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Research Article

Affluent Prognosis of Hepatitis C after Interferon Therapy and Disease Epidemiology in Rawalpindi, Pakistan

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Abstract: Hepatitis C (HCV) affects around 3% of the world population and, thus, remains a global threat. Globally, Pakistan is at second place with regard to incidence of HCV, as 4.5-8.0% of its population is infected with HCV. Diagnosis of hepatitis C patients after interferon therapy is poorly demarcated till today. Aim of the present study was to evaluate effect of interferon, ribavirin combined therapy on survival of hepatitis C patients. This study was conducted in District Head Quarter (D.H.Q.) Teaching Hospital, Rawalpindi, Pakistan to diagnose hepatitis C after interferon combined therapy of the patients. The study span was one year and included 237 chronic hepatitis C patients. Hepatitis C diagnosis was made by polymerase chain reaction (PCR). Treatment response was evaluated by medical reports. All patients were educated for the follow-up; however, only 143 (i.e., 60%) out of the total 237 patients completed the 6-month interferon combined therapy; the remaining 94 patients (i.e., 40% of total) discontinued the treatment. The treated patients included 59 (i.e., 41%) of total 143 malesand 84(i.e., 59%) total females. Among male patients,45 (i.e., 76%)out of total 59exhibited treatment success, while 14(i.e., 24%) exhibited treatment failure. In case of female patients, 68(i.e., 81%) out of total 84 revealed treatment success and 16 (19%) revealed treatment failure. Treatment success was attributed to multiple factors, while failure occurred because of non-adherence to the treatment protocol, unawareness of the complications and/or concurrent infection with HIV.

Keywords: HCV, interferon, ribavirin, prognosis, treatment response, epidemiology

1. INTRODUCTION

Hepatitis C (HCV) affects around 3% of the world's population [1, 2]. It remains a global threat. Pakistan has second highest incidence with 4.5-8.0% [3]. Studies were conducted on small targeted groups in Pakistan, which included health professionals, blood donors and drug abusers. Rate of incidence is much higher in rural areas than peri-urban [4]. This is troublesome because rural areas comprises of 66% of Pakistan population [5].

Hepatitis C is instigated by HCV. The name HCV was given to a virus that produces most transfusion-associated non-A non-B hepatitis. HCV was recognized and clone in 1989.The diameter of HCV is 50 nm and is enveloped RNA virus. HCV is placed in family flaviviridae, with a separate genus hepacivirus. Hepatitis C has genomic organization and sequence related to flaviviruses and pestiviruses [6-12]. It is also the cause of acute and chronic liver disease, cirrhosis and liver cancer. Globally it is the major causeof liver transplant [13]. "If 100 persons infected with HCV then out of 100, 75 to 85 may develop chronic infection during 20-30 years. While 10-20 may develop cirrhosis, and 1-5 patients die due to complications of HCV, like liver cancer [14].

The prime objective of treatment is to lessen inflammation, cirrhosis, fibrosis and HCC (Hepatocellular carcinoma) progression [15].Better treatment responses could be achieved by combination therapy as compared tomonotherapy.Treatment decisions could be influenced by HCV genotypes. Sustained virological response (SVR) was considered as successful treatment indicator, because of the absence of detectable HCV RNA in serum (50 IU/ml or less) 24 weeks after treatment completion [14].

Interferon has significant role inHCV viral replication reduction, normalization of liver tests

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and lessens hepatic inflammation. Interferon is the best treatment option for HCV [15]. Interferon-A is given subcutaneously in a dose of 3 million units 3 times a week, for 24 weeks. After one month of treatment, patients indicate reduction in ALT and HCV RNA levels will mostly show sustained viralogical response.After a single course of drug therapy about 42 % to 80 % could clear the virus [16].

Early detection and adherence to treatment are two important factors for better treatment [17]. Based on genomic diversity HCV about 100 different strains (numbered 1, 2, 3, etc.), many subtypes (designated a, b, c, etc.) and eleven major genotypes (designated 1-11) are identified [11]. Genotypes 1-3 have been distributedworldwide. Globally about 60% of HCV infections are due to 1a and 1b [12]. Viral genotypeinfluenceon the pathogenesis of liver is still controversial. Disease progression is affected by genetic, environmental and immunological factors.

Antiviral response has been predicted by infecting genotype. Interferon alone shows poor response to genotype 1 butshow more favorable response to genotypes 2 and 3 [1].

Early hepatitis C laboratory evaluation should include: coagulation studies, prothrombin time, complete blood count, ALT, direct and total bilirubin, alkaline phosphatase, AST, albumin, globulin and total protein. Diagnosis made by presence of anti-HCV in EIA test. Acute and chronic HCV could not be distinguished because tests are not yet developed. Children should not be tested younger than one year; becauseanti-HCV from the mother may proceed during that age [14-17].

According to W.H.O record about 3% of world population has been infected with HCV and 170 million chronic carriers are at risk to develop cirrhosis and liver cancer. All chronic carriers represent large reservoir for HCV to persist.Patients with cirrhosis are potential candidates for primary HCC but this progress is still unanswered.One reason may be hepatocyte destruction and regeneration repeated cycles over many years. Diagnosis is made by liver biopsy.Unlike HBV, HCV does not integrate into the host genome because it did not encode transforming protein, so HCV is not directly oncogenic [17]. Yearly incidence of HCC is 3-5% in hepatitis C patients. Determination of HCV RNA (quantitatively or qualitatively) is done by branched-DNA (bDNA) assays, polymerase chain reactions (PCR-based assays) and other tests [15].

Mode of HCV infection transmission is by percutaneous contact to plasma derivatives and contaminated blood. Contaminated needles and syringesare most important factors among injection drug users [16].

Hepatitis C is mostly preventable. As compared to HIV and hepatitis B, it could not be spread through casual contact; risk by sexual transmission is also low. New cases traced, could be prevented by education, complete distribution of safer drug and equipment, to support behavioral and social changes in life [15].

No vaccine is available against HCV. There exist extensive genetic variationamong different strains and genotypes of HCV that is a major obstacle for the development of vaccine. Virus species have significant antigenic variation [18, 19].

2. MATERIALS AND METHODS

2.1 Study Design

A cohort studywas carried out in D.H.Q Teaching Hospital Rawalpindi from December 2012 to December 2013. Patients with chronic hepatitis C infection, age 18 years or old and not treated with interferon and ribavirin were included in the study.

2.2. Inclusion Criteria for Interferon Combined Therapy

Patients with higher serum aminotransferase concentrations since 6 months, third generation ELISA (enzyme linked immunosorbent assay) positive HCV antibodies and detectable HCV RNA in serum were included in the study. Biopsy of liver was not mandatory.

2.3 Exclusion Criteria

Patients with decompensated liver cirrhosis, i.e., bleeding varices, presence of ascites, hepatic encephalopathy and spontaneous bacterial peritonitis were excluded from study.

The patients with prothrombin time exceeding the normal, serum albumin level lesser than 3.5 g/l, or significant cytopenia were excluded from the study. Hemoglobin values should be at least 13 g/dl for men and 12 g/dl for women before start of treatment.

Table 1. End treatment response in different age group of males.

Age group (yrs)	+ve PCR		-ve PCR		Unknown result		Relapser		S.V.R %		Total male %	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
< 20			1	50.0	1	50.0					2	2.0
21-30	4	11.1	14	38.9	17	47.2	1	2.8			36	35.3
31-40	4	13.8	14	48.3	11	37.9					29	28.4
41-50	6	21.4	15	53.6	7	25.0					28	27.5
51-60			1	14.3	6	85.7					7	6.9
Total	14	13.7	45	44.1	42	41.2	1	1.0			**102**	

Total male patients: 102

Table 2. End treatment response in different age group of females.

Age group (yrs)	+ve PCR		- ve PCR		Unknown result		Relapsers		S.V.R		Total female	
	No	%	No.	%	No.	%	No.	%	No.	%	No.	%
< 20	1	50.0	1	50.0							2	1.5
21-30	3	8.1	20	54.1	13	35.1	1	2.7			37	27.4
31-40	5	14.3	15	42.9	11	31.4	3	8.6	1	2.9	35	25.9
41-50	7	15.6	24	53.3	13	28.9	1	2.2			45	33.3
51-60			6	37.5	7	43.8	2	12.5	1	6.3	16	11.9
Total	16	11.9	66	48.9	44	32.6	7	5.2	2	1.5	**135**	

Total female patients: 135

Table 3. Complete 6 month treatment response.

Total number of cases	Male patients		Female patients	
	Number	Percent	Number	Percent
143	59	41	84	59

Total patients: 143

Table 4. Complete 6 month treatment response in male patients.

Total Male Patients	Treatment Success		Treatment Failure	
	Number	Percent	Number	Percent
59	45	76	14	24

Total male patients: 59

Liver diseases due to other causes or any other relevant disorders including hepatitis B virus or HIV co-infection, pre-existing psychiatric condition, previous organ transplantation, cardiovascular disease, seizure disorders, haemoglobinopathies, hemophilia and patients with auto-immune diseases and poorly controlled diabetes mellitus were also excluded from the study. Patients name, age, address, sex and ID card number were noted.

Patients were treated with combination of interferon alpha 2b plus ribavirin for 24 weeks. The dose of interferon alpha 2 b was3 mega units, subcutaneously three times a week. Ribavirin was given orally1200mg (more than 75 Kg body weight) or 1000mg (lesser than 75 Kg body weight) per day in two to three divided doses.

2.4 Blood Collection

Patient's assessment was done in the Out Patients Department (OPD) for safety, efficacy and tolerance at the end of 1st week and 2nd week, then every 4thweek for 24 weeks.

Initially fortnightly the hematological and biochemical profiles were checked by collecting blood from the patients and then monthly for successive 6 months. Treatment side effects were also noted down and were managed by the physician.

2.5 PCR Based Analysis

Serum HCV RNA was checked before start of treatment and then at 3rdmonth (12 weeks) and 6th month (24 weeks) of therapy and also 24 weeks after the completion of treatment.

Absence of serum HCV RNA at end of treatment and also 24 weeks after completion of treatment was primary end point which is known as sustained virological response (SVR) or end of treatment response. Serum ALT concentration normalization was secondary end point.

After checkup of the HCV infected patients by the physician, I personally attend the hepatitis C patients daily in medical outpatient department of D.H.Q Teaching Hospital Rawalpindi and investigating about their health condition, risk factor, comorbid, side effects of interferon and ribavirin and any other health problem.

2.6 Real-Time (RT)-PCR

Use the procedure as mentioned in primer bank for a PCR, primer bank for quantitative gene expression analysis as described by Wang and Seed [15]. Procedure was begun for real-time RT-PCR by using SYBR Green I with total RNA, gene specific primers. cDNA was used as template for real-time PCR.

2.7 Required Time

2 hours for cDNA synthesis.
2 hours for Real-time PCR.
0.5 hour for dissociation curve analysis.

2.8 Reagents and Equipment

Oligonucleotide Primers from Primer Bank gene specific primers could be retrieved. MGH DNA Core facility could provide these primers. To assess the quality of primer synthesis by both capillary electrophoresis, UV absorbance and all the primers were desalted.

2.9 Determination of Alanine Aminotransferase

In colorimetric method the amount of oxaloacetate or pyruvate produced as a result of reaction between oxoglutaric acid, aspartic acid, glutamic acid and alanine is estimated by forming 2,4 dinitrophenyl hydrazine. Its color in alkaline solution was red. The amount of color produced is proportional to the activity of the enzyme AST or ALT in serum of the patient. For the rate of reaction (Spectrophotometric method) the oxaloacetic acid and pyruvic acid produced were reacted with enzyme dehydrogenase. This needs NADH to reduce the keto acid. The decrease in absorbance due to formation of NAD from NADH was read at 340nm and was proportional to the amount of enzyme activity in the serum.

2.10 SCE Method

The activity of (formerly called transaminases) serum aminotransferases was measured as follows; UV test was optimized according to the SCE (Scandinavian Committee on Enzymes) recommendation.

On the following enzymatic reactions, the principle of the method was based;

ALT

L-Alanine + 2- Oxoglutarate ↔ L-Glutammate + Pyruvate

LHD

Pyuvate + NADH + H^+↔ L-Lactate + NAD^+

Table 5. Complete 6 month treatment response in female patients

Total Female Patients	Treatment Success		Treatment Failure	
	Number	Percent	Number	Percent
84	68	81	16	19

Total female patients: 84

Table 6. Correlation of ALT with PCR in male patients.

	During Treatment	PCR -ve		PCR +ve		Unknown PCR Results		Total males	
		No.	%	No.	%	No.	%	No.	%
ALT normal	at start	5	83.3			1	16.7	6	8.3
	At end	19	70.4	4	14.8	4	14.8	27	37.5
ALT high	At start	17	56.7	7	23.3	6	20.0	30	41.7
	At end	3	33.3	3	33.3	3	33.3	9	12.5
Total all groups		44	61.1	14	19.4	14	19.4	**72**	

Total male patients:72
Normal ALT values: Male: 9-43 U/L; Female: 9-36 U/L

Table 7. Correlation of ALT with PCR results in female patients.

	During Treatment	PCR -ve		PCR +ive		Unknown Results		Total females	
		No.	%	No.	%	No.	%	No.	%
ALT normal	at start	11	52.4	8	38.1	2	9.5	21	17.2
	At end	32	64.0	14	28.0	4	8.0	50	41.0
ALT high	At start	24	60.0	13	25.5	3	7.5	40	32.8
	At end	3	27.3	7	63.6	1	9.1	11	9.0
Total all groups		70	57.4	42	34.4	10	8.2	**122**	

Total female patients: 122
Normal ALT values: Male: 9-43 U/L; Female: 9-36 U/L

Table 8. Adverse Effects of interferon combined therapy on hematological parameters of male patients.

Parameters	Reference Range	Percent of patients	Number of patients
Anemia	13.5-17.5	60.9	28
Neutropenia	4000-11000	19.6	9
Thrombocytopenia	150000-450000	19.6	9

Total male patients: 72

Because of the oxidation of NADH to NAD^+ there was decrease in absorbance value at 340 nm. That was directly proportional to ALT activity in sample.

3. RESULTS AND DISCUSSION

3.1 End Treatment Response in Different Age Group of Males

Table 1 is for male patients. Total male patients were 102.In case of age group less < 20 years total 2(2%) patients were included. Out of which no patient show treatment failure, 1(50%) patient show treatment success, 1 (50%) patient had not follow up the treatment. No patients with relapse or S.V.R (sustained virological response) were identified.

In case of age group 21-30 years total 36(35.5%) patients were included out of which 4(11.1%) patients show treatment failure, 14(38.9) patients show treatment success, 17(47.2%) patients had either no follow up or were in start of treatment and 1(2.8%) patients wererelapses. No patient with S.V.R was identified.

In case of age group 31-40 years, 29(28.4%) patients were included in this group out of which 4(13.8%) patients showed treatment failure, 14(48.3%) patients showed treatment success. 11(37.9%) patients had either no follow up or were in start of treatment. No patients with relapse or S.V.R were identified.

In case of age group 41-50 years 28(27.5%) patients were included out of which 6(21.4%) patients showed treatment failure, 15(53.6%) patients showed treatment success, 7(25.0%) patients had either no follow up or were in start of treatment. No patient with relapse or S.V.R was identified.

In case of age group 51-60 years 7(6.9%) patients were included out of which no patients showed treatment failure, 1(14.3%) patients show treatment success, 6(85.7%) patients had either no follow up or were in start of treatment. No patients with relapse or S.V.R were identified.

At the end out of total 102 patients 14(13.7%) patients shown treatment failure, 45(44.1%) patients shown treatment success, 42(41.2%) patients had either no follow up or were in start of treatment.1(2.8%) patient had relapsed. No patient is identified with S.V.R.

3.2 End Treatment Response in Different Age Group of Females

Table 2 shows female patients. Total female patients in this study were 135.In case of age group < 20 years total 2(1.5%) patients were included out of which 1(50%) patient exhibited treatment failure, 1(50%) patient exhibited treatment success and no patient with relapse or S.V.R was identified.

In case of age group 21-30 years total 37(27.4%) patients were included out of which 3(8.1%) patients exhibited treatment failure, 20 (54.1%) patients showed treatment success, 13(35.1%) patients had either no follow up or were in start of treatment.1 (2.7%) patient relapses. No patient with S.V.R was identified.

In case of age group 31-40 years 35(25.9%) patients were included in this group out of which 5(14.1%) patients exhibited treatment failure, 15(42.9%) patients showed treatment success, 11(31.4%) patients had either no follow up or were in start of treatment. And 3(8.6%) patients exhibited relapse. Patient showed S.V.R is 1(2.9%).

In case of age group 41-50 years 45(33.3%) patients were included in this group out of which 7(15.6%) patients exhibited treatment failure, 24(53.3%) patients showed treatment success, 13(28.9%) patients had either no follow up or were in start of treatment, and 1(2.2%) patientwasrelapsed and no patient with S.V.R was identified.

In case of age group 51-60 years 16(11.9%) patients were included in this group out of which no patients showed treatment failure, 6(37.5%) patients exhibited treatment success, 7(43.8%) patients had either no follow up or were in start of treatment. Patients with relapse were 2 (12.5%) and 1 (6.3%) with S.V.R was identified.

At the end out of total 135 female patients 16(11.9%) patients exhibited treatment failure, 66(48.9%) patients exhibited treatment success, 44(32.6%) patients had either no follow up or were in start of treatment, 7(5.2%) patient had shown relapse and 2(1.5%) patients were identified with S.V.R.

3.3. Complete 6-month Treatment Response

During complete 6months treatment, during December 2012 to December 2013, total 237

numbers of patients with chronic HCV were enrolled.All patients were educated for follow-up, however 143 (60%) of 237 patients completed the 6 months interferon combined therapy. While remaining 94 (40%) of 237 quit the treatment. The treated cases includes 59 (41%) of 143 male and 84 (59%) of 143 female patients as in Table 3.

These 143 patients had completed their course with regular follow up.Male and female patients were further divided into separate tables. So their end treatment response could be clearly identified and compared.

3.4 Complete 6-month Treatment Response in Male Patients

Total 59 male patients who had completed the 6 monthstreatment, 45(76%) exhibit treatment success and 14(24%) male patients revealed treatment failure (Table 4).

3.5 Complete 6-month Treatment Response in Female Patients

Total 84 female patients who had completed the 6 monthstreatment, 68 (81%) exhibit treatment success and 16 (19%) male patients revealed treatment failure (Table 5).

3.6 Correlation of ALT with PCR

Total 194 patients were included, whose treatment was monitored after every 4 weeks till 24 weeks of treatment.Separate data was collected for male and female patients then tabulated. So that ALT couldbe easily compared with treatment failure and treatment success cases.

3.7 Male Patients

Table 6comprises of total 72 male patients out of them, 5 (83.3%) have normal ALT at start of treatment while 17(56.7%) patients had high ALT level. At end of treatment, 19 (70.4%) patients have normal level of ALT while 3 (3.3%) patients have high level of ALT.

In case of treatment failure patients, no patient found with normal level of ALT at start while 7 (23.3%) patients had high level of ALT at start. At end of the treatment there are 4 (14.8%) patients with normal levels of ALT while 3(3.33%) patients have high levels of ALT.

In case of those patients who had completed their 6 month treatment but did not came back to show their PCR results either it is +ve or -ve. In these type of patients 1 (16.7%) patient had normal levels of ALT at start and 6(20%) have high levels of ALT at start.

While 4(14.8%) patients had normal levels of ALT at end of the treatment, 3 (3.3%) have high levels of ALT. At the end total patients with normal levels of ALT at start of the treatment were 6(8.3%). Total patients who had high levels of ALT were 30(41.7%). Total patients with normal levels of ALT at end of the treatment were 27(37.5%) and with high levels of ALT were 9(12.5%).

3.8 Female Patients

Table 7 comprises of total 122 female patients, at start of the treatment 11(52.4%) patients have normal levels of ALT and 24(60%) patients have high levels of ALT. While at the end of treatment 32(64%) patients have normal levels of ALT and 3(27.3%) patients have high levels of ALT.

Patients with treatment failureat start, 8(38.1%) patients were found with normal levels of ALT, 13(25.5%) patients with high levels of ALT. While at the end of the treatment there were 14(28%) patients with normal levels of ALT and 7(63.6%) patients with high levels of ALT.

In case of those patients who completed their 6 months treatment but did not came back to check their PCR results either it is +ve or -ve. In these type of patients 2(9.5%) patients have normal levels of ALT at start and 3(7.5%) have high levels of ALT.At end of the treatment 4(8%) patients have normal levels of ALT while 1(9.1%) has high levels of ALT.

When we sum up total patients with normal levels of ALT at start of the treatment were 21(17.2%) while 40 (32.8%) with high levels of ALT. At end of the treatment normal levels of ALT were 50(41%) and patients with high levels of ALT were 11(9%).

3.9 Adverse Effects of Interferon Combined Therapy on Hematological Parameters

Adverse effects of interferon and ribavirin on blood were noted and tabulated in separate tables.Table 8 comprises of total 72 male patients out of which, 46 (64%) patients exhibited decline in hematological parameters. Detail is as follows 28(60.9%) patients develop anemia, 9 (19.6%)

patients develop neutropenia and 9(19.6%) patients develop thrombocytopenia.

Table 9 comprises of total 122 female patients out of which 71(58.2%) patients exhibited decreased in hematological parameters. Detail is as follows 50(70.4%) patients develop anemia, 15(21.1%) patients develop neutropenia and 6(8.5%) patients develop thrombocytopenia.

3.10 Liver Condition of Hepatitis C Patients

Liver condition of hepatitis C patients were monitored by USG abdomen test before the start of treatment and tabulated in Table 10. Total number of patients was 156 patients; patients with normal liver condition were 75(48.1%), while 43(27.6%) patients indicted coarse liver and 38(24.4%) patients exhibited fatty liver.

3.11 Side Effects

McHutchinson et al [20] discussed different side effects of interferon and ribavirin treatment, so I compared different side effects of my research work with his results. These side effects were compared in Table 11; total number of patients was 137. Which were compared as follows, in case of constitutional side effects McHutchinson et al. [20] wrote that fatigue, headache, myalgias, fever, arthralgias were 70%, 66%, 64%, 41%, 33% in patients, respectively, and I noted fatigue, headache, myalgias, fever, arthralgias in 37%, 26%, 56%, 85%, 22% in patients, respectively.

In case of gastrointestinal side effects, McHutchinson et al. [20] wrote that nausea, anorexia and diarrhea were 46%, 25%, 22% in patients respectively, and I noted nausea, anorexia, diarrhea in 18%, 23%, 4% patients, respectively.

In case of psychiatric side effects it was investigatedthat depression, irritability, insomnia was in 36%, 32%, 39% patients, respectively and according to present study depression, irritability, insomnia was in 43%, 44%, 22% patients, respectively.

In case of dermatological side effects it had been reported that pruritis, dermatitis, alopecia was in 19%, 28%, 32% patients respectively which is in contrast to McHutchinson et al. [20] as in this study, pruritis, dermatitis, alopecia was in 43%, 15%, 45% patients, respectively.

In case of respiratory side effects, McHutchinson et al. [20] noted cough and dyspnea in 14%, 18% respectively, according to present study cough and dyspnea was in 11%, 15% patients, respectively.

3.12 Prevalence in Rawalpindi

Rawalpindi has high prevalence rate of hepatitis C. Patients came from different areas of Rawalpindi to D.H.Q teaching hospital Rawalpindi. Total 237 patients with hepatitis C were administered in present study their area wise distribution is as follows:

19 cases in Gujar Khan, 17 cases in Dhok Hassu, 15 cases in Dhok Matkiyal, 13 cases in Dhokratta, 12 cases in Dakkhana Khas , 8 cases in Pir Wadhai, 7 cases in Railway Colony, 7 cases in Chorharpal, 7 cases in Fauji Colony Pir Wadhai, 6 cases in Khannapul, 5 cases in Dhok Chaudhry, 4 cases in Sihala, 4 cases in in Westridge Cantt, 4 cases in Chaklala, 4 cases in Airport Society sector 3, 4 cases in Kohota, 4 cases in Kalar Saeedan, 4 cases in Raja Bazar, 4 cases in Chakri, 3 cases in Shakriyal, 3 cases in scheme 3 Westridge, 3 cases in Hazara Colony Raja Bazaar, 3 cases in Tarnol, 3 cases in Tench Bhata, 3 cases in People Colony, 2 cases in Kohenoor Mills, 2 cases in Adyala Road, 2 cases in Pir Wadhai, 2 cases in Morgah, 2 cases in Afghan Citizens, 2 cases in Gulshan-e-Abad, , 2 cases in Zilaponch, 2 cases in Dhamiyal.

One case is found in each of the following areas: Mari JabarRawat, Sir Syed Chock Waqar-un-Nisa College, Chakamral, Sabzi mandi, Bahria Town, Mahala KarishPura, Scheme 7 Westridge, Gankal Mohra Khanna, Mahala Rehmat Abad Block F, Mahala dhok kala Khan, Adhwal, Islamabad Sector G 9/4, Mahala Shah Khalid Colony, Kohistan Colony, Chak jalalDin, Dakkhana Dahgal Colony, Zia ulHaq Colony, lahzarar, F7/4, Ali Purisl, Mohra, Mahala waris Khan, Mangtal Farooqia Chok, GawalaRoad, Morgha, Gulshanabad, Jinnah Road, Rehmatabad Rawalpindi Cantt, Chakbeli, Dhok malal, Rawat, Thana Chontra, Pindighap, Shah Khalid Colony Chaklala, Railway Workshop, Carriage Factory, Golra Shareef, Scheme 3 Chaklala, Banars Colony, Glass Factory, Chak Belli, Mohan Pura, Golra mor, DhokMustaqeem, Javaid Colony Tipu Road, Shams Abad, Scheme 3 High Court , Chaklala, Muslim Town, Rehmanpura near City Marriage Hall, Sector B 8, Rawat, Muree Road, Rawalpindi, DhokferozeDin, Haji Chok,

Table 9. Adverse effects of interferon combined therapyon hematological parameters of female patients.

Parameters	Reference range	Patients	
		percent	Number
Anemia	12.0-16.0	70.4	50
Neutropenia	4000-11000	21.1	15
Thrombocytopenia	150000-450000	8.5	6

Total hemale patients: 122

Table 10. Liver condition of hepatitis C patients.

Liver Condition	No. of Patients	Percent
Normal study	75	48.1
Coarse liver	43	27.6
Fatty liver	38	24.4

Total patients:156

Table 11. Adverse effects of interferon combined therapy.

Adverse Effects	MecHutchinson *et al* [20]	Present study results
Constitutional	**(Affected %)**	
Fatigue	70	37
Headache	66	26
Myalgias	64	56
Fever	41	85
Arthralgias	33	22
Gastrointestinal		
Nausea	46	18
Anorexia	25	23
Diarrhea	22	4
Psychiatric		
Depression	36	43
Irritability	32	44
Insomnia	39	22
Dermatological		
Pruritus	19	43
Dermatitis/Rash	28	15
Alopecia	32	45
Respiratory		
Cough	14	11
Dyspnea	18	15

Total patients: 137

Chakshahzad, Saddar, Khyaban e Sir Syed Sector 3,Chak Jalal Din, Muhanpura, Habib Colony, Said PurRoad, Pinddain, Benazir Chok, Mandra.

Mostly HCV-positive patients had a history of shaving by private barbers suggesting that the barbers shop was the key place for viral transmission. There was low awareness about sexually transmitted diseases amongst people. Another factor is that most Pakistanis believe that parenteral drugs are more efficient than oral drugs. There was little awareness in people about the various risk factors associated with HCV transmission. Treatment of hepatitis is very costly and is creating a huge burden on the country's economy. More stress should be given to the preventive measures of the disease in order to decrease the future health and economic burden; these include screened blood transfusions, proper sterilization techniques in clinics and hospitals, use of disposable syringes and razor blades. The government should take instantaneous steps to generate awareness among the general public.

4. CONCLUSIONS

Interferon combined therapy is an effective treatment for hepatitis C infection. Early detection and low viral load are important factors in treatment success. During the Interferon therapy the patients which indicate reduction in ALT levels and HCV RNA in 1st month of treatment, will mostly show sustained virological response (S.V.R).Than those who did not exhibit these changes. Many other factors also have an impact on cure rates. Treatment success rates are generally greater in those patients who haveyounger age, have minimal liver scarring (fibrosis), in a healthy weight range, have a high level of adherence to the treatment regimen and are not co-infected with hepatitis B or HIV. Many adverse effects were associated with interferon combined therapy that could be managed with diet and clinical measures.

This study suggested that the major causative factors towards increased HCV prevalence include un-checked blood transfusions, re-use of injection syringes, body piercing equipment, non-sterilized surgical equipment, dental and circumcision equipment. Awareness programs are required to decrease the future burden of HCV in the Pakistani population.

5. REFERENCES

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