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Original Research Paper

Pathology

EXPRESSION OF P53 IN COLORECTAL CARCINOMAS AND ITS CORRELATION WITH CLINICOPATHOLOGICAL PARAMETERS

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ABSTRACT Colorectal cancer is one of the most life-threatening gastrointestinal diseases encountered in clinical practice.1 The rectum is one of the most frequently involved sites and accounts for 25% of primary colorectal cancers.2 Accumulation of molecular alterations, including K-ras, P53, Bcl-2 and adenomatous polyposis coli, contribute to colorectal carcinogenesis.3 According to the literature, the deletion of p53 with the overexpression of p53 protein is correlated with a low rate of survival, thus being an independent prognosis factor.17 **Summary:** Overexpression of p53 protein is associated with high grade of colorectal carcinoma.

KEYWORDS : Colorectal carcinoma, p53 protein

INTRODUCTION

Colorectal cancer is one of the most life-threatening gastrointestinal diseases encountered in clinical practice.[1] Colorectal cancer is one of the most common cancers, affecting men and women equally.[2] It accounts for about 10% of all cancers and it is the fourth leading cause of cancer death globally and the second leading cause of death from malignancy in the industrialized world. [3, 4] The rectum is one of the most frequently involved sites and accounts for 25% of primary colorectal cancers.[2]. Accumulation of molecular alterations, including K-ras, P53, Bcl-2 and adenomatous polyposis coli, contribute to colorectal carcinogenesis.[3] A step-wise genetic model, comprising the genetic alterations of certain oncogenes and tumor-suppressor genes through the major chromosomal instability pathway, has been considered as the tumorigenic mechanism responsible for most (approximately 85%) of colorectal cancer cases.[6]

AIMS AND OBJECTIVES

1. To study the expression of p53 protein in colorectal cancers and to correlate with the type, stage and grade of the disease.
2. To correlate the clinical parameters like age, gender and site of tumor with stage and grade of the tumor.

MATERIALS AND METHODS

It is a prospective study for a period of two years. Forty cases of resected specimens of colorectal cancer submitted to the department of Pathology, CAIMS, Karimnagar for histopathological evaluation were studied. Clinical data was obtained from the patient's records and requisition forms accompanying the specimens to the department.

On arrival to the department, the specimens were adequately fixed in 10% neutral buffer formalin following which the evaluation of gross features was done. The gross details of specimens submitted for evaluation of malignancy were observed and recorded based on the protocol for evaluation of colorectal malignancy.

Inclusion Criteria:

1. Only resected specimens were considered.
2. Among the neoplastic lesions only malignant epithelial lesions are included.

Exclusion Criteria:

1. All benign lesions are excluded.
2. Tissues with necrotic areas in the tumor are excluded for IHC.

Representative tissue from resected colorectal specimens were subjected to routine processing for paraffin embedding. Four to five micron thick sections were taken from paraffin embedded blocks,stained with haematoxylin and eosin stain and studied.

All the 40 cases were subjected to IHC study for p53. Sections underwent histologic evaluation to select blocks without necrotic areas.

Assessement Of Expression Of P53:

Immunoreactivity for p53 was evaluated semi quantitatively according to the percentage of positive tumor nuclei, scored as follows:

1. None (score0): <5% positive cells
2. Weak (score1/+): 5-25% positive cells
3. Moderate (score2/++): 25-75% positive cells
4. Intense (score3/+++): >75% positive cells

All tumors showing p53 immunoreactivity (at least+) were considered to be positive.

OBSERVATIONS AND RESULTS

In the present study, 40 cases of colorectal carcinomas were evaluated for expression of p53 and correlated with the clinico-pathological features. In the present study, the age of the patients of colorectal carcinoma ranged from 14 to 70 years. Mean age of presentation is 52.5yrs. The peak incidence of colorectal carcinoma was seen in the fifth decade (37.5%).

Table-1: Distribution of cancer among different age groups:

Age range	No. of cases	Percentage
11-20	1	2.5
21-30	1	2.5
31-40	3	7.5
41-50	10	25
51-60	15	37.5
61-70	10	25
Total	40	100

In the present study 22 males (55%) and 18 females (45%) were present. The male to female ratio is 1.2:1.

Table-2: Proportion of males and females in the study

Gender	No. of cases	Percentage
Males	22	55
Females	18	45

In the present study, of the 40 cases of colorectal carcinoma, the presenting symptoms were pain abdomen in 14 cases (35%), constipation in 10 cases (25%), bleeding per rectum in 7 cases (17.5%), bleeding per rectum with constipation in 4 cases (10%), diarrhea in 2 cases (5%), pain abdomen with vomiting in 2 cases (5%), pain abdomen with bleeding per rectum in 1 case (2.5%).

Among the 40 cases of colorectal carcinoma, 37 were adenocarcinoma (92.5%) and 4 cases were mucinous carcinoma (7.5%).

Table-3: Distribution of histological types of the tumor:

Histological type	No.of cases	Percentage (%)
Adenocarcinoma	37	92.5%
Mucinous carcinoma	03	7.5%

In the present study, 18 cases (45%) were well differentiated, 18 cases (45%) were moderately differentiated and 4 cases (10%) were poorly differentiated. Among the 40 cases of colorectal carcinoma, 14 cases were in stage I (35%), 17 cases were in stage IIA (42.5%), 3 cases were in stage IIIA (7.5%) and 6 cases were in stage IIIB (15%) of TNM staging.

Table-4: Expression of p53 among cases in the study

P53 expression score	No. of cases	Percentage(%)
Score 0	10	25%
Score +	10	25%
Score ++	15	37.5%
Score +++	05	12.5%

Among the cases with positive p53 expression, most of the cases were scored++ i.e. 25-75% of malignant cells showed positive nuclear staining.

Table-5: P53 expression in relation to tumor grade

Tumor grade	No.of cases	P53 positive (%)	P53 negative (%)
Grade I	18	12 (66.6%)	6 (33.3%)
Grade II	18	15 (83.3%)	3 (16.6%)
Grade III	4	03 (75%)	1 (25%)
Total	40	30 (75%)	10 (25%)

Table 6: Bcl-2 and p53 expression in relation to tumor stage

Tumor stage	No. of cases	P53 positive (%)	P53 negative (%)
Stage I	14	09 (64.2%)	05 (35.7%)
Stage II	17	14 (82.3%)	03 (17.6%)
Stage III	09	07 (77.7%)	02 (22.2%)
Total	40	30 (75%)	10 (25%)

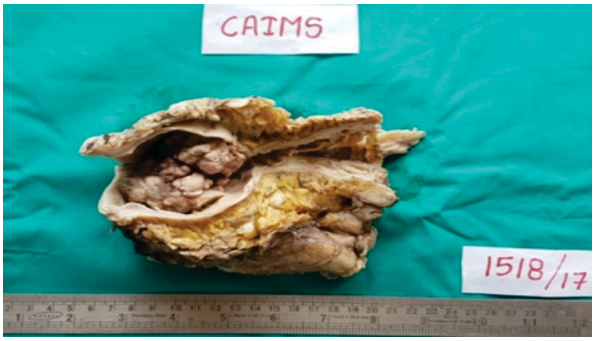
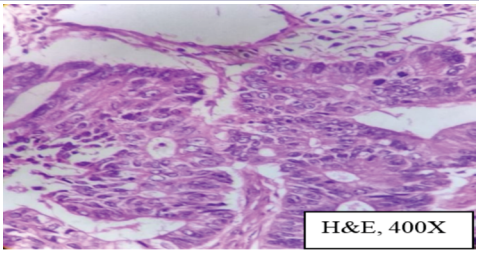
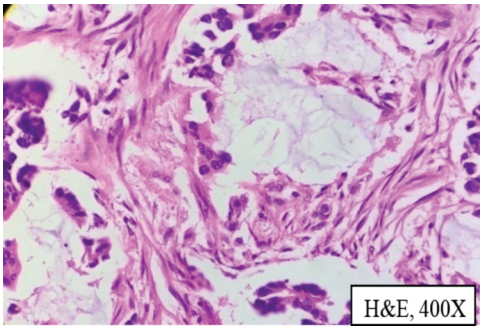


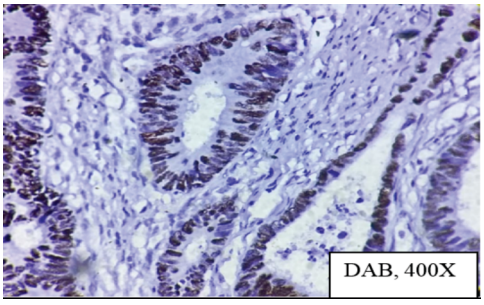
Image showing exophytic growth of the tumor in sigmoid colon obliterating the lumen



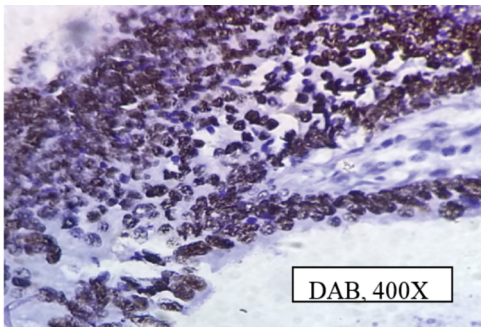
Moderately differentiated adenocarcinoma colon



Microscopic picture of mucinous carcinoma colon –showing nests of tumor cells floating in lakes of extracellular mucin



Picture showing positive p53 expression in well differentiated adenocarcinoma of colon



Picture showing positive p53 expression in poorly differentiated adenocarcinoma colon

DISCUSSION

Colorectal cancer is the third most common cancer worldwide with more than 1.2 million new cases diagnosed annually.[6] CRC exhibits several genetic alterations of which p53 abnormalities are frequent, occurring in more than half of cases.[7] The p53 transcription factor (encoded by gene TP53) is a key tumor suppressor, as it regulates several signaling pathways involved in carcinogenesis. Cells that fail to repair their DNA undergo apoptosis, but when the wild-type p53 is inactivated by the mutant p53, this mechanism collapses.[8]

In our study most of the cases of colorectal cancer are in the fifth decade (37.5%) and above which is similar to study by Mihalache et al[1]. In our study colorectal carcinomas showed slight male predilection, with 55% of

cases being males. This is similar to study done by RAEM Tollenaar et al[9], Nicholas FS Watson et al.[10]

In terms of degree of tumor differentiation (histopathological grading), the common forms were the well and moderately differentiated followed by poorly differentiated, which is similar to study done by Kavita Mardi et al[11].

Table-7: Comparison of p53 expression between various studies

Study (year)	Incidence of p53 expression (%)
AJM Watson et al12 (1996)	62.3%
RAEM Tollenaar et al9 (1998)	65%
Simonetta Buglioni et al13 (1999)	71.9%
O Petrisor et al6 (2008)	66%
Hunaldo Lima de Menezes et al15 (2010)	85.4%
Ban Qasim et al14 (2012)	78.78%
Komal Mahendra Ashar et al16 (2016)	72.9%
Kavitha Mardi et al11 (2017)	70%
Present study	75%

In our study p53 was expressed in 75% of cases of colorectal carcinoma. This was similar to the study done by Simonetta Buglioni et al[13] (71.9%), Ban Qasim et al[14] (78.78%) and Komal Mahendra Ashar et al[16] (72.9%). The p53 expression in various studies ranged from 62.3% to 85.4%.

Table-8: Comparison of grade of p53 expression among different study groups

Grade of p53 positivity	Petros C.Papagiorgis et al5 (2012)	Kavita Mardi et al11 (2017)	Present study
Score 0	30%	30%	25%
Score +	15%	16.6%	25%
Score ++	30%	26.6%	37.5%
Score +++	25%	26.6%	12.5%

While correlating grade of p53 positivity, a semi quantitative method was used. In our study most of the cases showed score 2, p53 expression which was similar to study by Petros C.Papagiorgis et al[5], which showed most of the cases with score o and score 2 positivity with distribution of 30% each.

According to the literature, the deletion of p53 with the overexpression of p53 protein is correlated with a low rate of survival, thus being an independent prognosis factor. Hamilton S.R et al showed that p53 negative tumors respond favorably to chemotherapy and radiotherapy.[17]

CONCLUSION

Majority of the patients of colorectal carcinoma were in their 5th decade with slight male predilection (M:F=1.2:1). Most of the patients had lesion in the right side of the colon i.e distal colon and rectum. Most of the cases of colorectal carcinoma were adenocarcinoma in TNM stage II. The expression of p53 was high in moderately differentiated Adenocarcinoma followed by poorly differentiated and low in well differentiated cases. Lymph node positive cases showed high p53 expression compared to negative cases.

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