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Risk Factors for Esophageal Cancer in Gadarif State in Eastern Sudan

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Abstract

Background: Esophageal carcinoma is not common disease in Sudan especially in eastern Sudan although it is neglected and patients usually presented at late stages of the disease. The main aim of this study is to identify the demographic, clinical and laboratory risk factors in Gadardif state.

Materials and Methods: This was a prospective analytical cross sectional study of one hundred and fifty patients for whom endoscopic examination was done, esophageal tissue biopsy was taken and examination was performed for these biopsies. A Statistical data collected by questionnaire.

Results: Family history was most risk factors for esophageal cancer in general 34(68%), while16 (32%) had no family history of malignancy followed by smoking which found in 22 (44% of patients in the study), while nonsmokers were found to be 28 (56% of patients in the study).

Conclusions: Here, we summarize there was association between family history, smoking and esophageal cancer.

Keywords: Esophageal Cancer, Risk Factors, Sudanese

1. Introduction

Esophageal cancer is among the ten most common malignancies worldwide and ranks as the sixth leading cause of death from cancer. It constitutes 7% of all gastrointestinal cancers and is one of the most lethal of all cancers [1]. Globally esophageal cancer ranks as the sixth most common cancer among males and ninth most common cancer among females. However, in India, it is the second most common cancer among males and the fourth most common cancer among females [2] The incidence of esophageal cancer varies greatly between developed and developing countries and a 50-fold difference has been observed between high and low-risk populations. It is more common in Asian than in western countries. The esophageal cancer belt is a geographic area of high incidence, which stretches from north-central China westward through Central Asia to northern Iran [1] esophageal cancer exists in two main forms with distinct etiological and pathological characteristics, squamous cell carcinoma (SCC) and adenocarcinoma. More than 90% of esophageal cancers worldwide are SCCs, although adenocarcinomas are more prevalent in the USA. SCC is often preceded by increased proliferation of esophageal epithelial cells leading to basal cell hyperplasia, dysplasia, and carcinoma in situ [3]. Tobacco smoking and alcohol drinking are strongly associated with the risk of esophageal SCC and to a lesser degree with the risk of esophageal adenocarcinoma. Reports from Southern India suggest that ESCC occurs in more than 80% of cases in chronic tobacco smokers that is further potentiated by heavy use of alcohol and additional prevailing risk factors, including nutritional factors and vitamin deficiencies [1]. Viral infection like HPV, CMV, HSV and EBV also are risk factors [4].

2. Materials and Methods

This was a prospective analytical cross sectional study. The study population consisted of 150 esophageal tissues diagnosed as esophageal squamous cell carcinoma. One section from each block measures four micrometers was cut and then stained in H&E to confirm diagnosis of each block. Then five sections were cut from each recruited block each section. Each section from the remainder three sections (measuring four microns) was floated in 70% ethanol and water bath (Electrothermal ser NO.18861434-China) at 40° C, consecutively. Each floated section was mounted on positive charge immune slide (Thermo Scientific- Italy) to detect immune expression of HPV, HSV, CMV, EPV and P53 in each sample all slides contained sections were dried in dry oven (WTC binder 7200 TUTTLINGEN, B28, NO.88485-USA) at $60c^0$ for 30 minutes. Paraffin wax sections were detected using immunohistochemistry. For IHCAb-3 (Clone K1H8) mouse monoclonal antibody biomarker was used to detect presence of HPV type (6, 11, 16, 18, 31, 33, 42, 51, 52, 56 and 58). LMP-1 biomarker was used to detect expression of EBV. Ab-1 rabbit polyclonal antibody biomarker was used to detect HSV primary antibody used to detect CMV and P53. All used biomarkers come from (Dako, Carpintera) was used to detect HR- HPV, HSV, CMV, EPV infections in paraffin sections using specific primer to each virus. Demographic data collected by questionnaire.

2.1. Statistic

All obtained results were analysed by Statistical Package for the Social Sciences (SPSS) version 20, with Pearson's chi-square test used to assess intergroup significance Ninety five (95%) confidence interval and p value was calculated (level of significance was set at P. value of 0.05).. Other variables, frequencies were calculated.

3. Results

A total of 150 samples from cases patients with histopathologically confirmed esophageal squamous cell carcinomas. The age of patients was ranged between 60 years and 87 years. Patients below 60 years of age were 41 (27.3%) while 109 (72.7%) their ages were 60 years and above (Figure 1).Sixty three 63 (42%) were well differentiated, while 87 (58%) were poor differentiated esophageal carcinoma diagnosed. There was male predominance where the females

constituted 22 (44%), while 28 (56%) were males (Figure 2).More than half of the patients in the study 27 (54%) were from Gedarif town, while 2 3 (46%) were from the rural areas. The majority of the patients had family history of malignancy in general 34 (68%), while16 (32%) had no family history of malignancy (Figure 3).Smokers were represented 22 (44% of patients in the study) while nonsmokers were found to be 28 (56% of patients in the study) (Figure4). Patients smoked less than 20 cigarettes per day were 15 (30% of the total number of patients) while those smoked 20 cigarettes and above per day were 7 (14% of the total number of patients) .When the patients asked about duration of smoking 9 (18% of the total number of patients) were smoked less than 10 years and 13 (26% were smoked 10 years and above. Most of the patients in the study were not alcohol drinkers 37 (74%), while 13 (26%) were alcohol users (Figure5). Ten of patients drinker for10 years and above while 3 of them drinker for less than 10 years, represented 20% and 6% of the total number of patients respectively. Majority of the patients in the study 34 (68%) used to intake hot drinks and foods, only 16 (32%) not used hot drinks and foods (Figure 6). History of swallowing corrosive materials was found in 16 (32%) and it was not found in the majority of the patients 34 (68%). Patients with history of esophageal reflux was found in 24 (48%) and it was not found in 26 (52%) of the patients (Figure 7). Changes of human papilloma virus infection were also examined for, they were found in more than half of the patients 27 (54%) and absent in 23 (46%) of them.

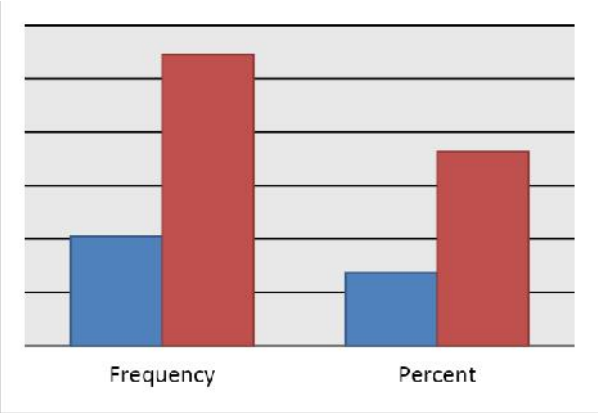

Fig 1: Frequency of age among study population

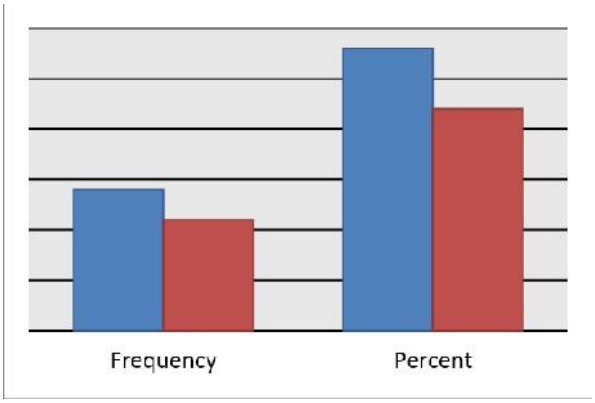

Fig 2: Frequency of gender among study group

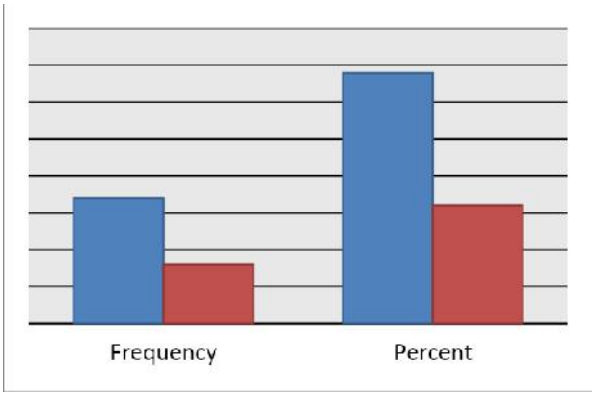

Fig 3: Frequency of family history of malignancy among study group

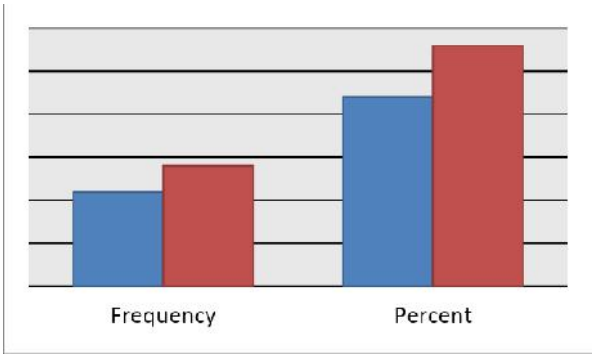

Fig 4: Frequency of smoking among study group

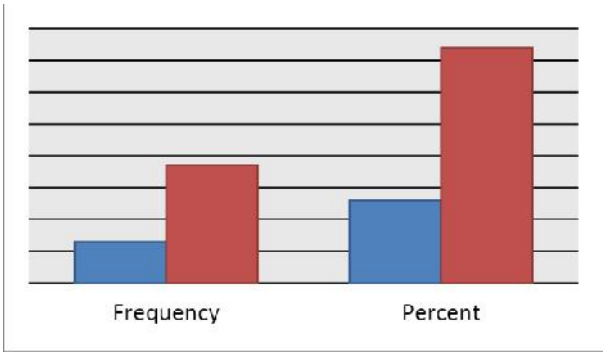

Fig 5: Frequency of alcohol drink among study group

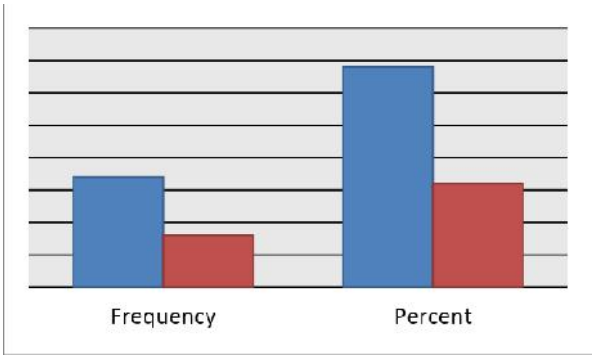

Fig 6: Frequency of intake hot drink and food among study group

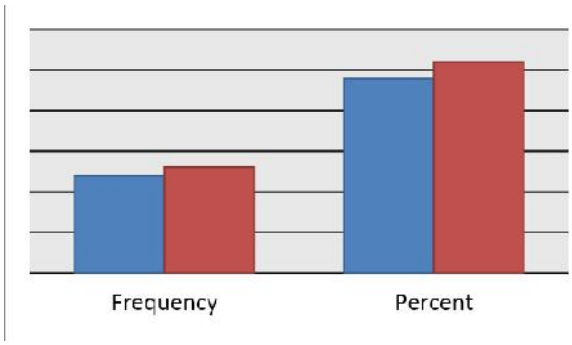

Fig 7: History of esophageal reflux among group study

The association between different risk factors and presence or absence of esophageal carcinoma:

The association between the age of the patients and presence and absence of esophageal carcinoma:

Presence of oesophageal cancer was found to be 29 (80.6%) in patient of 50 years and above and absent in 7 (19.4%) of them. It was found to be 6 (42.9%) in patients of less than 50 years and absent in 8 (57.1%) of them. Age is significantly associated with the occurrence of oesophageal carcinoma at P value of 0.01 and 95% CI 0.532 (0.285-0.995).

Table1: Showed the presence or absence of esophageal carcinoma by age

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Patient's Age <50 years	6 (42.9%)	8 (57.1%)	14 (100%)
Patient's Age ≥50 years	29 (80.6%)	7 (19.4%)	36 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between the sex of the patients and presence and absence of esophageal cancer:

Presence of oesophageal cancer was found in 20 (71.4%) of male and absent in 8 (28.6%) of them. It was also found in 15 (68.2%) of female and absent in 7 (31.8%) of them. there was no significant association between the sex of the patients and presence of cancer at P value of (0.8) and 95%CI 1.048 (0.724-1.516).

Table 2: Showed the presence or absence of oesophageal carcinoma by sex of the patient

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Male Patients	20 (71.4%)	8 (28.6%)	28 (100%)
Female Patients	15 (68.2%)	7 (31.8%)	22 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between the residence of the patients and presence or absence of esophageal cancer:

The oesophageal cancer was found in 20 (74.1%) of patients live in Gedarif town and 15 (65.2%) of patient live in rural areas .while it was absent in 7 (25.9%) and 8 (34.8%) of them respectively There was no significant association between the residence of the patients and presence of cancer at P value of 0.496 and 95% CI 1.136 (0.782-1.649).

Table 3: Showed the presence or absence of oesophageal carcinoma by residence of the patient

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Gadarif Residence	20 (74.1%)	7 (25.9%)	27 (100%)
Rural Residence	15 (68.2%)	8 (34.8%)	23 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between family history and presence or absence of esophageal cancer:

Oesophageal cancer found to be in 28 (82.4%) of the patients with family history of cancer and absent in 6 (17.6%) of them. While it found in 7 (43.8%) of patients with no family history of cancer and absent in 9 (56.3) of them .The association between patient with family history of cancer was found to be significant at P.value 0.005 and 95% CI 1.882 (1.057-3.352).

Table 4: Showed the presence or absence of oesophageal carcinoma by family history

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Presence of Cancer in Family	28 (82.4%)	6 (13.6%)	34 (100%)
Absence of Cancer in Family	7 (65.2%)	9 (34.8%)	16 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between use of tobacco and presence or absence of esophageal cancer:

Oesophageal cancer found in 15 (68.2%) of the patients used tobacco and absent in 7 (31.8%) of them. While it was found in 20 (71.4%) in patients did not used tobacco and absent in 8 (28.6%) of them .There was no significant association between use of tobacco and presence of cancer at P.value of 0.804 and 95% CI.955 (660-1.381).

Table 5: Showed the presence or absence of oesophageal carcinoma by use of tobacco

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Using Tobacco	15 (68.2%)	7 (31.8%)	22 (100%)
Not Using Tobacco	20 (71.4%)	8 (28.6%)	28 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between the number of cigarette/day and presence and absence of esophageal cancer:

Oesophageal cancer found to be in 5 (71.4%) in patients smoked 20 cigarette/day and above and absent in 2 (28.6%) of them. While it was found in 10 (66.7%) of patients smoked less than 20 cigarette/day and absent in 5 (33.3%) of them 'There was no significant association between the number of cigarette used per day and presence of the cancer at P value of 0.945.

Table 6: Showed the presence or absence of oesophageal carcinoma by number of cigarettes/day

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Non Smoking	20 (71.4%)	8 (29.6%)	28 (100%)
Smoking < 20 cigarettes /day	10 (66.7%)	5 (33.3%)	15 (100%)
Smoking ≥ 20 cigarettes /day	5 (71.4%)	2 (28.6%)	7 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between the duration of smoking and presence or absence of esophageal cancer:

Oesophageal cancer was found in 12 (92.3%) of patients smoked for 10 years and above and absent in 1 (7.7%) of them. It was found in 3 (33.3%) of patients smoked for less than 10 years and absent in 6 (66.7%) of them. There was significant association between the duration of smoking and presence of cancer at (P .value of 0.012).

Table 7: Showed the presence or absence of oesophageal carcinoma by duration of smoking

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Non Smoking	20 (71.4%)	8 (29.6%)	28 (100%)
Duration of Smoking< 10 years	3 (33.3%)	6 (66.7%)	9 (100%)
Duration of Smoking ≥10 years	12 (92.3%)	1 (7.7%)	13 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between alcohol intake and presence or absence of esophageal carcinoma:

The oesophageal cancer was found in 11 (84.6%) of the patients used alcohol and absent in 2 (15.4%) of them. It was found in 24 (64.9%) of patients not used alcohol and absent in 13 (35.1%) of them .There was no significant association between the use of alcohol and presence of the cancer (P.value0.181).

Table 8: Showed the presence or absence of oesophageal carcinoma by alcohol intake

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Using of Alcohol	11 (84.6%)	2 (15.4%)	13 (100%)
Not Using of Alcohol	24 (64.9%)	13 (35.1%)	37 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between the duration of alcohol used and presence and absence of the cancer:

The cancer was found in 1 (33.3%) of patients used alcohol for less than 10 years and absent in 2 (66.7%) of them .It was in 10 (100%) of the patients used alcohol for 10 years and above. There was significant association between the duration of alcohol used and presence of the cancer at P.value 0.036.

Table 9: Showed the presence or absence of esophageal carcinoma by duration of alcohol used

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Not Using of Alcohol	24 (64.9%)	13 (35.1%)	37 (100%)
Duration of Alcohol Using < 10 years	1 (33.3%)	2 (66.7%)	3 (100%)
Duration of Alcohol Using ≥ 10years	10 (100%)	0 (100%)	10 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between use of hot drinks and food and presence and absence of the oesophageal cancer:

The cancer found to be in 29 (82.4%) of the patients used hot drinks and foods and absent in 6 (17.6%) of them. It was found in 6 (40%) of patients not used hot drinks and foods and absent in 9 (60%) of them .There was significant association between the use of hot drinks and foods and presence of the cancer (P.value 0.005 and 95%CI 1.882(1.057-3.352).

Table 10: Showed the presence or absence of oesophageal carcinoma by use of hot drinks and food

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Using of Hot Drink & Foods	29 (82.9%)	6 (17.1%)	35 (100%)
Not Using of Hot Drink & Foods	6 (40%)	9 (60%)	15 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between the corrosive injury history and presence or absence of the esophageal cancer:

The cancer found in 11 (68.8%) of the patients had a history of corrosive injury and absent in 5 (31.3%) of them. It was found in 24 (70.6%) of the patients had no a history of corrosive injury and absent in 10 (29.4%) of them. There was no significant association between the history of corrosive injury and presence of the cancer at P.value0.895 and 95% CI.974 (.656-1.446).

Table 11: Showed the presence or absence of oesophageal carcinoma by history of corrosive injury

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Presence of Corrosive Injury	11 (68.8%)	5 (31.2%)	16 (100%)
Absence of Corrosive Injury	24 (70.6%)	10 (29.4%)	34 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between history of esophageal reflux and presence or absence of esophageal cancer:

The cancer found in 19 (79.2%) of the patients with oesophageal reflux and absent in 5 (20.8%) of them .It was found in 16 (61.5%) of the patients with no oesophageal reflux and absent in 10 (38.5%) of them .There was no association between presence of carcinoma and reflux (P. value 0.174).

Table 12: Showed the presence or absence of oesophageal carcinoma by history of oesophageal reflux

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Presence of Oesophageal reflux	19 (79.2%)	5 (20.8%)	24 (100%)
Absence of Oesophageal reflux	16 (61.5%)	10 (38.5%)	26 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

The association between human papilloma virus infection and presence or absence of esophageal carcinoma:

The cancer was found in 23 (85.2%) of the patients infected with human papilloma virus and absent in 4 (14.8%) of them. It was found in 12 (52.2%) of non-infected patients and absent in 11 (47.8%) of them .There was significant association between human papilloma virus infection and presence of the cancer at P. value 0.011 and 95% CI 1.63 (1.07-2.48).

Table 14: Showed the presence or absence of oesophageal carcinoma by human papilloma virus infection

Variables	Presence of oesophageal ca	Absence of oesophageal ca	Total
Infection of Human Papilloma Virus	23 (84.1%)	4 (14.9%)	27 (100%)
No Infection of Human Papilloma Virus	12 (52.2%)	11 (47.8%)	23 (100%)
Total	35 (70%)	15 (30%)	50 (100%)

4. Discussion

It was noticed that the esophageal carcinoma was a frequent gastrointestinal cancer and it was seen in daily life in GADC endoscopic and histopathological units. This finding is consistent with our national previous studies done by Prof. Elmakki in Khartoum University [5]. The affected age in our study was mainly people of fifty years and above this was shown by others study led by Mori M, et al 1990 also it was similar with that seen by Prof. Elmakki [5, 6].

The study showed that esophageal carcinoma had male predominance which constituted 71.4%, it was also shown in a previous study by Pisani P, et al at 1990 [7].

The patient with esophageal carcinoma is slightly higher in the town than the rural area. This may be because the health services and diagnostic tools are more accessible to the people in the urban areas then the rural ones. Esophageal carcinoma showed to be significant in patient with Family history of any other type malignancy, this was consistent with Czene K, et al findings in other previous study [8].

Use of tobacco and alcohol shown to be not a significant risk factor in this study, however it was significant in others studies If we look back to the demographic characteristics of the patients enrolled in the study, we get that females represent 44% of the study population. Smoking and alcohol consumption are not socially accepted among females in the Sudanese cultural background. When we interviewed our patients who use alcohol about the duration of drinking it, we found that esophageal carcinoma was diagnosed in all patient used alcohol for ten years and above. This finding was shown also by Wanp et al [9].

The majority of the Sudanese use warm privileges, but not all of them use hot ones. Tripe in the east part of Sudan usually use very hot drinks and food especially coffee and their locally made food, Asseeda. The study tested with fact and it was found that patient use hot drinks and food were more susceptible to esophageal carcinoma than those who used normal food. Study done in Iran by Islami F and others in 2009, noticed the same result and hot food as any other hot material is injurious to the mucosal surfaces [10].

The study showed that ingestion of corrosive material was not significant although it was significant in others studies [11]. These explained by the fact that the community in Gadarif is agricultural community and rarely use their chemical in their farms. Also females are rarely deal with chemical and other corrosive material. Also it might be explained by the fact that the sample size was not very large to high light the significance.

The majority of the patients in the study complained that they had esophageal reflux although it was not statistically significant. Other study led by Lagergre J and other in 1999 showed that there was significant association between esophageal reflux and carcinoma [12]. The insignificance might also explained by not very large sample size. Future studies with larger sample size may demonstrate the associations.

The human papilloma virus infection was documented to be a risk factor for dysplastic changes and squamous cell carcinoma of the uterine cervix [13]. Again other studies done by Syrjanen KJ in 2002 showed that it was significantly associated with esophageal carcinoma [14]. The current study showed that HPV infection was significantly associated with esophageal carcinoma correlating with the previous studies.

5. Conclusion

The esophageal carcinoma is not uncommon cause of morbidity and mortality in Sudan especially in the Eastern states. Patients with this condition are frequently seen in the surgical department and referred to the GADC for further diagnosis and management.

Demographic characteristics of patients, family history of carcinoma of any organ, personal habits such as smoking, alcohol drinking and taking hot privileges, esophageal corrosive injuries as well as disease like esophageal human papilloma virus infections might contribute to the disease and increase the risk of esophageal carcinoma.

The other factors like sex of the patients, residency of the patients, ingestion of corrosive materials and esophageal reflux although they did not significant at our p value and confidence interval but they were higher in the cancerous patient than in non-cancerous ones

Early detection of these risk factors and elimination of them will be of great value in decreasing the incidence of this disease and its complications such as physical weakness, difficulty of swallowing and bleeding and serious and difficult operative procedures.

6. Recommendations

Esophageal carcinoma is serious and killing disease. Avoidance of modifiable risk factor such as alcohol consumption cigarette smoking and intake of hot privileges will help in reducing the incidence. Correction of anemia epically among children, ladies and old individuals as well as follow up of patients with prolong duration of esophageal reflux and patients with strong family history of carcinoma.

Further studies recommended for environmental risk factors and genetic predisposition of the disease since the disease is more seen in a particular area in Sudan and in certain tribes. Active case detection, if practically and financially feasible will provide early detection and management.

Eastern part of Sudan is poor and the majority of these patients are very poor so social support for these patients are very important. More studies and researches in esophageal carcinoma and others esophageal disease is recommended.

References

1. Akbari MR, Malekzadeh R, Nasrollahzadeh D, Amanian D, Sun P, Islami F, Sotoudeh M, Semnani S, Boffeta P, Dawsey SM, Ghadirian P, Narod SA. Familial risks of esophageal cancer among the Turkmen population of the Caspian littoral of Iran. Int J Cancer. 2006 Sep 1; 119(5):1047-1051.
2. Kumar A, Chatopadhyay T, Raziuddin M, Ralhan R. Discovery of deregulation of zinc homeostasis and its associated genes in esophageal squamous cell carcinoma using cDNA microarray. Int J Cancer. 2007 Jan 15; 120(2):230-242.
3. Stoner GD, Gupta A. Etiology and chemoprevention of esophageal squamous cell carcinoma. Carcinogenesis. 2001 Nov; 22(11):1737-1746.
4. Chang F, Syrjanen S, Wang L, Syrjanen K (1992), Risk of esophageal cancer. Gastroenterology, Department of Pathology, University of Kuopio, Finland, Journal Article, Review, Research Support, Non-U.S. Gov't [1992, 103(4):1336-1348]
5. Mohamed Elmakki ahmed, (2006) MD, FRCSI, Department of surgery and toomback and smoking research centre , Both: the university of Khartoum and toomback research centre , Elfashir st, Elmatar residence, Khartoum, Sudan.
6. Mori M, Ohno S, T sutsui S, et al. (1990) Esophageal cancer in young patients. Ann ThoracSurg 1990; 49:284-6.
7. Pisani P, Parkin (1990) DM, Bray F, Ferlay J. Estimate of the world wide mortality from 25 cancers 1990;83:870-3.
8. Czene K, Lichtenstein P, Hemminki K. (2002). .Enviromental and heritable causes of cancer among 9.6 million individuals in the Swedish family- cancer database. 2002;99: 260-6.
9. WU AH, Wan P, Bernstein L.(2001). A multiethnic. Population-based study of smoking, alcohol and body size and risk of adenocarcinoma of stomach and esophagus (united statea) cancer causes control 2001; 12: 721-732.
10. Islami F, Pourshams A, Nasrollahzadeh D, et al. (2009)"Tea drinking habits and oesophageal cancer in a high risk area in northern Iran: population based case-control study". (2009) BMJ 338: b929.
11. Kenneth J. Vega, M.D., M. MazenJamaM.D.l (September 2000). Changing pattern of esophageal cancer incidence in New Mexico. Changing pattern of esophageal cancer incidence in New Mexico. The American Journal of Gastroenterology.Retrieved 2007-03-21.
12. Lagergren J, Bergström R, Lindgren A, Nyrén O. (1999). "Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma". N. Engl. J. Med. (1999) 340 (11): 825–31.

13. Rosai and Ackerman: Surgical pathology, ninth edition. 2004.
14. Syrjänen KJ. "HPV infections and oesophageal cancer". (2002)J. Clin. Pathol. 55 (10): 721–PMIDhttp://jcp.bmj.com/cgi/content/full/55/10/721

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