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ORIGINAL ARTICLE

Association of Interleukin-28b- Rs8099917 with Response to Treatment with Interferon A-2b & Ribavirin in Chronic Hepatitis C patients

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

ABSTRACT

Aim: To determine the association of interleukin-28b- RS8099917 with response to treatment with interferon α-2b & ribavirin in chronic hepatitis C patients
Methods: A case control study has been designed. Those who respond to standard therapy were classified as responders while those who didn't respond to standard regimen were referred as non-responders. A total of 219 (95 males, 124 females) patients were recruited. All the demographics and biochemical data were recorded that includes age, ALT and viral load. The data were analyzed using SPSS version 16.
Results: The data reveals that polymorphism of IL28B- RS8099917 does not affect the treatment outcome (p-value=0.65, OR=1.52). Similarly, both responders and non-responder groups were not consistent with HWE with p-value 0.9 and 0.23 respectively.
Conclusion: polymorphism of IL28B- RS8099917 does not affect the treatment outcome Large multicenter studies must be conducted with large sample size to further validate our findings.
Keywords: Hepatocellular carcinoma, Cirrhosis, Interferon, Ribavirin, IL28-B

INTRODUCTION

WHO report says up to 3% of human population is affected by HCV worldwide. About 150-200 million people are having HCV infection[1]. About 27% cases of liver cirrhosis and 25% of hepatocellular carcinoma throughout world occurs due to HCV and about 35,000 people are dying yearly due to HCV and its complications. There are different HCV genotypes all over the world, most common is genotype 1 to 3[2].

The objective of the study was to determine the association of interleukin-28b- RS8099917 with response to treatment with interferon α-2b & ribavirin in chronic hepatitis C patients

METHODOLOGY

A case control study was designed. 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 a full course.
Exclusion Criteria:

- Patients with ages above 50 years
- Patients with body mass index <18.5 & above 30.
- Patients with hepatic cirrhosis (diagnosed through Ultrasound)
- Patients co-infected with HBV/HIV & or with alcohol consumption

Sample collection: 5cc blood was drawn for genetic analysis. The demographics including age, gender, ethnicity, treatment strategy and other complications resulting from HCV were obtained from the patients at the time of sampling.

RESULTS

Table 1: Patients Demographics

	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	$2*10^3$-$1*10^7$	$1*10^3$-$2*10^7$	$1*10^3$-$2*10^7$

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Fig 1: Allelic distribution

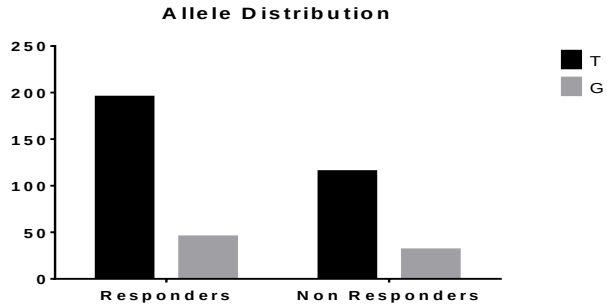

Fig 2: Genotypes distribution

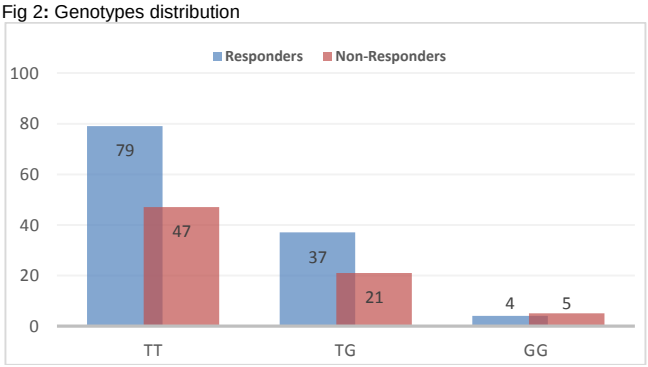

Table 2: Calculation of Hardy-Weinberg Equilibrium (HWE)

Responders				
Genotype	**Observed value**	**Predictive value**	**χ2**	**p-value**
TT	79	79.2	0.01	0.90
TG	37	36.6		
GG	04	4.2		
Non-responders				
Genotype				
TT	47	45.3	1.43	0.23
TG	21	24.4		
GG	05	3.3		

Table 3: Association between RS8099917 with Interferon response

T vs G	T	G	p-value	Odds Ratio
Responders	195	45	0.5981	1.168
Non-responders	115	31		
Total	310	76		
TT vs GG				
	TT	GG	p-value	Odds Ratio
Responders	79	04	0.30	2.10
Non-responders	47	05		
Total	126	09		
TT vs TG				
	TT	TG	p-value	Odds Ratio
Responders	79	37	1.0	0.95
Non-responders	47	21		
Total	126	58		

DISCUSSION

In control group, 59 were males while 72 were females. Similarly, in our cases, 36 were males while 52 were females. The mean age, ALT and viral load of both groups were 40.5±10/43±10, 107±102/132±110, $2*10^3$-$1*10^7$/$1*10^3$ -$2*10^7$ respectively.

Based on statistical analysis, the data reveals that polymorphism in IL28B rs8099917 does not showed any significant difference to treatment outcome between both cases and control group (p-value = 0.59). Similar results were also found in past where researcher did not found any significant treatment outcome in patient with IL28B rs8099917 polymorphism[3].

Studies including GWAS are failed in showing relationship between IL28-B polymorphism and sustained virological response in genotype 2 and 3 patients. Genome wide association studies have shown a strong association of IL28-B polymorphism with treatment outcome of CHC patients with combination therapy of interferon and ribavirin[4]. The most important and validated SNP relation to treatment outcome with combination therapy is rs12989860 and rs8099917. The rs 8099917 are having a strong association with HCV genotype 1 and 4. Several GWAS studies have found that rs8099917 is having association with NVR (Null virological response) and viral resistance which leads to failure of treatment[5].

Studies of Mangia et al[6] and Thomas et al[7] shows a possible role of IL28B in natural clearance of HCV genotype 2 from infected patients, implying that the lack of an apparent effect on natural clearance might be specific to HCV genotype 3. Hardy Weinberg equation is used to calculate the genetic variation of population at equilibrium. The Hardy–Weinberg principle, also called Hardy–Weinberg equilibrium (HWE), states that allele and genotype frequencies in a population will remain constant from generation to generation in the absence of other evolutionary influence[8].

In our study, both our cases and control were in HWE p-value = 0.90 and 0.23 respectively which means that there is no statistically significant difference between the observed and expected values. In this study, we can assume that polymorphism in IL28B rs8099917 does not shows any significant beneficial effect in treatment outcome in patient with CHC treated with Interferon and Ribavirin.

CONCLUSION

The IL28B rs8099917 polymorphism has no effect on patient with HCV (particularly those with genotype 3a) treated with ribavirin and interferon.

Conflict of interest: Nil

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