Erectile dysfunction in patients with liver cirrhosis; upper Egypt experience

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Abstract

Background normal sexual activity is an important issue in the quality of life for both males and females. Several diseases were associated with erectile dysfunction, unfortunately, data about erectile dysfunction in cirrhotic patients was scanty. This study was conducted to determine the prevalence and risk factors of erectile dysfunction in patients with liver cirrhosis. Method: a cross-sectional study was conducted on 200 patients with liver cirrhosis they were divided into three groups according to Child score and erectile dysfunction was studied by (IIEF-5) Questionnaire and penile Doppler. Results the prevalence of erectile dysfunction in the cirrhotic patient was 80%. the erectile dysfunction worsens with the worsening of the liver condition (Child C), also 20% of the cirrhotic patients had penile venous leakage which became 28.6% in advance liver cirrhosis (Child C). Multivariate logistic regression showed that advancing in age, Albumin less than 2.8 g/dl, INR 1.7-2.2, Hb>16 g/dl and Child C were predictors of erectile dysfunction in cirrhotic patients. Conclusion Erectile dysfunction was found in 80% of cirrhotic patients. It was more frequently observed in cirrhotic patients having an advanced disease (child C). Patients reporting ED had elevated INR, serum bilirubin, suppressed serum albumin, and elevated level of hemoglobin.

Introduction

Liver cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. It is generally considered to be irreversible in its advanced stages, at which point the only treatment option may be liver transplantation. Patients with liver cirrhosis are susceptible to a variety of complications, and their life expectancy is markedly reduced.

Erectile dysfunction (ED) is widespread in patients with liver cirrhosis, with prevalence varying from 25% to 92%. Some comorbidities and risk factors associated with ED may be found in males with liver cirrhosis as well, including alcohol use, hypertension, diabetes, metabolic syndrome and depression. Other factors that may be associated with ED include changes in sex hormones, malnutrition, and the use of drugs such as diuretics and nonselective beta-blockers.

ED is associated with poor health-related quality of life and depression. Health-related quality of life (HRQOL) measurements are recognized as an important part of the overall management of liver cirrhosis and targeting specific symptoms can improve HRQOL. ED in males with liver cirrhosis is one such symptom that needs attention.

So, we conducted this study to clarify the prevalence and risk factors of ED in cirrhotic patients in our locality (Upper Egypt).

Patients And Methods
Across section, the study was conducted on 200 cirrhotic patients in the period from January 2022 to November 2022 at Hepatology, gastroenterology and infectious diseases department, Al-Azhar university hospital, Assuit all of them were subjected to:

1. Full detailed History tacking.
2. Careful Clinical examination.
3. Routine laboratory investigations including CBC, serum creatinine, urea, ESR, and Liver function tests included alanine aminotransferase, aspartate aminotransferase, direct and total bilirubin, total protein, INR and albumin.
4. Classification into Child A, Child B and Child C according to Child Turcot Pugh Score.
5. Viral serology analysis included serology studies for HBV and HCV.
6. Serum testosterone level.
7. Erectile dysfunction evaluation by the Arabic version of the international index of erectile dysfunction (IIEF-5) Questionnaire. The IIEF-5 domain scores of the patients were calculated and ED was determined on the erectile function domain. (IIEF-5) the questionnaire is a 5-item questionnaire assessing five domains of male sexual function (erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction). The IIEF-5 scores range from 1 to 25. It was used to define ED and its severity: 4 or lower (no attempts at intercourse); 5 to 7 (severe ED); 8 to 11 (moderate ED); 12 to 16 (mild to moderate ED); 17 to 21 (mild ED); and 22 to 25 (“normal” erectile function, i.e., absence of ED)\(^7\).
8. Penile Doppler ultrasound was performed with the patient supine in a quiet, darkened room by the same operator using a machine (SIEMENS) with a 10 MHz linear array probe. An initial real-time examination, in both the transverse and longitudinal planes, was performed to study cavernosal anatomy and identify fibrous plaques. A rubber band tourniquet is placed around the base of the penis before injection. About 50-120 mg papaverine was injected into either corpus cavernosum using a 27- or 30-gauge needle. The penis was inspected for abnormal curvature and the shaft was palpated for fibrous thickening. The scanning is made from the base at the penoscrotal junction, with the examiner's wrist resting on the patient's pubis. The Doppler signals were recorded from the cavernosal artery over a non-tortuous segment close to the root of the penis and care was taken to ensure angle correction to 60° and sample gate 1 mm during sampling. The accurate location of the Doppler gate further ensured optimal waveform tracing. The following parameters were measured at peak response from the clearest waveform obtained: the peak systolic velocity (PSV), the end-diastolic velocity (EDV) and the Resistance index (RI), \(RI = \frac{PSV - EDV}{PSV}\). The velocity waveforms from both cavernosal arteries at the same points were recorded initially at 5 min. and 10 min. 15 min. and 20 min post-injection. Avascular anatomy was also assessed for anomalies in flow and morphology. A (PSV) of less than 25 cm/sec was used as the threshold for arterial insufficiency. An (EDV) of greater than 5 cm/sec was used to predict venous incompetence. The images were recorded and printed on paper\(^8\).
**Inclusion criteria:**

The included married male patient who had liver cirrhosis and aged between 18 and 55 years old.

**Exclusion criteria:**

1. Patients more than 55 years old or less than 18 years old.
2. Patients who were treated with Interferon therapy in the last year.
3. Patients with renal failure.
4. Patients with endocrinological disorders.
5. Patients with heart failure.
6. Patients with neurological or psychosomatic disorders.
7. Patients with hypertension.
8. Patients with diabetes mellitus.
9. Patients with organic causes of erectile dysfunction.

**Ethics consideration:**

-The study is conducted under Helsinki standards as revised in 2013 and approved by the ethics committee of Al-Azhar-Assiut Faculty of Medicine.

-Before any data was collected, each patient was informed about the study's purpose.

-Those who agreed to participate in the research provided verbal and written informed consent.

-The data's privacy was guaranteed.

**Statistical analysis:**

The collected data were revised, organized, tabulated and statistically analyzed using Statistical analysis of statistical package for social sciences (SPSS) for windows. (Version 26, produced by IBM SPSS Inc., Chicago, USA). Categorical variables were reported as numbers and percentages and continuous variables, as Mean ± standard deviation (SD), medians and range. Student t-test (two-tailed) and paired t-test were used to compare continuous data. Fisher’s exact test and the Qi square test were used to compare categorical data.

**Results**

The demographic profile of studied patients was showed in the table (1) the mean age was 45.8 years, 70% were smokers, 72.5% of them were HCV-related liver cirrhosis, 17.5% were HBV-related liver cirrhosis and the last 10% were cryptogenic liver cirrhosis. And as regards Child scores; 45% were (Child A), 20%
were (Child B) and the last 35% were (Child C). and testosterone levels were below normal in 35% of studied patients.

Table (1) demographic data of the studied patients:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Mean± SD</td>
<td>45.8 ± 8.1</td>
</tr>
<tr>
<td>Range</td>
<td>27-55</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>140 (70%)</td>
</tr>
<tr>
<td>No</td>
<td>60 (30%)</td>
</tr>
<tr>
<td>Couse of liver cirrhosis</td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>145 (72.5%)</td>
</tr>
<tr>
<td>HBV</td>
<td>35 (17.5%)</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>20 (10%)</td>
</tr>
<tr>
<td>Child Score</td>
<td></td>
</tr>
<tr>
<td>Child A</td>
<td>90 (45%)</td>
</tr>
<tr>
<td>Child B</td>
<td>40 (20%)</td>
</tr>
<tr>
<td>Child C</td>
<td>70 (35%)</td>
</tr>
<tr>
<td>Testosterone level</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>130 (65%)</td>
</tr>
<tr>
<td>Below than normal</td>
<td>70 (35%)</td>
</tr>
</tbody>
</table>

The baseline laboratory Data were shown in table (2)

Table (2) the baseline laboratory data
As regards the prevalence of ED among cirrhotic patients our study revealed that 80% of cirrhotic patients were ED table (3)

Table (3) the prevalence of ED in cirrhotic patients:

<table>
<thead>
<tr>
<th>Patients</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without ED</td>
<td>40 (20%)</td>
</tr>
<tr>
<td>With ED</td>
<td>160 (80%)</td>
</tr>
<tr>
<td>Mild ED</td>
<td>25 (12.5%)</td>
</tr>
<tr>
<td>Mild to moderate ED</td>
<td>25 (12.5%)</td>
</tr>
<tr>
<td>Moderate ED</td>
<td>45 (22.5%)</td>
</tr>
<tr>
<td>Severe ED</td>
<td>65(32.5%)</td>
</tr>
</tbody>
</table>

As regards the relation between ED and Age group our study showed that the age group (44-55) had a significantly higher prevalence of ED table (4).

Table (4): Relation of age groups with ED.
As regards the results of penile doppler 20% of the studied patients had penile venous leakage and 80% were normal penile doppler and our study showed no significant relationship between penile doppler results and ED (Table 5).

**Table (5) relation between penile doppler results and ED**

<table>
<thead>
<tr>
<th>Doppler</th>
<th>Normal patients (40)</th>
<th>Patients with ED (160)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal penile</strong> Doppler</td>
<td>35 (21.9%)</td>
<td>125 (78.1%)</td>
<td>&gt;0.05 NS</td>
</tr>
<tr>
<td><strong>N=160</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Venous leakage</strong></td>
<td>5 (12.5%)</td>
<td>35 (87.5%)</td>
<td></td>
</tr>
<tr>
<td><strong>N=40</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Chi-square test was used

**Statistically significant at p<0.05

As regard Frequency and severity of ED according to Child Classification (Table 6) our study showed that the better the liver function (Child A) had the less ED and the worse liver function (Child C) had the more ED with highly significant P-value (less than 0.0001)

**Table (6) Frequency and severity of ED according to Child Classification**
As regards the relation between ED and the cause of liver cirrhosis our study showed that ED was more prevalent in patients with HCV-related liver cirrhosis with significant P.Value (<0.001) table (7).

Table (7): relation between ED and the cause of liver cirrhosis

<table>
<thead>
<tr>
<th>Etiology of cirrhosis</th>
<th>Normal patients (40)</th>
<th>Patients with ED (160)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV-related N=35</td>
<td>15 (42.9%)</td>
<td>20 (57.1%)</td>
<td>&lt;0.001 S</td>
</tr>
<tr>
<td>HCV-related N=145</td>
<td>20 (13.8%)</td>
<td>125 (86.2%)</td>
<td></td>
</tr>
<tr>
<td>Cryptogenic N=20</td>
<td>5 (25.0%)</td>
<td>15 (75.0%)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi-square test was used  
**Statistically significant at p<0.05

As regards predictors of ED, we do multivariant logistic regression of ED in cirrhotic patients which revealed that Age group (44-55) years, Albumin less than 2.8 g/dl, INR range (1.7-2.2), Hemoglobin level more than 16g/dl and Child C can predict ED table (8)

Table (8) multivariant logistic regression of ED
Parameters | P-value | Odd's ratio | 95% Confidence interval | Lower | Upper
--- | --- | --- | --- | --- | ---
Age group 31-43 | 0.998 | 0.52 | | 0.65 | 1.57
Age group 44-55 | 0.002 S | 1.023 | | 0.02 | 0.9
Albumin 2.8-3.5 mg/dl | 0.998 | 0.09 | | 0.09 | 0.22
Albumin < 2.8 mg/dl | <0.001S | 1.42 | | 1.21 | 1.32
Total bilirubin 2 – 3 mg/dl | 0.997 | 0.21 | | 2.36 | 3.36
Total bilirubin > 3 mg/dl | 0.997 | 1.42 | | 1.78 | 4.012
INR 1.7 - 2.2 | 0.042S | 1.12 | | 0.13 | 0.34
Mild ascites | 0.998 | 0.52 | | 0.52 | 4.3
Moderate ascites | 0.52 | 0.89 | | 0.1 | 1.6
Marked ascites | 0.998 | 0.03 | | 0.39 | 1.36
Hb 12 – 16 g/dl | 0.999 | .000 | | 2.56 | 5.06
Hb > 16 g/dl | <0.001S | 1.62 | | 4.63 | 5.02
HCV-related cirrhosis | 0.994 | 0.09 | | 1.58 | 6.33
Cryptogenic cirrhosis | 0.998 | 0.25 | | 1.88 | 4.12
Child class B | 0.999 | 0.85 | | 5.12 | 8.36
Child class C | 0.02S | 1.12 | | 6.14 | 9.15

Discussion

in our study, 80% of studied patients had ED which Almost agrees with Huyghe et al., 2009 who found ED prevalence was 76% in End-stage liver disease candidates for liver transplantation ⁹.

Explanation of high frequency of ED in the cirrhotic patient may be due to lower metabolic clearance rates, lower total and free levels of testosterone, reduced testosterone responses to human chorionic gonadotropin stimulation, higher estradiol levels, higher luteinizing hormone and follicle-stimulating hormone levels and higher binding capacities of sex steroid binding globulin ¹⁰.

while Jagdish et al., 2022 had the nearer result as in this study, 72.3% of men with cirrhosis had ED ³. This variation in the reported prevalence of ED is likely due to differences in the assessment tools used and differences in the severity of cirrhosis. But the prevalence of ED is higher than the result of Kim et al/where the prevalence of ED was found to be 41.2% in his study ¹¹.

This difference is probably due to the patient selection criteria used for the evaluation of ED in these studies. In his study, patients were relatively young, all patients were in stable chronic disease status and all cirrhotic patients were at the compensated stage without deteriorating their hormonal or physical status.

Frequency and severity of ED according to Child Classification of cirrhotic patients included in the study revealed that patients of child C complained of ED more than child A with increased severity of ED in
patients of child C more than child A. 55(61.1%) patients of child A have ED & 20(22.2%) patients have severe ED. Where 65(92.9%) patients of child C have ED & 40(57.1%) patients have severe ED, these results are in agreement with Huyghe et al., 2009.

This may be due to changes in sex hormones, malnutrition, and the use of drugs such as diuretics and nonselective beta-blockers.

Results of penile Doppler in our study revealed that normal penile Doppler in 160 (80.0%) patients & venous leakage in 40 (20.0%) patients and the relation between penile Doppler results and Child classification of cirrhotic patients revealed that patients with child A have normal penile Doppler in 70(77.8%) patients & Venous leakage in 20(22.2%); patients with child B have normal penile Doppler in 40(100.0%) patients & Venous leakage in 0(0.0%); patients with child C have normal penile Doppler in 50(71.4%) patients & Venous leakage in 20(28.6%). Which is statistically significant as a P-value (<0.001).

To our knowledge, there is no reported paper revealing the relation between liver cirrhosis and venous leakage on penile Doppler. In this study, there is 40 (20.0%) patients have venous leakage which may be accidental and as there is 160 (80.0%) patients have normal penile Doppler and so these results support our conclusion that liver cirrhosis is the cause of ED in this patient.

Another notable result is the relationship between the etiology of cirrhosis and ED our study shows that patients with liver cirrhosis due to HBV have ED (57.1%) these results agree with the study of Kim et al where the prevalence of HBV-related Liver Cirrhosis was (36.7%) but Kim et al had smaller sample size than our study.

Also, patients who had HCV-related Liver cirrhosis had significantly Higher ED which was (86.2%) but Fábregas et al showed significant sexual dysfunction but with a lesser percentage (45.1%) which may be due to patient selection criteria used for the evaluation of ED. In his study, patients were relatively young, and our study had a larger sample size.

Also, our study showed a positive relationship between age and ED and the Age group (44-55) had a significantly higher prevalence of ED. This result was agreed with Maimone et al who concluded that Patients with ED were significantly older than those without ED (p.value = 0.006).

The explanation for this result is morphologic and physiologic mechanisms that are involved in the aging process play a key role in the development of sexual dysfunction in the absence of any other clinical or medical condition. Also, a meta-analysis done by Yoo et al concluded that Patients with ED were 5.8 years older (p < 0.001).

On contrary Kim et al concluded that age is not a risk factor for ED in cirrhotic patients but they had a smaller sample size.
As regards predictors of ED, multivariant logistic regression showed that Age group (44-55) years, Albumin less than 2.8 g/dl, INR range (1.7-2.2), Hemoglobin level more than 16g/dl and Chid C can predict ED. The explanation of patients with Hb >16 g/dl having ED may be due to increased hemoglobin levels associated with sluggish blood flow.

**Limitation:** The limitations of our study are: A relatively small number of the study population, a single center and a lack of controls chosen from the general population without liver disease.

**Conclusion**

Erectile dysfunction was found in 80 % of cirrhotic patients. It was more frequently observed in cirrhotic patients having an advanced disease (child C). Patients reporting ED had elevated INR, serum bilirubin, suppressed serum and elevated levels of hemoglobin.

**Declarations**

1. **Ethics approval and consent to participate:** -The study is conducted under Helsinki standards as revised in 2013 and approved by the ethics committee of Al-Azhar-Assiut Faculty of Medicine. Before any data was collected, each patient was informed about the study's purpose. Those who agreed to participate in the research provided verbal and written informed consent. The data's privacy was guaranteed.

2. **Consent for publication:** not applicable.

3. **Availability of Data and Material (ADM):** The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

4. **Competing interests:** no competing interests.

5. **Funding:** no funding support.

**References**


