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Prevalence and patterns of gastrointestinal cancers among obese patients, from a teaching hospital in Saudi Arabia

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Abstract: Background: Obesity is associated with many comorbidities. Several studies concluded that there is an association between obesity and different types of cancers. But the prevalence and patterns of gastrointestinal (GI) cancers among obese patients still need to be investigated. Objective: To determine the prevalence and patterns of GI cancers among obese and non-obese patients. Method: The current case-control study was performed using medical records of all adult patients who were diagnosed with GI cancers at King Abdulaziz University Hospital (KAUH) from January 2010 until May 2018, with a sample size of 834. We excluded participants who had a missing body mass index (BMI) value. SPSS 21 software package was used for data analysis. Result: 532 patients with GI cancer included in the study divided into non-obese and obese based on their BMI. Obese patients represented 22.9% (n=122) while 77.1 % (n=410) are non-obese. The mean age at diagnosis in obese was 56.63 years and in non-obese was 56.65 years. The mean BMI of obese was 34.18kg/m². There were more females in the obese group than non-obese (54.9% vs 34.9%, p=0.00007). The commonest tumor site in obese was colorectal cancer (CRC) followed by gastric and pancreatic cancers while in non-obese was CRC followed by gastric and esophageal cancers (p=0.348). There was no difference in the death rate among obese and non-obese (27.9% and 34.1%, p=0.194). Obese patients have higher positive lymph node than non-obese (p=0.236). Conclusion: Our study showed that GI cancers are common among obese females and the commonest sites are CRC, gastric and pancreatic cancers in obese than non-obese and screening obese female is highly recommended in our society. [Duaa J. Alhazmi, Dina H. Alsohaibi, Hamidh A. Almusayliem, Ola A. Bukhari, Aseel A. Alharbi, Aisha A.

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Key words: Obesity; body mass index; gastrointestinal cancer.

1. Introduction:

Obesity is defined as a body mass index (BMI) that is greater than or equal to 30 kg/m² and it is considered worldwide to be a significant problem, with a drastically increased incidence in recent years (Sun and Karin, 2012). Obesity has been associated with several illnesses such as cardiovascular disease, diabetes, and cancer (Martin-Rodriguez, Guillen-Grima *et al.*, 2015). The World Health Organization (WHO) categorizes BMI as underweight (<18.5 kg/m²), normal (18.5–24.99 kg/m²), overweight (25–29.9 kg/m²), and obesity (\geq 30 kg/m²) (WHO Expert Consultation, 2004). Additionally, the prevalence of obesity for both sexes was 13.2% worldwide, 19.5% in the middle east, and 35% in Saudi Arabia (Abarca-Gómez, Abdeen *et al.*, 2017).

Gastrointestinal (GI) cancer affects the function of digestive system organs such as the stomach, colon-rectum, liver, esophagus, and pancreas (Sung, Ng *et al.*, 2012). However, the most common GI cancer is colorectal cancer (CRC) worldwide and in Saudi Arabia, while in developing countries, it is gastric cancer (Jemal, Bray et al., 2011; Bazarbashi, Al Eid et al., 2017). Several studies concluded that there is an association between high BMI and different types of cancer such as CRC(Al-Sharif, Fayi et al., 2018), postmenopausal breast cancer, endometrial cancer, renal cell carcinoma, esophageal adenocarcinoma (Ri, Aikou et al., 2018; Steffen, Huerta et al., 2015), pancreatic cancer and liver cancer (Sun and Karin, 2012), ovarian cancer, advanced prostate cancer, gallbladder cancer, and gastric cardia cancer(Steffen, Huerta et al., 2015; Renehan, Tyson et al., 2008). However, a few studies showed that there is an inverse relationship between obesity and gastric non-cardia adenocarcinoma (Steffen, Huerta et al., 2015) and esophageal squamous cell carcinoma (Renehan, Tyson et al.,

2008).

Pathologically, the majority of the CRC clinicopathological characteristics included adenocarcinoma type (52%), a tumor size >5 cm, and lymph node metastasis (Aldiab, Al Khayal *et al.*, 2017). Another study performed in adult males with rectal cancer showed that most obese patients had larger tumor size compared to non-obese people (Bokey, Chapuis *et al.*, 2014). In contrast to distal gastric carcinoma (DG), proximal gastric cancer (PG) had a larger tumor size, a higher rate of lymph node metastases, and an advanced stage (Yu, Hu *et al.*, 2018).

In 2006, a study reported that 4% of cancer deaths in men and 16–20% of cancer deaths in women resulted from obesity (Calle, Rodriguez *et al.*, 2003). Obesity and overweight led to an increase in postoperative mortality in the patient who underwent surgery for gastric cancer (Struecker, Biebl *et al.*, 2017).

In Saudi Arabia, there is a lack of studies about the relationship between obesity and cancer. Thus, we aimed to determine the prevalence and patterns of GI cancer among obese and non-obese patients.

2. Materials and methods

The study was approved by the institutional review board (IRB) of king abdulaziz university. The present cross-sectional study was performed using the medical records of all adult cancer patients who presented to the department of general surgery of KAUH, Jeddah, the western region of Saudi Arabia, from January 2010 to May 2018. There were 834 cancer patients recruited into this study. The selected patients had GI cancer including esophageal, gastric, pancreatic, hepatic, and CRC and were over 18 years of age. Patients who had a missing BMI value were excluded.

The following data were extracted from each patient's records as the demographic data: age, sex, nationality, comorbidities, living or deceased, history of other cancers, history of receiving chemotherapy and radiotherapy, anthropometric measurement (height, weight, and BMI), and pathological factors (tumor site, histopathological type, size, grade, lymph node status, tumor margin, and TNM stage). The patients were divided into groups based on their BMI.

The data were inputted into Microsoft Excel 2016 version15.25 (Microsoft Corporation by Impress a Systems, Santa Rosa, California, USA), and all statistical analyses were performed using Statistical Package for Social Science (SPSS) Version 21, (IBM Corporation, Armonk, NY, USA). Categorical variables, such as sex, BMI groups, and cancer site and frequency were estimated and analyzed using the chi-square test to examine the association between the different variables. For continuous variables, the mean \pm standard deviation was determined, and the data were analyzed using a one-way ANOVA. The level of significance was set at p < 0.05.

3. Result

During the study period, 834 patients who were diagnosed with GI cancer at our hospital and 532 patients with GI cancer were included into the study. There were 302 patients who were excluded because of missing BMI values, the patient was diagnosed before 2010, or the patient was not a GI cancer patient.

The mean age, age at diagnosis, and BMI in the obese group were 59.41 (26–85) years, 56.63 (23–83) years, and 34.18 (30–48.4) kg/m², respectively. The mean overall BMI was 26.33 kg/m². Table 1 summarizes the clinicopathological characteristics of participants according to the BMI. Among 532 patients, 410(77.1%) had a BMI of <29.99 kg/m² and 122 (22.93%) had a BMI greater than 30 kg/m².

The only significant difference between obese and non-obese patients was their sex, where the greatest proportions of the obese patients were female (54.9% vs. 34.9%, P=0.00007) and more obese patients had hypertension (36.9% vs. 25.9%, P=0.017). There was no significant difference in the distribution of the patients' BMI with age (P=0.900), history of other cancers (P=0.620), and history of receiving chemotherapy or radiotherapy (P=0.755).

Diabetes (P=0.543) was higher among obese patients compared to non-obese group. Additionally, the death rate among non-obese, and obese groups was 34.1%, and 27.9%, respectively (P=0.194).

According to the cancer site, CRC had the highest prevalence (57.9%) followed by gastric cancer (18.2%). Similarly, CRC was the most common GI cancer type that affected obese patients followed by gastric cancer (P=0.348).

Most obese patients had a tumor <5 cm (P=0.190) in size, with a moderately differentiated grade (P=0.558), negative margin (P=0.339), positive lymph nodes (P=0.236) and relatively more advanced cancer (*P*=0.804). About 42.9% of tumors that were larger than 10 cm were in obese patients (*P*=0.190).

The most common histological type in obese patients is adenocarcinoma (P=0.403). However, in non-obese patients, adenocarcinoma was the most common followed by invasive adenocarcinoma.

Table 1. Clinicopathological c		•		
Clinical features	Total	Non-obese	Obese	Р
	(n=532)	(BMI<29.99) (n=410)	(BMI ≥30) (n=122)	
Age, years mean (SD)	59.28(13.224)	59.24(13.861)	59.41(10.863)	0.900465
Age at diagnosis mean (SD)		56.65(13.941)	56.63(11.235)	0.988392
Gender		, ,		0.000070
Male	322(60.5)	267(65.1)	55(45.1)	
Female	210 (39.5)	143(34.9)	67(54.9)	
Deaths	174(32.7)	140(34.1)	34(27.9)	0.194469
Comorbidities	224(42.1)	163(39.8)	61(50)	0.044237
Diabetes mellitus	184(34.6)	139(33.9)	45(36.9)	0.543140
Hypertension	151(28.4)	106(25.9)	45(36.9)	0.017666
Hyperlipidemia	27(5.1)	21(5.1)	6(4.9)	0.928219
Cancer Site	27(0.1)			0.347513
Esophageal Cancer	57(10.7)	50(12.2)	7(5.7)	0.0
Colorectal Cancer	308(57.9)	233(56.8)	75(61.5)	
Gastric Cancer	97(18.2)	75(18.3)	22(18)	
Hepatic Cancer	21(3.9)	15(3.7)	6(4.9)	
Pancreatic Cancer	49(9.2)	37(9)	12(9.8)	
History of other cancers	26(4.9)	19(4.6)	7(5.7)	0.619669
History of receiving chemotherapy or	<i>, , ,</i>	19(4.0)	7(3.7)	0.019009
radiotherapy	391(73.5)	300(73.2)	91(74.6)	0.755155
Tumor size				0.189645
<5 cm	141(58.5)	111(60)	30(53.6)	0.189045
5–10 cm	86(35.7)	66(35.7)	20(35.7)	
>10 cm	14(5.8)	8(4.3)	6(10.7)	
	14(3.8)	0(4.5)	0(10.7)	0.558408
Tumor grade G1	116(21.9)	86(20.6)	20(25.7)	0.338408
G2	116(31.8)	86(30.6)	30(35.7)	
G2 G3	171(46.8)	132(47)	39(46.4)	
	78(21.4)	63(22.4)	15(17.9)	0.402215
Histological type	12(2.0)	7(0.1)		0.403215
HCC	12(2.8)	7(2.1)	5(5.1)	
Cholangiocarcinoma	4(0.9)	3(0.9)	1(1)	
SCC	29(6.7)	26(7.8)	3(3.1)	
Adenocarcinoma	279(64.6)	215(64.4)	64(65.3)	
Ductal adenocarcinoma	8(1.9)	5(1.5)	3(3.1)	
Mucinous adenocarcinoma	27(6.3)	20(6)	7(7.1)	
Signet ring carcinoma	6(1.4)	5(1.5)	1(1)	
Neuroendocrine	6(1.4)	4(1.2)	2(2)	
Poorly cohesive carcinoma	1(0.2)	1(0.3)	0(0)	
Invasive adenocarcinoma	39(9)	32(9.6)	7(7.1)	
GIST	6(1.4)	3(0.9)	3(3.1)	
Adenocarcinoma with signet cell feature	13(3)	12(3.6)	1(1)	
Adenocarcinoma with neuroendocrine feature	2(0.5)	1(0.3)	1(1)	
Tumor margin				0.339343
Negative	173(88.7)	125(87.4)	48(92.3)	
Positive	22(11.3)	18(12.6)	4(7.7)	
Lymph node status				0.236104
Negative	93(42.5)	73(44.8)	20(35.7)	
Positive	126(57.5)	90(55.2)	36(64.3)	
T Stage	,			0.804107

Table 1. Clinicopathological	characteristics of pa	atients according to	BMI (kg/m^2)
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Tis	1(0.7)	1(0.9)	0(0)	
ТО	2(1.3)	2(1.9)	0(0)	
T 1	16(10.7)	12(11.3)	4(9.3)	
T2	26(17.4)	17(16)	9(20.9)	
T3	78(52.3)	57(53.8)	21(48.8)	
T4	26(17.4)	17(16)	9(20.9)	
N Stage				0.831870
N0	52(38.5)	37(38.1)	15(39.5)	
N1	51(37.8)	37(38.1)	14(36.8)	
N2	25(18.5)	17(17.5)	8(21.1)	
N3	7(5.2)	6(6.2)	1(2.6)	
M Stage				0.489542
Mx	2(6.7)	2(9.5)	0(0)	
M0	7(23.3)	4(19)	3(33.3)	
M1	21(70)	15(71.4)	6(66.7)	

Values are given as n (%). G1, well differentiated; G2, moderate differentiated; G3, poorly differentiated; HCC, hepatocellular carcinoma; SCC, squamous cell carcinoma; GIST, gastrointestinal stromal tumor

4. Discussion

cross-sectional In our current study. epidemiological and clinicopathologic characteristics and the prognostic factors for patients with different cancer locations were analyzed for obese patients with GI cancer. Participants in the present study had a 22.9% prevalence of obesity. Several studies reported that the prevalence of overall cancer was 33%, 7.7%, and 31.7% for obese people with a BMI >30 in Sweden, Canada, and the United States, respectively (Wolk, Gridley et al., 2001; Pan, Johnson et al., 2004; Greenlee, Shi et al., 2016). In 2016, a study found a strong association between overweight/obesity and GI cancers including CRC and pancreatic cancer (Whiteman and Wilson, 2016). In almost all countries, education and other measures of socioeconomic status are inversely associated with the prevalence of obesity (International Agency for Research on Cancer, 2002).

More obese females compared to obese males in our study had GI cancers. Similarly, two studies showed that, among obese persons, the rate of cancer was higher in females (Wolk, Gridley *et al.*, 2001; Arnold, Pandeya *et al.*, 2015). However, other studies reported that some types of GI cancers had a higher prevalence in men compared to women (Shin, Han *et al.*, 2017; Koyanagi, Matsuo *et al.*, 2018).

In this study, we found that in obese patients, the maximum age at diagnosis was 83 years, while the mean age in our study was 59.4 years and the mean age at diagnosis was 56.63 years. While some studies showed that the mean age of GI cancer diagnosis was 60.7–71 years for esophageal cancer, 66.8–73.1 years for gastric cancer (Anderson, Tavilla *et al.*, 2015), and >50 years for CRC (Ghalkhani, Ghojavand *et al.*, 2016). All these results suggest that the elderly are at higher risk of comorbidities and cancers.

Previous studies concluded that the obese population is more likely to develop CRC (Ma, Yang *et al.*, 2013) and esophageal cancer (International Agency for Research on Cancer, 2002). Moreover, we found that CRC, gastric cancer, and pancreatic cancer were the three most frequent types of cancer in obese patients. However, in non-obese people, CRC was the most common followed by gastric and esophageal cancers.

We found no significance between histopathological features and BMI, but we observed that there was a relatively higher frequency of obese patients who had positive lymph node and negative tumor margins compared to non-obese. Additionally, 42.9% of tumor >10 cm was in obese patients. Overall, we found that most tumors were <5 cm in all patients. Similar to our findings, one study conducted in gastric cancer patients showed that most tumors were <5 cm (Yu, Hu *et al.*, 2018).

Our study has several strengths. First, most of the results in the GI cancer field were similar to our findings with slight differences in the rates; this supports the good quality of our data, which can be used in another statistical study. Additionally, our results are based on clinical records, which supports conducting another study using the same sample. This is the first study done in Saudi Arabia about the prevalence of obesity among GI cancer patients.

However, there are several limitations to our study that should not be neglected. First, there were no data available on BMI and pathological reports, which could be overcome by changing the study design to a prospective study. In Saudi Arabia, the practice of autopsy is underestimated because of our religious and cultural beliefs, so most of our patients that had missing pathological reports were deceased before their tumor was resected or the biopsy was taken. Second, the sample size was inadequate because we investigated only five GI cancers at one hospital. We assume that the effect of obesity on patient outcomes might reach statistical significance with a larger sample size. Thus, we suggest conducting the study in several regions in Saudi Arabia and including all types of cancer.

In conclusion, the most common GI cancer site in obese patients are colorectal, gastric and pancreas in obese group. Moreover, obese females were more than males; thus, we highly recommend screening of obese female in our society.

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Disclosure about Potential Conflict of Interests

The authors declare that there is no conflict of interest regarding the publication of this article.

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