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GUT MICROBIOTA ALTERATION IN COLORECTAL CANCER AND ITS CLINICAL IMPLICATIONS

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Abstract:

Introduction: *Colorectal cancer is the second commonest cancer arising in the world. Colorectal cancer can present with an array of symptoms and approximately 35–48% of patients diagnosed with colorectal cancer have experienced rectal bleeding.* ***Objectives:*** *The main objective of the study is to analyse the role of gut microbiota alteration in colorectal cancer and its clinical implications.* ***Material and methods:*** *This descriptive study was conducted in King Edward Medical University during June 2019 to November 2019. Several studies have shown that numerous bacterial species appear to be associated with the pathogenesis of CRC and recent studies have provided a mechanism for the participation of gut microbiota in the progress of CRC.* ***Results:*** *The median age of the patients was 56 years (range: 20–86), and 73% were male. Most patients were married [85.6%], and more than half of the participants were high school educated or higher [77.8%] and unemployed 52.8%. The differences in microbial community abundance between the two groups were examined by statistical methods, and the significance of the differences was evaluated by FDR (false discovery rate). We screened out the species that caused the difference in the composition of the two groups of samples.*

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INTRODUCTION:

Colorectal cancer is the second commonest cancer arising in the world. Colorectal cancer can present with an array of symptoms and approximately 35–48% of patients diagnosed with colorectal cancer have experienced rectal bleeding. Even though the positive predictive value of rectal bleeding for colorectal cancer is low (<3%), it is regarded as an alarm symptom in persons over the age of 40 years [1]. Meanwhile, the majority of individuals who experience rectal bleeding do not report it to their general practitioner (GP). More surprisingly, studies have shown that colorectal cancer patients, who had experienced rectal bleeding, delayed help-seeking more often than patients who had not experienced rectal bleeding [2].

The possible association between rectal bleeding and patient delay differentiates colorectal cancer from most other cancers where bleeding appears to be associated with a short patient interval. Therefore, it is imperative that the factors contributing to this are examined and understood [3]. It has been assumed that the revealed association between rectal bleeding and long patient intervals is a consequence of patients attributing the rectal bleeding to benign causes such as hemorrhoids. Meanwhile, the results of one study of 93 patients who presented with rectal bleeding to their GP suggested that the relationship between rectal bleeding and the patient interval appeared to be modified by personal experiences [4]. Thus, it was found that those patients who had experienced rectal bleeding before and may had suffered from known benign rectal disorders were *less* likely to delay help-seeking than those who had never experienced rectal bleeding before. The proportion of patients who considers cancer when experiencing rectal bleeding is not known [5].

The gut contains a complicated environment that is settled by bacteria, fungi, and viruses. The total number may reach 100 trillion, and the number of microbe cells is estimated to be 10-fold more than the human cells. This densely resident microbial community consistently communicates with the host and also enhances the epithelial defense against pathogens, accelerates the maturity of the immune system, and absorbs the nutrition from ingested foods [6]. Despite the mucus layer, which consists of various macromolecules and secreted antimicrobial molecular and intercellular tight connection proteins, the gut microbiota also possess the capacity to defend pathogens by inducing IgG antibodies through recognition of their conserved antigen part of gram-negative bacteria [7]. The gut microbiota not only protect the local homeostasis, but also mediate the related organ. For example, an in-vivo experiment proved that the gut microbiota was manipulated by intestinal lectins to decrease alcohol-associated steatohepatitis [8].

Objectives

The main objective of the study is to analyse the role of gut microbiota alteration in colorectal cancer and its clinical implications.

MATERIAL AND METHODS:

This descriptive study was conducted in King Edward Medical University during June 2019 to November 2019. Several studies have shown that numerous bacterial species appear to be associated with the pathogenesis of CRC and recent studies have provided a mechanism for the participation of gut microbiota in the progress of CRC.

Inclusion criteria

- All those patients who were ready to participate in this study and having confirmed CRC.

Exclusion criteria

- Those who had used antibiotics or microecological agents within 2 months before enrolment.
- Those who suffer from chronic diseases such as hypertension, heart disease, and diabetes.

Data collection

All patients were interviewed and examined by a gastroenterologist. Accordingly, patients' informed through written consent was obtained from each patient before placing interview according to the strategies of the local institutes. After clinical assessment, all patients suffered anal examination and digital rectal review. The subjects were divided into two groups, one was CRC patients and second was control group. Data were collected in the clean environment of fresh feces (not less than 6 g), put in an aseptic sampling tube and sent to the laboratory, and kept at −80°C for inspection.

Statistical analysis

Each experiment was repeated three times and all data were displayed in mean±SD and analyzed through SPSS 19.0 (IBM, USA). T-test and one-way ANOVA were applied for measuring comparison among groups. $P<0.05$ was considered to have statistical meaning.

RESULTS:

The median age of the patients was 56 years (range: 20–86), and 73% were male. Most patients were married [85.6%], and more than half of the participants were high school educated or higher [77.8%] and unemployed 52.8%.

Table 01: Baseline characteristics

	***N* = 50**	**%**
Age		
Median	56	
Range	20–86	
Smoking		
Smoker	16	20.1
Non-Smoker	34	79.9
Marital status		
Married	19	85.6
Single	15	7.4
Widowed	12	5.2
Divorced	4	1.7
Educational level		
Elementary school	14	10.5
Middle school	7	11.8
High school	16	37.6
Undergraduate	7	32.3
Graduate school	6	7.9
Employment status		
Full-time job	22	35.8
Part-time job	6	11.4
Unemployed	22	35.8
Histology		
Tubular adenocarcinoma	16	70.3
Signet ring cell carcinoma	8	25.3
Mucinous carcinoma	3	2.2
Others	25	22
Adjuvant chemotherapy		
Platinum-based doublet (SP or FP)	36	67.5
TS-1 monotherapy	14	26.5

The median patient intervals in days are reported for patients, who reported changes in bowel habits, fatigue, pain, weight loss, and general indisposition either in combination with rectal bleeding or not in combination with this symptom.

Table 02: Median patient interval (in days) for the five symptoms occurring in ≥20% of the sample

	Changes in bowel habits	Pain	Weight loss	Fatigue	General indisposition
Median (IQI) patient interval when presented without rectal bleeding	16 (5–31)	14 (3–28)	18 (4–29)	17 (4–29)	10 (0–29)
	N=30 (22.1%)	N=25 (18.4%)	N=17 (12.5%)	N=26 (19.1%)	N=11 (8.1%)
Median (IQI) patient interval when presented together with rectal bleeding	61 (12–112)	31 (13–119)	38 (22–74)	34 (5–96)	31 (0–57)
	N=58 (42.6%)	N=22 (16.2%)	N=12 (8.8%)	N=38 (27.9%)	N=16 (11.8%)

DISCUSSION:

Several studies have shown that numerous bacterial species appear to be associated with the pathogenesis of CRC and recent studies have provided a mechanism for the participation of gut microbiota in the progress of CRC [9]. Some bacterial species like *Clostridium septicum*, *Enterococcus faecalis*, *Streptococcus bovis*, *Bacteroides fragilis*, *Helicobacter pylori*, *Escherichia coli* and *Fusobacterium* spp. have been detected and supposed to play a role in colorectal pathogenesis [10].

For example, *Streptococcus gallolyticus* (In the past *Streptococcus bovis*) is reported in nearly 20–50% and 5% of colon tumors and normal colon respectively. In CRC patients *Ruminococcus bromii*, *Clostridium clostridioforme* and *Bifidobacterium longum* have low prevalence compared to normal population [11]. Furthermore, in different studies a notably increase number of the *Bacteroides/Prevotella* and *Fusobacterium nucleatum* population is described in CRC population [12].

CONCLUSION:

It is concluded that diet is associated with increased incidence of CRC. Diet shapes the microflora and affects its metabolites and functions. Excessive intake of animal protein and fat (especially red meat and processed meat) will produce excessive secondary bile acid and hydrogen sulfide, leading to barrier dysfunction, inflammation, DNA damage, genotoxicity, and so on, which may increase the risk of CRC.

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