

# Evaluation of Depression in Hemodialysis Patients

Dr.Muhammad Anees, Dr.Haris Barki, Mahrukh Masood, Dr.Asim Mumtaz, Tahira Kausar.

## Abstract

**Objective:** The present study was conducted to identify risk factors for depression in patients under going hemodialysis. Incidence of depression was also measured.

**Study Design:** Cross-sectional prospective study.

**Place and duration:** Hemodialysis unit of Shalamar Hospital and Shaikh Zayed Hospital, Lahore from 1<sup>st</sup> Jan2006 to 30<sup>th</sup> April 2006.

**Subjects and Methods:** This study was conducted on all patients who were getting regular hemodialysis for more than three months. Beck's Depression Inventory- II (BDI-II; adapted in Urdu) was administered on all the patients who were able to read or understand it. Blood sample of all patients was drawn at the same time for routine hematological, biochemical parameters and viral markers (Anti HCV and HbsAg). Diagnosis was made according to the criteria mentioned in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM IV) for correlation of psychological variables with clinical, hematological and biochemical parameters.

**Results:** In this study 89 patients were enrolled, amongst them majority of them were male 52 (58.4%) and married 77 (86.5%). Major causes of renal failure were diabetes, hypertension and chronic glomerulonephrotis. Duration on dialysis was from 03 to 49 months with mean of  $19.64 \pm 11.7$ . Severity of depression was categorized in to mild, moderate and severe on the basis of BDI score. Majority of

the patients were moderately to severely depressed 50 (56.1%) and there was no gender difference in the prevalence of depression. Majority of patients were anemic, hypoalbuminemic and hyperkalemic.

**Conclusion:** Majority of patients under going hemodialysis were depressed. Major risk factors for depression came out to be hypertension, tachycardia, anemia and hepatitis C with disturbed liver function. Patients with anemia, hyperkalemia and hyponatremia had suicidal tendency. Patients with hypophosphatemia were having easy fatigability. Anti HCV was positive in 47% of patients. Illiterate patients had uncertainty regarding their illness which increased their depressive mood.

**Key Words.**Depression.hemodialysis

## INTRODUCTION

Depression plays a crucial role in the progression of chronic medical illnesses. A person with depression feels so hopeless that s/he abandons the will to survive. Consequently the person will fail to show compliance and the medical illness exacerbates due to lack of preventive measures. Moreover, loss of appetite creates nutritional deficiencies to make the things even worse. Deterioration of physical health would deepen the depression to create a vicious cycle. Chronic kidney disease is also a chronic medical illness. Independent of the cause of kidney disease physical fitness decreases with its progression till the development of end stage renal disease (ESRD). Patients on hemodialysis may manifest various psychiatric problems like affective disorders, dementia and personality disorders (1). Amongst all psychiatric disorders depression is the most important and common in patients with ESRD. Depression in dialysis patients not only effect mortality (2-4) but increased rate of hospitalizations (1-6) and dialysis withdrawal (7) is also very common.

Depression is also related with quality of life and increased cardiovascular morbidity (4, 8).Suicidal tendencies or attempt is significantly more common among dialysis patients than general population. (9)The incidence of depression in dialysis patients ranges from 10% to 66 %.( 10).This wide variation is due to different criteria and methods used to diagnose depression. (11) In Pakistan, due to paucity of indigenious researches exact incidence of depression in dialysis patients is not known, so this cross-sectional study was conducted to check the prevalence ratio of depression in two major dialysis centers of Lahore, Pakistan.

## **Material and Methods**

This study was conducted at hemodialysis units of Shalamar and Shaikh Zayed Hospital, Lahore, from 1<sup>st</sup> Jan 2006 to 30<sup>th</sup> April 2006. A self administered questionnaire- Beck Depression Inventory (BDI- II) comprising of 21 items; adapted in Urdu was filled by all the patients as a screening diagnostic tool. The questionnaire was filled out only by those patients who were able to read or understand it. Patients with dementia, delirium and who were unable to understand that questionnaire were excluded from the study. A performa consisting of relevant demographic variables (sex, education, marital status, number of children, family members, family system, any financial support, history of smoking and addiction) was also administered. Scoring of depression was done according to following severity levels: mild (depression scale 10-15), moderate (16 – 24 depression scale) and severe (25 and above)(12). At the same time pulse and blood pressure was checked and recorded. Blood sample of each patient was drawn for hematological (Hb) and biochemical parameters. Diagnostic criteria for depression was taken from Diagnostic and Statistical Manual of Mental Disorders, (DSM IV) criteria, to observe the relationship of important psychological variables with hematological and biochemical parameters (urea, creatinine, sodium, potassium, calcium, potassium, phosphorus, albumin, ALT, HbsAg, Anti Hcv).

STATISTICAL ANALYSIS: Data was analyzed on SPSS for windows (ver 12.00) and statistical significance was set at  $p < 0.05$ . Correlation was used for analysis of the data.

## RESULTS

Majority of the patients were male and married. Demographic data of dialysis patients is shown in Table No.1.

**Table No.1 Demographic data of hemodialysis patients (n=89)**

| No. | Data                     | Results=n (%)   |
|-----|--------------------------|---|
| 1   | Age                      | 49.64 $\pm$ 15.26 years   |
| 2   | Sex                      | Male 52(58.4%)<br>Female 37(41.6%)  |
| 3   | Duration of hemodialysis | 19.64 $\pm$ 11.7 months   |
| 4   | Education                | Nil 37(41.6%)<br>Primary 26(29.2%)<br>Matriculation 16(18%)<br>Graduation 7(7.9%)<br>Master 3(3.4%) |
| 5   | Marital status           | Married 77(86.5%)<br>Unmarried 12(13.5%)  |
| 6   | Smoking                  | NO 69(77.5%)<br>YES 20(22.5)  |
| 7   | Addiction                | NO 87(97.7%)<br>YES 2(2.2%)   |

**Table No.2 Depression Scores of hemodialysis patients (n=89)**

| <b>No</b> | <b>Depression Score</b> | <b>Mean± SD(%)</b><br><b>No.(%)</b> |           |
|-----------|-------------------------|-------------------------------------|-----------|
| 1         | Depression Scale        | 19.64 ±11.75                        |           |
| 2         | Depression Grade        | Nil                                 | 24(27%)   |
|           |                         | Mild                                | 15(16.9%) |
|           |                         | Moderate                            | 23(25.8%) |
|           |                         | Severe                              | 27(30.3%) |

**Table No.3 Clinical, hematological and biochemical parameters of hemodialysis patients (n=89)**

| No | Parameters             | Mean $\pm$ SD                |
|----|------------------------|------------------------------|
| 1  | Pulse                  | 81.97 $\pm$ 10.35 (per min)  |
| 2  | Mean arterial pressure | 100.69 $\pm$ 15.7 (mmHg)     |
| 3  | Hemoglobin             | 9.34 $\pm$ 1.71 (gm/dl)      |
| 4  | Urea                   | 146 $\pm$ 53.3 (mg/dl)       |
| 5  | Creatinine             | 9.87 $\pm$ 2.68 (mg/dl)      |
| 6  | Serum Sodium           | 136.5 $\pm$ 6.0 (mmol/lit)   |
| 7  | Serum Potassium        | 4.9 $\pm$ 1.0 (mmol/lit)     |
| 8  | Serum Calcium          | 8.14 $\pm$ 0.96 ( mg/dl)     |
| 9  | Serum Phosphorus       | 6.15 $\pm$ 1.89 (mg/dl)      |
| 10 | Serum Albumin          | 3.76 $\pm$ 0.60 (gm/lit)     |
| 11 | Serum ALT              | 41.77 $\pm$ 25.3 (units/lit) |

Major cause of end stage renal disease (ESRD) was diabetic nephropathy 41(46.1%) and hypertensive nephropathy 20(22.5%) followed by chronic glomerulonephritis, nephrolithiasis and miscellaneous. Eighty eight percent of patients were either 10 grade passed or under 10 grade. Family members were in the range of 01 to 30 with mean of seven members in each family. Depression scores of these patients are shown in Table. No.2. Hematological, biochemical parameters are shown in Table No.3. Blood pressure was not controlled and

majority of patients had anemia, hypoalbuminemia, and hyperphosphatemia.

More than fifty percent of patients were moderately to severely depressed.

## DISCUSSION

Depression is generally accepted to be the most common psychological problem in patients with ESRD (4, 13).

Depression is characterized by both cognitive and somatic features. The somatic characteristic of depression is similar to symptoms of uremia like anorexia, sleep disturbance, fatigue, gastrointestinal disorders and pain. (14-15) Due to this overlap of symptoms of uremia with depression it is usually neglected, under diagnosed and untreated. In our study, our majority of patients 65 (72%) were mild to severely depressed with mean scale of depression of  $19.64 \pm 11.75$  according to Beck Depression Inventory (BDI-II). This ratio came out to be same as that of a study conducted in Turkey (16).

There is substantial variation in the percentage of depression in dialysis patients (25%- 60%) in studies conducted in different geographical areas.(17-19). This wide variation is due to different criteria used for depression and social factors affecting the patients in different geographical regions.

This prevalence of depression in dialysis patients is much higher as compared to the general population of Pakistan which is 06% to 30%,(20-21) and patients of cancer (22) and coronary artery disease. (23).

Possible social factors that increases the severity of depression is illiteracy, financial constraints. Education has a very strong correlation ( $p$  value  $< .05$ ) with psychological parameters of depression like insomnia, fatigue, diminished interest which are also supported by other studies in Pakistan.(18,24)



Our majority of patients 79(88%) were either have passed their 10 grade or under 10 grade and most of them were depressed. The reason for relating education with lower depression scores is that education creates awareness about the disease and people feel more confident about their treatment and as a result feel less insecure about the strategies related to prevention of the disease. We found out that illiterate patients are ignorant about basic facts about treatment procedures, prevention strategies and they are less adherence to medical treatment. Their information is based on misperceptions of simple facts that not only affect their health but treatment also. Illiterate patients believe on treatment options which are not evidenced- based and by the time they reach dialysis center they feel disappointed with the illness and are physically fatigued. Imparting fact- based education or information to the illiterate patients; according to their intellectual level, can improve the psychological features and their general physical health. They will feel lesser insecure and uncertain regarding their illness; hence, lower the severity of depression. They become dependent which affects their quality of life.

Socioeconomic factors plays important role in depression. The health budget of the country is very low, average per capita income is 430US dollars and 35% of the population falls below the poverty line. Health and education are lowest on the priority of public. Dialysis costs about 250 US dollars/month and most of patients are unemployed this further aggravates financial burden on dialysis patients. Under these circumstances any financial support plays a major role in alleviating the problems of these patients. In our study although monthly income does not have statistically significant relationship with depression but patients who were

getting any financial support from NGOs, hospital and/ or organization were less depressed as compared to those who were not. Bokhari et al (25) has found that depression is positively associated with income level below 83 US dollars per month. Financial support encompasses the direct effects of depression. Another reason is that quality of dialysis delivered to hemodialysis patients is not up to the international standards. Low dose of dialysis leads to increased morbidity and mortality of hemodialysis patients. (26).Anees et al has done a study in which inadequate dialysis (i.e  $Kt/V < 1.4$ ) was done in majority (61%) of patients. (27) Major reason for inadequate dialysis was financial and social problems which further aggravates depression in these patients. Unemployment is also an important factor that puts further financial burden on hemodialysis patients and increases their depression. In our study majority of patients 46(51.7%) were unemployed. This large ratio of unemployment augments depression in these patients.

In female patients, prevalence of depression is twice as compared to male patients. This difference (between male and female) is present in a lot of studies done in Pakistan. (25, 28)

But in our study this gender difference is not seen in renal failure patients. Major reason for this effect is that as males are dominant and usually earning hand in our social setup, so when they suffer from this chronic disease they get more depressed than adult female. During dialysis, patients are also dependent on their spouse and partner due to comorbid diseases. Male patients feel loss of independence and authority and hence, scored higher on BDI-II. (29)

The other reason is that patients with renal failure have increased uremic toxins in their body which inhibits testosterone secretion. Testosterone has an inverse relation with depression. So, low testosterone level is directly related with depression. (30-32)

Hypertension plays major role in morbidity and mortality of dialysis patients. Patients who were having high blood pressure (Mean Arterial Pressure  $100+15.7$  mmhg) and tachycardia were statistically ( $p$  value $<0.05$ ) more depressed. This was also seen in a study conducted in Taiwan by Fan PI et al (33)

So if we control the blood pressure of these patients we can control depression in an easier way and need lesser amounts of antidepressant drugs. One problem is that usually dialysis patients don't take antihypertensive drugs on the day of dialysis so this high blood pressure may show high readings on the day of dialysis. To rule out this problem home monitoring of blood pressure can be done to further confirm and strengthen this perspective. As tachycardia has positive relationship with depression so if we give beta one blockers to these patients, then it will not only control blood pressure but also helps in settling depression.

Albumin is very important marker of nutritional status of hemodialysis patients. Hypoalbuminemia is a major risk factor for morbidity and mortality of hemodialysis patients (34-35). In our study patients who were hypoalbuminemic (Mean  $\pm$  SD  $3.76+0.60$  gm/dl ) they were having positive correlation ( $p$  value $<0.05$ ) with all psychological parameters of depression.

Betul Kalender et al (36) has also found same correlation in which patients with hypoalbuminemia have depression. Uremia leads to distaste of mouth, nausea and vomiting during and after dialysis, delayed gastric emptying, autonomic neuropathy leading to diarrhea and constipation, inadequate dialysis. Depression

leads to loss of appetite, sleep disturbance and gastrointestinal disorders. So symptoms of uremia and depression lead to malnutrition. There are very wrong concepts of dietary restriction of protein intake by quakes(hakims i.e non qualified medical personals), homeopaths and non renal physicians so all patients who go for dialysis are already hypoalbuminemic and malnourished. If we include psychiatrist and psychologist in the management of these patients and depression is properly treated with antidepressant medicines then the role of depression can be reverted back in malnutrition. There is need to do study on the depression and malnutrition while other factors have been ruled out.

In hemodialysis there is rapid shift of electrolytes from body which can lead to hyponatremia or hypernatremia. In our study hyponatremia (Mean+SD)  $136.54 \pm 6.0$  has statistically significant relationship with suicide. The symptoms of hyponatremia include nausea, malaise, lethargy and headache. These symptoms compound the misery of depressed uremic patients which may enhance suicidal ideation. The symptoms directly attributable to hyponatremia primarily occur with acute and marked reductions in the plasma sodium concentration and reflect neurologic dysfunction induced by cerebral edema (37-38).In this setting, the associated fall in plasma osmolality creates an osmolal gradient that favors water movement into the cells, leading in particular to brain edema. (39)

Anemia is very much prevalent in hemodialysis patients. In our study mean hemoglobin was 9.34 gm/dl which much is less than recommended for normal population .The symptoms of palpitation, sweating, dyspnoea and lethargy are important symptoms of anxiety. So, it is very much obvious that uremic patients have high anxiety level. In our patients most of the patients were having

tachycardia. For many studies it has been proven that mix anxiety and depression have higher incidence of suicidal ideation than in simple depression(44).

Phosphate and calcium metabolism are disturbed in hemodialysis patients. In our study hypophosphatemia has strong and statistically significant relationship with easy fatigability which may be due to the anxiety and depression or proximal myopathy. (40)

Hypophosphatemic leads to irritability and paresthesia. Both these symptoms are important feature of anxiety and depression (41) and proximal myopathy.

Hepatitis C positive patients have strong positive correlation with depression. Depression prevalence in untreated HCV-infected patients ranges from about 24% to 50 %.( 42-43)

In our study 42(47.2%) patients were hepatitis c positive and they were having disturbed liver function tests. This has a statistically strong correlation with all psychological parameters like easy fatigability, insomnia, diminished interest, suicide, irritable mood, sadness.

### **Implications.**

1. Findings have implications in improving the quality of dialysis patients with depression.
2. Treatment options should entail psychological treatment.
3. Proper information regarding nutrition, dietary habits should be provided to the patients.
4. Information to these illiterate patients can improve psychological variables and their general physical health

### **Limitations in this study.**

1. Depression was not measured at the start of the study. So, it can not be said that depressive phase of the patients is due to uremia or they were already depressed when they came for treatment.
2. Psychosocial functioning of the patients was not taken into account.
3. Somatic symptoms of depression can not be separated from the symptoms of uremia.
4. A multicentric study should be done to check the prevalence ratio.

## REFERENCE

1. Kimmel PL; Thamer M; Richard CM; Ray NF. Psychiatric illness in patients with end-stage renal disease. *Am J Med* 1998; 105(3):214-21)
2. Kimmel PL; Weihs K; Peterson RA. Survival in hemodialysis patients: the role of depression. *J Am Soc Nephrol* 1993;4(1):12-27.)
3. Kimmel PL; Peterson RA; Weihs KL; Simmens SJ; Alleyne S; Cruz I; Veis JH Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients.  
*Kidney Int* 1998 ;54(1):245-54.)
4. Kimmel PL; Peterson RA; Weihs KL; Simmens SJ; Alleyne S; Cruz I; Veis JH Multiple measurements of depression predict mortality in a longitudinal study of chronic hemodialysis patients, *Kidney Int* 2000; 57:2097-2098.
5. Hedayati SS, Grambow SC, Szezech LA, Stechuckak KM, Allen AS, Bosworth HB, 5 Physician-diagnosed depression as a correlate of hospitalization in patients receiving long term hemodialysis: *Am J Kidney Dis.* 2005;46(4):642-9.
6. Lopes AA; Bragg J; Young E; Goodkin D; Mapes D; Combe C; et al. Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe. *Kidney Int* 2002;62(1):199-207.
7. McDade-Montez EA, Christensen AJ, Cvengros JA, Lawton WJ; The role of depression in dialysis withdrawal: *Health Psychol.* 2006;25(2):198-204.

8. Elovainio M, Keltikangas-Jarvinen L, Kivimaki M, Pulkki L, Puttonen S, Heponiemi T, et al : Depressive symptoms and carotid artery intima-media thickness in young adults: The Cardiovascular Risk in young Finns study. *Psychosom Med* 2005;561-167
9. Kurella M; Kimmel PL; Young BS; Chertow GM: Suicide in the United States end-stage renal disease program. *J Am Soc Nephrol* 2005; 16(3):774-81. Epub 2005 Jan 19.
10. Lopes AA; Albert JM; Young EW; Stayathum S; Pisoni RL; Andreucci VE et al.  
Screening for depression in hemodialysis patients: associations with diagnosis, treatment, and outcomes in the DOPPS. *Kidney Int* 2004; 66(5):2047-53
11. Wuerth D; Finkelstein SH; Finkelstein FO; The identification and treatment of depression in patients maintained on dialysis. *Semin Dial* 2005 Mar-Apr; 18(2):142-61  
J. Mark & G. Williams (2<sup>nd</sup> Ed). 1992. The psychological treatment of depression. A guide to the theory and practice of cognitive behavior therapy.
12. J. Mark & G. Williams (2<sup>nd</sup> Ed). 1992. The psychological treatment of depression. A guide to the theory and practice of cognitive behavior therapy.
13. Finkelstein FO, Finkelstein SH. Psychological adaptation and quality of life of the patient with end stage renal disease. In: Brown E and Parfrey P, eds, *Complications of Long Term Dialysis*, Oxford University Press, Oxford: 1999; 168-187.
14. Kimmel PL: Depression in patients with chronic renal disease: What we know and what we need to know. *J Psychom Res*: 2002; 53:951-956.
15. Kimmel PL, Peterson RA: Depression in end stage renal disease patients: Tools, correlates, outcome and needs. *Semin Dial*; 2005: 1891-97.



16. Mukadder Mollaoglu. Depression and health related quality of life in hemodialysis patients. *Dialysis and Transplantation*.2004; 33(9):
17. Tyrrell J,Pature L,Cadec B,Capezzali E,Poussin G. Older patients undergoing dialysis treatment :cognitive functioning, depressive mood and health related quality of life. *Aging and Mental Health*. 2005; 9(4):374-9.
18. Lew SQ,Piraino B.Quality of life and psychological issues in peritoneal dialysis patients. *Seminars in dialysis*.18 (2):119-23.
19. A Nizami, S Abbas, F Aslam, FA Minhas, Najma Najam. Relationship between anxiety, depression, psychological well-being and quality of life in diabetic patients having hemodialysis *J Pak Psych Society* ; 2005; 2(2):80-4.
20. Gadit AA; Out-pocket-pocket expenditure for depression among patients attending private community psychiatric clinics in Pakistan: *The Journal of Mental Health Policy & Economics*.7 (1):23-8, 2004.
- 21.Ali BS,Rahbar MH, Naeem S,Tareen AL.Gul A,Samad L. Prevalence of and factors associated with anxiety and depression among women in a lower middle class semi-urban community of Karachi, Pakistan .*J of Pak Med A*.2002;52(11):513-7.
22. Iqbal A. Common type of mental disorders in adult cancer patients seen at Shaukat Khanum Memorial Cancer Hospital and Research Center. *J Ayub Med Coll*.2004;16(4):65-9.

- 23 .Bokhari SS, Samad AH, Hanif S,Hadique S, Cheema MQ,Fazal MA,Gul M et al.Prevalence of depression in patients with coronary artery disease in a tertiary care hospital in Pakistan.
- 24.Husain N,Garter R,Tomenson B,Creed F. Social factors associated with chronic depression among a population-based sample of women in rural Pakistan. *Social Psychiatry & Psychiatry Epidemiology*.2004; 39
- 25.Bokhari SS, Samad AH, Hanif S,Hadique S, Cheema MQ,Fazal MA,Gul M et al.Prevalence of depression in patients with coronary artery disease in a tertiary care hospital in Pakistan.
- 26.Chora B, Calemard E, Ruffet M, Chazol C, Terract J, Vanel T et al. Survival as an index of adequacy of dialysis. *Kidney Int*. 1992; 41:1286-91.
27. M Anees,Aizaz MA,Rizwan-ul-haq,Waqar A.Tahir S.Adequacy of haemodialysis.2002;12(11):692-695.
- 28.Khwaja AK,Qureshi R,Azam SI .Prevalence and factors associated with anxiety and depression among family practitioners in Pakistan.*JPMA*;2004;54(2):45-9.
29. Kimmel PL. Psychological factors in adult end stage renal disease patients with hemodialysis: correlates and outcome. *Am J Kidney Dis*.2000; 35(1):132-140.
30. Feldman HA,Goldstein I,Hatzichristou DG,Krane RG and Mckinaly JB; Impotence and its medical and psychosocial correlates: Results of Massachusetts Male Aging Study.*J Urol* 1994,151;54-61.
31. Benetae, Melman A: The epidemiology of erectile dysfunction .*Urol Clin N Am* 1995,22: 699-709.

32. AR Yousafzai, M Yoysaf, M Jan, A Badar. Serum testosterone levels in young male patients with major depression. *J Ayub Med Coll*; 2000; 12(2):31-2.
33. Fan PL, Shu CH, Shiang JC, Kuo TS, Lung FW: Hypertension-a possible vulnerability marker for depression in patients with end stage renal disease. *Nephron Clin Pract* .2006; 102(1):c43-50.
34. Bergstorm J, Alvstrand A, Furst P. Plasma and muscle free amino acids in maintenance hemodialysis patients without protein malnutrition. *Kidney Int* 1990;38:108-14.
35. Collins AJ, Ma JZ, Umen A, Keshaviah P. Urea index and other predictors of long term outcome in hemodialysis patients survival. *Am J Kidney Dis* 1994;23:272-82.
36. Betul Kalender, Aytul Corapcioglu Ozdemir, Gulturk Koroglu; Association of depression with markers of nutrition and inflammation in chronic kidney disease and end stage renal disease : *Nephrol Clin Practice* 2006;102:c115-c121
37. Rose, BD, Post, TW, *Clinical Physiology of Acid-Base and Electrolyte Disorders*, 5th ed, McGraw-Hill, New York, 2001, pp. 716-720, 761-764.
38. McManus, ML, Churchwell, KB, Strange, K. Mechanisms of disease: Regulation of cell volume regulation in health and disease. *N Engl J Med* 1995; 333:1260.
39. Strange, K. Regulation of solute and water balance and cell volume in the central nervous system. *J Am Soc Nephrol* 1992; 3:12. 37Ravid M; Robson M. Proximal myopathy caused by latorogenic phosphate depletion. *JAMA* 1976;20; 236(12):1380-1.
40. Ravid M; Robson M. Proximal myopathy caused by latorogenic phosphate depletion.

JAMA 1976;20; 236(12):1380-1.

41. Silvis SE; DiBartolomeo AG; Aaker HM: Hypophosphatemia and neurological changes secondary to oral caloric intake: a variant of hyperalimentation syndrome.

42. Am J Gastroenterol 1980; 73(3):215-2239 Lee DH, Jamal H, Regenstein FG, et al. Morbidity of chronic hepatitis C as seen in a tertiary care medical center. *Dig Dis Sci.* 1997; 42:186-191.

43. Serag HB, Kunik M, Richardson P, et al. Psychiatric disorders among veterans with hepatitis C infection. *Gastroenterology.* 2002; 123:476-82.

44. Thompson EA, Mazza JJ, Herting JR, Randell BP, Eggert LL, The mediating role of anxiety and depression and hopelessness on adolescent suicidal behavior. *Suicide life threat behavior.* 2005; 35(1):14-34.