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### END TREATMENT RESPONSE IN CHRONIC HEPATITIS C NAÏVE PATIENTS BY STANDARD INTERFERON THERAPY IN RURAL AREA OF SINDH

<sup>1</sup>Dr. Kuldeep Kumar, <sup>2</sup>Dr. Pooran Mal, <sup>3</sup>Dr. Kanwal Rai,  
<sup>4</sup>Dr. Hamid Nawaz Ali Memon, <sup>5</sup>Dr. Muntaha Irshad and <sup>5</sup>Dr. Pireh Memon

<sup>1</sup>Consultant Physician, M.K Hospital Hyderabad, Sindh Pakistan

<sup>2</sup>Assistant Professor, Department of Nephrology, Liaquat University of Medical and Health Sciences (LUMHS) Jamshoro

<sup>3</sup>Consultant Physician, Syed Abdullah Shah Institute of Medical Sciences (SASIMS), Sehwan Sharif Sindh Pakistan

<sup>4</sup>General Practitioner Zulekha Hospital Dubai United Arab Emirates

<sup>5</sup>Department of Medicine, Liaquat University Hospital Hyderabad

#### ABSTRACT:

**BACKGROUND:** Chronic hepatitis secondary to hepatitis C virus is more prevalent in district Tharparker of lower Sindh province that is why it is important to know the response of conventional interferon therapy in Chronic HCV naïve patients of the area.

**Objective:** to determine the end treatment response in chronic hepatitis c naïve patients by standard interferon therapy in rural area of Sindh

**PATIENTS AND METHODS:** A total of 146 patients with chronic hepatitis secondary to HCV included for treatment with conventional interferon and ribavirin therapy. The patients enrolled at district District Head Quarter Hospital Mithi @ Tharparker, Sindh, Pakistan. The real time PCR done in all patients to confirm active HCV infection, treatment with conventional interferon and ribavirin started for six months. At the completion of therapy, end of treatment response (ETR) calculated.

**RESULTS:** Among 146 treated patients, 124 (84.9%) showed end treatment response and HCV RNA on PCR was undetectable. While 22 (15.1%) patients had positive HCV RNA on real time PCR hence not responded to this treatment. Efficacy with conventional interferon was relatively better in age group of 25 to 40 years in both sexes.

**CONCLUSION:** It concluded that response with conventional interferon against chronic Hepatitis C virus patients in District Tharparker Sindh is approximately 85%. This high response rate may be due to the prevalence of IFN-responsive HCV genotypes in the area.

**KEYWORDS:** ETR, conventional Interferon, Ribavirin, Hepatitis C Naïve patients, Rural Area, Sindh.

#### Corresponding author:

**\*Dr. Pooran Mal,**

Assistant Professor,

Department of Nephrology,

Liaquat University of Medical and Health Sciences (LUMHS),

Jamshoro

**Email:** zulfikar229@hotmail.com

QR code



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**INTRODUCTION:**

Hepatitis C leads to chronic hepatitis and globally it is the major health issues with prevalence rate of 5% worldwide, more than 150 million patients are affected with chronic hepatitis. Among them more than 350 000 people die due to HCV related complications yearly [1]. Hepatitis C has affected around 5% general population of Pakistan with approximately 8.3 million people exposed to this virus thereby creating a huge pool of patients who might require treatment [2]. Over 10 studies reported from various institutions in Pakistan show that over 80% of hepatitis C virus infected population has genotype 3 [3] with a prevalence of between 75-90% [20,21]. The long-term effects of hepatitis C virus are highly variable from patients to patients and may result in minimal damage to extensive fibrosis, and cirrhosis of liver and may be associated with hepatocellular carcinoma (HCC) [4]. Up to now six genotypes of hepatitis c virus (HCV) has been found. In USA and Europe, genotype 1a and 1b is more common. The Mediterranean region has high prevalence with genotype 2 while 3a is more common in European intravenous drug abusers. In Middle East genotype 4 is more common. Pakistan has more patients with genotype 3 but genotype 1, 2 and 4 is also seen sporadically [5,6]. Pegylated interferon (PEG-INF) with ribavirin can be used for treatment in those patients who are non-responder to standard INF-a and ribavirin other than HCV genotype 1.<sup>4</sup> Viral load levels have no such important role in deciding duration or type of therapy since genotype 3 is treated with conventional treatment irrespective of the viral load [7,8]. The American and European studies does not recommend standard interferon for genotype 1 or 3; instead PEG-IFN is used with ribavirin [9,10]. Because in these countries the common genotype is 1 or 4; hence recommended therapy is PEG interferon with ribavirin.

In Pakistan, conventional INF-a is still used due to its cost effectiveness and considering that genotype 3 is more common in this region and will, therefore, show an excellent response with a sustained virological response (SVR) of 80% to 86.4% [11-15].

There are no recent local guidelines available for the management of HCV infected patients considering the diversity of our genotypes. Also there is no recent international published literature which recommends the use of standard Interferon (INF) with Ribavirin for management of naïve cases of hepatitis C virus in genotype other than genotype 1. Apart from Pakistan Society of Gastroenterology recommendation,<sup>14</sup> no other literature recommends to treat HCV standard interferon with ribavirin. This research was

conducted to find out the end treatment response (ETR) in naïve patients with chronic hepatitis C Infection who were receiving conventional interferon for six months period in Tharparkar District of Sindh Province. Currently Pegylated INF- $\alpha$  and Ribavirin for 24 to 48 weeks is approved as initial therapy, but is more costly. This study will help physicians to predict the success of therapy and specially to deal the chronic hepatitis C patients of remote area of Sindh who have economic constraints and are being treated through the Chief Minister's hepatitis prevention and control program.

**PATIENTS AND METHOD:**

This study is an observational case series study. It was conducted from January 2010 to February 2013 at District Head Quarter Hospital Mithi @ Tharparkar, Sindh, Pakistan. Total 146 adult Patients aged 16 to 60 years, of both sexes, having Anti HCV antibody positive on Elisa selected for this study, the sample size was calculated by Raosoft and the sample technique was non probability consecutive. Polymerase chain reaction (PCR) with Qualitative RNA (Ribonucleic acid) assay was done to confirm chronic hepatitis due to HCV infection. Patients with age younger than 15 years and older than 60 years, alcoholics, with co infection HBV and Delta Virus, clinical/biochemical and radiological criteria of liver cirrhosis and autoimmune hepatitis were excluded from study. PCR positive patients with normal cognitive functions, high normal ALT level, hemoglobin and platelets within normal range were selected to treat with INF- $\alpha$ 2a (3million units three times a week) with Ribavirin (1000-1200 mg/day) for 24 weeks. Liver function tests (LFT) and PCR for HCV RNA checked during and at the completion of therapy. The End of Treatment Response (ETR), defined as undetectable HCV RNA on PCR assay at 6 months or completion of therapy. SPSS software version 16.0 used analysis of data, the frequency and percentage was calculated for categorical variables while the mean  $\pm$ SD was calculated for numerical variables.

**RESULT:**

At the completion of therapy at six months result calculated. Among 146 patients, male were 98(67.1%) and 48 (32.9) were female; age mean was calculated 35.63 years. 124 (84.9%) patients had negative HCV RNA on PCR hence end treatment response (ETR) achieved, whereas 22 patients (15.1%) were positive for HCV RNA and not responded to this therapy.

Out of 124 patients 84(67.74%) were male and 40 (32.25%) were female in whom ETR was achieved while in 22 patients 14 (63.63) male patients and 8

(36.36) female patients ETR was not achieved. (Figure 2& 3) In this study better response observed with conventional interferon therapy in age group of 25-40 year. (Figure 1)

The overall end treatment response obtained was 84.9%.

**Table 1:END TREATMENT RESPONSE**

RNA IN PCR	Frequency	Percent	Valid Percent	Cumulative Percent
NOT DETECTED	124	84.9	84.9	84.9
DETECTED	22	15.1	15.1	100.0
Total	146	100.0	100.0	

**Bar Chart**

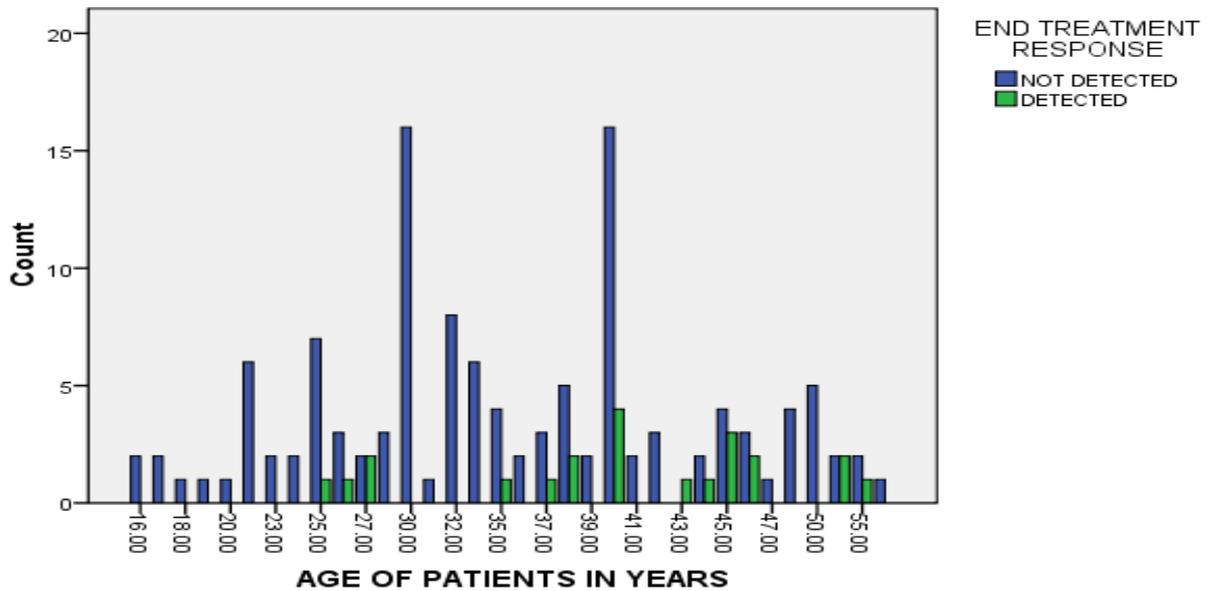


Figure 1

**GENDER OF PATIENTS=MALE**

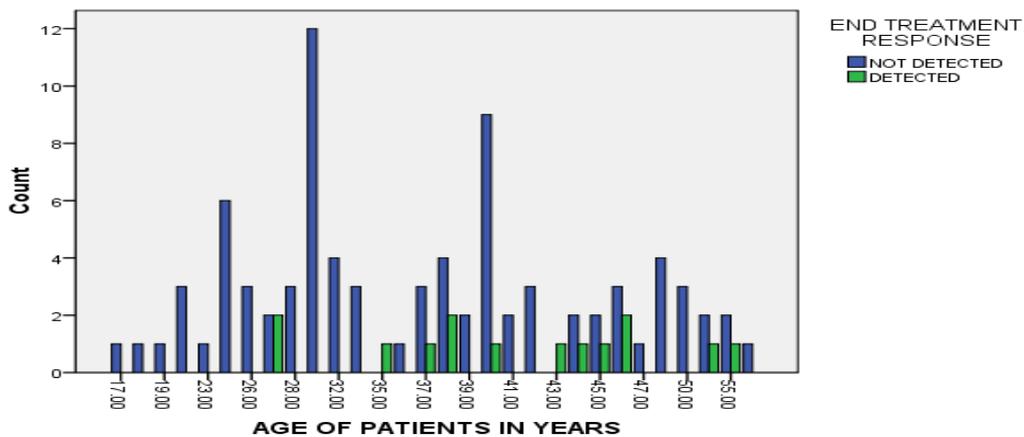


Figure 2 : ETR in Male Patients

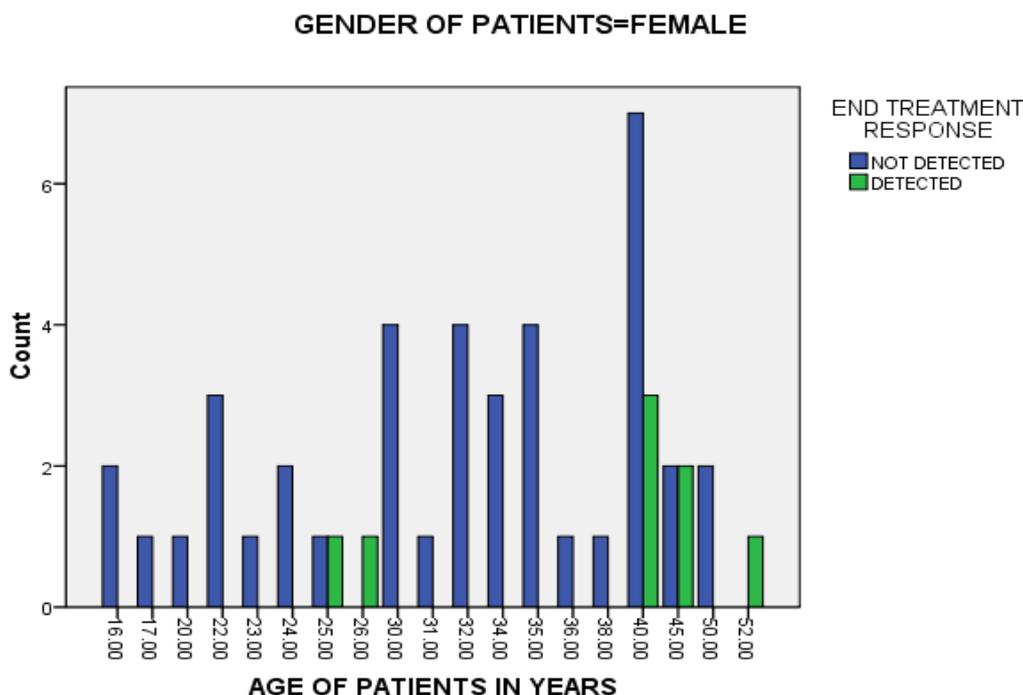


Figure 3: ETR in Female Patients

**DISCUSSION:**

Chronic hepatitis secondary to HCV infection is found endemically in different parts of the world with overall estimated prevalence of 3%. A large number of cases of cirrhosis of liver and liver cancer are found due to chronic HCV infection. A similar study from Khyber Pakhtunkhwa, Pakistan in HCV virus infections determined ETR rate 74.71%.<sup>12</sup> and End treatment response (ETR) was 89.3% was found in another study conducted at Combined Military Hospital, Quetta.<sup>15</sup> Cases of hepatitis C virus are rapidly rising in Pakistan. At present approximately 200 million people are infected with HCV all around the world and 3-4 million more people are acquiring HCV infection every year. WHO has reported that at present India is having more than 20 million HCV infected people as compared to sero-prevalence rate in our country is around 2.4%.<sup>1</sup> In different regions of our country sero-prevalence of HCV infection found between 2.2-13.5% in last few years.<sup>16</sup> The sero-prevalence rate reported in Mardan district Pakistan around 9%. The overall sero-prevalence was found to be 9% in district Mardan, Pakistan and the highest cases reported in Lahore.<sup>17,18</sup> In Pakistan studies were conducted to determine the ETR in patients treated with standard IFN in HCV patients because still this therapy is commonly used under chief Minister Programs in Government setups due to poverty of patients who cannot afford costly drugs. Those patients who fail to respond or relapse after treatment with conventional interferon the

pegylated INF therapy is recommended for retreatment of such cases while HCV genotype 1 treated with pegylated interferon showed sustained viral response (SVR) around 40-54% at approved dose of Pegylated interferon plus ribavirin for 48 weeks. On the other hand SVR was around 65-82% in patients with HCV genotypes 2 or 3 treated with pegylated IFN- $\alpha$  plus ribavirin at approved doses for 24 weeks. Our study determined the End of Treatment Response (ETR), defined as undetectable HCV RNA on PCR assay at the completion of six months IFN therapy, in patients with chronic HCV infection. The end treatment response (ETR) calculated was 84.9% and 15.1% patients found to have resistance to the treatment.

**CONCLUSION:**

Our study shows that with standard interferon antiviral therapy 84.9% showed positive response hence end treatment response achieved. This high response rate may possibly be due to genotype 2 or 3 and geographical difference and adherence of therapy.

**REFERENCES:**

1. Mohamed AA, Elbedewy TA, Serafy ME, El-Toukhy N, Ahmed W, El Din ZA. Hepatitis C virus: a global view. *World J Hepatol.* 2015 Nov 18; 7(26): 2676-2680.
2. Qureshi H, Bile K, Jooma R, Alam S, Afridi H. Prevalence of hepatitis B and C viral

- infections in Pakistan: findings of a national survey appealing for effective prevention and control measures. *Eastern Mediterranean Health Journal*. 2010;16:S15-23
3. Infectious Diseases Society of Pakistan. Volume 17 Issue 03. Jul-Sep 2008.
  4. EASL Clinical Practice Guidelines: Management of hepatitis C virus infection. *Journal of Hepatology* 2011 vol. 55 j 245–264.
  5. Simmonds P, Bukh J, Combet C, Deleage G, Enomoto N, Feinstone S, et al. Consensus proposals for a unified system of nomenclature of hepatitis C virus genotypes. *Hepatology*2005; 42:962-73.
  6. Idrees M, Riazuddin S. Frequency distribution of hepatitis C virus genotypes in different geographical regions of Pakistan and their possible routes of transmission. *BMC Infect Dis* 2008; 8:69.
  7. Sarwar S, Khan AA, Alam A, Butt AK, Shafqat F, Malik K, et al. Value of quantitative HCV RNA in management of chronic hepatitis C patients with genotypes 2 and 3. *Liver International*. 2005; 25:1275-6.
  8. Chow W, Gane E, Unit NLT, Hamid S, Jafri W, Lai M, et al. Asian Pacific Association for the Study of the Liver consensus statements on the diagnosis, management and treatment of hepatitis C virus infection. *Journal of gastroenterology and hepatology*. 2007; 22:615-33.
  9. Chevaliez S, Pawlotsky J-M. Diagnosis and management of chronic viral hepatitis: antigens, antibodies and viral genomes. *Best Practice & Research Clinical Gastroenterology*. 2008; 22:1031-48.
  10. Sarrazin C, Susser S, Doehring A, Lange CM, Muller T, Schlecker C, et al. Importance of IL28B gene polymorphisms in hepatitis C virus genotype 2 and 3 infected patients. *J Hepatol* 2011; 54:415-21.
  11. Aziz S, Qamar R, Ahmed I, Imran K, Masroor M, Rajper J, et al. Treatment profile of hepatitis C patients: a comparison of interferon alpha 2a and 2b treatment regimes. *J Coll Physicians Surg Pak*2010; 20:581-5.
  12. Ahmad B, Ali S, Ali I, Azam S, Bashir S. Response rates of standard interferon therapy in chronic HCV patients of Khyber Pakhtunkhwa (KPK). *Virology journal*. 2012; 9:18.
  13. Aziz S. Pegylated Interferon Treatment in HCV Genotype 2 and 3 Patients Refractory to Conventional Interferon. *Journal of the College of Physicians and Surgeons Pakistan*. 2012; 22:615-6.
  14. Hamid S, Umar M, Alam A, Siddiqui H, Qureshi H, Butt J. Member of the consensus panel. PSG consensus statement on management of hepatitis C virus infection - 2003. *J Pak Med Assoc*2004; 54:146-50.
  15. Jadoon SM, Jadoon S, Muhammad I. Response to standard interferon A2b and ribavirin combination therapy in chronic hepatitis C treatment naive patients. *J Ayub Med Coll Abbottabad*. 2010; 22:164-6.
  16. Chaudhary IA, Khan SS, Majrooh MA, Alvi AA. Seroprevalence of hepatitis-B and C among the patients reporting in surgical OPD at Fauji Foundation Hospital, Rawalpindi: Review of 5 year literature. *Pakistan Journal of Medical Sciences*. 2007;23:514-7
  17. Khan MSA, Khalid M, Ayub N, Javed M. Seroprevalence and risk factors of hepatitis C virus (HCV) in Mardan, NWFP: a hospital based study. *Rawal Med J*. 2004; 29:57-60.
  18. Almani S, Memon A, Qureshi A, Memon N. Hepatitis viral status in Sindh. *Professional Med J*. 2002; 9:36-43.