Role of Dietary Habits in the Development of Esophageal Cancer in the Doaba Region of Punjab

A
Thesis
Submitted to

For the award of

DOCTOR OF PHILOSOPHY (Ph.D.)

in

Nutrition and Dietetics

By

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2019

DECLARATION

I, Rachna Khosla, Research Scholar, Department of Food Technology and Nutrition certify that the work embodied in this Ph.D. thesis titled 'Role of Dietary Habits in the Development of Esophageal Cancer in the Doaba Region of Punjab' is my own bonafide work carried out by me under the supervision of Dr Beenu Tanwar, Assistant Professor at Dept. of Dairy Technology, Mansinhbhai Institute of Dairy and Food Technology, Mehsana, Gujarat and Dr Anil Panghal, Research & Consultancy Coordinator & Associate Professor at School of Agriculture, Lovely Professional University, Phagwara, Punjab.

The interpretations put forth are based on my understanding of the existing literature and the analysis of my research. The achieved results have not been published anywhere in the form of book or monograph. The matter embodied in this Ph.D. thesis has not been submitted for the award of any other degree or diploma or distinction in this or any other university. I declare that I have faithfully acknowledged, given credit to and referred to the research workers wherever their works have been cited in the text and body of the thesis. I further certify that I have not willfully lifted up some other's work, paragraph, text, data, result, etc. reported in the journals, books, magazines, reports, dissertations, theses or websites and included them in this Ph.D. thesis and cited as my own work.

Place : Phagwara (Ms. Rachna Khosla)

Date : 17th April 2019 Research Scholar

CERTIFICATE

This is to certify that the work incorporated in the thesis 'Role of Dietary Habits in the Development of Esophageal Cancer in the Doaba Region of Punjab' submitted by Ms. Rachna Khosla, Research Scholar, Department of Food Technology and Nutrition was carried out under our guidance. She has satisfactorily completed the course work and pre-submission requirement which is part of her Ph.D. programme. The work of other researchers has been acknowledged, given credit to and referred to wherever their works have been cited in the text and body of the thesis.

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ABSTRACT

Cancer is a pathological disorder in which cells grow rapidly in an uncoordinated manner with or without the presence of a stimulus. It is an intricate, multistage and multifactorial process involving alteration of genes, suppression of immune system and finally malignant transformation. Tumors of the esophagus are by and large malignant in nature with a very small fraction being benign. Esophageal cancer has two main sub-types, esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinma (EADC). Esophageal cancer (EC) ranks sixth, both as most common type of cancer and cause of cancer related deaths in India.

The present research 'Role of dietary habits in the development of esophageal cancer in the 'Doaba region' of Punjab' included four districts Kapurthala, Jalandhar, Hoshiarpur and Nawanshehar (Shaheed Bhagat Singh Nagar). This case-control study included 110 esophageal cancer patients along with age (±5years), gender and area matched 152 controls. Food frequency questionnaire for Doaba region was prepared, validated, pre-tested and filled during face to face interview. Statistical software SPSS 18.0 was used for descriptive and inferential statistical analysis.

Our study showed a higher incidence of esophageal squamous cell carcinoma (ESCC) type of EC and no familial cause. The study also revealed a higher incidence among females. On basis of occupation, manual workers and housewives showed greater incidence in our study. Other pre-disposing factors of significance for the increase in the incidence of EC appeared to be inhabitancy, age group of 50-70 years, illiteracy or low education level and low socio-economic status.

Dietary data reveals that total wheat and whole wheat flour intake has no significant impact on the incidence of esophageal cancer. Intake of '*basmati*' rice and maize was more amongst controls. Vegetables and fruit intake appeared to be protective.

The average number of monthly servings, indicating the total fat consumption was significantly more of all categories of fats and oils in case of patients. The consumption of nuts and oilseeds was significantly higher in case of the control group. The amount of tea consumption was significantly more in the patient group but the total milk consumption other than the amount consumed in tea was more in the

control group. The amount of non-aerated drink consumption was double in case of control group, which could have an impact on the incidence of esophageal cancer.

Logistic regression model revealed a significant impact of intake of maize flour, basmati rice, ‘roots & tubers’ and ‘other vegetables’ category of vegetables, fresh fruit and fresh fruit juice, paneer (cottage cheese), plain and sweet buttermilk, fats and oils and tea.

Various lifestyle factors too had an impact on the incidence of esophageal cancer. Regular meal timings were not found to be protective against ESCC. Non organic pesticides used to preserve grain could increase the incidence of esophageal cancer. Contaminants or improper handling of chopped fruits and vegetables could increase the risk of esophageal cancer. Higher percentage of patients discarded the water in which pulses were soaked. More people of control group than the patient group people consumed filter and ‘RO’ water. Number of smokers and their frequency of smoking were also observed to be more amongst the patients group.

In a nut shell, intake of fresh fruits, vegetables, certain milk products could be protective against esophageal cancer while high intake of fats and oils along with tea could increase the risk of esophageal cancer. Life style practices like handling of fruits and vegetables, discarding water in which pulses are soaked, amount and type of water consumed, grain preservation method and smoking could also increase the risk of esophageal cancer.

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to my thesis advisor Dr. Beenu Tanwar now Assistant Professor at Dept. of Dairy Technology, Mansinhbhai Institute of Dairy and Food Technology, Mehsana, Gujarat, who initiated and encouraged me to take up this research work and finally see me through with her pertinent advise, continuous support and valuable suggestions. I sincerely thank my thesis co-advisor Dr. Anil Panghal, Research & Consultancy Coordinator & Associate Professor at School of Agriculture, Lovely Professional University, Phagwara, Punjab, for his invaluable guidance, untiring help and constant encouragement. Their able guidance helped me achieve my goal.

Besides my advisors, I would like to thank my young and dynamic Head of Department Ms. Sawinder Kaur (Professor, Department of Food Technology & Nutrition, Lovely Professional University, Phagwara, Punjab) for her ever helping nature, timely and valuable advice which kept me moving towards my goal. I am also grateful to Dr. Navnidhi Chhikara (Assistant Professor, Department of Food Technology & Nutrition, Lovely Professional University, Phagwara, Punjab) for her motivation and cooperation.

I am grateful to all my teachers- Dr. Vishal Sarin, Dr. Anand Thakur and Dr. Abhineet Goel for introducing me to research methodology and various nuances of research. I am extremely obliged to the annual seminar panel experts for their grilling, which chiseled my research.

I acknowledge the cooperation of all the gastroenterologists of this region who provided me an opportunity to access their patients and gather data. I am also thankful to the staff of Lifeline Hospital, Nawanshehar, Gulati surgical Hospital, Hoshiarpur and BS Diagnostic Labs, Jalandhar who assisted me in data collection. Without the precious support of all of them it would not have been possible to conduct this research.

I am indebted to all the people who consented to be a part of this study. I owe my heartfelt gratitude to the patients who sat through the long questionnaire session

despite their grave illness and strained speech. Information imparted by them would be a stepping stone in helping esophageal cancer cases and general public.

My sincere thanks to Mr. Sanjay Tanwar who provided me critical help with statistical analysis.

Last but not the least, I express my deepest love and gratitude to my family and friends for bearing with my schedule and providing their unfailing support and sustained inspiration which helped me face all problems and successfully complete this study.

Place : Phagwara — Rachna Khosla

Date : 17th April 2019 — (41400063)

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INTRODUCTION

Cancer is a pathological disorder in which cells grow rapidly in an uncoordinated manner with or without the presence of a stimulus (Kumar, 2014). The intricate, multistage and multifactorial process of carcinogenesis involves alteration of genes, suppression of immune system and finally malignant transformation. It begins from a single cell due to the mutation of a few vital genes, brought about by DNA replication errors or exposure of DNA to free radicals and carcinogens. After this initiation more genetic/epigenetic changes occur in the cells leading to loss of control of cell proliferation and apoptosis, autonomy in growth signals, endless replicative power, unrelenting angiogenesis, tissue invasion and metastasis (Tabrez et al, 2013).

Cancer can affect any system and any part of the human body. The esophagus is a part of the upper gastrointestinal tract. It is about 10 inch long muscular tube that travels from back of the mouth, between the trachea and the spine, pierces the diaphragm and finally connects with the stomach at the cardia end. The esophagus in humans has a mucous membrane comprising of stratified squamous epithelium, lamina propria and muscularis mucosae. The rapid turnover of the epithelial layer of the esophagus and the mucous from the esophageal glands, protects it from the abrasive foods. Tumors of the esophagus are by and large malignant in nature with a very small fraction being benign. Esophageal cancer has two main sub-types. Esophageal squamous cell carcinoma (ESCC), which arises from the inner surface of the esophagus and esophageal adenocarcinma (EADC), which arises from the glandular cells present at the gastroesophageal junction. Patients of esophageal cancer have dysphagia with or without other symptoms like hoarseness of voice, cough, lymphadenopathy, heartburn and unintentional weight loss.

High incidence of EC is seen in countries of South America, Africa, Europe and Asia. The rate of incidence could vary five hundred folds in two regions just a hundred miles apart. The survival rate of EC cases is poor. Even after radical esophagectomy the 5 year survival rate is less than 20% in China and about 15% in US. The foremost cause of high mortality is delay in diagnosis. Most of the cases are diagnosed at III/IV stage. If detected early EC is treatable so esophageal screenings should be done regularly.

The incidence of EC showed disparity on various grounds. First, the incidence of ESSC is more in the developing countries while EADC is more in the developed ones. Secondly,

studies have reported gender disparity. Most of the studies have reported a higher incidence among men while some studies have not shown women to be at any advantage.

The field of medical science has developed in leaps and bounds, but EC still remains a disease of poor prognosis and high mortality. Like other cancers the process of esophageal carcinogenesis can be activated by a number of factors. Heredity, environment and diet are the major ones. Heredity is beyond our control, environment is partly under our control and diet is completely under our control.

In 1981, Doll and Peto estimated diet to be the cause of all avoidable cancers, today 38 years later we don't think different. The role of diet is unchallenged, but the knowledge of active mechanism and active substances is still incomplete. Various dietary studies have been conducted to identify the dietary components responsible for esophageal carcinogenesis. The results of studies carried out in various regions of the world have been varied and inconsistent. Over and under nutrition is considered one of the major risk factors in various cancers. Positive association has been reported between obesity and high mortality rate for cancer of various organs like esophagus, liver, gallbladder and breast, to count a few. Association between the incidence of esophageal cancer and dietary components, both nutritional and non-nutritional, has been documented by various researchers.

Cereals, pulses and legumes have been cultivated from prehistoric period. They form the major portion of human food all around the world and are the main constituents of the Mediterranean and Asian diets. Grains (cereals and pulses) contribute about half of the energy and protein required by an individual. Various Cancer research centers have reported an inverse association between whole grains, especially cereal fiber intake and reduction in total and cause specific mortality with cereal fiber being a potential protective constituent. On this ground the consumption of unprocessed cereals and/or pulses in every meal is advocated, however, these recommendations of whole grain consumption vary from country to country. Studies on the impact of pulses on the incidence of EC are few. These researchers found the vegetarian protein from pulses to have a significant cancer reduction impact.

Role of dietary fat in the etiology of cancer has been studied for more than half a century. Studies have been conducted on type and amount of fat and oil intake. Changes in lipid metabolism, disturbs the homeostatic balance controlling cell differentiation, cell proliferation and apoptosis resulting in neoplastic lesion. Role of nuts and oil seeds in decreasing the incidence of cancer and treatment is still in its infancy and needs more research before we label it as a protective food.

The act of fruits and vegetables in preventing or decreasing the risk of cancer has been studied for quite a few decades now. On the basis of case control studies various research agencies have reported 'probable' reduction to 'significant' reduction in the incidence of EC though the researchers are still divided in ranking fruits or vegetables as the prime protector from EC. The prospective studies conducted in Linxian (area of maximum incidence of EC in the world) have also mentioned low and seasonal intake of fruits and vegetables causing 'marginal deficiencies' or 'insufficiencies' of micronutrients like vitamin A, $B_{2,}$ C, E, and carotenoids as possible risk factor.

In the existing studies on consumption of animal products the consistency in results is missing. No steady correlation between EC and intake of milk and other dairy products has been reported. Milk protein has been found to possess anticarcinogenic, immunomodulatory, antihypertensive, hypocholesterolemic, antimicrobial properties. Their findings indicated the effectiveness of milk protein in the reduction of risk factor for cancer while other scientists have reported no or marginally inverse association between milk intake and the incidence of EC. A significant decrease in EC risk incidencewas noticed with high consumption of poultry including eggs and fresh fish in various regions of the world. Higher risk of ESCC and EADC with processed meat and red meat intake was reported though the researchers are divided in their opinion with regard to the cooking method of meat rather than the type of meat or its protein and fat content as the main culprit.

Mate, tea and other hot beverages have shown significant association with EC. The carcinogenic effect of hot beverages is due to the constituents of the herb, the temperature and amount of consumption or all these. Individually these factors have been studied but

how much impact these factors have together needs further investigation. Preparation method and constituents of common beverages like tea and coffee also vary from region to region. This too could have different influence on the incidence of EC.

Impact of aerated and non-aerated soft drinks is an understudied arena. Most of the studies have reported no association between the consumption of both type of soft drinks and the incidence of EC though some researchers have reported a positive correlation between the increased consumption of sodas and increased incidence of EC.

Various bioactive compounds that are non-nutritional, but biologically active are present along with macronutrients and micronutrients in the food groups like cereals, pulses, fruits, vegetables, spices and condiments. These bioactive compounds are called chemopreventers as they appear to be antioxidant, anticarcinogenic, antimutagenic and immunomodulators by nature. Dietary chemoprevention is considered to be a practical and financially viable method of controlling cancer.

India is a land of culinary diversity. The diversity of Indian diet is unknown to the rest of the world. The varied dietary patterns are a product of cultural and religious fusion which has existed for thousands of years. Studies conducted in various regions of India have documented varied results. The disparity in findings is obvious because of diverse food habits. Foods items and dishes specific to certain areas like *Kalakhar* of Assam, *noon chaiy* and preserved spice cakes of Kashmir, tea in Malwa region of Punjab and pickles in Kerala have been reported as probable risk factors for EC in their respective regions.

As we transcend from a developing to a developed nation our lifestyle especially our food selection is undergoing a sea change. Convenience foods are being preferred over traditional foods. Very little is known about its role in causation or prevention of cancer. Lifestyle factors like dietary practices, consumption of alcohol, tobacco, betel quid, betel nut, *paan masala* and various other environmental factors have been reported to lay deep influence on the development of cancers. Many researchers have reported their results on the role of alcohol, tobacco, betel nut and betel quid in the development of EC with conflicting outcomes. Individual research variations in the impact of tobacco smoking

and alcohol consumption on the incidence of EC include reports of no association, positive correlation of tobacco or alcohol individually or in tandem. A few researchers are of the opinion that it is not only the consumption of alcohol and tobacco but also their type that mattered.

Socio-demographic factors like age, gender, inhabitance, ethnicity and socioeconomic factors like family income, education and profession have been studied and the outcomes reported. Studies regarding association between these factors and the risk of EC too have shown incompatible results.

The task of microorganisms inhabiting the oral cavity and upper gastrointestinal tract in the risk of EC is also being studied by various researchers. Impact of prolonged medication of different categories is also under scrutiny.

Man lived in harmony with the environment from the warm tropics to the cold poles. Once immaculate region is now tarnished due to pollution. The amount and type of contaminants describe our environment and decide our health. This is the price we have paid to gain modernization and industrialization. Excessive use of fertilizers and pesticides for an agricultural boom, excess of heavy metals in soil, organic and inorganic chemical industrial waste dumped into water bodies, indoor air pollution from inefficient burning of household fuel, decreased holistic nutrition have increased the incidence of cancer.

The amount of research done in the field of cancer, especially in the area of etiology of esophageal cancer has not yielded definitive results. So far we could just identify unhealthy diet, lifestyle and environment as the causative risk factors for esophageal oncogenesis (Ruiz et al, 2014). Unhealthy diet is a broad term. Need of the hour is to see the effect of various foods in helping us decrease the burden of cancer. Better dietary measurements and multidisciplinary researches could help us achieve the goal of finding an association between EC and dietary habits to curb the rampant onward move of esophageal cancer. This vast area needs to be further explored to see not only the tip but

the complete iceberg with consistent and unequivocal results. We can then meet the problem head on and defeat it.

OBJECTIVES OF STUDY

1. To identify the various dietary risk factors associated with Esophageal Cancer specific to the Doaba Region of Punjab.
2. To determine the socio-demographic and socio-economic association of Esophageal Cancer in the 'Doaba Region of Punjab'.
3. To examine linkage of dietary habits with subtypes of Esophageal Cancer in this region.

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REVIEW OF LITERATURE

To determine the 'Role of dietary habits in the development of esophageal cancer in the Doaba region of Punjab', a review of previous researches was made to get the bird's view of the work done in this sphere of dietary impact on esophageal cancer (EC). An endeavour to study the accessible researches on diet in totality was made under following sub-heads.

2.1 Prevalence of Cancer

According to Globocan 2018, non-communicable diseases are the main cause of death in the world today. Cancer ranks as first or second cause of death among people less than 70 years of age in 91 of 172 countries of the world, third or fourth in another 22 countries and ranks fifth to tenth in India. The year 2018 also saw 18.1 million new cancer patients

and 9.6 million deaths due to cancer, about half of the cases (48.4%) and half of deaths (57.3%) being in Asia. The worldwide incidence of all cancers among men is 218.6/100,000 and 182.6/100,000 in women.

2.1.1 World Esophageal Cancer statistics

Out of the new cancer cases detected, esophageal cancer was reported in 572,000 cases, 399,699 being men and 172,335 women. Esophageal cancer (EC) is the seventh commonest cancer in terms of incidence (572,000 new cases) and sixth in terms of mortality (509,000 deaths). According to these statistics 1 in every 20 cancer deaths in the year 2018 was due to EC and 90% of these were due to esophageal squamous cell carcinoma (ESCC) (Globocan, 2018). Cancer is now the third leading cause of death in South East Asia. According to Asia Pacific Journal of Cancer Prevention (2010) the number of cancer cases would move from 979,786 in 2010 to 1,148,757 in 2020. Esophageal cancer with 42,513 cases in 2020 would be the third major contributor (13.4%) to TRC (tobacco related cancer) and second major contributor (18.6%) to digestive system cancers.

2.1.2 Indian Esophageal Cancer statistics

In India 2,258,208 people are suffering with cancer for the last five years, 49,369 being cases of EC. The year 2018 also saw 1,157,294 new cancer cases (570,045 men and 587,249 women) and 784,821 patients losing to cancer. In the year 2018 in India 52,396 new cases of EC were registered making it the sixth most common type of cancer in the country. 46,504 EC patients died because of EC in India in 2018 ranking EC as the sixth most common cause of cancer related deaths (Globocan 2018: India factsheet).

2.1.3 Punjab and Doaba Esophageal Cancer statistics

Punjab state cancer report (PSR 2013) revealed the incidence of cancer per 100,000 of population as 99.1 in Kapurthala, 87.3 in Jalandhar, 86.9 in Hoshiarpur and 79.4 in Nawanshehar amounting to an average of 88.1 in the Doaba region. According to the Population Based Cancer Registeries, Indian Council of Medical Research released a

report comparing the incidence of cancer in Punjab with the incidence in rest of the country. Number of esophageal cancer cases among men in Punjab was reported as 2.1-6.6/100,000 as compared to 2.9-46.2/100,000 in rest of India. Amongst women of Punjab the incidence was 3.2-8.9/100,000 as compared to 0.94-14.81 in rest of India (Labani et al, 2015).

2.2 Socio-demographic presence

Esophageal cancer (EC) is a global health problem and it exists in every country and every race of the world. The rate of incidence varies widely from one region to another. Higher incidence of EC has been reported in countries of South America & Africa, Iceland, France, United Kingdoms, India, Japan, region around the Caspian Sea with special reference to the 'Asian esophageal cancer belt'(Mao et al, 2012). 'Asian esophageal cancer belt' stretches from Turkey to Taihang mountain region of China passing through Iran, Mongolia and Kazakhistan (Yu et al, 1993). In India higher incidence of esophageal cancer has been reported from the north-eastern states of Assam, Nagaland and Mizoram. Incidence in other states is also on the rise.The incidence rate of EC showed great disparity when compared on the basis of gender, being 2-3 times more in males than females in America (Yang et al, 2016). In most of the areas of China the incidence among males and females is in the ratio of 3to 5:1 (Yang et al, 2012). In certain areas of Iran, the women are suffering equally (Islami et al, 2009) whereas in Gezira, Central Sudan, male to female ratio is 1:3.3 (Mohammed et al, 2012). A study in Uttar Pradesh, reported 3 fold more incidence and mortality in males than females (Rathore SS, 2012) while those conducted in Rajasthan (Kapoor et al, 2015) and Maharashtra (Giri et al, 2014) showed a higher incidence amongst females.

2.3 Types of Esophageal Cancer

Esophageal Cancer occurs in the tissues lining the inner surface or epithelium of the esophagus. Primarily EC has two subtypes. One that arises from the cells lining the upper part of the esophagus is esophageal squamous cell carcinoma (ESCC). The other which arises from the glandular cells present at the junction of the esophagus and stomach is esophageal adenocarcinoma (EADC) (Yu et al, 1993). Tumours of the esophagus are usually malignant with about only 0.5% of them being benign. Smooth muscle tumour (leiomyoma) or gastrointestinal stromal tumour (GIST) constitutes less than 10% of the total tumours. Leiomyosarcoma is a rare non-epithelial tumour occurring in the esophagus (Rathore, 2012). Occasionally small cell carcinoma is also seen in the esophagus. This resembles the small cell lung cancer and is relatively more sensitive to chemotherapy than EC of other types. ESCC and EADC can be differentiated on the grounds of pathogenesis, epidemiology, etiology and biological behavior pattern. Understanding and delineating the etiology of EC will be the cornerstone in curbing and finally eliminating EC (Zhang, 2013). Earlier 90% of EC cases were ESCC cases but with the increase in the incidence of obesity and gastroesophageal reflux disease in the developed countries a tremendous shift in the epidemiology of EC has occurred. The incidence of EADC is on the rise, showing comparatively less disparity between ESCC and EADC (Napier et al, 2014).

2.4 Dietary causes of esophageal cancer

Daily diet of most of the individuals is guided by customs and traditions, religion, area of inhabitance, season, financial status, personal likes and dislikes. Studies have been undertaken since early twentieth century to nail the cause of esophageal cancer with respect to food intake and dietary habits. Eating more or less causes over-nutrition, under nutrition, deficiencies or nutrient imbalance. Donaldson (2004) calculated that in a year around 90,000 casualties could be prevented if people maintained a normal weight with BMI lower than 25. Avoiding being overweight and gastroesophageal reflux could decrease the incidence of EC (Engel et al, 2003).

2.4.1 Nutritional Factors

Different diet components studied by various researchers around the world, to find the possible cause of EC have been discussed below (Table 2.4.1).

Table 2.4.1 Epidemiologic association between food macronutrients and the risk of Esophageal Cancer

Nutrient food source	Model	References
Positive association (higher consumption = enhanced risk)		
Animal protein (red meat)	Case control	Gallus et al (2009), Castellsague et al (2009), Ceglie et al (2011)
Saturated fat	Case control	Skeie et al (2016)
Carbohydrate from refined cereals	Case control	Bosetti et al (2000), Donaldson (2004).
Negative association (higher consumption = decreased risk)		
Vegetable Proteins (Pulses)	Case control	Gupta et al (2012)
Animal protein (white meat)	Case control	Gallus et al (2009), Ganesh et al (2009)
Unsaturated fats	Case control	Bosetti et al (2000), Psaltopoulou et al (2011),Gupta et al (2012), Mizoguch (2014), Donatella and Francesca (2016).
Carbohydrates from whole cereals	Case control	Eslamian et al (2013), Nour et al (2016), Skeie et al (2016).
Fruits and Vegetables	Review studies	Kubo et al (2010), Yang et al (2016).

Cereals

Studies conducted in late twentieth century showed positive association between amount of cereal consumed and the risk of having EC (Yu et al, 1993). Later in the year 2000, researchers found an inverse relation between pasta/ rice consumption and esophageal cancer. The probable reason for this finding was that earlier studies did not keep the type of cereal and amount of micronutrient into consideration, as in refined flour rather than

the whole cereals (Bosetti et al, 2000). Diets rich in refined cereals have been associated with an increased risk of esophageal cancer, not only because they are deficient in a number of protective micronutrients perhaps because of high glycemic index, glycemic load and consequently insulin- linked growth factors. High levels of glycemic index (GI) are related more to certain types of cancer than increased (GL) glycemic load (Donaldson, 2004). In another study of Kurdistan province of Iran the researchers found both GI and GL to have positive association with EC (Eslamian et al, 2013).Along with carbohydrates, proteins, fats, vitamins and minerals, cereals also have non starch polysaccharide (NSP) or dietary fiber in different amount. NSP provides no calories or essential macro or micro nutrients but is important not only for intestinal movement but functioning also. It decreases the pH of the intestine, binds with bile acid and decreases the transit time in the intestines (Srilakshmi, 2014). Bile acids are considered as one of the causes of colon carcinogenesis by the regulation of gene expression 11. Association between whole-grain foods and decreased esophageal cancer risk too has been reported (Gallus et al, 2007). World Cancer Fund Report (2007) declared an inverse correlation between whole grain bread and total cancer. A weak inverse association of cancer with refined and total grain intake in dose-response analysis was observed. The report also stated no correlation between cancer and the consumption of brown rice, white rice, total rice and breakfast cereals. Huang et al (2015) found an inverse association between whole grains, cereal fiber intake and reduction in total and cause specific mortality with cereal fiber being a potential protective constituent.Over-nutrition is linked with high intake of carbohydrates and obesity. There is a rise in the incidence of EADC and a significant association has been seen between carbohydrate intake and EADC. A positive relation has also been noticed between obesity and EADC (Mao et al, 2012). Zinc intake has been found to be significantly associated with esophageal and gastric cancer among Asians (Li et al, 2013). Perhaps high unprocessed cereal and whole pulses in Indian diet was the reason of low incidence of various cancers. We could lose this advantage by not giving importance to our traditional foods and replacing them with refined foods.

Pulses and Legumes

In the last quarter of twentieth century, studies showed the beneficial role of protein intake on EC. In 2002, Hangen and Bennink reported lower incidence of lab induced certain cancers and tumour multiplicity in rats consuming *Phaseolus vulgaris* (common beans). Beans are rich in functional compounds. Polyphenols like anthocyanins, flavonols present in beans have antioxidant, anti-inflammatory, anti-mutagenic and anti-carcinogenic properties (Ganesan et al, 2017). Various researches have suggested the positive role of fiber in preventing certain cancers. Wong et al (2010) worked on Japanese Hokkaido red beans and isolated a haemagglutinin which had antiproliferative effect on human hepatic cancer cells. It was unstable above 90°C. High doses of lectin phytohaemagglutinin present in various varieties of beans are toxic. It affects cell metabolism and can be done away with soaking and cooking at high temperature. Its mitogenic activity is used to enhance T-lymphocyte cell division and to inhibit cancer cell proliferation (Marko et al, 2010). The non digestible carbohydrates of pulses act as prebiotics which enhance the growth of lactobacilli and have an anti-inflammatory action. The fiber and antioxidants can have protective effect against certaintypes of cancer. Huang et al (2012) reported that selenium stimulates immune system, regulate cell proliferation and perform cytotoxic action against cancer cells.

Dry peas, chickpeas and faba beans have 20-30% dry weight protein. Peas have a good amount of tyrosine, lysine and histidine. Chickpea is rich in tryptophan, lysine and isoleucine while methionine and cystine are the limiting amino acids. They have antinutritive compounds like trypsin inhibitors, tannins, haemagglutinin, saponins and phytic acid (Yadahally et al, 2010) which are either destroyed or decreased on germinating and thermal food processing. Pulses and legumes (like lentil, chickpea, gram and beans) are the main source of protein in a vegetarian diet and they have been linked with reduced risk of cancer (Gupta et al, 2012). Soya beans and its products have been an important dietary component of East Asian cultures for many centuries, now it has been adopted by the West also. Soya bean is a rich source of proteins, carbohydrates and fats. It is favoured because of its non-nutritive secondary metabolites or

phytocemicals. Other than peptide lunasin, phytochemicals saponins and flavanoids it is popular for its isoflavones daidzein and glycitein (Messina, 2016).

Fats and Oils

Role of dietary fat in the etiology of cancer has been studied for more than half century. Changes in lipid metabolism, disturbs the homeostatic balance controlling cell differentiation, cell proliferation and apoptosis resulting in neoplastic lesion. Similarly saturated fats could have an impact on hormonal status, alter structure and functioning of cell membrane, cell signaling pathways, gene expression and could also affect the immune system (Othman, 2007) The studies on *vanaspati ghee* (hydrogenated vegetable oil) and *desi ghee* (clarified butter oil) are limited. Rani and Kansal (2012) reported the potential of cow *ghee* in down regulating the activity of enzymes involved in carcinogen activity and increases the detoxifying activities in specific tissues of rat models. Herr et al (2013) reported mustard oil to have antioxidative property that protects the damage of DNA. This suggests that source, origin, consumption pattern and nature of processing of various fats and oils have varied impact on oncogenesis.

Animal fats or saturated fats including butter showed positive correlation with higher incidence of esophageal cancer (Gupta et al, 2012).A protective effect was presented by monounsaturated and polyunsaturated fats. The Mediterranean diet is considered healthy because of the high percentage of mono and poly unsaturated fats in it. This is the reason for low incidence of EC in northern Italy than in southern Italy because in northern Italy people still follow the conservative traditional Mediterranean diet. The decrease in esophageal carcinogenesis on the consumption of olive oil is due to the type of fat-oleic acid, presence of vitamin E or polyphenols. These findings were independent of the amount of alcohol and smoking by an individual (Bosetti et al. 2000). Tuyns et al (2009) concluded that polyunsaturated fats had a significant protective effect.

Imbalance of omega 3:6 ratio could promote cancer. In animal studies omega 3 fats (DHA, EPA and alpha-linolenic acid) protect from cancer whereas omega 6 fats (arachidonic acid and linoleic acid) promote it. Changes in the n-6 and n-3 fatty acid

metabolism of the cell membrane alters the structure, function, enzyme activity, oxidative condition of cell and the signaling pathways. These happenings are an important feature in the sustenance and growth of neoplastic lesion and at the same time provide target for intervention or cancer modulation with the use of specific n-6, n-3 ratio (Othman, 2007; Abel et al, 2014). Ceglie et al (2011) found association between EC and meat & high fat intake though the findings were not very consistent. Schwab et al (2014) and He et al (2017) also reported an increased risk of EADC with increased consumption of high amount of total fat, saturated and mono unsaturated fat. A negative association was also found between partially hydrogenated vegetable oil trans-fatty acids and all types of cancer (Laake et al, 2013). Abel et al (2014) reported from the cancer tissue biopsy that a specific type of lipid profile was associated with the development and growth of malignant lesions. Flax seed, its oil and its lignan content decreases the tumour load especially the secoisolariciresinol diglycoside in lignan (Donaldson, 2004).

Role of nuts and oil seeds in decreasing the incidence of cancer and treatment is still in the initial stage and needs more research to find benefits other than antioxidants (Lang et al, 2015). It is too early to label amygdalin as a double edged sword which lowersresistance of cancer cells to treatment and secondly attack cancer cells with its cyanide content (Blaheta et al, 2016).

Milk and Milk Products

A marginal increase in the incidence of EC was observed with high consumption of milk (Bosetti et al, 2000) but no steady correlation between EC and intake of milk and other dairy products was noticed (Gallus et al, 2007). Tsuda et al (2000) proposed that conjugated linoleic acid could induce an inhibitory effect. Parodi (2015) reported that cow's milk components possess anti-cancer potential, accounted to increased levels of bifidobacterium and certain lactobacilli. Butyrate produced during fermentative activity of organisms promoted antiproliferation, apoptosis and differentiation in some cancer cells. Rumenic acid acted as a powerful anticarcinogen in experimental animals. These factors probably act together to fight the environmental insult and prevent cancer. In the beginning of twenty first century Lamprecht and Lipkin team (2001) reported the role of

calcium in cancer prevention of certain organs. Calcium forms insoluble soaps with bile acids and fatty acids in the gastrointestinal tract preventing cell damage, reducing cell proliferation and causes differentiation. Calcium improves signaling within the cells leading to differentiation and apoptosis in cancer cells. Oral enzymes especially proteases can have a direct anti-tumour and anti-metastatic effect on reaching systemic circulation (Donaldson, 2004). A few animal model studies reported the potential of bovine lactoferrin (bLF) in the chemoprevention of colon and various other cancers. Lactoferrin was found to exhibit antiviral, antifungal, antibacterial and antitumour activity. It also enhanced the immune system function in already immunocompromised animals. Alpha lactalbumin and casein hydrolyzates also demonstrated anti tumour activity (Zimecki and Kruzel, 2007). The milk constituents alpha lactalbumin and a casein degradation product, glycomacropeptide have been used together in health enhancing formula feeds for both infants and adults in addition to preventing and treating cancer (Artym and Zimecki, 2013). Rock (2011) stated that numerous bioactive substances in milk could have an impact on the risk and progression of cancer. Analysis of Bravi et al (2012) to study the impact of animal products on the risk of esophageal cancer revealed an increased risk of EC in the ‘high milk’ cluster of their sample. Park et al (2014) reported alpha casein and total casein as the proteins which promoted proliferation of PC3 and LNCaP in specific cancer cells but not IGF-1. Davoodi et al (2016) studied the anticarcinogenic, immunomodulatory, antihypertensive, hypocholesterolemic, and antimicrobial properties of milk. Their findings indicated the effectiveness of milk protein in the reduction of risk factor for cancer. Li et al (2017) also suggested an inverse correlation between dietary calcium intake and the risk of EC specifically ESCC in the Asian population but not in American and European population.

Meat, Fish and Poultry

Various researches conducted on vegetarian and non-vegetarian diet have varied results. Several reports revealed an inverse correlation between EC and various types of meat while many other report non-significant association. A higher risk of ESCC and EADC has been correlated with processed meat and red meat intake whereas the consumption of

fish and white meat were inversely correlated (Castellsagu'e et al, 2000; Gallus et al, 2007). High intake of poultry is related with a decrease in the risk of esophageal cancer. Intake of fresh fish decreased the incidence of EC by 20% in a study conducted in Mumbai (Ganesh et al, 2009).

Excessive consumption of meat cooked by barbecue method, frying or roasting at high temperatures is particularly associated with an increased risk of EC. These cooking methods produce high amount of organic compounds like heterocyclic amines which may raise the risk of EC (Cancer Research UK, 2014). In another study also grilled meat consumers were in the highest quintile for 2-Amino-1-methyl-6-phenylimidazo 4,5-b pyridine (PhIP) the main heterocyclic amine produced from cooking meats at raised temperature (Tang et al, 2007). Salted meat in the Uruguayan diet is considered a risk factor in EC because of its nitrodimethylamine content. Though an exogenous nitrosamine its impact is biologically plausible as nitrosamine exposure is related to EC. So far no concrete evidence against grilling, smoking and barbecuing as a cause of stomach or any other cancer has been found (World Cancer Fund Report, 2007). Meat is a rich source of proteins, vitamins, minerals and fats especially omega 3 fatty acid and linoleic acid. Incorporation of various spices makes cooking of meat different in India. (Devi et al, 2014). World Cancer Fund Report (2007) also stated that there was no significant evidence in terms of amount, consistency or quality to conclude any relation between egg, poultry, fish and meat consumption and the risk of esophageal cancer. People who consume large amounts of animal foods consume small amount of vegetables. The impact seen in certain studies is due to consumption of animal foods or lack of vegetables and other protective foods is hard to decipher.

Fruits and Vegetables

Fruits and vegetables add to the micronutrients and non nutritional components in the diet. Most of the case studies and meta-analysis have revealed an inverse association with EC. Stronger inverse association seen in case of citrus fruits than other fruits could support the importance of vitamin C but the debate is still on.

Higher intake of vegetables was found to be more effective than even citrus fruits. The possible explanation being the low energy and low sugar content (Bosetti et al, 2000). Findings of Yang et al (2016), Kubo et al (2010) and Castellsagu'e et al (2000) also endorsed the belief of protective nature of fruits and vegetables while a meta-study conducted in Japan showed fruits having more protective effect than the vegetables**.** Poor intake of fruits and vegetables, lack of vitamins especially A, C, riboflavin and mineral like selenium, may also increase the risk of cancer. Intake of pickled vegetables, preserved vegetables, salted foods and fermented bean products more than once a week increased the risk by 3.4 times in men aged 40 years and above (Hung et al, 2004). Case control studies support a considerable decrease in the risk of cancers of the esophagus, lung, stomach and colorectum with fruits and vegetables but cohort studies indicate about their protective nature only not the decrease in risk factor (Riboli and Norat, 2003). Some researchers found that consumption of fruits and vegetables decreased the incidence of both ESCC and EADC (Holmes et al, 2007). Polyphenols and ascorbic acid in fruits and vegetables were thought to protect from the polycyclic hydrocarbons produced by burning coal and wood (Yang et al, 2016).Dietary intake of flavanoes, flavanones, total flavanoids and anthocyanidins could reduce the risk of EC (Cui et al, 2016). Certain vegetables are packed with anticarcinogens like sulforophane in cruciferous family and lycopene in tomatoes. The protective nature of fruits and vegetables is not because of a few vitamins, minerals, fiber or phytochemicals but a group of them (Table 2.4.2), each having its own mechanism of action (Table 2.4.3). The peel and seeds of citrus fruits too are very good source of antioxidants (Singh et al, 2014).

Dark green leafy vegetables contain folic acid which plays an important role in the methylation of DNA and DNA synthesis along with vitamins-B6 and B12. Insufficient folic acid causes DNA strand breakage. Alcohol intake increases cancer risk because it is an antagonist of folate. Chlorophyll and its derivatives in green plants combine with various carcinogens (hydrocarbons, heterocyclic amine, aflatoxins, etc.) to form a hard complex which is difficult for the body to absorb and is thrown out.

International agency for research on cancer (IARC) reported (2003) 40-50% lower risk of EC in people having high intake of fruits and vegetables. American institute for cancer research (2007) summarized their findings by reporting low energy dense non-starchy vegetables and fruits to be probably protective against cancers of upper aerodigestive tract including esophagus. The prospective study conducted by Freedman et al (2007) and Yamaji et al (2008) suggested an inverse association between fruits and vegetable consumption and risk of ESCC only not EADC. An increased consumption of 100 ug/day of dietary folate decreased the risk of EC by 12% (Zhao et al, 2017).

Beverages

Mate Drink

Mate is a tea like beverage prepared from the plant Ilex paraguariensis in South America. High consumption of mate is the suspected cause of high incidence of EC in that region (Castellsagu'e et al, 2000; Andrici and Eslick, 2013). More than 50% researches have shown a notable rise in the risk of EC related to higher temperature of foods consumed (Islami et al, 2009). The effect of mate amount showed significant relation only in those who had it hot and not in those who had it at lower temperature. These two were independent risk factors.The carcinogenic effect is due to the components of the herb, to the temperature at which it is consumed or to both is still an unanswered question (Castellsagu'e et al, 2000). In 2007 World Cancer Report summarized the findings of various studies by relating the increased risk of EC with increased consumption of mate to the traditional way of drinking it hot from a gourd with a metal straw placed in the mouth like a tobacco pipe.Consistent with the thermal injury affect other beverages like hot soup, coffee with milk and tea also showed association with EC.

Soup

A positive association was indicated between EC and hot soups. Soups are indispensable part of the mediterranean diet and are consumed heavily in the central and northern Italy. Soups have a high salt content and are consumed hot. Ingestion of drinks at high temperature showed positive linkage to precancerous esophageal lesions (Bosetti et al, 2000).

Tea/Coffee

Tea is one of the most popular beverages. According to the manufacturing process tea is classified into three categories—green or non-fermented, oolong or half fermented and black or fermented. The constituents of green tea like EGCG or epigallocatechin-3gallate, EGC or epigallocatechin and ECG or epicatechin-3gallate have been found to curb tumourgenesis in various animal models (Zheng et al, 2012). Earlier also researchers had stated that green tea had the property of inhibiting esophageal carcinogenesis (Gao et al, 2006). However, Castellsagu'e et al (2000) observed the association between large volume of tea intake and its temperature with EC. Large volume was protective but high temperature increased the risk of EC about 4 folds. An Iranian study of Ghadirian was also consistent with these findings of EC (Castellsagu'e et al, 2000). The meta-analysis of epidemiological studies conducted in China and Japan observed insignificant chemopreventive effect of high, medium or low consumption of green tea but an interesting finding of green tea being protective in females was concluded. There could be a possibility of a sex hormone mediated pathway in the development of EC. Estrogen had an inhibiting effect while androgen had a promoting effect on EC. Researchers have shown the hormonal relation in the growth rate of metastatic squamous cell esophageal carcinoma also with estrogen inhibiting it and testosterone enhancing it.

In 2012, Dr Laurence Knott found that drinking black tea at temp. 70º C or higher increased the risk of EC (Cancer Research UK, 2014). The increase of intra-esophageal temperature depended not only on the temperature of the drink but more on the volume swallowed at a time. A study in Shanxi province of China too found major association between EC and thermal damage (Gao et al, 2006). The impact of temperature was evident when the quantity of the hot drink was large. The risk increased 2-4 folds with high temperature of the beverage. In Taiwan, increased risk of EC was correlated with the intake of overheated foods and preserved foods but was inversely correlated with the consumption of tea, fresh vegetables and fruits. (Hung et al, 2004). The initiation and development of EC by hot foods and beverages is possibly by both direct and indirect pathways. The chronic thermal insult to the mucosa could enhance the formation of RNS-

reactive nitrogen species and finally lead to the formation of nitrosamines of carcinogenic potential. Other possible cause is the weakening of the epithelial barrier due to repeated thermal injury. The weak epithelium is susceptible to various intraluminal carcinogens leading to ESCC (Tai et al, 2017).A study conducted in Tanzania, Munishi et al (2015) found hot milk tea to be an important factor for EC in the region. Das et al (2015) revealed an increase in the incidence rate of ESCC with a consumption of more than 3 cups of tea per day in their study conducted in a tertiary hospital of Punjab. Inverse association between coffee consumption and risk of esophageal cancer was reported in studies conducted by Castellsagu'e et al (2000) and Ren et al (2010). Wang et al (2016) and Miranda et al (2017) reported coffee to be protective against oral and pharyngeal cancer.

Many researchers have conducted studies to see the impact of beverages and their temperature but Wu et al (2011) reported an increased risk of esophageal cancer is associated with injury to the mucosa by big bite/sip, fast eating speed and high temperature. Chen et al (2015), Tai et al (2017) reported a positive association of hot food and beverage intake with the incidence of esophageal carcinoma in north western China.

Soft Drinks

Significant studies have not been conducted to see the impact of noncarbonated sugar-sweetened beverages on the incidence of cancer. Fuchs et al (2014) reported progression of certain cancers with the consumption of sugar-sweetened beverages.

Researchers studied the impact of carbonated soft drinks and EC in United States. The team found a significant association between the increased consumption of sodas and increased incidence of EC. Though they did not rule it out to be a chance correlation, they explained it on biological basis. Sodas distended the stomach, causing gastric reflux and finally EC. The study found that EC rates were increasing in all countries consuming more than twenty gallons of fizzy sodas ('Sodas raise cancer risk, U.S. study finds'- Reuters news item; May 17, 2004). A few more studies conducted to study this correlation, soda showed entirely opposite results. Studies of case-control nature

conducted in Sweden and Australia (Ibiebele et al, 2008) concluded that soda drinks had no association with increased risk of esophageal cancer. Mayne et al (2006), Johnson et al (2010) and Kubo et al (2010) too had similar findings.

The high incidence of ESCC in the population of Linxian is also associated with the use of pond water for cooking and drinking. It was rich in nitrates and nitrites formed by the oxidation of the organic nitrogenous material in water (Yang et al, 2016).

2.4.2 Non-Nutrient Components

Our daily diet could be directly or indirectly a source of carcinogens (Bathija, et al, 2014). Macro nutrients—proteins, fats and carbohydrates; and micronutrients—vitamins like folic acid, riboflavin, retinol, tocopherol, vit.B12 (especially methylecobalamine) and minerals like selenium, zinc, magnesium and calcium are known for their modulatory effects in experimental cancers. A study conducted in China showed that esophageal epithelial cells were sensitive to the deficiency of vitamin A and riboflavin. The study mentions the inhibitory effect of vitamins E and C on oncogenesis (Jiang et al, 2008). Though nutritional factors of diet appear to influence initiation and promotion of malignant growth, the role of non nutritional components is also gaining a lot of importance. Their anticarcinogenic and antimutagenic properties are emphasized. These properties have given them the name of bioactive compounds or chemopreventers. Chemoprevention is the process of blocking or reversing carcinogenesis in the early stages. It is an affordable, easily implementable approach that can help in controlling cancer.

Spices

Indian diet is full of a variety of spices and condiments. They are not only anti-inflammatory, antimicrobial, hypoglycaemic and hypocholesterolaemic in nature but also possess antioxidant, antimutagenic and anticarcinogenic qualities. Turmeric, ginger, anise, thyme, clove, cinnamon, mustard have been observed to be antimutagenic and antioxidative in nature. The non-nutrient dietary components (chemopreventers) act in different ways (Table 2.4.3). Chemopreventers inhibit carcinogenesis, inhibit or stimulate

enzyme activity, physically react and detoxify carcinogens or suppress their metabolic pathways. The chemopreventers mainly act by detoxification or antimutagenic processes at both the initiation and promotion steps of carcinogenesis. The antineoplastic effects of inducing and inhibiting agents in foods focus on specific monooxygenases like the aryl hydrocarbon hydroxylase (AHH), uridine diphosphate (UDP), uridine diphosphate glucuronyl transferase (UDPGT), and glutathione S transferase. Carcinogens bind to the DNA, RNA and proteins giving rise to mutagenic process leading to cell transformation and neoplastic changes. Antimutagens prevent this process by binding to the carcinogens or their metabolites, or by metabolizing and eliminating toxic xenobiotics.

Chemopreventers/ Phytochemicals

Various food groups—cereals, pulses, fruits and vegetables, spices and condiments, etc. not only contain macronutrients and micronutrients but also contain various micro constituents that are biologically active. The chemopreventers are a group of 25 types of phytochemicals that are safe, have low or no toxicity. (Table 2.4.2)

Table 2.4.2 Food sources of phytochemicals

Phytochemicals	Food source	Effect on EC	Reference
Fiber	Cereals, pulses, fruits and vegetables	• Inhibits cell growth rate by reducing cellular proliferation and promoting apoptosis • Lowers tumour necrosis factor α receptor 2 and interleukin affecting carcinogenesis process • May absorb carcinogens in GIT	McFadden et al, 2008 Ma Y et al, 2008 Brown et al, 1995
Carotenoids	Yellow/orange vegetables, fruits and dark green leafy vegetables	• May curb the oxidative stress caused by chronic acid reflux	Terry et al, 2000 Giri et al,2015
Allium compounds	Onion, garlic, chives, leeks	• Acts on cytochrome P450 and counteracts pro-carcinogen activation	Adaki et al, 2014

Dithiolthiones/ glucosinolates	Cruciferous vegetables	• Inhibition of enzymes responsible for activation of pro-carcinogens • Induction of enzymes important in mutagen elimination • Induction of cell cycle arrest • Inhibits NF-kB(nuclear factor kappa light chain enhancer of activated B cells)	Tortorella et al, 2015
Isothiocyanates	Cruciferous vegetables	• Causes cessation of growth and cell death selectively in cancer cells • Curtails cancer development by suppressing diverse cancer pathways e.g. neoangiogenesis, NFkB	Ruiz et al, 2016
Terpenoids	Oil of citrus fruit peel	• Inhibits cancer cell proliferation and metastasis through varied mechanisms	Huang et al, 2012
Phytoestrogens	Cereals, pulses, sorghum, millets, Soya beans, fruits and berries	• Lignan reduces the incidence of EADC and GE junction adenocarcinoma	Lin et al, 2013
Protease inhibitors	Cereals, barley, wheat, oats, rye, Soya beans, kidney beans and chick peas	• Prevents spread of cancer cells and suppresses tumour growth. • Inhibits degradation of extra cellular matrix, cancer invasion and metastasis	De Clerck et al, 2004 Herszenyl et al, 2014
Phytic acid	Cereals, nuts, seeds, sesame seeds, lima beans, peanuts, and soya beans	• Initiates apoptosis • Curbs cell proliferation • Changes cell cycle progression	Henderson et al,2012
Flavonoids	Fruits and vegetables	• Antioxidant, anti-inflammatory, antiviral, antiallergic and anti tumour characteristics	Tanwar and Modgil, 2012
Phenolic	Fruits,	• Inhibits tumour cell proliferation	Zhang et al,

compounds	vegetables and tea	• Induces apoptosis • Breaks DNA binding to carcinogens • Disturbs angiogenesis	2013
Plant sterols	Vegetables	• β sitosterol reduces the risk of ESCC	Liu et al,2013
Saponins	Soya beans, yam and colocasia	• Rhizoma Paridis Saponins decrease the release of prostaglandins • Promotes apoptosis and cell cycle arrest in • Esophageal cancer in rats • Inhibits COX-2 pathway	Yan et al, 2015

(Source: ICMR 2001)

Table 2.4.3 Non-nutrient chemopreventers – Mechanism of action

Category	Mechanism
Inhibitors of carcinogen formation	
Caffeic acid, ferulic acid	Inhibit *in situ* formation of carcinogen *eg* nitrosamines acid formation.
Blocking agents Isothiocyanates, diallylsulphide, ellagic acid, ferulic acid, dithiocarbamates.	Inhibit the activity of enzymes (cytochrome P 450) which convert procarcinogens to carcinogens
Inducing agents Isothiocyanates, sulpharaphane d-limonene, terpenoids and curcumin	Stimulate enzymatic system, which are involved in detoxification of carcinogens.

Trapping agents	
Ellagic acid, N-acetylcysteine.	Physically react with carcinogens and detoxify them.
Suppressing agents	
Selenium, isoflavones, phytoestrogens and epigallocatechin gallate (EGCG)	Suppress different steps in metabolic pathways required for tumour development.

(Source: ICMR 2001)

2.5 Lifestyle Practices in India

India has a spectrum of food or dietary practices uncommon to other parts of the world. Every region has its own specific food habits. Studies have been conducted in places like Kashmir, Assam, Kerala, Karnataka, Tamil Nadu, etc. with inconsistent outcome.

In Kashmir the etiology of ESCC appears to be the excessive use of salt, spices, deep fried foods and over brewing in copper utensils (Mir and Dar, 2009). Increased exposure of fruit growers to indiscriminate spraying of various fungicides and insecticides too should be considered for their synergistic impact on the increased risk of EC. Contamination of traditional dried foodstuff and spice cakes with bacteria and mycotoxins are also considered to be predisposing factors to EC (Mir and Dar, 2009). The alkalinity of prolonged simmering of salted tea with addition of sodium bicarbonate in copper utensils could be a predisposing factor for EC (Dar et al, 2015). Poorly differentiated EC patients had higher levels of copper than moderately or well differentiated tumour patients. A positive correlation between zinc deficiency and presence of TP53 mutation in the tumour was also noticed (Dar et al, 2008). High incidence of esophagitis in the population is the result of chronic exposure to pro-inflammatory agents like coarse or abrasive food, hot beverages and irritant dietary components leading to the occurrence of premalignant lesion. High consumption of local salted tea makes a multi pronged attack. Salt is an established irritant and possible cause for gastric cancer. Traditional preparation method formed considerable amount of N nitroso-compounds and had a high methylating activity. Tannin isolated from tea gave rise to ribosomal degranulation and showed genotoxicity to rat hepatocytes (Wani et al, 2013). High temperature of tea could cause thermal injury to esophageal mucosa and enhance mutagenesis.

Unlike the Kashmir study, the researchers in Coimbatore found no association between spicy, fried food, salted fish and esophageal cancer but a significant correlation between pickle consumption and EC (Chitra et al, 2004).

Assam in the north east of India has one of the highest incidences of EC in India. The study conducted in Assam (Phukan et al, 2001) too identified their unique traditional food item, *Kalakhar*, as a significant risk factor. A positive association between the consumption of very spicy foods, hot foods, hot beverages, left over foods and EC was alaso noticed by them (Table2.4.4).

2.5.1 Alcohol and Tobacco

According to the WHO global status report on alcohol and health (2014) 38.30% of world's population and 30% of Indian population consumed alcohol regularly. The individual average annual consumption in India is 4.3 litres. Organization for economic cooperation and development reported (2015) a consumption of 101-500 ml per capita per week of country liquor and 1-50 ml per capita per week of beer, imported alcohol and wine in Punjab. Global Adult tobacco survey (GATS) under WHO presented, 'India fact sheet 2009-2010'. According to these statistics 14.0% of Indian adults smoked tobacco, 25.9% used smokeless tobacco, 34.6% used tobacco in any form while the Punjab statistics of above categories were 0-10%,0-10% and 10-20% among persons of 15 years of age or more. Generally speaking alcohol is not considered a part of diet but because of its high caloric value and some nutrient content in the diet of some communities it is broadly studied. Tobacco smoking and alcohol drinking are considered to be the major risk factors for ESCC even though certain studies like that conducted in Linxian, China have shown no association between alcohol/ tobacco consumption and high incidence of EC (Yu et al, 1993). In Chennai and Trivandrum too, studies did not find a significant association between various types of alcohol traditionally consumed in Southern India (arrack, country liquor and toddy) in causation of all 3-oral, pharyngeal and esophageal cancer (Znaor et al, 2003). Most of the studies have shown that about 90% of EC cases are caused by alcohol drinking and tobacco smoking and the cessation of smoking alone significantly reduces the risk of developing EC (Castellsagu'e et al, 2000; Znaor et al, 2003). An Italian study showed that alcohol attributed a little more than tobacco smoking in causing EC. Statistically alcohol attributed about 52% and tobacco smoking 40% as the risk factors for EC (Franceschi et al, 1990). In a study in Karnataka, statistics showed

alcohol attributed a little more than 64%, tobacco smoking 56% and tobacco chewing 52% as risk factors for EC (Bathija et al, 2014). Individually they are harmful and together they are lethal. Their synergistic effect increases the risk of developing EC by 100 folds. In 2016, Yang et al estimated an increase of ESCC to the tune of 3-7 times in current smokers and 3-5 times in alcohol consumers with the incidence rate being manifolds in those who consume tobacco and alcohol both. Smoke of tobacco contains mainly nitrosamines and polycyclic aromatic hydrocarbons along with a significant amount of pro oxidative substances which produce ROS- reactive oxygen species. ROS is considered to play a role in carcinogenesis. Tobacco carcinogens dissolve in ethanol and transport to the cells with ease. This is considered to be the cause of the lethal synergy of alcohol and tobacco (Yang et al, 2016).

Impact of different types of liquor and tobacco consumption was also studied by a few researchers. A case-control study in Spain revealed that the intake of combination of hard liquors was more harmful for well being than low intake of wine. Similarly the type of cigarette mattered as black one was found to be more harmful than the blond one (Mao et al, 2011). A European study saw increased risk with consumption of alcohol, neat and without or less salad and snacks (Joshi et al, 2009). In Normandy, area in western France, high incidence of ESCC is attributed to the consumption of homemade alcohol (Mir and Dar, 2009). Samples of beer obtained from various Indian cities especially southern India contained N-nitrosodimethylamine in large quantity.

In a study conducted in Kashmir, use of *hooka* and *nass* too increased the risk of esophageal cancer (Dar et al, 2012). Mao et al had also reported similar findings in their population in 2011.Not only smoking but chewing of tobacco too has been found to be an important risk factor with odds ratio exceeding 2.5 (Chitra et al, 2004). In a study in Jammu, snuff (smokeless tobacco) was found to be the most significant risk factor for EC (Sehgal et al, 2012). Prevalence of tobacco and alcohol use can neither justify the decrease in the incidence of ESCC in the last 40 years in developed countries nor the racial difference in the incidence rate of ESCC (Yang et al, 2016).

2.5.2 Betel Nut and Betel Quid

Chewing of betel nut and betel quid with or without tobacco is an important risk factor for EC (Znaor et al, 2003; Chitra et al, 2004). It also adds to the carcinogenic effect of tobacco and alcohol. Contact of betel juice directly with esophageal mucosa too could contribute to carcinogenesis (Wu et al, 2006). It irritates the mucosa of the mouth and esophagus. Areca nut was reported to increase the risk of ESCC significantly and independently in the people of Asia (Akhtar, 2013; Garg et al 2014). Hossain et al (2015) found arecoline, the major alkaloid in betel or areca nut to be carcinogenic. Some polyphenols present in the nut are genotoxic as they form ROS or reactive oxygen species in the saliva of the chewer. Wang et al (2017) found histone methylation and acetylation related enzymes in the tissue of ESCC patients consuming betel quid.

2.6 Microbial and medicinal Impact

Helicobacter pylori is a bacteria considered to increase the risk of adenocarcinoma of the stomach and decrease the incidence of esophageal carcinoma (Kamangar et al, 2009). Turmeric was found to inhibit the growth of various strains of *Helicobacter pylori* (Sinha et al, 2003). Gao et al (2016) reported the presence of *Porphyromonas gingivalis* in 61% cancerous tissue and 12% adjacent tissue immunohistochemically in ESCC patients and not in normal esophageal mucosa. Similarly a catalytic endoprotease secretion, unique feature of *P.gingivalis and P.gingivalis* 16S rDNA was seen. Study conducted by Kamangar et al (2009) reported the use of H2 blockers and non-steroidal anti-inflammatory drugs and poor oral hygiene as some of the causative factors of esophageal cancer.

2.7 Socio-Economic Status

About 30 to 40 percent of all cancers can be prevented by simple changes in the lifestyle and dietary pattern of people. Researchers in U.S.A too found socioeconomic status as a

factor that was positively associated with EC (Brown et al, 2001). Over-nutrition and under-nutrition are considered as causative factors of EC. These can be linked to the socioeconomic status. Over-nutrition is associated with high socioeconomic status and under-nutrition with low socioeconomic status. Other reasons for nutritional imbalance could be lack of knowledge or awareness of protective foods. Low intake of micronutrients like vitamin A, C, E, riboflavin, zinc and selenium too could be the precipitating factor for EC. A study in India revealed 80% EC cases to be males between 41-60 years of age; 68% were from low socio-economic strata and 60% were not literate (Bathija et al, 2014). Similar findings were reported by Dar et al (2015). Gholipour et al (2016) reported low SES to be linked to lack of nutritious food, unhealthy environment, decreased and delayed access to health care which hindered early diagnosis, treatment and prognosis. The house hold combustible fuels too are considered as prospective risk factors (Rathore, 2012).

Table 2.4.4 Association between different factors, foods and risk of Esophageal Cancer

Factors/ Foods	Association (risk)	Reference
Temperature of food	Increased	Islami et al (2009), Castellsague et al (2000), Hung (2004), Chen et al (2017).
Size of bite/sip	Increased	Wani et al (2013), Wu et al (2011).
Pickles	Increased	Chitra et al (2004).
Chilies	Increased	Phukan et al (2000), Mir and Dar (2009).
Black tea	Increased	Wani et al (2013).

(tannin)		
Green tea	Decreased	Zheng et al (2012).
Salt tea	Increased	Mir and Dar (2009), Dar et al (2015).
Soda drinks	No association	Kubo et al (2010), Johnson et al (2010).
Smoke from solid fuel	Increased	Rathore (2012), Sapkota et al (2013)
Pollutants	Increased	Ceglie et al (2011), Tabrez et al (2013)

Fig 2.1 Protective and harmful foods in incidence of Esophageal Cancer

MATERIALS AND METHODS

Research is the systematic investigation of a particular concern or problem in order to establish facts and reach new conclusions. It involves formalized collection of data, information and facts for the advancement of knowledge. The actions taken and the application of specific techniques to collect process and analyse data impersonally and without bias is covered under methodology. To determine 'The role of dietary habits in the development of esophageal cancer in the Doaba region of Punjab' the current case-control study was conducted with the help of dietary and lifestyle survey.

The nature of our research demanded a case-control study. It falls under the category of observational study in which two groups differ in outcome when compared on the basis of causal attributes. Case-control studies help to identify potential factors contributing to a medical condition by comparing disease affected cases with people without that disease. Case-control study is a low cost, commonly used type of epidemiological study which can be carried out even by small teams or individual researchers. This kind of research design has been very effective in the study of rare disease or in cases where a little is known about the linkage between the risk factors and the disease. A number of important discoveries and advances such as association between tobacco smoking and lung cancer have been established as a result of case-control studies.

For effective and flawless data collection a face to face survey method was used as it has a very high survey response rate. This is because of the trust the respondent places in the researcher as it is in-person. The survey design involved the following steps.

3.1 Location/Region of study

3.2 Questionnaire design

3.2.1 Socio-demographic

3.2.2 Clinical picture

3.1 Location/Region of study

The present study was conducted in the 'Doaba region' of Punjab, a north western state of India. Doaba also referred to as 'Bist Doaba' derives its name from the fusion of two Persian words 'do' and 'ab' which means two waters. It literally means the land enclosed by two rivers, Beas in the north and Sutlej in the south. Its geographical coordinates are 31°20'N 76° 10'E. Districts of Jalandhar, Kapurthala, Nawanshehar (Shaheed Bhagat Singh Nagar) and Hoshiarpur constitute 'The Doaba Region'. Doaba region has a population of about 52 lakhs with nearly 65% people residing in villages.

Table 3.1.1 Population distribution of Doaba region

District	Rural (%)	Urban (%)	Total (in number)
Jalandhar	46.82	53.18	2,181,753
Hoshiarpur	78.80	21.20	1,582,793
Kapurthala	65.35	34.65	815,168
Nawanshehar	79.57	20.43	614,362
Doaba region	63.36	36.64	5,194,076

(Source: www.punjab.gov.in, 2011 census)

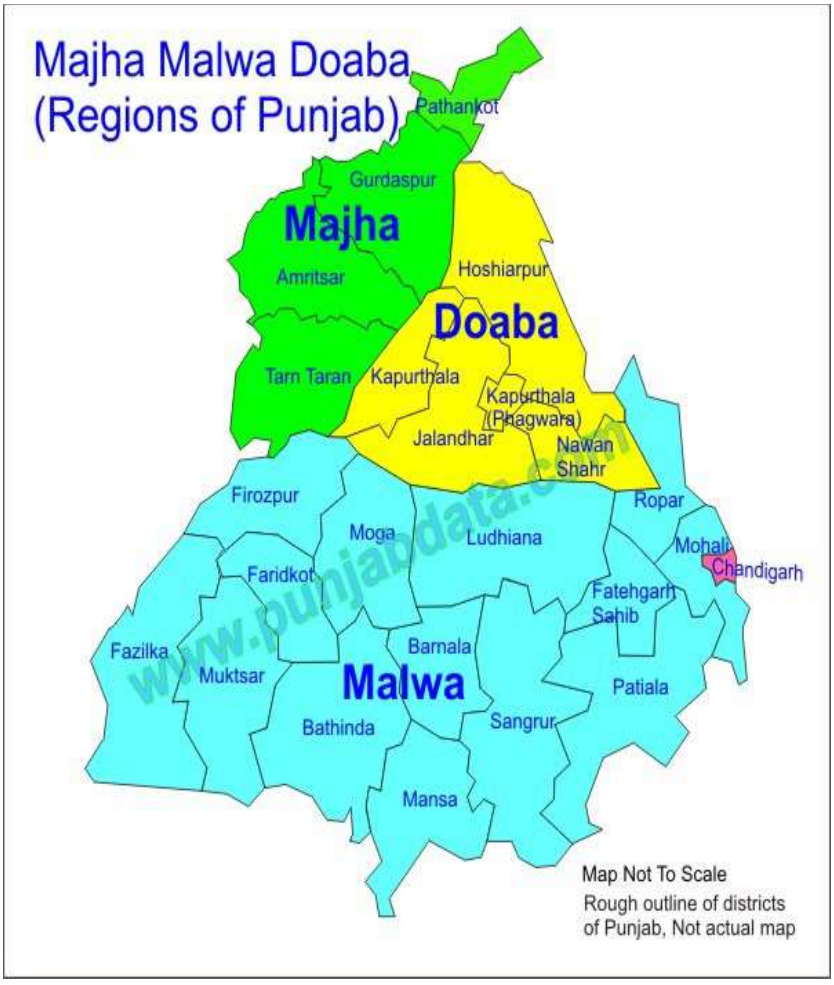

Fig 3.1 Map of Punjab showing Doaba region

3.2 Questionnaire design

Tradition, ethnicity, climate, availability of things and socio-economic status are some of the major factors that influence the dietary practices of a region. As no food frequency questionnaire (FFQ) for this region was available, a detailed FFQ was prepared keeping the above factors and various previous researches in mind. The questionnaire comprised structured dichotomous questions, multiple choice questions and open questions. The questionnaire consisted of three parts.

3.2.1 Socio-demographic

First part of the questionnaire was framed to gather socio-demographic and clinico-pathological information. This included questions regarding age, gender, height, weight, area, district, qualification, occupation, family income, symptoms and past medical history of the individual under study and family history of the individual specifically of cancer. This data was collected to know the vulnerability of various groups.

The age of the case was enquired to know the high risk group of people because review of literature suggested variation. We categorized the patients and the control group in the age groups of 0-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90, 91-100 years. People were grouped as male or female on the basis of gender as gender variation in the susceptibility of this disease has also been observed. The BMI of the person was calculated with the height and weight measures of the individual.

As the Doaba region comprises of four districts the questionnaire allowed for collection of data specific to each district. The rural/urban area of inhabitance was also ascertained. Areas were categorized as rural and urban on the basis of the governing body that is panchayat or municipal council/corporation. Panchayat is the governing body of a village, Municipal Council and Municipal Corporation are the governing body of a town and city respectively. The amenities available and the life style of the people varied according to the area they inhabit. Doaba has no large metropolitan or cosmopolitan city. The towns and cities have similar amenities and life style so urban and semi-urban was clubbed under the urban group.

Food habit was enquired to classify individuals into vegetarian, ovotarian (who consume egg along with vegetarian food) and non vegetarian groups because certain diseases are more common in vegetarians while non-vegetarians (who consume egg, meat fish and poultry) are vulnerable to some other.

Literacy, occupation and income have also been reported as factors of significance in influencing the incidence of EC. On these grounds educational, occupational and financial information of the subjects under study was also collected. Patients and controls

were listed as uneducated, less than matric, matric, +2, graduate, post graduate or any other. On the basis of occupation patients and controls were sorted under professional, businessman, agriculturist and housewife or 'anyother' group. Patients who had received professional qualification and were pursuing their career in the spheres like education, medical, non-medical, management, etc. were considered in the professional category. Those who were running their own business came under the category of businessman while those pursuing farming were categorized as agriculturists. Women who looked after their household chores only were categorized in the group 'housewife'. Any other category included all those individuals who were employed or self-employed in jobs like those of vendor, cobbler, laborer, tailor, cleaner, driver, etc.

The subjects under study were grouped on the basis of monthly household income to see the impact of socioeconomic status (SES) on the incidence of esophageal cancer in this region. The groups were of' less than 10,000, 10,000 to <20,000, 20,000 to <30,000, 30,000 to <40,000, 40,000 to <50,000 and >50,000 per month. Family size and ethnicity were also recorded.

3.2.2 Clinical picture

EC has various sub types such as esophageal squamous cell carcinoma, esophageal adenocarcinoma and a few less common such as blue cell tumour, signet ring cell tumour. Our questionnaire recorded incidence of each case to determine the prevalence of various sub types. History of symptoms was also gathered.

3.2.3 Medical history

Personal

Information of other medical problems and medication taken was gathered to see if any medical problem or abuse of any medicine was a predisposing factor for EC.

Family

The observations of various researchers reveal that contrary to public belief most of the cancers do not have heredity as their prime etiology. Family history of the incidence of malignancy was gathered to know the familial nature of EC in this region.

3.2.4 Dietary intake

Second part comprised of food intake. The Doaba region of Punjab has temperate type of climate with seasonal variation in terms of food items too. On the basis of dietary recall of one year from the time of the interview, an attempt was made to gather the information regarding dietary intake of the major food groups including cereals, pulses and legumes, fruits and vegetables, animal foods like meat, fish and poultry including eggs, milk and milk products. Variance in the impact of food groups in the development, prevention and cure of cancer has been observed.

The detail of food intake was taken on both aspects of amount and frequency. As the data had to be collected in terms of number (like *chappati),* volume (milk, tea, *dal*, sugar) the size of the *chappati*, volume of glass, bowl (*katori*) and spoon was categorized as small, medium, large and the spoons as teaspoon and tablespoon. Small, medium and large *chappati* were made of about 25, 30 and 35 grams of wheat flour. The glass volume of small, medium and large was taken as 200, 250 and 300 ml while the cup volume of small medium and large was taken as 150, 200 and 250 ml. Teaspoonful was considered as 5 grams and tablespoonful as 10 grams in quantity. While enquiring about the intake either these utensils or their cut outs were shown. The food frequency was classified as never, rare (once a month), occasional (once a fortnight), number of times in a week or a day. The foods which were not consumed even once a month were not considered.

S [Small] M [Medium] L [Large]

Plate 3.1 Picture showing portion size

Wheat is the staple diet of residents of Doaba. Rice and maize are the two other cereals consumed liberally though the consumption of maize flour is restricted to the winter season. Whole wheatflour and milled wheat flour are the most common types of wheat flour used mainly in the form of *chappati, naan, kulcha, parantha, bhatura* and *poori.*

Consumption of pulses is significant in Doaba region. Whole, split, and washed, all types of pulses are consumed as a savoury dish, snack and dessert.

The intake of both fruits and vegetables was studied. Though there is a seasonal variation in the availability of vegetables, this food group is an integral part of the Doaba diet. In our study vegetable intake was summed into three groups of roots and tubers, green leafy vegetables and 'other vegetables'. Fruit consumption was studied under the categories of fresh, tinned, dried, fresh fruit juice and packaged juice.

The non-vegetarian food (egg/meat/fish/poultry) consumption among the residents of Doaba is specifically bound by religion, customs and traditions than the consumption of any other food group. Meat included mutton, pork and organ meat like brain and liver. Along with the type and amount, preparation of animal foods has also been reported to increase the incidence of carcinogenesis. Intake data keeping all these parameters was enquired.

To study the impact of milk, consumption data of various types of available milk and its products like butter milk, curd, *paneer* (cottage chese) and cheese was collected.

Role of dietary fat in the etiology of cancer has been studied for more than half a century. Mustard oil, refined oil and *vanaspati ghee* are the commonly used plant fats while cream, butter and *desi ghee* (clarified butter) are the common animal fats used by people of Doaba region. Having a few nuts a day is a common feature of the Doaba diet. Eating pattern of this food group was also noted.

A daily Doaba diet includes a significant amount of beverages like tea, coffee, aerated and non aerated drinks, juice and butter milk. Out of all the beverages tea and buttermilk are the most popular beverages. Preparation of tea has lots of variation, especially in

terms of milk consumption. Other beverages consumed are coffee, aerated and non aerated drinks.

Having a beverage with snacks; main meal with various types of *achar* (pickle), *chutney* and *papad* as accompaniments, fruit, sweet meat, dessert or simply a piece of jaggery in the end is a common dietary practice in Doaba. To study the diet in totality information of all these foods consumed along with the intake amount and frequency was also recorded.

Accompaniments of beverages were broadly categorized as fried, sauté, steamed foods, nuts and any other. If people of Punjab are known for their sweet tooth, people of Doaba cannot be far behind. Intake of sugar and desserts was also studied.

3.2.5 General information (Lifestyle)

In the final part (III) of the questionnaire, information regarding dietary practices was gathered. This included information like meal timings, the temperature and texture of food, cooking details like vessels used, pre preparation, cooking methods practiced and preservation of the leftover food.

3.3 Validation and Pre-Testing

The FFQ prepared was scrutinized by 5 doctors and 5 dieticians and its validation tested. The suggestions given by them were considered and the question was altered if the suggestion was from majority of the experts. The questionnaire was pretested on 10% matched case- control people to help us plan the interview schedule.

3.4 Sample selection

Patients of both genders residing in the four districts of Doaba region getting upper gastrointestinal tract endoscopy done were selected for the study. All histopathologically confirmed cases of esophageal cancer those who consented to be a part of the study were considered for the research.

3.5 Data collection

As the aim was to study EC, the gastroenterologists of this region were contacted. Between October 2015 and April 2018 about 200 patients undergoing upper gastro-intestinal tract endoscopy, suggestive of or with a strong suspicion of EC and who consented to be a part of the study were selected. All patients undergoing endoscopic scrutiny were personally interviewed. The information was collected by face to face survey method from the patient or from the attendant in case of patients who had difficulty in speaking. Only histopathologically confirmed EC patients (110) were considered under the category of patients. Detailed information was collected from 110 patients and 152 control cases on various parameters in the pre-designed and pre-tested questionnaire. For every EC case studied a matched control was also studied. The matching was conducted on the basis of area, gender and age (±5 years).

3.6 Data analysis

The data collected was transferred to Excel sheet for further analysis. Equivalent values were obtained where there were different variants of the same food item, for example all milk products were converted into equivalent intake of milk. For convenience in comparison the collected data was presented in average and percentage. Statistical analysis was done by using descriptive and inferential statistics using Pearson chi square test for categorical data, Unpaired t-test to compare mean values between the two groups. Logistic regression used to see the effect of groups of variables on a dependent variable having only two categories. P-value equal to or less than 0.05 was considered as significant at 95% confidence level. The statistical package for the social sciences, SPSS 18.0 was used in the analysis.

RESULTS AND DISCUSSION

Data from the current case-control study to examine 'Role of dietary habits in the development of esophageal cancer' was analysed and results obtained which have been discussed under following heads.

4.1 Socio-demographic factors& Socio-economic factors

4.2 Cereals and Pulses

4.3 Vegetables and Fruits

4.4 Animal Products

4.5 Fats, Oils, Nuts and Oil seeds

4.6 Beverages

4.7 Lifestyle Practices

4.1 SOCIO-DEMOGRAPHIC FACTORS & SOCIO-ECONOMIC FACTORS

4.1.1 Socio-demographic factors

Variation in the incidence of esophageal cancer has been reported world wide on the parameters of area of inhabitance, age, gender and type of esophageal cancer of the patients. Effort was made to study the impact of these factors in the Doaba region of Punjab. The results obtained have been discussed below.

Effect of area of inhabitance

Total population of the Doaba region of Punjab is 5,194,076 (63.36% rural). Jalandhar is the most densely populated district in the Doaba region of Punjab with a total population of 2,181,753 with 53.18% being urban and 46.82% being rural population. Population of other three districts can be summed up as Hoshiarpur 1,582,793 (78.80% rural), Nawanshehar (SBS Nagar) 614,362 (79.57% rural) and Kapurthala 815,168 (65.35% rural). The data collected between October 2015 and April 2018 producedfollowing

statistics. Jalandhar had 62 cases, Hoshiarpur 27, Nawanshehar 11 and Kapurthala10 (Fig.4.1.1). More than half of the patients, 54.50%were from rural area and 45.50% from urban area. Our data revealed a higher incidence in the rural population of three districts Hoshiarpur (70.37%), Kapurthala (60.00%) and Nawanshehar (100.00%) which amounted to 70.08%cases from the rural areas of these three districts. These findings are in agreement with the already published data of greater incidence being in rural area (Kapoor et al, 2015). Kapoor et al (2015) conducted a study in Bikaner, India and reported 76% cases from rural and 24% from urban area. Dar et al (2013) reported more than 90% subjects to be from rural areas in Jammu and Kashmir.

Fig. 4.1.1 Distribution of esophageal cancer patients in Doaba region

The scenario in the most populated and urbanized Jalandhar district of the Doaba region is reverse. 61.30% of the EC cases of Jalandhar district were from urban areas. This is perhaps due to urbanization and the related environmental and lifestyle changes (Thakur et al, 2017).The other possible reasons of higher incidence of cancer in the urban areas of Jalandhar could be difference in nutritional intake, post-harvest handling malpractices (Panghal et al, 2018) and environmental pollution due to industrialization and mechanization (Yuan et al,2016).The water pollution (Nayyar,2015) and air pollution (Huang et al, 2017) contribute more cases of esophageal cancer in urban area. On considering the population density of the areas of incidence it was evident that the incidence was higher in urban areas with an average of 26.20 cases of esophageal cancer per million of the population (ppm) from urban areas and 18.20 cases of esophageal cancer per million of the population from rural areas. In districts of Jalandhar (32.7 ppm), Kapurthala (14.2 ppm) and Hoshiarpur (23.9 ppm) the incidence per million of population was more in the urban areas (Table 4.1.1; Fig. 4.1.2)

Fig. 4.1.2 Area based incidence of Esophageal Cancer Cases per million population

Effect of gender

Our study showed a little higher incidence (1.2:1) among women than men (Table 4.1.2) and endorses the findings of Kapoor et al (2015) and Giri et al (2014). Kapoor et al (2015) reported higher incidence among women (1.15:1) of North-West India in their study conducted in Rajasthan while Giri et al (2014) reported higher incidence amomg women (1.4:1) in western Maharashtra. In certain areas of Iran, the women are suffering equally (Islami et al, 2009) whereas in Gezira, Central Sudan, female to male ratio is3.3:1 (Mohammed et al, 2012). According to the interactive cancer atlas prepared by the National Cancer Registry Programme of India the highest incidence amongst females (10.8/100,000) was found in Meghalaya. The incidence rate of EC in the world showed great disparity on the basis of gender, being 2-3 times more in males than females in America (Yang et al, 2016). Globocan (2018) reported EC incidence in the ratio of 2.3:1 in men and women. The incidence of EC in China was more in males than females (3-5:1) in a study conducted by Yang et al (2016).

Fig. 4.1.3 Gender based distribution of Esophageal Cancer Cases in Doaba region

Effect of age

Cases of EC are rarely reported below 30 years of age even in areas of high incidence. US surveillance epidemiology and end results (SEER) registries, northern China and in northeastern Iran the incidence percentage is 0.5, 0.7 and 1.0 respectively (Kapoor et al, 2015). Our study showed (Table 4.1.3) an incidence of 1.81% (females-2, males-0) below or equal to 30 years and 5.45% (females-5, male-1) below or equal to 40 years of age whichis consistent with the findings of Chitra et al (2004). In the present study maximum incidence of 59.09% (females-37, males-28) was seen in the agegroup of 51-70 years (Figure 4.1.4). Chitra et al. (2004) reported 62% cases in the age group of 41-60, Giri et al. (2014) reported 30.43% in the age group of 50-60 years and 41.54% in the age group of more than 60 years of age. In the present study 57.27% (females-37, males-26) cases were above 60 years of age. Our study revealed the mean age of EC patients to be 61.79 years (63.45 years in men and 60.42 years in women), Dar et al (2013) reported mean age

of EC cases to be 61.6 years in Kashmir while in US the mean age was reported as 68 years (Kapoor et al, 2015).

Fig.4.1.4 Age (Years) Based Distribution of Esophageal Cancer Cases in Doaba region

Types of EC

Most of the EC cases reported during period of study were of ESCC (86.36%) and only 4.54% cases had EADC (Table 4.1.3). Zhang (2013) reported three times higher incidence of ESCC among blacks than whites but a higher incidence of EADC among whites.

Fig. 4.1.5 Incidence of Different types of Esophageal Cancer

ESCC is largely the disease of the developing countries and EADC of the developed ones (Zhang, 2013). Worldwide incidence of ESCC is much more than EADC. With the increase in the incidence of obesity and gastro-esophageal reflux disease in the developed countries a tremendous shift in the epidemiology of EC has occurred (Napier et al, 2014). Yang et al (2016) also reported as most of the cases of EC being ESCC especially in Asia though there has been a sharp increase in the incidence of EADC during the last 40 years in the western countries. Our results claim the same and are in accordance with the already published data (Table 4.1.3; Fig. 4.1.5).The findings of the present study also show no correlation between incidence of EC and family history at genetic level.

Effect of BMI

102 out of 110 patients did not have their weight record of pre-illness period. The current BMI (body mass index) was the outcome of the disease and not the cause of EC, hence comparing it with the BMI of the control group would be misleading. In view of this the effect of BMI on the incidence of EC was not studied.

4.1.2 Socio-economic factors

Socioeconomic status (SES) is not a biological cause of EC but it could be one of the major factors in influencing the risk of EC. It includes various dimensions like income/wealth, education, profession. These factors could have an impact by altering the type of environmental exposure, behavior, diet and life style due to the affect on the access to basic resources for maintaining good health (Dar et al, 2013). Gholipour et al (2016) also stated that low SES was linked to lack of nutritious food, unhealthy environment, decreased and delayed access to health care which hindered early diagnosis, treatment and prognosis.

Effect of Household income

Our findings revealed (Figure 4.1.6) that 33% subjects had a monthly family income of less than Rs.10,000 and 46% had the total family income of less than Rs. 20,000 per month (47% of them had a family size of 4 or more).Singhand Jemal (2017) studied the impact of SES on cancer in USA. Their findings revealed a varied pattern of incidence for specific cancers but a consistent pattern of increased incidence and mortality in groups living in deprived areas, having low income and low education. Greater wealth scores showed a decrease in ESCC risk in a study conducted in Kashmir (Dar et al, 2013). Higher SES has been associated with an increased rate of overall and private cancer screening irrespective of gender in a South Korean study (Kim and Kang, 2016). Our findings are in accordance with these findings (Table 4.1.4)

Fig. 4.1.6 Income (Rupees/month) of Esophageal Cancer Cases in Doaba region

Effect of Education

According to Indian census of 2011, a person aged 7 years and above who can both read and write in any language, is treated as literate. One who can only read and not write is not considered as literate. It is not necessary that a person should receive any formal education or pass any minimum education standard. Literacy rate of India according to 2011 census is 74.00% with 82.10% males and 65.50% females being literate. Literacy

rate of Punjab is 75.84% with 80.44% males and 70.73% females being literate. The education level is varied with 2.30% having no formal education, 9.03% less than primary, 17.38% primary, 12.43% middle, 16.97% matric, 9.37% senior secondary, 0.10% non-technical diploma, 0.95% technical diploma, 7.14% graduate or above and 0,42% unclassified. Literacy rate of rural and urban India is 67.80% and 84.10% whereas of Punjab is 71.40 and 83.20% respectively. In the Doaba region Hoshiarpur leads with 84.60% literacy, followed by Jalandhar 82.48%, Nawanshehar (SBSN) 79.78% and Kapurthala79.07%.The data collected indicates an inverse correlation between educationand Esophageal Cancer. Collected data revealedthat education played an important role in prevention from cancer disease. More than 80 patients from the data (Figure 4.1.7) were under matric (38% illiterate and 39% had a qualification of less than matric). Ljung et al (2013) considered education as an indicator of socio-economic status as it is easy to measure and doesn't change with health and phase of life. Higher education imparts more awareness about nutrition, dietary habits and diseases which helps in prevention from the disease. Education helps to make right food choices, maintain hygiene and take early medical help in case of need.Dar et al (2013) concluded that higher education had inverse association with ESCC risk in Kashmir. Statistical findings of illiteracy among the cases of some other researchers are Bathija et al (2014) 60%, Kapoor et al (2015) 66.15%. Our findings are consistent with already published data. It was evident from the study conducted in Doaba region (Table 4.1.5) that 38% cases were uneducated, 39% had schooling of less than matric (10^{th} standard) and 11% had schooling up to matric (10^{th} standard).

Fig. 4.1.7 Education Based Distribution of Esophageal Cancer Cases in Doaba region

Effect of occupation

10% of the patients in the present study were agriculturists (Table 4.1.5). Zhang et al (2003) reported pollution in well water by nitrogenous compounds of fertilizers used in farming to have a positive correlation with esophageal cancer.Organophosphates(OP) are most toxic and widely used pesticides and insecticides especially after organochlorinesbeing withdrawn from the market. They have both agriculture and household applications and have been the cause of acute lymphoblastic leukemia (Tabrez et al, 2013).The role of OP in the development of EC needs to be authenticated with studies of its level in blood of the patients (Kapoor et al, 2015). Dar et al (2013) concluded that farmers were at a greater risk of having ESCC than their counterparts in business or government jobs though this association did not exist in fully adjusted models. They also found a strong association between ESCC risk and strenuous occupational physical activity (Fig.4.1.8).

Fig. 4.1.8 Qualification/Profession based incidence of Esophageal Cancer

In Doaba region of Punjab more than half of the total patients were housewives (50.90%). It may be because of solid fuels being used in the household .Study conducted in central and Eastern Europe (Sapkota et al, 2013) had shown an increase in risk of upper aerodigestive tract cancers due to indoor air pollution from solid fuels.In the present study conducted in the Doaba Region of Punjab ‘any other’ category included manual workers.They had a high (36.40%) risk of incidence of EC (Table 4.1.5). Kim and Kang (2016) also reported similar findings in a study conducted in Korea. According to their study, more educated individuals and male office workers showed a higher incidence of private cancer screening as compared to manual workers in South Korea leading to greater incidence in manual workers. Sehgal et al (2012) reported 59%, Bathija et al (2014) reported 68% labour class and Kapoor et al (2015) reported nearly 50% of their cases to be from lower SES.

Table 4.1.1: Area based incidence of Esophageal Cancer Cases in Doaba region, Punjab

	Cancer Cases		Population		Incidence per million	
Districts	**Rural**	**Urban**	**Rural**	**Urban**	**Rural**	**Urban**
Hoshiarpur	19	8	1247969	334824	15.22	23.89
Jalandhar	24	38	1021388	1160365	23.49	32.74
Kapurthala	6	4	532712	282455	11.26	14.16
Nawanshehar	11	-	488857	125505	22.50	-
Total	60	50	3290926	1903149	18.23	26.27

Table 4.1.2: Area and Gender based incidence of Esophageal Cancer Cases in Doaba region, Punjab

District	No. of cases	Rural	Urban	Rural Male	Urban Male	Rural Female	Urban Female
Hoshiarpur	27	19	8	8	4	11	4
Jalandhar	62	24	38	9	16	15	22
Kapurthala	10	6	4	3	3	3	1
Nawanshehar	11	11	-	6	-	5	-
Total	110	60	50	26	23	34	27

Table 4.1.3 Incidence of cases on basis of Age, Gender and Types of esophageal cancer

Age (yrs.)	No. of cases	Male	Female	ESCC	EADC	Malignant Process	Other

0-20	-	-	-	-	-	-	-
21-30	2	0	2	2	0	0	0
31-40	4	1	3	3	0	1	0
41-50	16	7	9	14	1	0	1
51-60	31	15	16	26	3	2	0
61-70	34	13	21	31	1	0	2
71-80	18	9	9	16	0	0	2
81-90	4	3	1	2	0	2	0
91-100	1	1	-	1	0	0	0

Table 4.1.4 Income based incidence of Esophageal Cancer Cases

Monthly Income (Rupees)	Number	Male	Female
< 10,000	37	18	19
10,000- <20,000	51	21	30
20,000- <30.000	12	5	7
30,000- < 40,000	5	3	2
40,000- < 50,000	4	1	3
50,000 or More	1	1	-

Table 4.1.5 Qualification/Profession based incidence of Esophageal Cancer in Doaba region, Punjab

Qualification	No.	M	F	Professional	Businessman	Agriculturist	Housewives	Others
Unedu.	42	13	29	0	0	5	27	10

<Matric	43	19	24	0	0	4	23	16
Matric	12	8	4	0	0	1	4	7
10 +2	2	2	-	0	0	1	0	1
Graduate	7	3	4	1	1	0	2	3
Post Grad.	2	1	1	1	0	0	0	1
Any Other	2	2	-	0	0	0	0	2

(Others: Manual workers like street hawkers, cobblers, laborers, tailors, cleaners, drivers, etc.)

4.2 Cereals and Pulses

Cereals, pulses and legumes have been cultivated from prehistoric period. They form the major portion of human food all around the world and are the main constituents of the Mediterranean and Asian diets. Grains (cereals and pulses) contribute about 56% of energy and 50% of protein required by an individual (Aune et al, 2016). Health benefits of the whole grain foods have been known to man since the fourth century BC. Whole grains are consumed in the form of whole grain and multi grain bread, breakfast cereal in the West; brown rice and unrefined maize in the continent of Africa; unleavened bread and roasted grains as snacks in Asia.

4.2.1 Cereals

Three major cereals consumed in the Doaba region of Punjab are wheat, rice and maize. The consumption of these cereals was grouped under refined wheat flour, whole wheat flour, maize flour, basmati rice and regular rice. Data of the consumption of these groups in Doaba region revealed a variation in their consumption both in the amount and form. The t-test values reveal the variation in the consumption of certain food items in both the groups. The variation in case of cereals and pulses intake was observed in the consumption of whole wheat chappati with ghee, whole wheat stuffed fried parantha, refined wheat nan/kulcha, maize roti with fat, maize vegetable fried parantha, total amount of maize, basmati plain boiled rice, regular plain boiled rice, regular zeera rice along with split and washed dal, soya bean, rajmah, etc. group and karhi.

Fig. 4.2.1 Comparison of EC Cases (Patients) and Control Group Cereal consumers (Percentage based)

Fig.4.2.2 Comparison of EC Cases (Patients) and Control Group Cereal consumption (Intake amount based)

Wheat

Wheat or *Triticum aestivum* ssp plays a significant role in human nutrition as a dietary staple. 25 grams of wheat flour provides about 85 calories, 4.4 g of proteins, 18 g of carbohydrates and 0.6g of fats and. Bran, germ and endosperm are integral parts of the whole grain. Bran is a rich source of natural fiber, vitamins especially vitamin B complex and minerals; the germ layer contains oil, antioxidants, vitamin E, whereas the endosperm provides proteins and carbohydrates. In the second half of twentieth century this advantage was accredited to fiber and other bioactive substances (polyphenolic compounds) present in wheat bran and germ. With advent of new millennium, the consumer focus has shifted from energy providing food to foods containing phytochemicals possessing prophylactic properties of disease prevention and health promotion along with therapeutic powers. The extensive nutritional research conducted so far suggests that consumption of whole grains and their products decrease the incidence of chronic diseases like obesity, coronary heart disease, type II diabetes and various cancers (Malaguti et al, 2014).

Consumption pattern of different cereals viz refined wheat flour, whole wheat flour, maize, basmati rice and regular rice was observed (Table 4.2.1)**.** A difference in the consumption was observed. 26.31% of control group people consumed refined wheat flour while 35.45% patients consumed refined wheat flour (Fig. 4.2.1). Average number of servings of refined wheat flour consumed by the control group people was 125.67 per month amounting to a monthly intake of 2210.37 grams per month while the patients consumed 190.54 servings per month with an average amount of 2603.17 grams per month (Fig.4.2.2). A higher percentage of control group people (71.71%) consumed whole wheat flour as compared to 63.63% people of patient group, though the monthly number of servings and the amount of whole wheat flour is nearly same in both cases. These findings are a good indicator to direct our thinking to refrain from refined wheat flour. Whole wheat flour contains 12.5% total dietary fiber, 9.6% being insoluble dietary fiber and 2.9% being soluble dietary fiber (Gopalan, 2012). The consumption of refined wheat flour replacing the whole wheat flour led to low intake of dietary fibers and

polyphenolic compounds present in outer layer of wheat bran. Researchers have found a positive association between the intake of whole grain foods and reduced risk of chronic diseases (Slavin, 2004). The antioxidants have anti tumour behaviour in our body. They react with reactive oxygen species (ROS) and reactive nitrogen species (RNS) to prevent damage of biomolecules like proteins, lipids and DNA. Antioxidants scavenge free radicals and chelate metal ions also. Vitamin E and carotenoids were the first antioxidants to be isolated from wheat. The main carotenoids present are lutein and zeaxanthin (Kafui et al, 2003). Ferulic acid is another antioxidant present in wheat. The concentration of these antioxidants is higher in wheat germ and bran layer than in endosperm.

In case of cancer patients the average monthly intake amount of refined wheat flour was found to be negatively correlated with the intake amount of maize flour (r= -0.263, $p \leq 0.01$), whole wheat flour (r= -0.836, $p \leq 0.01$), milk (r= -0.200, $p \leq 0.05$) and animal fat (r= -0.202, $p \leq 0.05$) but positively correlated with the monthly average intake amount of meat (r= 0.203, $p \leq 0.05$), fowl (r= 0.243, $p \leq 0.05$) and total non veg. (r= 0.248, $p \leq 0.01$). Whole wheat intake showed a positive correlation with intake of maize flour (r= 0.379, $p \leq 0.01$), milk (r= 0.217, $p \leq 0.05$), buttermilk (r= 0.215, $p \leq 0.05$), total amount of milk intake (r= 0.244, $p \leq 0.05$), animal fat (r= 0.246, $p \leq 0.01$), total fat (r= 0.222, $p \leq 0.05$) and total sugar intake (r= 0.269, $p \leq 0.05$) (Table 4.2.2). Intake of whole wheat flour in case of Jalandhar patients (Table 4.2.3) was inversely correlated with the intake of refined wheat flour (r= -0.824, $p \leq 0.01$) and meat (r= -0.263, $p \leq 0.05$). Average monthly intake of refined wheat flour of Kapurthala patients (Table 4.2.4) was inversely correlated with whole wheat flour intake (r= -0.921, $p \leq 0.01$) and directly correlated with the intake of total fowl (r= 0.813, $p \leq 0.01$) and total non veg. (r= 0.820, $p \leq 0.01$). Patients data of Nawanshehar (Table 4.2.5) revealed a negative correlation of refined wheat intake with the intake of whole wheat flour (r= -0.870, $p \leq 0.01$) and total curd (r= -0.931, $p \leq 0.01$). A positive correlation was recorded on comparing the intake of whole wheat flour with the intake of total curd (r= 0.898, $p \leq 0.01$) and total meat (r= 0.635, $p \leq 0.05$). The patient's group of Hoshiarpur district (Table 4.2.6) showed a negative correlation between the

monthly average intake of refined wheat flour and whole wheat flour (r= -0.838, $p \leq 0.01$).

The total control group intake also revealed significant ($p \leq 0.05$) negative correlation of refined wheat flour intake with the intake of maize flour (r= -0.190); fowl (r= -0.187); total non veg. (r= -0.167); plant fat (r= -0.249) and total fat intake (r= -0.251). A strong negative correlation was also observed on comparing the refined wheat flour intake with the intake of whole wheat flour (r= -0.801, $p \leq 0.01$) and the amount of milk consumed (r= -0.222, $p \leq 0.01$). Data of control group intake of whole wheat flour showed a significant correlation ($p \leq 0.01$) with the intake of maize flour (0.339), fowl (0.237), buttermilk (0.247) and total fat intake. A significant correlation ($p \leq 0.05$) was also recorded on comparing the consumption of whole wheat flour with the consumption of total non veg. (0.182), milk (0.185), total milk (0.171) and plant fat (0.173) (Table 4.2.2). The mechanism by which dietary n-3 and n-6 PUFA protect or enhance tumor development, respectively, has not been fully investigated, but most of the proposed mechanisms are based on the metabolic fate of these fats and the subsequent biosynthesis of eicosanoids, which exert control over several systems. Fats, particularly saturated fats, may affect hormonal status, modify cell membrane structure and function, cell signaling transduction pathways, and gene expression, and they may even modulate functions of the immune system (Othman, 2007). The control group data also bared a significant ($p \leq 0.05$) negative correlation of whole wheat flour intake with refined wheat flour intake (r= -0.223) and total nuts intake (r= -0.242). Though in the initial stages, there is a growing lobby in favour of nuts as preventers of cancer, respiratory, cardiovascular and neurodegenerative diseases (González and Salas-Salvadó, 2006). Total fruit intake and whole wheat flour intake was also inversely correlated (r= -0.254, $p \leq 0.001$). Fruits are rich sources of micronutrients like carotenoids (including beta-carotene and lycopene), folate, vitamin C, vitamin D, vitamin E, quercetin, pyridoxine, and selenium which could play a protective role against occurrence of cancer (World Cancer Fund Report, 2007). A positive correlation with milk from tea (0.199) was also observed. The evidence on the relationship between milk and dairy products, and also diets high in calcium, and the risk

of cancer, points in different direction. Limited studies on relation between milk intake and esophageal cancer are not conclusive so far (World Cancer Fund Report, 2007). Oils sold as refined oils of cotton seed peanut, soyabean, rice bran etc. are used in the area of study along with mustard oil and vanaspati ghee. The processing of theses plant oils includes exposure to high temperature, degumming, bleaching, deodorizing, etc. which deprives them of protective polyphenols. Their indiscriminate use creates an imbalance between omega 3 and omega 6 fats in the body and increases the trans-fats level too. These factors are thought to predispose an individual to chronic diseases and cancer.

If we glance at the cereal consumption pattern per district, we observe a difference in them. Jalandhar control group (Table 4.2.3) revealed a negative correlation on comparing the intake of refined wheat flour intake with the intake of whole wheat flour (r= -0.829, $p \leq 0.01$), total fruit (r= -0.245, $p \leq 0.05$), total curd (r= -0.252, $p \leq 0.05$), fowl (r= -0.256, $p \leq 0.05$), plant fat (r= -0.370, $p \leq 0.01$), total fat (r= -0.313, $p \leq 0.01$) and nuts (r= -0.284, $p \leq 0.01$). A direct association was observed in the intake of fowl (r= 0.246, $p \leq 0.05$) and total sugar (r= 0.220, $p \leq 0.05$) with intake of whole wheat flour. Kapurthala district's control group (Table 4.2.4) showed a negative correlation of intake of whole wheat (r= -0.760, $p \leq 0.01$), milk (r= -0.513, $p \leq 0.05$) and animal fat (r= -0.550, $p \leq 0.05$) with the intake of refined wheat flour; while a positive correlation ($p \leq 0.05$) was recorded on the intake of whole wheat flour with the intake of fowl (0.534), fish (0.492), total non veg. (0.534), buttermilk (0.469) and total fat (0.491). A strong positive correlation ($p \leq 0.01$) was observed on comparing the whole wheat intake with the intake of eggs (0.657), and animal fat (0.736). Nawanshehar control group (Table 4.2.5) revealed a positive correlation between total legumes (r= 0.869, $p \leq 0.001$), total nuts (r= 0.665, $p \leq 0.01$).The intake of whole wheat flour was negatively correlated with the intake of refined wheat flour (r= -0.697, $p \leq 0.01$), legumes (r= -0.571, $p \leq 0.05$) and nuts (r= -0.732, $p \leq 0.01$). Hoshiarpur control data (Table 4.2.6) showed a negative correlation of whole wheat flour intake with refined wheat flour intake (r= -0.800, $p \leq 0.05$) but apositive correlation with the intake of vegetables (r= 0.426, $p \leq 0.05$) and the amount of milk consumed (r= 0.478, $p \leq 0.01$).

The logistic regression model with all independent variables of cereal and pulse group is given in the annexure. To find variables with maximum impact stepwise logistic regression was performed. The independent variables remaining in the tenth step of this stepwise regression model are presented in Table 4.2.8.From the table wheat and whole wheat chappati with ghee or butter does not appear to be protective at 95% confidence level (CL95%). The probability of the negative impact is very low as the 'B'value is extremely small (-0.008 and -0.01). This result could be due to the impact of some confounding agents.

Rice

Rice or *Oryza sativa* is one of the oldest cereals. It is believed to be cultivated for the past 5000 years. About half of world's population especially people of East and South Asia consume rice as the main cereal in their diet. Rice though not the staple diet, is relished by residents of Doaba region.

Rice grain (white milled) has about 7.3% protein which contains all ten essential amino acids with lysine as a limiting amino acid. The protein content consists of globulin 5%, albumin 10%, and prolamin 20% (Liangli et al, 2012). Chen et al (2010) isolated a prolamin which could enhance anti- leukaemia immune response when added to culture medium by inhibiting growth of human leukaemia U937 cells. Neutrase hydrolysate isolated from rice endosperm protein produced a peptide with scavenging property like alpha tocopherol (Zhang et al, 2009).

Broadly speaking rice is divided into basmati and non basmati or regular rice. Basmati rice consumption was found to be more amongst the control group. 66.45% cases of control group consumed 8.66 servings of basmati rice amounting to 577.43 grams per month while only 28.18% of cancer patients consumed 454.80 grams of basmati rice in 7.00 servings per month. Regular rice consumption was found to be less among the control group with only 35.52% opting for regular rice. Their average consumption was 336.30 grams in 6.04 servings while 65.45% patients had 5.04 servings of regular rice amounting to 324.20 grams.

Basmati rice is a special variety of rice grown in Indian subcontinent especially India. *Basmati* derives its name from two Hindi words '*bas*' and '*mati*' meaning full of aroma. The aroma of this long grain rice is due to the presence of 2-acetyle-1-pyrroline which is significantly more in *basmati* ricethan in other types of rice.*Basmati* rice is preferred not only because of aroma but also due to health benefits. A serving (50g raw) of rice provides about 170 calories, 39 gm of carbohydrates and 3.2 gm of proteins composed of eight essential amino acids, giving it a high nutritive value (Gopalan et al, 2012). It is low in fat because of the loss of germ layer during milling. It is a good source of thiamine, niacin, riboflavin, pyridoxine, pantothenic acid, vitamins E and K, phosphorus, calcium, potassium, zinc and iron. It has 20% more fiber and higher level of amylose. Amylose is linked with resistant starch a type of carbohydrate which takes longer to digest thus preventing an unhealthy blood sugar spike. Basmati rice fiber keeps the digestive tract hydrated. It binds with cholesterol and bile acids to eliminate them through faeces, protecting the gut from carcinogens and repairs DNA. Rice is healthy for even what it does not have like low fat and sodium levels. Most of the antioxidants present in fruits, vegetables and cereals like wheat, rice and oats are polyphenolic compounds with ferulic acid, p-coumaric acid, vanillic acid, caffeic acid and syringic acid being the main ones in whole grains (Tan and Norhaizan, 2017). Rice germ or constituents of rice bran have been found to have chemopreventive effects against carcinogenesis of esophagus, stomach, liver, colon and blader of rodents. Chemopreventive potential was observed by Henderson et al also in mouth, esophagus, liver, lung, breast and skin. The presence of antinutrient affects the availability of various nutrients. Trypsin inhibitor is primarily present in the outer embryo and bran not in the milled rice leaving the digestion of rice undisturbed. Haemagglutinin-lectin is another feature of concern as it binds to specific sites in the intestinal mucosa which are carbohydrate receptors thus hindering nutrient absorption. This antinutrient is inactivated on simple steam cooking. Though phytate is not affected by heat its presence is of little concern as it is located in the bran and not in milled rice.

The total patient group (Table 4.2.2) showed a positive correlation ($p \leq 0.05$) of total rice intake with total sugar intake (r= 0.205), fruits intake (r= 0.218) and fish intake (r= 0.243). Jalandhar patients data (Table 4.2.3) revealed that that those who consumed more fish consumed more rice too (r= 0.280, $p \leq 0.05$). Rice intake of Nawanshehar patients (Table 4.2.5) was negatively correlated with the intake of vegetables (r= -0.696, $p \leq 0.05$) and pulses (r= -0.636 $p \leq 0.05$). Hoshiarpur patients group (Table 4.2.6) showed a positive correlation of total rice intake with total sugar intake (r=0.438; $p \leq 0.05$) also with vegetable intake (r= 0.536; $p \leq 0.001$), fruits intake (r= 0.495, $p \leq 0.01$) and intake of pulses (r= 0.541, $p \leq 0.01$). Kapurthala data showed no significant dietary correlations with the intake of rice.

In the control group (Table 4.2.2) rice intake was negatively correlated with the intake of whole wheat flour (r= -0.264; $p \leq 0.01$). Jalandhar control group (Table 4.2.3) showed a negative correlation between the intake of rice and the intake of vegetables (r= -0.269; $p \leq 0.05$) while the Kapurthala control group (Table 4.2.4) showed a positive correlation between rice and the amount of milk consumed (r= 0.707; $p \leq 0.01$). Consumption of rice in the Hoshiarpur control group (Table 4.2.6) showed a negative correlation with whole wheat flour (r= -0.415; $p \leq 0.05$) but positive correlation with the intake of refined wheat flour (r= 0.431; $p \leq 0.05$), fowl (r= 0.578; $p \leq 0.01$) and total non veg. (r= 0.371; $p \leq 0.05$). Rice consumption of Nawanshehar control group (Table 4.2.5) showed negative correlation with the intake of fruits (r= -0.748; $p \leq 0.01$) egg (r= -0.532; $p \leq 0.05$) and meat (r= -0.525; $p \leq 0.05$). Fruits are rich sources of micronutrients like carotenoids (including beta-carotene and lycopene), folate, vitamin C, vitamin D, vitamin E, quercetin, pyridoxine, and selenium which could play a protective role in the risk of incidence cancer. The evidence on the relationship between milk and dairy products, and also diets high in calcium, and the risk of cancer, points in different direction. Limited studies on relation between milk intake and esophageal are not conclusive so far WCRF Report (2007).

Rice grain has plenty of bioactive substances. Lot of research needs to be done to know the factors affecting their bioavailability alone or in tandem with any other food groups,

and finally labeling them as potential health providers. Biological interactions of these dietary components in the body need to be scrutinized to do away with potential toxic effects and have synergistic impact of the phytochemicals.

On performing stepwise logistic regression,the independent variables remaining in the tenth step of the model are presented in Table4.2.8.The regression model (CL 95%) showed basmati rice to be protectiveagainst the risk of esophageal cancer. The impact of basmati plain boiled (B=0.093) and *zeera* seasoning preparation (B= 0.295) appeared to be protective against esophageal cancer along with *zeera* seasoned regular rice (B=0.177).

Maize

Similar to other cereals, *Zea mays* is also the member of the grass family Gramineae. A produce of 1,000 million tons in 2014 reveals its popularity in the human diet (FAO, 2015). Monocotyledon of maize comprises an embryo, an endosperm and bran. Kernel is packed with starch mainly amylopectin and amylose (72-73% of kernel weight) along with proteins (8-12% of kernel weight). Albumin, globulin, prolamin and glutelin are the main proteins and glutamic acid, the main amino acid (Shukla and Cheryan, 2001).Zeins are deficient in the amino acids lysine and tryptophan. De Mejia et al (2012) reported the healthy properties of cereal peptides like antithrombotic, anti hypertensive, anticancer, immunomodulatory, mineral-binding, antioxidant and antimicrobial. Li et al (2014) stated that cereal based proteins and peptides have a protective affect against various stages of cancer including initiation, promotion and progression.

Maize is consumed in the Doaba region of Punjab, mainly in the winter months. 77.63% people in the control group consumed 7.27 servings of maize amounting to an intake of 308.82 grams of maize per month whereas 43.63% people of the patient group consumed 200.00 grams of wheat flour in 4.64 servings. Bioactive peptides show anti-tumor behavior by different mechanisms (a) Initiating apoptosis by activating pro-apoptotic receptors, restoring p53 activity, cascade modulation and proteasome inhibition (b) regulating cellular mechanisms linked with proliferation of cells, their survival and

growth (c) regulation of immune system by increasing the tumour-associated antigens or by escalating disposition of cancer cells to be identified and eliminated by the immune system (Diaz-Gomez et al, 2017). HepG2 cells when treated with peptides isolated from Alcalase hydrolysates from different varities of maize increased apoptosis by about 4 times. Zhou et al (2015) reported maize peptides to be biologically active, mainly as antioxidants. They attributed the radical scavenging and reducing capacity to the amino acids present like leucine, lysine, proline, tyrosine, phenylalanine, alanine and histidine.

Patients dietary intake (Table 4.2.2) revealed a negative correlation between the intake of maize and refined wheat flour (r= -0.263; $p \leq 0.01$) but the intake of maize and animal fat (r= 0.256; $p \leq 0.01$) were positively correlated. In the Jalandhar control group (Table 4.2.3) the data showed a positive correlation between maize and whole wheat intake (r= 0.510; $p \leq 0.01$) but a negative correlation of maize intake with refined wheat flour intake (r= -0.345; $p \leq 0.01$) and sugar intake (r= -0.263; $p \leq 0.05$) was noticed. In Kapurthala the control group people (Table 4.2.4) who consumed more maize consumed more of milk products and the correlations were milk (r= 0.711; $p \leq 0.05$); curd (r= 0.670; $p \leq 0.05$) and total milk intake (r= 0.849; $p \leq 0.01$). Intake of maize showed correlation with the intake of pulses (r= 0.713; $p \leq 0.05$), animal fat (r= 0.791; $p \leq 0.05$), meat (r= 0.602; $p \leq 0.05$) and sugar (r= 0.623; $p \leq 0.05$) amongst Nawanshehar (Table 4.2.5) though only significant correlation of vegetables with maize intake (r= 0.506; $p \leq 0.01$) was seen in the Hoshiarpur control group (Table 4.2.6).

In the total control group the amount of maize intake was more in people who consumed more of fruits (r= 0.190; $p \leq 0.05$) and fowl (r= 0.238; $p \leq 0.01$). A negative association between the intake of maize and plant fat was also observed (r= -0.203; $p \leq 0.05$). Jalandhar control group's maize flour intake was positively correlated with the intake of whole wheat flour (r= 0.333; $p \leq 0.01$), fruits (r= 0.287; $p \leq 0.01$), tea (r= 0.253; $p \leq 0.05$) and indirectly associated with the intake of plant fat (r= -0.250; $p \leq 0.05$). Kapurthala control group's data showed positive correlation ($p \leq 0.05$) of maize intake with the intake of total non veg. (r= 0.505) and animal fat (r= 0.555). A strong positive correlation was observed between maize intake and the intake of whole wheat(r= 0.590; $p \leq 0.01$), egg (r=

0.775; $p \leq 0.01$), fowl (r= 0.643; $p \leq 0.01$) and buttermilk (r= 0.592; $p \leq 0.01$). Data of Nawanshehar control group showed a negative correlation between the intake of maize flour and total fat intake (r= 0.592; $p \leq 0.05$). A positive association between maize and vegetable intake (r= 0.506; $p \leq 0.01$) was seen in the Hoshiarpur control data.

The data findings synchronize with the existing studies. Besides being a source of macro and micro nutrients, maize is an important source of phytochemicals like carotenoids, phytosterols and phenolic. Carotenoids are a group of natural pigments ranging from yellow to red in colour. They can be broadly classified into two categories that are carotenes which have no oxygen only hydrocarbons and xanthophylls which contain oxygen too (Liangli et al, 2012). Numerous studies have reported the beneficial impact of carotenoid rich foods in combating cancer in different tissues (Takuji et al, 2012). Humans are incapable of synthesizing carotenoids and depend entirely on dietary supplements to meet the body requirements. Yellow corn is a good source of carotenoids, large quantities being mainly present in the horny and floury endosperm of the kernel more in sweet corn than waxy corn (Jiangfeng, 2016). Carotenes like alpha and beta carotene have 'provitamin A'property because they can be metabolized to vitamin A in the gut and tissue. High concentration of B-carotene was reported to function as a pro antioxidant. It acts as a potent chemopreventer by inducing apoptosis of cancer cells of colon, melanoma, leukemia and stomach (Liangli et al, 2012). Lutein and zeaxanthin are Xanthophylls with anti-tumour activity. Ferulic acid is a potent antioxidant which has anti-inflammatory and anticarcinogenic properties. Grains are the major source of ferulic acid. Corn has high amount of phytochemical content (Siyuan et al, 2018) which promote health because of their anti-inflammatory, antiatherogenic, antineoplastic, anti carcinogenic and antimicrobial properties to name a few (Ghosh and Konishi, 2007). Phytochemicals have been reported by Thomas et al (2015) to decrease the risk of cancer or its relapse after treatment.

On performing stepwise logistic regression,the independent variables remaining in the tenth step of the model are presented in Table4.2.8.The regression model (CL 95%)

revealed maize with fat/oil (B= 0.237) and with vegetables(B= 0.2) to be protective against the risk of esophageal cancer.

Table 4.2.1 Comparison of cereal consumption between Control Group and EC Cases (Patients)

Category	Refined wheat flour	Whole wheat flour	Maize	Basmati rice	Regular rice
Percentage of Consumers					
Control	26.31	71.71	77.63	66.45	35.52
Patients	35.45	63.63	43.63	28.18	65.45
Average no. of servings/month					
Control	125.67	213.62	7.27	8.66	6.04
Patients	190.54	217.88	4.64	7.00	5.04
Consumption Per Month(g)					
Control	2210.37	6551.74	308.82	577.43	336.30
Patients	2603.17	6629.86	200.00	454.80	324.20

Table 4.2.2 Correlation between Cereal intake and other food groups in EC Cases and Control Group

Cereal Intake of Total EC Cases				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.836**	-0.263**	
Maize		0.379**		
Total milk		0.244*		
Milk	-0.200*	0.217*		
Fruits				0.218*
Total fat		0.222*		
Animal fat	-0.202*	0.246**	0.256**	
Meat	0.203*			
Fowl	0.243*			
Fish				0.243*
Non -veg.	0.248**			
Buttermilk		0.215*		
Sugar		0.207*		0.205*
Cereal Intake of Total Control Group				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.801**		
Whole wheat				-0.264**
Maize	-0.190*	0.339**		
Fruits			0.190*	
Fowl	-0.187*	0.237**	0.238**	
Non-veg.	-0.167*	0.182*		
Milk	-0.222**	0.185*		
Buttermilk		0.247**		
Total milk		0.171*		
Plant fat	-0.249**	0.173*	-0.203*	
Total fat	-0.251**	0.253**		

Table 4.2.3 Correlation between Cereal intake and other food groups in EC Cases and Control Group of Jalandhar

Cereal Intake of Jalandhar EC Cases				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.824**	-0.345**	
Whole wheat			0.510**	
Meat		-0.263*		
Fish				0.280*
Pulses			-0.263*	
Cereal Intake of Jalandhar Control Group				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.829**		
Whole wheat			0.333**	
Vegetables				-0.269*
Fruits	-0.245*		0.287**	
Fowl	-0.256*	0.246*		
Curd	-0.252*			
Tea			0.253*	
Sugar		0.220*		
Plant fat	-0.370**		-0.250*	
Total fat	-0.313**			
Nuts	-0.284**			

Table 4.2.4 Correlation between Cereal intake and other food groups in EC Cases and Control Group of Kapurthala

Cereal Intake of Kapurthala EC Cases				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.921**		
Total milk			0.711*	
Milk			0.849**	
Curd			0.670*	
Fowl	0.813**			
Non -veg.	0.820**			
Cereal Intake of Kapurthala Control Group				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.760**		
Whole wheat			0.590**	
Eggs		0.657**	0.775**	
Fowl		0.534*	0.643**	
Fish		0.492*		
Non –veg.		0.477*	0.505*	
Fowl		0.534*	0.643**	
Milk	-0.513*			0.707**
Buttermilk		0.469*	0.592**	
Animal fat	-0.550*	0.736**	0.555*	
Total fat		0.491*		

Table 4.2.5 Correlation between Cereal intake and other food groups in EC Cases and Controls Group of Nawanshehar

Cereal Intake of Nawanshehar EC Cases

	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.870**		
Vegetables				-0.696*
Curd	-0.931**	0.898**		
Animal fat			0.791*	
Meat		0.635*	0.602*	
Sugar			0.623*	
Pulses			0.713*	-0.636*
Cereal Intake of Nawanshehar Control Group				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.697**		
Pulses	.869**	-0.571*		
Fruits				-0.748**
Eggs				-0.532*
Meat				-0.525*
Total fat			-0.592*	
Nuts	0.665**	-0.732**		

Table 4.2.6 Correlation between Cereal intake and other food groups in EC Cases and Control Group of Hoshiarpur

Cereal Intake of Hoshiarpur EC Cases				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.838**		
Vegetables				0.536**
Fruits				0.495**
Sugar				0.438*
Pulses				0.541**
Cereal Intake of Hoshiarpur Control Group				
	Amount of wheat	**Amount of whole wheat**	**Amount of Maize**	**Amount of rice**
Wheat		-0.800**		0.431*
Whole wheat				-0.415*
Vegetables		0.426*	0.506**	
Fowl				0.578**
Non-veg.				0.371*
Milk		0.478**		

4.2.2 Pulses

Pulses and legumes are two words usually used interchangeably as they both belong to the 'leguminosae'plant family. These plants produce their fruits as pods. Some varieties like peas and beans are eaten as green vegetables. Pulses are the dried edible seeds of the legume family. They are good sources of proteins (soya bean 36 gm, peanut 26gm per 100 gm), high in carbohydrates including non starch polysaccharides and low in fats (soyabean 8gm and peanut 47gm per 100gm are exceptions). Mono and poly unsaturated fatty acids are the main type of fats. Legumes are a good source of isoflavones, saponins and phytosterols. Some legumes are a source of deguelin, which is known for anti tumour effect. Pulses and legumes contribute about 2% of the total calories and 3.5% of the total proteins in the diets globally. The consumption is low in the communities consuming foods of animal origin and more in natives of parts of South America, Africa, Middle East and Asia where it is a staple food (World Cancer Fund Report, 2007). Indian yield of pulses is 661 Kg/ hectare with Punjab producing the maximum that is 905 Kg/ hectare (Status paper on pulses: farmer.gov.in/imagedefault/pestanddiseasescrops/pulses).

The collected data showed high percentage of Doaba people consuming pulses. Percentage of people consuming split and washed pulses is more in patients group (97.27%) than the control group (90.13%) though the number of monthly servings are similar that is 6.85 in case of patients and 6.71 in case of the control group. 59.87% people of the control group consumed split pulses with a monthly serving average being 4.02 whereas 85.45% people of patients group consumed 4.68 servings per month. Whole pulses were consumed by76.32% people of the control group with a monthly average serving of 5.13 while 98.18% people of patient group consumed whole pulses at an average of 5.32 monthly servings. Soya bean, lobia, rajmah, kabuli channa etc. was consumed by 92.76% people of the control group with an average monthly intake of 5.26 servings and 94.55% people of the patient group in 2.86 servings per month. *'Karhi'* is a spicy, savoury dish prepared with buttermilk and gram flour.

Fig. 4.2.3 Comparison of EC Cases (Patients) and Control Group Pulse consumers (Percentage Based)

Fig.4.2.4 Comparison of EC Cases (Patients) and Control Group Pulse consumption (Average servings/month based)

The consumption data was 89.47% control group people with average monthly serving being 2.10 and 76.36% patient group with 1.88 servings per month on an average. In the data of current study the consumption of pulses is similar in both the groups except for the intake of *channa, rajmah* and soya category.This category is consumed more by the control group. Logistic regression model also reveals the protective nature of this category. Soya beans are packed with phytoestrogens, saponins and phytosterols. Deguelin present in certain pulse has also been reported as antitumourogenic in experimental studies. Protease inhibitors have been reported to be linked with decreased cancer incidence. Pulses are a concenterated source of natural fibre. There is limited evidence of plant fibre being protective against esophageal cancer (World Cancer Report, 2007). The polypeptide, lunasin arrests cell division and causes apoptosis of malignant cells. The glycoprotein, lectin binds to selective carbohydrates and is therefore a part of various applications as medicine (Mejia et al, 2003). Research of Magee et al (2012) revealed the possibility of leguminous protease inhibitor concenterates of various legumes could possess anticancer properties similar to that of Bowman-Bir inhibitor of soyabean.

The patient group's intake of pulses revealed a strong positive correlation ($p \leq 0.001$) with the intake of animal fat (r= 0.461), total fat (r= 0.490) and total sugar (r= 0.401). In case of control group along with animal fat (r= 0.202; $p \leq 0.05$) and total fat intake (r= 0.374; $p \leq 0.01$), the intake of pulses showed a positive correlation with the intake of milk (r= 0.173; $p \leq 0.05$), curd (r= 0.173; $p \leq 0.05$), vegetables (r= 0.339; $p \leq 0.01$), fruits (r= 0.305; $p \leq 0.01$), plant fat (r= 0.262; $p \leq 0.01$), nuts (r= 0.363; $p \leq 0.01$). On comparing the Jalandhar sample we find the pulse intake of patients to be significantly correlated with the intake of maize (r= -0.263; $p \leq 0.05$),animal fat (r= 0.446; $p \leq 0.01$), total fat

(r= 0.452; $p \leq 0.01$) and sugar (r= 0.285; $p \leq 0.05$) whereas the pulse intake of the control group was significantly correlated with the intake of vegetables (r= 0.289; $p \leq 0.01$), fruits (r= 0.303; $p \leq 0.01$), curd (r= 0.194; $p \leq 0.01$), plant fat (r= 0.335; $p \leq 0.01$), total fat (r= 0.402; $p \leq 0.01$) and nuts (r= 0.418; $p \leq 0.01$). No significant correlation was registered from the Kapurthala patients data but the pulses intake of the Kapurthala control group showed a strong correlation of pulse and vegetable intake (r= 0.696; $p \leq 0.01$). Nawanshehar data of patients exhibited significant positive correlation of pulse intake with the intake of maize (r= 0.713; $p \leq 0.05$), animal fat (r= 0.846; $p \leq 0.01$), total fat (r= 0.767; $p \leq 0.01$), sugar (r= 0.757; $p \leq 0.01$) and a negative association with the intake of rice (r= -0.713; $p \leq 0.05$). The control group of the same area showed pulse intake's association with refined wheat flour (r= 0.869; $p \leq 0.01$), total milk intake (r= 0.523; $p \leq 0.05$), plant fat (r= 0.518; $p \leq 0.05$), total fat (r= 0.528; $p \leq 0.05$), nuts (r= 0.539; $p \leq 0.05$) and a negative correlation with the intake of whole wheat flour (r= -0.571; $p \leq 0.05$). Pulse intake in the Hoshiarpur patients was directly correlated with the intake of rice (r= 0.541; $p \leq 0.01$), plant fat (r= 0.384; $p \leq 0.05$),sugar (r= 0.474; $p \leq 0.05$) while the pulse intake of the control group revealed a significant positive correlation with the intake of buttermilk (r= 0.526; $p \leq 0.01$), total milk (r= 0.356; $p \leq 0.05$), animal fat (r= 0.462; $p \leq 0.01$), total fat (r= 0.471; $p \leq 0.01$) and sugar (r= 0.611; $p \leq 0.01$) With so many dietary correlations it is hard to isolate the cause perhaps this is the reason for no significant impact of pulses in the risk of esophageal cancer. The regression model too illustrates no significant impact.

In stepwise logistic regression, the independent variables remaining in thetenth step of the model are presented in the Table4.2.8.From the regression model (CL 95%) the channa, rajmah and soyabean group appears to be protective (B= 0.213) against the incidence of esophageal cancer while split pulses do not appear to be protective (B= -0.176).

Table 4.2.7 Comparison of consumption of pulses between Control Group and EC Cases (Patients)

	Percentage Consumer Of Pulses				
Sample	Split washed–urad/ channa/ masur/moong / tur	Split-moong/ urad	Whole-moong/ moth/ masur/ urad	Soya bean/ Lobia/ Raungi/ Rajmah/ Kale channae/ Kabuli channae	Karhi
Control	90.13	59.87	76.32	92.76	89.47
Patients	97.27	85.45	98.18	94.55	76.36
	Average Servings/ Month				
Control	6.71	4.02	5.13	5.26	2.10
Patients	6.85	4.68	5.32	2.89	1.88

Table 4.2.8 Logistics Regression (Stepwise) taking independent variables in the model (Wheat, Whole Wheat, Maize, Rice and Pulses) and eliminating one by one which have minimum effect.

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Independent Variables		B	df	Sig.	Exp (B)	95.0% C.I.for EXP(B)	
						Lower	Upper
Step 10[a]	WHEATChappatiWithgheebutter	-0.008	1	0.006	0.992	0.986	0.998
	WHEATChappatiNanKulcha	0.512	1	0.074	1.669	0.952	2.927
	WHOLEWHEATChappatiWithgheebutter	-0.01	1	<0.001	0.99	0.985	0.995
	MAIZEWithgheebutter	0.237	1	0.001	1.268	1.106	1.453
	MAIZEParanthawithveg	0.2	1	0.021	1.222	1.031	1.448
	BASMATIPlainboiled	0.093	1	0.005	1.098	1.029	1.171
	BASMATIZeera	0.295	1	<0.001	1.343	1.151	1.567
	REGULARZeera	0.177	1	0.023	1.194	1.025	1.391
	PULSESLEGUMESSplitwasheduradchannamasurmoongtur	-0.081	1	0.08	0.922	0.842	1.01
	PULSESLEGUMESSplitmoongurad	-0.176	1	0.011	0.839	0.733	0.96
	PULSESLEGUMESSoyabeanLobiaRaungiRajmahKalechannaeKabulichannae	0.213	1	<0.001	1.237	1.104	1.387
	Constant	0.016	1	0.977	1.016		

Table 4.2.9 Correlation between Pulse intake and other food groups in EC Cases and Control Group

Pulse Intake Total EC Cases					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Rice				-0.636*	0.541**
Maize		-0.263*		0.713*	
Total fat	0.490**	0.452**		0.767**	
Plant fat					0.384*
Animal fat	0.461**	0.446**		0.846**	
Sugar	0.401**	0.285*		0.757**	0.474*
Pulse Intake Total Control Group					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Milk	0.173*				
Wheat				0.869**	
Whole wheat				-0.571*	
Vegetable	0.339**	0.289**	0.696**		
Fruits	0.305**	0.303**			
Curd	0.194*	0.335**			
Tea		-0.267*			
Buttermilk					0.526**
Total milk				0.523*	0.356*
Animal fat	0.202*				0.462**
Plant fat	0.262**	0.335**		0.518*	
Total fat	0.374**	0.402**		0.528*	0.471**
Nuts	0.363**	0.418**		0.539*	
Sugar					0.611**

4.3 Vegetables and Fruits

Vegetables including fungi (mushroom) are the edible portion of the plant. This includes gathered or cultivated roots, leaves, bulbs, stalks and flowers. Some foods like cucumber

and tomato are fruits according to botanical classification but regarded as vegetables on culinary grounds. In this study the culinary vegetables were divided into three categories that are roots and tubers, green leafy vegetables and 'any other'. Similarly, in botanical terms the seed bearing part of a plant is called a fruit but in this study culinary fruits have been considered like apple, banana, orange and dried fruits like apricot.

4.3.1 Vegetables

In the present study the dietary source of vegetables was in the form of stuffing in *paranthas* or as a constituent of a preparation like *pulao/biryani* (Table 4.3.1), as a savoury dish or as an accompaniment in meals mainly in the form of pickle and *chutney* (Table 4.3.2). The findings of the collected data reveal an inverse association of varied significance between vegetables and the risk of incidence of esophageal cancer. 61.84% of the control group and 36.36% of the patient group consumed stuffed vegetable paranthas. On an average the two groups had 10.15 and 6.90 servings per month contributing 304.50 and 207.00 grams (g) of vegetables to the total average monthly intake of vegetables. Green leafy vegetables were consumed by 95.72% people of the control group and 98.18% people of the patient group, the average number of servings per month being 6.89 and 5.95 amounting to an average monthly vegetable intake of 997.63 grams in case of control group and 910.00g in the patient group. Similar observations were seen with regards to roots and tubers. 98.2% of the controls and 100% of the patient group people consumed roots and tubers. Their average monthly serving consumption was 16.29 and 10.21 amounting to an average monthly intake of 1629.00 and 1021.00 grams respectively. 98.29% control group and 100% of patient group people also consumed vegetables in the 'other vegetables' category with a little variation in their frequency of intake. Their average intake was of 18.16 and 16.63 servings per month. This amounted to an average intake of 1816.00 and 1663.00 g per month. Freedman et al (2007), Yamaji et al (2008) have also reported an inverse correlation of fruit and vegetable intake with the risk of cancer.

Pulao is a rice preparation along with vegetables. More people in the control group (31.58%) than in the patient group (10.00%) consumed vegetables in the form of *pulao* but the number of servings in case of patients (6.36) was almost double than those of the control group (3.35) amounting to a monthly average intake of 251.25 and 477.00g, respectively(Table 4.3.1).

Fig. 4.3.1 Comparison of EC Cases (Patients) and Control Group Vegetables consumers (Percentage based)

Pickles and *chutney* are common accompaniments in the Doaba diet. Pickles made in Indian subcontinent contain not only vegetables in brine/sugar and vinegar but oil and spices along with salt and/or sugar. *Chutney* usually does not contain oil. Salt and sugar are added for taste and/or preservation. A few preparations are consumed within a short period while others are preserved for a longer period. In Doaba region the main oil used in pickles is mustard oil while turmeric, fennel, fenugreek seed, carom seed, onion seed, cinnamon, clove are some of the main spices and condiments used along with chilies. These spices are rich in phytochemicals. Though high in sodium content pickles are low in saturated fats, good source of vitamins A and K, minerals like iron, potassium and manganese and a very good source of dietary fiber.Pickling makes hard-to-digest cellulose digestible. Consuming pickles with foods enhances the probiotic content of a meal. It also preserves the antioxidant power of foods which are sensitive to cooking methods. The judicious use of pickles could be beneficial. Chitra et al (2004), Hung et al (2004), Islami et al (2009), Mir and Dar (2009) have reported pickles to be a probable cause in increasing the risk of esophageal cancer. Islami et al (2009) reported a two-fold increase in the risk of EC associated with the consumption of pickled vegetables on the basis of retrospective studies with high heterogeneity.

Fig.4.3.2 Comparison of EC Cases (Patients) and Control Group Vegetable consumption (Intake amount based)

The consumption of *pickles* and *chutneys* in our study did not appear to be significant enough to cause an effect individually (Table 4.3.2). Total vegetable intake was positively correlated ($p \leq 0.05$) with intake of total fat (r= 0.197), total plant fat (r= 0.216) and total fish (r= 0.215) in case of total patient group. In case of individual districts, total vegetable intake showed a negative correlation with total rice (r= -0.696; $p \leq 0.05$) in case of Nawanshehar patients, a positive correlation ($p \leq 0.01$) with total rice (r= 0.536) and fruit (r= 0.564) intake in case and other food of Hoshiarpur patients. No significant correlation was established between total vegetable intake and other food groups in the data collected from Jalandhar and Kapurthala districts (Table 4.3.4).

In the total control group the total vegetable intake was positively correlated ($p \leq 0.05$) with milk (r= 0.202) and total milk (r= 0.170) intake while total pulses(r= 0.339) and total fruit (r= 0.220) intake was positively correlated at p value of ≤ 0.01. In case of individual districts Nawanshehar data showed no correlation but Kapurthala data revealed a positive correlation ($p \leq 0.01$) of total vegetables with total pulse intake (r= 0.696). Jalandhar data presented a significant correlation between total vegetable intake, intake of total pulses (r= 0.289; $p \leq 0.01$) and total animal fat (r= 0.215; $p \leq 0.05$). It also showed a negative correlation of total vegetables with total rice intake (r= -0.269; $p \leq <0.05$). Hoshiarpur district showed a positive correlation ($p \leq 0.05$) with whole wheat (r= 0.426), total curd (r= 0.426), total milk (r= 0.354), milk (r= 0.357) and total fat (r= 0.365). A positive correlation with total maize intake (r= 0.506; $p \leq 0.01$) was also noticed (Table 4.3.4).

Vegetables are packed with non nutritional anticarcinogenic micronutrients in the diet. The logistic regression model (CL95%) shows roots and tubers (B= 0.088) and 'other' vegetables (B= 0.058) to be protective against the risk of Esophageal Cancer (Table 4.3.5).

Table: 4.3.1 Comparison of Vegetable consumption between Control Group and EC Cases (Patients).

PERCENTAGE CONSUMERS					
Category	**Vegetables as stuffing in parantha**	**Green leafy veg.**	**Roots and tubers**	**Others**	**Vegetables in pulao**
Control	61.84	95.72	98.20	98.29	31.58
EC Cases	36.36	98.18	100.00	100.00	10.00
AVERAGE NO. OF SERVINGS/MONTH					
Category	**Vegetables as stuffing in parantha (no. Of servings /month)**	**Green leafy veg.**	**Roots and tubers**	**Others**	**Vegetables in pulao (no.of servings/ month)**
Control	10.15	6.89	16.29	18.16	3.35
EC Cases	6.90	5.95	10.21	16.63	6.36
CONSUMPTION PER MONTH (g)					
Category	**Vegetables as stuffing in parantha (amount intake/month)**	**Green leafy veg.**	**Roots and tubers**	**Others**	**Vegetables in pulao (amount intake/ month)**
Control	304.50	997.63	1629.00	1816.00	251.25
EC Cases	207.0	910.00	1021.00	1663.00	477.00

Table: 4.3.2 Comparison of pickle consumption between Control Group and EC Cases (Patients).

PERCENTAGE OF CONSUMERS		
Category (pickle)	**Control**	**EC cases**
MIXED	49.57	77.27
MANGO	33.33	10.91
LIME	29.05	5.45
LEMON	19.65	2.72
GINGER	19.65	2.72
INDIAN GOOSEBERRY	13.67	0.00
CARROT/CAULIFLOWER/TURNIP	17.94	0.90
GREEN CHILLI	17.94	7.27
RED CHILI(STUFFED)	7.69	0.00
Category (chutney)	**Control**	**EC cases**
MINT	63.8	80.00
CORIANDER	12.5	1.00
MANGO	15.79	0.90
ANY OTHER	1.97	0.00
AVERAGE NO. OF SERVINGS/MONTH		
Category (Pickle)	**Control (no.of servings)**	**EC cases (no.of servings)**
MIXED	8.44	3.11
MANGO	3.84	8.08
LIME	4.08	1.66
LEMON	1.65	2.60
GINGER	1.73	1.66
INDIAN GOOSEBERRY	1.50	0.00
CARROT/CAULIFLOWER/TURNIP	1.90	1.00
GREEN CHILLI	3.19	5.25
RED CHILI(STUFFED)	1.55	0.00
Category (Chutney)	**Control (no.of servings)**	**EC cases (no.of servings)**
MINT	3.78	1.51
CORIANDER	2.44	2.0

MANGO	1.15	1.0
ANY OTHER	11.0	0.00

Table 4.3.3 Correlation between Vegetable intake with other food groups in EC Cases and Control Group

Vegetable intake Total EC Cases					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Rice				-0.696*	0.536**
Fruits					0.564**
Total fat	0.197*				
Plant fat	0.216*				
Fish	0.215*				

Vegetable intake Total Control Group					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Whole wheat					0.426*
Maize					0.506**
Rice		-0.269*			
Pulses	0.339**	0.289**	0.696**		
Fruits	0.220**				
Curd					0.426*
Milk	0.202*				0.357*
Total milk	0.170*				0.354*
Total fat					0.365*
Animal fat		-0.215*			

4.3.2 Fruits

Like vegetables, fruits too are packed with non nutritional anticarcinogenic micronutrients in the diet. All dark coloured fruits, citrus fruits, grapes, apples, strawberries, plums, pineapple, melons are rich sources of phytochemical as discussed earlier. Citrus fruits are a very good source of vitamin C and other antioxidants like flavonoids, phenols, carotenoids, limonoids and pectin.

Fig. 4.3.3 Comparison of EC Cases (Patients) and Control Group Fruit consumers (Percentage based)

The fruits were classified into fruit category on the culinary basis. Dietary intake of fruits was as fresh fruits, tinned fruits, dried fruits, fresh juice and packaged juice. Fresh fruit was consumed by 96.60% controls and 98.20% patients. Controls consumed 2715.00 grams of fruits on an average in their 18.10 servings while the patients consumed 11.40 servings amounting to an average of 1710.00g per month. Tinned fruit and dried fruits consumption was very low. Only control group consumed these two fruit forms. 1.70% of controls consumed 6.50 servings amounting to 650.00 grams of tinned fruits. 2.56% of control group people also had 467.00 grams of dried fruit in 4.67 servings. 43.59% of controls and 6.36% patients consumed fresh juice on an average of 5.02 and 3.63 servings respectively leading to an average intake of 2259.00 and 1026.00g of fruits per group. In the form of packaged juice 9.40% controls and 5.45% patients had 145.20 and 193.20 grams of fruit in 3.63 and 4.83 servings on an average in a month (Table 4.3.5).

Fig. 4.3.4 Comparison of EC Cases (Patients) and Control Group Fruit consumption (Intake amount based)

The findings of the present study revealed an inverse association between fruit consumption and the risk of incidence of esophageal cancer. Our findings are consistent with those of Wang et al (2015) who conducted a meta-analysis of epidemiological studies. They reported an inverse association between risk of EC and fruit intake which

was consistent between cohort and case-control studies. Fruits especially citrus fruits contain bioactive compounds like beta- carotene and vitamin C. Carotenoids are regarded as nutritional scavengers of various malignancies including esophageal cancer. Carotenoids could interfere in cancer related pathways and the expression proteins involved in various steps of cell proliferation, differentiation, angiogenesis, apoptosis and detoxification of carcinogens, DNA damage and repair. Citrus fruits are a rich source of Vitamin C. Large intake of Vitamin C is correlated with a reduced risk of reflux esophagitis and EADC. American Institute of Cancer (2007) also concluded their report on various cohort and case-control studies in favour of Vitamin C. They found consistent and substantial evidence about the probable protective role of Vitamin C in reducing the risk of esophageal cancer. Dietary increase of 50 mg/day of Vit.C statistically decreased the incidence of EC by 13% (Bo et al, 2016). Antioxidants play a role more in hindering progression than initiation of the malignant process. On the basis of epidemiological studies Wang et al (2015) reported a decrease in incidence of esophageal cancer by about 37%. Rossi et al (2007) reported the protective effect of citrus fruits against esophageal cancer was due to flavanones. The interaction between fruits and medicines too should be considered to avoid adverse reactions (Bailey et al, 2013).

Correlation analysis revealed the association between total fruit intake and other food groups of EC patients (Tables 4.3.7). In the total patient group positive correlation ($p \leq 0.05$) was observed with total rice ($r = 0.218$), total milk ($r = 0.217$) and animal fat ($r = 0.208$). A stronger positive correlation ($p \leq 0.01$) was also seen with total fat intake ($r = 0.283$). In case of individual districts, Jalandhar patients data showed a positive correlation with the amount of total fat intake ($r = 0.314$; $p \leq 0.05$). No significant correlation was observed between fruits and other food groups in case of Kapurthala patient group. Nawanshehar patients data revealed a positive correlation ($p \leq 0.05$) between fruits intake, milk from tea ($r=0.706$), total fish ($r=0.710$), total meat ($r=0.646$) and total non-veg. intake ($r=0.632$). A strong positive correlation ($p \leq 0.01$) was also seen in Hoshiarpur patient group when fruit intake was considered in relation to rice ($r=0.495$) and total vegetable ($r=0.564$) intake. Control group data revealed many significant

correlations (Table 4.3.8). The total control group showed a significant positive correlation ($p \leq 0.05$) of total fruit intake with total maize ($r=0.190$) and total fowl ($r=0.203$) We observed a strong positive correlation ($p \leq 0.01$) of total fruit intake with the intake of total pulses ($r=0.305$), total vegetables ($r=0.220$), total curd ($r=0.435$), total milk ($r=0.275$), total fish ($r=0.318$), total non-veg. ($r=0.232$) and total nuts ($r=0.417$). In case of the Jalandhar control group a negative association was seen between total fruit intake and refined wheat intake ($r= -0.245$; $p \leq 0.05$). A positive correlation ($p \leq 0.05$) was noticed with milk ($r=0.226$) and total non-veg. ($r=0.245$) intake. A stronger correlation ($p \leq 0.01$) was observed in case of pulses ($r=0.303$), total curd ($r=0.491$), milk in buttermilk ($r=0.312$) total milk ($r=0.427$), total egg ($r=0.286$), total fish ($r=0.371$) and nuts ($r=0.471$). In case of Kapurthala control group the intake of fruits was less with progressing age ($r= -0.618$; $p \leq 0.01$) and a positive correlation between fruit and nut intake was noticed ($r=0.648$). Nawanshehar control data revealed a negative correlation with rice ($r= -0.748$; $p \leq 0.01$). It showed a positive correlation ($p \leq 0.05$) with total egg ($r=0.522$), total meat ($r=0.561$) and total non-veg. ($r=0.530$) but a strong positive correlation ($p \leq 0.01$) with animal fat ($r=0.654$). The Hoshiarpur group showed a positive correlation with animal fat intake ($r=0.340$; $p \leq 0.05$) and total curd ($r=0.730$; $p \leq 0.01$).

The logistic regression model (CL95%) shows fresh fruits ($B= 0.036$) and fresh fruit juice ($B= 0.774$) to be protective against the risk of Esophageal Cancer (Table 4.3.5).

Table 4.3.4 Comparison of Fruit consumption between Control Group and EC Cases (Patients).

PERCENTAGE OF CONSUMERS		
Category	**Control**	**ECCases**
Fresh fruit	96.60	98.20
Tinned fruit	1.70	0.00
Dried fruit	2.56	0.00
Fresh juice	43.59	6.36
Packaged juice	9.40	5.45
AVERAGE NO. OF SERVINGS/MONTH		
Category	**Control**	**ECCases**
Fresh fruit	18.10	11.40
Tinned fruit	6.50	0.00
Dried fruit	4.67	0.00
Fresh juice	5.02	2.28
Packaged juice	3.63	4.83
CONSUMPTION PER MONTH (g)		
Category	**Control (intake amount)**	**ECCases (intake amount)**
Fresh fruit	2715.00	1710.00
Tinned fruit	650.00	0.00
Dried fruit	467.00	0.00
Fresh juice	2259.00	1026.00
Packaged juice	145.20	193.20

Table: 4.3.5 Logistics Regression taking independent variables in the model (Vegetables and Fruits)

Variables in the Equation						
Independent Variables	B	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
VEGETABLESGreenLeafy	0.015	1	0.726	1.015	0.934	1.103
VEGETABLESRootsTubers	0.088	1	<0.001	1.091	1.044	1.141
VEGETABLESOthers	0.058	1	0.003	1.06	1.02	1.101
FRUITSFresh	0.036	1	0.003	1.036	1.012	1.061
FRUITSFreshjuice	0.744	1	<0.001	2.105	1.503	2.948
Constant	-3.709	1	<0.001	0.024		

Table 4.3.6 Correlation betweenFruit intake with other food groups in EC Cases and Control Group

Fruit intake Total EC Cases					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Rice	0.218*				0.495**
Vegetable					0.564**
Tea				0.706*	
Total milk	0.217*				
Total fat	0.283**	0.314*			
Animal fat	0.208*				
Fish				0.710*	
Total meat				0.646*	
NV				0.632*	
Buttermilk		0.279*			
Fruit intake Total Control Group					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Refined wheat		-0.245*			
Maize	0.190*	0.287**			
Rice				-0.748**	
Pulses	0.305**	0.303**			
Vegetables	0.220**				
Curd	0.435**	0.491**			0.730**
Milk		0.226*			
Total milk	0.275**	0.427**			
Animal fat				0.654**	0.340*
Total egg		0.286**		0.522*	
Total fowl	0.203*				
Total meat				0.561*	
Total fish	0.318*	0.371**			

	*				
Total NV	0.232**	0.245*		0.530*	
Nuts	0.417**	0.471**	0.648**		
Buttermilk		0.312**			

4.4 ANIMAL PRODUCTS

4.4.1 Milk/Dairy Products

There are wide variations in the personal, cultural and national consumption of the various food groups. Milk and dairy products are an integral part of the daily diet and are consumed in the raw, pasteurized or homogenized form. Milk is also processed into curd/ yogurt, cheese, channa (khoya) and concentrated milk while the milk fat is converted into cream, butter and ghee (clarified butter). The variation in nutritional composition of milk can be attributed to variation in species, breeds and type of feed of the ruminant. 100 grams of cow's milk contains about 3.40 g protein and 3.60 g fat (Gopalan, 2012). Saturated fatty acids constitute two thirds of the total fat, polyunsaturated fatty acids are about 4.00% and together they contribute half the energy of whole milk. Globally milk provides about 5.00% of the total dietary energy. The milk intake varies from less than 0.50% in African countries to 10-15% of dietary energy in USA and parts of Europe (WCR, 2007). Punjab contributes 8.00% to the total milk production and 6.00% to the total dairy output of India. Punjab recorded maximum per capita milk availability of 937 gram though Indian per capita milk availability was as low as 252 grams in 2014.

The dietary intake of milk and milk products in the most popular form was recorded. This included various types of available milk like cow milk, buffalo milk, pasteurized whole, toned and skimmed milk,curd like plain curd, *raita* and *dahi bhalla,* types of buttermilklike plain, salted, sweet, any other along with *paneer*(cottage cheese) and cheese(Table 4.4.1).

In the present study (Table 4.4.1) the consumption of cow's milk is more by control cases (30.77%) than cancer patients (18.18%) and the amount consumed by control group is

marginally more (22.08 servings/month) than the patients (20.10 servings/month). Buffalo's milk was consumed by 47.00% controls with the average number of monthly servings being 26.27 while 51.81% patient (EC cases) consumed 20.91 servings per month on an average. Pasteurised toned milk was consumed by 6.83% controls and 12.73% patients with an average monthly intake of 30.38 and 20.00 servings respectively.

Fig. 4.4.1Comparison of EC Cases (Patients) and Control Group Milk and Milk products consumers (Percentage Based)

Plain curd was consumed by 94.00% controls and 93.00% patients with an average monthly intake of 22.00 and 23.00 servings respectively. Raita was consumed by 49.00% controls and 3.60% patients with an average monthly intake of 7.10 and 23.00 servings, respectively. Dahi bhalla was consumed by 20.50% controls only with an average monthly intake of 1.92 servings. Other than raita the curd consumption was on similar pattern in both the groups. Raita is prepared by adding vegetables or tiny gram flour dumplings. Vegetables appear to be protective against esophageal cancer. Plain buttermilk was consumed by 66.00% controls and 77.00% patients with an average monthly intake of 16 and 14 servings each. Salted buttermilkwas consumed by 29.10% controls and 11.80% patients with an average monthly intake of 6.38 and 28.20 servings. Sweet buttermilk takers were 26.50% in the control group and 1.82% in the patient group. They consumed 2.55 and 3.00 servings on an average in a month.

Fig. 4.4.2 Comparison of EC Cases (Patients) and Control Group Milk and Milk products consumption (Intake amount based)

More people in the control group (79.48%) consumed paneer (cottage cheese) than patients (10.90%). Their consumption was double (once a week) than that of the patients (once a fortnight). Cheese was consumed by 3.41% controls only about 1.25 times a month.

To study the correlation of various food groups with milk and its products we grouped the intake of all the milk sources into five subgroups. Various types of drinking milk like

cow milk, buffalo milk, pasteurized whole, toned and skimmed milk were grouped into the category of milk; plain curd, *raita* and *dahi bhalla* were categorized as total curd; milk intake from all types of tea were considered as milk from tea; consumption of milk from all types of buttermilk as milk from buttermilk and the sum total of milk intake from all these sources as total milk (Table 4.4.2).

78.95% members of the control group consumed about 5855.00 grams of milk in a month while 80.91% of patients consumed 4245.00 grams of milk. Consumption of milk in the form of curd was 3855.71 grams by the controls (98.03%) and 3464.00 grams by the patients (94.55%). Amount of milk consumed as paneer and cheese was 485.0 grams and 250.0 grams respectively.

Tea is the most popular beverage and thus the maximum contributor to the total milk intake. 94.74% of controls and 100% patients consumed 7000.00 grams and 8176.00 grams of milk respectively as tea. Coffee takers were 31.58% controls only. Their average monthly consumption of milk as coffee was 692.71 grams. Buttermilk consumers were 78.29% controls and 88.18% patients with an average monthly intake of 1285.08 and1239.40 grams of milk respectively. All this summed up to an average monthly milk intake of 16965.36 grams by controls and 16305.0 grams by patients which amounts to about 565 and 543 grams per day respectively. Though the daily milk intake in both the groups is similar but the form is different. Patients consumed significantly more amount of milk as tea and our findings are coherent with the findings of Das et al (2015) while the subjects of the control group consumed more milk in other forms than in tea. Our results are in accordance with the findings of earlier researchers.Parodi (2015) reported that cow's milk components possess anti-cancer potential, accounted to increased levels of bifidobacterium and certain lactobacilli. Butyrate produced during fermentative activity of organisms promoted antiproliferation, apoptosis and differentiation in some cancer cells. Rumenic acid acted as a powerful anticarcinogen in experimental animals. These factors probably act together to fight the environmental insult and prevent cancer. Lamprecht and Lipkin team (2001) reported the role of calcium in cancer prevention of certain organs. Calcium forms insoluble soaps with bile acids and fatty acids in the

gastrointestinal tract preventing cell damage, reducing cell proliferation and causes differentiation. Calcium improves signaling within the cells leading to differentiation and apoptosis in cancer cells. Oral enzymes especially proteases can have a direct anti-tumour and anti-metastatic effect on reaching systemic circulation (Donaldson, 2004). Lactoferrin was found to exhibit antiviral, antifungal, antibacterial and antitumour activity. It also enhanced the immune system function in already immunocompromised animals. Alpha lactalbumin and casein hydrolyzates also demonstrated anti tumour activity (Zimecki and Kruzel, 2007). The milk constituents alpha lactalbumin and a casein degradation product, glycomacropeptide have been used together in health enhancing formula feeds for both infants and adults in addition to preventing and treating cancer (Artym and Zimecki, 2013). Rock (2011) stated that numerous bioactive substances in milk could have an impact on the risk and progression of cancer. Davoodi et al (2016) studied the anticarcinogenic, immunomodulatory, antihypertensive, hypocholesterolemic, and antimicrobial properties of milk. Their findings indicated the effectiveness of milk protein in the reduction of risk factor for cancer. Li et al (2017) also suggested an inverse correlation between dietary calcium intake and the risk of EC specifically ESCC in the Asian population but not in American and European population.

Correlation of consumption of milk and milk products with other food groups

The milk correlation matrix (Table 4.4.3) shows the p value along with the correlation value 'r'. It revealed that the cases who consumed more milk consumed less of refined wheat flour ($p \leq 0.05$, -0.200) and total meat ($p \leq 0.05$, -0.205). A positive association of milk intake was observed with the intake of whole wheat ($p \leq 0.05$, 0.217), fruits ($p \leq 0.05$, 0.217), curd ($p \leq 0.05$, 0.239), animal fat ($p \leq 0.05$, 0.233) and total fat ($p \leq 0.05$, 0.197). Those who consumed more milk also consumed more buttermilk ($p \leq 0.001$, 0.308) leading to an increased overall consumption of milk ($p \leq 0.001$, 0.426). Patients curd intake showed correlation with the intake of total fat ($p \leq 0.001$, 0.246) and overall milk consumption ($p \leq 0.001$, 0.505). Tea was a significant source of milk in many cases. Tea intake was showed correlation with the total intake of milk ($p \leq 0.001$, 0.709) and sugar ($p \leq 0.001$, 0.551). Buttermilk intake showed a correlation with the intake of whole

wheat (p ≤0.05, 0.215), milk (p ≤0.001, 0.308) and total milk consumption (p ≤0.001, 0.318). Intake of milk in any form increased the total milk intake. Total milk intake was more in the consumers of milk (p ≤0.001, 0.426), curd (p ≤0.001, 0.505), tea (p ≤0.001, 0.308), buttermilk (p ≤0.001, 0.318), sugar (p ≤0.001, 0.434). Those who consumed more milk consumed more animal fat (p ≤0.05, 0.227) and whole wheat flour (p ≤0.05, 0.244). Fish eaters consumed less milk (p ≤0.051, -0.195).

The data of all the four districts shows various correlations. The Jalandhar patients (Table 4.4.4) who consumed more milk consumed more buttermilk (p ≤0.001, 0.349), total milk (p ≤0.05, 0.254), animal fat (p ≤0.05, 0.294) and total fat (p ≤0.05, 0.294). Curd consumers had more dietary milk (p ≤0.05, 0.548) and total fat (p ≤0.05, 0.282). Tea intake showed a positive correlation with total milk (p ≤0.001, 0.794) and total sugar (p ≤0.001, 0.632) intake but a negative correlation with the intake of nuts (p ≤0.05, -0.254) and milk (p ≤0.05, - 0.254). Buttermilk consumers also consumed more fruits (p ≤0.05, 0.279), animal fat (p ≤0.05, 0.296) and milk (p ≤0.05, 0.349). Total milk intake revealed a positive correlation with intake of milk (p ≤0.05, 0.254), curd (p ≤0.001, 0.548), milk from tea (p ≤0.001, 0.794) and sugar (p ≤0.001, 0.476).

Kapurthala patients (Table 4.4.5) intake of maize showed significant correlation with the intake of milk (p ≤0.001, 0.849, curd (p ≤0.05, 0.670) and total milk (p ≤0.05, 0.711). Curd consumers also consumed more buttermilk (p ≤0.05, 0.758) and had higher total milk intake (p ≤0.001, 0.884). Along with curd, buttermilk takers had more milk from the source of tea (p ≤0.001, 0.781) showing a direct association with total milk intake (p ≤0.001, 0.883). The other category which increased total milk intake was the consumption of tea (p ≤0.05, 0.741). Intake of tea was also positively correlated with the consumption of sugar (p ≤0.05, 0.735).

Nawanshehar (Table 4.4.6) sample revealed an indirect correlation between curd and refined wheat flour intake (p ≤0.001, -0.931) and a positive association between curd and whole wheat intake (p ≤0.001, 0.898). Data also revealed that those who consumed more tea consumed more fruits also (p ≤0.05, 0.706).

Hoshiarpur cases (Table 4.4.7) correlation tables showed increased total milk intake in those who consumed more curd ($p \leq 0.05$, 0.419) and consumed more milk ($p \leq 0.001$, 0.818) or tea ($p \leq 0.001$, 0.716) but had no correlation with the intake of buttermilk. Milk intake was positively correlated with buttermilk intake ($p \leq 0.05$, 0.444) but negatively correlated with the total intake of eggs ($p \leq 0.05$,-0.421). Sugar intake was also directly linked with the intake of tea ($p \leq 0.001$, 0.534) and total milk consumption ($p \leq 0.05$, 0.395).

All people in the control group (Table 4.4.3) consumed milk in one form or the other with an average daily intake of about half a liter (as per above table). This is the reason for many correlations in this group. Total milk consumption was directly correlated ($p \leq 0.05$) with the intake of wheat (0.171), vegetables (0.170) and animal fat (0.182) and highly linked ($p \leq 0.001$) with the intake of fruits (0.275), milk (0.493), curd (0.502), milk from tea (0.661) and buttermilk (0.470). Buttermilk intake was strongly correlated ($p \leq 0.001$) with the intake of whole wheat (0.247), milk (0.363), curd (0.239) and animal fat (0.243). Tea consumers consumed more sugar ($p \leq 0.001$, 0.271) and less of milk ($p \leq 0.05$, -0.166), plant fat ($p \leq 0.05$, -0.167) and animal fat ($p \leq 0.001$, -0.222). Curd intake was positively associated with the age of the patient ($p \leq 0.001$, 0.260) along with the consumption of pulses ($p \leq 0.05$, 0.194), animal fat ($p \leq 0.05$, 0.201), fruits ($p \leq 0.001$, 0.435), milk ($p \leq 0.001$, 0.282), total fat ($p \leq 0.001$, 0.254) and total nuts ($p \leq 0.001$, 0.314). In the control group who drank more milk drank less tea ($p \leq 0.05$, -0.166) and ate less of refined wheat flour ($p \leq 0.05$, -0.222). Milk intake was directly correlated ($p \leq 0.05$) with the intake of whole wheat (0.185), pulses (0.173), vegetables (0.202) and total fat (0.177). Animal fat intake was strongly correlated with milk intake ($p \leq 0.001$, 0.296).

Intake of Jalandhar control group (Table 4.4.4) revealed inverse association of total milk intake with plant fat intake ($p \leq 0.05$, -0.213) and a strong positive correlation ($p \leq 0.001$) with fruits (0.427), milk (0.527), curd (0.614), milk from tea (0.626) and milk from buttermilk (0.521). Milk intake was strongly linked with intake of fruits ($p \leq 0.05$, 0.226), curd ($p \leq 0.001$, 0.385) and animal fat ($p \leq 0.001$, 0.392). Curd intake was directly

correlated with age of the individual ($p \leq 0.001$, 0.326) intake of pulses ($p \leq 0.05$, 0.335) and animal fat ($p \leq 0.05$, 0.267). A strong correlation with fruits ($p \leq 0.001$, 0.491), buttermilk ($p \leq 0.001$, 0.360) and nuts ($p \leq 0.001$, 0.317) intake was also observed. Refined wheat intake was found to be negatively correlated with curd intake. Consumption of tea was linked with maize ($p \leq 0.05$, 0.253), buttermilk ($p \leq 0.05$, 0.231) and sugar intake ($p \leq 0.001$, 0.367). Tea intake was found to be negatively correlated with the intake of pulses ($p \leq 0.05$, -0.267), plant fat ($p \leq 0.001$, -0.330) and total fat ($p \leq 0.001$, -0.394). Buttermilk intake was also positively correlated with fruit ($p \leq 0.001$, 0.312) intake.

Kapurthala (Table 4.4.5) control group's total milk intake was linked with milk from tea ($p \leq 0.001$, 0.644) while milk intake was positively correlated with rice intake ($p \leq 0.001$, 0.707) and negatively correlated with the intake of refined wheat flour ($p \leq 0.05$, -0.513). Curd was positively correlated with plant fat intake ($p \leq 0.001$, 0.834). People who consumed more buttermilk, consumed higher amount of whole wheat ($p \leq 0.05$, 0.469) and maize ($p \leq 0.001$, 0.592). Nawanshehar data (Table 4.4.6) revealed total milk intake to be negatively associated with fish intake ($p \leq 0.05$, -0.530), positively correlated with intake of pulses ($p \leq 0.05$, 0.523), tea ($p \leq 0.001$, 0.94) and plant fat ($p \leq 0.05$, 0.574). Tea intake was negatively linked with fish ($p \leq 0.05$, 0.586) and positively with plant fat ($p \leq 0.05$, 0.563) intake. Curd and milk intakes were also indirectly associated ($p \leq 0.001$, -0.679).

In the Hoshiarpur control group (Table 4.4.7) all those who consumed high amount of total milk also consumed more of pulses ($p \leq 0.05$, 0.356), vegetables ($p \leq 0.05$, 0.354), milk ($p \leq 0.05$, 0.424), curd ($p \leq 0.05$, 0.374), tea ($p \leq 0.001$, 0.706), sugar ($p \leq 0.001$, 0.609) and buttermilk ($p \leq 0.001$, 0.563). Buttermilk intake showed correlation with pulses ($p \leq 0.001$, 0.526), milk ($p \leq 0.001$, 0.644), curd ($p \leq 0.05$, 0.364), animal fat ($p \leq 0.001$, 0.583) and sugar ($p \leq 0.001$, 0.710). More curd intake was linked with more intake of vegetables ($p \leq 0.05$, 0.426), fruits ($p \leq 0.001$, 0.730), animal fat ($p \leq 0.001$, 0.419) and nuts ($p \leq 0.05$, 0.407). Increased milk intake was correlated with intake of whole wheat ($p \leq 0.001$, 0.478), vegetables ($p \leq 0.05$, 0.357) and sugar ($p \leq 0.05$, 0.349).

Table 4.4.1 Comparison of Milk and Milk Products consumption between Control Group and EC Cases (Patients)

Category	Control		EC Cases	
Milk	**Percentage of consumers**	**Avg. no. of monthly servings**	**Percentage of consumers**	**Avg. no. of monthly servings**
MILK				
Fresh cow	30.77	22.08	18.18	20.10
Fresh buffalo	47.00	26.27	51.81	20.91
Pasteuised full fat	3.41	22.75	0.90	15.00
Pasteurised toned	6.83	30.38	12.73	20.00
Pasteurised skimmed	4.27	18.80	0.00	0.00
CURD				
Plain	94.00	22.00	93.00	23.00
Raita	49.00	7.10	3.60	23.00
Bhalla	20.50	1.92	0.00	0.00
PANEER/CHEESE				
Paneer	79.48	4.05	10.90	2.08
Cheese	3.41	1.25	0.00	0.00
BUTTERMILK				
Plain buttermilk	66.00	16.00	77.00	14.00
Salted buttermilk	29.10	6.38	11.80	28.20
Sweet buttermilk	26.50	2.55	1.82	3.00
Any other	0.86	2.00	0.00	0.00

Table 4.4.2 Comparison of Milk consumption betweenControl Group and EC Cases (Patients)

PERCENTAGE CONSUMERS							
Category	**Milk**	**Curd**	**Paneer & Cheese**	**Tea**	**Coffee**	**Buttermilk**	**Total milk**
Control	78.95	98.03	80.26	94.74	31.58	78.29	100.00
EC Cases	80.91	94.55	10.91	100.00	0.0	88.18	100.00
AVERAGE MONTHLY CONSUMPTION (MILK)							
	Milk (gm)	**Curd (gm)**	**Paneer & Cheese (gm)**	**Tea (gm)**	**Coffee (gm)**	**Buttermilk (gm)**	**Total milk (gm)**
Control	5855.00	3855.71	485.90	7000.90	692.71	1285.08	16965.36
EC Cases	4245.00	3464.00	250.00	8176.00	0.0	1239.40	16305.00

Table 4.4.3 Correlation between Milk intake with other food groups in total EC Cases and Control Group

Milk intake in total EC Cases					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Whole wheat	0.217*			0.215*	0.244*
Fish					-0.195*
Fruits	0.217*				
Meat	-0.205*				
Milk	1	0.239*		0.308**	0.426**
Curd	0.239*	1			0.505**
Tea					0.709**
Buttermilk	0.308**				0.318**
Total milk	0.426**	0.505**	0.709**	0.318**	1
Animal fat	0.233*				0.227*
Total fat	0.197*	0.246**			
Sugar			0.551**		0.434**
Milk Intake in total Control Group					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Pulses	0.173*	0.194*			
Vegetables	0.202*				0.170*
Fruits		0.435**			0.275**
Milk	1	0.282**	-0.166*	0.363**	0.493**
Curd	0.282**	1		0.239**	0.502**
Tea	-0.166*				0.661**
Buttermilk	0.363**	0.239**			0.470**
Total milk	0.492**	0.502**	0.661**	0.470**	1
Animal fat	0.296**	0.201*		0.243**	0.182*
Plant fat			-0.167*		
Total fat	0.177*	0.254**	-0.222**		
Nuts		0.314**			
Sugar			0.271**		

Table 4.4.4 Correlation between Milk intake with other food groups in Jalandhar EC Cases and Control Group

Milk Intake of Jalandhar EC Cases					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Fish					-0.297*
Fruits				0.279*	
Milk			-0.254*	0.349*	0.254*
Curd					0.548**
Tea					0.794**
Buttermilk	0.349**				
Milk	0.254*	0.548*	0.794**		
Animal fat	0.294*			0.296*	
Plant fat					
Total fat	0.294*	0.282*			
Nuts			-0.254*		
Sugar			0.632**		0.476**
Milk Intake of Jalandhar Control group					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Pulses		0.335*	-0.267*		
Fruits	0.226*	0.491**		0.312**	0.427**
Milk		0.385**			0.527**
Curd	0.385**			0.360**	0.614**
Tea				0.231*	0.626**
Buttermilk		0.360**	0.231*		0.521**
Total milk	0.527**	0.614**	0.626**	0.521**	
Animal fat	0.392**	0.267*			
Plant fat			-0.330**		-0.213*
Total fat		0.298**	-0.394**		
Nuts		0.317**			
Sugar			0.367**		

Table 4.4.5 Correlation between Milk intake with other food groups in Kapurthala EC Cases and Control Group

Milk Intake of Kapurthala EC Cases					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Maize	0.849**	0.670*			0.711*
Curd				0.758*	0.884**
Tea				0.781**	0.741*
Buttermilk		0.758*	0.781**		0.883**
Total milk		0.884**	0.741*	0.883**	
Sugar			0.735*		
Milk Intake of Kapurthala Control Group					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Maize				0.592**	
Rice	0.707**				
Tea					0.644**
Total milk			0.644**		
Plant fat		0.834**			

Table 4.4.6 Correlation between Milk intake with other food groups in Nawanshehar EC Cases and Control Group

Milk Intake of Nawanshehar EC Cases					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Whole wheat		0.898**			
Fruits			0.706*		
Milk Intake of Nawanshehar Control Group					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Fish			-0.586*		-0.530*
Pulses					0.523*
Milk		-0.679**			
Curd	-0.679**				
Tea					0.946**
Total milk			0.946**		
Plant fat			0.563*		0.574*

Table 4.4.7 Correlation between Milk intake with other food groups in Hoshiarpurr EC Cases and Control Group

Milk Intake of Hoshiarpur EC Cases					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Eggs	-0.421*				
Fruits				0.398*	
Milk				0.444*	0.819**
Curd					0.419*
Tea					0.716**
Buttermilk	0.444*				
Total milk	0.819**	0.419*	0.716**		
Sugar			0.534**		0.395*
Milk Intake of Hoshiarpur Control Group					
	Milk	**Curd**	**Tea**	**Buttermilk**	**Total amount of milk**
Pulses				0.526**	0.356*
Vegetables	0.357*	0.426*			0.354*
Fruits		0.730**			
Milk				0.644**	0.424*
Curd				0.364*	0.374*
Tea					0.706**
Buttermilk	0.644**	0.364*			0.563**
Total milk	0.424*	0.374*	0.706**	0.563**	
Animal fat		0.419*		0.583**	
Nuts		0.407*			
Sugar	0.349*			0.710**	0.609**

4.4.2 Meat, Fish and Poultry

Dietary consumption of animal products is highly variable. There are wide variations in the personal, cultural and national consumption of this food group. Meat and poultry provides 8% of energy, 18% protein and 23% of fat in the diet by world statistics. Consumption of fish is more in coastal areas and islands. Asia and Oceania (Australia, Newzealand and surrounding island countries) consume more fish than other countries. In India the most common meats consumed are poultry, goat, pig, mutton, fish and bovine. Meat, fish and poultry consumption is influenced by culture, customs, traditions and particularly religion. Urbanization too has been the cause of increased consumption of meat. Popularity of chicken meat can be related to its versatility, lower cost and acceptance by all religions unlike beef which is forbidden to Hindus and pork being prohibited to Muslims. According to the survey conducted by FAO (Food and Agriculture Organisation) 20-42% Indians are vegetarian. In India per capita monthly consumption is mutton is 0.053 kg, pork 0.006 kg, chicken 0.059 kg, beef 0.037 kg and other meats 0.003 kg (Devi et al, 2014). 80% of men and 70% of women consume meat, fish and poultry not weekly but occasionally. Punjab has the fewest consumers of meat, fish and chicken. Meat is a rich source of proteins, vitamins, minerals and fats especially omega 3 fatty acid and linoleic acid. Incorporation of various spices makes cooking of meat different in India. (Devi et al, 2014). FAO (2012) reported Indian meat consumption to be below 5 kg/cap/year. Our findings are in accordance with the World Cancer Fund Report (2007).

In the present case-control study the dietary intake of non-vegetarian foods (egg, meat, fish and poultry) along with the type of preparation was studied in the EC and control group.

Fig. 4.4.3 Comparison of EC Cases (Patients) and Control Group Egg consumers/consumption (Percentage/Intake amount based)

Fig. 4.4.4 Comparison of EC Cases (Patients) and Control Group Meat consumers/consumption (Percentage/Intake amount based)

Table 4.4.9 shows the consumption practice of non-vegetarian food of the control and patient group (EC cases). 24.80% people of the control group consumed boiled egg with an average of 19.50 servings per month while 22.70% patients had only 5.76 servings of boiled egg per month. The preparation of fried egg or omelette had more takers in the control group than the patient group with a little variation in the intake frequency.25.64% control group candidates had 9.20 servings per month as compared to 20.00% of patients having 8.04 servings. Total percentage of controls consuming egg (Fig 4.4.3) was 38.16% with an average monthly serving of 18.29 whereas 30.00% patients consumed only 9.72 servings per month. According to the data, meat (Fig 4.4.4) in the grilled form was not a preferred choice as only 1.70% control group and 3.63% patients ate this preparation that too with a low monthly frequency of 1.00 and 2.00 respectively. Fried preparations of meat were consumed by 4.30% cases and 0.90% patients with monthly frequency as small as 1.60 and 2.00 respectively. Meat cooked in gravy was the most preferred meat preparation with 26.50% controls and 11.82% patients consuming it though the monthly frequency was of 2.25 and 2.07 servings only. 28.29% controls and 13.64% patients ate meat with a monthly average intake of 246.51 and 300.00 grams respectively. Fowl (Fig 4.4.6) was the most popular choice amongst the non-vegetarian foods. 6.83% control group people had grilled chicken with an average monthly frequency of 1.87 while 7.27% of the patient group had 2.62 servings of grilled fowl per month. Fried chicken was consumed by 2.60%controls and0.90% patients with an average monthly frequency of 2.00 servings in both groups. Curried preparation of fowl was consumed by 21.36% controls and 23.64% patients with an average monthly frequency of 2.32 and 2.69 servings respectively. Total fowl consumers were 28.94% in the control group and 26.36% in the patient group with an average monthly consumption of 368.18 and 393.10 grams each. Only 4.27% controls and 1.81% patients consumed grilled fish about once a month. The curried preparation was consumed about once a month by 2.56% people in the control group only. Most popular fish (Fig. 4.4.5) preparation was the fried fish which was the dietary constituent of 9.4% controls and

4.5% patients though the average monthly intake in a year was 1.4 and 1.2 servings respectively. 13.16% controls and 5.45% patients consumed fish with an average monthly intake in a year of 185.0 and 183.3 grams respectively.

Fig. 4.4.5 Comparison of EC Cases (Patients) and Control Group Fish consumers/consumption (Percentage/Intake amount based)

Fig. 4.4.6 Comparison of EC Cases (Patients) and Control Group Fowl consumers/consumption (Percentage/Intake amount based)

In our study the number of controls consuming egg and fish was significantly higher though there was a significant difference in the consumption amount of eggs only. Our study is in association with the findings of previous researchers. Brown et al (2001) concluded that high consumption of eggs was associated with 20.00% reduction in EC risk and Ganesh et al (2009) reported decreased incidence of EC by 20.00% in consumers of fresh fish.

Correlation of meat, fish and poultry consumption with other food groups

The correlation matrix results 'r' has been given belowalond with the p value. In case of the total patient group (Table 4.4.10)total non- vegetarian intake was strongly correlated ($p \leq 0.001$) with the intake of refined wheat flour (0.248), total eggs (0.320), total meat (0.835), total fowl (0.938) and total fish intake (0.626). Those who consumed egg consumed significant amount of meat ($r= 0.261$, $p \leq =0.001$) and fowl ($p \leq 0.001$; $r= 0.328$). Meat intake was positively correlated with the intake of refined wheat flour ($p \leq 0.05$; 0.203), total fowl ($p \leq 0.001$; 0.610) and total fish ($p \leq 0.001$; 0.582) intake. A negative link between the intake of milk and meat ($p \leq 0.05$; -0.205) was also noticed. Fowl eaters also consumed more of refined wheat flour ($p \leq 0.05$; 0.243) and fish ($p \leq 0.001$; 0.444). Fish consumption was positively associated with meat, fowl, total non veg., rice ($p \leq 0.05$; 0.243) and vegetables ($p \leq 0.05$; 0.215) though negatively correlated with the consumption of total milk intake ($p \leq 0.05$; -0.195).

District data showed similar correlations in case of non-vegetarian food choices but a little variation in case of correlation with other food groups. Amongst the Jalandhar patients (Table 4.4.11) total non veg. intake showed a strong positive correlation ($p \leq 0.001$) with the intake of egg (0.363), fish (0.431), meat (0.816) and maximum with fowl (0.932). Egg consumers also consumed more of fowl ($p \leq 0.001$; 0.305) and meat ($p \leq 0.001$; 0.378). Meat consumption was positively correlated with the intake of fowl ($p \leq 0.001$; 0.587) also but negatively correlated with the intake of whole wheat flour ($p \leq 0.05$; 0.263). Intake of fowl and fish were directly associated ($p \leq 0.001$; 0.274). Along with fowl and total non veg. intake fish intake was found to be significantly associated with the intake of rice ($p \leq 0.05$; 0.280) and total milk ($p \leq 0.05$; - 0.297). Total non veg. intake of Kapurthala patients (Table 4.4.12) showed a strong ($p \leq 0.001$) positive link with the intake of meat (0.846), fish (0.846) and fowl (0.938) along with the intake of refined wheat flour (0.820). Egg intake was associated with the intake of fowl only ($p \leq 0.001$; 0.801). All meat consumers consumed fish too ($p \leq 0.001$; 1.000). Fowl intake showed a positive correlation with the intake of refined wheat flour also ($p \leq 0.001$; 0.813). Nawanshehar patients (Table 4.4.13) total non veg. intake showed a significant positive correlation with the intake of fish ($p \leq 0.001$; 0.816), fowl ($p \leq 0.001$; 0.924), meat ($p \leq 0.001$; 0.934) fruits ($p \leq 0.05$; 0.632) and a negative correlation with nuts intake ($p \leq 0.05$;- 0.603). Egg consumers consumed more of fowl ($p \leq 0.05$; 0.617) and animal fat ($p \leq 0.05$; 0.620). Meat intake was positively correlated with the intake of fowl ($p \leq 0.001$; 0.737), fish ($p \leq 0.001$; 0.815), animal fat ($p \leq 0.05$; 0.668), fruits ($p \leq 0.05$; 0.646), whole wheat flour ($p \leq 0.05$; 0.635) and maize flour ($p \leq 0.05$; 0.602). Fowl intake showed a positive correlation with the intake of fish also ($p \leq 0.05$; 0.620). A negative correlation between fish and nuts intake was observed ($p \leq 0.05$; - 0.702). Along with total non veg., fowl and meat intake fish intake was directly associated with the intake of fruits ($p \leq 0.05$; 0.710). Data of Hoshiarpur patients (Table 4.4.14) revealed an indirect association between total non veg. intake and age of the patient ($p \leq 0.05$; - 0.395). A direct association of total non veg. intake was observed with the intake of eggs ($p \leq 0.001$; 0.857), meat ($p \leq 0.001$; 0.702) and fowl ($p \leq 0.001$; 0.038). Egg consumers consumed

more of meat (p ≤0.001; 0.550) and fowl (p ≤0.001; 0.829) but less of milk (p ≤0.05; - 0.421). Meat and fowl intake were also directly associated (p ≤0.001; 0.411).

The total control group data (Table 4.4.10) revealed a strong positive correlation (p ≤0.001) of total non veg. intake with the intake of eggs (0.295), fish (0.693), meat (0.870), fowl (0.932) and fruits (0.232). A positive correlation with the intake of whole wheat flour (p ≤0.05; 0.182), nuts (p ≤0.05; 0.174) and a negative correlation with refined wheat flour (p ≤0.05; 0.167) was also seen. Egg consumers consumed more of meat (p ≤0.001; 0.291), fowl (p ≤0.001; 0.248), fish (p ≤0.001; 0.219), curd (p ≤0.001; 0.260), animal fat (p ≤0.05; 0.189) and nuts (p ≤0.001; 0.203). Meat intake was directly associated with the intake of fowl (p≤0.001; 0.674), fish (p ≤0.001; 0.526) and nuts (p ≤0.05; 0.169). Fowl intake was positively correlated with the intake of whole wheat (p ≤0.05; 0.237) and maize (p ≤0.05; 0.238) flours, fruits (p ≤0.05; 0.203), animal fat (p ≤0.05; 0.194) and fish (p ≤0.001; 0.522) though negatively correlated with refined wheat flour intake (p ≤0.05; - 0.187). Fish intake was directly linked with nuts intake also (p ≤0.05; 0.169).

Total non veg. intake of the Jalandhar control group (Table 4.4.11) revealed strong positive correlation (p ≤0.001) with the intake of egg (0.397), meat (0.835), fowl (0.907) and fish (0.794). Direct link between total non veg. and fruit intake (p ≤0.05; 0.245) was also seen. Egg consumers also consumed more of fruits (p ≤0.001; 0.286), meat (p ≤0.001; 0.434), fowl (p ≤0.001; 0.306), fish (p ≤0.001; 0.265). Positive correlation (p ≤0.001) was observed between total non veg. intake and intake of eggs (0.644), meat (0.902), fowl (0.963) and fish (0.555) in Kapurthala control group (Table 4.4.12). Total non veg. intake was also directly associated with the intake of whole wheat (p ≤0.05; 0.477)and maize (p ≤0.05; 0.505) flours. Egg consumers consumed more of whole wheat (p ≤0.001; 0.657), maize flour (p ≤0.05; 0.775), and fowl (p ≤0.001; 0.731). Fowl intake was also directly linked with the intake of whole wheat flour (p ≤0.05; 0.534), maize flour (p ≤0.001; 0.643) and meat intake (p ≤0.001; 0.793). Positive correlation between fish intake and whole wheat flour intake (p ≤0.05; 0.492)was also noticed. Data of Nawanshehar control group (Table 4.4.13) showed a direct association between total non

veg. intake and intake of fruits (p ≤0.05; 0.530), meat (p ≤0.001; 0.985) and fowl (p ≤0.001; 0.983). An indirect association with sugar intake (p ≤0.05; - 0.570) was also observed. Egg intake was positively correlated with intake of fruits (p ≤0.05; 0.522), fish (p ≤0.001; 0.883), animal fat (p ≤0.05; 0.515) and nuts (p ≤0.05; 0.733). Egg intake was found to be negatively correlated with the intake of rice (p ≤0.05; - 0.532) and plant fat (p ≤0.05; - 0.536). Meat consumption was directly correlated with the intake of fruits (p ≤0.05; 0.561) and fowl (p ≤0.001; 0.942). Inverse correlation of meat intake with the intake of rice (p ≤0.05; - 0.525) and sugar (p ≤0.05; 0.520) was also recorded. Negative association between fowl intake with sugar intake (p ≤0.05; - 0.633) and fish intake with the intake of milk from tea (p ≤0.05; - 0.586), total milk (p ≤0.05; - 0.530) and plant fat (p ≤0.001; 0.720) was also observed. Amongst the Hoshiarpur control group (Table 4.4.14) total non veg. intake was positively correlated (p ≤0.001) with the intake of eggs (0.665), meat (0.945), fowl (0.951) and fish (0.540). Total non veg. intake was also correlated with the intake of rice (p ≤0.05; 0.578). Egg consumption was correlated with the intake of meat (p ≤0.001; 0.528), fowl (p ≤0.001; 0.647), fish (p ≤0.001; 0.664) and animal fat (p ≤0.05; 0.354). Meat intake was associated with the intake of fowl (p ≤0.001; 0.817), fish (p ≤0.001; 0.462) and fowl intake was correlated with the intake of rice (p ≤0.05; 0.578) and fish (p ≤0.05; 0.393)

Logistic regression model (CL 95%) revealed paneer (B= 0.496) and sweet buttermilk (B= 1.019) to be protective against esophageal cancer. The ‘B’ value ofplain buttermilk (-0.041) is too small to be considered as an influencing factor(Table 4.4.8). Non veg. group of meat, fish and poultry had no significant impact on the incidence of esophageal cancer (Table 4.4.15).

Table 4.4.8 Logistics Regression taking independent variables in the model (Milk products)

Variables in the Equation						
Independent Variables	B	Df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
MILKMILKPRODUCTS Fresh Cow’s	0.005	1	0.783	1.005	0.971	1.04

MILKMILKPRODUCTS Fresh Buffalo's	0.003	1	0.804	1.003	0.979	1.028
MILKMILKPRODUCTSPasteurised full fat	0.027	1	0.531	1.028	0.944	1.119
MILKMILKPRODUCTS Toned milk	-0.015	1	0.445	0.985	0.946	1.025
Curd Plain	-0.007	1	0.552	0.993	0.971	1.016
Curd Raita	0.048	1	0.141	1.049	0.984	1.118
Paneer	0.496	1	<0.001	1.642	1.379	1.955
ButtermilkPlain	-0.041	1	0.003	0.96	0.934	0.987
ButtermilkSalted	-0.02	1	0.413	0.98	0.933	1.029
ButtermilkSweet	1.019	1	0.003	2.771	1.403	5.472
Constant	-1.037	1	0.001	0.354		

Table 4.4.9 Comparison of Meat, Fish, Poultry consumption between Control Group and EC Cases (Patients)

Category	Control		EC Cases	
	Percentage of consumers	Avg. of monthly servings/amount	Percentage of consumers	Avg. of monthly servings/amount
EGG				
Boiled	24.80	19.50	22.70	5.76
Fried/ omelette	25.64	9.20	20.00	8.04
Egg intake	38.16	18.29	30.00	9.72
MEAT				
Grilled	1.70	1.00	3.63	2.00
Fried	4.30	1.60	0.90	2.00
With gravy	26.5	2.25	11.82	2.07
Meat intake	28.29	246.51 g	13.64	300.00 g
FOWL				
Grilled	6.83	1.87	7.27	2.62
Fried	2.60	2.00	0.90	2.00
With gravy	26.97	2.73	23.64	2.69
Fowl intake	28.94	368.18 g	26.36	393.10 g
FISH				
Grilled	4.27	1.00	1.81	1.00
Fried	9.40	1.40	4.50	1.20
With gravy	2.56	1.00	0.00	0.00
Fish intake	13.16	185.00 g	5.45	183.30 g

Table 4.4.10 Correlation between Meat, Fish and Poultry intake with other food groups in total EC Cases and Control Group

Meat, Fish and Poultry Intake of Total EC Cases					
	Total egg	**Total meat**	**Total fowl**	**Total fish**	**Total non-veg.**
Rice				.243*	
Vegetables				0.215	
Eggs		.261**	.328**		.320**
Meat	.261**		.610**	.582**	.835**
Fowl	.328**	.610**		.444**	.938**
Fish		.582**	.444**		.626**
Milk		-.205*			
Total milk				-.195*	
Meat, Fish and Poultry Intake of Total Control Group					
	Total egg	**Total meat**	**Total fowl**	**Total fish**	**Total non-veg.**
Whole wheat			0.237**		0.182*
Maize			0.238**		
Fruits			0.203*	0.318**	0.232**
Eggs		0.291**	0.248**	0.219**	0.295**
Meat	0.291**		0.674**	0.526**	0.870**
Fowl	0.248**	0.674**		0.522**	0.932**
Fish	0.219**	0.526**	0.522**		0.693**
Curd	0.260**				
Animal fat	0.189*		0.194*		
nuts	0.203*	0.169*		0.169*	0.174*

Table 4.4.11 Correlation between Meat, Fish and Poultry intake with other food groups in Jalandhar EC Cases and Control Group

Meat, Fish and Poultry Intake of Jalandhar EC Cases					
	Egg	**Meat**	**Fowl**	**Fish**	**Total NV**
Whole wheat		-0.263*			
Rice				0.280*	
Eggs		0.378**	0.305*		0.363**
Meat	0.378**		0.567**		0.816**
Fowl	0.305*	0.587**		0.274*	0.932**
Fish			0.274*		0.431**
Total milk				-0.297*	
Meat, Fish and Poultry Intake of Jalandhar Control Group					
	Egg	**Meat**	**Fowl**	**Fish**	**Total NV**
Whole wheat			0.246*		
Fruits	0.286**			0.371**	0.245*
Egg		0.434**	0.306**	0.265*	0.397**
Meat	0.434**		0.568**	0.584**	835**
Fowl	0.306**	0.568**		0.626**	0.907**
Fish	0.265*	0.584**	0.626**		0.794**
Nuts	0.266*	0.214*	0.254*	0.279**	0.285**

Table 4.4.12 Correlation between Meat, Fish and Poultry intake with other food groups in Kapurthala EC Cases and Control Group

Meat, Fish and Poultry Intake of Kapurthala ECCases					
	Egg	**Meat**	**Fowl**	**Fish**	**Total NV**
Egg			0.801**		
Meat				10.000**	0.846**
Fowl	0.801**				0.938**
Fish		10.000**			0.846**
Meat, Fish and Poultry Intake of Kapurthala Control Group					
	Egg	**Meat**	**Fowl**	**Fish**	**Total NV**
Whole wheat	0.657**		0.534*	0.492*	0.477*
Maize	0.775*		0.643**		0.505*
Egg			0.731**		0.644**
Meat			0.793**		0.902**
Fowl	0.731**	0.793**			0.963**
Fish					0.555*

Table 4.4.13 Correlation between Meat, Fish and Poultry intake with other food groups in Nawanshehar EC Cases and Control Group

Meat, Fish and Poultry Intake of Nawanshehar EC Cases					
	Egg	**Meat**	**Fowl**	**Fish**	**Total NV**
Whole wheat		0.635*			
Maize		0.602*			
Eggs			0.617*		
Fruits		0.646*		0.710*	0.632*
Meat			0.737**	0.815**	0.934**
Fowl	0.617*	0.737**		0.620*	0.924**
Fish		0.815**	0.620*		0.816**
Animal fat	0.620*	0.668*			
Nuts			-0.702*		-0.603*
Meat, Fish and Poultry Intake of Nawanshehar Control Group					
	Total egg	**Total meat**	**Total fowl**	**Total fish**	**Total non-veg0.**
Rice	-0.532*	-0.525*			
Fruits	0.522*	0.561*			0.530*
Eggs				0.883**	
Meat			0.942**		0.985**
Fowl		0.942**			0.983**
Fish	0.883**				
Milk from tea				-0.586*	
milk				-0.530*	
Plant fat	-0.536*			-0.720**	
Animal fat	0.515*				
Nuts	0.733*				
Sugar		-0.520*	-0.633*		-0.570*

Table 4.4.14 Correlation between Meat, Fish and Poultry intake with other food groups in Hoshiarpur EC Cases and Control Group

Meat, Fish and Poultry Intake of Hoshiarpur EC Cases					
	Total egg	**Total meat**	**Total fowl**	**Total fish**	**Total non-veg.**
Eggs		0.550**	0.829**		0.857**
Meat	0.550**		0.411*		0.702**
Fowl	0.829**	0.411*			0.038**
Milk	-0.421*				
Meat, Fish and Poultry Intake of Hoshiarpur Control Group					
	Total egg	**Total meat**	**Total fowl**	**Total fish**	**Total non-veg.**
Rice			0.578**		0.371*
Eggs		0.528**	0.647**	0.664**	0.665**
Meat	0.528**		0.817**	0.462**	0.945**
Fowl	0.647**	0.817**		0.393*	0.951**
Fish	0.664**	0.462**	0.393*		0.540**
Animal fat	.354*				

Table 4.4.15 Logistics Regression taking independent variables in the model (Meat products)

Variables in the Equation						
Independent variables	B	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
Total eggs	-0.034	1	0.081	0.966	0.93	1.004
Total meat	-0.002	1	0.259	0.998	0.996	1.001
Total fowl	0.002	1	0.076	1.002	1	1.003
Total fish	-0.004	1	0.181	0.996	0.991	1.002
Constant	-0.192	1	0.181	0.825		

4.5 FATS, OILS, NUTS AND OIL SEEDS

4.5.1 Fats and Oils

Fats are a concentrated source of energy, contributing about 30-40 percent of total dietary energy in diets of affluent countries of North America and Europe while it is only 20-30 percent in the Asian, African and Latin American diet with maximum consumption being in Greece. Dietary fat is composed of three molecules of fatty acids linked to a framework of glycerol. Fats are usually classified on the basis of their source, chemical configuration and use. Oils are liquid at ambient temperature, of plant or marine source and high in unsaturated fatty acids while, fats are solid or semi-solid at ambient temperature, usually from animal source and high in saturated fatty acids (World Cancer Fund Report, 2007). 'Nuts' commonly called dry fruit or culinary nuts are the edible portion of a seed or fruit which is enclosed in an inedible hard or brittle shell. The kernel is a rich source of protein, oils and B-vitamins. Popularly consumed nuts are almond, cashewnut, pistachio, walnut, pine nut and coconut while oilseeds like groundnut, mustard, soyabean, safflower, sunflower, sesame and flax are frequently grown for edible oils or consumption as such (Indiaagronet.com)

The pattern of fat and oil consumption was found to be significantly different in both the groups (Table 4.5.1). Number of cases of control group consuming any type of fat and oil is more than the patients except for the consumption of *vanaspati ghee* and cream. The average number of servings or amount of fat intake of all categories of fat were significantly more in case of all patients.Mustard oil was consumed by 89.74% control group people with an average of 58.63 servings per month while 79.09% patients on an average consumed 72.34 servings per month. Refined oil was consumed by 55.55% control group with an average of 56.93 servings and an average of 64.17 servings was consumed by 40.90% EC patients. 53.8% control group people consumed 30.20 servings per month of *desi ghee* (clearified butter) and 43.6% of EC cases consumed an average of 64.9 servings in a month. The intake of 11.7 butter and 3.70 cream servings by 34.2% and 11.88% control group people respectively was less than the patient's intake. The 16.4% and 10.92%patient's had 14.6 and 23.50 servings of butter and cream respectively. Monthly averages of 47.80 servings of *vanaspati ghee* were consumed by only 26.49% of the control group though 34.54% cases consumed 63.21 servings. Similarly, 1.71%

controls had a meagerly intake of 1.5 servings of cream. 1.82% cases had nearly six times that is about 8.5 servings of cream per month (Fig 4.5.1 and 4.5.2).

Fig. 4.5.1 Comparison of EC Cases (Patients) and Control Group Oils and Fats consumers (Percentage based)

The amount of total and individual fat and oil consumption was significantly more in case of patients than the control group. Our findings are in accordance with the findings of World Cancer Report (2007), Doherty et al (2011), Schwab et al (2014) and He et al (2017). World Cancer Report (2007) concluded that fat rich diets might increase the risk of certain types of cancer and indicated that high fat or energy dense diet increases the incidence of obesity which itself is a known risk factor for certain types of cancer. Doherty et al (2011) reported that patients in the highest quartile of total fat consumption were at a greater risk of developing reflux esophagitis (RE) and esophageal adenocarcinoma (EADC). They reported a positive correlation between high saturated and monounsaturated fat intake and risk of having both RE and EADC. Schwab et al (2014) and He et al (2017) also reported an increased risk of EADC with increased consumption of high amount of total fat, saturated and mono unsaturated fat. A negative association was also found between partially hydrogenated vegetable oil trans fatty acids and all types of cancer (Laake et al, 2013). Othman (2007) indicated the probable mechanism leading to carcinogenesis with increased fat intake. High fat intake promoted bile acid production which gets converted into secondary bile acids and cytotoxic compounds by the intestinal bacteria, resulting in the increase in ornithine decarboxylase, finally leading to enhanced proliferative activity of the colonic epithelium. Along with this, these compounds also speeds up cellular signals like protein kinase C, alter the phospholipid configuration of the cell membrane, modify prostaglandin metabolism, increase local inflammatory reaction and COX-2 activity while apoptosis is decreased. Recent study conducted on CD36, the precise protein found on the membrane of the cancer cells capable of metastasis is fatty acid dependent for its activity of metastizing.

Fig. 4.5.2 Comparison of EC Cases (Patients) and Control Group Oils and Fats consumption (Average servings/month based)

Various studies have associated a favourable outcome in cancer patients on consumption of n-3 fatty acids sources like flax seed and fish oils but an unfavourable result in patients on consumption of n-6 fatty acids sources like corn and safflower oils. PUFA (n-6) appears to hold tumurogenic properties. Abel et al (2014) reported from the cancer tissue biopsy that a specific type of lipid profile was associated with the development and growth of malignant lesions. Modifications in the cell membrane fatty acid (n-6, n-3) metabolism lead to changed membrane structure, function, enzyme activity, oxidative level and signaling pathways.

Studies suggest that fat soluble vitamins especially tocopherol, polyphenolic compounds, fatty acid structure or a combination of these factors have overall protective impact on cancer (Othman, 2007).Schwab et al (2014) and He et al (2017) also reported an increased risk of EADC with increased consumption of high amount of total fat, saturated and mono unsaturated fat. A negative association was also found between partially hydrogenated vegetable oil trans-fatty acids and all types of cancer (Laake et al, 2013).

Correlation between the intake of fats, oils and other foods

Every meal in the Doaba region has fats and oils. This group cannot be studied in isolation. The correlation tables revealed a few associations between fats and oil intake with other foods.

As is evident in (Table 4.5.2) the total fat intake of the patient group was positively correlated ($p \leq 0.05$) with the intake of vegetables ($r= 0.197$), milk ($r= 0.197$) and whole wheat ($r= 0.222$). A strong positive correlation ($p \leq 0.01$) was observed with the intake of food groups like pulses ($r= 0.490$), fruits ($r= 0.283$), curd ($r= 0.246$), plant fat ($r= 0.533$) and animal fat ($r= 0.643$). Plant fat intake was positively associated with vegetable intake ($r= 0.216$, $p \leq 0.05$) but negatively associated with the intake of animal fat($r= -0.305$, $p \leq 0.01$). Animal fat intake was negatively correlated with wheat intake ($r= -0.202$, $p \leq 0.05$) and positively associated ($p \leq 0.05$) with intake of fruits ($r=0.208$), sugar ($r= 0.243$), milk ($r= 0.233$) and total milk ($r= 0.227$). A strong positive correlation ($p \leq 0.01$)

was also seen between animal fat intake and pulses (r= 0.461), whole wheat (r= 0.246) and maize (r= 0.256).

Data of individual districts reveals correlations between various food groups, some similar to the total cases while other are different from total cases data. The Jalandhar group of cases (Table 4.5.3) data shows a positive correlation ($p \leq 0.05$) between total fat intake and pulses (r= 0.452), fruits (r= 0.314), curd (r= 0.282) and milk (r= 0.294). Those who consumed more fat consumed more plant fat (r= 0.574, $p \leq 0.01$) and more animal fat (r= 0.609, $p \leq 0.01$) too. Patients who had more of plant fat had less of animal fat (r= -0.300, $p \leq 0.05$). Animal fat intake showed a positive correlation with pulse (r= 0.446, $p \leq 0.01$) and milk(r= 0.294, $p \leq 0.05$) intake. In case of Kaputhala cases total fat intake bore a positive correlation only with plant fat (r= 0.653, $p \leq 0.05$), animal fat (r= 0.807, $p \leq 0.01$) and milk intake (r= 0.822, $p \leq 0.01$) (Table 4.5.4) Nawanshehar case data revealed a strong direct association ($p \leq 0.01$) of maize with animal fat (0.791) and of pulses with both total fat (0.767) and animal fat (0.846). Other positive correlations ($p \leq 0.05$) were seen of animal fat with intake of sugar (0.683), total fat (0.664), total eggs (0.620) and total meat (0.668). Plant fat intake showed a positive association with the intake of nuts only (r= 0.607, $p \leq 0.05$) (Table 4.5.5).The Hoshiarpur group of cases showed a positive correlation between plant fat and pulse intake (r= 0.384, $p \leq 0.05$). Animal fat intake had a positive correlation with total fat intake (r= 0.489, $p \leq 0.01$) but a negative correlation with plant fat intake (r= - 0.512, $p \leq 0.01$) (Table 4.5.6)

In case of the total control group (Table 4.5.2) a direct correlation ($p \leq 0.05$) of total fat intake with milk (0.177), total milk (0.231) was noticed A strong positive correlation ($p \leq 0.01$) of total fat intake was seen with whole wheat (0.253), pulses (0.374), curd (0.254), plant fat (0.673), animal fat (0.571) and nuts (0.298) intake. A strong negative correlation ($p \leq 0.01$) of total fat intake with intake of refined wheat (-0.251) and milk from tea (-0.222) was seen. Those who consumed more animal fat consumed more pulses (r= 0.202, $p \leq 0.05$), curd (r= 0.201, $p \leq 0.05$), milk (r= 0.296, $p \leq 0.05$), plant fat (r= 0.571, $p \leq 0.01$) and milk in buttermilk (r= 0.243, $p \leq 0.01$). Plant fat intake showed a positive correlation with intake of whole wheat (r= 0.173, $p \leq 0.05$), pulses (r= 0.262, $p \leq 0.01$),

total fat (r= 0.673, $p \leq 0.01$) and nuts (r= 0.327, $p \leq 0.01$) along with a negative correlation with refined wheat (r= - 0.249, $p \leq 0.01$), maize (r= - 0.203, $p \leq 0.05$), milk from tea (r= - 0.167, $p \leq 0.05$) and animal fat (r= - 0.224, $p \leq 0.01$).

District data bared different correlations. Jalandhar control group (Table 4.5.3) data showed a positive correlation ($p \leq 0.05$) of total fat intake with intake of whole wheat (0.217). There is a strong positive correlation ($p \leq 0.01$) of total fat intake with pulses (0.402), curd (0.298) and nuts (0.290). A negative correlation was also seen between total fat intake and refined wheat (r= -0.313, $p \leq 0.01$) along with milk from tea (r= -0.394, $p \leq 0.01$). Animal fat intake was directly associated with the intake of curd (r= 0.267, $p \leq 0.05$), milk (r= 0.392, $p \leq 0.01$) and total fat intake (r= 0.551, $p \leq 0.01$). Plant fat intake was directly interrelated with the intake of whole wheat (0.243, $p \leq 0.05$), pulses (r= 0.335, $p \leq 0.01$), total fat (r= 0.660, $p \leq 0.01$) and nuts (r= 0.371, $p \leq 0.01$). Plant fat intake was indirectly interconnected with the intake of refined wheat (r= - 0.370, $p \leq 0.01$), maize (r= - 0.250, $p \leq 0.05$), milk from tea (r= - 0.330, $p \leq 0.01$) and animal fat (r= - 0.264, $p \leq 0.05$). Kapurthala data (Table 4.5.4) showed a positive correlation between total fat intake and whole wheat intake (r= 0.491, $p \leq 0.05$). A direct association was also noticed between intake of plant fat and intake of curd (r= 0.834, $p \leq 0.01$), total fat (r= 0.655, $p \leq 0.01$) and nuts (r= 0.556, $p \leq 0.05$). Animal fat showed a direct link with the intake of whole wheat (r= 0.736, $p \leq 0.01$), maize (r= 0.555, $p \leq 0.05$), total fat (r= 0.679, $p \leq 0.01$), total fowl (r= 0.609, $p \leq 0.01$) and total non veg. (r= 0.544, $p \leq 0.05$). It also showed an inverse link with the intake of refined wheat (r= - 0.550, $p \leq 0.05$).In case of Nawanshehar control group (Table 4.5.5) the data revealed a positive association between total fat intake and pulse intake (r= 0.528, $p \leq 0.05$). A strong positive correlation was noticed between total fat and animal fat intake (r= 0.786, $p \leq 0.01$). An indirect association between total fat and maize intake was also observed (r= - 0.592, $p \leq 0.05$). The plant fat consumers of Nawanshehar showed a positive correlation with the intake of pulses (r= 0.167, $p \leq 0.05$), milk from tea (r= 0.167, $p \leq 0.05$), total milk and a negative correlation with total egg (r= - 0.536, $p \leq 0.05$) and total fish (r= - 0.720, $p \leq 0.01$) intake whereas animal fat intake was inversely associated with total egg intake (r=- 0.515, $p \leq$

0.05).Hoshiarpur data (Table 4.5.6) states a positive interconnection of total fat with the intake of pulses (r= 0.473, $p \leq 0.01$), vegetables (r= 0.365, $p \leq 0.05$), and plant fat (r= 0.764, $p \leq 0.01$) but plant fat intake showed a negative correlation with animal fat intake (r= - 0.357, $p \leq 0.05$). The intake of animal fat was directly interrelated with the intake of fruits (r= 0.340, $p \leq 0.05$), pulses (r= 0.462, $p \leq 0.01$), curd (r= 0.419, $p \leq 0.05$), total eggs (r= 0.354, $p \leq 0.05$), total sugar (r= 0.531, $p \leq 0.01$) and milk in buttermilk (r= 0.583, $p \leq 0.01$).

From the Logistic regression model (CL 95%) it appears that mustard oil (B= -0.012) and *vanaspati ghee* (B= -0.016) are not protective against esophageal cancer (Table 4.5.7).

Table 4.5.1Comparison of Oil and Fat consumption between Control Group and EC Cases (Patients)

Category	Control		EC Cases	
	Percentage consumers	Average no. of servings/month	Percentage consumers	Average no. of servings/month
Mustard oil	89.74	58.63	79.09	72.34
Refined oil	55.55	56.93	40.90	64.17
Vanaspati ghee	26.49	47.80	34.54	63.21
Desi ghee	53.8	30.2	43.6	64.9
Butter	34.2	11.7	16.4	14.6
Cream	11.88	3.70	10.92	23.5

Table 4.5.2 Correlation between Oil and Fat intake with various food groups in EC Cases and Control Group

Oils and Fats intake Total EC Cases			
	Animal fat	**Plant fat**	**Total fat**
Vegetable		0.216*	0.197*
Fruits	0.208*		0.283**
Curd			,246**
Sugar	0.243*		
Total milk	0.227*		
Plant fat			0.533**
Animal fat		-0.305**	0.643**
Milk	0.233*		0.197*
Wheat	-0.202*		
W,Wheat	0.246**		0.222*
Maize	0.256**		
Oils and Fats intake Total Control Group			
	Animal fat	**Plant fat**	**Total fat**
Maize		-0.203*	
Pulses	0.202*	0.262**	0.374**
Curd	0.201*		0.254**
Tea		-0.167*	-0.222**
Milk	0.296**		0.177*
Total milk			0.231*
Plant fat	0.571**		0.673**
Animal fat		-0.224**	0.571**
Nuts		0.327**	0.298**
Buttermilk	0.243**		

Table 4.5.3 Correlation between Oil and Fat intake with various food groups in Jalandhar EC Cases and Control Group

Oils and Fats intake Jalandhar EC Cases			
	Animal fat	**Plant fat**	**Total \fat**
Fruits			0.314*
Curd			0.282*
Plant fat	-0.300*		0.574**
Animal fat		-0.300*	0.609**
Milk	0.294*		0.294*
Buttermilk	0.296*		
Oils and Fats intake JalandharControl Group			
	Animal fat	**Plant fat**	**Total fat**
Maize		-0.250*	
Legumes		0.335**	0.402**
Curd	0.267*		0.298**
Milk	0.392**		
Tea		-00.330**	-00.394**
Total milk		-0.213*	
Total fat	0.551**	0.660**	
Animal fat		-0.264*	
Nuts		0.371**	0.290**

Table 4.5.4 Correlation between Oil and Fat with various food groups in Kapurthala EC Cases and Control Group

Oils and Fats intake Kapurthala EC Cases			
	Animal fat	**Plant fat**	**Total fat**
Plant fat			0.653*
Animal fat			0.807**
Milk			0.822**
Oils and Fats intake KapurthalaControl Group			
	Animal fat	**Plant fat**	**Total fat**
Maize	0.555*		
Curd		0.834**	
Total fat	0.679**	0.655**	
Fowl	0.609**		
NV	0.544*		
Nuts		0.556*	

Table 4.5.5 Correlation between Oil and Fat with various food groups in Nawanshehar EC Cases and Control Group

Oils and Fats intake Nawanshehar EC Cases			
	Animal fat	**Plant fat**	**Total fat**
Sugar	0.683*		
Total fat	0.664*		
Eggs	0.620*		
Meat	0.668*		
Nuts		0.607*	
Maize	0.791**		
Oils and Fats intake NawansheharControl Group			
	Animal fat	**Plant fat**	**Total fat**
Maize			-0.592*
Pulses		0.518*	0.528*
Tea		0.563*	
Total milk		0.574*	
Total fat	0.786**		
Egg	0.515*	-0.536*	
Fish		-0.720**	

Table 4.5.6 Correlation between Oil and Fat with various food groups in Hoshiarpur EC Cases and Control Group

Oils and Fats intake Hoshiarpur EC Cases			
	Animal fat	**Plant fat**	**Total fat**
Total fat	0.489**	0.499**	
Plant fat	-0.512**		
Oils and Fats intake HoshiarpurControl Group			
	Animal fat	**Plant fat**	**Total fat**
Fruits	0.340*		
Legumes	0.462**		0.471**
Vegetables			0.365*
Curd	0.419*		
Plant fat	-0.357*		0.764**
Egg	0.354*		
Sugar	0.531**		
Buttermilk	0.583**		

Table 4.5.7 Logistic Regression taking independent variables in the model (Oils and Fats)

Variables in the Equation						
Independent Variables	B	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
FATMustard oil	-0.012	1	0.018	0.988	0.979	0.998
FATRefined oil	-0.007	1	0.183	0.993	0.984	1.003
FATVanaspatighee	-0.016	1	0.002	0.984	0.975	0.994
FATDesi ghee	-0.005	1	0.242	0.995	0.988	1.003
FATButter	-0.003	1	0.77	0.997	0.973	1.02
Constant	0.869	1	0.065	2.385		

4.5.2 Nuts and oilseeds

Popularly consumed nuts are almond, cashewnut, pistachio, walnut, pine nut and coconut while oilseeds like groundnut, mustard, soya bean, safflower, sunflower, sesame and flax are frequently consumed. Nuts are used in the fresh, roasted, fried or salted form. They are consumed as snack, thickening agents or to prepare sweets, beverages, chutney to name a few. Other than for oil extraction, oil seeds are also used in the preparation of sweets, as topping, thickening agents and the like. Nuts are of great commercial value (indiaagronet.com). Perhaps for this reason some nuts have limited consumers and it is hard to significantly correlate the role of nuts and oil seeds in decreasing the incidence or treatment of various diseases especially cancer. Though in 2004 Donaldson reported flax seed's oil and lignin, especially the secoisolariciresinol diglycoside in lignin, to decrease the tumour load more research is needed to find benefits of nuts and oil seeds other than antioxidants in the prevention and treatment of various diseases (Lang et al,2015). It is too early to label amygdalin as a double edged sword which lowers resistance of cancer cells to treatment and secondly attack cancer cells with its cyanide content (Blaheta et al, 2016).

Our results show a significant (< 0.01) difference on't-test' which indicates a variation in the amount of nuts and oil seeds consumption between the patient and the control group. Nuts and oilseeds were consumed by 75% controls and 71.81% patients (EC cases). The amount of nuts consumed on an average per month in a year by the control group was 335.39 grams while the patient group average intake was 66.77 grams (Fig 4.5.3). Our findings are in accordance with the few studies conducted to study the impact of intake of nuts (dry fruit) and oilseeds on the risk of incidence of cancer and especially esophageal cancer. Wu et al (2015) concluded their systemic review and meta-analysis study by stating that nuts could play an important role in reducing the risk of incidence of esophageal cancer and more studies could help assess this relationship better by understanding the underlying mechanism. Golestan cohort study (Iran) conducted in a high-risk population revealed a statistically significant decrease of 29% in the risk of incidence of ESCC for each 5 gram of total nuts consumed per day. Their study included

peanuts, walnuts, mixed nuts and seeds (Hashemian et al, 2018). A study on tree nuts like almond, pistachio, cashew, walnut, pinenut and hazel nut was conducted by Nieuwenhuis and Brandt (2018).

Fig. 4.5.3 Comparison of EC Cases (Patients) and Control Group Nuts and Oilseeds consumers/consumption (Percentage/Intake amount Based)

Their findings of Netherland cohort study suggested an inverse association between the consumption of tree nuts and peanuts with ESCC, gastric non-cardia adenocarcinoma but not with other types of esophageal and gastric cancers.

Correlation data (Table 4.5.7) of total EC cases, Kapurthala and Hoshiarpur district EC cases revealed no significant correlation between nuts intake and the incidence of esophageal cancer (EC). Data of Jalandhar patients nut intake was negatively correlated with tea ($r=-0.254$, $p \leq 0.05$). Nawanshehar data showed a positive correlation of nuts intake with plant fat consumption ($r= 0.607$, $p \leq 0.05$) but a negative correlation with the intake of total non veg. ($r= -0.603$, $p \leq 0.05$) and total fowl ($r= -.0702$, $p \leq 0.05$).

In case of the control group (Table 4.5.7) data various correlations were recorded between nuts intake and other food groups. In the total control group information nuts intake was directly correlated ($p \leq 0.05$) with the intake of total egg ($r= 0.203$), total meat ($r= 0.169$), total fish ($r= 0.169$) and total non veg. ($r= 0.174$). A strong direct link (p value 0.01) was also seen with the intake of fruits ($r= 0.417$), pulses ($r= 0.363$), curd ($r= 0.314$), plant fat ($r= 0.327$) and total fat ($r= 0.327$). The Jalandhar control group data revealed a strong direct association ($p \leq 0.01$) of nuts intake with the intake of fruits ($r= 0.471$), pulses ($r= 0.418$), curd ($r= 0.317$), plant fat ($r= 0.371$), total fat ($r= 0.290$), total fish ($r= 0.279$) and total non veg.intake ($r= 0.285$). A significant association ($p \leq 0.05$) of nuts intake was also seen with the intake of total eggs ($r= 0.266$), total fowl ($r= 0.254$), total meat ($r= 0.214$) and buttermilk ($r= 0.341$). Fruit ($r= 0.648$, $p \leq 0.01$) and plant fat ($r= 0.556$, $p \leq 0.05$) intake had direct interrelation with the nuts intake in the Kapurthala population while the only correlation in the Hoshiarpur group was with curd intake ($r= 0.407$, $p \leq 0.05$). Nawanshehar data showed a significant correlation of nuts intake with

the intake of refined wheat flour (r= 0.665, $p \leq 0.01$), total egg (r= 0.733, p value 0.01) and pulses (r= 0.539, $p \leq 0.05$). Nuts intake was also seen to be indirectly associated with the intake of whole wheat (r= - 0.732, $p \leq 0.01$).

Table 4.5.8 Correlation between Nuts and Oilseeds intake and food groups in EC Cases and Control Group

Intake of Nuts and Oilseeds EC Cases					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Tea		-0.254*			
Plant fat				0.607*	
Non Veg.				-0.603*	
Fowl				-0.702*	
Intake of Nuts and Oilseeds Control Group					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Refined wheat flour		-0.284**		0.665**	
Whole wheat flour				-0.732**	
Fruits	0.417**	0.471**	0.648**		
Legumes	0.363**	0.418**		0.539*	
Curd	0.314**	0.317**			0.407*
Total Fat	0.298**	0.290**			
Plant fat	0.327**	0.371**	0.556*		
Egg	0.203*	0.266*		0.733**	
Fowl		0.254*			
Meat	0.169*	0.214*			
Fish	0.169*	0.279**			
Non Veg.	0.174*	0.285**			
Buttermilk		0.341*			

4.6 BEVERAGES

Beverage is a term used for any potable liquid intended for human consumption like milk, juices, tea, coffee, sugar sweetened non-aerated drinks, carbonated soft drinks and alcoholic drinks. Researchers all over the world have concluded that beverage intake does not decrease the food intake, however adds to the dietary sugar and saturated fats leading to increased calorie intake. The consumption of these beverages can either boost our health or mar it, hence the phrase 'We are partly what we drink!' The global functional foods and beverages market value was USD 129.39 billion in 2015 and is growing at a CAGR (compound annual growth rate) of close to 8.6 (Panghal et al., 2018). Neves et al (2011) reported that 1.60 trillion liter market of commercial beverages in 2009 was shared by hot tea (20.90%), bottled water (15.30%), milk (12.80%), aerated soft drinks (12.50%), beer (11.20%), hot coffee (8.20%), non aerated or still drinks (2.70%) and juices/nectar (2.60%).

4.6.1 Tea

Tea is the most consumed beverage and a dark horse after unparalleled water. Food and Agriculture Organization data reveals the consumption of six billion cups of tea per day world- wide (Stone Daniel, 2014). Tea is prepared in many ways. The most variable constituent of tea is milk. Its amount varies from a spoon or two in separate tea to only milk and no water in milk tea viz. tea (100% milk).

Our data revealed consumption of various types of tea in a single individual also hence the need of total tea intake to study the correlation with other foods. Tea (100% milk) was consumed by 25.6% of control group people and12.7% patients (EC cases) with a monthly average frequency of 48.8 and 64.4 servings respectively (Table 4.6.1). Tea prepared with half milk and half water viz. tea (50% milk) was consumed by 35% people of control group with a frequency of 58.9 servings while 20% of patients consumed 116.0 servings of this type of tea (50% milk). Regular tea had maximum takers with 53.85% people of control group and 71.82% patients consuming 80.4 and 117.5 servings on an average per month. 26.5 servings of separate tea were consumed by 5.13% people of

control group only. Total tea consumption was significantly more in the patient group. Our findings correlate with the findings of Munishi et al (2015) and Das et al (2015).

Fig. 4.6.1 Comparison of EC Cases (Patients) and Control Group Tea Consumers/Consumption (Percentage/Amount Based)

Patient's data revealed a negative correlation of regular tea intake with the intake of tea having100% milk (r= -0.196, p ≤0.05) and tea having 50% milk (r= -0.362, p ≤0.01) and positive correlation with the intake of plant fat (r= 0.195, p ≤0.05). In case of control group regular tea intake was negatively correlated with the intake of tea having 100% milk (r= -0.246, p ≤0.01) and tea having 50% milk (r= -0.436, p ≤0.01) and positively correlated with the total milk intake (r= 0.205, p ≤0.05). Both types of tea (100% milk and 50% milk) intake did not show any significant correlations in both the groups. As stated earlier some individuals consumed different types of tea during the day so the correlation of various foods with total tea intake was also studied. Total tea intake of patients was positively associated with the intake of total milk (r= 0.709, p ≤0.01) and sugar (r= 0.551, p ≤0.01). Data of control group revealed a negative correlation between total tea intake and intake of plant fat (r= -0.167, p ≤0.05), total fat (r= -0.222, p ≤0.01) and the amount of milk cnsumed (r= -0.166, p ≤0.05). A positive correlation of total tea intake with the intake of total milk (r= 0.616, p ≤0.05) and sugar (r= 0.271, p ≤0.01) was observed (Table 4.6.2).

Our study showed a significant difference in the amount of tea consumption of the two groups and is in coherence with the study conducted in a tertiary hospital of Punjab, India showed an increase in the incidence rate of ESCC with a consumption of more than 3 cups of tea per day (Das et al, 2015).

The logistic regression model (CL 95%) shows tea having 50% milk and regular teais not protective against the incidence of esophageal cancer.

4.6.2 Coffee

Coffee is also prepared in different ways and with variable amount of milk. Alicandro et al (2017) reported no association between coffee consumption and overall cancer risk. They found a pooled relative risk close to unity for cancers of esophagus, gall bladder, thyroid to name a few.

Fig. 4.6.2 Comparison of EC Cases (Patients) and Control Group Coffee Consumers/Consumption (Percentage/IntakeAmount Based)

Our data revealed the intake of coffee in case of the control group only. Coffee (100% milk) was consumed by 30.77%, coffee (50% milk) was consumed by 9.40%, regular coffee by 4.27% and black coffee by only 0.90% people of the control group. The average monthly amount of servings of coffee consumed by the control group people was 4.03, 2.27, 2.20 and 15.00 percent, respectively (Table 4.6.1). Inverse association between coffee consumption and risk of esophageal cancer was reported in studies conducted by Castellsagu'e et al (2000) and Ren et al (2010). Wang et al (2016) and Miranda et al (2017) have reported the protective nature of coffee against oral and pharyngeal cancer. In our study only control group people consumed coffee.

Correlation analysis between the intake of coffee and other food items was not performed because of few consumers and low monthly consumption in control group only and no consumers in the patient group.

4.6.3 Aerated and non-aerated drinks

Aerated drinks contain dissolved gas usually carbon dioxide from which it derives the name carbonated drink. The gas dissolves under pressure and is released as small bubbles on the removal of pressure giving it the popular 'fizz'. The level of carbonation varies in aerated drinks. Other major constituents of this carbonated water are a sweetener along with a colouring, flavouring and preserving agent. Sweeteners could be high-fructose corn syrup, sugar or its substitute or a combination of these. Combination of these or/and any other ingredients is product based. Lack of or very low amount of alcohol, categorizes these drinks into 'soft drinks'

In our study 52.14% of people of the control group and 74.54% patients (EC cases) consumed aerated drinks with an average monthly intake frequency of 3.69 and 3.08 servings while non aerated drinks were consumed by 50.42% people of the control group and 81.82% patients with an average monthly intake frequency of 8.94 and 4.70 servings. Our data does not reveal a significant variation in the consumption of aerated drinks between thetwo groups. The amount of non aerated drinks consumption is less, though double in case of the control group (Table 4.6.1).

Fig. 4.6.3 Comparison of EC Cases (Patients) and Control Group Soft Drinks Consumers/Consumption (Percentage/ IntakeAmount Based)

Aerated drink consumption revealed an indirect association with the intake of plant fat ($r= -0.240$, $p \leq 0.05$) and a direct association with total fowl intake ($r= 0.195$, $p \leq 0.05$) in case of the esophageal patients but no correlation in the control group. Intake of non aerated drinks was negatively correlated with the consumption of maize ($r= -0.239$, $p \leq 0.05$), total curd ($r= -0.249$, $p \leq 0.01$) and positively correlated with the intake of vegetables ($r= 0.223$, $p \leq 0.05$) in the patient group. The intake of non aerated drinks was directly associated with the intake of aerated drinks ($r= 0.289$, $p \leq 0.01$), total fowl ($r= 0.206$, $p \leq 0.05$) and total non veg. ($r= 0.175$, $p \leq 0.05$) in the control group (Table 4.6.2).

Our study is in accordance with the studies of Mayne et al (2006), Ibiebele et al (2008), Johnson et al (2010) and Kubo et al (2010) who concluded that soda drinks had no association with increased risk of esophageal cancer (Table 4.6.3).

The regression model (CL 95%) also reveals no significant impact of aerated and non aerated drinks on the incidence of esophageal cancer.

Table 4.6.1 Comparison of type of Beverage intake between the Control Group and EC Cases (Patients)

Category	Control		Patient	
	Percentage of consumers	Avg. monthly servings	Percentage of consumers	Avg. monthly servings
TEA				

100% milk	25.60	48.80	12.70	64.40
50% milk	35.00	58.90	20.00	116.00
Regular	53.85	80.40	71.82	117.50
Separate	5.13	26.50	0.00	0.00
COFFEE				
100% milk	30.77	4.03	0.00	0.00
50% milk	9.40	2.27	0.00	0.00
Regular	4.27	2.20	0.00	0.00
Black	0.90	15.00	0.00	0.00
SOFT DRINKS				
Aerated drinks	52.14	3.69	74.54	3.08
Non aerated drinks	50.42	8.94	81.82	4.70

4.6.4 Sugar

The consumption of sugar and jaggery (*gur and shakkar*) were included in this group. Our data revealed similar consumption in the patient and control group. All the patients and people of the control group consumed sugar or jaggery as such or in desserts. The average monthly consumption was 947.18 grams in the control group and 928.01 grams in the patient group (Fig 4.6.4). Myers AP (2012), Rippe JM (2016) and Meer et al (2018) reported no significant correlation between the intake of added sugar and the incidence of cancer. More studies could perhaps help put an end to the hot and controversial topic of added sugars and cancer.

Fig. 4.6.4 Comparison of EC Cases (Patients) and Control Group SugarConsumers/Consumption (Percentage/Intake amount Based)

Data of dietary added sugar (Table 4.6.4) intake in total patient group showed positive correlation with the intake of whole wheat flour (r= 0.207, p ≤0.05), rice (r= 0.205, p ≤0.05), pulses (r= 0.401, p ≤0.01), animal fat (r= 0.233, p ≤0.05), tea (r= 0.551, p ≤0.01) and total milk intake (r= 0.423, p ≤0.01). Jalandhar patient group data also revealed a positive correlation between added sugar intake and intake of tea (r= 0.632, p ≤0.01) and total milk (r= 0.476, p ≤0.01) and pulses (r= 0.285, p ≤0.05). Intake of Kapurthala patients showed a direct association between the intakes of added sugar and tea (r= 0.735, p ≤0.05). Nawanshehar patient data revealed a positive association of added sugar intake with the intake of maize (r= 0.623, p ≤0.05), pulses (r= 0.757, p ≤0.01) and animal fat (r= 0.683, p ≤0.05) while the Hoshiarpur data showed a positive correlation of added sugar intake with the intake of rice (r= 0.438, p ≤0.05), tea (r= 0.534, p ≤0.01), total milk intake (r= 0.395, p ≤0.05) and pulses (r= 0.474, p ≤0.05).

The total control group data (Table 4.6.4)revealed a positive correlation of added sugar intake with the intake of tea (r= 0.271, p ≤0.01). Added sugar intake was directly associated with the intake of tea (r= 0.367, p ≤0.01) and whole wheat flour (r= 0.220, p ≤0.05) in the Jalandhar control group. The intake of total fowl (r= -0.633, p ≤0.05), total meat (r=- 0.520, p ≤0.05) and total non veg. (r= - 0.570, p ≤0.05) were negatively correlated with the intake of sugar in Nawanshehar control group while milk (r= 0.349, p ≤0.05), buttermilk (r= 0.710, p ≤0.01), total milk (r= 0.609, p ≤0.01) maize (r= 0.611, p ≤0.01)and animal fat (r= 0.531, p ≤0.01) were positively correlated with the intake of added sugar in the Hoshiarpur group.

Table: 4.6.2 Correlation of intake of beverages with other foods in the EC Cases and Control group

Beverages Intake of EC Cases						
	Tea(100 % milk)	**Tea(50% milk)**	**Regular tea**	**Total tea**	**Aerated drinks**	**Non aerated drinks**
Tea (100% milk)			-0.196*			
Tea (50% milk)			-0.362**			
Maize						-0.239*
Fowl					0.195*	
Vegetables						0.223*
Curd						-0.249**
Plant fat			0.195*		-0.240*	
Total milk				0.709**		
Sugar				0.551**		
Beverages Intake of Control Group						
	Tea(100 % milk)	**Tea(50% milk)**	**Regular tea**	**Total tea**	**Aerated drinks**	**Non aerated drinks**
Tea (100% milk)			-0.246**			
Tea (50% milk)			-0.436**			
Maize						0.289**
Fowl						0.206*
Vegetables						0.175*
Curd				0.166*		
Plant fat			0.205*	0.616*		
Total fat				0.222**		
Total milk				0.167*		
Sugar	0.202*			0.271**		

Table: 4.6.3 Logistic Regression taking independent variables in the model (Beverages)

Variables in the Equation						
Independent Variables	B	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
Tea(100% milk)1	-0.007	1	0.185	0.993	0.982	1.003
Tea (50% milk)1	-0.009	1	0.023	0.991	0.984	0.999
TeaRegular1	-0.012	1	<0.001	0.988	0.983	0.994
AeratedDrinks	-0.084	1	0.09	0.92	0.835	1.013
NonAeratedDrinks	0.003	1	0.868	1.003	0.968	1.04
Constant	0.756	1	0.012	2.131		

Table: 4.6.4 Correlation of Sugar and other foods in EC Cases and Control Group

Sugar Intake of EC Cases					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Rice	**0.205***				**0.438***
Maize				**0.623***	
Tea	**0.551****	**0.632****	**0.735***		**0.534****
Total milk	**0.434****	**0.476****			**0.395***
Animal fat	**0.243***			**0.683***	
Pulses	**0.401****	**0.285***		**0.757****	**0.474***
Wheat	**0.207***				
SugarIntake of Control Group					
	Total	**Jalandhar**	**Kapurthala**	**Nawanshehar**	**Hoshiarpur**
Maize					0.611**
W.wheat		0.220*			
Tea	0.271**	0.367**			
Milk					0.349*
Total milk					0.609**
Animal fat					0.531**
Fowl				-0.633*	
Meat				-0.520*	
Non Veg.				-0.570*	
Buttermilk					0.710**

4.7 Lifestyle Practices

The observations of various researchers reveal that contrary to public belief most of the cancers do not have heredity as their prime etiology. Lifestyle factors like dietary practices, consumption of alcohol, tobacco, betel quid, betel nut, *paan masala* and various other environmental factors have a deep influence on the development of cancers (Anand et al, 2008). Greater influence of diet and environment both of which are modifiable makes most cancers preventable. Keeping this in mind the final part (III) of the questionnaire was designed.

Worldwide incidence of esophageal squamous cell carcinoma (ESCC) is much more than esophageal adenocarcinoma (EADC). With the increase in the incidence of obesity and gastroesophageal reflux disease in the developed countries, a tremendous shift in the epidemiology of EC has occurred with an increase in the incidence of EADC (Napier et al, 2014). Common causes of gastroesophageal reflux are intra-abdominal pressure, hiatal hernia, abnormal tone and relaxation of lower esophageal sphincter, chemistry of gastric contents, spicy food and alcohol(Goljan, 2013).Obesity, delayed stomach emptying, eating large meals or eating late at night, spicy fried foods, alcohol, smoking and medications like aspirin are regarded as the predisposing factors for gastroesophageal reflux disease (GERD).

Our data revealed that 89.09% patients (EC cases) and 82.23% control group people had a dietary pattern of two major and two minor meals. Only one patient and 11 people of the control group had no fixed dietary pattern. 10 of the patients and 12 people of the control group had two major meals and tea twice. 80.90% patients and 65.9% people of control group had regular meal timings, the difference being significant (χ^2= 7.25, p $\leq$0.01) on Pearson Chi-square test. Regular meal timings are important to avoid gastritis which is one of the known causes of EADC. In our study 86.36% cases were suffering from ESCC in which gastritis does not have a significant roll (Goljan, 2013). Our findings are in accordance with previous research studies. 20.00% of the patients and 29.60% of the control group people slept within an hour of their meal. 68.18% of the

patients and 56.57% of the controls had a gap of 1-2 hours between their meal and sleep timings at night. Analysis indicates that dietary pattern may not be associated with increased risk of esophageal carcinoma.

Many researchers have conducted studies to see the impact of overheated foods including beverages. Increased risk of esophageal cancer was associated with injury to the mucosa by big bite/sip, fast eating speed and high temperature (Hung et al, 2004; Gao et al, 2006; Islami et al, 2009; Mir and Dar, 2009; Wu et al,2011). Drinking black tea at temperature of 70ºC or higher increased the risk of EC (Cancer Research UK, 2014). 99.00% of patients and 81.58% of control group people consumed food after 5.0 minutes of its heating.

Food of 80.90% patients and 78.28% control group people was cooked to soft texture which was consumed in medium size bites (53.63% patients and 69.07% control group people) after chewing it well (89.09% patients and 86.18% control group people). Hung et al (2004) reported an association between EC and the consumption of preserved foods. Our data revealed 0% and 1.97% consumers among patients and control group of frozen, tined or 'ready to use' preserved foods respectively.

Patients (61.81%) and control (44.07%) group respondents procured wheat grain and got it milled rather than buying wheat flour. About 4.00% respondents in both the groups preserved grain with an organic preservative and 58.18% patients and 41.45% control used non organic preservatives. It indicates that food grains preserved with non organic preservatives increase risk of cancer. Our findings are in accordance with the findings of Huang et al (2012) and Tabrez et al (2013) who reported that exposure to pesticides could increase the incidence of cancer.

Persistent infection and inflammation have been reported to favour tumourigenesis while some pathogens and anti-tumour immune responses could lead to a decrease in the risk of carcinogenesis. Oikonomopoulou et al (2013) found it hard to explain this dichotomous behaviour while revaluating the hygiene hypothesis. In our study also hygiene was taken care of by both the groups. 99.09% patients and 99.34% controls washed their hand

before cooking, 93.64% patients and 98.03% controls washed hands before eating, 96.36% patients and 93.42% controls washed staked utensils before using and all patients and controls washed fruits and vegetables before consuming. Patients (98.00%) washed fruits and vegetables before chopping, 1.00% washed after chopping while the remaining washed both before and after chopping the vegetables. In the control group 62.00% washed fruits and vegetables before, 23.00% after and 15.00% both before and after chopping. This variation was significant on Pearson Chi-square test. Washing removes contaminants, preservatives or other chemicals from fruits and vegetables. Contaminants or improper handling of chopped fruits and vegetables could increase the risk of cancer. Our findings are in coherence with Tabrez and co-workers (2013).

Household air pollution due to inefficient combustion of solid fuel and kerosene costs millions of lives per year worldwide.Rathore (2012) reported household combustible fuels to be prospective risk factors for esophageal cancer. Sapkota et al (2013) in their research on indoor air pollution reported an association between prolonged use of wood and cancer of esophagus and pharynx. Household air pollution had a carcinogenic effect on lungs which could lead to cancer of other sites including aero-digestive tract (Josyula et al, 2015). In our study 53.64% patients cooked food on gas, 10.00% on *chula* and 35.45% used a combination of gas and chula amounting to 45.45% people using *chula* completely or partially. In control group only 24.34% people used chula partially or completely for cooking. These findings are in accordance with the findings of the above researchers and should be confirmed with further studies.

Poorly differentiated EC patients had higher levels of copper than moderately or well differentiated tumour patients in a study conducted in Kashmir (Mir and Dar, 2009). Not much research has been done to rule out the contribution of various types of cookware. Aluminium and steel combination was the most used combination in the kitchen cookware (patients 90%, controls 48.03%). Combination of aluminum and nonstick cookware was used by 11.84% controls only. Only aluminum cookware was used by 1.82% patients and 26.97% controls. Total aluminum consumers were similar in both the groups (47.73% patients and 46.38% controls), steel cookware was used by 48.64%

patients and 35.74% control. Non stick cookware was used by 0.91% patients and 11.91% controls. Iron, aluminum and steel have no negative impact on health. BPA or bisphenol-A is an estrogen mimicking toxic compound used in plastics. It can migrate from plastic food containers into food and has been associated with cancer. Plastic containers or covers in microwave should not be used (Anand et al, 2008). 92.73% patients and 72.37% control group people did not use microwave. Those who used microwave, made use of microwave safe plastic containers (3.64% patients and 28.95% controls). Significant Pearson Chi-square test shows the disparity in the consumption pattern but is not significant on logistic regression.

Soaking followed by cooking enhanced the concentration of cellulose, hemicelluloses, lignin and pectin content and increasing the health benefits of chickpea (Vashishtha and Srivastava, 2011). Soaking improves starch and protein digestibility, availability of minerals such as zinc and iron, synthesis of enzymes like phytase, polyphenols oxidase, breakdown of oligosaccharides linked to aglycone, reduction of bound fructose and saponoins. Minor nutrients and non nutrients like vitamin B specifically thiamine, phytic acid, polyphenols are leached into the soaking water of pulses (Yildirim and Oner, 2011; Agarwal, 2016). In our study pulses were soaked by all patients and 96.05% people of the control group but 90.0% of patients and 54.61% control group people discarded the soaking water losing the water soluble non-nutritive, bioactive compounds which are chemopreventive in nature. Baking soda was not consumed by patients and by only 7.89% people of the control group hence no conclusions can be drawn regarding the association between baking soda and esophageal cancer.

In our study 4.55% patients and 24.34% controls had food within an hour of preparation, 18.18% patients and 21.71% controls had food within 1 to 3 hours of preparation, 34.55% patients and 15.13% controls had food between 3 to 6 hours, 37.27% patients and 30.26% controls had food within 6 to 9 hours while 5.45% patients and 8.55% controls had food within 9 to 12 hours of preparation. This variation was found to be significant on Pearson Chi-square test (χ^2= 28.114, p $\leq$0.01). 96.36% patients and 88.82% controls consumed the leftover food in the next meal but 5.45% patients and 8.55% controls disposed off the

leftover food and did not consume it. 76.36% patients and 90.1% controls stored cooked food by refrigeration. 3.64% patients kept the leftover food both at room temperatures and in refrigerator. The difference in handling the cooked food shows a significant difference (χ^2= 16.392, p $\leq$0.01). These findings are in accordance with the positive association between the consumption of leftover stale foods and EC reported earlier (Phukan et al, 2001; Mir and Dar, 2009).

All the patients and controls used piped water. 97.27% patients and 62.50% controls consumed fresh tap water, 2.73% patients and 37.50% controls had filter and reverse osmosis treated water. It indicates that poor water quality could increase the risk of cancer (χ^2= 43.706, p $\leq$0.01). Our results are coherent with the other studies related to quality of water (Zhang et al., 2003; Ebenstein, 2008; Zhang et al., 2014; Nayyar, 2015). Both patients (99.09%) and controls (96.05%) had water after meals. They reported a daily intake of 3-glasses in case of 60.0% patients and 49.34% controls and 6-8 glasses in case of 34.55% patients and 36.84% controls. Consumption of 9-11 glasses of water was recorded in 5.45% patients and 9.21% controls. Only 4.61% controls consumed more than 11 glasses of water per day. No data is available on piped water and especially the amount of water consumed which could probably help in keeping the esophageal mucosa healthy by neutralizing the irritants.

65.45% patients and 42.76% people of the control group had less spicy food while 25.45% patients and 46.05% controls had medium spicy food. Very spicy food was consumed by 6.36% patients and 9.21% controls (χ^2= 14.326, p $\leq$0.01). Spices are dried parts of a plant like seeds, root, bark which are used to flavor and colour a dish. They contain lot of non-nutrient phytochemicals and antioxidants like tannins, polyphenolic compounds, flavonoids and essential oils which help in prevention of cancer. Our findings are in accordance with the study of Chitra et al (2004) who reported that spices do not increase the incidence of esophageal cancer. Fried dishes were prepared about 1-3 times a week by 90.91% patients and 69.74% people of control group while 2.73% patients and 19.74% controls prepared fried dishes 4-7 times a week. Mustard oil as frying medium was used by 69.09% patients and 68.42% controls while 18.18% patients

and 9.87% controls used refined oil as frying medium. Our findings are in accordance with the study of Chitra and co-workers (2004) who reported that fried food did not increase the incidence of esophageal cancer. Free radical formation in the frying oil during re-frying has been reported to increase the risk of cancer. 87.27% patients and 77.63% controls used the leftover frying oil for normal cooking and did not reuse it for frying.

Aerated drinks including plain soda were consumed by 91.82% patients and 84.87% controls about 2 to 4 times a week while 4.55% patients and 11.18% controls had an average weekly frequency of 5-7. There was a small fraction of patients and control group who had an average weekly intake of 7-10 or more than 10 servings per week. The consumption amount is less than 1 serving a day in 87.79% persons studied and its significant impact on the incidence of EC is unlikely which is in synchronization with the findings of Johnson et al (2010) and Kubo et al (2010).

According to the WHO global status report on alcohol and health (2014) 38.30% of world's population and 30.00% of Indian population consumed alcohol regularly. The individual average annual consumption in India is 4.30 litres. Organization for economic cooperation and development reported (2015) a consumption of 101-500 ml per capita per week of country liquor and 1-50 ml per capita per week of beer, imported alcohol and wine. One drink measure of beer, alcohol and spirits was specified as 150 ml of wine, 330 ml of beer and 30 ml of hard liquor (Mao et al, 2012). In our study only 23.00% patients and 18.00% controls consumed alcohol. Less than five drinks a week were consumed by 44.00% each of alcohol consuming patients and controls, 5-11 drinks/week were consumed by 8.00% and 26.00% of alcohol consuming patients and controls respectively while 32.00% patients and 15.00% controls amongst the alcohol consumers consumed more than 30 drinks/week. Considering all alcohol consumers, 8.00% patients and 4.00% controls had it neat, 76.00% patients and 70.00% controls had liquor with water, 4.00% patients and 26.00% controls consumed liquor with soda while only 12.00% of patients consumed with water or soda. Joshi et al (2009) reported a higher incidence in people consuming neat alcohol, without or with a little amount of salad and

snacks. The duration of consumption of alcohol among the alcohol consumers varied with more than 20 years in 72.00% patients and 67.00% controls and less than 20 years in 28.00% patients and 34.00% controls. The Pearson Chi-Square test reveals no significant variation in the intake amount and pattern of alcohol consumption between the esophageal cancer patients and the control group to record an impact on the incidence of EC. Our findings are in association with the findings of Yu et al (1993), Znaor et al (2003) and Yang et al (2016). Organization for economic cooperation and development (2015) reported an increase in alcoholism by 55% between 1992 and 2012.Yang et al (2016) stated that alcohol consumption could neither justify the decrease in the incidence of ESCC in the last 40 years in developed countries nor the racial difference in the incidence rate of ESCC.

Global Adult tobacco survey (GATS) under WHO presented, 'India fact sheet 2009-2010'. According to these statistics 14.00% of Indian adults smoked tobacco, 25.90% used smokeless tobacco, 34.60% used tobacco in any form while the Punjab statistics were 0-10,0-10 and 10-20 percent respectively among persons of 15 years of age or more. The data of current study revealed 17.00% (19) patients and 7.00% (10) controls to be smokers with a significant Pearson chi-square value (χ^2= 7.414, p $\leq$0.01). In the smoker group of this study 89.00% (17) patients and 60.00% (6) controls smoked 'bidi', none of the persons smoked hooka while 11.00% (2) patients and 20.00% (2) control smoked cigarette. Cigar was smoked by 20.00% (2) smokers of smoker control group only. Frequency of smoking amongst the smokers of the study was more than 30 per week in case of 84.00% (16) patients and 60.00% (6) controls. 31.00% patients and 30.00% controls of the smokers had a history of smoking for less than 20 years while 69.00% patients and 70.00% controls had been smoking for more than 20 years(χ^2= 11.607, p $\leq$0.05). Alcohol and smoking both were reported by 12.00% (13) patients and 7.00% (10) controls. Consumers of *pan masala* and *zarda* were few. *Pan masala* was consumed by 0.66% controls only. *Zarda* was consumed by 4.55% patients and 3.29% controls. Unfiltered *zarda* was consumed by 3.64% patients and 1.32% controls while rest of *zarda* consumers had filtered zarda. 1.82% patients gave a history of 20-30 years of

consumption and a history of more than 30 years was presented by 1.82% patients and 1.32% controls.

Sehgal et al (2012), Bathija et al (2014), Yang et al (2016) have considered tobacco to be a major risk factor for EC. Castellsagu'e et al (2000) and Znaor et al (2003) reported a significant decrease in the incidence of EC with the cessation of smoking alone.

Chewing of betel nut and betel quid with or without tobacco is an important risk factor for EC. Contact of betel juice directly with esophageal mucosa too could contribute to carcinogenesis (Wu et al, 2006). Polyphenol and alkaloid like arecoline present in areca nut were reported to increase the risk of ESCC significantly and independently (Akhtar, 2013; Garg et al 2014; Hossain et al, 2015). Wang et al (2017) found histone methylation and acetylation related enzymes in the tissue of ESCC patients consuming betel quid. In our study only 0.66% (1) control consumed betel quid.

Gao et al (2016) reported the presence of *Porphyromonas gingivalis* in 61 cancerous tissue and 12 adjacent tissue immunohistochemically in ESCC patients and not in normal esophageal mucosa. Similarly a catalytic endoprotease secretion, unique feature of *P. gingivalis* and *P. gingivalis* 16S rDNA was seen. In our study 25.45% patients and 13.83% controls had problem of the oral cavity especially problem with the teeth. This significant difference could influence the incidence of esophageal cancer.

The logistic regression model (CL 95%) shows an impact of meal timings, handling of fruits and vegetables after chopping, discarding soaking water, type and amount of water consumed and smoking on the incidence of esophageal cancer.

Table 4.7.1 Logistic regression (for all the variables fails to execute the model.) So stepwise forward LR logistic regression was applied and presented below:

Variables in the Equation							
Independent Variables		B	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
						Lower	Upper
Step 11[k]	Do_you_have_regular_meal_timing	-1.312	1	0.006	0.269	0.106	0.682

	s_						
	How_long_after_heating_do_you_have_food_	3.927	1	0.016	50.76	2.072	1.24E+03
	In_what_form_do_you_procure_wheat	-1.06	1	0.018	0.346	0.144	0.836
	Do_you_wash_fruits_and_veg	-3.424	1	<0.001	0.033	0.008	0.132
	Do_you_discard_the_soaking_water	-1.281	1	0.007	0.278	0.109	0.708
	Which_water_do_you_drink	-2.59	1	<0.001	0.075	0.022	0.261
	How_many_glasses_of_water_do_you_drink_day	-0.996	1	0.007	0.369	0.18	0.758
	Is_your_foodBland__Less_spicy__Spicy__Very_Spicy	-0.759	1	0.025	0.468	0.242	0.908
	If_yes_then_Do_you_smoke_bidi_hookah_cigarettecigar_	-1.766	1	0.027	0.171	0.036	0.815
	Since_when_are_you_smoking	-2.124	1	<0.001	0.12	0.048	0.297
	How_much_do_you_smokeweek	3.268	1	<0.001	26.247	6.988	98.588
	Constant	3.552	1	0.488	34.872		

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APPENDIX

Logistics Regression taking independent variables in the model (Wheat, Whole Wheat, Maize, Rice and Pulses)

Variables in the Equation						
					95.0% C.I.for EXP(B)	
	B	df	Sig.	Exp(B)	Lower	Upper
WHEATChappatiWithgheebutter	-0.006	1	0.06	0.994	0.987	1
WHEATChappatiPlainfried	-0.003	1	0.838	0.997	0.973	1.022
WHEATChappatiStuffedfried	-0.038	1	0.39	0.963	0.882	1.05
WHEATChappatiNanKulcha	0.624	1	0.035	1.866	1.046	3.329
WHOLEWHEATChappatiWithgheebutter	-0.01	1	<0.001	0.99	0.984	0.995
WHOLEWHEATChappatiPlainfried	0.014	1	0.184	1.014	0.994	1.034
WHOLEWHEATChappatiStuffedfried	0.037	1	0.162	1.038	0.985	1.094
WHOLEWHEATChappatiAnyother	0.002	1	0.8	1.002	0.99	1.014
MAIZEWithgheebutter	0.225	1	0.002	1.252	1.085	1.445
MAIZEParanthawithveg	0.172	1	0.064	1.187	0.99	1.424
BASMATIPlainboiled	0.106	1	0.003	1.112	1.037	1.192
BASMATIZeera	0.277	1	0.001	1.32	1.121	1.554
BASMATIPulao	0.044	1	0.614	1.045	0.88	1.242
REGULARPlainboiled	0.024	1	0.484	1.024	0.958	1.095
REGULARZeera	0.192	1	0.015	1.212	1.038	1.415
PULSESLEGUMESSplitwasheduradchannamasurmoongtur	-0.084	1	0.083	0.92	0.836	1.011
PULSESLEGUMESSplitmoongurad	-0.176	1	0.016	0.839	0.727	0.968
PULSESLEGUMESWholemoongmothmasururad	-0.075	1	0.113	0.928	0.846	1.018
PULSESLEGUMESSoyabeanLobiaRaungiRajmahKalechannaeKabulichannae	0.202	1	0.001	1.224	1.088	1.378
PULSESLEGUMESKarhi	0.117	1	0.427	1.124	0.842	1.5
Constant	-0.025	1	0.971	0.975		

ANNEXURE-I

QUESTIONNAIRE

Chief Investigator : Dr Beenu Tanwar
Co-Chief Investigator : Dr. Anil Panghal
Investigator : Rachna Khosla

We would like to request you to be a part of the clinical research on-

'Role of dietary habits in the development of esophageal cancer in the Doaba region of Punjab'

Being a part of this research is entirely voluntary and not mandatory. You could talk to others or to us to have a clear picture or more information regarding this study. Please spare some time to carefully go through the following information and decide whether you wish to take part in this research.

The following information sheet provides:

Purpose of the study and the role of the participants.

Detailed information about the conduct of the study.

Purpose and your role in this study

1. What is the purpose of this study?

Esophageal cancer is third most common cancer in men and fourth most common in women. In this research we aim to identify the causative dietary habits of esophageal cancer in our area. This knowledge could give us clues for the prevention or cure of esophageal cancer.

2. Why have you been chosen?

You have been referred to a gastroenterologist for a suspicion of esophageal abnormality. We intend studying at least 300 cases in next 2 years.

3. Do you have to take part?

You can volunteer if you wish. Information provided by you would be kept confidential and used for research purpose only. If you do agree, you would be given this information sheet and requested to sign a consent form. You would still be free to withdraw at any step without giving reason. It would not affect your treatment or relationship with the doctor.

4. What have you to do?

Your treatment would continue as required and planned. You would have to spare just half an hour to know about the study, sign a consent form, go through the questionnaire and fill it. No blood sample would be taken or medicine given to you in this period by us. You could refuse to answer any question in the questionnaire. Rest assured that the

information provided by you would be kept confidential. Questionnaire would be filled at your convenience.

5. Advantages and disadvantages of taking part?

We do not foresee any disadvantage in taking part in this study. .The information provided by you would be a donation/gift to mankind as it may help us identify the potential food items in causing esophageal cancer. It could then change the course of prevention, diagnosis, treatment and follow up of esophageal cancer patients. These changes may also be of help in your follow up.

6. Contact details about the study

In case of any problem, concern or question regarding the study please do not hesitate to contact the investigator or chief investigator on the provided contact nos. We would be happy to answer your queries and help you.

Chief Investigator: 9888928265
Co-Chief investigator: 9988049760
Investigator: 9872342995

Information about the conduct of the study

This study is being conducted as a part of PhD research in the department of Food Science and Nutrition at Lovely Professional University; Phagwara, Punjab. It is a pure academic venture with no financial gains to any person associated with this study.

The questionnaire has been reviewed by the experts in the fields of gastrentology and nutrition & dietetics.

Important results of the study could be published or presented at meetings involved with this field of cancer. We assure you that no individual would be identified in any report in any manner. Only the results would be discussed not individuals.

Thank you for sparing your valuable time to read this sheet. Should you wish to participate in this study we would give you a copy of this sheet and the signed consent form for your record.

INFORMED CONSENT FORM

I, the undersigned, confirm that (please tick box as appropriate):

1.	**I have read and understood the information about the project, as provided in the Information Sheet dated _____.**	☐
2.	**I have been given the opportunity to ask questions about the project and my participation.**	☐
3.	**I voluntarily agree to participate in the project.**	☐

4.	**I understand I can withdraw at any time without giving reasons and that I will not be penalised for withdrawing nor will I be questioned on why I have withdrawn.**	☐
5.	**The procedures regarding confidentiality have been clearly explained (e.g. use of names, pseudonyms, anonymisation of data, etc.) to me.**	☐
6.	**If applicable, separate terms of consent for interviews, audio, video or other forms of data collection have been explained and provided to me.**	☐
7.	**The use of the data in research, publications, sharing and archiving has been explained to me.**	☐
8.	**I understand that other researchers will have access to this data only if they agree to preserve the confidentiality of the data and if they agree to the terms I have specified in this form.**	☐
9.	**Select only one of the following:** • **I would like my name used and understand what I have said or written as part of this study will be used in reports, publications and other research outputs so that anything I have contributed to this project can be recognised.** • **I do not want my name used in this project.**	☐ ☐
10.	**I, along with the Researcher, agree to sign and date this informed consent form.**	☐

Participant: **Signature & Date**

Researcher: **Signature & Date**

LOVELY PROFESSIONAL UNIVERSITY

DEPARTMENT OF FOOD TECHNOLOGY AND NUTRITION

Chief Investigator : Dr. Beenu Tanwar

Co-Chief Investigator: Dr. Anil Panghal

Investigator : Rachna Khosla

Introduction

Esophageal cancer is on the rise in this part of the country. We are conducting a study to see if dietary habits and esophageal cancer bear some relation. In the hope to discover

this relationship we are asking a volley of questions to people with esophageal problem [both confirmed malignant and benign] and with no esophageal problem.

Certain questions may appear vague or personal. They are neither to test or judge you nor to frame an opinion about you. Please take your time and answer all questions. Please do not hesitate to answer them as all your answers would be confidential and used for medical research only to discover the link between dietary habits and health. If you still feel uncomfortable you are free to refrain from answering such a question and write DK [don't know] or CA [can't answer] in front of the question.

GENERAL INFORMATION

Age : ☐☐ yrs. Gender Male ☐ Female☐

Height : ☐☐☐ cm Weight ☐☐☐ Kg

Area :---------- Rural ☐ Urban ☐ Semiurban ☐

District :---------- Code ☐☐☐☐☐☐

Phone no. : ☐☐☐☐☐☐☐☐☐☐☐

Food habit : Vegetarian ☐, Non vegetarian ☐, Ovotarian ☐

Qualification : Uneducated ☐< Matric ☐ Matric ☐ +2 ☐ Graduate ☐ Post Graduate ☐

Any other ----------

Occupation : Professional ☐, Businessman ☐, Agriculturist ☐, Housewife ☐, Any other ☐

Monthly income (Rs.): < 10,000 ☐ 10,000 to <20,000 ☐, 20,000 to < 30,000 ☐, 30,000 to <40,000 ☐, 40,000 to < 50,000 ☐, > 50,000 ☐

Family size : Adults ☐; Children ☐ Ethinicity :----------

Clinical picture

Dysphagia (difficulty in swallowing) Yes ☐; No ☐. If yes, to Solids ☐, Semisolids ☐, Liquids ☐

Weight loss (without effort) Yes ☐; No ☐

Feeling of pressure, pain or burning in the chest Yes ☐; No ☐

Increasing indigestion or acidity Yes ☐; No ☐. Cough Yes ☐; No ☐.

Hoarseness of voice Yes ☐; No ☐. Difficulty in speaking Yes ☐; No ☐

Histopathological report : Benign ☐ ; Malignant ☐ ; NA ☐

Medical history

Personal

Are you having any other medical problem. Yes ☐, No ☐

Name of the problem----------

Do you take any medicine regularly? Yes ☐, No ☐

If yes, then name of the medicine/s-(with duration)----------

Do you take any medicine occasionally? Yes ☐ , No ☐

If yes then name of the medicine/s (with duration)----------

Family

Is any family member having any type of cancer? Yes ☐, No ☐

If yes, Relation---------- Type & site of cancer ----------
Period----------

Please mark your portion size in the picture

S [small] M [medium] L [Large]

How often do you eat the following?

Foods	Times you have eaten various foods				
	Amount	Never	Occasional/	Per week	Per day

			Rare	1 time	2 times	3-4 times	5-6 times	1 Time	2 times	3 or more times
Cereals										
Chappati	Wheat	☐	Whole wheat☐	Maize	☐	Multig rain	☐	Any other	☐	
With ghee/butter		☐	☐	☐	☐	☐	☐	☐	☐	☐
Tandoori		☐	☐	☐	☐	☐	☐	☐	☐	☐
Cooked on fire		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
Parantha		☐	☐	☐	☐	☐	☐	☐	☐	☐
Plain fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Stuffed fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Stuffed non-fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Nan/Kulcha		☐	☐	☐	☐	☐	☐	☐	☐	☐
Bhatura/Poori		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
Rice	Basmati	☐	Regular ☐	Sela☐	Any other	☐				
Plain boiled		☐	☐	☐	☐	☐	☐	☐	☐	☐
Zeera		☐	☐	☐	☐	☐	☐	☐	☐	☐
Pulao		☐	☐	☐	☐	☐	☐	☐	☐	☐
Biryani veg.		☐	☐	☐	☐	☐	☐	☐	☐	☐
Biryani non-veg.		☐	☐	☐	☐	☐	☐	☐	☐	☐
Khichri		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
PULSES &LEGUMES										
Split washed – urad/channa/masur/moong/tur		☐	☐	☐	☐	☐	☐	☐	☐	☐
Split-moong/urad		☐	☐	☐	☐	☐	☐	☐	☐	☐
Whole-moong/moth/masur/urad		☐	☐	☐	☐	☐	☐	☐	☐	☐
Soya bean/Lobia/Raun		☐	☐	☐	☐	☐	☐	☐	☐	☐

gi/Rajmah/Kale channae/Kabuli channae										
Karhi		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
VEGETABLES										
Green Leafy		☐	☐	☐	☐	☐	☐	☐	☐	☐
Roots & Tubers		☐	☐	☐	☐	☐	☐	☐	☐	☐
Others		☐	☐	☐	☐	☐	☐	☐	☐	☐
FRUITS										
Fresh		☐	☐	☐	☐	☐	☐	☐	☐	☐
Tinned		☐	☐	☐	☐	☐	☐	☐	☐	☐
Dried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Fresh juice		☐	☐	☐	☐	☐	☐	☐	☐	☐
Packaged juice		☐	☐	☐	☐	☐	☐	☐	☐	☐
EGG										
Boiled		☐	☐	☐	☐	☐	☐	☐	☐	☐
Fried/Omlette		☐	☐	☐	☐	☐	☐	☐	☐	☐
Poached		☐	☐	☐	☐	☐	☐	☐	☐	☐
MEAT										
Steamed		☐	☐	☐	☐	☐	☐	☐	☐	☐
Grilled		☐	☐	☐	☐	☐	☐	☐	☐	☐
Fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Boiled		☐	☐	☐	☐	☐	☐	☐	☐	☐
With Gravy		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
FOWL										
Steamed		☐	☐	☐	☐	☐	☐	☐	☐	☐
Grilled		☐	☐	☐	☐	☐	☐	☐	☐	☐
Fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Boiled		☐	☐	☐	☐	☐	☐	☐	☐	☐
Broiled		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
FISH										

Steamed		☐	☐	☐	☐	☐	☐	☐	☐	☐
Grilled		☐	☐	☐	☐	☐	☐	☐	☐	☐
Fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Boiled		☐	☐	☐	☐	☐	☐	☐	☐	☐
With Gravy		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
MILK & MILK PRODUCTS										
Fresh -Cow's		☐	☐	☐	☐	☐	☐	☐	☐	☐
Fresh-Buffalo		☐	☐	☐	☐	☐	☐	☐	☐	☐
Pasteurised full fat		☐	☐	☐	☐	☐	☐	☐	☐	☐
Toned milk		☐	☐	☐	☐	☐	☐	☐	☐	☐
Skimmed milk		☐	☐	☐	☐	☐	☐	☐	☐	☐
Curd										
Plain		☐	☐	☐	☐	☐	☐	☐	☐	☐
Raita		☐	☐	☐	☐	☐	☐	☐	☐	☐
Bhalla		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
Paneer		☐	☐	☐	☐	☐	☐	☐	☐	☐
Cheese		☐	☐	☐	☐	☐	☐	☐	☐	☐
BEVERAGES										
Tea										
Full milk		☐	☐	☐	☐	☐	☐	☐	☐	☐
Half milk		☐	☐	☐	☐	☐	☐	☐	☐	☐
Regular		☐	☐	☐	☐	☐	☐	☐	☐	☐
Black		☐	☐	☐	☐	☐	☐	☐	☐	☐
Separate		☐	☐	☐	☐	☐	☐	☐	☐	☐
Coffee										
Full milk		☐	☐	☐	☐	☐	☐	☐	☐	☐
Half milk		☐	☐	☐	☐	☐	☐	☐	☐	☐
Regular		☐	☐	☐	☐	☐	☐	☐	☐	☐
Black		☐	☐	☐	☐	☐	☐	☐	☐	☐
Separate		☐	☐	☐	☐	☐	☐	☐	☐	☐

Aerated Drinks		☐	☐	☐	☐	☐	☐	☐	☐	☐
Non Aerated Drinks		☐	☐	☐	☐	☐	☐	☐	☐	☐
Buttermilk (Lassi)										
Plain		☐	☐	☐	☐	☐	☐	☐	☐	☐
Salted		☐	☐	☐	☐	☐	☐	☐	☐	☐
Sweet		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
FAT										
Mustard oil		☐	☐	☐	☐	☐	☐	☐	☐	☐
Refined oil [Name]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Vanaspati ghee		☐	☐	☐	☐	☐	☐	☐	☐	☐
Desi ghee		☐	☐	☐	☐	☐	☐	☐	☐	☐
Butter		☐	☐	☐	☐	☐	☐	☐	☐	☐
Malai		☐	☐	☐	☐	☐	☐	☐	☐	☐
Cream		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
NUTS & OILSEEDS										
Peanut		☐	☐	☐	☐	☐	☐	☐	☐	☐
Almond		☐	☐	☐	☐	☐	☐	☐	☐	☐
Cashew nut		☐	☐	☐	☐	☐	☐	☐	☐	☐
Sesame seed [Til]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Pistachio nut [Pista]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Pine nut [Nezae]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Walnut [Akhrot]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
MISCELLANEOUS										
Bread		☐	☐	☐	☐	☐	☐	☐	☐	☐
Biscuits		☐	☐	☐	☐	☐	☐	☐	☐	☐
Papad roasted on flame		☐	☐	☐	☐	☐	☐	☐	☐	☐

Papad fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Pickle [Achar]										
Mango [Aam]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Lime [Nimboo]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Lemon [Galgal]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Ginger [Adrak]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Indian Gooseberry [Amla]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Carrot/Cauliflower/Turnip [Gaajar/Gobi/Shalgam]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Green chilli [Hari mirch]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Red chilli stuffed [Lal mirch]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Karonda		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
Chutney										
Mint [Pudina]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Coriander [Dhania]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Mango [Aam]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐
Sugar		☐	☐	☐	☐	☐	☐	☐	☐	☐
Jaggery [Gur]		☐	☐	☐	☐	☐	☐	☐	☐	☐
Shaker		☐	☐	☐	☐	☐	☐	☐	☐	☐
Artificial sweetener [Name]		☐	☐	☐	☐	☐	☐	☐	☐	☐
SAVOURY										
Fried		☐	☐	☐	☐	☐	☐	☐	☐	☐
Saute		☐	☐	☐	☐	☐	☐	☐	☐	☐
Steamed		☐	☐	☐	☐	☐	☐	☐	☐	☐
Nuts		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐

DESSERTS										
Milk Based		☐	☐	☐	☐	☐	☐	☐	☐	☐
Flour Based		☐	☐	☐	☐	☐	☐	☐	☐	☐
Plain cake		☐	☐	☐	☐	☐	☐	☐	☐	☐
Pastry		☐	☐	☐	☐	☐	☐	☐	☐	☐
Any other		☐	☐	☐	☐	☐	☐	☐	☐	☐

General questions:

How many meals do you have/day? 2 major & 2 minor ☐, 2 major & twice tea ☐, small frequent meals☐, no fixed pattern ☐

Do you have regular meal timings? Yes ☐, No ☐

When do you go to bed [after last meal]? Immediately ☐, < 1 hr. ☐, 1-2 hrs. ☐, >2-3 hrs. ☐, > 3 hrs. ☐

How long after heating do you have food? Immediately ☐, 5 mins. ☐ more than 5 min ☐

How long after boiling do you have tea/coffee/milk? Immediately ☐, 5 mins. ☐ more than 5 min ☐

In what form do you procure wheat? Grain ☐ , Atta ☐

Do you add preservative to grain ? Yes ☐, No ☐

If Yes : Non organic (Chemical) ☐ , organic ☐

Do you have Frozen ☐, Tinned ☐, Ready to use foods ☐? Yes ☐, No ☐

How frequently (meals per week)? <1 ☐, 1-3 ☐,4-7 ☐, > 7 ☐

Do you wash hands before cooking? Yes ☐, No ☐

Do you wash hands before eating? Yes ☐, No ☐

Do you wash staked utensils before using? Yes ☐, No ☐

Do you wash fruits and veg. ----Before chopping ☐, After chopping ☐?

Food is cooked on ------Gas ☐, Stove ☐, Chula ☐?

Which type of utensils are mostly used to cook food--- Brass ☐, Copper ☐,Aluminium ☐, Iron ☐, Steel ☐, Non stick ☐.

Do you use brass utensils without tin plating ? Yes ☐; No ☐

Do you use microwave for Cooking ☐, Heating ☐, None ☐?

Which type of utensil do you use in microwave? Microwave safe Plastic ☐, Microwave safe Glass ☐, Any other☐

Do you soak legumes and pulses before cooking ? Yes ☐; No ☐

Do you discard the soaking water? Yes ☐; No ☐

Do you cook with baking soda? Yes ☐; No ☐.

How frequently (meals per week)? <1 ☐, 1-3 ☐,4-7 ☐, > 7 ☐

Is your food very soft ☐, soft ☐, retains bite ☐ when cooked?

Is your bite small ☐, medium ☐, large ☐?

Do you chew a little ☐ or chew very well ☐?

After how much time do you eat the cooked meal ---Within 1 hour ☐, 1-3 hrs. ☐,> 3-6hrs. ☐>6-9hrs.☐, >9-12 hrs. ☐.

What do you do with the leftover food?—Use it --In the next meal ☐, Next day ☐, Use a few days later ☐, Dispose it off ☐
How do you store cooked meal? Room temp. ☐, Refrigerate ☐, Freeze ☐
Which water do you drink? Fresh tap water ☐, Filter water ☐, RO water ☐
Do you drink water after the meal? Yes ☐; No ☐
How many glasses of water do you drink /day? 3-5 ☐, 6-8 ☐, 9-11☐, >11 ☐
Is your food--- Bland ☐, Less spicy ☐, Spicy ☐, Very Spicy ☐
How frequently do you prepare fried dishes at home ?(meals per week) <1 ☐, 1-3 ☐,4-7 ☐, > 7 ☐
What is the frying medium? Mustard oil ☐, Refined oil ☐, Vanaspati ghee ☐, Desi ghee ☐
What do you do with frying medium? Use for normal cooking ☐, Reuse till a refill is required ☐, Refill and reuse till thick and dark ☐
How many soda drinks do you have per week? <2 ☐, 2-4 ☐, 5-7 ☐ , 7-10 ☐, >10 ☐
Do you take alcohol? Yes ☐; No ☐
If yes then, how many drinks/week do you take? <5 ☐, 5-11 ☐, 12-30 ☐, > 30 ☐
[1 drink = 150 ml of wine, 330 ml. of beer and 30 ml of hard liquor]
Do you have it --- Neat ☐, With soda ☐, With water☐?
Since when are you having alcohol? < 10 yrs. ☐, 11-20 yrs. ☐, 21-30 yrs. ☐, > 30 yrs. ☐
Do you smoke? Yes ☐; No ☐
If yes then, Do you smoke bidi ☐ , hookah ☐, cigarette ☐, cigar ☐
How much do you smoke/week? <5 ☐, ,5-11 ☐, 12-30 ☐, >30 ☐
Since when are you smoking? < 10 yrs. ☐, 11-20 yrs. ☐, 21-30 yrs. ☐, > 30 yrs. ☐
Do you consume betel quid? Yes ☐; No ☐
How many/week? < 1 ☐, 1-3 ☐, 4-7 ☐, 8-10 ☐, > 10 ☐
Does it contain tobacco? Yes ☐; No ☐
Does it contain betel nut? Yes ☐; No ☐
Since when are you taking betel quid? < 10 yrs. ☐, 11-20 yrs. ☐, 21-30 yrs. ☐, > 30 yrs. ☐
Do you take pan masala? Yes ☐; No ☐
If yes then how much pan masala do you take/week?
Since when are you taking pan masala? < 10 yrs. ☐, 11-20 yrs. ☐, 21-30 yrs. ☐, > 30 yrs. ☐
Do you consume zarda? Yes ☐, No ☐
If yes, then is the zarda filtered ☐ or unfiltered ☐?
How much zarda do you consume /week?
Since when are you cosuming zarda? < 10 yrs. ☐, 11-20 yrs. ☐, 21-30 yrs. ☐, > 30 yrs. ☐
Do you have any oral problem? Yes ☐; No ☐

We appreciate your co-operation in providing the information and supporting this study.

THANK YOU!

ANNEXURE-II

MASTER SHEETS KEY

The information collected from every individual of the control and the patient (EC cases) group was transferred to the Excel sheet for analysis.

General Information :

Age has been recorded in years, height in centimeters, weight in kilograms, gender as M (male) or F (female). District name has been entered as J (Jalandhar) K (Kapurthala) N (Nawanshehar) or H (Hoshaiarpur). Food habit has been filled as V (vegetarian) N (non vegetarian) or O (ovotarian). Area, qualification, occupation and monthly income have been entered according to the number of the ticked option. Like in the following case Occupation : Professional ☐, Businessman ☐, Agriculturist ☐, Housewife ☐, Any other ☐.

The information gathered about occupation has been coded as '1' for professional, '2' for businessman, '3' for agriculturist, '4' for housewife and '5' for anyother. Type of EC and medical problem has been also recorded.

Dietary Information :

The intake of food choice has been entered as the number of servings per month. The foods not consumed were coded as zero. One medium sized chappati, Paranthi, stuffed parantha, slice of bread, three-fourth medium sized katori of rice has been taken as one cereal serving. Similarly one medium sized katori of vegetable and fruit has been taken as one serving. Medium sized glass of milk or tea and a teaspoon of sugar or oil have been taken as one serving. The total amount of various food items has been calculated by summing up the product of serving number with the serving amount like the total amount of wheat was calculated with a chappati as 30 grams of wheat, tandoori roti as 35 g, parantha as 40 g, nan/kulcha as 25g, poori/bhatura as 40g and dalia etc as 40 g.

Life Style :

Whole information has been coded according to the number of the selected option as in the question – 'In what form do you procure wheat? Grain ☐ , Atta ☐', grain option has been coded as '1' and atta option has been coded as '2'. The question which was'not applicable', like the amount of alcohol consumed in case of a teetotaler, has been marked zero.