ORIGINAL RESEARCH

Association of gall bladder stones and Coeliac disease in children

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ABSTRACT
Aims and Objective: to create awareness regarding association of gall bladder disease and coeliac disease in children. **Material and methods:** During school health program from April 2016 to March 2018 in urban and rural areas of district Amritsar, Punjab, India, we diagnosed 53 cases of coeliac disease with help of tissue transglutaminase antibodies as screening test in children having a triad of anaemia, failure to thrive and bowel disturbance and confirmation by anti endomysial antibodies and gut biopsy. Routine work up also included abdominal ultrasound. **Results:** out of 53 cases,4 have gall bladder stones. Out of 4, 2 were solitary and 2 were having multiple calculi. Only one patient was having pain in right upper quadrant of the abdomen and in rest 3 it was an incidental finding. **Conclusion:** Children with celiac disease should be assessed regularly for presence of gall bladder stones.

Keywords: celiac disease, gall bladder, stones

INTRODUCTION

Celiac disease (CD) is an immune-mediated disorder induced by gluten consumption in a subset of people with a specific HLA-DQ genetic background. Indeed, all patients developing CD have one or more MHC-DQ2 and/or MHC-DQ8 heterodimer-related allelic variants [1]. However, HLA-DQB1 alleles HLA-DQB1*02 and, to a lesser extent (in terms of allelic frequency in CD patients), HLA-DQB1*0302 are the most important for CD susceptibility [2,3]. Notably, this genetic background is required, but not sufficient, for the development of CD following gluten exposure. Indeed, only 3–4% of these HLA-DQ-predisposed individuals will develop CD during their lifetimes, indicating that additional (epi)genetic and/or environmental factors play a substantial role in CD etiopathogenesis [4,5].

The primary target of celiac disease is the gastrointestinal tract, and the diagnostic hallmark of celiac disease is gluten-sensitive enteropathy characterized by intraepithelial lymphocyte infiltration and variable degrees of villous atrophy of the small intestine; [1,4] however, celiac disease is a systemic disorder, as numerous other tissues and organs are affected in >50% of patients [6].

The liver is one of the most commonly affected extra-intestinal organs by CD. Unexplained hypertransaminasemia with non-specific histologic hepatic changes is the most common hepatic presentation of CD; this "cryptogenic" liver disorder (ranging from mild to severe liver dysfunction) frequently leads to CD diagnosis in asymptomatic (silent) patients and typically resolves within one year of a gluten-free diet (GFD). Specific autoimmune liver diseases, such as autoimmune hepatitis and autoimmune cholangitis, which are diagnosed more frequently in CD patients than in the general population, are not gluten sensitive. Recent evidence suggests that CD is also a risk factor for non-alcoholic fatty liver disease [6,7,8]. In addition to the liver, the biliary tract can be specifically affected in patients with CD; specifically, gallbladder function can be altered.

Cholecystokinin is a hormone that is synthesized and secreted by I-cells from the proximal small intestine mucosal epithelium in response to a meal with fat and protein [9]. After CCK is secreted, it enters the circulation and stimulates the contraction of the gallbladder and the relaxation of the Oddi sphincter. This then stimulates the release of bile in the gallbladder into the small intestine [10]. Before a

gluten-free diet (GFD), the gallbladder becomes large, lax, and lazy in celiac disease patients [11], which poses a risk for the formation of biliary sludge and gallstones. Gall bladder disease or malfunction can be associated with coeliac in children. It can cause pain in the upper right quadrant of the abdomen, or it can be incidental finding on routine ultrasound.

Thus the present study was conducted to create awareness regarding association of gall bladder disease and coeliac disease in children.

MATERIAL AND METHODS

During school health program from April 2016 to March 2018 in urban and rural areas of district Amritsar,Punjab,India, we diagnosed 53 cases of coeliac disease with help of tissue transglutaminase antibodies as screening test in children having a triad of anaemia, failure to thrive and bowel disturbance and confirmation by anti endomysial antibodies and gut biopsy. Routine work up also included abdominal ultrasound.

RESULTS

Out of 53 cases,4 have gall bladder stones. Out of 4, 2 were solitary and 2 were having multiple calculi. Only one patient was having pain in right upper quadrant of the abdomen and in rest 3 it was an incidental finding.

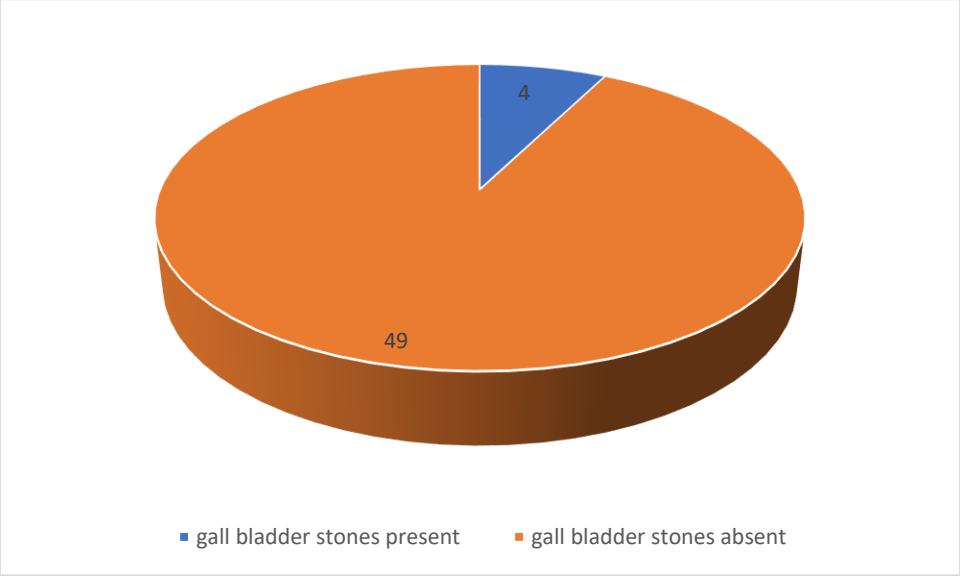

Figure 1: prevalence of gall bladder stone in patients with celiac disease

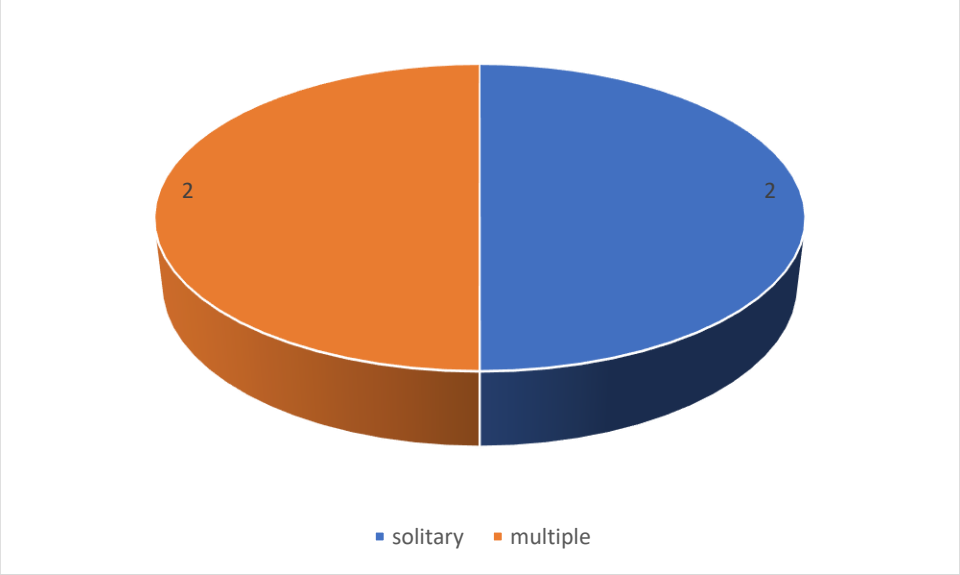

Figure 2: Nature of stones

DISCUSSION

As per above results, incidence of gall bladder disease was more in coeliac disease children as compared to general population. Celiac Disease (CD) is an immune-mediated disorder which primarily affects the small intestine, but extra-intestinal organs are often affected by the pathological process [12]. Wang HH et al summarized relationship between coeliac disease

and gallstones because defective intestinal cholecystokinin secretion markedly increases susceptibility to cholesterol gallstones via a mechanism involving dysmotility of both the gallbladder and the small intestine. Because gluten free diet can significantly improve the coeliac enteropathy, early diagnosis and therapy in coeliac patients is crucial for preventing the long-term impact of cholecystokinin deficiency on the biliary and intestinal consequences. When gluten is reintroduced, clinical and histologic relapse often occurs in coeliac patients [13]. In patients at diagnosis, elevated somatostatin levels were associated with increased gallbladder fasting volume, whereas decreased cholecystokinin secretion was responsible for the reduced gallbladder emptying. Gluten-free diet reversed these abnormalities [14]. Maton et al concluded that cholecystokinin immunoreactivity cochromatographing with cholecystokinin-octapeptide was responsible for 50%-60% of circulating cholecystokinin in normals and in treated patients but the small amount of cholecystokinin that was released in untreated patients with celiac disease cochromatographed with cholecystokinin-33/39 and there is a reversible defect of gallbladder emptying and cholecystokinin release in celiac disease[15].In another study, Plasma CCK was measured in 20 celiac patients (normal mucosa: n=6; infiltrative type: n=6; atrophic type=8) and 9 controls, before and after ingestion of a polymeric or a semi-elemental meal. Significant decreases in basal CCK plasma (B 0.6 [95% CI, 0.3-1.3] pmol/l; $p<0.003$) and postprandial CCK area under curve (AUC 34 [19-61] pmol/l x 120 min, $p<0.0001$) were observed in patients with an atrophic mucosa compared with treated patients (B 1.6 [1.0-2.4] pmol/l, AUC 267 [172-414] pmol/l x 120 min) or healthy volunteers (B 1.0 [0.7-1.4] pmol/l, AUC 186 [131-264] pmol/l x 120 min)[16].

CONCLUSION

CCK(Cholecystokinin) is the hormone responsible for gall bladder contraction. The bulk of this hormone is produced in duodenum. Active coeliac disease can cause a reduction of duodenal production of CCK. This can abnormally decreased gall bladder contraction in coeliac patients resulting in stone production. So, it is the result of decreased production of endogenous production of CCK and not a lack of end organ responsiveness.

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