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Nutritional Assessment of Egyptian Adults with Hepatic and Gastrointestinal Malignancies: Cross sectional study

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ABSTRACT

Background: Malnutrition is a frequent problem in cancer patients. Malnutrition and weight loss are associated with worse outcome, impaired quality of life, and performance status in cancer patients. **Objective:** The study aimed to assess the nutritional status of patients with stomach, colorectal, and hepatic malignancies in relation to different sociodemographic and clinicopathological characteristics. **Method:** This cross-sectional study included 298 incident cases (85 liver, 93 stomach, and 120 colorectal cancers) enrolled during the period from January 2018 to September 2019. The instrument of this study consisted of Socio-demographic, clinicopathological characteristics, and the Mini Nutritional Assessment (MNA) questionnaire. **Results:** Malnutrition was found in 39.6% of all patients; 49.5% of stomach, 39.2% of colorectal, and 29.4% of liver cancer patients. The independent factors that significantly predict malnutrition were tumor type (OR: 3.4: 95%CI: 1.6-7.1 - stomach vs. liver) and (OR: 1.8, 95%CI: 0.9-3.6 - colorectal vs. liver), psychological problems (OR: 3.8: 95%CI: 2.1-6.8), low performance status (OR: 5.6: 95%CI: 1.8-17.9), and smoking (OR: 1.9: 95%CI: 1.1-3.4). **Conclusion:** Malnutrition is prevalent among gastrointestinal and liver cancers. It is more frequent in stomach cancer cases than in liver cancer cases. The independent factors that significantly predict malnutrition were: tumor type, psychological problems, low performance status, and smoking

INTRODUCTION

Malnutrition is either illness-related (secondary to one or more diseases/injury), non-illness-related (caused by environmental/behavioral factors), or both. In gastric cancer patients 13% are malnourished before gastrectomy and 29% become malnourished after gastrectomy [1]. Malnutrition and weight loss are associated with worse outcome, impaired quality of life, and performance status in cancer patients. Malnourished patients have 2.5 times more risk of death compared to well-nourished patients.[2] Therefore, cancer patients should be maintained in a good nutritional status to improve the effect of anticancer therapy, increase the ability to overcome stress, and minimize the side effects of treatment. Early nutritional screening and nutritional assessment for cancer patients should be established as an essential step in preventing malnutrition in cancer patients. Nutritional assessment should be followed by the appropriate, timely, and cost-effective nutritional intervention.[3]

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There are different methods for assessing nutritional status in patients with malignant neoplastic diseases. Several questionnaires were constructed to assess nutritional status, as the mini nutritional assessment (MNA) score, designed initially for elderly patients.[4]

Liver cancer is the most commonly diagnosed cancer in Egypt in both sex; it is the first most common cancer among males and the second among females. Colon cancer represents the seventh most common cancer among males and the tenth among females. The age-standardized incidence rates are 61.8, 2.3, 4.7, and 1.3 per 100,000 population for liver, stomach, colon, and rectum, respectively.[5]

Up to our knowledge, it is the first Egyptian study to assess the nutritional status of these tumors. This study aimed to assess the nutritional status of patients with stomach, colorectal, and hepatic malignancies and to relate nutritional status to different sociodemographic and clinicopathological characteristics.

METHOD

It is a cross-sectional hospital-based study including 298 recently diagnosed Egyptian patients with cancer (85 liver cancer, 93 stomach cancer, and 120 colorectal cancer). The sample was consecutive sample that involves taking every patient who meets the selection criteria. Patients were recruited from different departments of a large oncology institute in Egypt during the period from January 2018 to September 2019. The study was approved by the Institutional Review Board (approval No: 201617063.3), and all participants signed informed consent. All procedures followed the ethical standards of the 1964 Helsinki declaration and its later amendments. The questionnaire was anonymous, and all obtained data were kept confidential.

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Only incident cases of liver, stomach, and colorectal cancers of both sexes, aged >18 years with pathologically proved malignancy at diagnosis before starting any treatment were included in that study. Patients with multiple primary sites, metastases at diagnosis, and those receiving any type of cancer treatment were excluded from the study.

Data were collected in a data collection sheet from direct patient interview, patients' medical records, laboratory data, and nutritional assessment questionnaire. Sociodemographic data included age, sex, marital status, residence, occupation, education, special habits as smoking, alcohol, and exercise and clinical data included unintentional weight loss and its amount, weight, height, body mass index, performance status.

Mini Nutritional Assessment (MNA) questionnaire (4) was used to calculate the MNA Score. The full form MNA questionnaire consists of 18 items grouped into two subtitles: 6 screening questions (section I) and 12 assessment questions (section II). The MNA includes body mass index (BMI), weight loss, arm and calf circumference, appetite, medication, general and cognitive health, dietary matters, the autonomy of feeding, self-perception of health and nutrition, and subjective judgment of malnutrition. The maximum score in the MNA test is 30 points, 14 points obtained by screening questions (< 7 indicating malnourished, 8-11: at risk of malnutrition, 12-14: normal nutritional status), and 16 related to assessment questions. Based on the final score, subjects were classified into three groups: malnourished (score < 17), at risk for malnutrition (17–23.5), and normal nutritional status (24–30). The normal and those at risk of malnutrition were combined for statistical purposes. As part of the MNA questionnaire, each participant underwent a clinical examination, including measurement of mid-arm circumference (MAC), calf circumference (CC), weight, and height.

Statistical analysis

Data management and analysis were done using IBM© SPSS© Statistics version 25 (IBM© Corp., Armonk, NY, USA). Numerical data were explored for normality using the Kolmogorov-Smirnov test. Chisquare or Fisher's tests were used to compare between the independent groups with respect to categorical data, as appropriate. Comparisons

Table 1: Baseline characteristics and nutritional status of the three studied groups

	Liver cancer n=85	Stomach cancer n=93	Colorectal cancer n=120	P-value
Sociodemographic				
Age (years)	57±12 [a]	52±12 [b]	51±14 [b]	0.003
Sex (Men/Women)	54/31	58/35	61/59	0.112
Residence				
Urban	61 (71.8)	66 (71.0)	93 (77.5)	0.506
Rural	24 (28.2)	27 (29.0)	27 (22.5)	
Education level				
Illiterate	23 (27.1) [a]	35 (37.6) [a]	38 (31.7) [a]	
Primary & preparatory school	34 (40.0) [a]	31 (33.3) [a,b]	28 (23.3) [b]	0.036
High school	28 (32.9) [a]	27 (29.0) [a]	54 (45.0) [a]	
Smoking	41 (48.2)	44 (47.3)	40 (33.3)	0.051
Alcohol drinking	9 (10.6)	11 (11.8)	20 (16.7)	0.375
Routine exercise practice	8 (9.4)	16 (17.2)	15 (12.5)	0.315
Prescribed medicine (day)				
No	9 (10.6) [a]	23 (24.7) [b]	41 (34.2) [b]	0.001
Yes	76 (89.4)	70 (75.3)	79 (65.8)	
Comorbidity				
No	2 (2.4) [a]	23 (24.7) [b]	41 (34.2) [b]	<0.001
Yes	83 (97.6)	70 (75.3)	79 (65.8)	
Psychological problems				
No	48 (56.5)	59 (63.4)	62 (51.7)	0.234
Yes	37 (34.5)	34 (36.6)	58 (48.3)	
Anthropometric measurements				
Weight (kg)	76.5±14.6[b]	68.1±17.1[a]	73.7±17.3[b]	0.003
Unintentional weight loss (kg)	6.5 (1.0-23.0)	8.0 (1.0-60.0)	10.0 (1.0-42.0)	0.106
Unintentional weight loss (%)	6.2 (1.0-28.7) [a]	11.0 (1.3-55.0) [a, b]	13.4 (1.0-40.0) [b]	0.035
Height (cm)	163.0±8.0	165.0±10.0	163.5±9.0	0.246
BMI (kg/m^2)	28.8±5.4[b]	25.1±6.3[a]	27.8±6.4[b]	<0.001
MAC (cm)	26.1±3.6[b]	24.5±4.3[a]	25.8±4.0[b]	0.018
CC (cm)	36.2±4.0[a]	33.2±5.0[b]	34.4±5.0[b]	<0.001
Nutritional Status				
MNA score				
Malnourished	25 (29.4) [b]	46 (49.5) [a]	47 (39.2) [a, b]	
At risk of malnutrition	52 (61.2)	34 (36.6)	57 (47.5)	0.026
Normal	8 (9.4)	13 (14.0)	16 (13.3)	
MNA score				
Malnourished	25 (29.4) [b]	46 (49.5) [a]	47 (39.2) [a, b]	0.024
Normal & at risk	60 (70.6)	47 (50.5)	73 (60.8)	

Data are expressed as mean ±standard deviation, median (range), or number (%). BMI: Body mass index, MAC: Mid-arm circumference, CC: Calf circumference, MNA: Minimal Nutrition Assessment score, Groups sharing the *same letter are not significantly different. Comorbidity includes hypertension, diabetes mellitus, and hepatitis C virus. p<0.05 indicates statistical significance*

between two groups were made using the Student's t-test or Mann-Whitney test according to the normality of distribution. Comparisons between more than two groups were performed by the

Table 2: Nutritional status (according to MNA) and its relation to sociodemographic characteristics, performance status, psychological status, and hospitalization

	Total n=298	Malnourished n=118	Normal & at risk of malnutrition n=180	P-value
Age (years)	53±13	52±14	54±13	0.154
Sex				
Male	173	68 (39.3)	105 (60.7)	0.904
Female	125	50 (40.0)	75 (60.0)	
Residence				
Urban	220	89(40.5)	131 (59.5)	0.611
Rural	78	29 (37.2)	49 (62.8)	
Education level				
Illiterate	96	39 (40.6)	57 (59.4)	0.257
Primary & preparatory school	93	42 (45.2)	51 (54.8)	
≥ High school	109	37 (33.9)	72 (66.1)	
Smoking				
Non-smoker	173	61 (35.3)	112 (64.7)	0.072
Current & past smoking	125	57 (45.6)	68 (54.4)	
Alcohol				
Nondrinker	258	101 (39.1)	157 (60.9)	0.687
Current & past drinker	40	17 (42.5)	23 (57.5)	
Routine exercise				
No	259	102 (39.4)	157 (60.6)	0.845
Yes	39	16 (41.0)	23 (59.0)	
Prescribed medicine (day)				
No	73	27 (37.0)	46 (63.0)	0.680
Yes	225	91 (40.4)	134 (59.6)	
Comorbidity				
No	66	27 (40.9)	39 (59.1)	0.887
Yes	232	91 (39.2)	141 (60.8)	
Psychological problems				
Yes	129	68 (52.7)	61 (47.3)	<0.001
No	169	50 (29.6)	119 (70.4)	
Performance status				
0	34	4 (11.8)	30 (88.2)	<0.001
1	100	25 (25.0)	75 (75.0)	
2	108	43 (39.8)	65 (60.2)	
3 & 4	56	46 (82.1)	10 (17.9)	
Length of hospitalization (days)	10 (1-60)	12 (2-60)	10 (1-60)	<0.001
Number of hospitalizations	1 (1-15)	1 (1-15)	1 (1-15)	0.174

Data are expressed as mean ± standard deviation, median (range), or number (%). p<0.05 indicates statistical significance

ANOVA test or Kruskal-Wallis test according to the normality of distribution. To measure the independent effect of different factors on the nutritional status of cancer patients, factors that had a significance level < 0.10 were selected to enter into stepwise logistic regression analysis. Logistic regression was used to estimate the odds ratio (OR) and 95% Confidence Interval (95%CI). All tests

Table 3: Pathological factors and their relationship to nutritional status (according to MNA)

	n	Malnourished n=118	Normal & at risk of malnutrition n=180	P-value
Tumor type (n= 298)				
Liver cancer	85	25 (29.4)	60 (70.6)	
Stomach cancer	93	46 (49.5)	47 (50.5)	0.024
Colorectal cancer	120	47 (39.2)	73 (60.8)	
LN involvement (n= 298)				
Yes	148	67 (45.3)	81 (54.7)	0.047
No	150	51 (34.0)	99 (66.0)	
Grade (stomach, colorectal) (n= 194)				
Grade I	34	16(47.1) [a, b]	18 (52.9)	
Grade II	121	46 (38.0) [b]	75 (62.0)	0.017
Grade III	39	25 (64.1) [a]	14 (35.9)	
AJCC stage (stomach, colorectal) (n= 212)				
High stage	63	30 (47.6)	33 (52.4)	0.474
Low stage	149	63 (42.3)	86 (57.7)	
BCLC staging for liver cancer (n= 85)				
Stage (A)	37	7 (18.9) [b]	30 (81.1)	
Stage (B)	19	2 (10.5) [b]	17 (89.5)	<0.001
Stage (C)	16	6 (37.5)[a, b]	10 (62.5)	
Stage (D)	13	10 (76.9) [a]	3 (23.1)	

AJCC: American joint committee on cancer staging system, BCLC: Barcelona Clinic Liver Cancer staging system, LN: lymph node. Groups sharing the same letter are not significantly different. p<0.05 indicates statistical significance were two-sided. A p-value < 0.05 was considered significant.

RESULTS

Liver cancer patients were significantly older than the stomach (p=0.018) and colorectal cancer (p=0.004). Higher educational level was more common in colorectal cancer patients than liver cancer patients (p=0.036). Otherwise, the three groups were comparable demographically and regarding special habits. Liver cancer cases take much more medications than stomach and colorectal cancer cases (p=0.018 and p < 0.001, respectively). Also, liver cancer cases suffer from several comorbidities (as hypertension, diabetes mellitus, and hepatitis C) compared to stomach and colorectal cancer cases (p<0.001 for both). The weight of stomach cancer patients was significantly lower than that of either liver (p=0.003) or colorectal cancer patients (p=0.042). Body mass index (BMI) was significantly lower in stomach cancer cases compared to the liver (p=0.001) and colorectal cancer (p=0.004). Colorectal cancer patients showed significantly higher unintentional weight loss percentage compared to liver cancer patients (p=0.035). Mid arm circumference (MAC) was significantly higher in liver cancer than stomach cancer (p=0.026). Calf circumference was higher in liver cancer compared to either stomach (p<0.001) or colorectal cancer (p=0.038). There was no significant difference between the three cancers in height and unintentional weight loss (Table 1). A minority of patients had normal nutritional status ranged from 9.4% in liver cancer to 14% in colorectal cancer at presentation. Malnutrition was significantly more frequent in stomach cancer (49.5%) than liver cancer (29.4%) (p=0.012) (Table 1).

According to the MNA score, 118 patients of the whole studied group (39.6%) were malnourished. Malnourished and normally nourished patients were comparable regarding demographic characteristics. Malnourishment showed a borderline association with smoking (p = 0.072). Malnourishment was significantly associated with a psychological problem, low performance status, and prolonged hospital stay, p <0.001 (Table 2).

Table 4: Predictors of malnutrition using MNA

Factors	OR	95% C.I. for OR	p-value
Tumor type			0.006
Tumor type (Stomach vs. liver)	3.4	1.6-7.1	0.002
Tumor type (Colorectal vs. liver)	1.8	0.9-3.6	0.118
Psychological problems	3.8	2.1-6.8	<0.001
Performance status (PS)			<0.001
PS (1) vs. PS (0)	2.8	0.9-9.1	0.089
PS (2) vs. PS (0)	5.6	1.8-17.9	0.004
PS (3&4) vs.PS (0)	43.9	11.9-162.4	<0.001
Smoking	1.9	1.1-3.4	0.032

OR= Odds Ratio, CI = confidence interval, PS: performance status. P-value≤ 0.05 is considered significant

As shown in table (3), 49.5% of stomach cancer cases were malnourished, while less than one-third (29.4%) of liver cancer cases were malnourished (p=0.012). Malnutrition was significantly associated with lymph node involvement (p=0.047). Higher grade stomach and colorectal tumors were significantly associated with malnourishment (p=0.012). Malnourishment was significantly more frequent in stage D liver cancer patients (76.9%) compared to those with stage A and B (p<0.001, for both).

Using multivariate logistic regression, the only independent factors that significantly predict nutritional status were the tumor type, psychological problems, performance status, and smoking (Table 4).

DISCUSSION

The study demonstrated that 39.6% of patients with gastrointestinal (GIT) malignancies were malnourished according to the MNA score. Nearly half of stomach cancer patients were malnourished versus 39.2% of colorectal and 29.4% of liver cancer patients. Tumor type (location), psychological problems, poor performance status, and smoking are the independent factors predicting malnutrition.

The MNA score predicts the nutritional status accurately in patients with liver tumors (Tsai et al., 2011). The MNA questionnaire has a good level of reliability, with internal consistency, estimated by Cronbach's alpha of 0.83. Test-retest reliability, according to the intraclass correlation coefficient (ICC), is 0.89 for the total MNA score.[8]

Previous studies reported variable figures about the prevalence of malnutrition in patients with GIT cancers. In stomach cancer, Jin et al. [9] reported a high incidence of malnutrition of 65%, while in Japan in 2018 Fujiya et al.[10] found that only 13% of gastric cancer patients are malnourished before gastrectomy. In 2017, Daniele et al. [11] reported that 46.1% of colorectal cancer patients were at risk of malnutrition, and 24.5% were malnourished. In 2018, among Chinese patients with geriatric stomach and colorectal cancer, about 47.8% were at risk of malnutrition.[12] At Taiwanese hospital, Huang et al.[13] in 2019 detected a 33.4% prevalence of malnutrition among liver cancer patients, while in France (2018) Gyan et al.[14] found a higher percentage of 55%. Another Korean study found a prevalence of 28.1% of malnutrition in colorectal cancer patients [15](Kwag et al., 2014), a figure lower than that in the current study. We believe that the variability in the prevalence of malnourishment reported in different studies might be attributed to the differences in other influential factors. These factors include - for example - age, sex, socioeconomic standards, and disease stage in addition to the actual nutritional status before diagnosis of cancer.

Malnutrition in cancer patients can be attributed to several causes. It can be caused by systemic effects of cancer or by the hosts' response to cancer and by chemoradiotherapy. Cancer can directly lead to loss of appetite and decreased bodyweight, resulting in the deficiency of several minerals and vitamins, such as iron, folate, and vitamin B12.[16] Protein-energy malnutrition (PEM) is frequently recognized in cancer patients. PEM is associated with decreased physical strength, reduced tolerance to cancer treatment, reduced survival, and longer hospitalization time.[11]

Patients with GIT malignancies, in particular, are at high risk of malnutrition through causing anorexia, nausea, vomiting, GIT obstruction, and malabsorption. Radiotherapy (RT) and, more importantly, chemoradiotherapy (CRT) are known factors that lead to malnutrition in colorectal cancer. Chemoradiotherapy is usually much more toxic than RT alone and causes marked weight loss and reduced serum albumin concentration.[14]

In stomach cancer, malnutrition depends on tumor type, location, disease stage, treatment, and type of nutritional assessment method.[17] Besides, treatment modalities, including chemo- and radiotherapy, and surgery are known to lead to acute and chronic consequences that restrict eating and exert a significant impact on nutritional status. Then resulting anorexia decreases food intake and induces psychological distress leading to loss of body weight and malnutrition.[18] Besides, surgery aggravates malnutrition in patients with gastric cancer, induces severe immunosuppression, and affects prognosis.[19] In advanced gastric cancer, malnutrition can be caused by GIT obstruction and bleeding.[20] In most patients with radical gastrectomy, the body's immune function and nutritional status decline due to malnutrition before surgery in some patients.[21]

In liver cancer patients, the host systemic immune-inflammatory response is the most pathogenic factor in malnutrition. This is particularly essential in patients with hepatocellular carcinoma (HCC) because of underlying infection in most cases and the concomitant illness, fibrosis, and cirrhosis that contribute to impaired nutritional status.[22]

The most common clinical symptoms in liver cancer are decreased food intake and diarrhea. Long-term decreased food intake or diarrhea will inevitably result in malnutrition, which results in poor prognosis in liver cancer cases.[23] Also, reduced food intake may impair immunity.[24]

Multivariate analysis showed that tumor type (location), psychological problems, low performance status, and smoking could independently predict malnutrition in the current study. Stomach cancer was more at risk of malnutrition than liver cancer (OR: 3.4, 95%CI: 1.6-7.1). Colorectal cancer carries almost twice the risk of malnutrition as liver cancer (OR: 1.8, 95%CI: 0.9-3.6). In Victoria, Australia, (2019) Marshall et al.[25] reported comparable results using multivariate analysis showing that tumor type was independently associated with malnutrition. The risk of malnutrition was increased in patients with upper GIT tumors (OR: 3.8, 95%CI: 2.4-6.0) and those with colorectal cancer (OR: 1.6, 95% CI: 1.1-2.5).

Malnutrition was found to be high for patients with cancer in the digestive organs[26], but low for those with lymphomas and breast cancer[27]. In Korea (2010) Wie et al.[7] found that malnutrition was more prevalent in patients with liver and stomach cancer than other cancer sites. They reported moderate and severe malnutrition in 29.7%, 52.6%, 31.5% for stomach, liver, and colorectal cancers, respectively.

In agreement with the current results, Saka et al.[28] identified depression as a risk factor for malnutrition. Depression leads to a lack of appetite, loss of interest in self-care, apathy, and physical weakness. While depression causes anorexia and, consequently, malnutrition, the latter might further impair appetite via the secretion of TNF-α and other mediators.[29] Another study in the Netherlands reported that depression and smoking were independent risk factors for malnutrition. Smoking was associated with an increased risk of malnutrition. This association may be linked to how tobacco reduces appetite and promotes inflammatory reactions.[30]

In the current study, there was a significant association between performance status and malnutrition in GIT malignancies ($p<0.001$). Similar findings were reported in 2019 by Zhang et al.[31] who conducted a cross-sectional study in the United States. The study reported that ECOG performance status score was associated with malnutrition in older patients with cancer (OR: 1.57, 95%CI: 1.24-2.00). Also, Also, a longitudinal cohort study conducted in Sweden in 2009 by Johansson et al.[32] reported that patients with functional dependence exhibited poor nutritional status according to the MNA score.

CONCLUSION

Malnourishment is a common finding in patients with GIT malignancies accounting for 43.7%; it was more common in stomach cancer (49.5%) than colorectal cancer (39.2%). At presentation, only a minority of the patients were well-nourished. Thus, timely and early nutritional screening and nutritional assessment are essential to avoid serious effects of malnutrition on patient's health and outcome of treatment. The independent factors that significantly predict malnutrition were tumor type, psychological problems, low performance status, and smoking.

Study limitations

Sometimes participants were not able to recall data such as previous weight. Also, during recruitment of cases, some people refuse to participate in the study, 350 patients were approached and 298 accepted to participate (acceptance rate 85%).

Recommendations

Nutritional screening and nutritional assessment must be done for all cancer patients in their first visit and during follow up in a simple and non-invasive way to identify patients at risk of malnutrition and determine the degree of malnutrition. Also, educational sessions for nutrition during treatment are recommended for prevention of possible development of malnutrition due to different types of treatment modalities, especially chemo- and radiotherapy. Proper management of malnourished patients and those at risk to face any nutritional challenges before significant weight loss or before other clinical/biological signs of malnutrition appear. Nutrition specialists should be available in specialized clinics for the process of assessment and consultation about the nutritional status of cancer patients.

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