ORIGINAL RESEARCH PAPER

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TO DETERMINE THE PREDICTORS OF NONALCOHOLIC FATTY LIVER DISEASE AND NONALCOHOLIC STEATOHEPATITITS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

KEY WORDS:

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) refers to the accumulation of fat mainly triglycerides in hepatocytes that results from insulin resistance. It is the most common chronic liver disease in the western world. The clinicopathologic spectrum of NAFLD ranges from bland hepatic steatosis which is clinically associated with similar long term prognosis as compared to general population to nonalcoholic steatohepatitis (NASH) which when associated with increase liver fibrosis, may progress to cirrhosis and liver failure as such distinguishing between NASH with and without fibrosis has important implications for management and patient counseling.

AIMS AND OBJECTIVES The aim of the study is to determine the predictors of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in patients with type 2 diabetes mellitus.

MATERIALS AND METHODS The study consisted of evaluating fibrosure as diagnostic and prognostic test for NAFLD disease taking liver biopsy as gold standard. The study was conducted on 50 inpatients of department of medicine, patna medical college and hospital patna from october 2016 to September 2018 who fulfilled inclusion and exclusion criteria.

SUMMARY AND CONCLUSION The study to evaluate fibro sure test as diagnostic modality for diagnosis of NAFLD taking liver biopsy as gold standard has given following conclusions : In patients with provisional diagnosis of nonalcoholic fatty liver disease based on clinical history and radiological investigation fibrosure test can be used as diagnostic test and also for staging of the disease since it has very high sensitivity and positive predictive value and higher fibrotest scores correlate well with higher stages of fibrosis on liver biopsy. Definite diagnosis of the condition can only be done on liver biopsy.Fibrosure test has both diagnostic value as well as prognostic value. This is because of the fact at higher score of fibrotest the sensitivity and positive predictive value of the test is close tyo ideal diagnostic test and there is direct relationship between fibroscore and degree of fibrosis on liver liver biopsy.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) refers to the accumulation of fat mainly triglycerides in hepatocytes that results from insulin resistance. It is the most common chronic liver disease in the western world. The clinicopathologic spectrum of NAFLD ranges from bland hepatic steatosis which is clinically associated with similar long term prognosis as compared to general population to nonalcoholic steatohepatitis (NASH) which when associated with increase liver fibrosis, may progress to cirrhosis and liver failure as such distinguishing between NASH with and without fibrosis has important implications for management and patient counseling.

NAFLD is a growing medical problem affecting any age range with a reported prevalence of 9.6% among adolescents and pre adolescents and 34% among patients aged 30 – 65 years. However the reported prevalence of this condition varies based on study population and diagnostic modality used. For instance, liver biopsies performed in otherwise healthy potential liver donors revealed a prevalence of 20% whereas studies using MR spectroscopy reported a prevalence of 34% In general population. Studies usuing idiopathic elevations in liver enzymes as a case definition yielded a wide NAFLD prevalence of 8% to 75%.

Liver biopsy is the gold standard for confirming the diagnosis and staging of the disease. In addition to this it is the only investigation that can reliably distinguish between simple steatosis and NASH. The prognosis of NAFLD depends on the severity of liver injury and fibrosis. Mortality in patients with NASH particularly those with advanced fibrosis and cirrhosis is increased as compared to general population of same age and gender. Additionally the identification of early cirrhosis or advanced bridging fibrosis may alter management, as such patients should undergo Upper G.I.Endoscopies to screen for varices and periodic liver ultrasound imaging to screen for hepatocellular carcinoma. Hence in the absence of clinical and radiological features of cirrhosis, liver biopsy remains the only way to reliably assess prognosis. Given the higher prevalence in the population, the invasive nature of liver biopsy,the paucities of effective therapies ,however, often there is an understandable reluctance to perform liver biopsies for the sole purpose of confirming the diagnosis. In most patients therefore, the diagnosis of suspected NAFLD is based on clinical and laboratory data, and imaging studies with appropriate exclusion of other liver conditions. Also the potential drawbacks of liver biopsies are sampling error, inadequate size, variability in interpretation, cost and associated morbidity.

Different indices have been proposed to make the diagnosis of NASH and in an attempt to increase the predictive accuracy of noninvasive markers of liver fibrosis, multiple serum markers have been combined into mathematical models to produce predictive scores. Fibrosure is one algorithm consisting of six variables : alpha 2 globulin, haptoglobin, apolipoprotein A 1 gamma glutarmyltranspeptidase (GGT), total bilirubin and alanine transaminase (ALT). the fibrotest score is calculated from the results of six parameters blood test, combining six serum markers with the age and gender of patients. Studies have shown that a score of less than 0.3 (range 0-1) provided an NPV of 98% for the presence of bridging fibrosis or cirrhosis, whereas a score of greaterthan 0.7 provided a 60% positive predictive value for bridging fibrosis or cirrhosis. However 33% of individuals had a score between 0.3 to 0.7 indicating that fibrotest cannot predict the severity of liver fibrosis in one third of patients with NAFLED.

The present study is aimed to evaluate the sensitivity and specificity of FIBROTEST or FIBROSURE test as predictor of NAFLD in patients with type 2 diabetes mellitus.

AIMS AND OBJECTIVES

The aim of the study is to determine the predictors of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in patients with type 2 diabetes mellitus.

MATERIALS AND METHODS

The study consisted of evaluating fibrosure as diagnostic and prognostic test for NAFLD disease taking liver biopsy as gold standard. The study was conducted on 50 inpatients of department of medicine, patna medical college and hospital patna

from october 2016 to September 2018 who fulfilled inclusion and exclusion criteria.

Inclusion criteria

Diagnosed patients of type 2 diabetes mellitus aged 40 years or more who were taking oral hypoglycaemic agents. Duration of illness was not a consideration for inclusion in study group.

Exclusion criteria

- Any amount of alcohol consumption based on careful history
- Patients of diabetes mellitus on insulin therapy
- Significant comorbidities precluding a liver biopsy
- History of jejuno-ileal bypass or small intestinal resection
- Patients with chronic viral hepatitis
- Patients taking any drug which can itself cause stetosis or steatohepatitis
- Patients of hypo or hyperthyroidism

After selecting patients based on strict inclusion and exclusion criteria, ultrasonography of whole abdomen of each patient was ordered and all patients with a fatty liver of grade 2 or more were selected for further investigation. In all those patients where liver function tests were suggestive of NASH, liver biopsy was done. All patients who had a biopsy diagnosis of intermediate or high grade of NASH (biopsy score of 3 to 4 has intermediate likelihood of NASH while biopsy score of 5-8 had a high likelihood of NASH) were further investigated for calculation of fibroscore of each patient.

For calculation of fibroscore, each patient was ordered following investigation in addition to the routine investigation : liver function test, alpha-2 macroglobulin, haptoglobin, apolipoprotein A1.

The fibrotest score is calculated from the results of six parameters blood test (mentioned above) , combining six serum markers with the age and gender of the patient.

OBSERVATIONS

FIBROSURE RESULTS 1

FIBROTEST RESULTS	TOTAL NUMBER OF PATIENTS
SCORE OF EQUAL OR GREATER THAN 0.7	19
>0.3BUT <0.7	25
SCORE OF EQUAL OR LESS THAN 0.3	6

BIOPSY RESULTS

BIOPSY SCORE (RANGE 2 – 8)	TOTAL NUMBER OF PATIENTS
SCORE LESS OR EQUAL TO 2	0
SCORE 3 – 4	5
SCORE 5 – 8	45

SUMMARY AND CONCLUSION

The study to evaluate fibro sure test as diagnostic modality for diagnosis of NAFLD taking liver biopsy as gold standard has given following conclusions :

1. In patients with provisional diagnosis of nonalcoholic fatty liver disease based on clinical history and radiological investigation fibrosure test can be used as diagnostic test and also for staging of the disease since it has very high sensitivity and positive predictive value and higher fibrotest scores correlate well with higher stages of fibrosis on liver biopsy. Definite diagnosis of the condition can only be done on liver biopsy.
2. Fibrosure test has both diagnostic value as well as prognostic value. This is because of the fact at higher score of fibrotest the sensitivity and positive predictive value of the test is close tyo ideal diagnostic test and there is direct relationship between fibroscore and degree of fibrosis on liver liver biopsy.
3. The cut off value of fibroscore for diagnosis of diagnosis of disease if taken at 0.3 has a very high sensitivity and positive predictive value for diagnosis but at the cost of specificity. If the cut off value is taken to be 0.7 (which was concluded in largest trial evaluating fibrotest) the sensitive and positive predictive value decreases marginally. Considering increasing prevalence of nonalcoholic fatty liver disease higher sensitivity is desired. Therefore cut off value for diagnosis of NAFLD should be taken at values of fibroscore equal or greater than 0.3.
4. The fibrosure test can be used for prognostication of patients of NAFLD. Scores of fibrosure correlate well with the degree of fibrosis on liver biopsy. Therefore a higher score of fibrotest not only helps in the diagnosis of disease but also indicates advanced stage of fibrosis and hence such patient need to be treated on urgent basis.
5. Considering the limitations of liver biopsy and increasing incidence and prevalence of NAFLD as a cause of chronic liver disease non invasive test like fibrosure should be used more commonly as a diagnostic and prognostic test for effective diagnosis and management.
6. Since the results of fibrosure test depend on the cut off value taken it should not be used alone for making diagnosis and treatment of the patient. The decision should be taken on the basis of clinical history, laboratory investigations, suitable radiological examination and fibroscore results.

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