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Dysplasia in Ulcerative Colitis Patients in Kashmir Valley

Baba Iqbal Khaliq[1], Danish Rafiq Khan[2], Yawar Bhat[1], Mohamad Iqbal Lone[3], Khalil Mohamad Baba[4], Hameed Raina[5]

- 1:Postgraduate Department of Pathology
- 2: Senior resident Department of Pathology
- 3:Additional Professor, Department of Pathology
- 4:Professor and Head, Department of Pathology
- 5:Postgraduate Department of Gastroenterology

Sher-i-Kashmir Institute of Medical Sciences Srinagar India - 190011.
E mail : drbabaiqbal@gmail.com

ABSTRACT

Background: *Patients with long-standing ulcerative colitis (UC)and Crohn's disease of the colon are at an increased risk of developing colorectal neoplasia (dysplasia and colorectal carcinoma.) In inflammatory bowel disease (IBD) the development of colorectal carcinoma (CRC) occurs through an inflammation-dysplasia-carcinoma pathway. the diagnosis and grading of dysplasia in IBD plays a decisive role in the management of patients and reducing cancer related mortality.*

Aim: *To identify dysplasia in IBD patients and preventing progression to invasive colorectal carcinoma by proper intervention at right time.*

Methodology: *5 years hospital based prospective study extending from June 2009 to June 2014.*

Results: *Out of 210 confirmed IBD patients 21 (10%) developed dysplasia over a period of time. All Crohn's disease and indeterminate colitis patients were negative for dysplasia. Out of 182 ulcerative colitis patients 21 (11.53%) developed dysplasia. low grade dysplasia was present in 17 (9.34%) patients and high grade dysplasia was present in 4 (2.19%) patients. Dysplasia was higher in patients with extensive colitis and long disease duration.*

Conclusion: *Periodic endoscopic surveillance biopsies are must in IBD patients to rule out dysplasia and prevent progression to development of colorectal carcinoma and morbidity and mortality associated with it.*

Keywords: Dysplasia, colorectal carcinoma, Inflammatory bowel disease

(IBD), Ulcerative colitis (UC), Crohn's disease (CD).

INTRODUCTION

Both forms of IBD are associated with an increased incidence of gastrointestinal cancer, in addition, both begin relatively early in life and persist for long periods, leading to decreased quality of life indices and a greater than two fold increase in mortality rate.[1-4] It was generally believed that chronic idiopathic ulcerative colitis (IUC) and Crohn's disease were rarely seen in underdeveloped nations, including middle eastern, Asian and African countries.[5,6,7]

The last 2 decades have seen an increase in the reports of both ulcerative colitis (UC) and Crohn's disease (CD) from Asian countries. [8-11]

Patients with long-standing ulcerative colitis (UC) and Crohn's disease of the colon are at an increased risk of developing colorectal neoplasia (dysplasia and colorectal carcinoma.[12,13] In inflammatory bowel disease (IBD) the development of colorectal carcinoma (CRC) occurs through an inflammation-dysplasia-carcinoma pathway.[13] In contrast to patients with sporadic CRC, individuals with IBD-related CRC have an increased incidence of synchronous malignancies, an absence of adenomatous polyps preceding the development of carcinoma, and a more rapid rate of progression of colonic mucosa to dysplasia.[12-22]

Although CRC, complicating ulcerative colitis and Crohn's disease, only accounts for 1–2% of all cases of CRC in the general population, it is considered a serious sequela of the disease and accounts for one in six of all deaths in IBD patients.[12-22]

Colorectal cancer, the most lethal long term complication of chronic inflammatory bowel disease (IBD), is the culmination of a complex sequence of molecular and histologic derangements of the intestinal epithelium that are initiated and at least partially sustained by chronic inflammation. Dysplasia, the earliest histologic manifestation of this process, plays an important role in cancer prevention by providing the first clinical alert that this sequence is underway and serving as an endpoint in colonoscopic surveillance of

patients at high risk for colorectal cancer.[15-22]

The diagnosis and grading of dysplasia in endoscopic surveillance biopsies play a decisive role in the management of patients with IBD.[15,16,17,18]

The current approach to surveillance is grounded in the concept of an inflammation-dysplasia-carcinoma sequence, with dysplasia representing a premalignant phase during which intervention can prevent or minimize the complications associated with invasive cancer. Dysplasia, the earliest histologic manifestation of this process, plays an important role in cancer prevention by providing the first clinical alert that this sequence is underway and serving as an endpoint in colonoscopic surveillance of patients at high risk for CRC. The diagnosis and grading of dysplasia in endoscopic surveillance biopsies plays a decisive role in the management of patients with IBD.[15-22]

MATERIAL AND METHODS

This Hospital based five years prospective study was done in the department of pathology, Sher-i-Kashmir Institute of Medical Science (SKIMS), Srinagar Kashmir extending from June 2009 to June 2014. Histopathologically and endoscopically confirmed cases of IBD 0n regular follow up were included in the study, patients who did not come for follow up were excluded from the study. During this period follow up endoscopic surveillance biopsies of 210 IBD patients were studied for dysplasia. Dysplasia was divided into negative for dysplasia, low grade, high grade and indefinite for dysplasia. Indefinite group was sent for repeat endoscopic biopsies. Biopsies received in 10% formalin were processed as per the standard procedure and studied by two senior most pathologists in the department of pathology for dysplasia.

RESULTS:

Age of the IBD patients ranged from 1 to 80 years. Mean age was 39.75 years. Maximum number of IBD cases were seen in the age group 20-30 years (49 cases, 23.33%), followed by 40-50 years (43 cases,

20.47%) and 30-40 years age group (42 cases, 20%). Only in (2 cases 0.95%) age was less than ten years. Males were 127 (60.5%) cases of inflammatory bowel disease and females were 83 cases (39.5%). Male: Female ratio was 1.53:1.

Pain abdomen, Bloody diarrhoea, Diarrhoea, and Hematochesia were dominant symptoms. Extra intestinal manifestations in the form of arthritis was present in four patients (1.90%).

Mean duration of disease was 2.43 years. Duration of disease was less than 1 year in 78.57% patients, 1to 10years in 14.76% patients and greater than 10 years in 5.71% patients.

Haemorrhagic spots, ulcerated, erytematous and friable areas, loss of vascularity and oedema were dominant endoscopic findings. (graph 1)

Ulcerative colitis was present in 182 patients (86.6%), Crohn disease in 26 patients (12.38%) and Indeterminate colitis in 2 patients (0.95%). All Crohn's disease and indeterminate colitis patients were negative for dysplasia. Out of 182 ulcerative colitis patients low grade dysplasia was present in 17 (9.34%) patients and high grade dysplasia was present in 4 (2.19%) patients. Dysplasia was higher in patients with extensive colitis and long disease duration.

This hospital based study thus proves that IBD patients are at the risk of developing dysplasia which may progress to the development of colorectal carcinoma if ignored.

Thus IBD patients should be educated and encouraged to attend the hospital out-patient department regularly and periodic endoscopic surveillance biopsies should be taken to rule out dysplasia, so that proper intervention at the right time can prevent development of colorectal carcinoma and mortality associated with it in these patients.

DISCUSSION:

This study included total of 210 confirmed IBD case. Males were 127/210 (60.5%) cases of Inflammatory bowel disease and females were 83/210 cases (39.5%). Male: Female ratio was 1.53:1. This pattern is similar to most studies from Asian countries[23,24,25,26] but is unlike western experience[11,27,28]. This difference may relate

to the custom that males are likely to seek medical advice more commonly than females in relation to colorectal disease.

In this study age ranged from 1 to 80 years. The youngest patient was less than one year old and eldest patient was 80 years old. Mean age is 39.75 years and Standard deviation of 16.04. Maximum number of cases 49 (23.33%) were seen in the age group 20-30 years, followed by 43 (20.47%) cases in 40-50 years age group years, 42 (20%) cases were in the age group of 30-40 years, 30 (14.28%) cases were in 50-60 age group, 23cases (10.95%) cases were in 10-20 years age group 19 (9.04%) cases were in 60-70 years age group, 2 (0.95%) cases were in 70-80 years age group and 2 (0.95%) cases were belonged to less than 10 years age group. This is almost similar to studies by Das et al.[29], Ghoshal et al.[30], Pai et al.[31] and

Mean duration of disease was 2.43 years. Duration was less than 1 year in 78.57% patients, 1 to 10 years in 14.76% patients, greater than 10 years in 5.71% patients. In Ulcerative colitis duration of disease varied from less than one year to twenty years while in Crohn's disease duration of disease varied from less than one year to three years. In this study mean duration was shorter than studies from west by M Leidenius et al[18], this is because of shorter period of follow up in our study.

Ulcerative colitis was present in 182 patients (86.6%), Crohn's disease in 26 (12.3%) patients and indeterminate colitis in 2 (0.95%). Results were similar to study by from middle east by Mohammad B. Satti et al[14], Mohammad Al Fadda et al[32] and but different from study by Sawczenko A et al[33] from UK and studies from America.[11,27,28,34]

Number of biopsy bits received varied from one to twenty nine. In 61 (29%) cases number of bits were four and in 48 (22.9%) case number of bits were three. The number of bits was much lower to rule out dysplasia with 90% confidence as reported by Rubin et al[21].

Out of total 210 IBD patients 189, IBD patients (90%) were negative for dysplasia, 21 (10%) IBD patients developed dysplasia. All Crohn's disease and indeterminate colitis patients were negative for dysplasia.

Out of 182 Ulcerative colitis patients, dysplasia was present in 21

(11.53%) patients, of which Low grade dysplasia was present in 17 (9.34%) patients and High grade dysplasia was present in 4 (2.19%) patients, 161 (88.46%) ulcerative colitis patients were negative for dysplasia. Results are almost similar to studies by Leidenis et al[18], but less than studies by Friedman et al[35].

Dysplasia was present in those patients who had either longer duration of disease, higher age group or extesive colitis. High grade dysplasia was present in four patients, in all four patients age was above fifty years, one patient was in the age group of 50-60 years, two patients were in the age group of 60-70 years, one patient was in age group of 70-80 years, similar to studies by Gyde and Colleagues [17] , Leidenis et al [18] Ekbom A et al. from Sweden [19], Taylor BA et al [20] Friedman et al [35] , Connell et al [36] . All the four patients of ulcerative colitis with high grade dysplasia underwent colectomy, none of them had developed adenocarcinoma. Patients with low grade dysplasia were kept on close follow up.

CONCLUSION

This study confirms the development of dysplasia in IBD patients. This study only gives the insight into the development of dysplasia in IBD patients in this geographical area because of shorter duration of study and hospital based nature and emphasises the need for much bigger population based studies with long term follow up.

Thus IBD patients should be educated and encouraged to attend the hospital out-patient department regularly and periodic endoscopic surveillance biopsies should be taken to rule out dysplasia, so that proper intervention at the right time can prevent development of colorectal carcinoma in these patients. Endoscopists should take multiple four quadrant biopsies to increase the yield of diagnosis in terms of dysplasia. furthermore newer techniques like chromoendoscopy, magnification endoscopy, narrow band imaging and confocal laser endomicroscopy should be used to diagnose dysplastic lesions at the earliest and prevent development of carcinoma in these patients.

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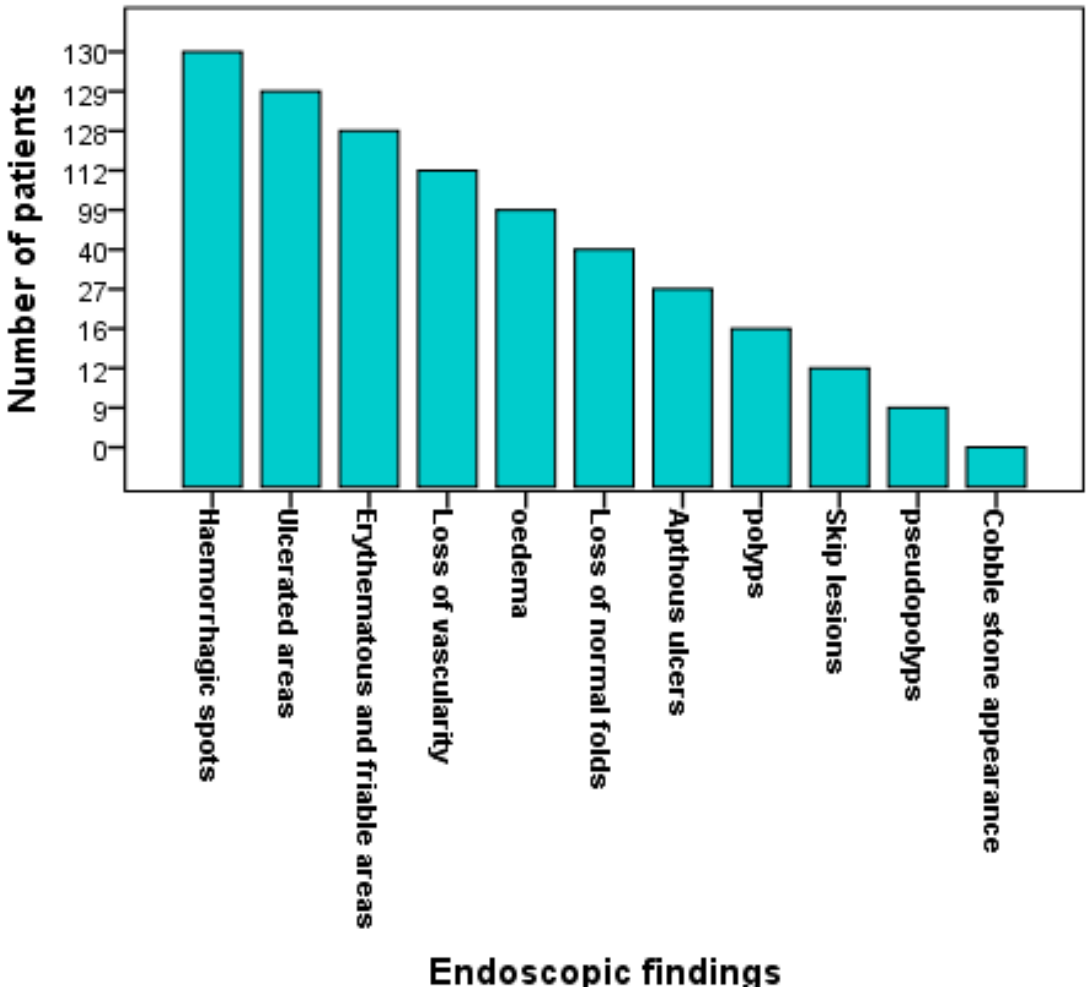


(graph 1)

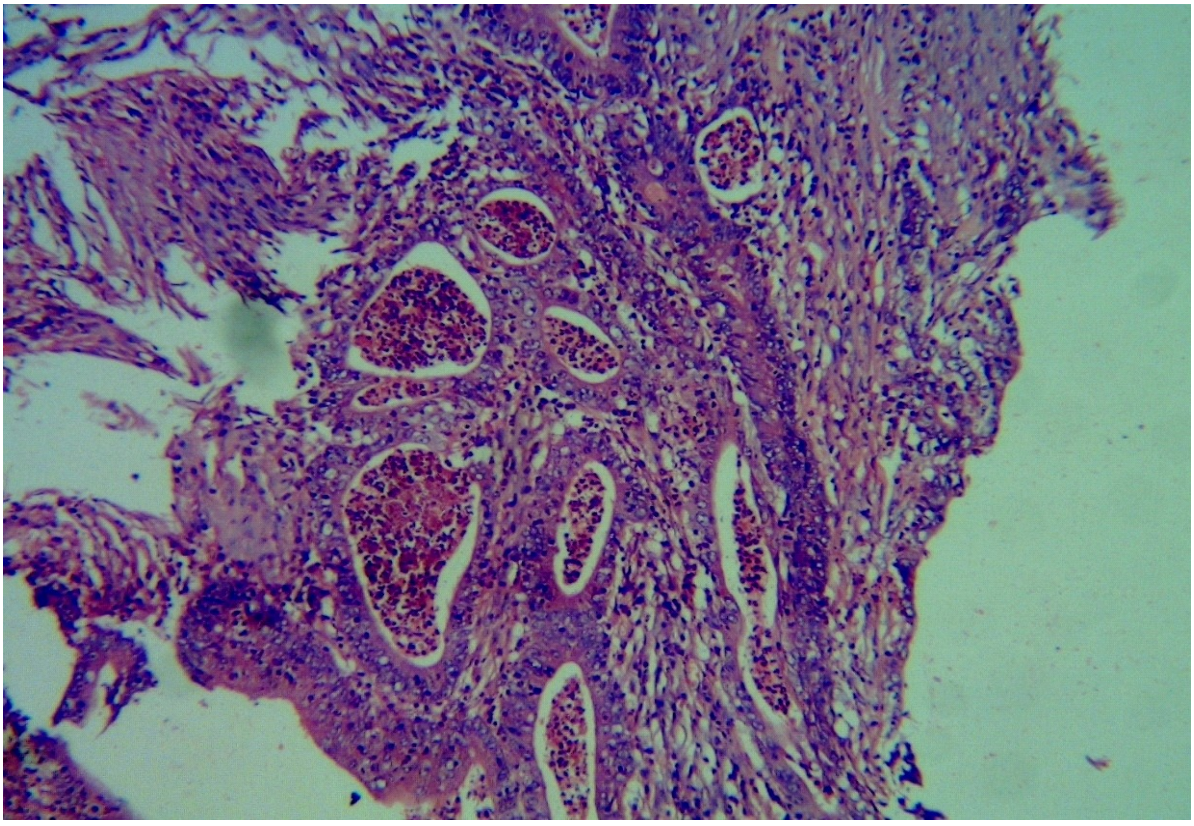
Distribution of cases according to Dysplasia (table 1)

Dysplasia	Ulcerative colitis	Crohn disease	Indeterminate colitis
Negative	161 (88.46%)	26 (100%)	2 (100%)
Low grade	17 (9.34%)	0 (0%)	0 (0%)
High grade	4 (2.19%)	0 (0%)	0 (0%)
Total	182 (100%)	26 (100%)	2 (100%)

Age group involved in dysplasia (table 2)

Age group in years	Low grade dysplasia	High grade dysplasia
Up to 10	0 (0%)	0 (0%)
10-20	1 (5.9%)	0 (0%)
20-30	3 (17.6%)	0 (0%)
30-40	4 (23.5%)	0 (0%)
40-50	4 (23.5%)	0 (0%)
50-60	2 (11.8%)	1 (25%)
60-70	2 (11.8%)	2 (50%)
70-80	1 (5.9%)	1 (25%)
Total	17 (100%)	4 (100%)

microphotographs



Microphotograph of a case of ulcerative colitis showing crypt abscess and high grade dysplasia. H&E stain (10X).

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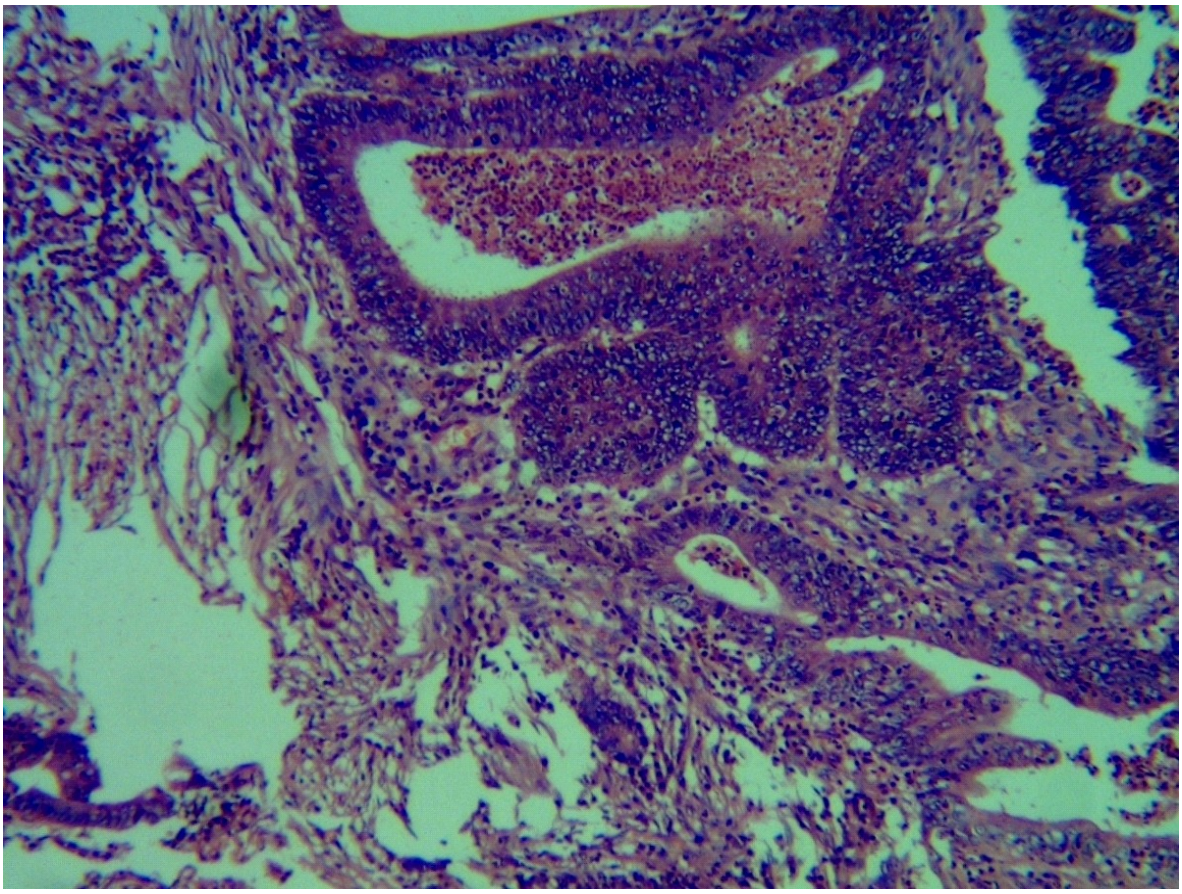

Microphotograph of a case of ulcerative colitis showing crypt abscesses and high grade dysplasia. H&E stain (10X).