FREQUENCY AND TYPE OF DYSPLASIA IN ULCERATIVE COLITIS IN COLORECTAL BIOPSIES

Shagufta Iram, Muhammad Tahir Khadim, Syed Salman Ali, Unaiza Jamil, Kiran Mumtaz

Combined Military Hospital Multan/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To determine the frequency and type of dysplasia in ulcerative colitis in colorectal biopsies.
Study Design: Cross sectional analytical study.
Place and Duration of Study: Department of Histopathology, Combined Military Hospital Multan, from Oct 2016 to Apr 2017.
Methodology: A total of 68 cases of ulcerative colitis were included in the study. Data was analyzed by using SPSS version 18. Variables like age and duration of disease gender and categories of dysplasia (low grade and high grade) were calculated. Chi-square test was applied.
Results: The age of patients ranged from 20 to 70 years with a mean age of 40.64 ± 13.9 years. In our study, most of the patients 22 (32%) belong to 21-30 years. Out of 68 cases of ulcerative colitis, 38 (56%) cases were diagnosed as negative for dysplasia, 20 cases (29%) were diagnosed as positive for low grade dysplasia and 10 (15%) cases were diagnosed as positive for high grade dysplasia.
Conclusion: The frequency of dysplasia in ulcerative colitis varies in different countries of world. A significant number of cases of ulcerative colitis in our study showed dysplastic changes. Surveillance colonoscopy and detection of dysplasia at early stages is effective in reducing mortality in ulcerative colitis.

Keywords: Colorectal biopsies, Dysplasia, Ulcerative colitis.

INTRODUCTION

Ulcerative colitis is a chronic and relapsing inflammation of colonic mucosa with variable extension from rectum towards cecum. It is a disease of adults and is more common in western countries including United States and United Kingdom and is less frequent in Asia, Japan and South America. However, in the past few years, its incidence is increasing in Asian countries[1]. Patients with ulcerative colitis are at increased risk of developing colorectal carcinoma. Risk of dysplasia increases 8 to 10 years after the development of mucosal lesions in cases of ulcerative colitis. Patients with pancolitis are at increased risk than those with left sided disease[2]. Greater frequency and severity of active inflammation, genetic factors, and presence of primary sclerosing cholangitis are associated risk factors for development of dysplasia[3]. Colorectal carcinoma (CRC) on ground of ulcerative colitis may develop from non-dysplastic mucosa to indefinite dysplasia, low grade dysplasia, high grade dysplasia and finally to invasive adenocarcinoma. Therefore surveillance programmes using colorectal biopsies are recommended to reduce risk of CRC and mortality in ulcerative colitis[4].

International studies show wide variation in dysplasia from 2% to 17.2%[5,6]. The rationale of our study was to determine the actual magnitude of dysplasia in our population, so that appropriate management should be done in these patients. This will help to decrease morbidity of the disease and also shorten their prolonged hospital stay once they are properly diagnosed and managed. This will also help to relieve psychological, financial and social stress from the suffering family.

METHODOLOGY

This cross-sectional analytical study was carried out at department of Histopathology, Combined Military Hospital, Multan from

Correspondence: Dr Shagufta Iram, Department of Pathology, Combined Military Hospital, Multan Pakistan
Email: drshag55@gmail.com
Received: 12 Jul 2017; revised received: 11 Jun 2019; accepted: 02 Jul 2019

October 2016 to April 2017, after the approval of ethical committee. Sample size was calculated using WHO sample size calculator with confidence level 95%, anticipated population proportion 17.2%[5] and absolute precision 9%. A total of 68 colorectal biopsies of ulcerative colitis were selected by non-probability, consecutive sampling technique, between 20-70 years of age, of both genders, after taking informed consent. Poorly fixed specimens, specimens with scanty tissue and metastatic carcinoma were not included in the study. The specimens were fixed in 10% buffered formalin, grossed and stained with Hematoxylin and Eosin to examine morphology. Biopsy specimens were examined for dysplasia and classified into low grade and high grade dysplasia. Special stains like Periodic Acid Schiff were performed whenever required. In order to minimize the bias, all results were verified by the supervisor having more than 15 years of experience. All the data were entered into the predesigned performa.

Data was analyzed by using SPSS version 18. The quantitative variables like age and duration of disease were presented by calculating mean and standard deviation. The qualitative variables like gender and categories of dysplasia (low grade and high grade) were presented by calculating frequency and percentages. Post stratification, chi-square and Fisher exact test were applied. *p*-value less than or equal to 0.05 was taken as significant.

RESULTS

During the study, a total of 68 colorectal biopsies of ulcerative colitis patients were included. Distribution of cases according to age groups, gender, disease duration and categories of dysplasia were summarized in table-I & fig-1. A significant statistical association was seen between disease duration and dysplasia, *p*-value being 0.001.

Table: Distribution of cases according to age, gender and disease duration.

Variable	Cases (n)	Percentage (%)	Ulcerative Colitis			*p*-value
			Negative for dysplasia	Low grade dysplasia	High grade dysplasia	
Age Groups						
21-30	22	32.4	19	3	-	-
31-40	20	29.4	7	11	2	
41-50	9	13.2	5	2	2	
51-60	10	14.7	4	2	4	
61-70	7	10.3	3	2	2	
Gender						
Male	50	73.5	25	15	10	0.091
Female	18	26.5	13	5	-	
Disease Duration						
<8 years	27	39.7	24	3	-	0.001
>8years	41	60.3	14	17	10	

Chi-square test applied.

The age of patients ranged from 20 to 70 years with a mean age of 40.64 ± 13.95 years. In our study, most of the patients 22 (32%) belonged to age group 21-30 years. There were 50 (74%) males and 18 (26%) females with a male to female ratio of 3:1.

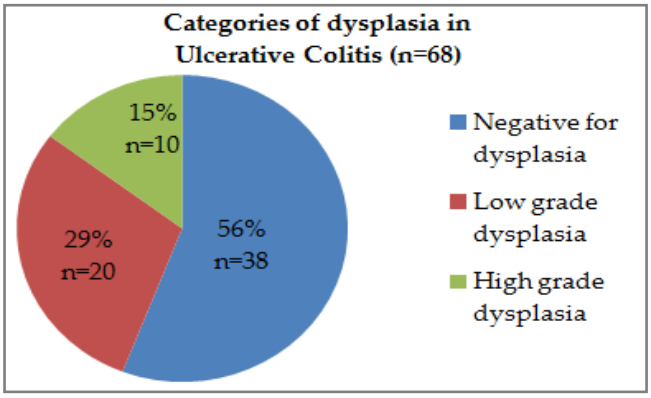

Figure-1: Distribution of dysplasia in ulcerative colitis.

Out of 68 cases, 27 cases (40%) had duration of less than 8 years and 41 cases (60%) had duration of more than 8 years. The mean disease duration was 1.60 ± 0.49 years.

Out of 68 cases of ulcerative colitis, 38 (56%) cases were diagnosed as negative for dysplasia, 20 cases (29%) were diagnosed as positive for low grade dysplasia, 10 (15%) cases were diagnosed as positive for high grade dysplasia (fig-2).

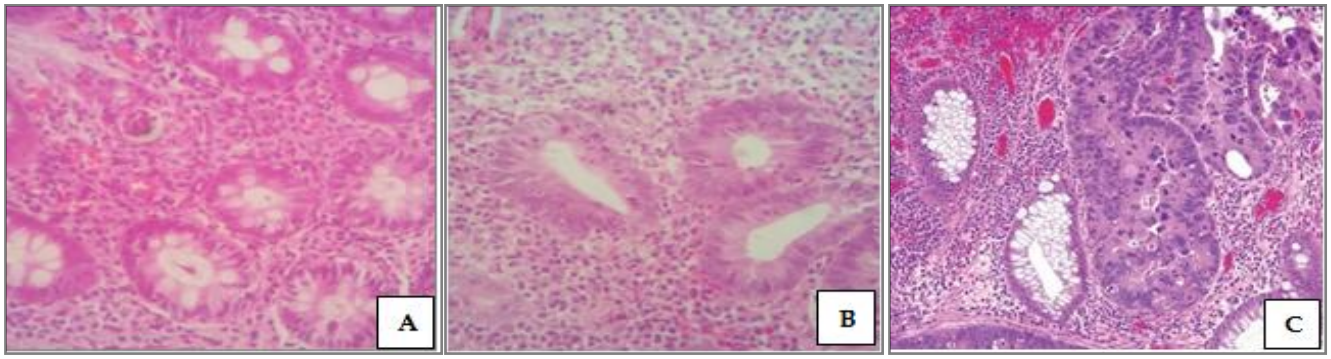

Figure-2: Photomicrographs showing Ulcerative Colitis with a. Negative for dysplasia b. Low grade dysplasia c. High grade dysplasia.

DISCUSSION

Ulcerative colitis has strong association with colorectal carcinoma (UC-CRC). UC-CRC patients are younger and have frequent multiple cancerous lesions and show signet and mucinous ring cell carcinomas[7]. Risk factors for colorectal carcinomas include younger age of patients, longer duration of disease, greater anatomical extent of colon, the severity of inflammation and presence of primary sclerosing cholangitis[8]. Colorectal cancer is the most common malignancy all over the world. It is the second most common cancer among females and third most common cancer in males[9].

Dysplasia in ulcerative colitis is classified into negative for dysplasia, indefinite for dysplasia, low grade dysplasia and high grade dysplasia. In low grade dysplasia, there is nuclear hyperchromasia and basilar orientation of nuclei. In high grade dysplasia, there are pleomorphic and hyperchromatic nuclei with luminal orientation of nuclei[10,11].

The implications for patient management are to continue regular follow-up for negative for dysplasia and indefinite for dysplasia, to institute short-term follow-up for low grade dysplasia and to consider colectomy for high grade dysplasia following confirmation of the diagnosis[10,11].

A prospective study was performed in India in ulcerative colitis patients at high risk of colorectal dysplasia by magnifying chromocolonoscopy. The study indicated 29 (70.7%) out of 41 eligible patients (a median age of 46yrs) having clinical symptoms for the last 10 years, underwent colonoscopy. Out of 29, sixteen had extensive colitis. Out of these 16 cases, low grade dysplasia was seen in 5 patients (17.2%) and high grade dysplasia was seen in 3 (10.3%). Only one out of 3 cases of high grade dysplasia, one underwent surgery for adenocarcinoma[5].

In another study by Murphy and Kalkbrenner, 329 patients (15%) out of 2130 patients were found, having at least 1 focus of dysplasia preoperatively. The association of chronic ulcerative colitis with low grade dysplasia and high grade dysplasia in surgical specimens was 2% and 3% respectively[6].

The mean age in our study was 40.64 ± 13.95 years, which was in concordance with a study carried out by Murphy *et al*[6], mean age in this study was 49.7%. The peak age group in our study was 21-30 years. It was comparable to study carried out in Egypt by Sandouk *et al*[10] in which most of the patients were young. Majority of the patients in our study were males as seen in

studies conducted by Murphy *et al*[6], and Watanabe *et al*[11]. However, in the study conducted by Kim *et al*[12], majority were females.

In our study low grade dysplasia was seen in 29% cases and high grade dysplasia is seen in 15% cases. 56% cases were diagnosed as negative for dysplasia. While in study carried by Murphy *et al*[6], low grade dysplasia is seen in 2% cases and high grade dysplasia in 3% cases which indicates high incidence of dysplasia in our population.

In a study carried out by Fumery *et al*[13], 1 patient (2%) had low grade dysplasia and high grade dysplasia was also in 1 case (2%). However, study conducted by Katsanos *et al*[14], dysplasia was seen in 69 cases (9.4%) in association with Ulcerative colitis. The study by Kekilli *et al*[15], showed low incidence of dysplasia in ulcerative colitis patients. Colorectal cancer was found in only 3 cases (1.1%) among 275 ulcerative colitis patients. Jess *et al*[16] showed 29 cases (4%) of low grade dysplasia. However, low grade and high grade dysplasia was 8.5% in a study carried out by Rozen *et al* and Rosenstock *et al*[17,18].

Relatively less is known about the development of dysplasia in the Asian populations, particularly Pakistani population. The results of this study will help in establishing the relationship between ulcerative colitis and dysplasia.

CONCLUSION

Endoscopic survelliance should be highly recommended in chronic ulcerative colitis for detection of dysplasia so that early management should be done to prevent morbidity and mortality from colorectal carcinoma. Moreover correlation between genetic changes and clinicopathologic features will also help in future to develop new treatment plans. International and regional collaboration is necessary to reach ideal public awareness.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Zhiquin W, Palaniappan S, Ali RAR. Inflammatory bowel disease-related colorectal cancer in the Asia- Pacific region: past, present, future. Intest Res 2014; 12(3): 194-204.
2. Kristina A. Matkowskyj, Zongming E. Chen, M. Sambasiva Rao, Guang-Yu Yang. Dysplastic lesions in inflammatory bowel disease. Arch Pathol Lab Med 2013; 137(3): 338-50.
3. Yashiro M. Ulcerative colitis associated colorectal cancer. World J Gastroenterol 2014; 20(44): 16389-97.
4. Rogler G. Inflammatory bowel disease cancer risk, detection and surveillance. Dig Dis 2012; 30(Suppl-2): 48-54.
5. Shivakumar BM, Lakshmankumar B, Rao L, Bhat G, Suvarna D, Pai CG. Colorectal neoplasia in long standing ulcerative colitis- a prospective study from a low prevalence area. Colorectal Dis 2013; 15(8): e462-68.
6. Murphy J, Kalkbrenner KA, Pemberton JH, Landmann RG, Heppell JP. Dysplasia in ulcerative colitis as a predictor of unsuspected synchronous colorectal cancer. Dis Colon Rectum 2014; 57(8): 993-98.
7. Vu M, Chang J, Chen J, Shih D. Inflammatory bowel disease associated colorectal cancer. J Gastrointest Dig Syst 2012; (Suppl-8): 002-10.
8. Deroche TC, Xiao SY, Liu X. Histological evaluation in ulcerative colitis. Gastroenterology Rep 2014; 2(3): 178-92.
9. Fatima A, Hagger, Robin P, Boushey. Colorectal cancer epidemiology: incidence, mortality, survival and risk factors. Clin Colon Rectal Surg 2009; 22(4): 191-97.
10. Sandouk F, Jerf F, Al-Halabi MH. Precancerous lesions in colorectal cancer. Gastroenterol Res Prac 2013; 2013: 457901.
11. Watanabe T, Konishi T, Kishimoto J, Kotake K, Muto T, Sugihara K. Ulcerative colitis-associated colorectal cancer shows a poorer survival than sporadic colorectal cancer: a nationwide Japanese study. Inflamm Bowel Dis 2011; 17(3): 802-08.
12. Kim B, Barnett JL, Kleer CG. Endoscopic and histological patchiness in treated ulcerative colitis. Am J Gastroenterol 1999; 94(11): 3258-62.
13. Fumery M, Pineton de Chambrun G, Stefanescu C, Buisson A, Bressenot A, Beaugerie L et al. Detection of Dysplasia or Cancer in 3.5% of Patients With Inflammatory Bowel Disease and Colonic Strictures. Clin Gastroenterol Hepatol 2015; 13(10): 1770-75.
14. Katsanos KH, Stamou P, Tatsioni A, Tsianos VE. Prevalance of inflammatory bowel disease related dysplasia from a referral centre in northwestern Greece. J Crohns Colitis 2011; 5(1): 19-23.
15. Kekilli M, Daqli U, Kalkan IH, Tunc B, Disibeyaz S, Ulker A, et al. Low incidence of colorectal dysplasia and cancer among patients with ulcerative colitis: a Turkish referral centre study. Scand J Gastroenterol 2010; 45(4): 434-39.
16. Jess T, Loftus EV, Velayos FS, Harmsen WS, Zinsmeister AR, Smyrk TC, et al. Incidence and prognosis of colorectal dysplasia in inflammatory bowel disease: A population-based study from Olmsted County, Minnesota. Inflamm Bowel Dis 2006; 12(8): 669-76.
17. Rozen P, Baratz M, Fefer F, Gilat T. Low incidence of significant dysplasia in a successful endoscopic survelliance program of patients with ulcerative colitis. Gastroenterol 1995: 108(5): 1361-70.
18. Rosenstock E, Farmer RG, Petras R. Surveillance for colonic carcinoma in ulcerative colitis. Gastroenterol 1985; 89(6): 1342-46.