IMPAIRED GLUCOSE TOLERANCE IN HCV/HBV CIRRHOSIS

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SUMMARY

Impaired glucose tolerance (IGT) is more frequently observed in cirrhosis. As many as 70% cirrhotics have IGT and recent studies suggest that hepatitis C viral infection may be an additional risk factor for the development of diabetes mellitus. We studied 349 cases of cirrhosis liver retrospectively for evidence of IGT and its relation to HBV and HCV infection. Three hundred and forty nine patients with cirrhosis were studied. Two hundred and seventy three of them had their spot random blood sugar (RBS) checked. Patients with a RBS of more than 180 were separated and their HCV and HBV status assessed. Of 273 patients, blood sugar ranged between 56 to 503 mg/dl with a mean of 132.48 ± 69.22. Fifty two patients had RBS more than 180. They were considered to have IGT. Out of the 52 patients with IGT, 29 were males and 23 females HBV was found in 13(25%) 8 were males 5 females, HCV in 22(42.3%), 13 males and 9 females. And 18(34.6%) were negative for both HBV and HCV. These results were comparable with studies elsewhere. Statistical analysis revealed no association between IGT and HBV (Table-1) and Non HB, HC group (Table-3). There was highly significant association between IGT and HCV p=0.01 (Table-2).

INTRODUCTION

Cirrhosis liver in not uncommon in our country and due to the increased incidence of hepatitis B and C infection the incidence is further increasing. Prevalence of IGT is higher in cirrhosis than non cirrhotics.[1] Recent studies suggest that hepatitis C virus infection may be an additional risk factor for the development of diabetes mellitus.[6] IGT is well known in patients with cirrhosis. Blood glucose is abnormally increased in response to an oral and intravenous infusion of glucose and the hyperglycemia is long lasting. Hyperinsulinaemia is also present in these patients pointing to defective insulin action in cirrhosis. The decreased insulin activity which is the main determinant of IGT[3] is caused by a combined receptor/post receptor defect[4] Hyperinsulinaemia has been related to either increased insulin secretion

SIGNIFICANCE OF HBV POSITIVE PATIENTS WITH IGT

	RBS > 180 mg/dl	RBS < 180 mg/dl	Total
HBs Ag Positive	13	63	76
HBs Ag Negative	39	158	197
Total	52	221	273

P=0.374 > 0.05 insignificant

TABLE – 1

or to diminished harmone degradation by diseased liver, this issue has not yet been settled.[5] HCV and HBV are established causes of chronic liver disease and cirrhosis. They seem to occur more frequently in diabetics than in general population. The association may reflect epidemiological circumstances because of the frequent parenteral exposure of diabetics. On the other hand the hepatitis virus particularly HCV can affect not only liver but also several tissues outside liver resulting in a wide spectrum of extrahepatic manifestations and morbid conditions, to which diabetes mellitus has been included.[6] A retrospective analysis of data on 349 patients with cirrhosis liver was done. 52 patients had IGT. HBV and HCV prevalence was determined. Patients with both B and C negative were considered controls and comparisons done.

MATERIAL AND METHODS

349 patients were diagnosed cirrhosis liver based on clinical signs of cirrhosis (Ascites, Varcies), and ultrasound findings of shrunken irregular liver with dilated portal vein, splenomegaly and ascites. 273 patients had their RBS checked. Patients with RBS more than 180 mg/dl were separated and considered to have IGT. These patients were screened for the prevalence of HBV and HCV.

RESULTS

273 patients had their blood sugar checked. Blood sugar levels ranged between 56-503 mg/dl with a mean of 132.48 and ± 69.722. Hepatitis B and C were checked in all patients. Out of 273 patients 76 were positive for HBV and 80 were HCV positive. 52 patients had RBS more than 180 mg/dl. Amongst the 52 patients with IGT 22(42.3%) had HCV positive 13(25%) were positive for HBV and 18(34.6%) were negative for both B and C. Statistical analysis wee done and a highly significant association between IGT and HCV P=0.01 (Table-2).

DISCUSSION

Patients with liver disease are known to have a higher prevalence of glucose intolerance. The reasons for this are many: there is hyperinsulinaemia, insulin resistance and an abnormal glucose metabolism. Resistance to insulin seems to be due to a defective insulin action caused by a receptors/post receptor defect.[4] As many as 70% of cirrhotic have IGT.[1] The association between diabetes and cirrhosis is recognised for any years and this association may be explained by many reasons. It may be due to alcoholism, haemochromatosis and possibly autoimmune conditions or it may be the caused of coexisting liver abnormalities.

SIGNIFICANCE OF HCV POSITIVE PATIENTS WITH IGT

	RBS > 180 mg/dl	RBS < 180 mg/dl	Total
HCV Positive	22	58	80
HCV Negative	30	163	193
Total	52	221	273

P=0.019 < 0.05 very significant

TABLE – 2

SIGNIFICANCE OF NON B NON C PATIENTS WITH IGT

	RBS > 180 mg/dl	RBS < 180 mg/dl	Total
Non B and C	18	100	118
	34	121	155
Total	52	221	273

P=0.10 > 0.05 insignificant

TABLE – 3

Non alcoholic steatohepatitis (NASH) is associated with diabetes and in turn to cirrhosis. NASH resembles alcoholic hepatitis histologically without alcohol use. Predisposing risk factors for the development of NASH include female sex, obesity, hyperlipidaemia and uncontrolled diabetes mellitus. Several studies have documented a clear association between the presence of NASH and the development of underlying cirrhosis in up to 10% of the cases. The association between NASH and diabetes and in turn cirrhosis now raises the possibility of additional predictors of disease progression in chronic viral hepatitis. There is now accumulating evidence that diabetes in turn may be implicated in the development of cirrhosis.[11]. Viral hepatitis B and C are established causes of cirrhosis. An increased coincidence is observed between diabetes and cirrhosis liver. The higher frequency of cirrhosis in diabetics compared with the normal population can be explained partly by the possible higher risk of cirrhosis like fatty degeneration and more frequent inflammatory diseases of bile duct and others.[12] Simo R et al have reported a higher prevalence of hepatitis C virus infection in diabetic patients and even suggest a direct role in the development of diabetes.[13] The prevalence of IGT is high in HCV related cirrhosis than others. Grimbert S et al in a case controlled study reported that diabetes was more prevalent in patients with chronic hepatitis C than with other liver diseases and that diabetes mellitus occurred in the absence of risk factors.[14] Mason et al found 33% patients wit HCV related cirrhosis to have diabetes. Our observation of 42% prevalence is some what higher than this but it could be explained on the basis of genotype of HCV. In Mason et al study the HCV genotype mostly encountered was 2 a and in our study genotyping has not been done. Alison et al found 50% patients to have diabetes with HCV positive cirrhosis.[9] Fraser et al found the prevalence of diabetes to be 39% in HCV positive cirrhosis.[10] In an other study 500 Asian patients with HBV infection were prospectively studied. End point was development of cirrhosis 5-8 years follow up showed 71 developing cirrhosis. Out of these 15 (21.2%) had diabetes mellitus diagnosed 2-15 years prior to recognition of cirrhosis, only 1.9% of the remaining 429 non cirrhotic had diabetes mellitus previously diagnosed. Additionally diabetes of more than 5 years duration before the development of cirrhosis was significantly more frequent in cirrhotic versus non cirrhotic controls (87% vs 33%) implying that the hyperglycaemia was not the result of cirrhosis. There is an increased rate of hepatocellular failure in cirrhotic patients who also have diabetes mellitus.[14] Age, cirrhosis and HCV infection were found to be significant variables associated wit diabetes by univariate analysis by Mason et al. The logistic regressions analysis confirmed that age and HCV infection were independent risk factors for diabetes. Fraser et al have also confirmed this observation. Mason et al in their excellent study determined that cirrhosis was an independent risk factors for diabetes. The prevalence of diabetes is also lower in patients wit alcohol related liver disease alone as compared with those wit chronic HCV infection. Mason et al also observed that HCV infection can not be considered to be a cause of diabetes and that the prevalence of extrahepatic syndromes associated with HCV infection like

benign monoclonal gammopathy and mixed cryoglbulinaemia and the improvement in glucose tolerance during antiviral therapy strengthen the association of HCV infection and diabetes. This association does not seem to be antibody related as circulating level of Islet cell antibody levels are not raised in diabetes with HCV infection.

The reported higher prevalence of IGT and diabetes in HCV positive cirrhosis patients raises some very interesting questions which need to be answered by well planned prospective studies. The main quarries needing explanation are whether HCV is a cause of diabetes in cirrhosis or diabetes enhances the progress of hepatitis C infection to cirrhosis. Recently a significant association was found between steatosis and hepatic fibrosis in a cohort of patients with chronic hepatitis C virus infection, implying a synergistic affect of steatosis on chronic viral hepatitis and progression of liver fibrosis.

In Conclusion hepatitis C viral infection is closely associated with IGT and/or diabetes mellitus, the correlation needs further study to ascertain any causal relation between the two. Also further assessment of the effect of right glycaemic control on the progression/regression of hepatic damage is needed through prospective studies on patients with diabetes mellitus and hepatitis C viral infection.

CONCLUSION

HCV infection is associated with IGT. The association of HBV with IGT in cirrhosis is not as significant as HCV. The association needs to be further studied in relation to the causes of diabetes mellitus. It also need to be evaluated whether steatosis caused by diabetes mellitus plays a role in progression of chronic hepatitis to cirrhosis.

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