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Blood biochemical markers and risk factors for esophageal cancer: A study in Gezira State, Sudan

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Abstract

Esophageal cancer (EC) poses a significant health challenge in Sudan, particularly in the Gezira State, yet the associated risk factors and biochemical markers remain understudied. This study investigated the relationship between various biochemical markers, dietary habits, and lifestyle factors with EC in this region. A cross-sectional study was conducted at the National Cancer Institute in Wad-Medani, Gezira State, Sudan, from 2021 to 2022, involving 50 participants. Data on dietary habits, smoking, and alcohol consumption were collected using a structured questionnaire, and hemoglobin, albumin, and serum protein levels were measured. The study found a significant association between gender and EC, with a higher prevalence in females (64%, p=0.021). Most patients were diagnosed with locally advanced EC and exhibited reduced serum albumin and total protein levels. A significant correlation was observed between cancer stage and albumin levels (p=0.000), as well as between obesity and EC stages (p=0.046). These findings highlight the importance of considering socio-demographic factors and biochemical markers in the risk assessment and management of EC in Sudan.

Keywords: Esophageal cancer; Biochemical markers; Risk factors; Albumin; Serum protein

1. Introduction

Esophageal cancer is a malignant neoplasm arising from the esophageal epithelium, with a significant global health burden, particularly in developing countries. Despite advancements in diagnostic and therapeutic strategies, the prognosis for esophageal cancer remains poor. Early detection and identification of risk factors are crucial for improving patient outcomes, (Cheifetz *et al.,* 2011). Sudan, particularly the Gezira State, has been reported to have a high incidence of esophageal cancer. However, the underlying risk factors and associated biochemical markers remain poorly understood. Several studies have suggested a strong association between dietary factors, lifestyle habits, and genetic predisposition in the development of esophageal cancer, (Moawia *et al.,* 2012).

This study aims to investigate the association between various biochemical markers and risk factors, including dietary habits, smoking, and alcohol consumption, with esophageal cancer in Gezira State, Sudan. By identifying these factors, we hope to contribute to early detection, prevention, and improved management of esophageal cancer in the region.

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2. Material and methods

2.1. Study Setting

This study was conducted at the National Cancer Institute (NCI) in Wad-Medani, Gezira State, Sudan, from 2021 to 2022. The NCI, provides comprehensive cancer care to patients throughout Sudan.

2.2. Study Participants

This study employed a cross-sectional design to assess the potential link between selected biochemical markers, dietary habits (with a focus on both the types and amounts of food intake), and the prevalence of esophageal cancer. The study sample consisted of male and female patients aged between 20 and over 60 years who were actively receiving medical attention at NCI during the designated study period.

2.3. Inclusion Criteria

Eligible participants were those who fulfilled the predetermined study specifications and presented with a confirmed diagnosis of esophageal cancer.

2.4. Exclusion Criteria

Individuals were excluded from the study if they had a documented history of any other malignancy prior to their esophageal cancer diagnosis.

2.5. Data collection

Risk factors for esophageal cancer were assessed through a structured questionnaire administered to participants at the National Cancer Institute clinics in Wad-Medani after diagnosis. Interviews elicited data on dietary habits (type, quantity, frequency, smoking, and alcohol consumption). A five-page questionnaire, including a food frequency questionnaire (FFQ), was administered. Fifty participants completed the questionnaire. Hemoglobin, albumin, and serum protein levels were also measured.

2.6. Laboratory Analyses

2.6.1. Total Protein Measurement

Total protein concentrations in the collected samples were quantitatively determined using spectrophotometry. This technique involves measuring the absorbance of light by the sample at specific wavelengths. In this study, measurements were conducted across a wavelength range of 200-400 nm, which is appropriate for the detection of peptide bonds and aromatic amino acids, the primary light-absorbing components of proteins. A standardized protein assay, adhering to the guidelines established by the National Committee for Clinical Laboratory Standards (NCCLS 2000), was employed to ensure accuracy and reproducibility of the measurements. This assay provides a reliable method for determining the total protein content in biological samples.

2.6.2. Serum Albumin Measurement

Serum albumin levels, a key indicator of nutritional status and liver function, were quantified using the Bromocresol Green (BCG) dye-binding method. This colorimetric assay is based on the principle that albumin binds specifically to BCG dye, resulting in a shift in the dye's absorbance spectrum (NCCLS 2000).

2.6.3. Hemoglobin Measurement

Hemoglobin concentration was determined spectrophotometrically at 540 nm using the cyano-methemoglobin method (NCCLS, 2000). A 20 µL sample was mixed with 200 µL of hemolyzing reagent, incubated for 10 minutes at room temperature, and the resulting absorbance compared against a standard curve generated with a known hemoglobin concentration.

2.7. Serum Albumin Levels in Patients

In adults, serum albumin levels are categorized as follows: normal (35-50 g/L), mildly undernourished (28 to <35 g/L), moderately undernourished (21 to <28 g/L), and severely undernourished (<21 g/L). Normal blood hemoglobin levels range from 13.5-17.5 g/dL in men and 12-15.5 g/dL in women.

2.8. Statistical analysis

All data were statistically analysed by using Statistical Package for the Social Sciences (SPSS) version 22.

3. Results

3.1. Demographic Characteristics and Esophageal Cancer Prevalence

Table (1) illustrates that the study population predominantly consisted of individuals over 60 years old (46%), with a significant female predominance (64%, p=0.021). Table (2) demonstrates the geographic distribution of esophageal cancer (EC), with Gezira state displaying the highest prevalence (52%). Blue Nile and Kassala States each exhibited 8%, while other states ranged from 2% to 6%. Age distribution did not significantly correlate with EC (p = 0.056). While the prevalence of EC through the respondents depend on their tribes as follow: the highest percentage of EC patients was in Kawahla (14%), Lahween (10%), Rifa'iya (8%), Gali (8%), Shukriya (6%), Agileia (4%), Hadandawa (4%), Bin Amer (4%), Zaghawa (4%), and others tribes collectively were (38%).

Table 1 Distribution of respondents according to their demographic characteristics: gender and age (n=50)

Characteristic	Category	Frequency (n)	Percentage (%)	p- value
Gender	Male	18	36	0.021*
	Female	32	64	
Age (years)	20 – 40	9	18	0.056
	40 – 60	18	36	
	> 60	23	46	
Total		50	100	

*P-value considered significant at less than 0.05 levels

Table 2 Prevalence of esophageal cancer among respondents by state and tribe (n = 50)

State	Frequency (n)	Percentage (%)	Tribe	Frequency (n)	Percentage (%)
Gezira	26	52	*Kawahla*	7	14
Blue Nile	4	8	*Lahween*	5	10
Kassala	4	8	*Rifa'iya*	4	8
Sennar	3	6	*Gali*	4	8
Northern	3	6	*Shukriya*	3	6
Halfa	3	6	*Agileia*	2	4
Kordofan	2	4	*Hadandawa*	2	4
Red Sea	2	4	*Bin Amer*	2	4
Gedaref	1	2	*Zaghawa*	2	4
Khartoum	1	2	Other Tribes	19	38
Darfur	1	2			
Total	50	100	Total	50	100

3.2. Association of age, gender, body weight with EC stages

In Table (3) Most patients (23/50) were elderly males (> 60 yrs.) with locally advanced EC. Grade two obesity was associated with the highest incidence of locally advanced EC (19/50). Only one female patient presented with metastatic stage of EC, while no cases of early-stage cancer were observed. A significant association was found between obesity

levels and three cancer stages (p=0.046). No significant association was found between age (p=0.403) or gender (p=0.055) and three cancer stages.

Table 3 Association of age, gender, body weight with EC stages (n = 50)

Variable	Stage			Total (n)	p- value
	Early (n)	Metastatic (n)	Local advance (n)		
Age (year)					0.403
20-40	0	0	9	9	
40-60	0	1	17	18	
Above 60	0	0	23	23	
Total	0	1	49	50	
Gender					0.055
Male	0	0	18	1	
Female	0	1	31	49	
Total	0	1	49	50	
Weight					0.046*
Under weight	0	0	1	1	
Normal weight	0	0	9	9	
Over weight	0	1	14	15	
Obesity class1	0	0	6	6	
Obesity class 2	0	0	19	19	
Obesity class3	0	0	0	0	
Total	0	1	49	50	

*P-value considered significant at less than 0.05 levels

3.3. Correlation of serum protein levels with esophageal cancer stage

As shown in Table (4), the majority of EC patients displayed a moderate reduction in total protein (5.0-8.0 g/dL) levels. The majority of EC patients were diagnosed with locally advanced disease and exhibited reduction in total protein levels ranging from less than 5.0 to 8.0 g/dL.

Table 4 Blood biochemical indices of esophageal cancer patients (n = 50)

Biochemical Index	Classification	Range (g/dL)	Frequency n	Percentage (%)
Hemoglobin	Severe	< 7.4	4	8
	Moderate	7.4 - 10.4	41	82
	Mild	> 10.4	5	10
	Normal	12.0 - 17.5	0	0
	Total		50	100
Albumin	Severe	< 2.1	1	2
	Moderate	2.1 - 2.8	48	96
	Mild	2.8 - 3.5	1	2

	Normal	3.5 - 5.0	0	0
	Total		50	100
Total Protein	Severe	< 5.0	1	2
	Moderate	5.0 - 8.0	49	98
	Mild	> 8.0	0	0
	Normal	6.0 - 8.0	0	0
	Total		50	100

3.4. Association of serum albumin with esophageal cancer stage

As shown in Table (5), a majority of EC patients (47/50) were diagnosed with locally advanced disease and exhibited serum albumin levels ranging from 7.4 to 10.4 g/dL. Statistical analysis revealed a significant correlation (p=0.000) between cancer stage and albumin levels.

Table 5 Association between serum albumin levels and esophageal cancer stage (n = 50)

Albumin Level (g/dL)	**Stage**			**Total (n)**	**p- value**
	Early (n)	**Metastatic (n)**	**Local advance (n)**		
Severe (< 7.4)	0	0	1	1	0.000*
Moderate (7.4 - 10.4)	0	1	47	48	
Mild (> 10.4)	0	0	1	1	
Normal (12.0 - 17.5)	0	0	0	0	
Total	0	1	49	50	

*P-value considered significant at less than 0.05 levels

4. Discussion

While age distribution among participants approached significance (p=0.056), gender demonstrated a significant association with EC development (p=0.021), with a higher prevalence observed in females (64%).

It is noticeable in these results that there is a close relationship between the geographical areas inhabited by patients with oesophageal cancer. Most of them were from Gezira state and nearby states such as Sennar, Kassala and Gedaref. This may be due to the proximity of the NCI in Gezira state to their areas of residence. There is also the distribution of tribes such as the Kawahla and Rifa'iya in central Sudan, i.e., in Gezira state, and the Beni Amer and Hadandawa in eastern Sudan.

Our findings regarding the geographical distribution of EC in Sudan are supported by Najla et al., (2015), which identified Guhaina and Jaali ethnicities as prevalent among EC patients, with a concentration in Gezira and Alqadarif states. This aligns with our observation of higher patient numbers from these areas. However, Mohamed et al., (2016) reported differing cancer incidence rates across Sudanese states, noting significantly higher rates in Northern Sudan, River Nile, and Khartoum compared to Al Gedarif and other regions. Notably, they found a proportionally higher frequency of EC in Kassala, diverging from the national trend. Asombang et al., (2019) also highlighted geographical variations in EC rates, attributing them to population density and dietary habits, which supports our observation of increased patient numbers from specific states. These studies collectively underscore the complex interplay of ethnicity, geographical location, and lifestyle factors in EC distribution within Sudan, emphasizing the need for region-specific investigations.

Consistent with findings from Conway et al., (2023), Ahmed et al., (2022), and Sara et al., (2020), our study underscores the importance of considering socio-demographic factors in EC risk. These studies advocate for public health measures incorporating genetic screening and comprehensive investigations into environmental and dietary influences. Our study, with a 95.86% response rate, revealed a demographic profile predominantly female (68.8%) and under 50 years

(57.8%). Existing literature supports the association between older age and increased EC risk, potentially due to cumulative exposure to risk factors. Similarly, male gender is often linked to higher EC incidence, possibly due to lifestyle factors. Obesity, a recognized EC risk factor, may contribute to chronic inflammation and GERD, influencing tumor aggressiveness and prognosis. The stage of EC at diagnosis, significantly impacting treatment outcomes, is influenced by age, gender, and body weight. Understanding these complex interactions is crucial for developing effective EC prevention, early detection, and treatment strategies.

Multiple studies (Kong et al., 2020; Kubo et al., 2009, 2010) indicate that deviations in serum total protein, encompassing albumin and globulin levels, correlate with diverse cancers, including esophageal carcinoma. Serum total protein, a composite measure of these proteins, is a recognized indicator of systemic physiological status. Specifically, hypoalbuminemia, potentially resulting from malnutrition, has been observed in cancer patients and may adversely affect prognosis and therapeutic response. This discussion examines the potential clinical significance of serum total protein alterations in esophageal cancer.

Consistent with previous research, this study confirms the prognostic significance of serum albumin levels in EC. Wang et al., (2023) demonstrated that severe hypoalbuminemia post-minimally invasive esophagectomy (MIE) predicted anastomotic leakage (AL) in neoadjuvant chemotherapy (NCT)-treated EC patients, aligning with our observations. Similarly, Wu et al., (2015) identified pre-therapeutic albumin as a key prognostic factor for short- and long-term outcomes following esophagectomy, supporting its integration into preoperative assessments. Our findings also partially corroborate Nassri et al., (2014), who reported albumin as an independent predictor of early mortality in EC.

5. Conclusion

This study provides valuable insights into the risk factors and biochemical markers associated with esophageal cancer in Gezira State, Sudan. The predominance of EC in females, the correlation between obesity and cancer stage, and the significant association between reduced serum albumin levels and advanced EC highlight the need for targeted screening and preventive strategies. The observed geographical distribution of EC cases underscores the influence of regional factors, including dietary habits and environmental exposures. Further research is warranted to explore these factors in detail and to develop effective interventions to reduce the burden of EC in this region.

Compliance with ethical standards

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Disclosure of conflict of interest

All authors have no conflict of interest.

Statement of ethical approval

Ethical approval was obtained from Faculty of Agricultural Sciences, University of Gezira ethical committee as well as Ministry of Health Gezira State ethical committee.

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Statement of informed consent

Informed verbal consent was obtained from all individual participants included in the study.

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