

Extra Intestinal Manifestations of 100 cases of Ulcerative Colitis and its correlation with extent and behavior of disease

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ABSTRACT

Aim: To identify frequency of extra intestinal manifestations, correlate them with the extent of involvement of colon and severity of disease and determine the effect of presence of extra intestinal manifestation on relapsing/ remitting pattern of disease in patients of ulcerative colitis.

Study Design: Case control type of cohort study carried out in Mayo Hospital, Lahore.

Results: Colonoscopic extent shows that there were 27% patients who had proctitis, 22% had distal colitis, 13% had left sided colitis, 17% had extensive colitis, 15% had pancolitis and 6% had pancolitis with backwash ileitis. Colonoscopic severity shows that 26% had grade II, 21% had grade III and 53% had grade IV. EIM were observed in 6%, out of which only 1(16%) had proctitis while 3(50%) had pancolitis and 2(34%) had pancolitis with backwash ileitis. Extra intestinal manifestations were significantly higher in patients with pancolitis and pancolitis with backwash ileitis..

Conclusion: Frequency of EIM in our study was 6% and its presence is significantly associated with extent of disease but has no significant association with behavior of disease.

Keywords: Colonoscopy, Extra intestinal manifestations (EIM), ulcerative colitis

INTRODUCTION

Ulcerative colitis (*Colitis ulcerosa*, UC) is a type of inflammatory bowel disease (IBD). It is a form of colitis, a disease of the large intestine that results in characteristic ulcers, loss of vascularity and erythema in the colon. The major symptom of active disease is usually diarrhea mixed with blood. While the cause is still unknown, several, possibly interrelated etiologies have been suggested. A genetic component to the etiology of ulcerative colitis can be hypothesized based on¹ aggregation of ulcerative colitis in families, identical twins concordance rate of 10% and dizygotic twin concordance rate of 3%², ethnic differences in incidence of disease and identification of genetic markers and linkages. Levels of sulfate-reducing bacteria tend to be higher in persons with ulcerative colitis. This could mean that there are higher levels of hydrogen sulfide in the intestine^{3,4}. The clinical presentation of ulcerative colitis depends on the extent of the disease process. The disease is usually accompanied with different degrees of abdominal pain, from mild discomfort to severely painful cramps. Ulcerative colitis is normally classified by the extent of involvement into:

- Distal colitis⁵ i.e., Proctitis, Proctosigmoiditis, Left-sided colitis,
- Extensive colitis i.e., involvement of colon beyond splenic flexure.
- Pancolitis

Hepatobiliary disease is another common extra intestinal manifestation of UC in children. Chronic

active hepatitis, granulomatous hepatitis, amyloidosis, fatty liver and pericholangitis are some of the intrahepatic manifestations of IBD. Extra hepatic manifestations include cholelithiasis and primary sclerosing cholangitis. *Neutrophilic Myositis* is also an Extra Intestinal manifestation of Ulcerative Colitis⁶. Another study shows that *sensorineural hearing loss* is an extra intestinal manifestation⁷ of Ulcerative Colitis. *Presence of Extra Intestinal Manifestations is well established*. Its prevalence and frequency in our population is not documented and it can be different from western data due to varied dietary habit, different life style and races. Moreover, impact of presence of Extra Intestinal Manifestation on extent and severity of disease is still largely unknown. We are also unaware whether disease course i.e., frequency of relapse and outcome of disease is different in those with Extra Intestinal Manifestations. We have planned a study to address these issues.

MATERIALS AND METHODS

This study is carried out in the department of internal medicine, medical out door and medical wards of Mayo Hospital, Lahore. One year after every patient found a case of ulcerative colitis in 100-patients. Conventional non-probability consecutive sampling technique was used. Patients with history of diarrhea who may or may not be associated with bleeding, diagnosed to have U.C. confirmed by colonoscopic biopsy results, patients with age above 12 years were included while patients with age below 12 years, patients with the history of diarrhoea of <3-week

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duration, Patients with non-conclusive colonoscopic biopsy, patients with concomitant diseases which can result in manifestations as can be seen with ulcerative colitis were excluded.

Case control type of cohort study. Data collection: 100-consecutive patients fulfilling selection criteria were selected. Detailed clinical history i.e. duration of diarrhea, frequency of stools, consistency of stool, presence or absence of blood and mucous in stools was taken. Associative symptoms like abdominal pain, fever, myalgia, arthralgia and fatigue were inquired. Past history, Systemic examination also recorded. The laboratory investigations i.e. complete blood count, stool complete examination and x-ray chest.

All patients treated as per standard protocol with sulfasalazine, oral steroids, steroid enema or azathioprine depending upon the extent & severity of disease. Patients followed at 1-month, 3-month, 6month and 1-year and monitored for number of relapses and duration of remissions. A standard proforma was used for collection of data with history of diarrhea who may or may not be associated with bleeding, diagnosed to have U.C. confirmed by colonoscopic biopsy results.

The collected information was entered into SPSS version 20 and analyzed through its statistical program. The *quantitative variables* like age, weight, pulse, temperature and duration of presenting complaints was given in the form of tables, Mean \pm SD and Histograms. The *qualitative variables* like gender, clinical history etc. was presented in the form of tables, ratio and pie charts. The results of Ulcerative Colitis i.e. acute exacerbation and duration of remission was compared in those with and without extra intestinal manifestations, using Chi Square test. "P" value will be considered significant as < 0.05 .

RESULTS

Total 100 patients were enrolled in this study who suffered from ulcerative colitis. Among these 50 were male and 50 were female. Mean duration of diarrhea was 23.84 \pm 21.45 months. Mean for frequency of stool was 6 \pm 2.18. Detailed history showed that 79% suffered from nocturnal diarrhea. 3% had history of skin pigmentation, 5% had history of muscle pain, 10% had history of joint pain, 1% had history of painful leg swelling and 2% had family history of ulcerative colitis.

There were 2 patients having tachycardia while 12 were having hypotension. Temperature was also noted. There were 8 patients who had high grade fever. General physical examination was done for each patient. There were 39 patients who were anemic, 1 patient had skin pigmentation, 1 patient had tender joints and 1 patient had tender leg

swelling. Stool for occult blood was done for all patients which was positive for 56 patients. Gall bladder stones were present in 3 patients while common bile duct was normal in all. Colonoscopic examination showed that 27 patients had proctitis, 22 had distal colitis, 13 had left sided colitis, 17 had extensive colitis, 15 had pancolitis and 6 had pancolitis with backwash ileitis. Colonoscopic severity of disease showed that 26 patients had granular but non friable mucosa, 21 patients had friable mucosa and 53 had friable mucosa plus ulcerations.

Histopathology results of patients showed that 21% had mild acute and chronic inflammatory cells but intact epithelium and 79% had heavy acute and chronic inflammatory cells with crypt distortion and abscess. Extra intestinal manifestations were observed in 6 patients. There were 2 who had arthritis, 3 had cholelithiasis and 1 had deep vein thrombosis as extra intestinal manifestation. Progress of disease was followed at 1st, 3rd, 6th, and at 12th month after discharge.

Total 27 patients suffered from proctitis, among these only 1 patient had extra intestinal manifestation, 22 had distal colitis while 13 had left sided colitis and 17 suffered from extensive colitis among whom none of them had EIM and 6 patients had pancolitis with backwash ileitis and among these 2 had EIM. Significant association was present between extra intestinal manifestations and colonoscopic extent of disease. Colonoscopic severity shows that there were 26 patients who had granular but non friable mucosa and 21 patients had friable mucosa and among these, none of them had extra intestinal manifestations, 53 patients had friable mucosa plus ulcerations and among these 6 patients had extra intestinal manifestations.

On follow up, relapse of disease was noted in 20 patients within 1 month, in 15 patients between 1-3 months, 9 had relapse between 3-6 months while 6 had relapse at 6-12 months of follow up. Total 6 patients who had extra intestinal manifestations, 3 had relapse during 1 year follow up. The remaining 94 patients had no extra intestinal manifestation and among these 45 had relapse. No significant association was present between relapse and extra intestinal manifestations.

DISCUSSION

Ulcerative Colitis (UC) is characterized by recurrent episodes of continuous inflammation limited to the mucosal layer of colon and rectum. In our study, 27% patients had proctitis, 22% had distal colitis, 13 had left sided colitis while extensive colitis was present in 17% of patients whereas pancolitis was present in 15% and 6% patients had pancolitis with backwash ileitis. Similar results were seen in a study done in

Korea which reported that among 94 patients, proctitis was noted in 34%, left sided colitis in 35.1% and extensive colitis in 30.9%⁸. This study also shows similarity with a study done in Singapore on 235 patients out of which 24.3% had proctitis, 20.8% had proctosigmoiditis, 17.7% had left sided colitis and 37.6% had pancolitis⁹. The population based study from India revealed that out of 23 patients, 44% had proctosigmoiditis, 40% had left sided colitis and 16% had pancolitis. The commonest presentation in the case series from Thailand was left sided colitis in 58% of patients¹⁰. So there is no significant difference of our study about extent of disease from above mentioned studies. There is no definite evidence that extent of UC is different among Asian population¹¹. In our study during clinical course of one year follow up, total 48% had relapse and 52% patients remained in remission. In a study, cumulative probability of relapse after UC diagnosis for Korean patients was 30.2% after one year, 58.8% after 3 years, 72% after 5 years and 88.4% after 10 years¹².

In our study 6 patients had extra intestinal manifestation (EIM). Among them, 2 had arthritis, 3 had cholelithiasis and 1 had deep vein thrombosis (DVT). Pokharna studied 46 patients and reported that 6% patients had EIM¹³. Frequency of EIM in Indian patients ranging from absence of such manifestations to prevalence is up to 18%. Kochhar et al reported EIM in 35% of patients. Habeeb et al encountered EIM in 18% patients^{14,15,16}. However study conducted by Khan in Peshawar in 2011 reported EIM in 26% patients admitted to a tertiary care Hospital in Peshawar¹⁷. Another study conducted by Huma et al in Karachi on 189 patients with non specific UC has been reviewed but in this study EIM were not discussed¹⁸.

Our study shows that EIM is associated with extent of disease but there is no significant association with behavior and activity of disease. Quite a number of studies emphasize the correlation of extent of UC and development of EIM and also association with disease activity. In their study, Mosebach et al also came to the conclusion that UC activity was significantly greater in patients with EIM. Muhammad et al also concluded that UC activity was greater in patients with EIM¹⁹.

This difference is due to certain factors which may include life style parameters, geographical and racial distribution, certain genetic factors due to which frequency, severity and impact of these EIM in UC patients are less.

CONCLUSION

Frequency of extra intestinal manifestations (EIM) in our study of patients with Ulcerative Colitis is 6%. Prevalence of EIM is significantly associated with

extent of disease but not adversely affected by behavior of disease.

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