Prevalence of Chronic Liver Disease Among the Patients of Celiac Disease and Effect of Gluten-Free Diet on Outcome of Liver Disease: A Prospective Study

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Abstract

Objectives: Descriptive reports of liver involvement in celiac disease (CD) are sparse, and the effect of a strict gluten-free diet (GFD) on the course of liver injury is also poorly understood. We conducted a study on 94 adult patients with CD and found that 39 of them were having chronic liver disease as well. We further followed patients of CD with CLD with strict Gluten-free diet (GFD) for six months.

Methods: We screened 94 patients of CD for CLD and found 39 patients to have CLD as well. We further followed these 39 patients of CD with CLD for six months with strict gluten-free diet. Follow up was done in terms of Child Pugh score. We recorded their clinical as well as laboratory findings after 1 month, 3 months and 6 months and compared them with those at the time of recruitment.

Results: The liver involvement was found in 39 (41.5%) out of 94 patients celiac disease.

Mean Child-Pugh score on admission was 10.22±1.09 and on first follow-up mean Child-Pugh score was 7.38±1.47 was found to be statistically highly significant (p <0.001)

Mean Child-Pugh score on admission was 10.15±1.09 and on second follow-up 7.33±1.33 respectively and was statistically highly significant (p <0.001)

Mean Child-Pugh score on admission was 10.12±1.09 and on third follow-up mean Child-Pugh score was 6.31±0.93 respectively was statistically highly significant (p <0.001)

Introduction

Prevalence of liver involvement in celiac disease is not much studied in India partly because of lack of awareness, investigation facilities and expertise in the field of gastroenterology. Liver involvement in CD has a wide spectrum of manifestations ranging from an asymptomatic isolated elevation of hepatic transaminases to severe liver insults like the chronic liver disease, cirrhosis, acute liver failure and even end-stage liver disease. CD is an important cause of hypertransaminasemia. Indeed, it has been reported in about 40% of adults and in 54% of children with a classical presentation of CD at the time of diagnosis. Conversely, CD is present in about 9% of patients with chronic unexplained hyper-transaminasemia.

Descriptive reports of liver involvement in celiac disease (CD) are sparse, and the effect of a gluten-free diet (GFD) on the course of liver injury is poorly understood.

A GFD leads to normalization of serum transaminases in 75% to 95% of patients with CD especially with isolated hypertransaminasemia, usually within a few months of good adherence to the diet. Even a severe liver failure is also potentially treatable by a gluten-free diet, even in the patients who are listed for liver transplantation.

Material and Method

This study was a prospective study, conducted in the Department of Medicine in collaboration with Department of Gastroenterology, Sardar Patel Medical College & Associated Group of Hospitals, Bikaner (Rajasthan) from September 2013 to October 2014.

Adult patients attending Gastroenterology OPD, Medicine OPD and admitted in Medicine Wards, S.P. Medical College and Associated Group of Hospitals, Bikaner with the diagnosis of celiac disease (CD) were initially recruited in the study. Informed written consent was taken from all patients, after confirming their diagnosis by IgA-tTG antibody test, upper GI endoscopy and the duodenal biopsy.

Inclusion criteria

1. Patients > 15 years of age
2. Proven cases of ‘celiac disease’ (CD) based on aforementioned criteria
3. Patients who have given written informed consent
4. Patients who were well motivated to follow strict GFD.

Exclusion criteria

1. Patients having known cause of liver disease
2. Terminally ill patients.

Among these 94 patients, we identified 39 cases who also had liver dysfunction. Diagnosis of CLD was based on the demonstration of splenomegaly, ascites and other signs of portal hypertension clinically and/or abdominal ultrasonography (USG), the presence of varices in upper GI endoscopy together with the presence

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of at least one of the four of the following features:\textsuperscript{13}

1. Hypoalbuminemia (serum albumin < 3.0 gm/dL) with reversal of albumin: globulin ratio.
2. Persistent elevation of prothrombin time (>5 sec. above control), which is not correctable by parenteral vitamin K.
3. One or more episodes of hepatic encephalopathy.
4. The presence of clinical stigmata of CLD like palmar erythema, parotid swelling, finger clubbing, gynecomastia, spider naevi.
5. Supportive evidence of CLD in the abdominal sonography included the presence of coarse echogenic liver pattern with dilated portal and splenic vein, and splenomegaly.\textsuperscript{13}

We excluded all other known causes of liver disease like alcohol, viral, autoimmune, toxic, iron and copper overload related liver disease by detailed history, thorough physical examination and appropriate investigations like CBC, Slit Lamp Examination, HBsAg, Anti-HCV, IgM Anti HCV Antibody, Autoimmune markers (ANA, ASMA, Anti LKM-1), Serum ceruloplasmin level, Serum α-1 antitrypsin level, once diagnosis of celiac disease associated CLD was made and these cases were included for further study.

Then, we followed these patients with strict gluten-free diet (GFD) for six months. The follow-up was done in terms of Child-Pugh score, which is the prognostic indicator of severity of CLD and is a constellation of 5 features namely encephalopathy, ascites, serum bilirubin, prothrombin time (INR) and serum albumin.\textsuperscript{14}

We observed their symptoms and signs, routine blood investigations, liver biochemical test results, including alanine transaminase, aspartate transaminase, alkaline phosphatase, and bilirubin levels, on every follow up after one month, after three months and after six months and compared them to those at time of diagnosis.

Data was analyzed by statistics package for social sciences (SPSS, Chicago-10) statistical software. Before comparing the groups studied, each variable was tested for normality distribution. The mean values of discrete variables were calculated along with their 95% confidence interval or percentages. Then, data was processed using the Chi-square test, Student's t-test.

**Results**

The liver involvement was found in 39(41.5%) patients with CD. All the patients had elevated liver biochemical test results (aspartate transaminase, alanine transaminase, bilirubin, and/or alkaline phosphatase) at the time recruitment.

Mean SGOT on admission was 140.77±30.03 IU/L and on first follow-up 47.83±36.02 respectively, and the difference was statistically highly significant (p <0.001). Mean SGPT on admission was 134.19±30.08 IU/L and on first follow-up 53.00±31.44 respectively. Mean SAP on admission was 348.69±100.71 and on first follow-up 264.41±116.34 respectively. Mean total bilirubin on admission was 3.23±0.70 and on first follow-up 1.33±0.35 respectively. Mean direct bilirubin on admission was 1.33±0.35 and on first follow-up 0.43±0.42 respectively. Mean indirect bilirubin on admission was 1.93±0.50 and on first follow-up 0.87±0.45 respectively. Mean total protein on admission was 3.80±0.47 and on first follow-up 4.98±0.81 respectively. Mean serum albumin on admission was 2.29±0.27 and on first follow-up 3.26±0.62 respectively. Mean prothrombin time on admission was 26.11±5.32 and on first follow up 17.63±3.06 respectively. Mean INR on admission was 2.02±0.40 and on first follow-up, 1.38±0.22 respectively (Table 1).

Mean Child-Pugh score on admission was 10.15±1.09 and on second follow-up mean Child-Pugh score was 7.33±1.33 and we observed that all the differences were statistically highly significant (p <0.001) (Table 1).

Mean SGOT on admission was 143.06±30.95 IU/L and on third follow-up 39.43±25.26 respectively. Mean SGPT on admission was 135.25±31.23 IU/L and on third follow-up 50.62±23.56 respectively. Mean SAP on admission was 349.43±103.16 and on third follow-up 244.39±116.04 respectively. Mean total bilirubin on admission was 3.21±0.73 and on third follow-up 1.06±0.27 respectively. Mean direct bilirubin on admission was 1.30±0.32 and on third follow-up 0.36±0.25 respectively. Mean indirect bilirubin on admission was 1.94±0.53 and on third follow-up 0.70±0.16 respectively. Mean protein on admission was 3.81±0.49 and on third follow-up 5.24±0.55 respectively. Mean serum albumin on admission was 2.29±0.29 and on third follow-up 3.26±0.56 respectively. Mean prothrombin time on admission was 26.37±5.58 and on third follow-up 16.87±2.84 respectively. Mean INR on admission was 2.02±0.42 and on third follow-up 1.29±0.21 respectively (Table 1).

Mean Child-Pugh score on admission was 10.12±1.09 and on third follow-up mean Child-Pugh score was 6.31±0.93. We observed that all the differences were statistically highly significant (p <0.001) (Table 1).

**Discussion**

Despite the large body of literature documenting CD-associated liver disease, descriptive studies in this setting are sparse. The effect of a
gluten-free diet on the course of liver disease, also remains uncertain.

In our study, we found that out of 94 cases of CD, 39 cases were diagnosed to have CLD as well, indicating that in the present study, the prevalence of CLD among the patients of CD was 41.5%.

Prevalence and clinical manifestation of hypertransaminasemia in celiac disease a 12-month follow-up study comprising 178 patients done by Novacek et al in 1999 has shown that 72 patient (42.4%) had raised AST and/or ALT levels at the time of diagnosis.15

Similar data were also seen by Alberto Rubio-Tapia et al in the study ‘the liver involvement in celiac disease’ in 2007, who observed hypertransaminasaemia in 40% of adults and 54% children with a classical presentation of celiac disease.15

In a study ‘Adult celiac disease and hepatopathy’ done by Morillas et al in 1991, they found that prevalence of significant hepatic disease in patients with celiac disease was 60.87%.16

In a study done by Volta et al in 2008, they found that about 50% patients of the untreated celiac disease had hypertransaminasemia as an expression of a mild liver impairment characterised by a histological picture of non-specific hepatitis (celiac hepatitis).17

Similar results were also observed by Green et al in ‘AGA technical review on the evaluation of liver chemistry tests’ in 2002 and emphasized that CD needs to be excluded before considering a diagnosis of cryptogenic cirrhosis.19

Almost similar results on GFD were also observed in a study done by Volta et al in 1998 as well as by Bardella et al in 1999.20 In 2002, Kaukinen et al done a study on 185 Finnish patients and found that dietary treatment may prevent progression to hepatic failure, even in cases considered for liver transplantation.19

In another study by Barbero Villares, et al in 2008 and showed that 40- 85% cases of celiac disease had improvement in their disease and liver disease was resolved after strict GFD for variable duration.20

Conclusion

In conclusion, chronic liver involvement in CD is an underestimated and potentially treatable cause of liver failure affecting 40-50% cases.

We strongly recommend screening of CLD in every case of CD because early diagnosis and treatment with gluten-free diet (GFD) not only delay or stop the progression of liver damage in these cases but also can improve already damaged the liver, even in cases of the end stage liver disease.

References
