International Journal of Advances in Medicine
Rahman MM et al. Int J Adv Med. 2021 Dec;8(12):1799-1803
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20214514

Original Research Article

Status of microsatellite instability in different histomorphological patterns of colorectal carcinoma among a group of Bangladeshi people

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Received: 03 July 2021
Revised: 27 August 2021
Accepted: 18 October 2021

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ABSTRACT

Background: This cross- sectional observational study was carried out with an aim to look for microsatellite instability (MSI) status in colorectal carcinoma and their association with different histomorphological patterns and biological behavior of colorectal carcinoma.
Methods: This cross-sectional observational study was done in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University Hospital (BSMMU), Dhaka, Bangladesh during September 2014 to October 2015. A total of 39 surgically resected sample of colorectal carcinoma were included. Consent from each patient was taken. The samples were histopathologically evaluated according to the standard protocol. The statistical analyses were done using Statistical packages for social sciences (SPSS 15) for Windows.
Results: A total of 39 cases of colorectal carcinoma were included in this study. Majority of the patients (55.5%) was in 6th decade in MSI and 29.1% were MSI absent group. The mean age was found 47.67±10.97 years in present group and 47.84±14.26 years in absent group. The difference was not statistically significant ($p>0.05$). TNM stage with MSI was observed. The mean CEA level was 100.74±103.66 and 60.43±91.72. The mean Hb was 9.72±1.99 % and 9.92±2.17, the range was 7.2-12.2 and 4.6-13.4 among the groups. The mean difference was not statistically significant ($p>0.05$). Ulcerated was 3 (33.3%) and 19 (64.5%). Stage 3 tumor was 4 (44.4%) and 16 (51.6%). Grade 2 tumor was 5 (55.6%) and 17 (58.0%).
Conclusions: For the first time in Bangladesh, this study was undertaken to evaluate the microsatellite instability (MSI) status in colorectal cancer tissue and their association with different histomorphological patterns of colorectal carcinoma.

Keywords: Colorectal carcinoma, Histomorphology, Microsatellite instability

INTRODUCTION

The incidence of colorectal carcinoma varies considerably throughout the world, being one of the leading cancer sites in the developed countries.[1] Approximately 6% of the population will develop colorectal cancer during their course of life.[2] In 2013 it was estimated that there will be 142,820 new cases of colon and rectum cancer and an estimated 50,830 will be die of this diseases.[3] With respect

of other types of cancer, colorectal carcinoma occupied the third place both in men (after bronchopulmonary and gastric cancer) as well as in women (after mammary gland and cervical cancer).[4] The incidence of this cancer is as much as 30-fold lower in India and in this subcontinent, presumably as a result of lifestyle changes and diet. The estimated incidence rate of colorectal carcinoma in Bangladesh is 2.3%.[6] Males are affected slightly more than females.[7] Cancer occurring in the young (<40 years of age) are usually located on the distal colon and rectum which tend to show features associated with aggressive behavior.[8]

Molecular genetic mechanisms are diverse and recent data suggest two main pathways: A mutational pathway and microsatellite instability. Both pathways involve the step wise accumulation of multiple mutations but the gene involved and the mechanisms differ.[9] Assessment of MSI may be used as a first screening to identify individuals who may have hereditary non- polyposis colorectal cancer and should receive more extensive genetic analysis.[11] The MSI status of CRC is an extremely useful marker for population-based screening programs that aim to identify individual and families with their hereditary cancer condition. Microsatellite instability has also been proposed as a prognostic marker and predictor of the response of chemotherapy in colorectal carcinoma.[10] It has been recommended that a panel of 5 microsatellites should be used as a reference slandered (BAT 25, BAT26, D5S346, D2S123, D17S250) for carcinomas of the colon. If two or more of these markers show MSI, the lesion is classified as high- frequency microsatellite instability (MSI-H), if only one marker shows MSI, it is classified as low-frequency microsatellite instability (MSI-L); If no marker shows MSI it is classified as microsatellite stable (MSS).[12] Though MSI is important for therapeutic and prognostic purpose, till date no such studies have been carried out in our country to find out their status in Bangladeshi patients with CRC. So, this study was planned to evaluate the MSI status of the colorectal carcinoma of Bangladeshi patients and compare their status with some relevant parameters.

METHODS

This cross-sectional observational study was done in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University Hospital (BSMMU), Dhaka, Bangladesh during September 2014 to October 2015. A total of 39 surgically resected hemicolectomy, abdominoperineal resection (APR) and partial colectomy sample of colorectal carcinoma were included in this study. The samples were histopathologically evaluated according to the standard protocol. Consent from each patient was taken before conducting the study. The statistical analyses were done using Statistical packages for social sciences (SPSS 15) for Windows. Consent from each patient was taken with their signature on the form before conducting the study. The samples were collected from BSMMU and other private hospitals. The samples were kept in 10% buffered formalin for 24 hours for proper fixation. Gross examination of the sample and section of blocks were done according to standard surgical pathology protocol and processed by routine histopathology procedure.

Inclusion criteria

Surgically resected hemicolectomy, abdominoperineal resection (APR) and partial colectomy sample of colorectal carcinoma. 30 years to 60 years of age.

Exclusion criteria

Below 30 years and over 60 years. The patients who were not given consent. Severely in patients.

RESULTS

It was observed that majority (55.5%) of the patients was in 6th decade in MSI group and 29.1% were in 6th decade MSI absent group. (Table 1) The mean age was found 47.67±10.97 years in MSI present group and 47.84±14.26 years in MSI absent group. The difference was not statistically significant (p>0.05) between two groups. TNM stage with MSI of the study patients was observed. It shows that 3 (33.3%) patients T2N0Mx and T3N2Mx in MSI group and 5 (19.4%) and 7 (22.6%) in no MSI group respectively. (Figure 1) The mean CEA level was found 100.74±103.66 in MSI group and 60.43±91.72 in no MSI group (Table 2).

Table 1: Distribution of the study patients by age according to MSI status (n=39).

	MSI Present, n=9		MSI Absent, n=30		P value
Age (years)	**n**	**%**	**n**	**%**	
≤30	1	11.1	5	16.1	
31-40	2	22.3	6	19.4	
41-50	1	11.1	6	19.4	
50-60	5	55.5	8	29.1	
>60	0	0.0	5	16.0	
Mean±SD	47.67	±10.97	47.84	±14.26	0.973[ns]
Range (min-max)	30	-60	25	-75	

Table 2: LV invasion, PN invasion, tumor border, circumferential margin according to MSI status (n=39).

	MSI Present, n=9		MSI Absent, n=30		P value
CEA level	**N**	**%**	**N**	**%**	
≤5	1	11.1	9	29.03	
>5	8	88.9	21	70.97	
Mean±SD	100.74	±103.66	60.43	±91.72	[a]0.266[ns]
Range	3.23	-348.2	1.25	-425	
Hb					
<10	5	55.5	17	54.7	
≥10	4	44.5	13	45.3	
Mean±SD	9.72	±1.99	9.92	±2.17	[a]0.805[ns]
Range	7.2	-12.2	4.6	-13.4	

Table 3: CEA level and Hb level according to MSI status (n=39).

	MSI Present, n=9		MSI Absent, n=30	
Growth pattern	**N**	**%**	**N**	**%**
Exophytic	1	11.1	10	32.3
Ulcerated	3	33.3	19	64.5
Annular	4	44.4	1	3.2
Infiltrating	1	11.1	0	0
Tumor stage				
Stage 1	3	33.3	8	25.8
Stage 2	1	11.1	4	16.1
Stage 3	4	44.4	16	51.6
Stage 4	1	11.1	2	6.5
Tumor grade				
Grade 1	2	22.2	7	22.6
Grade 2	5	55.6	17	58.0
Grade 3	2	22.2	6	19.4

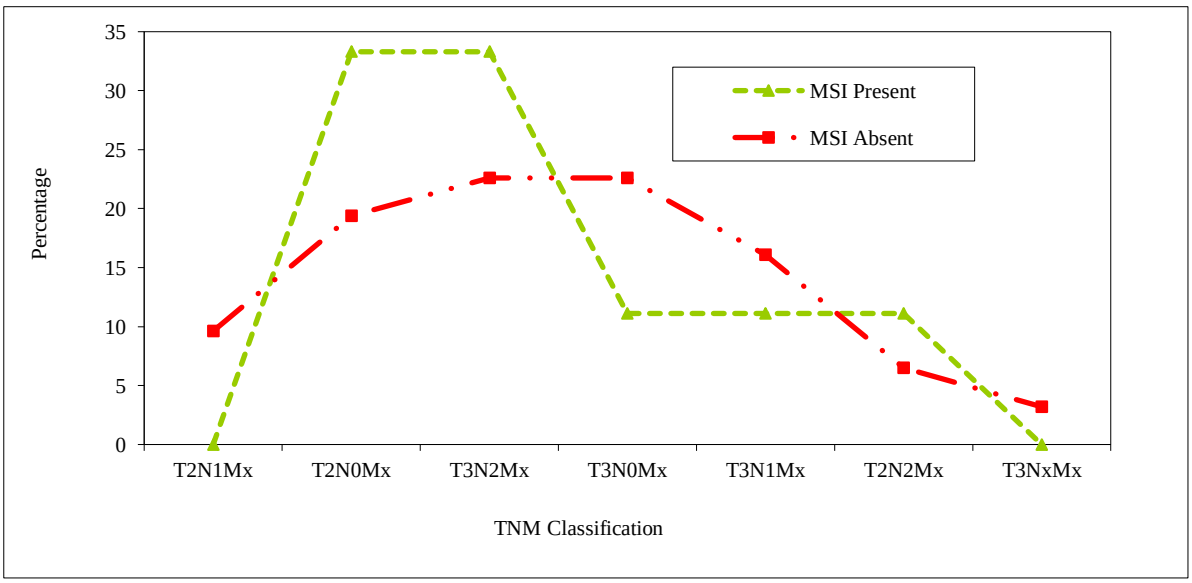

Figure 1: TNM stage correlated with MSI.

The mean Hb was found 9.72±1.99 % in MSI group and 9.92±2.17 in no MSI group, the range is from 7.2-12.2 in MSI present group and 4.6-13.4 in MSI absent group. The mean difference was not statistically significant (p>0.05) between two groups. (Table 2) Ulcerated was found 3 (33.3%) in MSI group and 19 (64.5%) in no MSI group. Stage 3 tumor was found 4 (44.4%) in MSI group and 16 (51.6%) in no MSI group. Grade 2 tumor was found 5

(55.6%) in MSI group and 17 (58.0%) in no MSI group (Table 3).

DISCUSSION

This cross-sectional observational study was carried out with an aim to look for MSI status in colorectal carcinoma in a group of Bangladeshi patients and to find out possible association between different histomorphological features (histological type of tumor, grade, location, lymph node metastasis etc) of colorectal carcinoma. A total of 39 surgically resected sample of colorectal carcinoma were included in this study. Patient with colonic biopsy histologically confirmed as adenocarcinoma of the colon, no history of chemotherapy or radiotherapy before surgery, cases accompanied by complete clinical information, availability of fresh unfixed colorectal cancer specimen and availability of normal uninvolved colonic tissue at least 5 cm away from the tumor were enrolled in this study. In this study it was observed that regarding the association between age with MSI status it was observed in this present study that majority (55.5%) of the patients was in 6th decade in MSI present group and 29.1% were in the decade MSI absent group. (Table 1) The mean age was found 47.67±10.97 years in MSI present group and 47.84±14.26 years in MSI absent group. (Table 1)

A study found 33% LV invasion in MSI positive cases. In this series it was observed that most (55.0%) of the patients with colotrectal carcinoma were in the 5th decade or above and their age range was from 25 to 75 years with a mean age of 47.8±13.46 years.[11] Dhall observed higher mean age in patients having colotrectal carcinoma, which were 59 years varied from 28-95 years, 66 years varied from 36-86 years and 68 years varied from 35-91 years respectively.[10] Similarly, Gurzu have observed the average age of their patients was 64.74±8.49 year, which all are higher with the current study. In Bangladesh have observe the average age of their patients were 46.6±14.8 and 42.9±13.7 respectively, which are lower than the current study.[12,18,17] In this study it was observed that colotrectal carcinoma was more common in male subjects, where 55.0% and 45.0% cases were male and female respectively. As regards to the incidence of colotrectal carcinoma, found in their studies that the incidence of colotrectal carcinoma were 77.5%, 77.6% and 76.2% respectively observed in male subjects.[12] On the other hand, 49.1% in male and 50.9% in female had colotrectal carcinoma.[10]

According to TNM classification of the study patients it was observed that, one fourth (25.0%) of the patients had T3N2Mx classification followed by (22.5%) had T2N0Mx. (20.0%) had T3N0Mx and (15.0%) had T3N1Mx. Salminen (2005) obtained (19.0%) patients presented with $T_3N_2M_x$, (18.0%) were $T_2N_0M_x$, (27.0%) had $T_3N_2M_x$ and (23.5%) had T3N1Mx. This observation is more or less similar to the above-mentioned study (Figure 2).

Limitations of the study

The study has come limitations which are as the study was conducted upon a small size of population which is too small to conclude over the commonest and burning issue and the study was conducted in a very limited area to represent. More extensive investigations could not be done due to lack of resources which would produce mor3e informative study. The study time was very limited to represent as overall result.

CONCLUSION

For the first time in Bangladesh, this study was undertaken to evaluate the microsatellite instability (MSI) status in colorectal cancer tissue and their association with different histomorphological patterns of colorectal carcinoma, but there was no statistically significant association was found in between MSI status with morphology and different histopathological features.

Recommendations

The study recommends case control study with large sample size.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Rahman MM, Imam S, Nessa S, Raza AKMM, Arjuman F, Kamal M. Status of microsatellite instability in different histomorphological patterns of colorectal carcinoma among a group of Bangladeshi people. Int J Adv Med 2021;8:1799-803.