

# Rate of Depression among Hepatitis C Patients Treated with Interferon Alpha and Ribvirin

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## ABSTRACT

**Aim:** To find the prevalence of depression in patients receiving interferon and ribavirin therapy

**Study design:** Prospective

**Place and duration of study:** Bahawal Victoria Hospital, Bahawalpur from July 2011 to June 2012.

**Methods:** Total 522 patients of Hepatitis C +ve screened by PCR for HCV RNA were included according to inclusion criteria. An approval was taken from Ethical Committee and informed consent was also taken from the patients.

**Results:** In our study of 522 patients 260(60%) male and 175(40%) females were positive quantitatively for HCV RNA by PCR. Majority of the patients were in age group 34-41 years (Age Group C), 231(53.10%) the study population. Depression was found during screening in 87(20%) of patients at base line level. These patients were excluded from the study. Depression was found in 170(39%) after treatment with IFN- $\alpha$  & ribavirin. Out of these patients 94(55.3%) had mild, 61 patients (36%) had moderate, 9 patients 5.3% had severe depression and 6(3.5%) patients had very severe depression. Depression of varying degrees is associated with IFN- $\alpha$  & ribavirin and needs effective control with antidepressants.

**Conclusion:** Uninterrupted interferon therapy could be ensured to combat depression.

**Keywords:** Hepatitis C, depression, interferon.

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## INTRODUCTION

HCV affects 180 million people Worldwide.<sup>1</sup> Interferon  $\alpha$  (IFN  $\alpha$ ) was the first effective treatment of this disease, more recently IFN  $\alpha$  and Ribavirin has shown good efficacy in treatment of HCV<sup>2</sup>. Twenty to thirty percent of patients treated with pegylated interferon and ribavirin report depression during therapy and an indication for decreasing the dose or even discontinuation<sup>3</sup>.

Pathophysiological mechanism that causes the neuropsychiatric side effects particularly depression is unclear although various hypotheses have been suggested, a disturbances of serotonin neurotransmitters may be one reason<sup>4,5</sup>. Early identification of depression by questioning during follow up visits is critical to subsequent management, As there is high prevalence of depression in the general population undiagnosed psychiatric disorder patients receive treatment with IFN  $\alpha$  and Ribavirin without psychiatric care.

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## METHODS AND ANALYSIS

It was a prospective study done at Bahawal Victoria Hospital, Bahawalpur from July 2011 to June 2012. Total 522 patients of Hepatitis C+ve screened by PCR for HCV RNA were included according to inclusion criteria. An approval was taken from Ethical Committee and informed consent was also taken from the patients. Demographic data of the patients were collected on predesigned proforma. Interferon alpha and ribavirin therapy was advised to the all patients for six months by the physician. For the purpose of liver transaminases and CBC blood samples were obtained at patient's medical visit for analysis.

Patients were divided into five age groups. Group A consisted of patients having age 18-25 years, Group B consisted of patients having age 26-33 years, Group C 34-41 years, Group D 42-49 and Group E consisted of 50 years and above.

Before the start of the treatment, all 522 patients were assessed for the presence of depression by using a diagnostic interview based on diagnostic & statistical manual of mental disorders (DSM-IV)<sup>6</sup>. Out of 522 patients, 87 patients already had depression. These were excluded from the study according to exclusion criteria.

Development of depression during the study was diagnosed using DSM-IV diagnostic criteria about the 12<sup>th</sup> week of therapy. To find the magnitude of severity of depression, the affected patients were

rated by administering Hamilton Depression Rating Scale (HDRS)<sup>7</sup>. Patients of both genders between 18-55 years of age, detectable HCV infection in PCR having ALT >40 U/L (normal 40 U/L) were included in the study. Patients having cirrhosis, coinfection with hepatitis B, severe cardiac disease, severe neurological disease and depression were excluded from the study.

## RESULTS

Total 435 patients of Hepatitis C+ve screened by PCR for HCV RNA were included in this study. Age group and gender wise distribution of patients shown in table No.1 Out of these 260(60%) patients were male and 175 (40%) were female. In age Group A, there were 6(1.38%), in age Group B 67 (15.40%), in age Group C 231(53.10%), in age Group D 111(25.52%) and in age Group E there were 20(4.60%) patients. Maximum number of patients were in age Group C (Table 1).

Table 1: Age and gender distribution

Age Group	Male	Female	Total
Group A 18-25 years	4 (66.7)	2 (33.3)	6 (1.38)
Group B 26-33 years	45 (67.2)	22 (32.8)	67 (15.40)
Group C 34-41 years	130 (56.3)	101 (43.7)	231 (53.10)
Group D 42-49 years	67 (60.4)	44 (39.6)	111 (25.52)
Group E ≥50 years	14 (70.0)	6 (30.0)	20 (4.60)
Total	260 (60)	175 (40)	435

Fig. 1: Patients with suicidal ideation

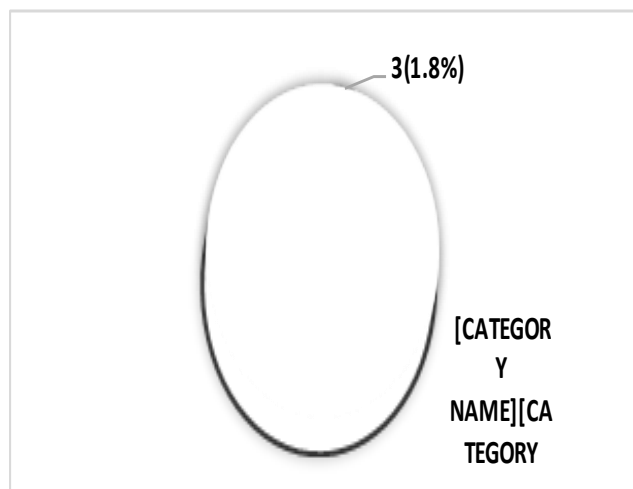
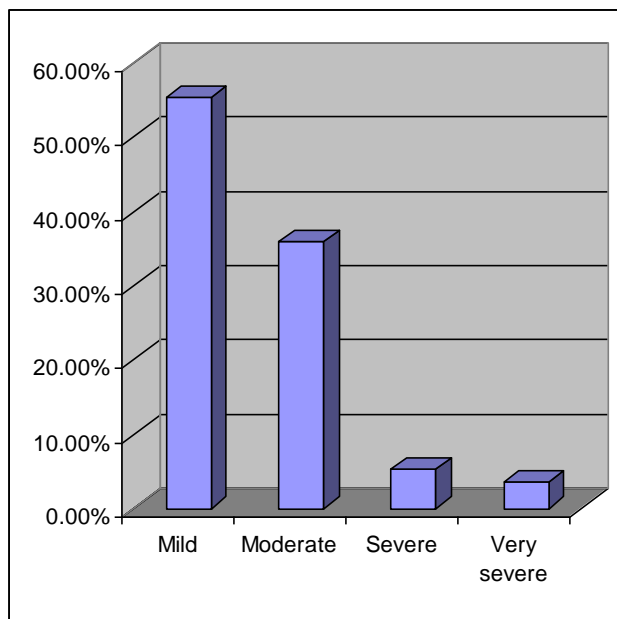


Fig. 2: Patients with varying degrees of depression (n=170)



Serum ALT levels were elevated in 130 that is 30% of patients at the baseline level; these levels remain elevated until 8 weeks of treatment with IFN- $\alpha$  in 63 patients that is 15 % of the study population, then the levels declined whereas in the rest 15% the levels remained elevated even at the end of the study period.

## DISCUSSION

HCV infection is a very common infectious disease and its prevalence in Pakistanis 4.9%<sup>8</sup>. Pakistan is an endemic zone for HCV due to the reuse of syringes, inadequate blood screening processes, illiteracy and poor socio-economic conditions of the country.

Medical treatment of HCV is still unsatisfactory because it is expensive and frequently not well tolerated due to somatic side effects and psychological problems. Most important barrier is depression and anxiety and it may induce suicidal ideation.<sup>9</sup> Thus the understanding, early recognition, and treatment of psychiatric side effects is of key importance, as this may increase the probability of successful antiviral therapy.

The mechanism of this depression is largely speculative. The proposed reason may be that IFN  $\alpha$  and Ribavirin may induce proinflammatory cytokines tumor necrosis factor interleukin 1 and interleukin 6 to promote sickness behavior and may also have effect on Hypothalamic Pituitary adrenal axis.<sup>10</sup> Recent attention has focused on relationship of IFN  $\alpha$  and Ribavirin to alterations in serotonin activity. Serum level of tryptophan is reduced during IFN  $\alpha$  and Ribavirin therapy. There is increased activity of

serotonin transporter that could decrease synaptic serotonin concentration and contribute to depression<sup>11</sup>.

In our study IFN  $\alpha$  and Ribavirin induced depression was seen after 12 weeks of treatment, A study reports that depressive events with IFN  $\alpha$  and Ribavirin occurred more frequently during the first 24 weeks of therapy than during later period of 48 weeks<sup>12,13</sup>. In our study depression was found in 170(39%) patients, this percentage coincides with the study of Shakoor A<sup>14</sup> which is also showing 39% patients to be depressed. In another study of Shah M<sup>15</sup> also showing 38% patients to be depressive, this value is also comparable with our study. In another study a very high prevalence was reported in which adverse Psychiatric events occurred in 77% of patients in clinical trials with PEG interferon alpha2b and the most common psychiatric effects depression were ranging from 25-34%. 3(4%) out of 75 patients developed suicidal ideas<sup>16</sup>. This result of study having suicidal ideation, is 2.2 times higher as compared to our study which is reflecting 3(1.8%) patients with suicidal ideation. Another study of Shakoor A<sup>14</sup> is reporting 30% suicidal ideation which is very high than our study. Another study reported that depression is common in Hepatitis C and is exacerbated by interferon depression occurred in 51.43% of patients after 12 weeks<sup>17</sup>.

## CONCLUSION

All out efforts should be made to optimize the treatment of HCV, which will include patients compliance and managing the side effects, this will avoid dose reduction and discontinuation of IFN  $\alpha$  and Ribavirin, questioning during follow up visits is critical to subsequent management and is a useful research tool. Therefore early recognition and effective treatment of psychiatric side effects of IFN  $\alpha$  and Ribavirin is needed. Involvement of serotonin pathways favors the use of SSRI. Multidisciplinary management concepts in the future during Hepatitis C therapy is essential to minimize the dropout rate and to increase effective response to treatment with IFN  $\alpha$  and Ribavirin.

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