

Correlation Between Aspartate Aminotransferase/ Alanine Transferase Ratio (AST/ALT Ratio) and Stage of Liver Fibrosis in Patients with Chronic Hepatitis

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Abstract— Fibrosis is hallmark histologic event of chronic liver disease. Liver biopsy remains the gold standard for diagnosis and assessment of liver fibrosis in patients with chronic hepatitis. However, its invasive procedure and can have complication, not suitable for continous observation of liver fibrosis. The aspartate aminotransferase-alanin transferase ratio (AST/ALT ratio) has been used to evaluate prognosis of liver fibrosis and non-invasive proseduce for chronic hepatitis patients. To evaluate correlation between AST/ALT ratio and the stage of histologic liver fibrosis in chronic hepatitis patients. The study was restrospective design, where liver biopsy specimen has been collected from fourty chronic hepatitis patients during period Januari 2012 to December 2015. All histological slides were reviewed by two pathologists for evaluating histologic liver fibrosis by using Metavire score system. Patients characteristic were descriptifly analized, AST/ALT ratio and the stage of fibrosis were analized by using Spearman's correlation. The 40 patients were identified. The mean of age was 41 years, 70% patients were male. The number of patients with stage F1, F2, F3 and F4 of fibrosis respectively were 2 (5%), 16 (40%), 11 (27,5%), and 11(27,5%). The mean of AST/ALT ratio was $1,45 \pm$ (SE mean 0,14) . We found that there was statistically significant positive correlation between AST/ALT ratio with the stage of fibrosis ($r = 0,843$; $p \text{ value} < 0,01$). AST/ALT ratio was correlated with the stage of fibrosis. It is recommended to used the ratio as prediction of pogrressive liver functional impairment.

Keywords— liver fibrosis, AST/ALT ratio, chronic hepatitis, metavir scoring, liver enzym.

I. INTRODUCTION

Chronic viral hepatitis is the most common underlying cause of cirrhosis and hepatocellular carcinoma in worldwide. Chronic viral hepatitis is a syndrome of persisting hepatotropic viral infection usually associated with chronic inflammation, hepatocyte injury and progressive fibrosis. The fibrosis of liver is the common pathologic process of all chronic liver disease, as result from excessive

accumulation of extracellular matrix. Several investigations show that advance fibrosis is reversible, although end-stage cirrhosis is irreversible and the patients can survive with liver transplant.[1], [2].

When the liver damage is chronic, excess fibrous connective tissue accumulates , this condition is continuing from necrosis, inflammation, remodelling and tissue repair. The process eventually distorts from normal parenchyme structure of the liver and impairs its function [2]. Development of scarring during chronic liver disease represent a balance between new deposition in a liver dynamically producing and degrading matrix. The fibrosis can regress by eliminating the viral activity and infection has now been demonstrated in all form of chronic viral hepatitis [3]. Assessment of hepatic injury secondary to hepatitis, particularly the extent of fibrosis, is extremely important for effective treatment planning and monitoring disease progression , evaluating the current stage of fibrosis is crucial for determination of whether the fibrosis could be reversed with treatment [3]. Liver fibrosis assessment methods can be divided into two methods, they are invasive and non invasive. Liver biopsy is an invasive method that has long been considered to be the gold standard for evaluating the stage of liver fibrosis. This technique allows physicians to obtain diagnostic information not only on fibrosis, but also on many other liver injury process, such as inlammation, necrosis, steatosis, hepatics deposits of iron or cooper. Liver biopsy also important for

treatment planning, assessment of treatment outcome, and for supplementary assessment of hepatic pathology. However, this process is action invasive, need the observation of significans side effects susceptibility of error technical sampling, under staging and variability in interpretation from expert . Furthermor because of its risk , inconvinience, cost and serial liver biopsy is not practical to monitoring disease progression and treatment effect [1], [4], [5].

Currently, the development of non invasive method that can accurately predict initial disease stage and fibrosis progression in the first stage is a high priority and required in medical. Routinely obtained blood test such as serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), AST/ALT ratio, and platelete have been proposed as indirect marker of advanced fibrosis in patients with chronic hepatitis [4], [5]. Assessment of liver cell injury is performed by estimation of serum aspartate aminotransferase and serum alanine aminotransferase. These enzyme are normally released into plasma at a constant rate due to programmed cell death (apoptosis) of hepatocyte, it is increased when there is damage at liver cell membrane. Aminotransferases are sensitive indicator of hepatocyte injury. The pattern of aminotransferase elevation, increasing AST/ALT ratio can be helpfull to diagnose in patients with chronic hepatitis [6], [7]. The ratio of serum AST/ALT was describe by De Ritis and known as De Ritis ratio. De Ritis described AST/ALT as useful indicator of hepatitis. For normal individual, De Ritis ratio vary from 0,7–1,4. In most of the acute hepatocellular disease, De Ritis ratio is <1, Chronic disorder such as alcoholic, cirrhosis and chronic active hepatitis have de Ritis ratio greater than 1 [9], [10].

The aim of study is to evaluate correlation between non invasive measurement AST/ALT ratio and the stage of histologic liver fibrosis in patients with chronic hepatitis.

II. METHODS

The study was carried out as retrospective design. The study was performed on medical record of eligible fourty patients with chronic hepatitis who

had undergone liver biopsy at Haji Adam Malik Hospital in Medan, Indonesia during January 2012 to December 2015. The study protocol was confirmed according to the guidelines of the Medical Ethical Committee of Medical Faculty of University of Sumatera Utara.

All histologic slide from specimen of liver biopsy were reviewed by two pathologists who did not know about the patient details and clinical data. Fibrosis of liver was scoring using the METAVIR score system. Fibrosis was grouped into five categories, they are : F0 : no fibrosis, F1: portal fibrosis without septa, F2 : portal fibrosis with a few septa, F3 : numerous septa without cirrhosis. F4: cirrhosis.

Serum data of level aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were collected from patients medical record and data base. AST/ALT ratio of all the patients were calculated , and the value AST/ALT ratio and stage of liver fibrosis were compared. Demographic profile of all the patients were recorded and analyzed . Spearmen’s rank correlation coefficient (p) were carried out to assess correlation between ratio.

III. RESULT

The 40 patients were identified. The average age was 41 years, and 70% patients were male. The average AST/ALT ratio was $1,45 \pm (SE \text{ mean } 0,14)$. We found that there was statistically significant positive correlation between AST/ALT ratio with stage of fibrosis ($r= 0,843$: $p \text{ value } < 0,01$).

TABLE I
STAGE OF LIVER FIBROSIS

| Stage | n | % |
|-------|----|------|
| 1 | 2 | 5 |
| 2 | 16 | 40 |
| 3 | 11 | 27,5 |
| 4 | 11 | 27,5 |

Stage of liver fibrosis in patients with chronic hepatitis was determined according to the METAVIR score system . The number of patients with stage F1, F2, F3, F4 of fibrosis respectively were 2 (5%), 16 (40 %) , 11 (27,5%) and 11 (27,5%).

TABLE II
AST/ALT RATIO

| | AST | ALT | AST/ALT |
|--------------------|--------|--------|---------|
| Mean | 99,78 | 69,28 | 14,543 |
| Std. Error of Mean | 22,006 | 18,538 | 0,14359 |
| Minimum | 14 | 10 | 0,60 |
| Maximum | 617 | 736 | 5,31 |

Mean level of aspartate aminotransferase (AST) were increased in patients with chronic hepatitis (99,78±18,5), mean of alanine aminotransferase (AST) level were also elevated (69,28±18,53). While mean of aspartate aminotransferase (AST)/ alanine amonitransferase (ALT) ratio markedly raised in patients with chronic hepatitis (1,454±0,143).

Spearman's correlation coefficient were used to assess the correlation between AST/ALT ratio and the stage of fibrosis ($r=0,843$; p value $<0,01$).

IV. DISCUSSION

Chronic liver disease may result from various creating both infectious (viral, parasite) and non-infectious (alcohol, autoimmune) which may asymptomatic even for many years. Evaluation of patients with liver disease should be directed at establishing the etiologic diagnosis, estimating the disease severity (grading) and establishing the disease stage. Liver biopsy staging is one of the main factors influence the decision to indicate therapy for chronic hepatitis patients. The therapy should be indicated for chronic hepatitis patients with significant fibrosis (F2-F4) because of the risk of evolution to cirrhosis and its complications. However, liver biopsy is an invasive method, can be error and has serious complications such as bleeding, perforation, and even death. Alternative methods to assess liver fibrosis having a number of advantages over histology including low cost, non-invasive and the absence of contraindications such as thrombocytopenia or coagulopathy [12].

Several non invasive biochemical tests are useful in the evaluation and management of patients with hepatic diseases. Assessment of liver cell injury is done by the estimation of serum aspartate transaminase or AST (formerly glutamic oxaloacetic transaminase or SGOT) and serum alanine

transaminase or ALT (formerly glutamic pyruvic transaminase or SGPT) [9].

Aminotransferase are enzymes, which sensitive indicators of hepatocyte injury. These enzymes are normally released into plasma at a constant rate due to programmed cell death of hepatocytes but its permeability is increased when there is damage to liver cell membrane. The pattern of the aminotransferase elevation, that is, De Ritis ratio can be helpful diagnostically and predict the stage of liver fibrosis [9]. In our study, we found that there is positive correlation between AST/ALT ratio and stage of liver fibrosis. Gianinni et all have studied that the AST/ALT ratio is correlated with both stage of liver fibrosis and clinical evaluation in patients with chronic hepatitis and progressivity of liver impairment is reflected by an increase in the AST/alt ratio. Some studies conclude that patients with cirrhosis hepatic have AST/ALT ratio ≥ 1 and correlated with stage of liver fibrosis and clinical symptom. Many study have combined other parameters like prolonging prothrombin time and platelet count with the reversed aminotransferase ratio for the more accurate diagnose in patients with chronic hepatitis. Siddiqi et al found that prolonged prothrombin time and combine with AST/ALT ratio > 1 can prove a more specific predictive value for detection of hepatic cirrhosis in patients with chronic liver disease.

V. CONCLUSIONS

The result revealed that 5%, 40%, 27,5% and 27,5% patients show stage 1, 2, 3, 4 of liver fibrosis. As showed in Table II, the level of biomarker liver enzymes aspartate aminotransferase, alaninie transferase and aspartate aminotransferase/alaninie transferase ratio (AST / ALT) ratio were increased in patient with chronic hepatitis.

The AST/ALT ratio based on laboratory test result is correlated with histological stage of liver fibrosis and liver impairment in patients with chronic hepatitis. This ratio is an important for diagnostic and prognostic tools to predict the fibrosis of chronic hepatitis.

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CONFLICT OF INTEREST

The study protocol was confirmed according to the guidelines of the Medical Ethical Committee of Medical Faculty of University of Sumatera Utara. There is no conflict of interest.

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