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STUDY TO KNOW THE MAJOR DETERMINANTS OF SUSTAINED VIRAL RESPONSE AS GENOTYPE OR VIRAL RESPONSE IN CHRONIC HEPATITIS C PATIENTS

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Abstract:

Objective: *This study was conducted to evaluate the predictive power of some additional factors in our population taking conventional interferon. Thus, we can reduce the rate of relapse and therefore improve the sustained viral response.*

Study design: *An observational study.*

Location and Duration: *In the medicine Unit II of Services Hospital Lahore for one year duration from July 2017 to July 2018.*

Methods: *The qualitative variables, age, ALT at the beginning of treatment, sex, abnormal alanine aminotransferase (ALT), HCV genotype at the beginning of treatment, and the achievement of the Final Treatment Response (ETR) were recorded. Sustained viral response and the viral load of HCV are quantitative variables. 75.3% of the 235 patients reached the ETR, while only 76.8% of them reached the sustained viral response. ETR and sustained viral response were statistically correlated with patient age, sex, ALT, viral load and HCV genotype.*

Results: *ETR was found to be 75% in male gender and 76% in females. SVR was 2.158 times higher in males than females and 2.98 times higher in ETR than younger than 40 years. ETR was found to be 75% in patients with abnormal onset ALT and 54% in patients with abnormal baseline ALT. ETR was found in 76% of subjects with decrease viral load and sustained viral response value was 24.29 times higher in patients with low viral load and the relationship was significant statistically ($p = 0.000$). Genotypes 3a, 2a, 3b, 2b and patients with incomprehensible HCV had an ETR of 77%, 72%, 81%, 75%, and 68%, respectively, and the relationship was statistically insignificant ($p = 0.856$) with genotype 3a. , 2a, 3b, 2b and non-typeable SVR values were 58%, 54%, 64.5%, 65% and 21%, respectively, and the relationship was significant statistically ($p = 0.025$).*

Conclusion: *Overall sustained viral response with standard ribavirin and interferon therapy was low in subjects and was due to marked erosion of patients after reaching ETR; Otherwise, SUSTAINED VIRAL RESPONSE was 76.8% in the participants for follow-up.*

Key words: *chronic hepatitis C virus (HCV), HCV viral load, HCV genotype, end of treatment.*

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INTRODUCTION:

Hepatitis C is caused by hepatitis C virus (HCV) infection. 3% of the Global population, 6% of Pakistan's nation is infected with the virus, while the most common virus genotype is 3. Pegylated interferon is a better option than conventional management for hepatitis C in chronic stage, and is now considered the standard treatment for infected patients[1-3]. Due to the significant difference in cost, standard interferon-ribavirin combination therapy remains the preferred regimen for genotypes 2 and 3, particularly in developing countries[4-6]. The virus, which cannot be detected at the last of the 24-week or 48-week treatment period, is known as the (ETR) end-of-treatment response. Relapse is determined as the re-emergence of RNA of HCV in serum after stopping treatment[7]. Therefore, the HCV test should be done once a year for minimum 2 years after completing treatment to note recurrence. If the patient relapses or does not respond to conventional interferon, a new treatment with pegylated interferon is required[8]. A large number of patients with recurrent and unresponsive to conventional interferon and ribavirin treatment require expensive treatment with pegylated interferon[9]. Even after the large expenditure of patients, the response rate will be only 20% to 11% compared to 93% for treating naive patients[10]. A BMI higher than 30 was linked with poor response therapy.

MATERIALS AND METHODS:

This is an observational study conducted between July 2017 to July 2018 for one year duration from August 2017 to August 2018 in the Medicine Unit II of Services Hospital Lahore. During this period, a total of 317 patients were treated with conventional ribavirin and interferon. 235 patients who completed the treatment with regular visits were included in the study. Qualitative variables were sex, abnormal alanine aminotransferase (ALT), HCV genotype, ETR success and SVR success rate at the beginning of treatment, age, ALT amount and load at the beginning of treatment. HCV had quantitative variables. All data were interpreted with negative or positive values. For the presentation of qualitative variables, frequencies and ranges were calculated and mean and standard deviations were calculated for quantitative variables. The data were retrospectively evaluated in SPSS version 17.

RESULTS:

Two hundred and thirty-five patients with chronic viral hepatitis C who received interferon treatment with ribavirin were included in the study, 28.5% were male and 71.5% were female. The mean age (year) of the patients was 10.27 ± 38.43 ± SD, the mean ALT (UI / L) was 54.22 ± 74.54 ± SD, and the mean viral load (IU / ml) as 1732056,663. Genotype 3a (47.2%), genotype 2a (23.2%), genotype 3b (13.2%), genotype 2b (8.5%) and genotype (8.1%) were found in most patients. Irreplaceable Only 7 (3%) patients had ALT in their normal range at the beginning of interferon therapy and 228 (97%) patients had abnormal ALT (Table 1, 2).

Table 1: Quantitative Factors associated with SVR in chronic hepatitis C patients of Azad Kashmir (n=235)

Quantitative variables	Minimum	Maximum	p-value
Age of patients (years)	20	60	0.013
ALT (IU/L)	45	86	0.393
Viral Load (millions IU/ml)	1.6	10.5	0.003

Of the 235 patients, 177 (75.3%) responded to the last treatment (ETR), while only 135 (76.7%) received a SVR. ETR and SVR were statistically correlated with patient age, gender, ALT (IU / L), viral load (IU / ml) and HCV genotype. ETR was found in 76% of men (51 of 67) and 75% of women (126 of 126), and the association was not significant statistically (p = 1,000).

Table 2: Qualitative Factors associated with ETR in chronic hepatitis C patients of Azad Kashmir (n=235)

Qualitative variables	ETR achieved (n=177)	ETR not-achieved (n=58)	Likelihood Ratio	p-value
Male	51 (76%)	16 (24%)	0.032	1.000
Female	126 (75%)	42(15%)	0.010	1.000
<40 yrs of age	99 (76%)	32 (24%)	0.010	1.000
≥40 yrs of age	78 (75%)	26 (25%)		
ALT(IU/L) abnormal	172(75%)	56(25%)	0.057	0.683
ALT (IU/L) normal	5(71%)	2(29%)		
Viral load(IU/ml) high	78(75%)	26(25%)	0.010	1.000
Viral load(IU/ml) low	99(76%)	32(24%)		
HCV genotype a	85(77%)	26(23%)	1.327	0.856
HCV genotype a	39(72%)	15(28%)		
HCV genotype b	25(81%)	6(19%)		
HCV genotype a	15(75%)	5(25%)		
Untypable	13(68%)	6(32%)		

The sustained viral response was 52% in men (67 in 35), 60% in women (101 in 168). Although SVR was 2.158 times higher in women than men, this relationship was not statistically significant (p = 0.149). SUSTAINED VIRAL RESPONSE was found in 62.5% (82 of 131), 52% of patients aged 40 and over (54 of 104) in patients younger than 40 years of age. Although SVR was 2.98 times higher in younger patients under the age of 40 compared to those under 40 years of age, this relationship was not statistically significant (p = 0.088). ETR was found to be 75% in patients with abnormal onset ALT (228 to 172) and in 71% of patients with normal ALT (7/5) and the relationship was not statistically significant (p = 0.683). SUSTAINED VIRAL RESPONSE was found to be 54% in patients with abnormal initial ALT (228 in 124) and 86% (7/6) in patients with normal ALT.

Table 3: Qualitative Factors associated with SVR in chronic hepatitis C patients of Azad Kashmir (n=235)

Qualitative variables	SVR achieved (n=136)	SVR not-achieved (n=99)	Likelihood ratio	p-value
Male	35(52%)	32 (48%)	2.158	0.149
Female	101(60%)	67 (40%)		
<40 yrs of age	82 (60%)	52 (40%)	2.98	0.088
≥40 yrs of age	54 (49%)	53 (51%)		
ALT(IU/L) abnormal	130 (57%)	98 (43%)	3.054	0.134
ALT (IU/L) normal	6 (86%)	1 (14%)		
Viral load(IU/ml) high	42 (40.4%)	62 (59.6%)	24.29	0.000
Viral load(IU/ml) low	94 (71.7%)	37 (28.3%)	11.15	0.025
HCV genotype a	64 (58%)	47 (42%)		
HCV genotype a	29 (54%)	25 (46%)		
HCV genotype b	20 (64.5%)	11 (35.5%)		
HCV genotype a	13 (65%)	5 (35%)		
Untypable	4 (21%)	15 (79%)		

Although sustained viral response was 3.054 times higher in patients with normal ALT than patients with abnormal ALT, this relationship was not statistically significant (p = 0.134). Viral load was labeled as ≥400,000 IU / mL, high viral load, Viral load <400,000 IU / mL, low viral load. ETR was found in 75% of patients with high viral load (78 of 104) and 76% of patients with low viral load (99% of 131) and the relationship was not statistically significant (p = 1,000). SVR was found in 37.5% (104%) of patients with high viral load and 69.5% (91 of 91) in those with low viral load. In patients with low viral load, the SVR was 24.29 times higher than in those with high viral load and the relationship was statistically significant (p = 0.000). HCV Genotypes 3a, 2a, 3b, 2b and 77%, 72%, 81%, 75% and 68% ETR were not significant in HCV Genotype patients (p = 0.856). 3a, 2a, 3b, 2b and undetectable had respectively 58%, 54%, 64.5%, 65% and 21% SVR, and the relationship was statistically significant

(p = 0.025). The atypical genotype was unfavorable for SVR.

DISCUSSION:

Pakistan is a high-load state of hepatitis C patients. The role of predictive factors in reducing the rate of treatment failure in these patients with hepatitis C is very important[11-12]. The best way to guide antiviral therapy in these patients is to treat patients who only respond continuously[13]. However, the positive estimation of a continuous virological response is still not easy, although various base estimates have been determined: genotype two or three, a basal viral load of below than 2 to 3.5 million copies / mL (581,111-1,018,020 IU / mL) not only portal fibrosis, but female gender and age under 40 years were determined. In the retrospective analysis of chronic HCV cases taking interferon therapy, ETR was 75.3% and SVR was only 76.8%[14]. Poynard et al Found that in the optimal population with all the characteristics of the positive prediction, standard combination therapy with IFN-plus ribavirin had a continuous virological response rate of 79%. This means that if we consider positive predictors for treating patients with hepatitis C, sustained viral response can be improved[15]. Retrospectively, in our study, we found that SVR was 24.29 times more (p = 0.000) in patients with low viral load compared to patients with high viral load, and that the non-transient genotype was not suitable for SVR(p = 0.000). = 0.025). In 2004, Ferenci, 18 found that the ongoing viral response was 1.5-fold higher in patients with hepatitis C with low viral load (<2 million copies per milliliter, 800 IU / mL) compared to patients with high viral load. Muto et al. Patients with a viral load greater than 2,000,000 copies per milliliter or greater than 800,000 IU / mL have the worst reactions.

CONCLUSION:

The total sustained viral response given to treatment with standard ribavirin and interferon was low in patients and was more dependent on the loss of patients after reaching ETR; Otherwise, SVR was 76.8% for those who followed. Assessment of predictive response factors such as viral load and genotype may help to individualize treatment, patient selection, and reduction in an increasing number of patient groups that do not respond and do not reappear.

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