DOI: https://doi.org/10.53350/pjmhs2216334

ORIGINAL ARTICLE

Treatment of Hepatitis C Disease with Standard Therapy and its Correlation with Specific Genotype of Interleukin

UMAR ALEEM[1], FALAK NAZ[2], RAHMAN SHAH[3], SAIFULLAH KHAN KHALIL[4], NAJEEB ULLAH[5], NAIMAT ULLAH[6]
[1]Associate professor. Pharmacology Deptt., Saidu Medical College, Swat
[2]Demonstrator, Khyber Medical College, Peshawar
[3]Associate professor. Pharmacology Deptt. Swat Medical College, Swat
[4]Assistant Professor, Pharmacology Deptt, Kabir Medical College, Peshawar
[5,6]Assistant Professor, Pharmacology Deptt., Saidu Medical College, Swat
Correspondence to Dr. Umar Aleem, Associate professor. Pharmacology Deptt. Saidu Medical College, Swat

ABSTRACT

Aim: To determine the association of interleukin-28b- RS12980275 with response to treatment with interferon α-2b & ribavirin in chronic hepatitis c patients
Methodology: A case control study was designed that includes219 HCV patients treated with INF and Ribavirin. Out of 219, 95 were males while 124 were females. They are classified into two groups. Those achieved sustained virological response (SVR) and those who did not sustained virological response (Non-SVR). All the demographics and biochemical data were recorded on a Performa that includes age, ALT and viral load. The data were analyzed using SPSS version 16.0.
Results: Patients having IL28B-rs12980275 AG genotypes respond better to interferon and ribavirin treatment (p-value=0.01, OR=2.91). Furthermore, HWE was also calculated for both groups in which the responders do not corresponds to HWE (p-value= <0.001) while the non-responders were found to be consistent with HWE (p-value= 0.31).
Conclusion: Polymorphism in IL28B (rs12980275) was found to be significantly associated (p-value = 0.009) with the treatment outcome in patient with hepatitis C receiving standard therapy regimen (Interferon + Ribavirin).
Key words: Hepatitis C, polymorphism, Interferon

INTRODUCTION

About 3% of the cases with chronic hepatitis C are all over the world. The prevalence of HCV is highly variable and higher in Egypt i.e. 6-8%. This may be due to IV antischistosomal therapy in the region. In USA, it is about 1.8 %[1].

Hemophilic patients have prevalence rate is about 98%, and the prevalence is variable in hemodialysis patients[2].

METHODOLOGY

This case control study was conducted. Sampling was done from major health care centers of D.I.Khan and experimental work was done in IBMS, KMU.
Inclusion Criteria: Patients with CHC who have completed therapy
Exclusion Criteria

- Patients above 50 years of age.
- BMI <18.5 or above 30.
- Cirrhotic patients, Patients complicated with metabolic disorders.

Sample Collection: About 5cc blood was drawn. All the samples were stored at 4°C. The demographic data includes age, gender, ethnicity, treatment strategy and other complications resulting from HCV.

RESULTS

Table 1: Characteristics of cases and controls

	SVR	Non-SVR	Total Cases
Gender (M/F)	59/72	36/52	95/124
Age (mean ±SD)	40.5 ± 10	43 ± 10	41.5 ± 10
ALT (mean±SD)	107 ± 102	132 ± 110	119 ± 105
Viral Load	2*103-1*107	1*103-2*107	1*103-2*107

Table 2: rs12980275 Genotypes distribution

	A	G	AA	GG	AG
Responders	123	156	57	9	9
Non Responders	27	42	74	34	8
Total	150	198	131	43	17

Received on 19-09-2021
Accepted on 26-02-2022

Table 3: Calculation of Hardy-Weinberg Equilibrium (HWE)

Responders				
Genotype	**Observe value**	**Predictive value**	**χ2**	**p-value**
AA	57	50.4	26.41	0.000
GG	09	22.1		
AG	09	2.4		
Non-responders				
Genotype	Observe value	Predictive value	χ2	p-value
AA	74	72.1	1.01	0.31
GG	38	41.9		
AG	08	6.1		

Table 4: Association between rs12980275 with Interferon response

A vs G					
	A	**G**	**p-value**	**Odds Ratio**	**Confidence interval**
Responders	123	156	0.4988	1.22	0.71- 2.1
Non-responders	27	42			
Total	150	198			
AA vs GG					
	AA	GG	p-value	Odds Ratio	Confidence Interval
Responders	57	74	0.002	3.25	1.22 – 4.22
Non-responders	9	38			
Total	66	108			
AA vs AG					
	AA	AG	p-value	Odds Ratio	Confidence Interval
Responders	57	9	0.6052	0.6847	0.248-1.88
Non-responders	74	8			
Total	131	17			

DISCUSSION

In responders group, 57 (66%) shows AA genotypes, 9(4.1%) shows GG and AG respectively while in non-responders, 74(33.8%) shows AA, 34(15.5%) shows GG and 8(3.6%) shows AG genotypes. These results were similar with previous studies conducted on 220 patients who were chronic hepatitis C it is found that homozygous genotype AA was present in responder group in much higher proportion 62% then non responder 37.5% and

genotype AG was found in increase proportion in non-responder group that is 46.7% then in responder group which is 25%.This result showing that AA genotype of rs12980275 has strong association in our population studied. Previously AA homozygous was found to have association in response to treatment and AG was in non-responder HCV Chilean patients[7]. The Hardy-Weinberg Equilibrium (HWE) was calculated for responders and non-responders. The responders were not consistent with HWE (p-value = 0.000) while the non-responders were found to be consistent with HWE (p-value = 0.31)

Regarding association of Interleukin-28B- rs12980275 with response to treatment with Interferon α-2b & ribavirin, the results show significant association to the treatment outcome. Individuals with AG genotypes respond better to Interferon α-2b & ribavirin treatment. (p-value = 0.09). This particular SNP (rs 12980275) was also reported by GWAS on different populations, as strong SNP in association with chronic hepatitis C treatment[5].

In another study, it is found that rs12980275 is a very strong positive predictor of response to non-PEG. Also it is found that AA genotype attained fast virological response to treatment in comparison to those who carries non AA loci[8]. It has also been found that homozygous CC at 12989860, AA at 12980275 and TT at rs8099917 are significantly more common in patients who are having infection with genotype 2 and 3 than genotype 1 in Caucasian patients only and it also confirms the findings reported by McCarthy et al[6].

Our study showed that IL-28B genes polymorphism rs12980275 have association with chronic HCV treatment in Pakistan population. It is also reported that 3SNP's, which is highly associated with favorable response to treatment in chronic hepatitis C patients infected with genotype1 is rs 12989860[3], rs12980275 (4), rs8099917[3].

These findings of different studies may help us in determining the treatment outcome in chronic hepatitis C patients by detecting responders and non-responder patients, which will be beneficial in decreasing side effects of the drugs and will also have effect on cost of the treatment.

CONCLUSION

Polymorphism in IL28B (rs12980275) was found to be significantly associated (p-value = 0.009) with the treatment outcome in patient with hepatitis C receiving standard therapy regimen (Interferon + Ribavirin). Furthermore, we have found that patients having AG genotypes of IL28B (rs12980275) respond better with the standard regimen of hepatitis C.

REFERENCES

1. Lehman EM, Wilson ML. Epidemiology of hepatitis viruses among hepatocellular carcinoma cases and healthy people in Egypt: International journal of Cancer. 2009;124(3):690-7.
2. Alavian SM, Mirahmadizadeh A, Javanbakht M et al. Effectiveness of methadone maintenance treatment in prevention of HCV transmission among injecting drug users. Hepatitis monthly. 2013;13(8).
3. Ge D, Fellay J, Thompson AJ et al. Genetic variation in IL28B predicts HCV treatment-induced viral clearance. Nature. 2009;461(7262):399-401.
4. Rauch A, Kutalik Z, Descombes P et al. Genetic variation in IL28B is associated with chronic hepatitis C and treatment failure: Gastroenterology. 2010;138(4):1338-45. e7.
5. Tanaka Y, Nishida N, Sugiyama M et al. Genome-wide association of IL28B with response to pegylated interferon-α and ribavirin therapy for chronic hepatitis C. Nature genetics. 2009;41(10):1105-9.
6. McCarthy JJ, Li JH, Thompson A et al. Replicated association between an IL28B gene variant and a sustained response to pegylated interferon and ribavirin. Gastroenterology. 2010;138(7):2307-14.
7. Venegas M, Villanueva RA, González K et al. IL28B polymorphisms associated with therapy response in HCV patients. World journal of gastroenterology: WJG. 2011;17(31):3636.
8. Lagging M, Askarieh G, Negro F et al. Response prediction in chronic hepatitis C by assessment of IP-10 and IL28B-related single nucleotide polymorphisms. 2011