

COMPARISON BETWEEN FIB-4 SCORE AND APRI SCORE AS AN INDICATOR OF THE SEVERITY OF CIRRHOSIS IN CHRONIC HEPATITIS B PATIENTS AT DR SOETOMO GENERAL HOSPITAL FOR THE 2018-2021 PERIOD

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Abstract

Cirrhosis is a condition characterized by the presence of regenerative nodules among the liver tissue which is experiencing fibrosis. Cirrhosis is caused by chronic liver damage, where the biggest cause is chronic infection with the hepatitis B virus. This study was conducted to compare the APRI score and FIB-4 score as an alternative that can be used as an indicator of the severity of cirrhosis in chronic hepatitis B patients who are hospitalized in RSUD DR Soetomo in the period June 2018-June 2021. This research was carried out in an observational analytic manner using patient medical record data.

In this study, the total population of cirrhotic patients with chronic hepatitis B etiology was 51 patients, and 35 patients were included in the inclusion criteria. 23 patients were male and 12 were female. The average age of the patients was 54.49 years with the youngest being 27 years and the oldest being 86 years. The majority of patients were in the severity of Child C and Child B, namely 15 patients and 14 patients. The prevalence of cirrhosis cases with chronic hepatitis B etiology in the inpatient ward of DR Soetomo Hospital for the period June 2018-June 2021 is 17.11%.

FIB-4 median value in the category Child A 2.493, Child B 4.365, and Child C 6.5. The FIB-4 interval values in the Child A category are 0.8-9.7, Child B is 0.8-14.9, and Child C is 2.2-17.8. The median APRI value in the Child A category was 0.743, Child B 2.121, and Child C 2.493. The APRI interval values in the Child A category were 0.5-1.8, Child B 0.2-7.9, and Child C 0.2 -7.9. Based on the Kruskal wallis method, a significance value of FIB-4 is 0.067 and APRI is 0.018, meaning that APRI can be used as an indicator.

The conclusion of this study is that the APRI score has better results to be used as an indicator of the severity of cirrhosis in chronic hepatitis B patients.

Keywords: Liver Cirrhosis, Chronic hepatitis B, CTP Score, FIB-4 Score, APRI score

1. Introduction

Cirrhosis is a condition where there are regenerative nodules surrounded by areas of fibrosis, a result of chronic liver damage. This condition can cause portal hypertension and end stage liver disease (Schuppan D & Afdhal Nezham H, 2008). According to Hsiang et al, the most common etiology of cirrhosis is chronic hepatitis B (37.3%), followed by alcoholic liver disease (24.1%), then chronic hepatitis C (22.3%). and non-alcoholic fatty liver disease (16.4%) (Stasi C et al., 2015). Of the 350 million people who have chronic hepatitis B infection, if it is not treated, it is estimated that around 8-20% of people will experience cirrhosis over a 5 year period, 20% of this number will experience liver decompensation. In the world, it is estimated that around 30% of cirrhosis cases and 45% of HCC cases are associated with chronic hepatitis B. In developed countries, NASH, HCV and alcoholic liver disease are the most common causes of cirrhosis, but in developing countries HBV and HCV are the most common causes (Sharma B & John S, 2020; Barbu LA et al., 2017; Samji Naga Swetha, 2017).

The cause of the highest morbidity and mortality from cirrhosis is caused by complications of portal hypertension and hyperdynamic circulation, where around 90% of cirrhosis patients will experience portal hypertension (Sharma B & John S, 2020; Barbu LA et al., 2017). The diagnosis of liver cirrhosis can be made through clinical findings in patients such as jaundice and ascites, then by laboratory examination to see the function of the liver, findings such as thrombocytopenia, low albumin levels, increased bilirubin levels are signs of decreased liver function. Imaging such as MRI, MRE, CT and ultrasound can also detect changes in the liver that indicate cirrhosis. The biopsy method is carried out to confirm the staging of the patient's liver condition, the etiology of the cause of cirrhosis can also be determined with this method, mainly used to assess the stage of fibrosis (Wiegand J & Berg T, 2013).

Child-Turcotte-Pugh Score or CTP Score, is used to predict mortality rates in liver cirrhosis patients. The prognostic value of the CTP score has been proven over the last 30 years. An analytical study proves that the CTP score can be used as an independent indicator for ascites, ruptured oesophageal varices, subclinical encephalopathy, hepatocellular carcinoma, liver surgery, alcoholic cirrhosis, decompensated HCV-related cirrhosis, primary sclerosing cholangitis, primary biliary cirrhosis and Budd–Chiari syndrome (Durand F & Valla D, 2005). Interpretation of the CTP Score is carried out by classifying cirrhosis into 3 categories, A, B, and C. Based on the score of 5 laboratory and clinical criteria from the patient. Survival rates for 1 year and 2 years from these categories are 100% and 85% (A), 80% and 60% (B), and 45% and 35% (C) (Tsoris A, Marlar Clinton A, 2019; Sharma B & John S, 2020).

Fibrosis based on four factors or FIB 4 score is a non-invasive method used to estimate the presence of fibrosis in the liver caused by various etiologies, one of which is Hepatitis B and Hepatitis C infections. The

formula for this method is $(\text{Age (Years)} \times \text{AST (U/L)} / \text{Platelet}(10^9 \times \sqrt{\text{ALT U/L}})$. FIB 4 score using a cut off value of <1.45 has an NPV of 94.7% and a sensitivity of 74.3% for advanced fibrosis. At a cut off value of >3.25 this method has a PPV of 82.1% with a specificity of 98.2% for diagnosing advanced fibrosis in patients with Hepatitis C infection (Pichard VA et al, 2007).

The aspartate aminotransferase-platelet ratio score or APRI score was first used by Wai et al in 2003, which has a sensitivity of 30% and a specificity of 93% (Seipalla G et al., 2020). The APRI score can be calculated using the formula $(\text{AST/Upper limit of AST} \times 100) / \text{platelet count}$, if the result is <0.5 , it means there is no fibrosis or only a little fibrosis, then if the result is 1.5, it means fibrosis has occurred. severe disease or cirrhosis. According to Shaheen et al. APRI score can predict the level of fibrosis that occurs in chronic hepatitis C patients with an APRI score <0.5 having an NPV of 72%, and an APRI score >1.5 having a PPV of 87% (Supriyanto I et al., 2012).

For this reason, it is necessary to carry out research regarding the comparison between FIB 4 score and APRI score to predict the severity of cirrhosis because both are methods that can be used as alternatives that are safer, more cost effective and easier to carry out, and it is necessary to know the comparison of each method. to find out a better method.

2. Methods

Researcher use medical record of patient with liver cirrhosis that caused by chronic hepatitis B infection that admitted in the DR Soetomo General Hospital from June of 2018 until June of 2021 that contain all the variable needed to assess CTP score, APRI score and FIB-4 Score. Researcher then process the data using Statistical Programme for Social Science (SPSS) with Shapiro Wilk method to determine if it's a normal distribute data. ANOVA or Kruskal Wallis non parametric test will be used to determine which is the superior to assess degree of liver cirrhosis based on CTP score between APRI and FIB-4 Score

3. Discussion

35 patients was sampled in this study, It was detected that 43% or 15 people had the severity of cirrhosis in the Child category C, next is 40% or 14 people have some degree of severity of cirrhosis Child B category, and the remaining 17% or 6 people have a degree of severity Child category A cirrhosis.

4 patients in Child A category had scores FIB-4 1.45-3.25. Then for Child B and Child C, the FIB-4 value was >3.25 is the largest, namely 9 and 12 patients. FIB-4 interval value at each CTP Score category, namely, Child A 0.8-9.7, Child B 0.8-14.9, Child C 2.2-17.8 Child A category has a median FIB-4 score of 2.409, category Child B has a median value of 4.365, and the median value is in category patients Child C is 6.5. Intervals from FIB-4 in each CTP Score category, Child A 0.8-9.7, Child B 0.8-14.9, Child C 2.2-17.8

4 patients in Child A category had APRI value 0.5-1.5. For Child B and Child C, the APRI value is >1.5 the largest were 9 and 12 patients. Interval value on each CTP category is 0.5-1.8 for Child A, 0.2-7.9 for Child B, and 0.2-7.9 for Child C. Child A category has a median APRI value of 0.743, patients with the severity of cirrhosis category Child B has a median APRI value amounted to 2.121 and patients with the severity of cirrhosis in the Child Child category C has a median APRI value of 2.493

The significance value is obtained through the Kruskal Wallis test FIB-4 got a result of 0.063 and APRI got a result of 0.018. FIB-4 does not can be used as an indicator of the severity of cirrhosis based on CTP because the significance value is $>5\%$. APRI can be used indicator because the significance value is $<5\%$. This result was obtained with using a cut off for each score based on the definition operational variables. Research conducted in 2007 which discussed Correlation between FIB-4 and liver biopsy results and Fibroscan examination It was found that the FIB-4 value <1.45 had an NPV value of 94.7% for elimination it is likely that the patient has severe fibrosis and cirrhosis. Mark FIB-4 >3.45 has a PPV value of 82.1% for diagnosing results Fibroscan ishak F3-F4, and using these values successfully diagnosed based on its classification in 72.8% of the 848 patients who did liver biopsy examination. FIB-4 at this value also has a correlation strong against Fibroscan examination where the results are consistent at 92.1% cases for FIB-4 <1.45 and 76% for FIB-4 >3.25 . (Vallet-Pichard et al., 2007) In a study comparing APRI with screening Fibroscan in 2019 obtained a cutoff value for patients with results Fibroscan F4 or cirrhosis, namely APRI >0.65 which has a sensitivity of 85.5% and specificity 77%. (Muhlifa Saputri, R and Murti, 2019) APRI and FIB-4 as indicators of F3/F4 or patient fibrosis staging who experience advanced fibrosis and cirrhosis in chronic hepatitis C patients have good results. At the cutoff value >0.64 for APRI to get results AUC 0.82, sensitivity 72%, specificity 83%, PPV 88%, NPV 63%, then FIB-4 with a cutoff value >1.46 has an AUC of 0.854, sensitivity 81.5%, specificity 79%, PPV 85.5%, and NPV 71%. These two indicators has a strong correlation with Fibroscan examination for Differentiate staging from fibrosis. (Husni, Anniwati and Lukitasari, 2019; Papadopoulos et al., 2019).

Use of APRI and FIB-4 in chronic hepatitis C patients for diagnose the degree of fibrosis stage F4 or cirrhosis using values cut off 0.65 for APRI and 1.63 for FIB-4 results that FIB 4 is better in terms of AUC, PPV, and NPV than APRI, although the difference is not significant. (Papadopoulos et al., 2019). Other research stated that by using a cut off of 3.25 from FIB-4 and 2.0 from APRI, these two indicators can predict the presence of cirrhosis or fibrosis stage F4 in chronic hepatitis C patients with AUC results for FIB-4 of 0.855 and for APRI 0.767, meaning FIB-4 has better results in predict the presence of cirrhosis (Rungta et al., 2021). Other studies that carried out also gave similar results for the AUC values of FIB-4 and APRI when used as an indicator of the presence of cirrhosis or F4, even though using different cut off values. (Loaeza-del-Castillo et al.,) Researchers did not find any sources that discussed performance FIB-4 and APRI in assessing the severity

of cirrhosis in hepatitis patients B chronic. This research obtained results when FIB-4 and APRI were used as an indicator of the severity of cirrhosis based on the CTP score with using the cut off stated in the operational definition of that variable APRI had better results, with significant results carried out using the Kruskal Wallis method, namely 0.018 compared to the significance results FIB-4 is 0.063. APRI compares favorably with FIB-4 in differentiate the severity of cirrhosis based on the CTP score. 2008; Parikh, Ryan and Tsochatzis, 2017; Catanzaro et al., 2021).

4. Conclusion

1. It can be seen that the median FIB-4 value increases with each increase degree of severity of cirrhosis based on CTP score
2. It can be seen that the median APRI value increases with each increase degree of severity of cirrhosis based on CTP score
3. Based on the Kruskal Wallis test there is no difference from the FIB-4 value score for each degree of severity of cirrhosis based on the CTP score, with values $p > 5\%$
4. Based on the Kruskal Wallis test, it was found that there were differences in values APRI score for each degree of severity of cirrhosis is based on the CTP score, with p value $< 5\%$
5. Apri score can be used as an indicator of severity cirrhosis based on CTP score and had better results compared with FIB-4 score

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