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# Baseline Depression as Risk Factor and Interferon Induced Depression in Hepatitis C Patients

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The major goal of the present study was to investigate the impact of baseline depression as a risk factor for the subsequent development of interferon induced depression in hepatitis C patients. The sample consisted of 57 hepatitis C patients diagnosed and scheduled for interferon alpha therapy in different hospitals of Peshawar. Interrupted Time Series Design was used as the analytic approach. The Siddiqui-Shah Depression Scale (Siddiqui & Shah, 1997) was administered to measure depression in these patients at baseline, at week 24$^{th}$, and after completion of the treatment. Results revealed that hepatitis C patients having higher baseline depression experience significantly higher levels of depression during and after completion of the treatment than those with low baseline depression. The data support hypotheses and inferred an easy way to identify patients who would be at a higher risk of developing interferon induced depression during the therapy. The findings concluded that

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systematic screening and treatment of depression at pre-interferon stage, during the course, and after completion of the therapy was essential for good adherence to antiviral treatment. Findings have important clinical implications in terms of neuropsychiatric safety of the interferon therapy.

*Keywords.* Hepatitis C, interferon alpha therapy, depression, patients.

Hepatitis C virus is a major health problem on global scale (Hoofnagle, 1997). The world-wide prevalence rate of this disease is 2.2 to 3% which is approximately 130 to 170 million infected people and three to four million are newly affected every year. Hepatitis C infection is likely to result in nearly 3, 50,000 deaths per year (Hepatitis C Facts, 2014). According to World Health Organization (2014) in Pakistan death rate because of hepatitis C is 0.47 per 100,000. The prevalence rate of hepatitis C varies widely geographically with low rates in Western Europe, for example, 0.6% in Germany and North America, 1.8% in United States, and higher rates in developing countries (Shepard, Finelli, & Alter, 2005). In some countries there are higher hepatitis C infection rates, for example, in Egypt (22%), in Pakistan (4.8%), and in China (3.2%) prevalence rate has been reported which is significantly higher than in countries of Western Europe or North America (Report on World Hepatitis C Day, 2014). The standard treatment approved by the Federal Drug Authority for the hepatitis C virus (HCV) is the pro-inflammatory cytokine interferon alpha (IFN-α), a multifunctional protein which is found to be effective in 40 to 80% of patients, and is most effective for patients infected with certain common genotypes of the hepatitis C virus (Bacon, 2004). Currently the advanced treatment of HCV includes the development of pegylated recombinant interferon (PEG-IFN-α) given subcutaneously once per week with oral ribavirin (RBV), an anti-viral drug given daily (Fried et al., 2002; Nesic *et al.*, 2004). The same therapies are given in Pakistan for treatment of hepatitis C (Zuberi *et al.*, 2008). The duration of therapy ranges from 24 to 48 weeks, depending on the HCV genotype (Wilkins *et al.*, 2010), and 40 to 80% of the patients have a Sustained Virological Response (Fried *et al*., 2002) when receiving this treatment. Despite increase in Sustained Virological Response (SVR), the side effects of this treatment present a major health problem (Fried *et al.*, 2002; Kraus, Schafer, Csef, & Scheurlen, 2005; Loftis, & Hauser, 2004).

Numerous researchers have associated neuropsychiatric disorders with the IFN-α therapy (Dieperink, Willenbring, & Ho, 2000; Yates &

Gleason, 1998). Wolfelschneider, Schreiber, Markou, Gieler, and Brosig's (2006) study examined a 26years old inpatient with hepatitis C infection. During the course of treatment with IFN-α patient developed depressive symptoms, agitation, somatization and lacked in response to medication, resulting in discontinuation of the therapy. The patient was referred to psychotherapy. After psychological treatment, patient was discharged and IFN-α was successfully re-administered and completed. It was concluded that ward based psychosomatic psychotherapy can be effective in treating and reducing psychological impact of IFN-α induced depression. Some researchers (Pavlovic, Delic, Maric, Vukovic, & Gasic, 2011) investigated depressive symptoms and risk of depression in 74 patients with chronic hepatitis C patients treated with PEG IFN-α therapy plus oral Ribavirin and compared their self-rating scores of depression with the observed score. Results revealed significant increase in the depression scores on the three follow-up visits as compared to baseline depression scores. Further, significant correlation was found between the observed rating scores on the Hamilton Depression Rating Scale (1960) and the Zung Self Rating Depression (Zung, 1965). In a meta analyses, Goeb *et al*. (2005) searched the electronic data bases up to 2005 in order to review psychiatric side effects of IFN-β in multiple sclerosis patients. Out of 150 articles which were reviewed, 16 studies revealed the occurrence of both depression and suicide in multiple sclerosis patients treated with IFN-α BIα / Iβ. Numerous studies demonstrated that among patients treated with IFN-β Iα/ Iβ, the side effects occurred during the initial phase of the therapy and resulted in discontinuation of the treatment in 0.2 to12.5% of the patients (European Study Group on Interferon beta-1b, 1998; Kayser, Louiz,& Guillin, 2001; Zephir *et al.*, 2003).

Moving along same lines it can be argued that if psychological and behavioral vulnerabilities are risk factors for development of subsequent depression during IFN-α treatment, then pre-existing vulnerability of developing psychiatric disorders (such as behavioral problems, baseline personality or other mood disorders & higher baseline depressive symptoms) may place these patients (having pre-existing vulnerability) at risk for worsening symptoms if treated for HCV using interferon-based therapies. In an early study on cancer patients Capuron and Ravaud (1999) found that those cancer patients having depression scores on a pre-treatment depression scale had a higher risk of becoming depressed during the subsequent IFN-α treatment. These results are similar to findings of other studies which suggest that patients having a past history of psychiatric disorders,

particularly of major depression, are more vulnerable to develop depression during subsequent IFN-α treatment (Castera, Constant, & Henry, 2006; Raison, Borisor, & Broadwell, 2005). In his study of pre-treatment levels of depression, David *et al*. (1999) tested the hypothesis that if increase in depression after the start of antiviral therapy for multiple sclerosis is a function of the pre-treatment levels of depression. Depression levels in 56 multiple sclerosis patients with a confirmed diagnosis of relapsing form of the disease were measured 3 times, that is, 2 weeks (time1) and 2 days (time2) pre-treatment, and 8 weeks (time 3) after start of the therapy. Findings demonstrated that compared to time 2, the level of depression was significantly higher at time 1 and time 3. These findings suggest that increase in the level of depression for these patients most likely reflect the pre-treatment levels of depression. In another study Udina *et al.*, (2012) reviewed risk factors for and rates of depression in hepatitis C patients from the earliest data available up to 2011 on line. The results revealed 0.25% and 0.28% incidence of depression at the $24^{th}$ and $48^{th}$ weeks of the treatment. Female gender, low educational levels, history of psychiatric disorders including major depression, higher levels of Interleukin-6 (IL-6) and depressive symptoms at baseline predicted major depression during treatment.

Another important question regarding interferon induced depression is that at which week of therapy patients experience higher level of depression so that preventive measures can be focused particularly on that period of therapy. To address this issue, Medeiros, Kayo, Medeiros, Lima, and Mello (2014) in a recent study examined rate and severity of depression in 50 Brazilian hepatitis C patients treated with PRG IFN plus ribavirin. Depression in participants was assessed at$12^{th}$, $24^{th}$, and $48^{th}$ weeks of therapy using the Beck Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh 1961) and the Center for Epidemiological Studies-Depression (Radloff, 1977). Results showed the highest levels of depression occurred at week $24^{th}$ of the therapy. Similar findings were also reported by Udina *et al.*, (2012). Patients having a history of alcohol and substance abuse had a higher risk of depression. Research suggests that all patients treated with IFN-α therapy develop some side effects as a result of treatment, whether neuro-vegetative symptoms (somatic aspects of risk behavior) or depressive symptoms (specific to behavioral parts of the sickness behavior). Both of these are measurable through depression rating scales. Thus, a person's higher baseline score on one of the scales may remain higher throughout the course of treatment and that patient may be more at risk of becoming depressed during the treatment and consequently,

require some additional psychological treatment (Raison, Demetrashvili, Capuron, & Miller, 2005). If this is the case, then, the scores of the patients on the depression scale should increase relative to time, which has been supported by numerous studies (Dan, Martin, & Crone, 2006; Dieperink, Ho, Thuras, & Willenbring, 2003; Fried *et al.*, 2002; Kraus *et al.*, 2005; Kraus *et al.*, 2008; Lotrich, Rabinovitz, Gironda, & Pollock, 2007).

Robaeyes *et al.*, (2007) studied depression in 49 chronic hepatitis C patients having acquired hepatitis C as a result of substance use (cocaine, heroin, or LSD) who were treated with either IFN-α or PEG IFN 2β. Two symptoms dimensions, vegetative depressive (diurnal variation, lack of sleep, loss of appetite, loss of weight, loss of sex drive, constipation, and fatigue) and cognitive depressive (loss of interest in normal routine activities, loss of pleasure, isolation, and withdrawal) were constructed. No significant difference in both cognitive and vegetative depressive symptoms at baseline was found. After four weeks of treatment, however, the mean vegetative Zung score was higher among patients who later developed depression compared to other patients. However, increase in vegetative depression at fourth week after the start of IFN-α reliably predicted subsequent development of depression in HCV patients. Because of these side effects numerous studies agree that hepatitis C patients with psychological depression should not be prescribed to IFN therapy (Dieperink *et al.*, 2000; Lauer, & Waller, 2001).

One of the major causes of liver diseases and death worldwide is the HCV (World Health Organization, 2014). According to a recent report 18 million individuals in Pakistan have been infected with hepatitis. The disease is spreading rapidly due to the lack of availability of a vaccine against hepatitis C (World Hepatitis Day, 2014, July 28). The standard treatment for HCV includes interferon alpha combined with oral ribavirin, a successful antiviral drug but having a profile with significant, psychiatric side effects. The most common among them is depression which has been reported by numerous studies (Capuronet *et al.*, 2004; Dieperinket *et al.*, 2000; Schaefer, Capuron, & Friebe, 2012). Due to these side effects patients either reduce the dose or discontinue therapy altogether. Keeping in view the empirical findings mentioned in the introductory section the present study was designed to investigate the effect of a primary psychological risk factor, that is, baseline depression on the subsequent development of depression in hepatitis C patients to identify preventive measures which may alleviate depressive symptoms during treatment.

### Hypotheses

Based on prior research following hypotheses were formulated and tested.

1. The baseline depression scores on the Siddiqui-Shah Depression Scale of hepatitis C patients will increase during the interferon treatment.
2. The post-treatment scores of hepatitis C patients with higher baseline scores on the depression scale will be significantly higher after completion of the therapy.

## Method

### Participants

The sample consisted of 57 hepatitis C patients (women) scheduled for interferon treatment with an age range of 30 to 65 years ($M$ = 55.61, $SD$ = 8.24). As design of the study required to measure depression in participants three times points, i-e, at baseline (pre-treatment) at week 24$^{th}$ (during treatment) and at 48$^{th}$ week (after completion of the treatment) and the authors were women therefore, it was more convenient for them to select women patients only. The duration of symptoms of the illness before diagnosis in the sample was five to six months. The minimum educational level of the sample was 6 years of schooling, while the maximum was matriculation. All the participants were unemployed. Majority of patients were of low socioeconomic status. The size of sample was calculated using software, Sample Size Determination in Health Studies (Lawanga, & Lemeshow, 1991).Convenience sampling technique was used to select the sample from different hospitals of Peshawar. Hepatitis C patients, previously untreated with interferon were included. Patients who had co-infection, such as hepatitis A, hepatitis B, or other liver diseases (e.g., hepatic carcinoma), patients having being diagnosed with uncontrolled neurological diseases (e.g., epilepsy), serious cardiovascular diseases, endocrine diseases, and patients having addiction to psychoactive drugs were not included.

### Study Design

Interrupted Time Series Design was used to measure depression levels in hepatitis C patients at pre-interferon treatment, 24$^{th}$ weeks after the start and after completion of the treatment (at 48$^{th}$ weeks).

## Measures

**Personal Informational Sheet.** The Personal Information Sheet was designed to collect demographic information such as age, education, previous medical conditions, previous treatment with interferon, and current or previous use of antidepressant drugs.

**Siddiqui-Shah Depression Scale (SSDS).** The SSDS (Siddiqui & Shah, 1997) measures depression both in non-clinical and clinical populations. The scale consists of 36 items related to depression. Each item is scored according to the following four categories: *Never* (0), *Sometime* (1), *Usually* (2), and *Always*, (3). The subject is required to answer each item by choosing one of the four responses. Total score is obtained by summing all items; while possible score ranges from 0-108. The author established the reliability of the scale using spilt half and internal consistency methods. The alpha correlations for clinical and non-clinical groups were .91 and .89, respectively. The correlation of the scale with the Zung Depression Self Rating Scale (Zung, 1965) is .55 ($p < .001$), and with psychiatric rating of depression, correlation was reported to be .40 ($p<.05$). In the present study, reliability computed for SSDS is .82.

## Procedure

Patients diagnosed with hepatitis C and were scheduled for interferon therapy were contacted and invited to participate. The assistance of the concerned doctors and other paramedical staff was needed to reach the eligible patients directly. Prior to participation in the study each patient was informed about the study protocols and requirements, and written consent was obtained. The participants were ensured about confidentiality of the obtained information in order to maintain their dignity and respect. The scale was administered on each participant. On the basis of the baseline scores the participants were classified into two groups. The criteria for this classification were as follow: All those participants who obtained higher baseline scores (above 40) on the depression scale were grouped separately from those who achieved low scores on the scale. The same depression scale was again administered on the participants at $24^{th}$ week during the therapy and after completion of the treatment (at $48^{th}$ week). The results of three data points, that is, pre- IFN (baseline) and during the IFN treatment (at week $24^{th}$) and pre- IFN and post- IFN (at $48^{th}$ week) were compared.

## Results

The Paired Sample *t*-test was used to determine significance of difference between two groups of participants because both groups received same treatment at three times points and there was no control group. Repeated Measures Analysis of Variance were computed to determine the significance of difference between high and low baseline depression scorers across three time measure, that is, pre-interferon, at 24th weeks of therapy, and after completion the treatment.

Table 1

*Mean Baseline Difference between Hepatitis C Patients on Siddiqui-Shah Depression Scale (N = 57)*

| Groups Hepatitis Patients | Baseline Depression Scores | | | | 95%CI | | Cohen's |
|---|---|---|---|---|---|---|---|
| | *n* | *M*(*SD*) | *t* (55) | *p* | *LL* | *UL* | *d* |
| High BLDS | 31 | 41.65(7.20) | 8.02 | .00 | 14.10 | 23.50 | 2.17 |
| Low BLDS | 26 | 22.85(10.42) | | | | | |

*Note*. BLDS = Baseline Depression Scorers, LL=Lower limit, UL=Upper limit

Result in Table 1 shows significant difference between two groups of participants on the Siddiqui-Shah Depression Scale (Siddiqui & Shah, 1997) at baseline. On the basis of these scores participants were divided in two groups.

Table 2

*Mean Pre and Time 1 IFN Difference on Siddiqui-Shah Depression Scale (N = 57)*

| Groups of Hepatitis C Patients | Pre-IFN | At 24th Week | | | 95% CI | | |
|---|---|---|---|---|---|---|---|
| | *n* | *M* (*SD*) | *M* (*SD*) | *t* (*df*) | *p* | *LL* | *UL* | Cohen's *d* |
| High BLDS | 31 | 41.65 (07.20) | 49.13 (18.57) | 2.00 (30) | .05 | 0.14 | 15.11 | .54 |
| Low BLDS | 26 | 22.85 (10.42) | 23.08 (8.33) | .22 (25) | .82 | 1.88 | 2.35 | .02 |

*Note.* IFN=Interferon, BLDS=Baseline Depression Scorers; LL=Lower limit, UL=Upper limit

Results in Table 2 reveal significant difference between two groups of patients. Hepatitis C patients having higher baseline

depression level have scored higher on the SSDS at 24th week (time, 1) of the INF therapy than low baseline depression scorers. These results support our first hypothesis.

Table 3

*Mean Pre and Post IFN Difference on Siddiqui-Shah Depression Scale (N= 57)*

| Groups of Hepatitis C patients | Pre-IFN | At 24th Week | | | 95% CI | | |
|---|---|---|---|---|---|---|---|
| | *n* | *M (SD)* | *M (SD)* | *t(df)* | *p* | *LL* | *UL* | Cohen's *d* |
| High BLDS | 31 | 41.65 (7.20) | 49.94 (19.76) | 2.12(30) | .04 | 0.33 | 16.25 | .65 |
| Low BLDS | 26 | 22.85 (10.42) | 23.70 (7.83) | .51(25) | .77 | 1.77 | 3.47 | .03 |

*Note:* IFN=Interferon, BLDS=Baseline Depression Scorers; LL=Lower limit, UL=Upper limit

Results presented in Table 3 demonstrate that hepatitis C patients having higher baseline depression have scored significantly higher on the Siddiqui-Shah Depression Scale (Siddiqui & Shah, 1997) as compared to those with low baseline depression score at week 24th and post-IFN therapy. We can safely assume that hepatitis C patients having higher baseline depression experience higher depression after completion of interferon treatment. These results support our second hypothesis.

Table 4

*Repeated Measure ANOVA for Depression Scores across Three Time Points (N= 57)*

| Groups of Hepatitis C Patients | *n* | Pre-IFN *M (SD)* | 24th Week *M(SD)* | Post IFN *M(SD)* | *F* | *p* |
|---|---|---|---|---|---|---|
| High BLDS | 31 | 41.65 (7.20) | 49.94(19.76) | 49.94(19.78) | 4.52 | .04 |
| Low BLDS | 26 | 22.85(10.42) | 23.70 (7.83) | 23.69 (7.83) | .44 | .51 |

*Note:* IFN=Interferon, BLDS=Baseline Depression Scorers; LL=Lower Limit, UL=Upper Limit

Results in Table 4 show significant difference in high and low baseline depression scorers on the SSDS. The obtained mean scores of the high baseline depression scorers on the depression scale in three

time points is higher than low baseline depression scorers which support our both hypothesis.

Table 5

*Post Hoc Analysis for Comparing Mean Difference for Depression Scores across Three Time Points*

| Groups of Hepatitis C | | | Difference | | | 95% CI | |
|---|---|---|---|---|---|---|---|
| Patients | *i* | *j* | *i-j* | *SE* | *p* | *LL* | *UL* |
| High BLDS | Baseline | 24th Week | 7.48 | 2.70 | .05 | 15.11 | 0.14 |
| | | Post IFN | 8.29 | 3.89 | .04 | 16.25 | 0.33 |
| | 24th Week | Baseline | 7.48 | 3.73 | .05 | 0.14 | 15.11 |
| | | Post | .80 | 1.04 | .44 | 2.93 | 1.31 |
| | Post | Baseline | 8.29 | 3.89 | .04 | 0.33 | 16.25 |
| | | 24th Week | .80 | 1.03 | .44 | 1.31 | 2.93 |
| | Baseline | 24th Week | .23 | 1.03 | .82 | 2.35 | 1.89 |
| | | Post IFN | .84 | 1.27 | .51 | 3.47 | 1.78 |
| Low BLDS | 24th Week | Baseline | .23 | 1.03 | .82 | 1.88 | 2.35 |
| | | Post | .61 | .61 | .32 | 1.88 | 0.65 |
| | Post | Baseline | .84 | 1.27 | 51 | 1.77 | 3.47 |
| | | 24th Week | .61 | .61 | .32 | 0.65 | 1.88 |

*Note:* IFN= Interferon; BLDS= Baseline Depression Scorers; LL=Lower Limit; UL=Upper Limits

*$p<.05$

Table 5 reveals result of Post Hot test carried out using LSD which demonstrates significant difference between means of baseline and week 24th, baseline and post, between means of week 24th and baseline and between post and baseline in the high baseline depression scorers. Among low baseline depression scorers results show no significant difference between obtained means in three times on SSDS. These results clearly support our hypotheses.

## Discussion

The purpose of current study was to investigate the effect of baseline depression on interferon induced depression in hepatitis C patients.

The first hypothesis of the study assumed that depression score on the Siddiqui-Shah Depression Scale of hepatitis C patients will be higher during the interferon treatment. The results revealed significant difference between high and low baseline depression scorers in terms of depression on the Siddiqui-Shah Depression Scale. Hepatitis C patients having high baseline depression scores experienced higher

levels of depression as compared to those with low baseline depression scores during the treatment. These results are in accordance with earlier research showing that patients with higher levels of depression at pre-IFN treatment are more vulnerable to develop depression during the antiviral treatment (Castera *et al*., 2006; Heinze, Egberts, & Rotzer, 2010; Malaguranera *et al.*, 1998; Majer *et al.*, 2008; Raison *et al.*, 2005). Numerous studies reported that presence and severity of depressive symptoms at baseline are predictive of subsequent development of mood disorders in patients treated with interferon treatment (Dieperink *et al*., 2003; Pavlovic *et al.*, 2011). The findings of current study concerning second hypothesis are consistent with numerous researches. For example, Mahajan, Avasthi, Grover and Chawla (2014) examined the effect of baseline depression on subsequent development of depression among 82 hepatitis C patients. The participants were assessed at baseline and at $2^{nd}$, $4^{th}$, $8^{th}$, and $12^{th}$ weeks of therapy using the Patient Health Questionnaire (Spitzer, Kroenk, & Williams, 1999) the Mini International Neuropsychiatric Interview (Sheehan, Lecrubier, & Sheehan, 1998) and the Beck Depression Inventory (Beck *et al.*, 1961). Their results showed that patients having certain depressive symptoms at baseline, that is, social withdrawal, feeling tired, loss of pleasure in normal routine activities, and in work and appetite loss, were more likely to develop significantly higher levels of depression than those having no baseline depressive symptoms.

In a more recent study Sarker, Sarker, Berg, and Schafer (2015) investigated sadness and cognitive impairment as predictor for interferon alpha induced depression in 91chronic hepatitis C patients who previously not received interferon treatment. Depression of these patients was measured on single item (sadness) of the Montgomery Asberg Depression Rating Scale (MADRS; Montgomery & Asberg 1979), the Beck Depression Inventory (Beck *et al.,* 1961) and cognitive functions were assessed using the Trail Making Test A/B (TMT A/B; Arnett & Seth, 1995). All these patients (without history of psychotic disorders) were examined before, $14^{th}$, $8^{th}$, and $2^{nd}$ weeks, during the treatment, and after $2^{nd}$,$4^{th}$,$12^{th}$, and $24^{th}$, weeks of the therapy. Result showed a significant association between higher baseline MADRS scores and depression during the treatment. Further low baseline TMT-A and TMT-B score was predictive of severe depression.

In an early study, Johnson *et al*., (1998) compared depressive symptoms of drug users with the hepatitis C patients non-treated with IFN, and with non-infected substance abusers. Findings revealed that 57.2% of the hepatitis C patients (who were using drugs) and 48.2%

of no-infected substance abusers showed significant symptoms of the depression. These authors concluded that IFN induced depression might, in part, be associated with pre-existing depression, especially in the substance abusers. Pereira *et al.,* (2014) in an epidemiologic study examined rate and severity of depression in 50 Brazilian patients with hepatitis C at week $12^{th}$, $24^{th}$, and $48^{th}$weeks. Their result showed that patients obtained highest depression scores at $24^{th}$ weeks of the treatment. Further, significant correlations between scores on the baseline somatic subscale of the Beck Depression Inventory (Beck *et al.,* 1961) and overall scale scores were found. Patients having previous history of alcohol and substance abuse developed higher levels of depression. Numerous studies reported 13% to 44% incidence of IFN- induced depression in hepatitis C patients (Manns *et al.,* 2001) but large randomized trail studies using standardized methods of evaluation revealed 20% to 30% incidence (Fried *et al*., 2002; McHutchison *et al.,* 1998). Higher levels of depression at baseline play a major role in development of subsequent depression during the IFN treatment. Numerous researches have addressed this issue and found depressive symptoms before the interferon treatment as risk factor for development of depression during treatment (Diepeink *et al.,* 2000; Heinzeet *et al.,* 2010; Raison *et al.,* 2005). The results of the current study are in line with the available research evidence and clearly support our first hypothesis.

Our second hypothesis postulated that post-treatment scores of hepatitis C patients with higher baseline scores on the depression scale will be significantly higher after completion of the therapy. The results revealed that hepatitis C patients who obtained higher baseline scores on depression scale scored significantly higher on the depression scale after completion of the treatment. A comparison of mean difference between depression scores (baseline & post-IFN) of high and low baseline depression scorers shows a clear difference in depression experienced by these patients. These results demonstrate that patients having higher levels of depression at baseline experienced higher depression after completion of the treatment. These findings match with results of numerous prior researches most of which were conducted in the west (e.g., Castera *et al.,* 2006; Dieprink *et al.,* 2003; Rainson *et al.*,2005), which suggest that hepatitis C patients with higher levels of depression at pre-interferon therapy experience significantly higher depression during and after completion of the treatment. Our findings regarding second hypothesis are consistent with several studies. For example, the study by Berati *et al*., (2005) which examined effect of baseline depression on interferon induced depression in 36 hepatitis C patient at pre- treatment, 2 times,

that is, at 1st and 2nd month during, and after completion of the therapy and found a strong positive correlation between depression scores at baseline and one month after the treatment. Our findings are also consistent with Reichenberg, Gorman, and Dieterich's study (2005) on depression and cognitive impairment in which they examined 50 hepatitis C patients at baseline, 14 times during treatment, four times post treatment and found major depressive disorders in 82% of patients at first week of the therapy, while higher levels of baseline depression were associated with severe depressive symptoms during and after completion of the treatment. Similarly, the findings of present study are consistent with Evon *et al.*'s research (2009) which examined the effect of baseline depression and social support in 400 hepatitis C patients (197 African American & 203 Caucasian) at baseline and at week 4th, 12th, 24th, and 24th weeks after completion of the treatment and found that patients having higher baseline depression were more likely to develop major depressive episodes and were more likely to discontinue the therapy as compared to those with low baseline depression scores.

Some researchers studied effect of low dose INF-α therapy in patients with malignant melanoma and found that higher pre-treatment depression scores correlated with the subsequent increase in the depression score during and after INF-α treatment (Heinze *et al.*, 2010; Majer *et al.*, 2008). Our findings with reference to second hypothesis are also consistent with the literature mentioned above.

## Implications

The findings of the current study have important implications. At initial stage of hepatitis C assessment, screening and identification of the baseline depression should be included as a part of the treatment so that to get maximum clinical benefits from treatment. Patients with clear symptoms of depression should be subjected to adequate psychological therapies and treatment should be continued till enough stability in psychological treatment is ensured. An improved psychological management of these risk factors may allow gastroenterologist to continue and get success in treatment, and not to exclude from treatment patients that are deemed as high risk.

## Limitations and Suggestions

The current study has certain limitations which should be taken into consideration by future researchers. There are certain other

variables that predict depression in hepatitis C patients. These include female gender, low socioeconomic status, low educational level and patients with substance abuse. There is a dire need to study the effects of these other variables by future researchers. The current study investigated the impact of baseline depression on development of depression during one point that is, at week 24$^{th}$and after completion of the treatment. The evaluation of depression more than two points in hepatitis C patients is recommended. In present study, a self rating scale was used to measure depression of the sample. Assessment by the psychiatrists of the same risk factor in the sample could provide a cross check with data which might reveal more valid results. Thus, future researchers need to examine interferon induced depression in patients using both self reports and experts ratings.

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