Research Article

Chronic HCV Patients' Liver Histology, Not Responding or Relapsing the Ribavirin and Conventional Interferon Therapy: A Descriptive Case Series Research Held at CMH, Lahore

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ABSTRACT

Objective: Our research was aimed at the liver histology evaluation of the hepatitis C chronic patients, who relapsed or they were non-responders in the previously held therapies.

Methods: Design of the research was descriptive case series which was held in the CMH, Lahore (HematologyDepartment) in the timeframe of February, 2016 – January, 2017. Sample of the research included a total of 109 cases diagnosed with hepatitis C, all the patients were the cases of relapsed or non-responders to ribavirin and conventional interferonfor a period of twenty-four weeks, these patients were treated through liver biopsy. Fibrosis and inflammatory activity as we observed showed that the assessment of the liver biopsies was according to the classification of the Batts-Ludwig. Statistical analysis was made through SPSS – 15.

Results: Maximumnumber of the cases was female in the total sample as observed 57 females (52.3%) which were diagnosed with the genotype virus of hepatitis C [3]. In the total sample there were 100 cases (91.7%) were of non-responders and 9 cases of relapses (8.3%). The factor of mean age was observed as (38.9±8.8) years. An elevated level of the serum aminotransferase was observed in the non-responders. According to the classification of the Batts-Ludwig,inflammation (Grade – 0) was absent in the relapsers and non-responders; 51cases were in Grade – I (46.8%); 47 cases were in Grade – II (43.1%); 10 cases were observed in Grade – III (9.2%) and 1 cases (0.9%) was observed in Grade – IV. Stage zero fibrosis was observed in ten cases (9.2%); 34 cases were observed with stage one (31.2%);36 cases were observed with stage two (33.0%); 13 cases were observed with stage three (11.9%) and 16 cases were of stage four (14.7%).

Conclusion: It is concluded that if the outcomes fail to reduce the incidence to hepatitis C virus or fail in the eradication of the said incidence, ribavirin therapy and conventional interferon were effective in the progression halt of the fibrosis and necroinflammation and fibrosis.

Keywords: Hepatitis C, Relapser, Non-responder, Conventional interferon and Ribavirin.

INTRODUCTION

Chronic infection of hepatitis C virus (HCV), with its sequelae, has become one of the important healthcare issues of Pakistan. According to the estimates of (WHO)almost 180 – million already has been affected by this virus; among these infected cases a total of 130 – million are the cases of choronic HCV and also face the risk of the progression of the cancer and liver cirrhosis.Newly infected cases are adding up annually at the rate of 3 – 4 million per year and chronic cases are observed in the range of 40 – 60 percent [1]. The situation demands for an Antiviraltherapy that can address the issue in hand and also manage the patients of HCV infection

whether new or chronic cases asa sustained virologic response (SVR); as this therapy possibly can stop the progression of the fibrosis. It also decreases the hepatocellular carcinoma risk with improved rate of survival [2, 3]. The Genotypes "3a & 3b"are prevalent in most of the cases in the Pakistani genotypes of HCV which are responsive to the ribavirin and interferon in the shape of a combined therapy [4 – 6].With the help of a conventional interferon – alpha three million units thrice per week having routine ribavirin as 800 – 1200mg for a period of six months, 3 randomized, controlledtrials in the research held at Taiwan, Sweden and Italy reflected higher rates of SVR for the first time as 43, 40 and 47 percent respectively [7]. Important tool considered is liver biopsy that determines the treatment response in the relapsers and non-responders of (IFN – 3) plus ribavirin therapy and their association to the biochemical and clinical characteristics. Our research was aimed at the liver histology evaluation of the hepatitis C chronic patients, who relapsed or they were non-responders in the previously held therapies.

PATIENTS AND METHODS

Design of the research was descriptive case series which was held in the CMH, Lahore (Hematology Department) in the timeframe of February, 2016 – January, 2017. Sample of the research included a total of 109 cases diagnosed with hepatitis C, all the patients were the cases of relapsed or non-responders to ribavirin and conventional interferon for a period of twenty-four weeks, these patients were treated through liver biopsy. Fibrosis and inflammatory activity as we observed showed that the assessment of the liver biopsies was according to the classification of the Batts-Ludwig. Statistical analysis was made through SPSS – 15. Ethical permission was taken from the hospital committee. Total female and males were 109 (above seventeen years) and they underwent chronic hepatitis C serological evidence byquantifiable serum HCVribonucleic (RNA) and anti – HCV antibody test. These patients had already been treated with conventional interferon (one course)three million units three times in a week and in addition to that ribavirin 800 – 1200 mg on regular basis daily for a period of twenty-four weeks. These cases as mentioned were made a part of the research. We informed and took permission from the patients about the research and also explained them the protocol of the research. A consultant was detailed for the carrying out of biopsies. Concomitant evidence of the infection of the B virus or D virus, decompensate cirrhosis, human immune deficiency (HIV) infection, intravenous drug abuse or alcohol, pregnancy,autoimmune disease and malignancy were not included in the research. Quantitative variables were calculated through Mean and SD.

RESULTS

In the total sample of 109 male and female ratio was as 57 females (52.3%) and 52 males (47.7%). The factor of mean age was observed as (38.9±8.8) years as shown in Table – 1. In the total sample of the research 100 patients (91.7%) never gained undetectable HCV RNA (PCR, qualitativepolymerase chain reaction testing) at the time of first treatment. They were considered as non-responders; whereas, 9 cases (8.3%) were observed with an undetectable HCV RNA at the time of therapy; whereas, it had become HCV RNA positiveafter the discontinuation of the medication and they were graded as relapsers. We observed Genotype – I in 29 cases (26.6%) and Genotype – IIIin 78 cases (71.6%). Two patients were observed with missing Genotype.Inflammation of Grade – I was observed in 51 cases (46.8%); 47 cases were observed with Grade – II (43.1%); 10 cases (9.2%) were observed with Grade - IIIone case was of Grade – IV as (0.9%). Stage zero fibrosis was observed in ten cases (9.2%); 34 cases were observed with stage one (31.2%); 36 cases were observed with stage two (33.0%); 13 cases were observed with stage three (11.9%) and 16 cases were of stage four (14.7%) as shown in Table – II.

Chronic Hcv Patients' Liver Histology, Not Responding or Relapsing the Ribavirin and Conventional Interferon Therapy:

Table – I: Demographics and baseline characteristics number =109

Characteristic		Non-responder n=100 (91.7%)	Relapser n=9(8.3%)
Sex	Male	48	4
	Female	52	5
	Age (mean ± SD)	39.19±8.91	35.89±8.35
HCV genotype	1	27	2
	3	73	6
	Missing	1	
function	Total bilirubin (mg/dl)	0.811±0.28	0.71±0.25
	Aspartate aminotransferase (U/L)	75.40 ±52.11	42.3±9.27
	Alanine aminotransferase (U/L)	68.46± 43.56	54.43±36.42
Abdominal ultrasound	Normal	40	4
	Hepatomegaly	16	3
	Hypoechoic liver	5	1
	Coarse liver &	8	0
	Splenomegaly	2	0
	Coarse liver	29	1
	Hemoglobin (g/dl)	12.3±2.33	12.1±1.24
	White blood cell count (/ml)	6412±2354	6722.22±2429.39
	Platelet count (×103/ml)	205±90	246±97

Table – II: Comparison of histo-pathological characteristics by Batts-Ludwig classification=109

Histological severity* Batts-Ludwig classification		Non-responder n=100		Relapser n=9	
		Number	Percentage	Number	Percentage
Grade of Inflammation	0	0	0	0	0
	1	48	48	3	33.3
	2	42	42	5	55.6
	3	9	9	1	11.1
	4	1	1	0	0
Stage of fibrosis	0	10	10	0	0
	1	31	31	3	33.3
	2	33	33	3	33.3
	3	11	11	2	22.2
	4	15	15	1	11.1

Comparison of histopathological characteristics
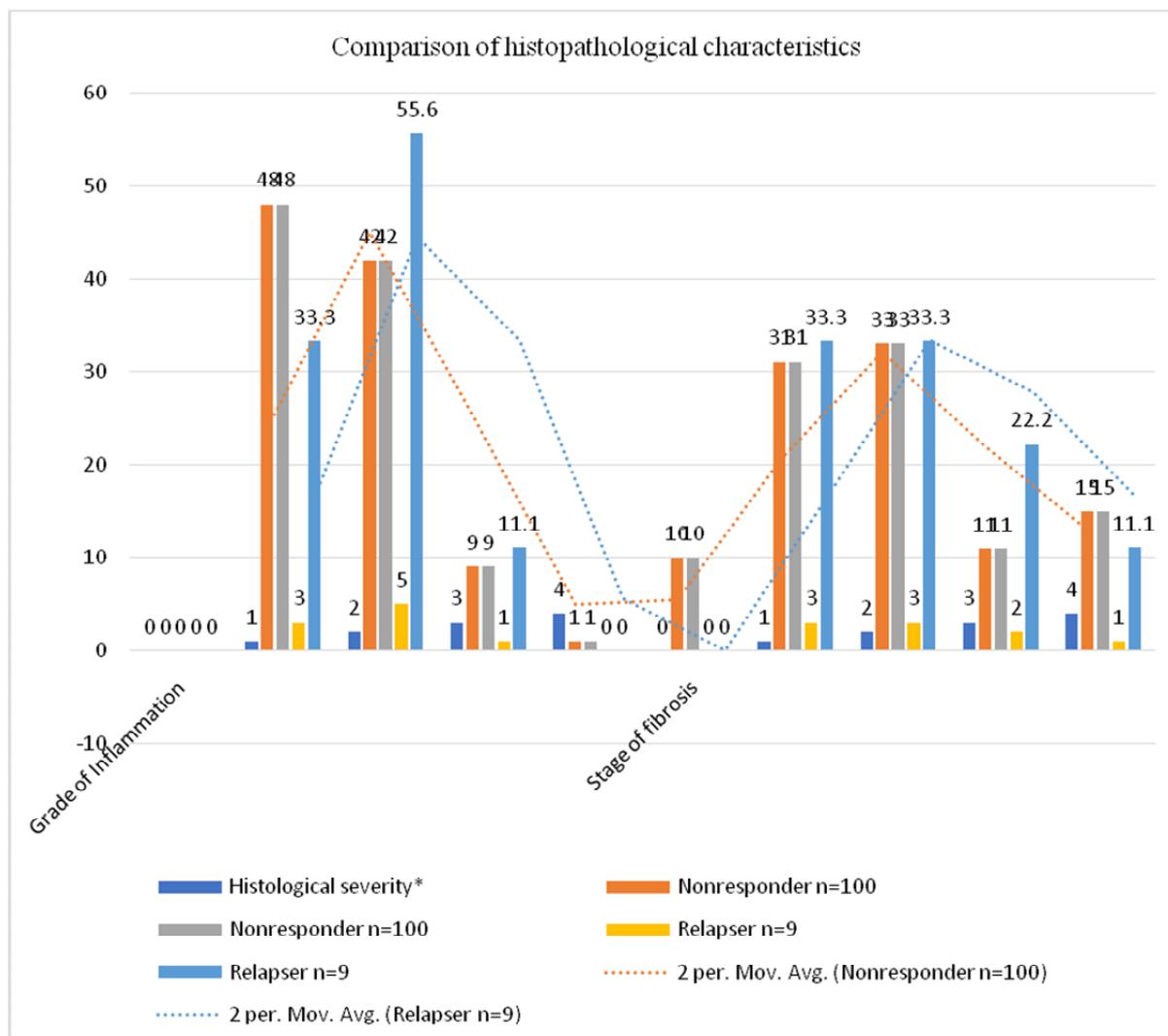
*Severity of the Histology: A grade is known as the portal degree, lobular and periportal activity which includes portal inflammation, liver cell degeneration, piecemeal necrosis, lobularinflammation and necrosis. The stage is known as the liver fibrosis extent.

DISCUSSION

The patients of Chronic hepatitis C which are relapsers and non-responders to ribavirin and conventional interferon (IFN) are known to be the most difficult clinical challenges in the setting of Pakistan. Available care standard for the treatment of the chronic hepatitis C combined with the pegylated interferon (PEG-IFN) therapy with ribavirin on the basis of the weight, has an SVR value of 70% – 90% in the patients of Asia when compared to the patients of Caucasian Area (50% – 80%) [8, 9].Pakistan is an underdeveloped country which faces the chronic HCV patients burden and this burden is increasing day by day. The prescription of the incidence is very difficult.

In the patients of Pakistan diagnosed with chronic hepatitis C, it is indicated through clinicalobservations that SVR which is obtained with the help of ribavirin and conventional IFN is more in comparison to the West [10]. For the severity evaluation of chronic liver disease, the hepatic fibrosis is known to be the primary endpoint. To assess the hepatic fibrosis gold standard consideration is given to the biopsy of liver [11]. In this research women were dominant in the incidence of HCV infection over males. Non-responders were observed with the factor of mean age as (39.19±8.9) years and the factor of mean age in the relapsers was observed as(35.89±8.3) years, counted as the productive

part. A number of cases were non-responders toconventional IFN therapy; whereas, relapsers were observed as 8.3% of the total sample population. Common most Genotype was observed as the Genotype III and I in the non-responders. Shin states in his Korean cohort research conducted on the patients of chronic hepatitis C that above fifty years of age was a risk factors for the relapsers in the cases of Genotype – I,higher levels of baseline HCV RNA; whereas, lower treatment adherence was important in the patients of Genotype II and III [12]. Our patients were not observed with older age as a factor of risk. Genotype influenced the responses of the treatment to an antiviral therapy including IFN plus ribavirin and higher SVR is with HCVGenotype II 0r III against the patients of HCV Genotype – I [13].A number of cases were relapsers and non-responders as we observed in our research having Genotype – III, it also reflects the HCV common genotype in the patients of Pakistan [14]. Higher levels of aminotransferase were observed in non-responders than the relapsers.Basso indicates about elevation of alanine aminotransferase (ALT) at the later stage ofan HCVRNA antiviral therapy in the negative patients which was linked to virologicrelapse [15].Our research outcomes forward that the level of aspartateaminotransferase (AST) and mean ALT were raised in the groups of non-responders than relapsers. The absence of baseline liver biopsy was a limitation of the research along with non-adherence of the levels of baseline HCV RNA. Another limitation of the research was the non-availability of the virological responses.

CONCLUSION

It is concluded that if the outcomes fail to reduce the incidence to hepatitis C virus or fail in the eradication of the said incidence, ribavirin therapy and conventional interferon were effective in the progression halt of the fibrosis and necro inflammation and fibrosis.

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