

Erectile dysfunction: Burden of disease in chronic liver disease patients in a developing country

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ABSTRACT

Objective: To measure the frequency of erectile dysfunction (ED) in patients of liver cirrhosis and to correlate the severity of erectile dysfunction with severity of liver disease.

Study Design: A descriptive cross sectional study.

Place and Duration: Medicine Department of Jinnah Medical College Hospital Karachi during from April 1, 2017 to March 31, 2018.

Methodology: Adult males confirmed patients of liver cirrhosis having active sexual life either admitted or attending OPD were included. Clinically and biochemically confirmed cases of cirrhosis of liver through serum albumin, Prothrombin time were requested to fill the IIEF-5 questionnaire. Patients were examined clinically for presence of jaundice, ascites and hepatic encephalopathy. Statistical Analysis was between erectile dysfunction and stage of liver disease.

Results: A total of 331 patients were taken and mean age of patients was 51.4 years. The frequency of erectile dysfunction was found to be 80.1%. About 74.3% patients had CTP-A, 84% had CTP-B while 97.4% patients had CTP-C. Significant correlation ($p = 0.489$, $p\text{-value} < 0.001$) was seen between severity of erectile dysfunction with liver disease.

Conclusion: Our findings relate that chronic liver disease has a high occurrence of erectile dysfunction.

Keywords: Alcohol, Chronic Liver Disease, Cirrhosis, Erectile Dysfunction, Jaundice, Viral Hepatitis.

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INTRODUCTION

Cirrhosis is a common disease all over the world including our region and it leads to various complications that have been well studied and reported in the literature¹. These include ascites, esophageal and rectal varices, encephalopathy, spontaneous bacterial peritonitis and hepato-renal syndrome

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to name a few². It also leads to poor quality of life and hormonal changes including changes in levels of sex hormones³. It also affects the sexual functions of the patient including decreased libido and erectile dysfunction (ED) in males.

Standardized evaluation of ED was a difficult task. In 1997 a questionnaire was developed named IIEF, for patients of erectile dysfunction and assessing the efficacy of Sildenafil⁴. It has been used since then gold-standard tool for assessing efficacy⁵. IIEF involves 15 questions on five domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction^{4,6}.

Till date there are no reports of ED in cirrhotic males from Pakistan using IIEF-5 scale. Chronic liver disease is stated in terms of dysfunction of liver like decreased albumin and vitamin K dependant clotting factors affecting Prothrombin time and portal hypertension causing splenomegaly, ascites, encephalopathy and hepato-renal syndrome. This study was conducted to document the frequency of ED in cirrhosis using IIEF-5 scale.

The study is conducted to determine the frequency of erectile dysfunction (ED) in patients of liver cirrhosis and to correlate the severity of erectile dysfunction with chronic liver disease (by CTP score).

METHODOLOGY

This a descriptive cross sectional study was conducted in Medicine Department of Jinnah Medical College Hospital Karachi during 12 months from April 1, 2017 to March 31, 2018. Sample size was calculated for population proportion with specified absolute precision method. Assuming the anticipated population proportion of erectile dysfunction in at 31.4% (p);⁷ the sample size is estimated to be as 331 patients. Inclusion Criteria consists of all adult male confirmed patients of cirrhosis of liver having sexual relationship. Exclusion Criteria shows patients with chronic renal failure, severe cardiac de compensation, myocardial infarction in last three months, unstable angina pectoris in the last three week, neuropsychiatric disorders, alcoholics, epilepsy, stroke, spinal cord injury and multiple sclerosis, hypospadiasis, epispadiasis, phimosis, balanitis were excluded from the study. Informed consent was taken. The approval from the Ethical Committee for Medical Research was obtained.

Clinically and biochemically confirmed cases of cirrhosis of liver were requested to fill the IIEF-5 questionnaire⁶ to assess for erectile dysfunction and its severity. A postgraduate resident was helping the subjects in filling the proforma using their native language. Total of the score obtained was done. Patients were examined clinically for presence of jaundice, ascites and hepatic encephalopathy to calculate Child Pugh Score for severity of chronic liver disease. Following laboratory investigations were also being carried out.

Serum Bilirubin Total, serum Albumin and Prothrombin time. All these tests were carried out by Hitachi automated biochemistry analyzer using Merck kits.

Data Analysis: Data was analyzed by SPSS 20. Frequencies and percentages were calculated for ascites, hepatic encephalopathy, severity of liver cirrhosis, erectile dysfunction (ED), severity of ED and age groups. Mean± Standard Deviation (SD) was calculated for age, bilirubin, serum albumin, INR, age and international index of erectile dysfunction-5 (IIEF-5). The correlation between severity of erectile dysfunction and severity of liver cirrhosis (By child pugh's grade) was done by spearman's rank correlation at 5% level of significance. Stratification was done with respect to age to see the effect of ED.

RESULTS

A total of 331 patients with liver cirrhosis participated in our study. The mean age of patients was 51.4 (±9.8) years. Majority of patients 150 (45.3%) had age between 51 – 60 years.

Mean (±SD) of total bilirubin came out to be 1.73 mg/dl, Albumin was 3.6 (±0.2) g/dl and Prothrombin Time was 78 (±3) %. Severity of liver cirrhosis was assessed by child pugh's classification (A, B and C). Out of 331 cirrhotic cases, 187 (56.5%) cases had A-class, 106 (32%) cases had B-class while 38 (11.5%) patients had C-class.

Erectile dysfunction (ED) was measured by using international index of erectile function-5 (IIEF-5), the frequency of erectile dysfunction was found to be 265 (80.1%).

Out of 265 ED cases, frequency of severe (IIEF = 1- 7) erectile dysfunction was seen in 132 (49.8%) cases, moderate (IIEF = 8 - 11) ED was seen in 59 (22.3%), mild to moderate (IIEF = 12- 16) ED was seen in 46 (17.3%), while mild (IIEF = 17- 21) ED was seen in 28 (10.6%) patients.

Frequency of erectile dysfunction was high in relatively older patients (age 51 - 60 years). 150 (56.6%) cases had age 51 – 60 years, 85 (32.1%) cases had age > 60 years while 30 (11.3%) cases had ≤ 50 years.

It was observed that frequency of erectile dysfunction increases with severity of cirrhosis as depicted by child Pugh score.

Significant correlation ($\rho = 0.489$, $p\text{-value} < 0.001$) was seen between severity of erectile dysfunction with liver disease (by child's pugh score) shown in Table-I.

Table-I: Correlation between severity of erectile dysfunction and severity of liver cirrhosis (by child PUGH's grade) (n = 265)

Erectile Dysfunction Severity	Child-Pugh's Classes Frequency n(%)		
	A	B	C
Severe	62 (44.6)	50 (56.2)	20 (54.1)
Moderate	32 (23)	18 (20.2)	9 (24.3)
Mild to Moderate	27 (19.4)	14 (15.7)	5 (13.5)
Mild	18 (13)	7 (7.9)	3 (8.1)

$\rho = 0.489$, $p\text{-value} < 0.001$

Keys:

Using International index of Erectile Function (IIEF)

Severe = 1 - 7

Moderate = 8 - 11

Mild to Moderate = 12 – 16

Mild = 17 - 21

DISCUSSION

Erectile dysfunction (ED) was explained by the National Institutes of Health Consensus Development Conference as the consistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance⁸. Thus, ED is becoming an increasing problem worldwide irrespective of ethnic group.

Recent studies have shown an easy way to evaluate ED by self-reported questionnaires. The international index of erectile function (IIEF)⁹, which has excellent reliability and sensitivity developed by Rosen et al. for evaluating male erectile function⁶.

Erectile dysfunction (ED) is frequently problematic in patients with chronic liver diseases¹⁰ such as hemochromatosis¹¹, alcoholic liver disease¹² or liver transplant patients¹³, leading to worsening quality of life in those patients. Hepatic cirrhosis is associated with hypogonadism and signs of feminization irrespective of the direct toxic effect of ethanol upon the testes. Cardinal features of hypogonadism such as decreased libido, testicular atrophy, low testosterone levels, infertility, reduced secondary sex hair and gynecomastia are seen in men with chronic liver disease.

Using IIEF-5, there was a high chance of erectile dysfunction, 80.1% to be precise in patients with liver disease. The prevalence in United States is 32%¹⁴ among the male

population and about 26% in Japan.¹⁵ Lee et al¹⁶ studied prevalence of NAFLD and female sexual dysfunction were 67/470 (14.3%) and 238/470 (50.6%), respectively. Gentile et al¹⁷ reported an extensive study, diabetes mellitus and stage of liver disease (cirrhosis vs chronic hepatitis) were the only independent predictors of ED in multivariate analysis.

In our study, patients were relatively older. Overall mean (\pm SD) age of patients with liver cirrhosis was 51.4 (\pm 9.8) years (Range = 30 – 65 years) and mean (\pm SD) age of ED patients was 53.9 \pm 10.3 years (Range = 35 – 65 years). In this study proportion of ED in patients with cirrhosis increased with grades of Chronic liver disease, as 74.3% cases had class A, 84% cases had class B while 97.4% cases had class C.

Frequency of severe erectile dysfunction was 49.8%, followed by moderate ED was 22.3%, mild to moderate ED was 17.3%, while mild ED was 10.6%. Apart from this the proportion of patients with severe and moderate ED increased with disease (cirrhosis) severity and proportion of mild ED was relatively stable. Significant correlation ($\rho = 0.489$, p -value<0.001) was seen between severity of erectile dysfunction with severity of liver disease (by child's pugh score) as shown in Table.

These results show that the severity of liver cirrhosis has increased erectile dysfunction. The plasma level of testosterone is decreased in chronic liver disease, and that plasma testosterone concentration was correlated with disease severity,¹⁸ however, whether or not the reduced level of testosterone is contributory to sexual dysfunction in patients with liver cirrhosis, as there was no significant effect of testosterone treatment on improvement of erectile dysfunction in patients with alcoholic liver disease⁹.

Paternostro declared the importance of portal hypertension by analyzing and stating that along with commonly known risk factors such as arterial hypertension and diabetes mellitus, liver dysfunction and portal hypertension too play a vital role in the evolvement of ED¹⁹. A study in Taiwan stated that erectile dysfunction improves after living donor liver transplantation²⁰. Another factor that can contribute to erectile dysfunction in cirrhotic patients is protein malnutrition.

CONCLUSION

These results show that liver disease is related to erectile dysfunction in patients with chronic liver disease.

Priorities of future studies: Although a reasonable amount of knowledge has been achieved from the recent surge in the disease and subsequent investigations, further studies are needed.

Population of men with liver cirrhosis is characterized by a high frequency of lack of sexual activity, and by a high prevalence of ED and should be targeted by interventions to improve sexual functioning. These preliminary data need further validation in prospective trial using more comprehensive questionnaires.

Limitations: By this study we know that we usually do not take into account this aspect of cirrhotic liver disease and hence it remains neglected. We admit that our study did not intervene to correct the condition. We just looked into the burden of disease.

AUTHOR'S CONTRIBUTION

Kumar R: Conceived idea, Designed research methodology, Editing of manuscript.

Riaz SU: Data collection, Statistical analysis, Manuscript writing.

Kumar A: Data collection, Statistical analysis, Manuscript writing.

Kumar A: Literature review, Final approval of manuscript.

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REFERENCES

1. El Soud Ali AA, Mohamed HI, Badr EA, Mohamed MA. Study of the relation between diabetes mellitus and hepatic encephalopathy in patients with liver cirrhosis. *Menoufia Med J* 2014;27:296-300
2. Al Khalloufi K, Laiyemo AO. Management of rectal varices in portal hypertension. *World J Hepatol.* 2015;7(30):2992–2998. doi:10.4254/wjh.v7.i30.2992
3. Chong CA, Gulamhussein A, Heathcote EJ, Lilly L, Sherman M, Naglie G, et al. Health-state utilities and quality of life in hepatitis C patients. *Am J Gastroenterol* 2003;98(3):630-638.
4. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997;49(6):822-830.
5. Gazzaruso C, Coppola A, Pujia A, Falcone C, Collaviti S, Fodaro M, Gallotti P, Solerte SB, Giustina A, Pelissero G, Luzi L, Montalcini T. Erectile dysfunction as a predictor of asymptomatic coronary artery disease in elderly men with type 2 diabetes. *J Geriatr Cardiol.* 2016 Sep;13(6) 552-556. doi:10.11909/j.issn.1671-5411.2016.06.011. PMID: 27582774; PMCID: PMC4987428.
6. Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Pena BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 1999;11(6):319-326.
7. Berrada S, Kadri N, Mechakra-Tahiri S, Nejari C. Prevalence of erectile dysfunction and its correlates: a population-based study in Morocco. *International journal of impotence research.* 2003; 24;15(S1):S3.
8. Seid A, Gerense H, Tarko S, Zenebe Y, Mezemir R. Prevalence and determinants of erectile dysfunction among diabetic patients attending in hospitals of central and northwestern zone of Tigray, northern Ethiopia: a cross-sectional study. *BMC endocrine disorders.* 2017;17(1):16.
9. Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Pena BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot*

- Res 1999;11(6):319-26.
10. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT. Hepatic encephalopathy--definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. *Hepatology* 2002; 35(3): 716-721.
 11. J. H. McDermott, C. H. Walsh, Hypogonadism in Hereditary Hemochromatosis, *The Journal of Clinical Endocrinology & Metabol*, 2005; 90(4): 2451–2455,
 12. Huo S, Scialli AR, McGarvey S, Hill E, Tügertimur B, Hogenmiller A, et al. (2016) Treatment of Men for “Low Testosterone”: A Systematic Review. *PLoS ONE* 11(9): e0162480. <https://doi.org/10.1371/journal.pone.0162480>
 13. Huyghe E, Kamar N, Wagner F, Yeung SJ, Capietto AH, El-Kahwaji L, Muscari F, Plante P, Rostaing L. Erectile dysfunction in liver transplant patients. *Am J Transplant* 2008;8(12):2580-2589.
 14. McCool ME, Zuelke A, Theurich MA, Knuettel H, Ricci C, Apfelbacher C. Prevalence of female sexual dysfunction among premenopausal women: a systematic review and meta-analysis of observational studies. *Sexual medicine reviews*. 2016; 1;4(3):197-212.
 15. Shirai M, Ishii N, Takanami M, Suzuki M, Oishi M. et al. Japanese validation of the international index of erectile function (IIEF). *Int J Impot Res* 1999;14:1-28
 16. Lee JY, Shin DW, Oh JW, Kim W, Joo SK, Jeon MJ, et al. Non-alcoholic fatty liver disease as a risk factor for female sexual dysfunction in premenopausal women. *PLoS ONE*.2017; 12(8): e0182708.
 17. Ivan G, Ferdinando F, Riccardo BA, Riccardo S, Emanuela Z, Biagio P,et al. Prevalence and risk factors of erectile dysfunction in patients with hepatitis B virus or hepatitis C virus or chronic liver disease: results from a prospective study. *Sexual Health*. 2018; 15, 408-412.
 18. Abdo AA. Health-related quality of life of Saudi hepatitis B and C patients. *Ann Saudi Med*. 2012;32(4):397–403. doi:10.5144/0256-4947.2012.397
 19. Paternostro R, Heinisch BB, Reiberger T, Mandorfer M, Schwarzer R, Seeland B. Erectile dysfunction in cirrhosis is impacted by liver dysfunction, portal hypertension, diabetes and arterial hypertension. *Liver International*. 2018;38;8: 1427-1436.
 20. Chien Y, Chiang H, Lin P, Chen Y. Erectile function in men with end-stage liver disease improves after living donor liver transplantation. *BMC Urology*. 2015;15:83.