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ANALYSIS OF RISK FACTORS AFFECTING DEVELOPMENT OF LIVER METASTASIS IN RECTAL CANCER PATIENTS

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Abstract:

Objectives of the study: *The main objective of the study is to find the risk factors affecting development of liver metastasis in rectal cancer patients.*

Methodology of the study: *This descriptive study was conducted in Holy Family Hospital, Rawalpindi during March 2018 to October 2018. The data was collected from 50 patients through non-random sampling technique. All those patients who were suffering from colorectal cancer were included in this study. Patients with primary cancer in another organ were excluded. Lymph node involvement was divided into N0, N1 and N2. All stage III and IV patients received neo-adjuvant chemotherapy. The neo-adjuvant chemotherapy will not be considered as a comparative factor in subsequent analyses, because it is strongly associated with tumor stages. According to the NCCN guideline, all CRC patients in stage II or more advanced CRC received a 5-Fu-based chemotherapy for at least 8 cycles postoperatively.*

Results: *The data was collected from 50 patients. Only 10-20% of the patients with liver were aged below 50 years. On clinical staging, 2(7.7%) patients had stage II disease, 22(84.6%) had stage III, and 2(7.7%) patients had stage IV disease. Pre-op CEA levels were missing in 2(7.6%) cases, 15(57.6%) had normal and 9(34.6%) had raised serum CEA levels. All the 26(100%) patients received neo-adjuvant chemoX R T. On histopathology, 18(69%) patients had stage III disease. Specimen resection margins were negative for disease in 25(96%) patients. Post-op CEA levels were also missing in 2(7.6%) patients, while 12(46%) patients each had raised and normal CEA levels at 6-month follow-up.*

Conclusion: *It is concluded that tumor depth, lymph node metastases, post-op serum CEA level s an d complete tumor response on histopathology can affect the development of metachronous liver lesions in patients having undergone curative surgical resection for rectal cancers.*

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INTRODUCTION:

Metachronous liver metastasis (MLM) occurs in 20–40% of colorectal cancer (CRC) patients following surgical treatment. Colorectal cancer (CRC) is the third most common cancer worldwide in males and the second in females, with an estimated 1.2 million new cases diagnosed per year. To date, surgical resection offers the only chance for potential curative therapy. However, even after radical surgery, more than 30% CRC patients develop metastases. Common sites of metastases from CRC include liver and lung while metachronous bone metastasis (MBM) occurs infrequently and is indictable of poor patient prognosis [1].

Rectal cancer is one of the most commonly diagnosed cancers worldwide and is counted among the leading causes of cancer-related deaths. The prognosis is closely related to the extent of disease at presentation as determined by Dukes and American Joint Committee on Cancer (AJCC) classifications. Metastases from colorectal cancers are common and develop in 40-60% patients. The existence of metastases classifies patients into M1 and stage IV of AJCC classification [2]. The most common metastases site from rectal cancer is liver and about 50% patients develop hepatic metastases during the course of their disease, with 20-25% of these presenting with synchronous liver metastases [3]. In about 1/3rd of the patients with synchronous or metachronous liver metastases, and the liver is the only site of metastatic disease. In particular, the median survival for patients with untreated colorectal cancer liver metastases ranges from 4.5 months to 21 months with a survival rate of only 0-3%. Advances in adjuvant treatment after primary curative surgical resection of colorectal cancer have shown the potential of a decrease in the number of metastatic cases even though the two-year survival is limited to 40% at best [4].

Objectives of the study

The main objective of the study is to find the risk factors affecting development of liver metastasis in rectal cancer patients.

METHODOLOGY OF THE STUDY:

This descriptive study was conducted in Holy Family Hospital, Rawalpindi during March 2018 to October 2018. The data was collected from 50 patients through non-random sampling technique. All those patients who were suffering from colorectal cancer were included in this study. Patients with primary cancer in another organ were excluded. Lymph node involvement was divided into N0, N1 and N2. All stage III and IV patients received neoadjuvant chemotherapy. The neoadjuvant chemotherapy will not be considered as a comparative factor in subsequent analyses, because it is strongly associated with tumor stages. According to the NCCN guideline, all CRC patients in stage II or more advanced CRC received a 5-Fu-based chemotherapy for at least 8 cycles postoperatively.

Statistical analysis

The collected data were analyzed using SPSS version 21.0. Continuous variables were presented as mean ± standard deviation (SD) compared using the independent sample t test, whereas categorical variables were expressed as frequency compared using the Pearson chi-square (χ^2) test.

RESULTS:

The data was collected from 50 patients. Only 10-20% of the patients with liver were aged below 50 years. On clinical staging, 2(7.7%) patients had stage II disease, 22(84.6%) had stage III, and 2(7.7%) patients had stage IV disease. Pre-op CEA levels were missing in 2(7.6%) cases, 15(57.6%) had normal and 9(34.6%) had raised serum CEA levels. All the 26(100%) patients received neoad juvant chemoX R T. On histopathology, 18(69%) patients had stage III disease. Specimen resection margins were negative for disease in 25(96%) patients. Post-op CEA levels were also missing in 2(7.6%) patients, while 12(46%) patients each had raised and normal CEA levels at 6-month follow-up. Only 1(3.8%) patient had complete tumor response on histopathology.

Table-1: Descriptive statistics with bivariate analysis.

Variables		Liver metastasis		*p*-value
		Yes	No	
		26 (6.0%)	408 (94.0%)	
Age	<50 YEARS	16 (7.4%)	201 (92.6%)	0.832
	>50 YEARS	10 (4.6%)	207 (95.4%)	
Sex	MALE	18 (6.3%)	266 (93.7%)	0.225
	FEMALE	8 (5.3%)	142 (94.7%)	
cTNM	STAGE I	0 (0%)	5 (100%)	0.299
	STAGE II	2 (4.7%)	41 (95.3%)	
	STAGE III	22 (5.9%)	354 (94.1%)	
	STAGE IV	2 (20%)	8 (80%)	
Clinical nodal status	N 0	1 (1.8%)	56 (98.2%)	0.039
	N 1	5 (5.4%)	88 (94.6%)	
	N2	19 (6.7%)	264 (93.3%)	
	N 3	1 (100%)	0	
Pre-operative CEA*levels	NORMAL	15 (5%)	286 (95%)	0.212
	RAISED	9 (8.3%)	100 (91.7%)	
NEOADJUVANT TREATMENT	NO	4 (9.8%)	37 (90.2%)	0.292
	YES	22 (5.6%)	371 (94.4%)	***
pTNM	NO DISEASE	1 (1.1%)	88 (98.9%)	0.006
	STAGE I	3 (4.8%)	59 (95.2%)	
	STAGE II	2 (2.8%)	70 (97.2%)	
	STAGE III	18 (8.8%)	187 (91.2%)	
	STAGE IV	2 (33.3%)	4 (66.7%)	
COMLPETE RESPONSE	NO	25 (7.2%)	320 (92.8%)	0.03
	YES	1 (1.1%)	88 (98.9%)	***
MARGIN CLEARENCE	NO	1 (3.4%)	28 (96.6%)	0.47
	YES	25 (6.2%)	380 (93.8%)	***
Histopathology status	WELL DIFF	3 (5.1%)	56 (94.9%)	0.133
	MOD DIFF	19 (7.9%)	223 (92.1%)	
	POOR DIFF	3 (6.2%)	41 (93.8%)	
	NO RESIDUAL	1 (1.2%)	88 (98.8%)	
POSTOPERATIVECEA* LEVELS	NORMAL	12 (3.4%)	339 (96.6%)	0.001**
	RAISED	12 (21.1%)	45 (78.9%)	
OUTCOME STATUS	ALIVE	2 (0.7%)	271 (99.3%)	0.001**
	DEAD	7 (18.9%)	30 (81.1%)	
	DISEASED	17 (15.3%)	94 (84.7%)	
	LOST F/U	0	13 (100%)	

DISCUSSION:

Rectal tumours are associated with increased mortality rate even after complete curative surgical resection of the primary tumour and it is mostly due to tumour recurrence. Almost half of patients undergoing resection for primary rectal cancer develop metastasis at some point during their surveillance [5]. Primary metastatic site is liver and accounts for almost 50% of the cases. Even after improvement in chemotherapeutic and biological agents, chances of recurrence cannot be reduced and patient's survival is rarely longer than 3 years [6]. After curative surgical resection of primary rectal cancer, if patients develop hepatic metastasis the chances of curative treatment still exist and it depends upon the disease status, its extent and available treatment options [7].

During the past two decades, the five-year survival rates for hepatic rectal metastases patients have almost doubled from 3 0% to 6 0%. The introduction of new chemotherapeutic agents and the shift in the criteria of surgical resection were the main factors in this

progress [8]. Current criteria of liver resection for a metastatic liver lesion depend only on what should be left after hepatic resection. The amount of liver remnant after resection should not be less than 20% of total liver volume for normal patients and about 30% or more for cirrhotic patients [9]. Our study showed that recurrent liver metastasis after curative primary rectal cancer surgery depends on several factors like T stage of the tumor, lymph node metastasis (N stage of tumor) and post-op serum CEA levels [10].

CONCLUSION:

It is concluded that tumor depth, lymph node metastases, post-op serum CEA level s an d complete tumor response on histopathology can affect the development of metachronous liver lesions in patients having under gone curative surgical resection for rectal cancers.

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