DOI: https://doi.org/10.53350/pjmhs2023175688

ORIGINAL ARTICLE

Association Between Body Mass Index (BMI) and Occurrence of Esophageal Cancer

MEHWISH JABEEN[1], GHULAM HAIDER[2], SANA SEHAR[3], BERKHA RANI[4] , SANA NASIR[5] , MUHAMMAD OWAIS KHAN[6] , SONA DEVI[7] , SHUMAILA NAWAZ KHAN[8]

[1,5,,7,8]Medical Doctor, Department of Medical Oncology , Jinnah Postgraduate Medical Centre Karachi
[2,3,4]Post Graduate Trainee, Department of Medical Oncology, Jinnah Postgraduate Medical Centre Karachi
[6]Medical Doctor, Department of Medical Oncology, Jinnah Postgraduate Medical Centre Karachi
Correspondence to: Mehwish Jabeen, Email: jabeenmehwish38@gmail.com, Cell: 03363191865

ABSTRACT

Aim: Esophageal cancer, one of the leading causes of cancer deaths globally, has been linked to body mass index (BMI). Studies have shown varying associations between BMI and different subtypes of esophageal cancer, namely adenocarcinoma and squamous cell carcinoma. However, there is limited literature from Pakistan on this topic. This study aims to investigate the association between BMI and the occurrence of esophageal cancer in a Pakistani population.

Methods: A prospective observational study was conducted at the Oncology Department of Jinnah Postgraduate Medical Center, Pakistan. Participants included patients over 18 years old with suspected adenocarcinoma or squamous carcinoma of the esophagus. The study utilized a non-probability consecutive sampling technique, and data was collected using a predefined proforma. The association between BMI and types of esophageal carcinoma was analyzed using Chi-square tests.

Results: The study found a statistically significant relationship between increasing BMI and the risk of developing esophageal adenocarcinoma. Conversely, a lower BMI was associated with a higher risk of squamous cell carcinoma. These findings align with existing literature that suggests different BMI associations with esophageal cancer subtypes.

Conclusion: This study underscores the distinct relationships between BMI and different types of esophageal cancer. It highlights the importance of considering BMI as a factor in the risk assessment for esophageal cancer, particularly in the Pakistani population.

Keywords: Esophageal Cancer, Body Mass Index (BMI), Adenocarcinoma, Squamous Cell Carcinoma

INTRODUCTION

Esophageal cancer is amongst the most common neoplastic causes of death worldwide, accounting for an estimated 400,000 deaths annually [1]. Several epidemiological studies have reported on the relationship between esophageal cancer and body fatness, usually measured indirectly by body mass index (BMI). In general, these studies have tended to show that BMI is associated positively with the risk of adenocarcinoma of the esophagus, but inversely with the risk of squamous cell carcinoma [2-4]

In a study by Engeland et al., it was found that compared with normal weighted (BMI 18.5-24.9 kg/m2) an increased risk of esophageal adenocarcinoma (OA) was observed in overweight men (BMI 25-29 kg/m2): RR=1.80 (95% CI: 1.48-2.19) and in obese men (BMI ≥30kg/m2): RR=2.58 (95% CI: 1.81-3.68) [5]

In a study conducted to explore the impact of body mass index (BMI) in patients with esophageal squamous cell carcinoma (ESCC), it was revealed that disease-free survival of the low and high BMI groups was significantly worse than that of the normal BMI group ($P < 0.0001$ between the low and normal BMI groups; $P = 0.0076$ between the normal and high BMI groups). Disease-free survival of the high BMI group was significantly worse than that of the normal BMI group in the propensity score-matched cohort ($P = 0.0020$). Multivariate analysis in this cohort demonstrated that high BMI was an independent prognostic factor (hazard ratio 2.949, 95 % confidence interval, 1.132–7.683) [6]. Evidence reveals that higher values of body mass index are associated with adenocarcinoma of the esophagus [7].

A number of papers have reported the relationships between body mass index (BMI) and esophageal cancer have been published [5-8]; however, these results are inconsistent. There is also a paucity of literature from Pakistan. Therefore, we plan to undertake the present study to find the association between body mass index with types of esophageal carcinoma.

The study had aimed to evaluate the association between body mass index (BMI) and occurrence of esophageal cancer among patients presenting at The Oncology Department, Jinnah Postgraduate Medical Center, Pakistan.

MATERIALS AND METHODS

A prospective observational study was undertaken at the Oncology Department, Jinnah Postgraduate Medical Center, Pakistan between [dates].

Patients with suspected adenocarcinoma or squamous carcinoma of the esophagus who were aged over 18 years were included. Those who did not give consent of participation were excluded.

Using OpenEpi software, an online sample size estimator, the sample size had been determined. By keeping the mean BMI in SCC and ADC as 18.8 ± 3.5 and 21.4 ± 5.8 kg/m2, confidence level of 95%, and a margin of error as 5%, a sample size in each group had been calculated as 54 and a total sample size of 108 was determined.

A non-probability consecutive sampling technique was used to recruit participants. A predefined proforma was used to record the data of each patient. Data had been documented from the patient's medical records after procuring the ethical review boards' approval. All demographic information like age, marital status, gender, ethnicity, body mass index, type of esophageal carcinoma, grade or stage of cancer, etc. was documented in the proforma by the researcher.

The study commenced after acquiring the approval from the institutional review board (IRB) of the institute. Before the study could be started, the aims and objectives were narrated to the patients and informed consent was obtained from the participants. All patients presenting to the OPD, department of oncology, Jinnah Postgraduate Medical Center, Karachi with confirmed diagnosis of esophageal carcinoma.

All demographics including age, sex, race, Body Mass Index (BMI, kg/m2), calculated from the weight and height using Cronk & Roche's formula (1982): BMI = weight divided by the squared height in meters were recorded at baseline. The weight of the patient was evaluated using a weight machine and the weight to the nearest decimal fraction was recorded in a predefined proforma. The height was measured using a stadiometer and height to the nearest decimal was recorded. Using the formula as above, BMI of each patient was determined.

Patients were labeled as either adenocarcinoma or squamous esophageal carcinoma. The patients in each group (Group A: adenocarcinoma and Group B: squamous carcinoma) were categorized according to the BMI. Following BMI categories were used to assess the patients: below 18.5 – underweight range; between 18.5 and 24.9 – healthy weight range; between 25 and 29.9 – overweight range; and between 30 and 39.9 – obese range.

Data was analyzed using IBM SPSS software. The categorical values including the gender, BMI categories, and type of esophageal carcinoma were presented as frequency and proportions. The continuous variables including BMI, age were presented as mean and standard deviation. The association between type of esophageal carcinoma and BMI was determined using a Chi square test. A P value of ≤ .05 was considered statistically significant

The patients were provided with the confidence that the data would be analysed in a confidential manner without the involvement of any outside parties. The data was retained by the main author. There was no collection or recording of any private information, such as an address or mobile phone number.

RESULTS

Table 1 compares demographic characteristics between patients with adenocarcinoma and squamous cell carcinoma. It shows statistically significant differences in weight and BMI between the two groups, indicating a correlation between these factors and the type of esophageal cancer.

Table 1: Demographic Characteristics of Patients

Study Variables	Overall (108)		Adenocarcinoma (n=50)		Squamous (n=58)	
	Mean ± SD	P-Value	Mean ± SD	P-Value	Mean ± SD	P-Value
Age (In years)[#]	49.68±14.08	0.055*	53.40±13.61	0.044*	46.47±13.80	0.238
Height (In cm)	164.52±11.58	0.181	166.33±11.66	0.254	162.96±11.38	0.105
Weight (In kg)	60.49±19.90	0.000**	77.16±14.93	0.105	46.12±9.92	0.002**
BMI (In kg/m^2)	22.19±6.46	0.000**	27.84±4.29	0.001**	17.33±3.23	0.000**
Age at Diagnosis	48.10±14.02	0.109	52.34±13.57	0.050*	44.44±13.46	0.160

#: Age is presented as mean ± sd
*Significant at p<0.05, **Significant at p<0.01

Table 2: Association of participants Characteristics among Patients with adenocarcinoma and squamous

Study Variables	Adenocarcinoma (n=50)	Squamous (n=58)	P-Value
Gender			
Male, n(%)	18(36.0%)	31(53.4%)	0.069
Female, n(%)	32(64.0%)	27(46.6%)	
Ethnicity			
Sindhi, n(%)	8(16.0%)	13(22.4%)	0.473
Urdu, n(%)	10(20.0%)	17(29.3%)	
Punjabi, n(%)	9(18.0%)	7(12.1%)	
Pushtoons, n(%)	16(32.0%)	17(29.3%)	
Others, n(%)	7(14.0%)	4(6.9%)	
Marital status			
Married, n(%)	34(68.0%)	41(70.7%)	0.954
Unmarried, n(%)	15(30.0%)	16(27.6%)	
Divorced, n(%)	1(2.0%)	1(1.7%)	
Employment status			
Business, n(%)	1(2.0%)	3(5.2%)	0.094
Employed, n(%)	24(48.0%)	18(31.0%)	
Student, n(%)	0(0.0%)	4(6.9%)	
Unemployed, n(%)	25(25.0%)	33(56.9%)	
Educational status			
illiterate, n(%)	11(22.0%)	7(12.1%)	0.329
Primary, n(%)	12(24.0%)	17(29.3%)	
Secondary, n(%)	15(30.0%)	12(20.7%)	
Graduate, n(%)	9(18.0%)	15(25.9%)	
Profession, n(%)	3(6.0%)	7(12.1%)	
Family History of Cancer			
Yes, n(%)	10(20.0%)	11(19.0%)	0.892
No, n(%)	40(80.0%)	47(81.0%)	
Family History of Obesity			
Yes, n(%)	22(44.0%)	13(22.4%)	0.845
No, n(%)	28(56.0%)	45(77.6%)	
Symptoms			
Dysphagia, n(%)	4(8.0%)	5(8.6%)	0.981
Cough, n(%)	10(20.0%)	10(17.2%)	
Neck Pain, n(%)	9(18.0%)	10(17.2%)	
Weakness, n(%)	12(24.0%)	18(31.0%)	
SOB, n(%)	13(26.0%)	12(20.7%)	
GERD, n(%)	2(4.0%)	3(5.2%)	
Grade of Cancer			
Grade 1, n(%)	3(6.0%)	5(8.6%)	0.041*
Grade 2, n(%)	31(62.0%)	34(58.6%)	
Grade 3, n(%)	14(28.0%)	12(31.1%)	
Grade 4, n(%)	0(0.0%)	1(1.7%)	
Grade 2 & 3, n(%)	2(4.0%)	0(0.0%)	
Clinical Staging			
Stage 1, n(%)	4(8.0%)	2(3.4%)	0.671
Stage 2, n(%)	10(20.0%)	13(22.4%)	
Stage 3, n(%)	26(52.0%)	28(48.3%)	
Stage 4, n(%)	10(20.0%)	15(25.9%)	
Lifestyle			
Addiction, n(%)	34(68.0%)	36(62.1%)	0.658
Diet, n(%)	9(18.0%)	10(17.2%)	
Exercise, n(%)	7(14.0%)	12(20.7%)	
Comorbid			
HTN, n(%)	27(54.0%)	29(50.0%)	0.557
Grade 2, n(%)	17(34.0%)	19(32.8%)	
Grade 3, n(%)	3(6.0%)	8(13.8%)	
Grade 4, n(%)	3(6.0%)	2(3.4%)	
Site of Metastasis			
Brain, n(%)	3(6.0%)	9(15.5%)	0.501
Lung, n(%)	11(22.0%)	16(27.6%)	
Liver, n(%)	11(22.0%)	13(22.4%)	
Bone, n(%)	14(28.0%)	11(19.0%)	
Peritoneum, n(%)	3(6.0%)	3(5.2%)	
Liver, Lung, Bone, n(%)	4(8.0%)	5(8.6%)	
Liver, Bone, n(%)	2(4.0%)	1(1.7%)	
Liver, Lung, n(%)	2(4.0%)	0(0.0%)	

Applied Chi-Square test
OR= Odd Ratio, HTN= Hypertension, DM= Diabetes Mellitus, SOB= Shortness of Breath, GERD= Gastroesophageal Reflux Disease

Table 3: Association of Body Mass Index among Patients with Esophageal Carcinomas (adenocarcinoma and squamous)

Body Mass Index (kg/m^2)	Adenocarcinoma (n=50)	Squamous (n=58)	OR	P-Value
<18, n(%)	3(6.0%)	45(77.6%)	0.018	0.000**
>18, n(%)	47(94.0%)	13(22.4%)		
BMI Classification				
Underweight, n(%)	3(6.0%)	48(82.8%)	N.A	0.000**
Normal, n(%)	5(10.0%)	7(12.1%)		
Overweight, n(%)	26(52.0%)	3(5.2%)		
Obese, n(%)	16(32.0%)	0(0.0%)		

Applied Chi-Square test

DISCUSSION

The association between BMI and the risk for the development of esophageal cancer and its subtypes has been evaluated in numerous studies. However, most studies focused on the impact of BMI on any one subtype of esophageal cancer rather than comparing the different subtypes. The present research studied BMI and the risk of developing esophageal cancer, squamous cell carcinoma, or adenocarcinoma.

Our findings indicated a statistically significant relationship between increasing BMI and the risk of developing esophageal cancer. However, the histological subtype of cancer associated with high BMI was esophageal adenocarcinoma. It was also revealed that low BMI contributed to the development of esophageal cancer but of a different subtype, i.e., squamous cell carcinoma. These findings were consistent with the study by Brenner et al., where a statistically significant relationship between BMI and its association with tumor development has been documented. [9]

In a study by Tian et al., the relationship between BMI and esophageal cancers was analyzed. The study noted that two histological subtypes of esophageal cancer, particularly EADC, and ESCC, were linked with different risk factors. It was revealed that since individuals with a much higher BMI suffered from a higher prevalence of gastroesophageal reflux disease, it led to the development of Barrett's esophagus in such individuals, a premalignant condition leading up to EADC. [10] Hence why EADC was more common in individuals who were overweight.

A similar study conducted in the Korean population highlighted that individuals with a BMI of less than 18.5 kg/m^2 were found to have a 73% increased risk of developing esophageal cancer compared to people with a normal BMI. On the other end of

the spectrum, it was also noted that individuals with a greater BMI of more than 25 kg/m^2 had a 30% lower risk of developing esophageal cancer. When the protective effect of low BMI against esophageal cancer was studied, it was identified that a low weight contributed to the development of squamous cell carcinoma, while weight gain reduced its risk.[11]

A negative association was found between BMI and cancer development in another study aimed at understanding the factors contributing to esophageal cancer development. [12] However, this conclusion was mainly based on the population comprising Asians, with very few individuals suffering from obesity. The application of BMI as a marker for obesity has been used widely, and its associations with esophageal cancer development have been supported in numerous case-control and cohort studies [13, 14, 15].

A large case-control study conducted in the Australian population also showed factors including high BMI and long-term weight gain to a reduced risk of developing esophageal squamous cell carcinoma. It was revealed that there was a 35% reduction in the risk of developing cancer per 5-unit increase in BMI. [17]

The underlying pathological reasoning behind the negative association between BMI and esophageal squamous cell carcinoma development is unclear. Some studies have shown that a poor diet leading to low BMI contributes to esophageal squamous cell cancer development. [18] Among the Asian population, a low BMI secondary to a diet deficient in micronutrients or malnutrition are implicated as causes that lead to a much higher risk of developing esophageal squamous cell carcinoma. [19]

A study was conducted to assess the association of nutritional status with esophageal squamous cell carcinoma. It aimed to determine whether nutritional status played a role in the anticancer immune response in patients. The findings suggested that a good nutritional status is essential to augment the antitumor immune response, and that nutritional supplementation decreased the rate of development of an invasive tumor. [20]

Our study was limited by a small low sample size. Additionally, BMI was calculated using the weight and height collected only once at baseline. However, the weight and other parameters of the participants may have changed during subsequent follow-ups.

CONCLUSION

The study establishes a significant association between body mass index (BMI) and esophageal cancer subtypes in a Pakistani population. It reveals that a higher BMI significantly increases the risk of esophageal adenocarcinoma, whereas a lower BMI is more associated with squamous cell carcinoma. These findings are consistent with global research trends and emphasize the role of BMI as a critical factor in esophageal cancer risk assessment. The study highlights the need for targeted public health strategies and personalized medical approaches considering BMI in the prevention and management of esophageal cancer in Pakistan.

REFERENCES

1. Ferlay J,Bray F,Pisani P,Parkin DM. GLOBOCAN 2002: cancer incidence, mortality and prevalence worldwide. IARC CancerBase No. 5. version 2.0. Lyon: IARC Press, 2004.
2. Ryan AM,Rowley SP,Fitzgerald AP,Ravi N,Reynolds JV. Adenocarcinoma of the oesophagus and gastric cardia: male preponderance in association with obesity. Eur J Cancer 2006; 42: 1151– 8.
3. Lindblad M,Rodriguez LA,Lagergren J. Body mass, tobacco and alcohol and risk of esophageal, gastric cardia, and gastric non-cardia adenocarcinoma among men and women in a nested case-control study. Cancer Causes Control 2005; 16: 285– 94.
4. Engeland A,Tretli S,Bjorge T. Height and body mass index in relation to esophageal cancer; 23-year follow-up of two million Norwegian men and women. Cancer Causes Control 2004; 15: 837– 43.
5. Engeland A, Tretli S, Bjørge T. Height and body mass index in relation to esophageal cancer; 23-year follow-up of two million Norwegian men and women. Cancer Causes Control. 2004 Oct;15(8):837-43. doi: 10.1023/B:CACO.0000043434.21558.ea. PMID: 15456997.
6. Watanabe, M., Ishimoto, T., Baba, Y. et al. Prognostic Impact of Body Mass Index in Patients with Squamous Cell Carcinoma of the Esophagus. Ann Surg Oncol 20, 3984–3991 (2013). https://doi.org/10.1245/s10434-013-3073-8
7. Henry MA, Lerco MM, Ribeiro PW, Rodrigues MA. Epidemiological features of esophageal cancer. Squamous cell carcinoma versus adenocarcinoma. Acta Cirurgica Brasileira. 2014;29:389-93.
8. Kort EJ, Sevensma E, Fitzgerald TL. Trends in esophageal cancer and body mass index by race and gender in the state of Michigan. BMC gastroenterology. 2009 Dec;9(1):1-7.
9. Brenner DR. Cancer incidence due to excess body weight and leisure-time physical inactivity in Canada: implications for prevention. Preventive medicine. 2014 Sep 1;66:131-9.
10. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. Journal of gastroenterology and hepatology. 2020 May;35(5):730-43.
11. Choi YJ, Lee DH, Do Han K, Yoon H, Shin CM, Park YS, Kim N. Joint effects of low body mass index and alcohol consumption on developing esophageal squamous cell cancer: A korean nationwide population-based cohort study. Asian Pacific Journal of Cancer Prevention: APJCP. 2017;18(7):1881.
12. Yang J, Liu X, Cao S, Dong X, Rao S, Cai K. Understanding esophageal cancer: the challenges and opportunities for the next decade. Frontiers in oncology. 2020 Sep 10;10:1727.
13. Cancer Genome Atlas Research Network. Integrated genomic characterization of oesophageal carcinoma. Nature. 2017 Jan 1;541(7636):169.
14. Chen W, Sun K, Zheng R, Zeng H, Zhang S, Xia C, Yang Z, Li H, Zou X, He J. Cancer incidence and mortality in China, 2014. Chinese journal of cancer research. 2018 Feb;30(1):1.
15. Castro C, Bosetti C, Malvezzi M, Bertuccio P, Levi F, Negri E, La Vecchia C, Lunet N. Patterns and trends in esophageal cancer mortality and incidence in Europe (1980–2011) and predictions to 2015. Annals of oncology. 2014 Jan 1;25(1):283-90.
16. Lahmann PH, Pandeya N, Webb PM, Green AC, Whiteman DC, Australian Cancer Study. Body mass index, long-term weight change, and esophageal squamous cell carcinoma: Is the inverse association modified by smoking status?. Cancer. 2012 Apr 1;118(7):1901-9.
17. Liu J, Wang J, Leng Y, Lv C. Intake of fruit and vegetables and risk of esophageal squamous cell carcinoma: a meta-analysis of observational studies. International journal of cancer. 2013 Jul 15;133(2):473-85.
18. Abnet CC, Arnold M, Wei WQ. Epidemiology of esophageal squamous cell carcinoma. Gastroenterology. 2018 Jan 1;154(2):360-73.
19. Chen MF, Hsieh CC, Chen PT, Lu MS. Role of nutritional status in the treatment outcome for esophageal squamous cell carcinoma. Nutrients. 2021 Aug 28;13(9):2997.