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Congestion Index of Portal Vein in the Evaluation of Liver Disease

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ABSTRACT

Introduction: *The invention of Doppler has made it possible to study the hemodynamics of blood flow in the human body. Non-alcoholic fatty liver disease (NAFLD), chronic viral hepatitis and alcoholic liver cirrhosis are three most common disorders affecting the liver. In our study congestion index of portal vein was studied in normal subjects as well as in these three groups of patients.*

Aim of the study: *To evaluate the efficacy of congestion index to distinguish normal subjects from those with Non-alcoholic Fatty liver disease, Alcoholic chronic liver disease and Chronic Viral Hepatitis.*

Materials and Methods: *A descriptive comparative study was done in Government Medical College, Thrissur for a period of eleven months and 401 subjects were studied. Sampling was done by Purposive sampling of patients attending the Ultrasound OPD in department of Radiodiagnosis and Medicine OPD. Patients diagnosed to have Chronic Viral Hepatitis (CVH), Chronic alcoholic liver disease, Non-alcoholic fatty liver disease and Normal subjects were included in the study.*

Results and Discussion: *The median congestion index was calculated. The values are as follows. In normal subjects-0.021, NAFLD patients-0.027, CVH patients-0.050 and Alcoholic cirrhotic patients-0.060. There is significant difference in congestion index between the different population groups studied & hence it can be used to indicate the presence of liver disease. There is significant difference in the congestion index between pediatric and adult patients affected with NAFLD, with pediatric patients having lower values of congestion indices indicative of less severe disease. There is no significant difference in the congestion index of different age groups studied in the normal population.*

Conclusion: *Congestion index shows promise in distinguishing normal subjects from patients with liver disease. Doppler can be used in clinical settings as an alternative test to Liver biopsy to detect the presence or absence of liver disease when the biochemical and serological markers of liver disease are ambiguous or could not be done.*

Keywords: *congestion index, NAFLD, Alcoholic Cirrhosis, Chronic viral hepatitis*

INTRODUCTION

Chronic alcoholism causes a spectrum of liver disease ranging from mild fatty liver to cirrhosis. Cirrhotic patients develop portal hypertension and are at increased risk of variceal bleeding[1]. Liver biopsy is considered as the gold standard in the diagnosis of liver cirrhosis. But it is prone to sampling error (Only 1/50000 part of liver is sampled by liver biopsy) and has the disadvantage of being an invasive procedure. Hepatic venous portal gradient is the gold standard in diagnosis of portal hypertension but has the same disadvantage of being an invasive procedure[1]. Ultrasonography is an established imaging modality in the diagnosis of liver cirrhosis and portal hypertension, especially when the aetiology is obvious. Liver surface nodularity and portal vein dilatation >13 mm are specific indicators of liver cirrhosis and portal hypertension respectively and are widely used clinically in the diagnosis of cirrhosis[2]

Hepatitis C, a common blood-borne infection, is found in approximately 2 percent of adults. Chronic infection is associated with serious morbidity and mortality (e.g., cirrhosis, hepatocellular carcinoma). Testing for hepatitis is recommended for at-risk populations, and confirmatory testing includes quantification of virus by polymerase chain reaction[3]

The diagnosis of NAFLD requires confirmation of hepatic steatosis by imaging or liver biopsy with clinical exclusion of excessive (>20 g/day) alcohol ingestion. Ultrasound, computed tomography, or magnetic resonance studies can confirm the presence of hepatic steatosis with a comparatively high degree of accuracy. Biopsy is thought to be the gold standard for diagnosis and is the only investigation able to distinguish between simple steatosis and NASH or stage the degree of fibrosis. The decision to perform a liver biopsy must be individualised and may be useful when there is diagnostic uncertainty[4] .Since liver biopsy is the gold standard in the diagnosis of NAFLD, a standard non invasive test is yet to become available for the diagnosis of Fatty liver disease.

Non-alcoholic fatty liver disease, chronic viral hepatitis and alcoholic liver cirrhosis are three most common disorders affecting the liver. They are also the three most common cause of end stage liver disease worldwide. Liver biopsy is indicated in all these diseases, for diagnosis, estimation of fat content in liver cells in NAFLD, for estimating the degree of liver damage in viral hepatitis and assessing the extent of liver cirrhosis in alcoholic patients. Doppler & Ultrasound are the only noninvasive imaging modalities that visualize liver and the portal vein hemodynamics in real time and can measure the flow characteristics such as flow velocity, portal vein diameter and area, portal blood flow. Doppler ultrasound is non-invasive and when compared to biopsy has no patient discomfort. It is also fast and easily reproducible technique that can study the hemodynamic alterations in the liver, especially in portal vein. Congestion Index was first described by Moriyasu et al as a reliable indicator to differentiate between chronic viral hepatitis and alcoholic cirrhosis. It is defined as the ratio of Portal Vein Area (by B-mode Ultrasound) to the Portal Vein Velocity (by Doppler Ultrasound).Since then, many authors have evaluated the congestion Index for many different clinical applications in diseases involving the liver. This study is to evaluate congestion index, a simple, inexpensive, non-invasive and accurate tool to differentiate alcoholic cirrhosis, NAFLD and viral hepatitis as an alternative to liver biopsy.

OBJECTIVES

To evaluate the efficacy of congestion index to distinguish normal subjects from those with Non-alcoholic Fatty liver disease, Alcoholic chronic liver disease and Chronic Viral Hepatitis.

MATERIALS AND METHODS

A descriptive comparative study was conducted involving patients referred for Ultrasonography of the abdomen for a period of 11 months from December 2015 to October 2016 in the Department of Radio diagnosis, Government Medical College, Thrissur and Department of Medicine, Government

Medical College, Thrissur with the approval of the Institutional Ethics Committee. Sample size was calculated by the formula Sample size= (Zα) ^2 [SD] ^2 / (d^2) where the symbol ^ means 'to the power of'; * means 'multiplied by', Z α- Z score for α error when α error is 5%, Zα= 1.96, SD is the standard deviation of congestion index between the study groups (chronic viral hepatitis) which is 0.029, "d" is the precision of the study; d =10% of SD, d=10/100 * 0.029=0.0029 based on the study by Moriyasu etal[14]

Sample size= (Zα) ^2 [SD] ^2 / (d^2)

= [(1.96) ^2 * (0.029) ^2] / (0.0029) ^2

=384

Based on the above formula the sample size was calculated as 384 subjects.

The Inclusion Criteria were patients diagnosed to have Chronic Viral Hepatitis, Chronic alcoholic liver disease, Non-alcoholic fatty liver disease. Normal subjects were also included in the study. The diagnosis was made by biochemical tests (serum triglyceride levels), serological markers (hepatitis B & C antibodies) and Ultrasound findings (coarse /fatty or normal echo pattern and surface nodularity). The Exclusion criteria were patients with idiopathic portal hypertension, portal vein thrombosis, right heart failure, patients on vaso active drugs such as beta blockers and diuretics, patients with history of variceal bleeding, patients with co-existing acute hepatitis B and HCV infection. Sampling was done by purposive sampling of all patients attending the Ultrasound OPD in Department of Radiodiagnosis.

All patients were evaluated by biochemical, microbiological and radiological investigations which include serum triglyceride level, Serological markers of hepatitis and Ultrasound. This is followed by Doppler ultrasound evaluation of portal vein cross sectional area and portal vein velocity and congestion index is calculated using the formula ,Congestion index =cross sectional area/blood flow velocity (cm/sec) .The Doppler measurements are made using MINDRAY DC8 ultrasound machine with a curved array transducer.

The data is collected and tabulated with Microsoft excel. Variables are expressed in terms of medians and quartiles as it is a non-parametric data. Analysis is done using SPSS software.

RESULTS

Data was collected from 401 patients who underwent Ultrasound scan in the Department of Radio Diagnosis, Government Medical College, Thrissur. Tests for normality was done using Shapiro Wilk test for congestion index and the data was found to be non normal in distribution. (W=0.9210; reject normality (p<0.0001)). Hence for tests of significance, non parametric tests were applied (Kruskal Wallis test and Mann Whitney U test) and quantitative data was expressed in terms of medians and quartiles.

Table 1 Median congestion indices in different study populations

Study Population	Median Congestion Index	1st quartile	4th quartile
Normal Population	0.021	0.015	0.029
NAFLD	0.027	0.017	0.036
Chronic Viral Hepatitis	0.050	0.030	0.070
Alcoholic Liver Disease	0.060	0.050	0.075

Most of the normal subjects recorded a congestion index of 0.02-0.03.Median congestion index in normal population-0.021 with 1st quartile of 0.015 and 4th quartile of 0.029.There was no significant difference in the congestion index between different age group in normal subjects (p value=0.1, Kruskal Wallis test).

Median congestion index in NAFLD -0.027 with 1st quartile of 0.017 and 4th quartile of 0.036. Congestion index of normal subjects and NAFLD patients were compared with Mann Whitney U test with test value of 3867 and p value 0.006. Hence significant difference in congestion index is present between the Normal subjects and patients with NAFLD. There is no significant difference in the congestion index between different age groups studied in the Fatty Liver disease. (P value 0.3, Kruskal Wallis test)

Median congestion index in chronic viral hepatitis -0.050 with 1st quartile of 0.030 and 4th quartile of

0.070. Congestion index of normal subjects and Chronic Viral hepatitis patients were compared with Mann Whitney U test and test value of 2036 and p value <0.001 were obtained. Hence significant difference in congestion index is present between the Normal subjects and patients with Chronic viral hepatitis. There is no significant difference in the congestion index between different age groups studied in Chronic Viral Hepatitis Patients. (P value 0.24, Kruskal Wallis test)

Median congestion index in patients with alcoholic cirrhosis-0.060 with 1st quartile of 0.050 and 4th quartile of 0.075. Congestion index of normal subjects and alcoholic cirrhosis patients were compared with Mann Whitney U test with test value of 670 and p value < 0.001. Hence significant difference in congestion index is present between the Normal subjects and patients with Alcoholic cirrhosis. There is no significant difference in the congestion index between different age groups studied in the alcoholic cirrhotics. (P value 0.45, Kruskal Wallis test)

DISCUSSION

In the normal population group, 7 paediatric and 93 adult patients were studied and there was no significant difference in the congestion index between adult and paediatric patients. The median congestion index in our study in the normal population is about 0.021 with 1st quartile 0.015 and 4th quartile 0.029.This is different from the original study by Moriyasu et al where the mean congestion index in the normal population was found to be 0.070 +/- 0.029. This difference could be attributed to the inter-observer variability or to the difference in race of the population studied. The inter observer difference in congestion index could be attributed to the wide range of velocities obtained when the Doppler angle is changed from 0 to 60 degrees (up to 60 degrees of Doppler angle is considered acceptable for clinical usage). [5]

In fatty liver disease, congestion index has not been studied previously. In our study, the median congestion index in the Non-alcoholic fatty liver disease population is about 0.027 with 1st quartile 0.017 and 4th quartile 0.036. Our study is the first to observe congestion index in NAFLD and there is significant difference in the congestion index between normal population and fatty liver disease population (p value 0.01).

In our study, the number of males affected with fatty liver disease is more (60%) compared to females. This is in agreement with the study by Singh et al in which the prevalence of fatty liver disease is found to be more common in males than females in India[6]. Also a study by Mohan et al found the prevalence to be more common in males in south Indian population and our study is representative of Kerala population and is in agreement with this study[7]. In the study by Amarapurkar et al, Fatty liver disease was found to be more common in people older than 40 years[8] .In our study also NAFLD was found to be more common in patients more than 40 years(67 %),but about 33% of people were below 40 years of age implying an increase in NAFLD among younger people.

NAFLD is a spectrum of diseases where quantity of fat deposition affects the severity of disease. If the fat deposition is very high, then oxidative stress may occur and may result in Non alcoholic steato hepatitis (NASH). NASH is associated with more increased risk of progression to cirrhosis[9].In our study, we did not assess the severity of fat deposition among the population studied. This may account in part for the very high values of congestion index (>0.05 to 0.1 in some patients) observed in some of the patients in the study population. However further studies based on the severity of fat deposition with relation to the congestion index are required to confirm it.

Seven pediatric (<13 years) patients were affected with NAFLD. These patients had a median congestion index of 0.012 compared with the adult population who had a median congestion index of 0.025(p value <0.01 Mann Whitney U test).This could be due to the fact that mechanisms operating at cellular level are different in paediatric and adult patients, with histopathologically visible changes such as hepatocyte ballooning and Mallory Denk

bodies observed less frequently in paediatric than adult patients. This could account for the relatively subtle changes seen in congestion index of paediatric patients affected by NAFLD than adult patients.[10] Also the prevalence of NAFLD in children is increasing with changing lifestyles and it is as high as more than 10 % according to study by Alterio et al[11]. NAFLD is expected to become the leading cause of liver pathology, liver failure and indication for liver transplantation in childhood and adolescence. But it is understudied and under estimated in most places.[10-13]

Congestion Index in Chronic Viral Hepatitis (CVH)

The median congestion index in the chronic viral hepatitis group is found to be 0.050 with 1st quartile 0.030 and 4th quartile 0.070,whereas the mean congestion index in chronic viral hepatitis in the original study by Moriyasu was found to be 0.11+/- 0.08. Similar to the congestion index in normal population and fatty liver, there is no agreement between the congestion index between this study and the study by Moriyasu et al[14] . There is significant difference in the congestion index between Normal Population and Chronic Viral Hepatitis Group (p value<0.01, Mann Whitney U test) implying that portal vein hemodynamics are significantly altered in patients with chronic viral hepatitis. This is in agreement with the study by Dubanova et al in which congestion index showed significant difference between groups with mild viral hepatitis and clinically severe viral hepatitis. [15] In our study none of the patients belonged to the paediatric age group (<12 years) implying the fact that chronic viral hepatitis is uncommon in paediatric population except during perinatal period when the serotransmission from mothers results in increased rates of infection. Even in hepatitis endemic populations the seroprevalence of children is low compared to the adults[16,17].According to the study by Lea et al, increasing duration of infection with cirrhosis is associated with increasing congestion indices, implying that hepatitis has an insidiously progressive course with cirrhosis as the ultimate end point of disease[18].

Congestion Index in Alcoholic cirrhosis

All the patients with alcoholic cirrhosis were above 18 years of in our study. This is in contrast to the western population where the prevalence of alcoholic liver disease is high in teenagers and adolescents which may be due to difference in drinking habits .[19-22] Mean Congestion Index in the alcoholic cirrhosis patients is 0.060 with 1st quartile 0.050 and 4th quartile 0.075. There is significant difference in the congestion index between alcoholic cirrhosis patients and Normal subjects. (P value <0.01 Mann Whitney U test).The congestion index described by Moriyasu et al[14] in alcoholic cirrhosis patients was 0.17, but in our study the congestion index in alcoholic cirrhosis is reduced. It is also reduced compared to the study by Bintintan et al where the congestion index in alcoholic cirrhosis patients was found to be 0.15[23] and the study by Huang et al where the mean congestion index in cirrhotics was calculated to be 0.15[24] .But in study by Erdozain Sosa et al, the congestion index was found to be lower with a range of 0.05-0.09 and patients with lower congestion index found to be at significantly lower risk of variceal bleeding than patients with higher congestion index[25] .Congestion index is definitely a good predictor of the presence of liver cirrhosis with several authors reporting higher congestion index in alcoholic patients with decompensated cirrhosis. Congestion index can also be evaluated as a parameter to predict the severity of liver disease in patients diagnosed with alcoholic cirrhosis. Also it can be used to stage the disease as early or late cirrhosis. Further analytical studies may confirm the use of congestion index as a significant prognostic factor in the evaluation of several liver diseases.[26-28]

Limitation of Study

NAFLD, Chronic Viral Hepatitis and Liver Cirrhosis are a spectrum of liver diseases. Hence their congestion indices may be normal during the early stages of disease. The duration of disease was not taken into consideration.

CONCLUSION

There is significant difference in congestion index between the normal population and the three disease groups studied which are NAFLD, Chronic Viral Hepatitis and Alcoholic liver disease. Hence congestion index may be used to suggest the presence or absence of these liver diseases. Congestion index between paediatric and adult patients affected with NAFLD showed significant difference; paediatric patients showed lower values of congestion indices which may be indicative of less severe disease. Different age groups studied in the normal population did not show any significant difference in the congestion index. The mean congestion index recorded in our study are lower than the congestion indices originally described by Moriyasu, which could be partly because of the racial differences of study population and partly due to inter-observer variability. Further studies are needed to test this hypothesis.

CONFLICT OF INTEREST

No conflict of interest

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