CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.2593212

Available online at: http://www.iajps.com ***Research Article***

FACTORS AFFECTING EARLY VIRAL LOAD DECLINE AMONG CHRONIC HEPATITIS C PATIENTS RECEIVING PEGYLATED INTERFERON PLUS RIBAVIRIN THERAPY

Shaista Ahmed[1], Firasat Waqar[2], Aisha Javed[3], Sadia Iqbal[4], Afshan Siddiqui[5], Muhammad Muneeb[6] & Aatir H. Rajput[7].

Associate Professor – Department of Medicine, Abbasi Shaheed Hospital, Karachi[1],
Assistant Professor – Department of Medicine, Abbasi Shaheed Hospital, Karachi[2& 3],
Assistant Professor – Department of Medicine, Dow University Hospital, Karachi[4 & 5],
Coordinator – Dept. of Medical Education, Indus Medical College Hospital, T.M.K[6],
Postgraduate Resident – Department of Psychiatry, Liaquat University of Medical & Health Sciences and Sir Cowasjee Jehangir Institute of Psychiatry, Hyderabad.

Article Received: December 2018 **Accepted:** February 2019 **Published:** March 2019

Abstract:

This observational study was conducted upon a sample of 108 chronic HCV patients (chosen via non-probability – consecutive sampling) presenting to the Dept. of Medicine - Abbasi Shaheed Hospital, Karachi from February 5, 2018 to August 31, 2018. As per the standard protocol, a dose of pegylated interferon-α2a was administered at week 1 and then weekly with daily oral ribavirin for 24 or 48 weeks. Genotyping and quantification of hepatitis C virus (HCV) RNA were done using molecular methods. Clinical and serological (viral load) data obtained was analyzed using SPSS version 21.0 and MS. Excel 2013. Out of 108 participants 71 were males and 37 were females, with a mean age of 38 years for males and 23 years for females. A total of 53 patients were infected with HCV genotype 1, 47 with genotype 2 and 8 with both genotypes 1 and 2. At the end of follow-up, 87 patients attained sustained virological response (SVR). After accounting for confounders, body mass index (BMI) and genotype were related to viral load decline at day 2, baseline viral load and high-density lipoprotein (HDL) cholesterol levels were correlated with viral load decline between days 2 and 28. Genotype, baseline viral load and BMI independently predicted rapid virological response. After careful consideration of the results, it can be concluded that HCV genotype, baseline viral load, pre-treatment BMI and HDL have a significant effect on early viral load decline of chronic HCV patients with interferon-based therapy.

Keywords: *Viral Load, HCV, Pegylated Interferon-α2a, Ribavarin and Sustained Viral Response.*

Corresponding author:

Dr. Shaista Ahmed,

Associate Professor – Department of Medicine, Abbasi Shaheed Hospital, Karachi, Corresponding Email: shaistaahmed.dr@gmail.com

Contact Number: +92-333-3179504.

QR code

Please cite this article in press Shaista Ahmed et al., ***Factors Affecting Early Viral Load Decline Among Chronic Hepatitis C Patients Receiving Pegylated Interferon Plus Ribavirin Therapy.,*** *Indo Am. J. P. Sci, 2019; 06(03).*

INTRODUCTION:

Hepatitis C virus (HCV) infection is the major cause of chronic liver disease and hepatocellular carcinoma worldwide. [1] The goal of treating chronic HCV patients is to eradicate the virus or, in a clinical term, to attain a sustained virological response (SVR; defined as undetectable serum HCV RNA level at 24 weeks after treatment cessation). [2]

However, currently approved pegylated interferon (PEG-IFN) plus ribavirin (RBV) therapy has many unpleasant side effects and is only effective in a certain proportion of HCV patients. [3] Therefore, identifying baseline and on-treatment factors predictive of SVR in HCV patients is important in terms of increasing efficacy, avoiding unnecessary side effects and saving medical costs.

Several factors have been linked to the therapeutic response of HCV patients, including viral factors, [4] host factors, [5] metabolic factors, [6] histological factors, [7] the regimen used [8] and the duration of infection. [9] Among these factors, early viral kinetics following therapy has become increasingly recognized and is widely used in both clinical trials and daily practice. [10]

Considering the clinical significance of early viral kinetics, it is thus reasonable to investigate the association of other predictors with viral load decline. These attempts not only provide information on individualized treatment, but also elucidate the underlying mechanisms of these predictors. Although patients in our part of the world (south-east Asia) are more likely to achieve an SVR to combination therapy than Caucasians with HCV, [11] the influence of various host and viral factors on early viral load decline in our part of the world among HCV patients deserves further study. [12]

Thus, this study recruited treatment naive patients with HCV and administered a combination therapy of PEG-IFN-a2a plus RBV, in an attempt to generate much needed evidence in this regard (the effect of various host, viral and metabolic factors on early viral load decline). The results shall prove helpful in providing a basis for future interventional research.

METHODOLOGY:

This observational study was conducted upon a sample of 108 chronic HCV patients (chosen via non-probability – consecutive sampling) presenting to the Dept. of Medicine - Abbasi Shaheed Hospital, Karachi from February 5, 2018 to August 31, 2018. Chronic HCV infection was defined as the positivity of both anti-HCV antibodies and serum HCV RNA for >6 months. As per the standard protocol, a dose of pegylated interferon-α2a was administered at week 1 and then weekly with daily oral ribavirin for 24 or 48 weeks. Genotyping and quantification of hepatitis C virus (HCV) RNA were done using molecular methods. Clinical and serological (viral load) data obtained was analyzed using SPSS version 21.0 and MS. Excel 2013.

Inclusion Criteria:

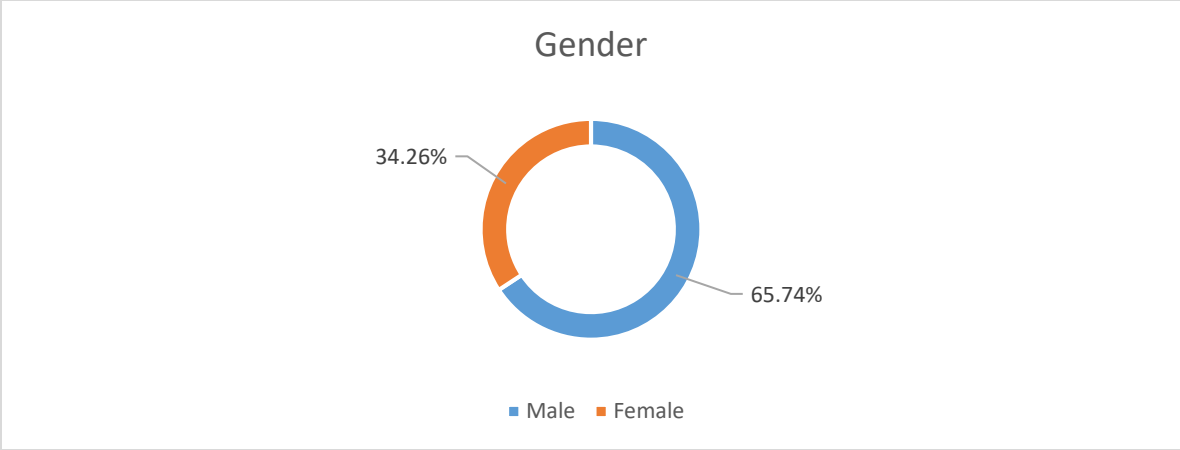
Consenting patients (of both genders and all ages) presenting with chronic HCV (defined as the positivity of both anti-HCV antibodies and serum HCV RNA for >6 months and had serum alanine aminotransferase (ALT) levels ≥2× the upper limit of normal on two occasions within the past 6 months) were included in the study.

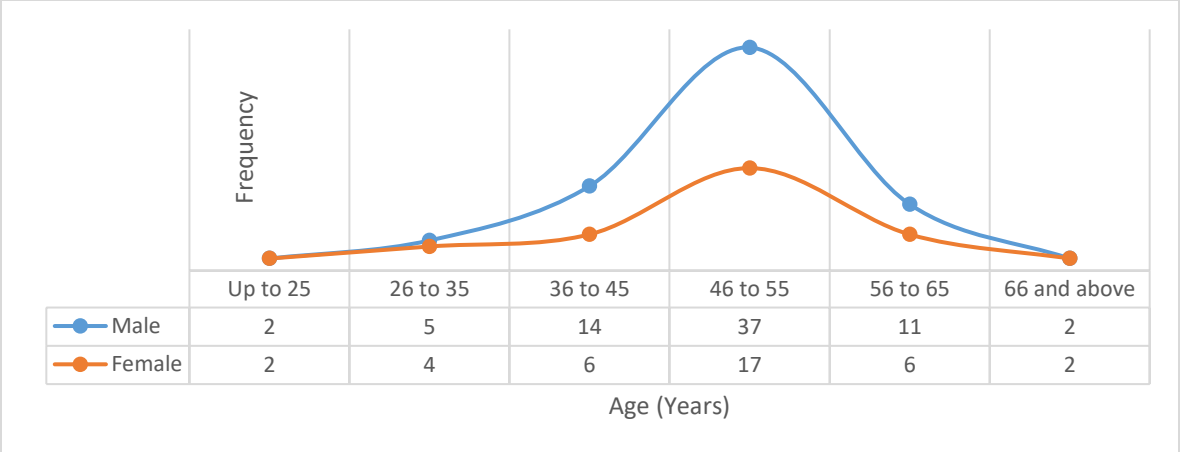
Exclusion criteria:

Non-consenting patients and patients who had received prior interferon, other experimental antiviral or immunosuppressive therapy were excluded from the sample. Also excluded were, patients positive for hepatitis B surface antigens or HIV antibodies, patients with a history or serological evidence of autoimmune liver disease, inheritable disorders (such as haemochromatosis or Wilson's disease), renal insufficiency, a history of excess alcohol intake (daily alcohol consumption >20 g) or active drug abuse.

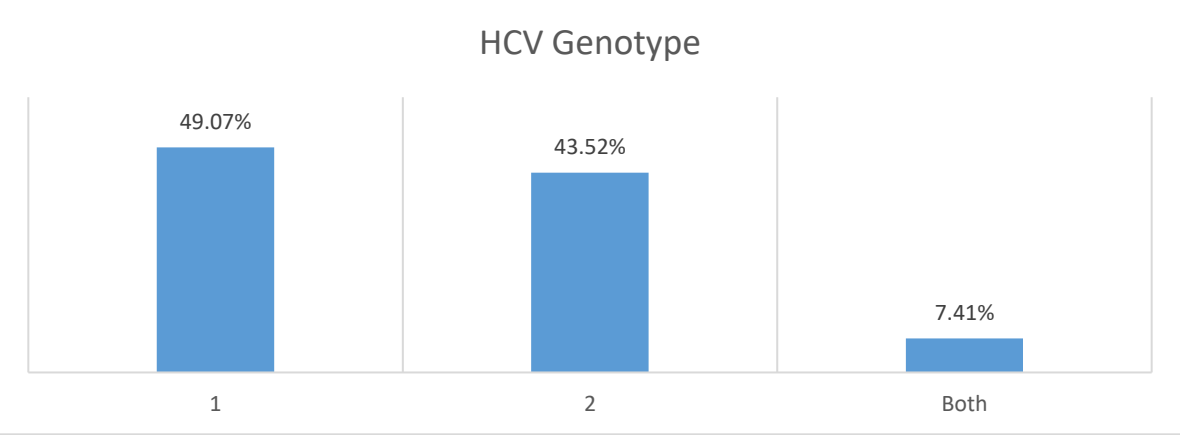
RESULTS:

Out of 108 participants 71 were males and 37 were females, with a mean age of 51 years for males and 45 years for females.





A total of 53 patients were infected with HCV genotype 1, 47 with genotype 2 and 8 with both genotypes 1 and 2.



At the end of follow-up, 87 patients attained sustained virological response (SVR). After accounting for confounders, body mass index (BMI) and genotype were related to viral load decline at day 2, baseline viral load and high-density lipoprotein (HDL) cholesterol levels were correlated with viral load decline between days 2 and 28. Genotype, baseline viral load and BMI independently predicted rapid virological response.

Characteristic	2-tailed sig
B.M.I ($kg/m^{2)}$	P = 0.05
Genotype 2	P < 0.01
HDL (mg/dl)	P = 0.08
HCV RNA, log_{10} (IU/ml)	P < 0.01

DISCUSSION:

Studies on early viral kinetics during treatment of chronic HCV infection have greatly improved our understanding about the pathophysiology of HCV infection and thus, harbored several clinical implications. For example, knowing the influence of various factors on HCV dynamics could help individualize antiviral treatment. [13]
In this study, we found that genotype, baseline viral load, BMI and pretreatment HDL were independently associated with early viral load decline and that genotype, baseline viral load and the viral load decline at day 28 were independent predictors of SVR. These data could optimize current standard of care and elucidate the underlying mechanisms of these predictors. [14]

A previous pilot study from Taiwan demonstrated a better virological response rate than the Western report (genotype 1 patients received 6 months of PEG-IFN-α2b plus RBV had an SVR up to 65.8%). [15] In addition, data to support shorter treatment duration for genotype 2 patients were also noted.

On the basis of these observations, the Bureau of National Health Insurance in Taiwan allows the reimbursement of 24-week rather than 48-week interferon-based treatment for HCV genotype 1 patients. This is the reason why only most of our genotype 1 patients received a 48-week treatment and fewer of them received a 24-week treatment. [16]

The use of viral load decline is inherently limited by the value of PCR negativity, and thus the decline cannot be greater than the difference between the baseline viral load and the value of PCR negativity. However, the viral load decline could render the information other than HCV RNA negativity in monitoring on-treatment virological response. Therefore, the combination of these qualitative and quantitative data will be more informative to practicing physicians. [17]

The duration of HCV infection, a known predictor of the therapeutic efficacy, was not included in our analyses because of possible recall bias. These data will certainly help clinicians optimize current therapy for HCV and elucidate the underlying mechanisms of these predictors.

CONCLUSION:

After careful consideration of the results, it can be concluded that HCV genotype, baseline viral load, pre-treatment BMI and HDL have a significant effect on early viral load decline of chronic HCV patients with interferon-based therapy.

REFERENCES:

1. Wedemeyer H, Dore GJ, Ward JW. Estimates on HCV disease burden worldwide–filling the gaps. Journal of viral hepatitis. 2015 Jan;22:1-5.
2. Innes HA, McDonald SA, Dillon JF, Allen S, Hayes PC, Goldberg D, Mills PR, Barclay ST, Wilks D, Valerio H, Fox R. Toward a more complete understanding of the association between a hepatitis C sustained viral response and cause-specific outcomes. Hepatology. 2015 Aug;62(2):355-64.
3. Younossi ZM, Stepanova M, Nader F, Henry L. Patient-reported outcomes of elderly adults with chronic hepatitis C treated with interferon-and ribavirin-free regimens. Journal of the American Geriatrics Society. 2016 Feb;64(2):386-93.
4. Wen SC, Cheng LC, Hsu JH, Lai HW, Shih PC, Tsai CC, Kuo WH. Assessment of baseline pretreatment factors and on-treatment virological response to predict sustained virological response in patients with chronic hepatitis C treated with

pegylated interferon and ribavirin. Advances in Digestive Medicine. 2017 Mar;4(1):4-11.
5. Sreejith Vasudevan S, Kavimandan A, Kalra N, Nayak B, Thakur B, Das P, Gupta SD, Panda SK, Acharya SK. Demographic profile, host, disease & viral predictive factors of response in patients with chronic hepatitis C virus infection at a tertiary care hospital in north India. The Indian journal of medical research. 2016 Mar;143(3):331.
6. Rehermann B. HCV in 2015: Advances in hepatitis C research and treatment. Nature Reviews Gastroenterology & Hepatology. 2016 Jan 21;13(2):70.
7. Akhtar E, Manne V, Saab S. Cirrhosis regression in hepatitis C patients with sustained virological response after antiviral therapy: a meta-analysis. Liver International. 2015 Jan;35(1):30-6.
8. Kohli A, Osinusi A, Sims Z, Nelson A, Meissner EG, Barrett LL, Bon D, Marti MM, Silk R, Kotb C, Gross C. Virological response after 6 week triple-drug regimens for hepatitis C: a proof-of-concept phase 2A cohort study. The Lancet. 2015 Mar 21;385(9973):1107-13.
9. Simmons B, Saleem J, Heath K, Cooke GS, Hill A. Long-term treatment outcomes of patients infected with hepatitis C virus: a systematic review and meta-analysis of the survival benefit of achieving a sustained virological response. Clinical Infectious Diseases. 2015 May 17;61(5):730-40.
10. Fourati S, Guedj J, Chevaliez S, Nguyen TH, Roudot-Thoraval F, Ruiz I, Soulier A, Scoazec G, Varaut A, Poiteau L, Francois M. Viral kinetics analysis and virological characterization of treatment failures in patients with chronic hepatitis C treated with sofosbuvir and an NS 5A inhibitor. Alimentary pharmacology & therapeutics. 2018 Mar;47(5):665-73.
11. Vutien P, Hoang J, Brooks Jr L, Nguyen NH, Nguyen MH. Racial disparities in treatment rates for chronic hepatitis C: analysis of a population-based cohort of 73,665 patients in the United States. Medicine. 2016 May;95(22):212-218.
12. Raja R, Baral S, Dixit NM. Interferon at the cellular, individual, and population level in hepatitis C virus infection: Its role in the interferon-free treatment era. Immunological reviews. 2018 Sep;285(1):55-71.
13. Ferenci P. Predictors of response to therapy for chronic hepatitis C. InSeminars in liver disease 2004 May (Vol. 24, No. S 2, pp. 25-31). Copyright© 2004 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA..
14. Mihm U, Herrmann E, Sarrazin C, Zeuzem S. Predicting response in hepatitis C virus therapy. Alimentary pharmacology & therapeutics. 2006 Apr;23(8):1043-54.
15. Davis GL, Wong JB, McHutchison JG, Manns MP, Harvey J, Albrecht J. Early virologic response to treatment with peginterferon alfa-2b plus ribavirin in patients with chronic hepatitis C. Hepatology. 2003 Sep;38(3):645-52.
16. Poynard T, Marcellin P, Lee SS, Niederau C, Minuk GS, Ideo G, Bain V, Heathcote J, Zeuzem S, Trepo C, Albrecht J. Randomised trial of interferon α2b plus ribavirin for 48 weeks or for 24 weeks versus interferon α2b plus placebo for 48 weeks for treatment of chronic infection with hepatitis C virus. The Lancet. 1998 Oct 31;352(9138):1426-32.
17. Alonso R, Pèc F, López-Roa P, Alcalá L, Rodeño P, Bouza E. HCV core-antigen assay as an alternative to HCV RNA quantification: A correlation study for the assessment of HCV viremia. Enfermedades infecciosas y microbiologia clinica (English ed.). 2018 Mar 31;36(3):175-8.