

Original Research

To determine the correlation of colorectal malignancy and ulcerative colitis

¹Harmanpreet Kaur, ²Aguilera Alvarez Victor Hugo, ³Rimsha Rahim Vohra, ⁴Lydia George, ⁵Bibimariyam Nasyrlaeva, ⁶Srinidhi Cheeti, ⁷Hari Krishna Uppalapati, ⁸Shafeena Vengasseri, ⁹Ramya Dhatri, ¹⁰Poojan Parmar, ¹¹Pallab Sarker, ¹²Vyshnav RajagopalMenon, ¹³Maheen Jalil, ¹⁴Jasmine Proudian

¹M.B.B.S., Government Medical College, Amritsar, Punjab, India;

²Adjunct Professor, Universidad Autonoma De Baja California, Mexico;

³Graduate, ¹³MBBS, Dow University of Health Sciences, Pakistan;

⁴Medical student MS4, St Martinus University School of Medicine, USA;

⁵MD, Moscow State University of Medicine and Dentistry, Russia;

⁶Medical Student, ChalmedaAnandRao Institute of Medical Sciences, Telangana, India;

⁷St.Martinus University Faculty of Medicine, Curacao;

⁸M.B.B.S, Karuna Medical College, India;

⁹MD, Department of Obstetrics and Gynaecology, Gandhi Medical College, Secunderabad, Telangana, India;

¹⁰MD, Our Lady of Fatima University, India;

¹¹ Honorary Medical Officer, Sher-E-Bangla Medical College, Bangladesh;

¹²Student, Washington University of Healthcare and Science, India;

¹⁴Royal College of Surgeons in Ireland (RCSI), Ireland

ABSTRACT:

Aim: To determine the correlation of colorectal malignancy and ulcerative colitis. **Methods:** All patients with a verified diagnosis of UC were included in this research. Clinical, endoscopic, histological, and radiologic data were used to confirm the diagnosis using the widely recognised Lennard-Jones criteria. Cancers discovered within a year after a UC diagnosis were excluded. 200 patients were examined. CRC was identified and confirmed by two skilled gastrointestinal pathologists. Biopsies were obtained during colonoscopy when there was an aberrant pit pattern according to Kudo's categorization. **Results:** A total of 200 UC patients were included in the study. In all, 2 of the 200 individuals were identified with UCCRC by both colonoscopy and biopsy pathology, excluding malignancies developed within 1 year of the UC diagnosis. The total risk of cancer was 1%. All UCCRC patients had had regular colonoscopy exams. The clinical characteristics of the UC group and the UCCRC group, half of the UCCRC patients were men. The mean age at the time of CRC diagnosis was 55.5 ± 5.12 , compared to 49.50 ± 4.69 for UC patients ($P 0.01$). According to the Truelove-Witts index grading method, 50 percent of UCCRC patients and 20.20 percent of UC patients had severe disease. When the UCCRC patients were diagnosed, half were in an advanced state. All four individuals suffered from severe colitis. Gender and the use of 5ASA/sulfasalazine or corticosteroids, on the other hand, were not identified as protective or risk factors for UCCRC; the difference was not significant. **Conclusions:** Patients with UC are at an increased risk for CRC. However, the prevalence of CRC in India remains lower than that in the world.

Key words: Colorectal cancer, ulcerative colitis, ulcerative colitis-associated colorectal cancer

Received: 14 May, 2022

Accepted: 17 June, 2022

Corresponding author: Jasmine Proudian, Royal College of Surgeons in Ireland (RCSI), Ireland

This article may be cited as: Kaur H, Hugo AAV, Vohra RR, George L, Nasyrlaeva B, Cheeti S, Uppalapati HK, Vengasseri S, Dhatri R, Parmar P, Sarker P, Menon VR, Jalil M, Proudian J. To determine the correlation of colorectal malignancy and ulcerative colitis. J Adv Med Dent Scie Res 2022;10(7):1-5.

INTRODUCTION

Colorectal cancer (CRC) is a well-known side effect of ulcerative colitis (UC).^{1,2} According to a meta-analysis, the risk of CRC rises with the length of UC, and the estimated cumulative risk of CRC 30 years from the commencement of UC is 18%.

³Nonetheless, the clinicopathological characteristics of UC-CRC are not entirely understood. There has been debate about whether the prognosis of UC-CRC is worse than that of sporadic CRC. Some studies have shown that UC-CRC patients had a worse 5-year survival rate than sporadic CRC patients, whilst

others have found that both groups of patients have identical 5-year survival rates.⁴⁻⁸ The difference may be attributed to a number of factors. One factor might be the small number of UC-CRC instances. Because UC-CRC is substantially less prevalent than sporadic CRC, most prior research only analysed a limited number of UC-CRC patients. As a consequence, only a few studies have compared survival between stage-matched UC-CRC cases and sporadic CRC cases. Another key explanation might be racial variations among the study individuals. Most earlier research have been undertaken in Western nations, and there have been no investigations of large series of UC-CRC patients in an Asian community, most likely due to Asians having a lower frequency of UC than Caucasians.^{9,10} The prognosis of UC-CRC in Asian people, however, is largely unknown.

MATERIALS AND PROCEDURES CHOOSING A PATIENT

All patients with a verified diagnosis of UC were included in this research. Clinical, endoscopic, histological, and radiologic data were used to confirm the diagnosis using the widely recognised Lennard-Jones criteria.¹¹ The majority of patients were recommended to have a mapping colonoscopy during their initial visit, followed by annual followup colonoscopies after 7 years of illness. As a result, participants were only included in the research if they had had a colonoscopy. Cancers discovered within a year after a UC diagnosis were excluded. 200 patients were examined. CRC was identified and confirmed by two skilled gastrointestinal pathologists.

METHODOLOGY

Biopsies were obtained during colonoscopy when there was an aberrant pit pattern according to Kudo's categorization.

The patients' full medical history, including earlier colonoscopies and pathology results, was reviewed. At the time of the final followup, patient records were evaluated for demographic information, endoscopic characteristics, surgical methods, and vital status. All patients' data on gender, age, illness site, disease duration, colonoscopic followup, 5-aminosalicylic acid (5ASA), and steroid medication were gathered for analysis. The amount of inflammation was determined using histology and colonoscopy reports, as well as barium enema X-ray findings, as documented in medical records at the time of the UC diagnosis. The prevalence of UCCRC was calculated, and clinical features of these individuals were examined. CRC was characterised in terms of the colorectum's eight segments, which are as follows: cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, and rectum. The localisation was recoded as right colon (cecum, ascending or transverse colon), left colon (splenic flexure and descending and sigmoid colon), or rectum for

statistical analysis. According to the International Classification of Diseases for Oncology, the cancer location was categorised.¹² The TNM classification was used to determine the degree of cancer at the time of diagnosis.¹³ The duration in years between the diagnosis of UC and the diagnosis of CRC was defined as the followup time.

STATISTICAL INVESTIGATION

The 2 test was used to examine the relationships between category variables. The two-tailed Student's t test was used to compare mean ages. To examine the influence of various risk variables on the development of UCCRC, Cox's proportional hazards regression was used to obtain univariable and multivariable hazard ratios. The odds ratios and 95% confidence intervals were computed. SPSS was used to analyse all of the data.

25.0 application software (SPSS, Inc., Chicago, IL, USA). P 0.05 was regarded as statistically significant.

RESULTS

A total of 200 UC patients were included in the study [Table 1]. In all, 2 of the 200 individuals were identified with UCCRC by both colonoscopy and biopsy pathology, excluding malignancies developed within 1 year of the UC diagnosis. The total risk of cancer was 1%. All UCCRC patients had had regular colonoscopy exams. The clinical characteristics of the UC group and the UCCRC group are shown in Table 1 shows that half of the UCCRC patients were men. The mean age at the time of CRC diagnosis was 55.5±5.12, compared to 49.50±4.69 for UC patients (P 0.01). According to the Truelove-Witts index grading method, 50 percent of UCCRC patients and 20.20 percent of UC patients had severe disease. When the UCCRC patients were diagnosed, half were in an advanced state. All four individuals suffered from severe colitis.

ULCERATIVE COLITIS TUMOUR FEATURES IN ULCERATIVE COLITIS PATIENTS

All of the patients had advanced to complete colitis by the time they were identified with CRC. 50 percent of the tumours were found in the rectum, 50 percent in the sigmoid colon, and 50 percent in the transverse and right colon. The proportion of CRC stages upon diagnosis in UC patients was as follows: 50% in situ and 50% in Stage I. For all instances of CRC, the histological type was known, and the distribution was as follows: 50% had significant atypical hyperplasia and 50% had well-differentiated adenocarcinoma. In terms of therapy, a whole proctocolectomy with end ileostomy (EI) was done on one patient (50 percent) and a subtotal colectomy with EI was performed on one patient (50 percent) (50 percent).

In ulcerative colitis patients, risk factors for ulcerative colitis As indicated in Table 1, there were statistically significant differences between UC and

UCCRC patients in terms of gender, age, duration of UC, pathological alterations, illness extent, and whether corticosteroids or 5ASA medicines were taken. We used logistic regression to further investigate these variables. Table 2 shows that illness duration and severe colitis have been identified as risk factors for UCCRC. Symptom activity was also associated with colitisCRC. The findings also

revealed that having UC for more than ten years, having whole colon lesions, and having severe inflammatory lesions were risk factors for UCCRC. Gender and the use of 5ASA/sulfasalazine or corticosteroids, on the other hand, were not identified as protective or risk factors for UCCRC; the difference was not significant [Table 2].

Table 1: The clinical characteristics between UC-CRC and UC patients

Gender	UC-CRC	UC
Male	1	110
Female	1	88
Age		
Below 30	0	12
30-50	1	85
50-70	1	101
	55.5±5.12	49.50±4.69
The length of the course	16.0	1.1
The extent Left colon and rectum or sigmoid colon (%)		
Entire colon lesions	2(100)	85(42.93)
Severity of disease (%)	1 (50)	40 (20.20)
5-ASA (%)	2 (100)	180 (90.91)
Corticosteroids (%)	1 (50)	110 (55.55)

Table 2: UC cancerous risk factor analysis

Risk factors	χ^2	P value	OR (95% CI)
Gender	0.045	0.74	1.33 (0.187-7.96)
The length of the course (>10 years)	7.11	0.007	7.74(1.117-65.22)
The extent			
Entire colon lesions	6.01	0.015	1.01 (1.011-1.02)
Severity of disease	9.11	0.002	12.52 (1.256-129.52)
5-ASA	3.23	0.077	0.18(0.021-1.69)
Corticosteroids (%)	0.51	0.51	2.19 (2.244-22.36)

DISCUSSION

Ulcerative colitis is linked to a significantly higher risk of colonic dysplasia and CRC. The risk is projected to be 1.55 times greater than that of nonUC controls.¹⁴ Since the diagnosis of UC 810 years ago, the cancer risk has increased by 0.5 percent every year.¹⁵ Despite accounting for just 2% of all CRC cases, CRC was responsible for 15% of UC-related fatalities. Numerous research have been conducted in Western nations, and the risk of CRC in UC differed significantly across studies. Many variables, including the research design, may explain this difference. Furthermore, studies have shown that CRC incidence rates in UC patients vary regionally, with residents of the United States and the United Kingdom being at a greater risk than Scandinavians and inhabitants of other nations. Data from Asian nations were few, perhaps because of the lower UC prevalence. A nationwide population study in South Korea found that the prevalence of CRC in UC patients was 0.37 percent,¹⁶ whereas it was 0.94 percent in India.^{17,18} The prevalence of UCCRC is expected to rise at the same time. A recent

metaanalysis¹⁹ found that the risk of UC patients acquiring CRC has declined over the previous six decades, with the risk of CRC in UC being lower than that reported by Eaden et al.²⁰ in 2001. With improved inflammation management, increased colectomy rates, the use of chemopreventive medicines, and better adherence to endoscopic monitoring programmes in high-risk patients, the prevalence of CRC in UC patients seems to have reduced over the previous several decades. Furthermore, Jess and colleagues did a metaanalysis of population-based cohort studies to evaluate the risk of CRC in UC patients. The authors also concluded that the previous metaanalysis done by Eaden et al. underestimated the long-term risk of CRC among individuals with UC in these population-based cohorts.²⁰ However, information on the incidence, features, treatment options, and prognosis of UCCRC in China is limited. The current research examines the prevalence of UCCRC and survival rates in China during a 12-year period. The findings from this single-center retrospective analysis revealed that the prevalence of CRC in Chinese UC patients was 1

percent. This research found a lower incidence of UCCRC than the worldwide metaanalysis, which is consistent with earlier studies from other Asian nations. A multicenter retrospective study²¹ found that the period prevalence of CRC in Chinese UC patients was 0.87 percent, which was comparable to our findings, indicating that, although there is a tendency of decreasing risk of developing CRC in UC patients, this trend is also validated by our investigation.

Several variables might explain the low occurrence. First, although the prevalence of UC in China has grown in recent years, it is still lower than in Western nations. Second, inflammatory severity is a risk factor for CRC in UC.²²

The likelihood of developing chronic UC is mostly determined by the disease's length and severity. According to research, a range of inflammatory factors, including tumour necrosis factor alpha, interleukin (IL31), IL6, IL²³, and nuclear factor B, predominate the relevant network signalling pathways in UC inflammation and play a major role in the cancer process.²³ According to earlier research, three of the four UCCRC patients in the present cohort had the illness for more than ten years and all had severe colitis or pancolitis. The statistical analysis also demonstrated that CRC in UC patients was associated with illness duration of more than 10 years and severe colitis.

Given the hypothesis that chronic inflammation is the most essential element in malignant transformation, it is reasonable to believe that antiinflammatory medication, such as 5ASA or steroid usage, may protect UC patients against malignant transformation. 5ASA and thiopurines, in particular, are hypothesised to either reduce or raise the risk of cancer development in IBD patients.²⁴ However, whether they can prevent CRC advancement in UC patients is debatable. According to Eaden et al., sulfasalazine may lower the risk of colon cancer by 75%, but it has no effect on the risk.²⁵ Bernstein said that 5ASA medicines had no protective effect in UC patients. The present investigation discovered no link between 5ASA or corticosteroid usage and UCCRC. The incidence of CRC was comparable for 5ASA and thiopurine users and nonusers, indicating that these therapies may not be preventive against UCCRC.

Gyde et al.²⁶ examined 35 individuals with CRC in a retrospective cohort of 823 patients with UC onset between 1945 and 1965 and found that the age at the beginning of IBD symptoms was related to the colitisCRC interval. Patients who were diagnosed with UC at an early age had a greater risk of CRC. Patients with UC who smoked had a decreased risk of CRC than nonsmokers. Gender studies in the United States and Canada revealed that twothirds of UCCRC patients were men. Furthermore, the literature suggests that primary sclerosing cholangitis, diabetes, and appendix resections for malignancy are risk factors for UC; however, these variables were not

examined in the current retrospective investigation. Endoscopic monitoring is still a valuable tool for identifying UCCRC. Regular colonoscopy screenings might aid in the early detection of typical hyperplasia or CRC and the prompt administration of appropriate therapy, lowering the incidence of UCCRC and death.²⁷

CONCLUSION

We discovered that the cumulative risk of CRC was significant in UC patients, although it was lower than in Western nations. While there is a tendency of decreasing risk of getting CRC in UC patients, our investigation confirms this trend. Disease duration of more than ten years and severe colitis were found as major risk factors for CRC development. The UCCRC interval was affected by symptoms but not by gender or the administration of 5ASA/sulfasalazine or corticosteroids.

REFERENCES

1. vanStaa TP, Card T, Logan RF, et al. 5-Aminosalicylate use and colorectal cancer risk in inflammatory bowel disease: a large epidemiological study. *Gut*. 2005;54:1573–1578.
2. Baumgart DC, Sandborn WJ. Inflammatory bowel disease: clinical aspects and established and evolving therapies. *Lancet*. 2007;369: 1641–1657.
3. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut*. 2001;48:526–535.
4. Jess T, Loftus EV Jr, Velayos FS, et al. Risk of intestinal cancer in inflammatory bowel disease: a population-based study from Olmsted County, Minnesota. *Gastroenterology*. 2006;130:1039–1046.
5. Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. *Gastroenterology*. 2006;130:1030–1038.
6. Aarnio M, Mustonen H, Mecklin JP, et al. Prognosis of colorectal cancer varies in different high-risk conditions. *Ann Med*. 1998;30:75–80.
7. Gyde SN, Prior P, Thompson H, et al. Survival of patients with colorectal cancer complicating ulcerative colitis. *Gut*. 1984;25:228–231.
8. Lavery IC, Chiulli RA, Jagelman DG, et al. Survival with carcinoma arising in mucosal ulcerative colitis. *Ann Surg*. 1982;195:508–512.
9. Whelan G. Epidemiology of inflammatory bowel disease. *Med Clin North Am*. 1990;74:1–12.
10. Yang SK, Loftus EV Jr, Sandborn WJ. Epidemiology of inflammatory bowel disease in Asia. *Inflamm Bowel Dis*. 2001;7:260–270.
11. Lennard-Jones JE. Classification of inflammatory bowel disease. *Scand J Gastroenterol Suppl* 1989;170:2–6;16
12. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM et al. International Classification of Diseases for Oncology. ICD-0. Geneva: World Health Organization; 2000
13. Ferretti S, Patriarca S, Carbone A, Zanetti R. TNM classification of malignant tumours, VII edition 2009.

- Changes and practical effects on cancer epidemiology. *EpidemiolPrev* 2010;34:125-8
14. Jess T, Loftus EV Jr, Velayos FS, Harmsen WS, Zinsmeister AR, Smyrk TC, *et al.* Risk of intestinal cancer in inflammatory bowel disease: a population-based study from olmsted county, Minnesota. *Gastroenterology* 2006;130:1039-46.
 15. Herszenyi L, Miheller P, Tulassay Z. Carcinogenesis in inflammatory bowel disease. *Dig Dis* 2007;25:267-9
 16. Kim BJ, Yang SK, Kim JS, Jeon YT, Choi H, Han DS, *et al.* Trends of ulcerative colitis-associated colorectal cancer in Korea: A KASID study. *J GastroenterolHepatol* 2009;24:667-71
 17. Venkataraman S, Mohan V, Ramakrishna BS, Peter S, Chacko A, Chandy G, *et al.* Risk of colorectal cancer in ulcerative colitis in India. *J GastroenterolHepatol* 2005;20:705-9.
 18. Yun J, Xu CT, Pan BR. Epidemiology and gene markers of ulcerative colitis in the Chinese. *World J Gastroenterol* 2009;15:788-803
 19. Castaño-Milla C, Chaparro M, Gisbert JP. Systematic review with meta - analysis: The declining risk of colorectal cancer in ulcerative colitis. *Aliment PharmacolTher* 2014;39:645-59.
 20. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: A meta - analysis. *Gut* 2001;48:526-35
 21. Gong W, Lv N, Wang B, Chen Y, Huang Y, Pan W, *et al.* Risk of ulcerative colitis - associated colorectal cancer in China: A multi-center retrospective study. *Dig Dis Sci* 2012;57:503-7.
 22. Gupta RB, Harpaz N, Itzkowitz S, Hossain S, Matula S, Kornbluth A, *et al.* Histologic inflammation is a risk factor for progression to colorectal neoplasia in ulcerative colitis: A cohort study. *Gastroenterology* 2007;133:1099-105.
 23. Johansson M, Jönsson M, Norrgård O, Forsgren S. New aspects concerning ulcerative colitis and colonic carcinoma: Analysis of levels of neuropeptides, neurotrophins, and TNFalpha/TNF receptor in plasma and mucosa in parallel with histological evaluation of the intestine. *Inflamm Bowel Dis* 2008;14:1331-40
 24. vanSchaik FD, van Oijen MG, Smeets HM, van der Heijden GJ, Siersema PD, Oldenburg B. Thiopurines prevent advanced colorectal neoplasia in patients with inflammatory bowel disease. *Gut* 2012;61:235-40.
 25. Eaden J, Abrams K, Ekbom A, Jackson E, Mayberry J. Colorectal cancer prevention in ulcerative colitis: A case - control study. *Aliment PharmacolTher* 2000;14:145-53
 26. Gyde SN, Prior P, Allan RN, Stevens A, Jewell DP, Truelove SC, *et al.* Colorectal cancer in ulcerative colitis: A cohort study of primary referrals from three centres. *Gut* 1988;29:206-17
 27. Rubin DT, Kavitt RT. Surveillance for cancer and dysplasia in inflammatory bowel disease. *GastroenterolClin North Am* 2006;35:581-604