal value<40iu/ml.

Table 3: Distribution of liver biopsy stages in the study.

| Liver biopsy stage | No.(%) |
|--------------------|------------|
| 1 | 1 (2.5%) |
| 2 | 10 (25.6%) |
| 3 | 18 (46%) |
| 4 | 7 (18%) |
| 5 | 2 (5%) |
| 6 | 1 (2.5%) |
| Total | 39 (100%) |

Table 4: Relation between viral load and liver enzymes.

| Liver enzymes | Viral load <600000 iu/ml | Viral load >600000iu/ml | Total No. (%) |
|---------------|--------------------------|-------------------------|---------------|
| <40iu/ml | 53(84.1%) | 17(63%) | 70(77.8%) |
| >40iu/ml | 10(15.9%) | 10(37%) | 20(22.2%) |
| Total | 63 | 27 | 90 |

P=0.028

Discussion. The program arranged by ministry of health by screening every patient before any intervention procedure lead to increase the number of cases seen in our health institute, however ,the overall prevalence in our country is still 0.3%.Most of the patients discovered to be HCV Ab +ve during routine screening before elective surgery or interventional medicine , or during blood donation or screening of the family of infected persons or screening patient with chronic renal failure on hemodialysis⁽¹⁾. For this reason we have to emphasize the importance of screening of at risk individuals and the importance of making the test easily accessible for the population⁽⁸⁻¹³⁾.Most patients enrolled in our study were male 66(73.3%) compared to 24(26.7%)patients were female, this what was found in other study' the explanation for this difference between male and female can be referred to that in our community less

women subjected to screening test for HCV Ab compared to male and most of the blood donors are among male gender .Male gender is associated with more rapid progression to cirrhosis and HCC. The reason for this association is not clear, and hormonal effects on fibrogenesis have been suggested. Estrogen inhibits proliferation and activation of hepatic stellate cells in vitro. In addition, fibrosis appears to accelerate in postmenopausal women. Age range of our study was between 18-63years, Mean age of patients was 41.4year ,most of the patients lie in the young and middle age group range. Most of our patients had low viral load (less than 600000 iu/ml in 63patient(70%) while 27 patients (30%) had viral load >600000iu/ml .There was no significant correlation between pretreatment viral load and the age of the patients at presentation, this is the condition found in other study. there was better end treatment virological response when pretreatment viral load low, this relation confirmed statistically(p value<0.05) this consistent with other study 'In this study; there was a significant correlation between viral load and liver enzymes as shown in table (4),this what found in other study.The most common genotype was 1 occurring in 50% of the patients followed by genotype 4 (36.7) this is similar to other study in our country and similar to nearby area like turkey and Iran but different from other area like Syria.

In conclusion, Most common presentations was incidental during blood donation or during screening before interventional medical procedure. Hepatitis C was more common among the male gender , most of our patient have low viral load <600000 IU/ml .There was significant association between the viral load and liver enzymes but There was no correlation between pretreatment viral load neither to the age of the patient nor to the stage of liver fibrosis or genotype .The predominant genotype was 1 occur in 50% followed by genotype 4 .Most of our patients got early virologic response .End treatment virological response was seen in only 37.78% which has significant association with genotype, early virological response . Attempts to improve adherence to therapy and the early detection together with treatment of complications are needed to achieve better response to therapy.

References

1. Jacqueline G. O'Leary,Gary L. Davis, Hepatitis C.In:Mark Feldman . LawrenceS.Friedman. and Lawrence J.Brandt . *Sleiseger and Fordtrans Gastrointestinal and Liver Disease* Saunders9th Ed , 2010 pp 1313 - 1335 .
2. Choo QL , Kuo G, Weiner AJ, Overby LR , Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A , non-B viral hepatitis genom *Science*. 1989;244:359-62
3. Te HS, Jensen DM. Epidemiology of hepatitis B and C viruses: a global overview. *Clin Liver Dis*. 2010;14:1-21, vii .
4. Alter MJ, Kruszon-Moran D, Nainan OV, McQuillan GM, Gao F,Moyer LA, Kaslow RA, Margolis HS: The prevalence of hepatitisC virus infection in the United States, 1988 through 1994. *N Engl J Med* 1999,341:556-562 .
5. Alter MJ, Gerety RJ, Smallwood LA,et al. Sporadic non-A, non-B hepatitis: frequency and epidemiology in an urban U.S. population. *J Infect Dis* 1982; 145:886 .

6. Murphy EL, Bryzman SM, Glynn SA, et al. Risk factors for hepatitis C virus infection in United States blood donors. NHLBI Retrovirus Epidemiology Donor Study (REDS). *Hepatology* 2000; 31:756.
7. Alter HJ, Houghton M. Clinical Medical Research Award. Hepatitis C virus and eliminating post-transfusion hepatitis. *Nat Med* 2000; 6:1082-6.
8. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ: The risk of transfusion-transmitted viral infections. The Retrovirus Epidemiology Donor Study. *N Engl J Med* 1996; 334:1685-90.
9. 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; 28:628-40
10. Tahan V, Karaca C, Yildirim B et al. Sexual transmission of HCV between spouses. *Am J Gastroenterol* 2005; 100: 821-4 .
11. Sun DX, Zhang FG, Geng YQ, Xi DS. Hepatitis C transmission by cosmetic tattooing in women . *Lancet* 1996; 347:541.
12. Tumminelli F, Marcellin P, Rizzo S, Barbera S, Corvino G, Furia P, et al. Shaving as potential source of hepatitis C virus infection. *Lancet* 1995;345:658.
13. Conte D, Fraquelli M, Prati D, et al. Prevalence and clinical course of chronic hepatitis C virus (HCV) infection and rate of HCV vertical transmission in a cohort of 15,250 pregnant women. *Hepatology* 2000 ; 31:751-5 .
14. Parés A, Barrera JM, Caballería J, et al. Hepatitis C virus antibodies in chronic alcoholic patients: association with severity of liver injury. *Hepatology* 1990; 12:1295 .
15. Mendenhall CL, Moritz T, Rouster S, et al. Epidemiology of hepatitis C among veterans with alcoholic liver disease. The VA Cooperative Study Group 275. *Am J Gastroenterol* 1993; 88:1022.
16. Wasley A, Grytdal S, Gallagher K, et al. Surveillance for acute viral hepatitis—United States, 2006. *MMWR* Surveill Summ 2008; 57:1-24 .
17. Blackard JT, Shata MT, Shire NJ, Sherman KE: Acute hepatitis C virus infection: A chronic problem. *Hepatology* 2008; 47:321-31.
18. Jules L. Dienstag . CHRONIC HEPATITIS in. Dan L. Longo , Anthony S. Fauci, Carol A. Langford' *HARRISON'S Gastroenterology and Hepatology* . Mc Hill Grow Medical.2010;403 .