

## **RELATIONSHIP BETWEEN THE MELD SCORE WITH SEVERITY ERECTILE DYSFUNCTION IN CIRRHOTIC PATIENTS**

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### **ABSTRACT**

Background: Liver cirrhosis is a pathological condition that describes the end stage of hepatic fibrotic which progressively ongoing that signed by distortion from hepar architecture and the formation of the regenerative modulus. Liver cirrhosis causes impairment in most of the liver function including the hormonal balance and metabolism of steroids. In the male patients, liver cirrhosis causes hypogonadism and feminization. Sexual dysfunction in cirrhotic patients is still underestimated and underdiagnosed. The most common sexual dysfunction in male cirrhotic patients is impotence or erectile dysfunction. Erectile dysfunction (ED) is define as a persistence inability to reach and/ or maintain enough erection to satisfy the sexual activity. International Index of Erectile Function 5/IIEF-5 could mark erectile dysfunction. Despite the prevalence of erectile dysfunction is high in patients with liver cirrhosis, only a few studies revealing the relationship between severity of liver cirrhosis and severity of erectile dysfunction.

The purpose of this study is to determine the correlation between MELD score and severity of erectile dysfunction (IIEF-5 score) in cirrhosis patients.

This study is observational with a cross-sectional method. Subjects were patients with liver cirrhosis, male, age 18 to 65 years old, married, have a partner, and agreed participated to this study. We used Pearson the correlation to assess correlation between severity of liver cirrhosis (Child Pugh score) and severity of erectile dysfunction (IIEF-5 score) if the data were distributed normally and *Spearman* correlation if the distribution is abnormal.

Keywords: liver cirrhosis, MELD score, erectile dysfunction, IIEF-5, correlation.

### *Abstrak*

*Latar belakang: Sirosis hati adalah kondisi patologis yang menggambarkan tahap akhir fibrotik hepatic yang semakin berlanjut yang ditandai dengan distorsi dari arsitektur hepar dan pembentukan modulus regeneratif. Sirosis hati menyebabkan kerusakan pada sebagian besar fungsi hati termasuk keseimbangan hormonal dan metabolisme steroid. Pada pria, sirosis hati menyebabkan hipogonadisme dan feminisasi. Disfungsi seksual pada pasien sirosis masih diremehkan dan kurang terdiagnosis. Disfungsi seksual yang paling umum pada pasien pria*

*dengan sirosis adalah impotensi atau disfungsi ereksi. Disfungsi ereksi (DE) didefinisikan sebagai ketidakmampuan untuk mencapai dan / atau mempertahankan ereksi yang cukup untuk memuaskan aktivitas seksual. Indeks Internasional Fungsi Ereksi 5 / IIEF-5 dapat menandai disfungsi ereksi. Meskipun prevalensi disfungsi ereksi tinggi pada pasien dengan sirosis hati, hanya sedikit penelitian yang mengungkapkan hubungan antara tingkat keparahan sirosis hati dan tingkat keparahan disfungsi ereksi.*

*Tujuan: Tujuan dari penelitian ini adalah untuk mengetahui korelasi antara skor MELD dan tingkat keparahan disfungsi ereksi (skor IIEF-5) pada pasien sirosis. Penelitian ini bersifat observasional dengan metode cross-sectional.*

*Metode: Subjek penelitian adalah pasien sirosis hati, pria, usia 18 sampai 65 tahun, menikah, memiliki pasangan, dan setuju berpartisipasi dalam studi ini. Kami menggunakan korelasi Pearson untuk menilai korelasi antara tingkat keparahan sirosis hati (skor Child Pugh) dan tingkat keparahan disfungsi ereksi (skor IIEF-5) jika data didistribusikan secara normal dan korelasi Spearman jika distribusinya abnormal.*

***Kata kunci:*** *sirosis hati, skor MELD, disfungsi ereksi, IIEF-5, korelasi*

## INTRODUCTION

Cirrhosis of the liver is a pathological condition that describes the final stage of hepatic fibrosis, which lasts progressively characterized by distortion of the liver architecture and nodule formation regenerative<sup>1</sup>. Clinically, cirrhosis described as a compensation or decompensation. Decompensation means cirrhosis with one or more complications of the following symptoms: jaundice, ascites, hepatic encephalopathy or variceal bleeding. Ascites is usually the first marker. Ascites was produced from sinusoidal hypertension and sodium retention. Hepatorenal syndrome, hyponatremia and spontaneous bacterial peritonitis (SBP) can also describe the decompensation, but in this patient, the first time is always the case ascites. Compensated cirrhosis patients do not obtain these symptoms.

Classification of Child-Turcotte-Pugh (CTP) has become the

reference for more than 30 years to assess the prognosis of liver cirrhosis. Scores CTP has limitations because it comes from some of the experienced variables that affect the prognosis empirically. Among several new prognostic scores of liver cirrhosis reported in the literature, the score Model of End-Stage Liver Disease (MELD) is the best alternative to CTP score. MELD scores are prepared to overcome the limitations and replace CTP score. This score is composed based on a group of variables that are meaningful and independent of output through multivariate analysis<sup>4</sup>. MELD scores are very useful in patients with cirrhosis of the liver with a wide variety of disease severity and etiology of cirrhosis even in patients who have unexplained causes<sup>5</sup>.

Cirrhosis of the liver causes disturbances in the majority of liver function, including hormonal balance and metabolism of steroid<sup>6</sup>. In men, liver cirrhosis causes occur

hypogonadism and feminization <sup>6,7</sup>. Sexual dysfunction in patients with liver cirrhosis is still underdiagnosed and underestimates <sup>8</sup>. Erectile dysfunction (ED) is defined by persistent inability to attain and/or maintain an erection sufficient for satisfactory sexual activity <sup>9</sup>. Erectile dysfunction can be assessed by the International Index of Erectile Function 5 / IIEF-5 <sup>10</sup>. The assessment is validated by the Indonesian Medical Association in 1999. Most of the research in Indonesia also uses these instruments for the diagnosis of erectile dysfunction. The prevalence of ED in patients with cirrhosis are by 93% (age 30-79 years) largely ED weight (43%) <sup>11</sup>.

ED high prevalence in patients with liver cirrhosis, but the data is still limited research, few studies revealing the relationship between the degrees of severity of cirrhosis of the liver with the degree of erectile dysfunction.

The aim of research is to determine the relationship between MELD score with the severity of erectile dysfunction (IIEF-5 scores), in patients with liver cirrhosis.

## **MATERIAL AND METHODS**

The study design was cross-sectional. Subjects were patients with

liver cirrhosis treated at the clinic of Internal Medicine at the Hospital Dr. Sardjito, in January 2014 to December 2014. Inclusion criteria male, age 18 to 65 years old, married, has a life partner, willing to follow the research, Diagnosis of liver cirrhosis was established by ultrasound checkup, supported by clinical and laboratory data from medical records.

Exclusion criteria were patients with (1) cognitive disorders / communication, (2) diabetes mellitus, (3) Congestive heart failure, (4) a history of stroke, (5) Chronic kidney disease, (6) malignancy, (7) a history of prostate surgery, (8) a history of spinal trauma, (9) peripheral arterial disease, (10) the symptoms of major depression (BDI score > 31), (11) symptoms of severe anxiety.

Liver cirrhosis patients who met the inclusion and exclusion criteria were included in the study. All study subjects given an explanation and signed a letter of approval of participation in the study. Demographic data, clinical and laboratory parameters were collected from all study subjects. The chronology of the study were shown in Figure 1.

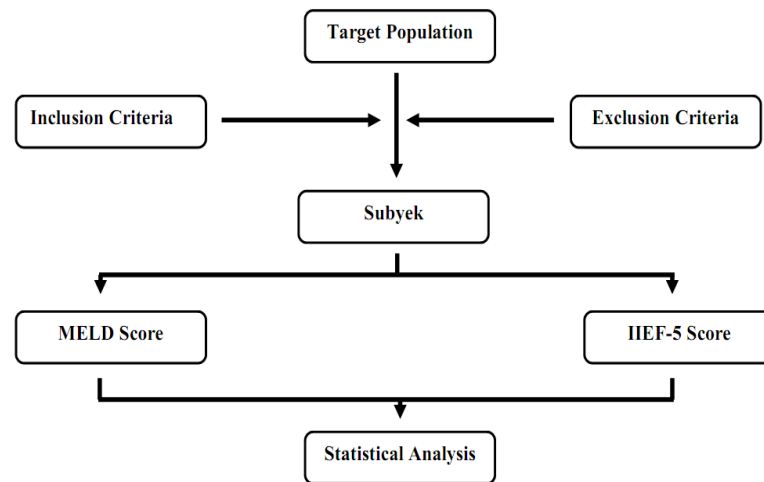


Figure 1. Flow Research

MELD scores assessed by a research assistant, using laboratory data (levels of bilirubin, albumin, INR (international normalized ratio), serum creatinine. Values obtained expressed as a MELD score. The degree of erectile dysfunction determined was by the International Index of Erectile Function 5 / IIEF-5). Patients fill the IIEF-5 is guided by a research assistant. Having obtained the IIEF-5 score and MELD score then performed statistical analysis.

Univariable analysis is conducted with descriptive analysis to look at the characteristics of the subject. Categorical data will be seen on the frequency distribution with the percentage proportion, while the numeric data will be the mean and standard deviation.

For bivariable analysis with independent variable / independent and dependent variable/ depending on the form of scale, the numerical data analysis using Pearson correlation

test for numerical distribution data but if the data is not normally distributed using Spearman correlation test 12. The correlation is very strong giving values ( $r = 0.80 - 1.00$ ); strong ( $r = 0.60$  to  $0.79$ ); moderate ( $r = 0.40$  to  $0.59$ ); low ( $r = .20-.39$ ); very low ( $r = 0.00$  to  $0.19$ ) 13.

## RESULT AND DISCUSSION

The research of correlation between the severity of liver cirrhosis (MELD score) with the degree of erectile dysfunction (IIEF-5 score) in the patient with liver cirrhosis is a cross sectional research. Subject of the research is the patient with liver cirrhosis conducting outpatient treatment in the polyclinic of Gastro-Entero-Hepatologi in the section of Internal Medicine in Dr. Sardjito Hospital Yogyakarta since November 2014 to November 2015.

There are 40 patients appropriate with the inclusion criteria and research exclusion. All of male patients with the mean age of  $48.93 \pm 10.30$  years. Most of the cause of liver cirrhosis is hepatitis B amount 25 patients (62.5%). The distribution of patients is based on the duration of suffering hepatic cirrhosis with the median 1 (1-27 years). Median score MELD is 13.5 (4-37) and the median score of IIEF-5 is 14 (5-25).

To understand the correlation between MELD score with the IIEF-5

score was conducted a correlation pearson test if the data distribution is normal and spearman test if the distribution is abnormal. In this research obtained the existence of correlation between the MELD score and IIEF-5 score with the p-value 0,001 and r score is -0.748 and the determination coefficient is  $r^2$  55.95%. It could be concluded that if the upgrading of MELD score so will be found reduction in IIEF-5 score with the moderate correlation with the correlation strength 55.95%.

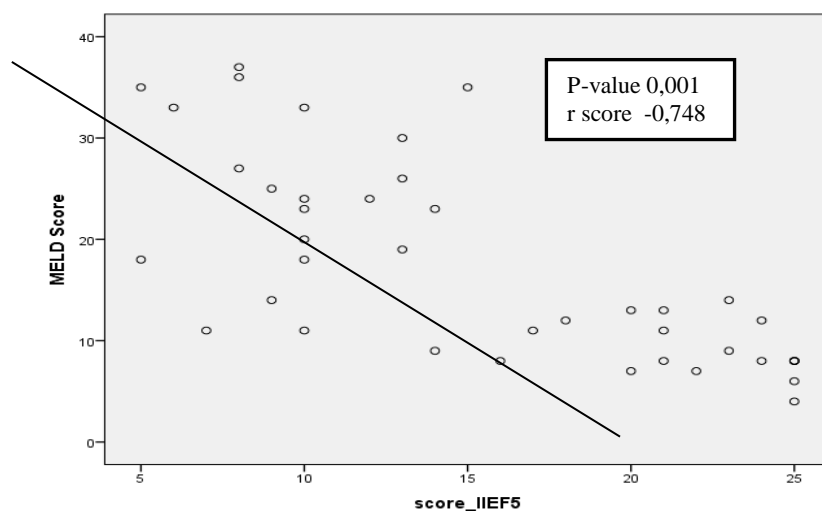
**Table 1** Basic Characteristics of the Subject of Research on Patient with Liver Cirrhosis, n= 40

Characteristics	Mean $\pm$ SD or n (%)
Demographic	
Age	48.93 $\pm$ 10.30
Education	
Completer Elementary School	13 (32.5)
Completer Junior High School	8 (20)
Completer Senior High School	15 (37.5)
Completer D3/S1	4 (10)
Clinically	
History of Smoking	
No	23 (57.5)
Yes	1 (2.5)
History	16 (40)
Alcohol Consumption	
No	36 (90)
History	4 (10)
Cause of Cirrhosis	
Hepatitis B	25 (62.5)
Hepatitis C	7 (17.5)
NAFLD	1 (2.5)
Other	7 (17.5)
The duration of suffering cirrhosis (year)	1 (1-27)
MELD Score	13.5 (4-37)
IIEF-5 Score	14 (5-25)
The circle of upper arm	10.8 $\pm$ 4.74
BDI score	10.8 $\pm$ 4.74
HAM-A score	6 (1-20)
Laboratory	

Haemoglobin (mg/dl)	10.66±1.96
GDS (mg/dl)	99.5 (72-172)
Creatinin (mg/dl)	0.98 (0.54-2.86)
Total Bilirubin (mg/dl)	2.15 (0.3-41.40)
INR	1.46 (1-3.62)
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Pharmacological	
Spironolactone dosage (mg)	50 (0-200)

Notes : ES : Elementary School, JHS: Junior High School, SHS : Senior High School, D3/S1 :Diploma 3/ Scholar, NAFLD: *Non Alcoholic Fatty Liver Disease*, MELD: *Model of End Stage*

*Liver Disease*, IIEF-5: *International Index of Erectile Function 5*, BDI: *Beck Depression Inventory*, HAM-A: *Hamilton Anxiety Scale*, GDS: *Blood sugar at one time*, INR: *International Normalized Ratio*.



The result of this research is similar with the research conducted by Toda et al (2005), the increase of severity degree in Erectile Dysfunction has positive correlation with the increase of

child pugh class (P <0.05). Muhammad et al (2012), cirrhosis patient with ED incline to the high severity group (child C) (p <0.000).

**Table 3.** Correlation of various variable potential to be confusing factor of erectile dysfunction

Variable	IIEF-5 Score	
	Correlation Coefficient (r)	p value
Age	-0.193	0.232
Education	NA	0.619
Occupation	NA	0.351
Smoking History	NA	0.357
Alcohol Consumption History	NA	0.08
Upper Arm Circle	0.287	0.73
BDI Score	-0.136	0.401
HAM_A Score	-0.23	0.154
Hemoglobin	-0.23	0.44
Sspironolactone Dosage	-0.356	0.024*

Information \*) p score < 0.05, BDI: *Beck Depression Inventory*, HAM-A: *Hamilton Anxiety Scale*

Spironolactone was used on the patient with asites. Side effect of spironolactone as the consequence of direct effect anti androgen. That side effect related with the dosage and the duration of usage (Finger and Slang, 2007).

## CONCLUSION

From this research can be concluded that there is negative correlation with the moderate strength degree between MELD score (the degree of severity in liver cirrhosis) with the IIEF-5 score (the degree of erectile dysfunction).

## Reference

1. Nurdjanah, S. 2009. Sirosis Hati. In: A. W. Sudoyo, B. Setiyohadi, I. Alwi, et al. (eds.) *Buku Ajar Ilmu Penyakit Dalam*. Jakarta: InternaPublishing, 668-673.
2. Garcia-Tsao, G. & Lim, J. 2009. Management and Treatment of Patients with Cirrhosis and Portal Hypertension: Recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. *Am J Gastroenterol*; 104:1802–1829.
3. McCormick, P. 2011. Hepatik Cirrhosis. In : Sherlock's Diseases Of The Liver And Biliary System 12Th Ed., A John Wiley & Sons, Ltd., Publication, 103-117.
4. Durand, F. O. dan Valla, D. 2005. Assessment of the prognosis of cirrhosis: Child–Pugh versus MELD. *Journal of Hepatology*, 42, S100-S107.
5. Chan, H.L.Y., Chim, A.M.L., Lau, J.T.F., Hui, A.Y., Wong, V.W.S., Sung, J.J.Y. 2006. Evaluation of model for end-stage liver disease for prediction of mortality in decompensated chronic hepatitis B. *Am J Gastroenterology* 101:1516-23
6. Kruszynska, Y. T. dan Bouloux, P. M. 2007. The effect of liver disease on the endocrine system. In: J. Rodes (ed.) *textbook of hepatology : from basic science to clinical practice* Malden mass: Blackwell.
7. Karagiannis, A. dan Harsoulis, F. 2005. Gonadal dysfunction in systemic diseases. *European Journal of Endocrinology* 152, 501-513.
8. Shabsigh, R. 2006. Epidemiology of Erectile Dysfunction. In: J. J. Mulcahy (ed.) *Male Sexual Function A Guide to Clinical Management* Humana.
9. Impotence, N. C. C. 1993. NIH consensus development panel on impotence. *JAMA*, 270, 83 - 90.
10. Rosen, R. C., Riley, A., Wagner, G., Hosterloh, I., Kirkpatrick, J. dan Mishra, A. 1997. The International Index of Erectile Function (IIEF): A

- multidimensional scale for assessment of erectile dysfunction. *Urology*, 49, 822-830.
11. Toda, K., Miwa, Y., Kuriyama, S., Fukushima, H., Shiraki, M., Murakami, N., *et al.* 2005. Erectile dysfunction in patients with chronic viral liver disease: its relevance to protein malnutrition. *J Gastroenterol* 40, 894-900.
  12. Tumbelaka A.R., Riono P., Wirjodiarjo M., Pudjiastuti P., Firman K. 2002. Pemilihan uji hipotesis dalam S Sastroasmoro dan S Ismail (eds) Dasar dasar metodologi penelitian klinis edisi kedua . Jakarta , Sagung Seto, 240-258.
  13. Sugiyono 2004. Statistik Non Parametris Untuk Penelitian. Bandung, Alfabeta.
  14. Huyghe, E., Kamar, N., Wagner, F., Capietto, A. H., El-Kahwaji, L., Muscari, F., *et al.* 2009. Erectile dysfunction in end-stage liver disease men. *J Sex Med*, 1395-1401.
  15. Finger, W. W. dan Slangue, M. A. 2007. Pharmacological agent causing male sexual dysfunction. *In*: F. R. Kandeel (ed.) *Male Sexual and Reproductive Dysfunction: Male Sexual Dysfunction: Pathophysiology and Treatment*. New York: Informa Healthcare.