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ORIGINAL ARTICLES

Depression within Hepatitis C virus patients: A case control study

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ABSTRACT

Background: The prevalence of depression is increased in patients with chronic hepatitis C virus (HCV) patients even in the absence of interferon (IFN) therapy. The aim of this work was to study the prevalence of depression in a cohort of Egyptian HCV naiive to treatment patients at early stage of the disease ,and the cofactors that may affect development of depression. **Patients and methods:** HCV compensated naïve to treatment patients as well as age and sex matched controls were studied for depression manifestations using the Beck inventory depression questionnaire. **Results:**75 male compensated naïve to treatment HCV patients of mean age 40.5± 5 years as well as 75 age and sex matched healthy controls were grouped into groups 1 and 2 respectively. Prevalence of mild mood disturbance, borderline clinical depression, moderate depression ,severe depression and extreme depression in group 1 versus group 2 were (17.3%vs 21.3%, 14.7%vs 12%, 10.7%vs 4%,2.7%vs 0% and 2.7% vs 0% respectively) with no statistical difference between the 2 groups($p>0.05$) .The mean depression score of group 1 (112.2±2) was significantly higher than that of group 2 (8.5±2) $p<0.05$. Within the HCV group age and ALT level were positively correlated to the score of depression($p<0.001$ and $p<0.05$ respectively). **Conclusion:** Although at early stages of HCV it seems that there is no significant difference in the prevalence of depression as compared to the general population, yet there is a significantly higher grade of depression within HCV patients, which is positively correlated to age and degree of hepatic inflammation.

Key words: HCV, depression, Beck depression inventory .

Introduction

The prevalence of depression is increased in patients with chronic hepatitis C virus (HCV) infection where several aetiological mechanisms are thought to be involved as, premorbid psychiatric disease, genetic disposition to affective disorders, socio-economic factors, stigmatization, possibly HCV neuroinfection (Hjerrild, S., *et al*., 2010) and changes in cerebral metabolism (Weissenborn, K., *et al*., 2009) even in the absence of IFN-alpha therapy, comorbid depression, cognitive decline, and especially fatigue are common in patients suffering HCV (Giunta, B., *et al*., 2007) This necessitates early identification and treatment of these symptoms that impact the patient's mental health, functional ability and overall quality of life (Saunders, 2008) and of particular importance, to diagnose and manage depression which constitutes one of the relative contraindications to Interferon (IFN) therapy (Hjerrild, S., *et al*., 2010) and deprive a considerable percentage of patients their chance to be administered the standard of care (SoC). Of notable importance is the relative scarcity of literature in studies tackling depression in HCV patients naïve to treatment, as compared to studies dealing with depression in HCV patients during their course of the SoC, together with the fact that screening for depressive symptoms in nonpsychiatric medical settings is rather exception that routine, and in a high proportion of patients depression is neither recognized nor treated adequately (Uzun, S., *et al*., 2009) Thus the aim of this work was to study the prevalence of depression among a cohort of compensated naïve to treatment HCV patients in comparison to healthy controls, as well as studying the sociodemographic and medical cofactors that would possibly represent risk factors for developing depression in this cohort of patients.

Patients and methods:

Study population:

This is a prospective case control cross sectional study that included 75 chronic compensated HCV hepatitis C infected male patients as proved by HCV-RNA by polymerase chain reaction(PCR) (group 1) and

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75 age and sex matched healthy controls (group2). Both groups gave informed consent for participation in the study before enrollment.

The following were considered as exclusion criteria from the study:

1-Age:less than 18 years or older than 55 years .
2-Decompensated chronic liver disease (ascites, oesophgial varices, hepatic encephalopathy).
3- History of Interferon alpha and/or ribavirin treatment in the last 6 month.
4-Patients with any other chronic disease such as diabetes, renal failure, psychiatric disorder, alcoholic, ischaemic heart disease.
5- Malignancy of whatever nature.
6- Drug history of neuropsychiatric drugs.

Methods:

All patients were subjected to the following:-

1-Full history taking and thorough clinical examination .
2-Liver enzymes ;alanine aminotransferase(ALT), aspartate aminotransferase(AST), total serum bilirubin, direct serum bilirubin, serum albumin,
3-Fasting blood glucose, 2 hours post prandial blood glucose, and renal profile.
4- Complete blood count (CBC).
5-Abdominal ultra sound examination.

Both groups were subjected to:

Beck Depression Inventory questionnaire:

The Beck Depression Inventory (BDI) is a self –administered 21 item self-report rating inventory measuring characteristic attitudes and manifestations of depression (Beck *et al*.1961).

Interpreting the Beck Depression Inventory:

The questionnaire is formed of 21 questions, After the questionnaire has been completed, we added up the score for each of the twenty-one of counting the number to the right of each question the patient marked. The highest possible total for the score would be sixty-three. This would mean that the patient circled numbered three on all twenty-one questions. The lowest possible score for each question is zero; the lowest possible score for the test would be zero. The total score ranges from 0 to 63, with higher scores indicating more severe depression. Scores from 0 to10 indicates no depression. Scores from 11 to 16 indicates mild mood disturbance. Scores from 17 to 20 indicates borderline clinical depression. Scores from 21 to 30 indicates moderate depression. Scores from 31 to 40 indicates severe depression, and scores from 41 to 63 indicates extreme depression. This questionnaire has been extensively validated in various populations, including patients with chronic HCV infection.

Statistical analysis:

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 16.
Description of quantitative variables as mean, SD and range.
Description of qualitative variables as number and percentage.
Unpaired t-test was used to compare two groups as regard quantitative variable in parametric data (SD<50% mean).
Mann Whitney test was used to compare quantitative variables in non parametric data (SD>50% mean).
Chi—square test was used to compare two groups as regard qualitative variable.
Correlation co-efficient test (r) test was used to rank variables against each others either positively or inversely.
P value >0.05 insignificant.
P<0.05 significant.
P<0.01 highly significant

Results:

This case - control study included 75 male patients with chronic hepatitis C, and 75 age and sex matched healthy controls. There was no statistically significant difference as regards socio-demographic data between the

2 groups (p>0.05) as shown in (table 1) that comprised age, occupation and special habits that was confined to smoking as there were no alcohol users or abusers within the studied population. Also, all biochemical analysis showed no statistical significant difference between both groups, apart from total serum bilirubin and AST that were both significantly higher among the HCV group (p<0.01) as shown in table 1.

Based on Beck's depression inventory 52% of HCV patients and 62.7% of controls had no manifestations of depression, 17.3% of HCV patients and 21.3% of controls had mild mood disturbance, 14.7% of HCV group and 12% of the control group showed borderline clinical depression, 10.7% of the HCV group and 4% of the control group had moderate depression, 2.7% of the HVC group and 0% of the control group had severe depression and finally 2.7% of the HCV group and 0% of the control group had extreme depression, where all these values showed no statistical significant difference between both groups using the Chi square test (p>0.05) as shown in table 1. But, on comparing the mean depression score between both groups the HCV group showed a significantly higher score than the control group (112.2 versus 8.5% respectively) p<0.05 as shown in table 1. Age and ALT were the only variables correlated to depression within the cases (r=0.23 p<0.001 and r=0.2 p<0.05 respectively) as shown in table 2. This was represented graphically in Fig 1 that shows the positive correlation between age and depression score, and fig 2 that shows the lack of a correlation between HCV-RNA value and the score of depression .

Table 3 showed no significant factor associating depression, whether occupation, age or the presence of cryoglobulinemia.

Table 1: Characteristics of the studied groups.

Variables	Cases N=75	Controls N=75	P
Age	40.5±5	39.9±6	>0.05
Profession			
Manual	50(66.7%)	22(29.3%)	>0.05
Clerk	17(22.7%)	35(46.7%)	
Professional	8(10.7%)	18(24%)	
Smoking			
No	48(64%)	45(60%)	>0.05
Yes	27(36%)	30(40%)	
Depression			
No depression	39(52%)	47(62.7%)	>0.05
Mild mood disturbance	13(17.3%)	16(21.3%)	
Borderline clinical depression	11(14.7%)	9(12%)	
Moderate depression	8(10.7%)	3(4%)	
Severe depression	2(2.7%)	0	
Extreme depression	2(2.7%)	0(0%)	
Score (mean±SD)	112.2±2	8.5±2	<0.05
Laboratory results			
RBCs (10^6/ml)	4.3+0.2	4.2+0.1	>0.05
Hb(g/dL)	12.8+2	12.9+2.3	>0.05
TLC(10^3/ml)	6.1±1	6.7±2	>0.05
PLT(10^3/ml)	199±56	193±24	>0.05
ALT(U/L)	14.6+2	18+3	>0.05
AST(U/L)	47.5+8	18.5+4	<0.001
Total Bil (mg/dL)	0.73+0.11	0.55+0.2	<0.001
Direct Bil	0.3±0.02	0.1 ±0.02	>0.05
Albumin(g/dL)	4.1+2	4.5+1.6	>0.05
FBS(mg/dl)	83+3	83.7+4	>0.05
PPBlgl(mg/dl)	120±8	119.5±10	>0.05
Urea(mg/dl)	0.86±0.2	0.85±0.1	>0.05
Creatinine (mg/dl)	12.3±5	10±3	>0.05

RBCs= red blood cells, Hb=haemoglobin, TLC=total leucocytic count, PLT=platelets,
ALT=alanine transaminase, AST=aspartate transaminase, FBS=fasting blood sugar, PPBlgl=postprandial blood glucose,

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Table 2: Correlation between depression score and different variables among cases.

Variables	Depression score	
	r	P
Age	0.23	<0.001
RBCs	0.19	>0.05
HB	0.05	>0.05
WBCs	0.17	>0.05
Platelets	0.14	>0.05
ESR	-0.10	>0.05
ALT	0.20	<0.05
AST	0.11	>0.05
Total bilrubin	0.07	>0.05
Direct bilrubin	-0.08	>0.05
Serum albumin	0.11	>0.05
FBS	-0.10	>0.05
2hpp	0.16	>0.05
Cr	-0.01	>0.05
Urea	0.12	>0.05
HCV-RNA	0.13	>0.05
PT	-0.17	>0.05
INR	0.08	>0.05
PVD	0.02	>0.05

RBCs= red blood cells, Hb=haemoglobin, TLC=total leucocytic count, PLT=platelets, ALT=alanine transaminase, AST=aspartate transaminase, FBS=fasting blood sugar, PPBlgl=postprandial blood glucose,PT=prothrombin time ,INR=international randomized ratio ,PVD=portal vein diameter

Table 3: Associated factors with depression among cases

Variables	Depression		P
	No	Yes	
Manual	26(66.7%)	24(66.7%)	
Clerk	8(20.5%)	9(25%)	>0.05
Professional	5(12.8%)	3(8.3%)	
Age	40.8±2	35.4±4.8	>0.0
Cryoglbulins	5(13.2%)	10(27.8%)	>0.05

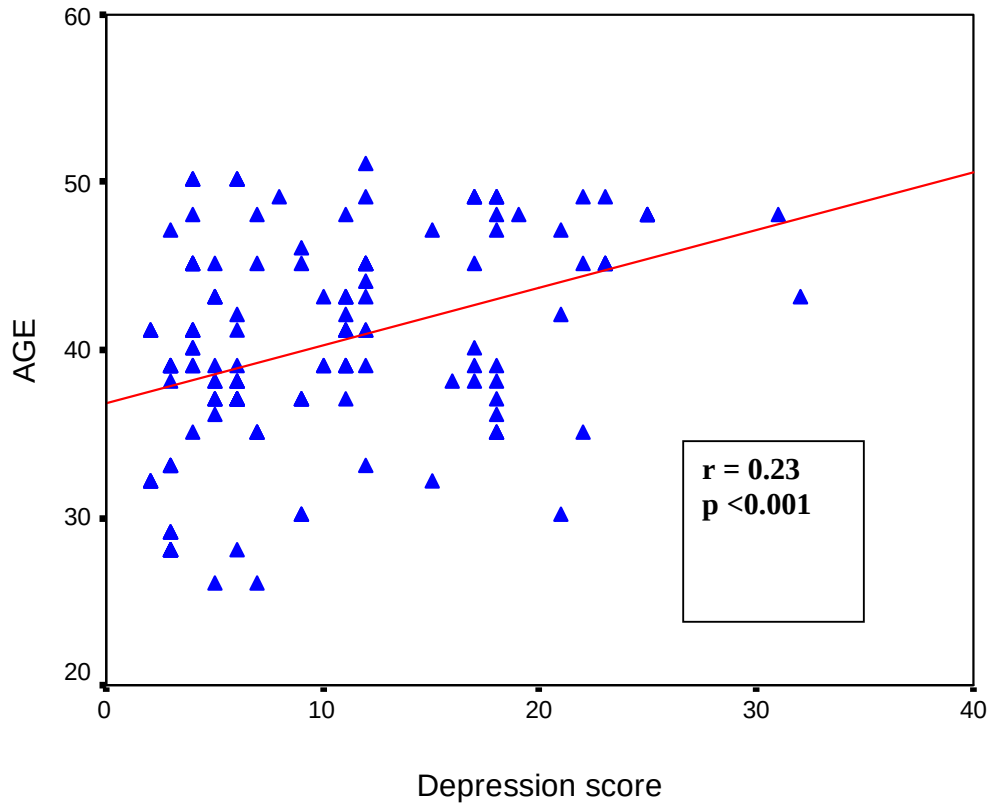

Fig. 1: Scattered plot representation of the correlation between depression score and age

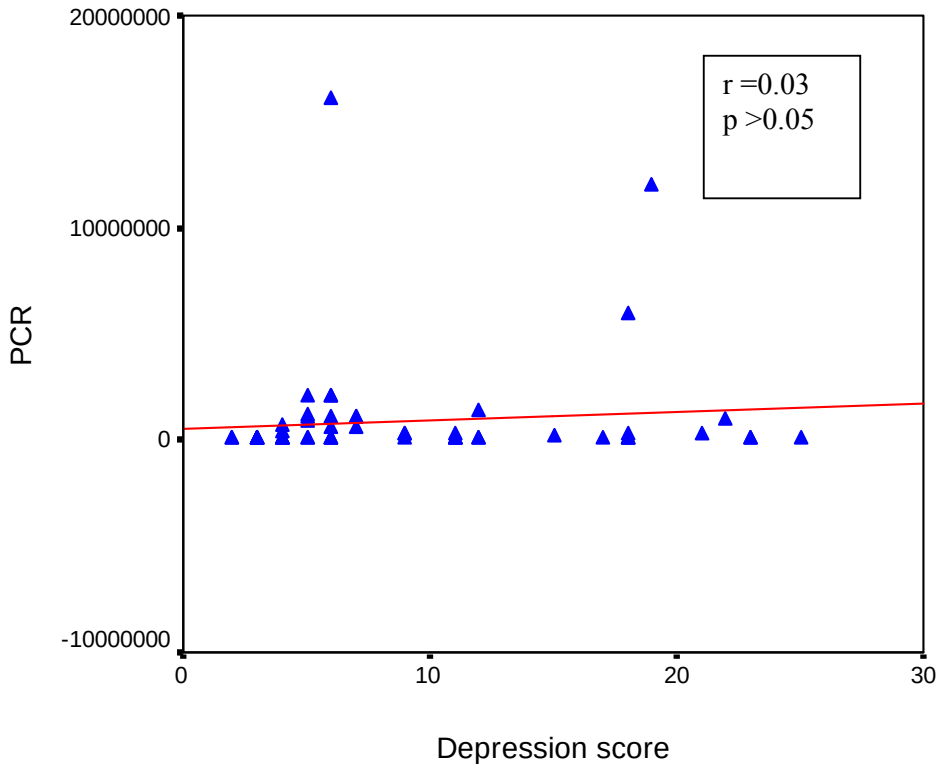

Fig. 2 Scattered plot representation of the correlation between depression score and PCR

Discussion:

HCV is one of the few infections, in addition to HIV, which is heavily linked to psychiatric disorders (Rifai, M.A., *et al*., 2006) It is generally well established that patients diagnosed with chronic HCV report a variety of associated psychosocial problems including a reduction in health-related quality of life (HQOL) (Foster, G.R., C. Hepatitis, 1999) increase in symptoms of depression and anxiety (Fontana, R.J., *et al*., 2002) and are at greater risk for stigmatizing experiences both from the general public and those in the healthcare system (Zickmund, S., *et al*., 2003).

In this work we searched for depression within HCV cases in comparison to controls using the BDI that measures both the affective and somatic components of depression as well as the depth of depression. On basis of the BDI, 52% of the HCV patients were totally free of any psychiatric disorders , while 48% showed a variety of disorders ranging from mild mood disturbance to extreme depression, if we exclude patients with mild mood disturbance the prevalence of patients showing different grades of depression within the HCV group would be 31%. The prevalence of depressive disorders within HCV patients ranged between 28% and 59% among different studies (Danoff, A., *et al*., 2006; Dwight, M.M., *et al*., 2000; Gallegos-Orozco, *et al*., 2013). The present study revealed a significantly higher depression score among HCV cases as compared to controls which supports the data of Danoff and his coworkers in 2006 (Danoff, A., *et al*., 2006) who on a background of studying sexual dysfunction in HCV male patients, found the median of BDI score to be significantly higher among HCV patients than in control subjects (9 and 5 respectively), which accords with the results by Dwight and his co-workers in (Dwight *et al*, 2000), who found significantly higher mean BDI score among HCV patients than among controls, 12 and 4 respectively . Moreover, Danoff and his colleagues in (Danoff *et al* 2006) found a significantly higher prevalence of depression among HCV patients (47.3%) than among the control group (23.8%), which differed from the results of the current study that in terms of prevalence of overall depression as well as the prevalence of different levels of depression revealed no statistical significance between cases and controls. The current results showed the prevalence of severe and extreme depression among HCV infected patients to be 5.4% , which was shown by Leutscher and his group to be 6% (Peter Derek Christian Leutscher, 2010)

Whether the development of depression within HCV patients correlates to the severity of the disease or not is an important research point ,it has been suggested by Gallegos-Orozco and his group in (Gallegos-Orozco *et*

al, 2003) that emotional disturbances in chronic HCV patients occurred independently of underlying liver disease severity as they found no significant differences in depression scores between cirrhotics and chronic HCV. The present work studied compensated HCV patients at relatively early stages of the disease where cirrhotics were not enrolled, and the results showed depression to be correlated to the ALT level , yet no correlation was found between depression and HCV-RNA levels as measured by PCR. To our opinion this warrants further investigating the correlation between the degree of hepatic inflammation and its impact on psychiatric manifestations in particular depression .

We put into consideration sociodemographic factors that may influence development of depression in HCV patients, among which age was the only factor found to be significantly correlated to depression which is similar to the pattern in the normal population , where two early studies (Murrell, S.A., *et al*., 1983; Mirowsky, J. and C.E. Ross,1992) found age to be significantly correlated to depression in the general population which could be attributed to age-related decline in central serotonergic function may make older individuals more vulnerable to depression and possibly render depressive episodes more frequent, more severe, and less amenable to treatment (Lerer, B., *et al*., 1996).

On studying other social factors that may affect development of depression within HCV patients, we focused on occupation , and classified patients according to their jobs into manual workers, clerks and professional (lawyers, physicians, engineers) where we did not find any statistical significance between the prevalence of any of this professional categories within HCV patients showing depression.

The correlation between smoking and depression in HCV patients is scarce in literature as all studies searched for this correlation in studying depression in the general population and not in HCV patients. The present study showed that there is no significant correlation between depression and smoking among cases, on the contrary to the study of Anda and his group (Anda, R.F., *et al*., 1990) who found depressive symptoms to be positively correlated with current smoking and negatively correlated with likelihood of quitting smoking**,** it is to be noted that the age of their studied population was higher than ours (53.3±6 and 40.6±5 respectively) , also, their applied questionnaire for assessment of depression *(Epidemiologic Studies Depression Scale)* did not differentiate between mild, moderate or severe depression.

An earlier study (Hughes, J.R., *et al*., 1986). Reported a 49% prevalence of current smokers with major depressive disorder in study of psychiatric outpatients . In conclusion HCV patients show a significantly higher mean depression score than controls. Age and the degree of liver inflammation are positively correlated to the degree of depression.

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