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A Study on Treatment Options and Response Evaluation, Disease Patterns and Known Risk Factors in Carcinoma Oesophagus in a Rural Hospital

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Background: Oesophageal carcinoma is the eighth most common cancer worldwide and the sixth most common cause of cancer-related mortality. In India, as per WHO, GLOBOCAN 2020, oesophageal carcinoma is the 5th most common cancer with an incidence of 4.8%. Various risk factors are associated with development of oesophageal cancer, most commonly tobacco (smoked and smokeless) consumption, alcohol consumption, diet less in fruits and vegetables, non-vegetarian diet, excessive use of spices and hot beverages. Squamous cell carcinoma and adenocarcinoma constitute 95% histology of all oesophageal tumors. Various surgical procedures are done depending on the stage and site of the disease. Combining chemotherapy and radiation therapy as the initial therapeutic approach, either alone or followed by an attempt at operative resection, seems beneficial. When administered with radiation therapy, chemotherapy produces a better survival outcome than radiation therapy alone. Approaches to palliation include repeated endoscopic dilatation, the surgical placement of a gastrostomy or jejunostomy for hydration and feeding, the endoscopic placement of an expansive metal stent to bypass the tumour, and radiation therapy. Most carcinoma oesophagus cases are diagnosed late. This study was done to observe treatment modalities, treatment outcomes and known risk factors in carcinoma oesophagus patients presented in the department of radiation oncology in a rural hospital.

Abstract:

Aims and objectives: To study the treatment options and response evaluation, disease patterns and known risk factors in carcinoma oesophagus patients reported in a rural hospital

Settings and Design: A descriptive observational study

Material and Methods: After approval of institutional ethical committee, all the diagnosed cases of carcinoma oesophagus presented to Oncology department were included in this study. Patients were then be evaluated by detailed history, general & systemic examination followed by hematological and relevant radiological investigations. TNM staging was done. Patients were treated with radiation therapy and chemotherapy depending upon the staging and intent of treatment.During treatment and after completion of treatment, patientswere assessed for acute treatment toxicities,then on first follow up (after one and a half months) and every three months according to (CTCAE version 5). On each follow up patients were evaluated clinically and by required hematological and radiological investigations. Thereafter, the response evaluation of the treatment was assessed according to RECIST criteria (version 1.1)

Result: The study wasconducted on 44 histologically diagnosed carcinoma oesophagus patients out of which 23 were males and 21 were females. The most commonly used substance abuse was smokeless tobacco (SLT) in various forms. 79.5% of the patients had history of consumption of spicy food and 95.5% patients were having

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consumption of hot beverages, mainly tea. The major presenting complaint was dysphagia reported by 97.7% patients. Squamous cell carcinoma (SCC) was the most common histopathology seen in the study group with 32 (72.7%) patients. The most common site in our study was the lower thoracic oesophagus with 19 (43.2%) patients. 27% of oesophageal carcinoma patients were diagnosed and reported in an advanced or metastatic stage. 25% of the patients did not take treatment and defaulted after reporting to the department. 59.09% of the total patients took radiation treatment in the form of neoadjuvant, radical, adjuvant or palliative treatment. Acute toxicities during radiation treatment and incidence of oesophageal stricture after radiotherapy were seen more in cervical oesophagus patients. Late toxicities were almost similar in all patients. Local and distant disease failure was observed in 11.8% patients whose primary site wasmiddle thoracic oesophagus. Response assessment showed a greater number of complete response in cervical oesophagus patients. Most of the patients with locally advanced disease had progressive disease. 16.7% patients defaulted to follow-up after treatment.

Conclusion: Oesophageal carcinoma is an important health issue in India and worldwide due to its incidence, management, prognosis and mortality. A multidisciplinary team management to ascertain the diagnosis, and multimodality treatment approach is required for the management of oesophageal malignancy depending upon the site, stage, histology, and general condition of the patient. In the current study, the delay in reporting may be due to low literacy and awareness regarding oesophageal malignancy, socioeconomic reasons, and patients reporting only when symptoms increase. This can be reduced and early diagnosis can be achieved by awareness programs and educating the population regarding dietary risk factors and risks caused by substance abuse.

Keyword: esophagus cancers, radiotherapy, chemotherapy

I. INTRODUCTION:

Oesophageal carcinoma is considered a serious malignancy concerning prognosis and mortality rate. In India, as per WHO, GLOBOCAN 2020, oesophageal carcinoma is the 5th most common cancer with an incidence of 4.8%. Carcinoma oesophagus is unique among gastrointestinal tract malignancies because it embodies two distinct histopathologic types: squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma and adenocarcinoma constitute 95% histology of all oesophageal tumors. Various risk factors are associated with development of oesophageal cancer, most commonly tobacco (smoked and smokeless) consumption, alcohol consumption, diet less in fruits and vegetables, excessive use of spices and hot beverages. Other major risk factors include gastroesophageal reflux disorder (GORD), consumption of smoked food and pickles. Various surgical procedures are done depending on the stage and site of the disease. Combining chemotherapy and radiation therapy as the initial therapeutic approach, either alone or followed by an attempt at operative resection, seems beneficial. When administered with radiation therapy, chemotherapy produces a better survival outcome than radiation therapy alone. The use of preoperative chemotherapy and radiation therapy followed by oesophageal resection appears to prolong survival compared with surgery alone, according to several randomized trials and a meta-analysis. Approaches to palliation include repeated endoscopic dilatation, the surgical placement of a gastrostomy or jejunostomy for hydration and feeding, the endoscopic placement of an expansive metal stent to bypass the tumour, and radiation therapy. Most carcinoma oesophagus cases are diagnosed late. Depending upon the site of malignancy, various surgical options are considered, followed by radiation therapy with or without chemotherapy. An increase in diagnostic modalities, advancement in surgical procedures and improved radiation therapy techniques have helped in the early diagnosis and treatment of carcinoma oesophagus over the last 20 years. This study is done to observe treatment modalities, treatment outcomes and known risk factors in carcinoma oesophagus patients presented in department of radiation oncology in a rural hospital.

II. METHODOLOGY:

After Institution ethical committee approval, all the diagnosed cases of carcinoma oesophagus presented to the Oncology department were included in this study. Patients were then evaluated by detailed history (with an emphasis on patterns of substance abuse and dietary patterns) and general & systemic examination followed by hematological and relevant radiological investigations. TNM staging was done. Patients were planned for curative or palliative treatment with various modalities depending upon the site of primary, histology and general condition of the patient. Patients requiring radiation treatment and chemotherapy were given in the department. Patients were assessed for acute toxicities during treatment and late toxicities after completion of

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treatment on the first follow-up (after one and a half months) and later every three months. On each follow-up, patients were evaluated clinically and by required hematological and radiological investigations. Thereafter, the response evaluation of the treatment given to each patient was assessed according to RECIST Criteria (version 1.1)

III. RESULTS:

In our study 44 biopsy proven oesophageal cancer patients were included out of which 23 were males and 21 were females. The most common age group affected was 61-70 years. (31.8%). The general informations of the patients are mentioned in table 1. The most commonly used substance abuse was smokeless tobacco (SLT) in various forms like raw tobacco, gutkha, and mishri. Patterns of substance abuse among patients in the current study are given in graph 1. The most common dietary risk factor was consumption of hot beverages like tea seen in 95.5%. Detailed dietary factors are mentioned in graph 2.

Most of the patients in this study belong to rural populations and have low socio-economic status. The literacy rate among the study group was 72.72%, with 23 (52.3%) patients received till primary education.

The most common presenting complaints of the patients in the study group was dysphagia of various grades, seen in 43 (97.73%) patients.

Squamous cell carcinoma (SCC) was the most common histopathology seen in the study group with 32 (72.7%) patients. Other histologies arementioned in table 2.

Seven (15.9%) patients were diagnosed and reported in metastatic stage. Two patients were locally advanced with stage IV A.

Cervical oesophagus was the primary site in seven patients out of which six (85.7%) patients took treatment.

There were five upper thoracic oesophagus patients in the study group out of which three (60%) patients took treatment and two (40%) patients defaulted. All three patients received curative radiation treatment.

The middle thoracic oesophagus was the second most common site of primary with 13 (29.5%) patients, out of which two (15.3%) patients were with distant metastasis (stage IV B). 10 patients took treatment and three patients defaulted.

Lower thoracic oesophagus was the most common site of primary with 19 (43.18%) patients of which four (21.1%) patients were metastatic at the time of diagnosis. 14 (73.68%) patients took treatment and five (26.31%) patients defaulted treatment.

The treatment modalities given to the patients are summarized in table 3.

Total 23 (52.27%) patients out of 44 patients received radiation treatment either with curative or palliative intent. Of that 19 (82.6%) patients were treated with 3DCRT technique and the remaining 4 patients (9.09%) were treated with IMRT technique.

The acute toxicities were assessed on radiation treatment during the study period as shown in table 4.

Late toxicities of dysphagia, nausea, and stricture were assessed which is shown in table 5.

From the current study, it is observed that acute toxicities and incidence of oesophageal stricture post-radiation treatment were more in cervical oesophagel cancer patients.

A total of 26 patients took curative treatment and out of which 17 (65.38%) patients completed treatment. In those two (11.8%) patients developed recurrence at the primary site. Both patients were middle thoracic oesophagus patients.

Response evaluation was done according to the site of primary tumorand is shown in graph 3. Cervical oesophagus patients had a maximum number of complete response (CR) with four (80%) patients.

IV. DISCUSSION:

In India, as per WHO, GLOBOCAN 2020, oesophageal carcinoma is the 6th most common cancer with an incidence of 4.8% (1).

Mamta Srivastava et al. in 1995 in a study on nutritional risk factors in carcinoma oesophagus conducted among 75 patients reported that increased risk was associated with low intake of fruits and vegetables, non-vegetarian diet and consumption of spicy food and tea at hot temperatures (2).It was observed in our study that dietary risk factors can cause carcinoma oesophagus in the absence of various addictions. In the study, 11 (25%) patients were without any history of substance abuse, and with dietary risk factors like spicy, oily, and smoked food. Spicy and oily food may aggravate other known risk factors of carcinoma oesophagus like oesophagitis, Plummer-Wilson syndrome, and Gastroesophageal reflux disease (GORD), by causing more irritation to the mucosal lining and may increase the risk. This could be one of the reason in our study for higher incidence of lower thoracic oesophagus malignancies as well as slightly higher female incidence.

In the present study, dysphagia was the chief complaint in 97.7% patients which was similar to the study by Vanita Noronha et al. in 2016 in which, 96% of the patients presented with chief complaint of dysphagia(3).

One (2.3%) patient with upper thoracic oesophageal cancer had a history of carcinoma vallecula for which the patient took chemoradiation 10 years back. Another female (2.3%) patient with primary in cervical oesophagus had history of carcinoma right breast for which she underwent surgery and took chemotherapy and radiation therapy 12 years back. In these cases, the incidence of oesophageal malignancy secondary to previous radiation treatment cannot be ruled out.

Dhaval Choksi et al.in 2020 has reported that there was a significant increase in the gastroesophageal junction tumors and adenocarcinoma in the recent years (4).

In the current study, the delay in reporting may be due to low literacy and awareness regarding oesophageal malignancy, lack of screening for oesophageal cancers, socioeconomic reasons, and patients reporting only when symptoms increase. This can be reduced and early diagnosis can be achieved by awareness programs and educating the population regarding dietary risk factors and risks caused by substance abuse.

A total of 10 patients among middle thoracic oesophagus took treatment out of which two underwent radical surgery (both stage III B) of which one patient received adjuvant chemoradiation and the other patient reported late due to post surgery comorbidities and had liver metastasis on evaluation.VPN Krishnaramaiah et al. in 2014 conducted a prospective study among 37 patients on Quality of life after oesophagectomy in patients with carcinoma of oesophagus, reported that there was no significant improvement in quality of life except emotional function in patients undergoing transhiatal and transthoracic oesophagectomy, but significant relief of dysphagia was there (5).

The acute toxicities were assessed on radiation treatment during the study period. Nausea was seen more in cervical oesophagus patients with four (80%) patients out of five having grade 1 nausea. Skin reactions were observed more in cervical oesophagus patients, which may be due to the skin folds in the neck and surface irregularities. Dysphagia was observed more in patients of the cervical oesophagus. Patients of the upper and middle thoracic oesophagus developed dysphagia less compared to the cervical and lower thoracic oesophagus.

Response evaluation was done according to the site of primary tumoras shown in graph 3. Cervical oesophagus patients had maximum number of complete response (CR) with four (80%) patients. Response evaluation in the current study could not be compared due to less sample in the study group, low socio-economic status of the rural population for follow-up and investigations and less patients reported regularly for follow-up

It was observed that dysphagia has significantly decreased after treatment compared to pre-treatment. The incidence of post radiation oesophageal stricture was more in cervical oesophagus. Virendra Bhandari et al.in 2019 in a study of long-term survival and late toxicities in 54 carcinoma oesophagus patients receiving chemoradiation treatment reported similar results stating 54.35% patients had Grade 0 dysphagia and 32.6% patients had Grade1 dysphagia after 1 month of chemoradiation treatment (6).

V. CONCLUSION:

Oesophageal carcinoma is an important health issue in India and worldwide due to its incidence, management, prognosis and mortality. A multidisciplinary team management to ascertain the diagnosis, and multimodality treatment approach is required for the management of oesophageal malignancy depending upon the site, stage, histology, and general condition of the patient. In the current study, the delay in reporting may be due to low literacy and awareness regarding oesophageal malignancy, socioeconomic reasons, and patients reporting only when symptoms increase. This can be reduced and early diagnosis can be achieved by awareness programs and educating the population regarding dietary risk factors and risks caused by substance abuse.

Limitation:

Limitations of the study were small sample size and shorter follow up among the patients as a result of which long term follow up record could not be maintained.

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Tables and Graphs

Table 1 : General information of the patients

Age Group	Frequency	Percentage (%)
21-30	1	2.3
41-50	7	15.9
51-60	13	29.5
61-70	14	31.8
71-80	8	18.2
>80	1	2.3
H/O Alternative Medication	8	18.2
Feeding support	23	52.3
Chief Complaint		
Dysphagia	43	97.7
Weight loss	6	13.64
Nausea and vomiting	4	9.09
Site		
Cervical oesophagus	7	15.9
Upper Thoracic	5	11.4
Middle Thoracic	13	29.5
Lower Thoracic	19	43.2

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Table 2 : Histology of the tumor

Histology	Frequency	Percentage (%)
Squamous cell Carcinoma	32	72.7
Adenocarcinoma	8	18.2
Neuroendocrine Tumour	2	4.5
Poorly Differentiated Carcinoma	1	2.3
Carcinoma in-situ	1	2.3

Table 2 : Treatment Modalities Given to Carcinoma Oesophagus Patients

Treatment Modality	Cervical	Upper Thoracic	Middle Thoracic	Lower Thoracic	Total
NACT	1	0	1	1	3
Surgery	0	0	1	4	5
Neoadjuvant CTRT	0	0	0	1	1
Radical RT	0	2	0	1	3
Radical CTRT	4	1	5	2	12
NACT+ Radical CTRT	0	0	0	1	1
Surgery+Adjuvant CTRT	0	0	1	0	1
Palliative RT	0	0	1	1	2
Palliative Chemo	0	0	1	1	2
Palliative RT + Palliative Chemo	1	0	0	2	3
Did not take treatment	1	2	3	5	11

Table 3 : Site wise Acute Toxicities

Acute Toxicities	Cervical Oesophagus (5)	Upper Thoracic Oesophagus (3)	Middle Thoracic Oesophagus (7)	Lower Thoracic Oesophagus (7)
Skin Reaction				
Grade 0	1	2	5	5
Grade 1	3	1	2	2
Grade 2	1	0	0	0
Grade 3	1	0	0	0
Dysphagia				
Grade 0	0	0	0	0
Grade 1	0	1	2	2
Grade 2	4	2	4	5
Grade 3	1	0	1	0
Nausea				
Grade 0	0	1	1	1
Grade 1	4	0	3	3
Grade 2	1	2	3	3
Mucositis				
Grade 0	1	3	7	7
Grade 1	3	0	0	0
Grade 2	1	0	0	0

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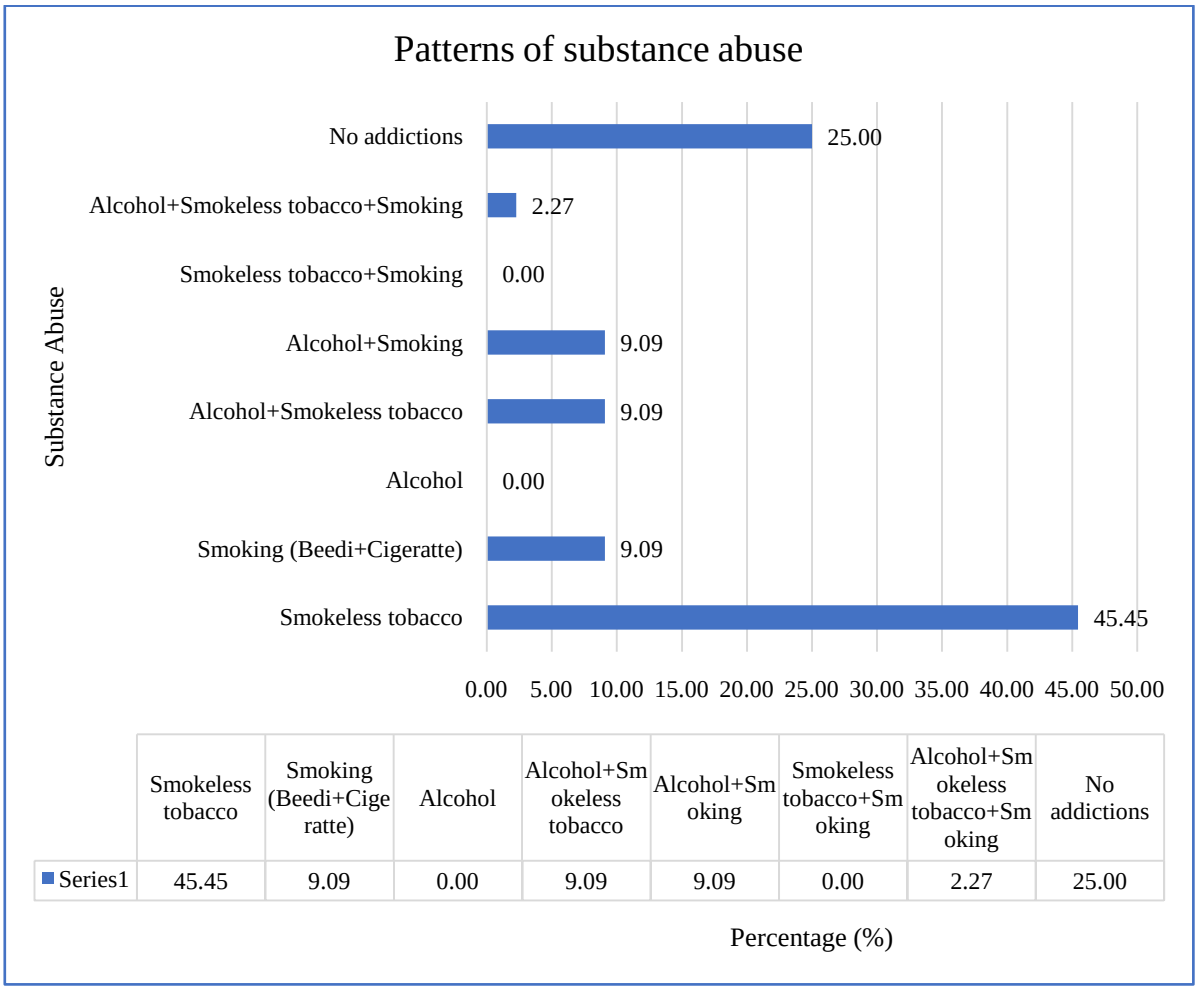
Tabe 4 : Site wise Late Toxicities After Radiation treatment

Late Toxicities	Cervical Oesophagus (5)	Upper Thoracic Oesophagus (3)	Middle Thoracic Oesophagus (5)	Lower Thoracic Oesophagus (6)
Dysphagia				
Grade 0	1	1	3	2
Grade 1	4	2	2	4
Nausea				
Grade 0	3	3	3	3
Grade 1	2	0	2	3
Incidence of Oesophageal Stricture	2	1	1	0



Graph 1: Patterns of substance abuse among study group

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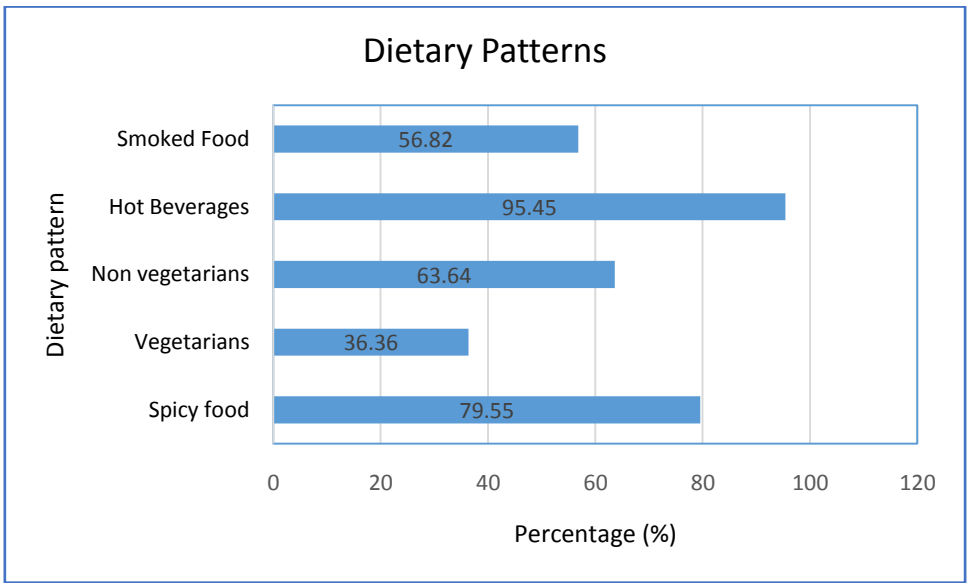
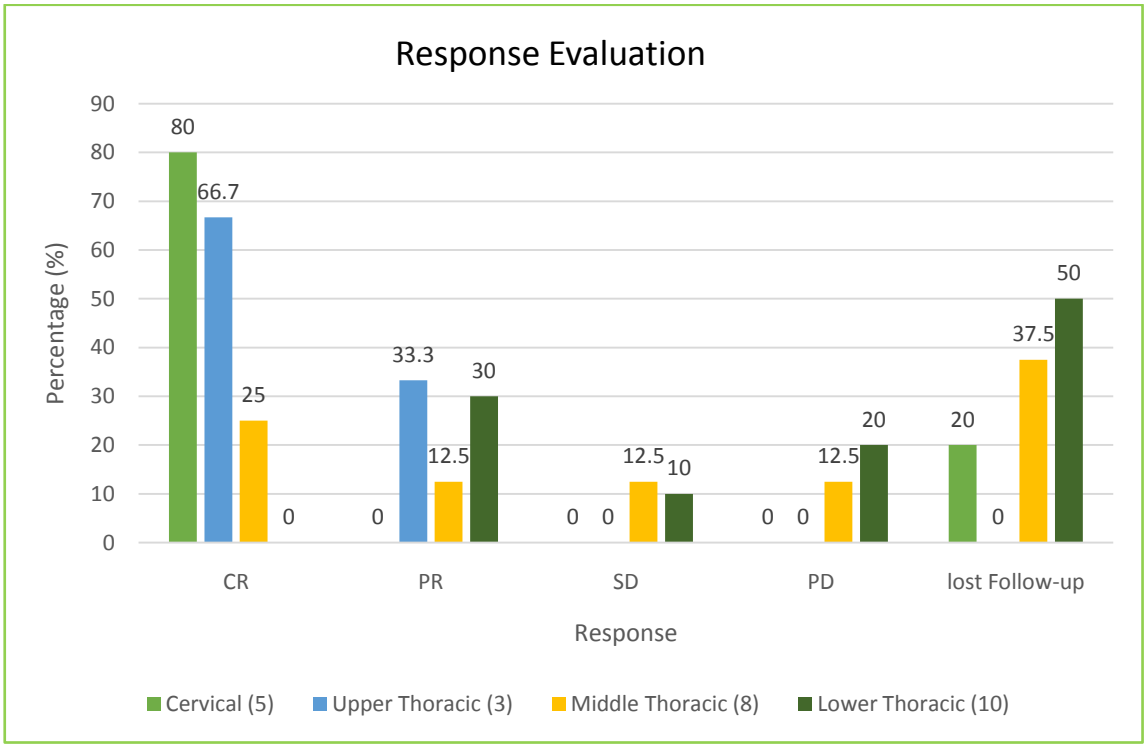


Graph 2 : Dietary factors among the study participants



Graph 3 : Response evaluation of carcinoma oesophagus patients who took curative treatment