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Implementation of a Clinical Nutrition Clinic for Cancer Patients. Will It Improve Health Outcomes?

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1. Abstract

1.1. Background: Cancer exerts a massive burden on society in both developed and developing countries. Cancer is becoming more common as the population grows and ages, as well as the incidence of identified risk factors rises.

1.2. Aim: The review aimed to establish a clinic for cancer patients in which a balanced diet will be adjusted to them based on investigations of the relationship between food product consumption, dietary intake, and the occurrence of side effects, tumour development, and associated illness in cancer patients undergoing chemotherapy.

1.3. Methods: Clinical nutrition clinic structure was mentioned with significance of each individual in the clinic team. Furthermore, a literature search was done to collect different evidences supporting the review aim.

1.4. Discussion: Several studies indicated that dietary changes have a promising positive effect on chemotherapy side effects like GIT side effects, tumour incidence and growth, and so improving patients' quality of life.

1.5. Conclusion: The collected data showed that dietary intake with specific food products have a significant impact on the health status of cancer patients including the side effects of chemotherapy, radiation and co morbidities. A dietary approach focused on the exclusion or limited intake of specific food products, as well as diet improvement, might minimize chemotherapy-induced problems and hence should be considered in clinical practice.

2. Introduction

According to dietary guidelines for cancer patients, it is advised to analyze nutrient intakes, changes in body weight and BMI since cancer diagnosis, nutritional assessment, and repeat review depending on clinical stability [1]. The energy requirements and biology of the tumour, the body's reaction to the existence of the tumour, and the influence of therapies all contribute to increased caloric requirements in cancer patients [2].

Chemotherapy treatments are associated with a variety of nutrition-related symptoms such as loss of appetite, nausea, vomiting, and taste changes, all of which interfere with patients' ability to eat and enjoy meals, resulting in impaired nutritional intake, nutritional status deterioration, and decreased quality of life. And so, drug treatment to promote appetite may result in higher food intake, weight gain, and better quality of life [3].

Furthermore, DNA methylation is a frequent epigenetic alteration that affects gene expression, and abnormal DNA methylation patterns are considered a cancer hallmark. Micronutrients, bioactive chemicals, and mycotoxins all have the ability to influence DNA methylation patterns and so contribute to cancer prevention and onset [4].

In one-carbon metabolism and other DNA methylation processes, micronutrients like as choline, folate, betaine, and methionine function as cofactors or methyl donors. Curcumin, epigallocatechin-3-gallate, genistein, quercetin, resveratrol, and sulforaphane are dietary bioactive compounds that reactivate essential tumour

suppressor genes by correcting aberrant DNA methylation patterns, and hence have shown potential against various cancers. On the other hand, fungus-infested agricultural foods are a source of potent mycotoxins that promote carcinogenesis [4].

It is observed that cancer cells are excessive users of metabolic fuels, such as glucose, amino acids, and fats. Dietary interventions could lead to improved outcomes with little or no additional toxicity. Indeed, some data show that diet interventions could potentially reduce chemotherapy side effects. Unfortunately, the vast majority of the discourse has been based on opinion and anecdotal evidence, and a paucity of scientifically validated diet interventions can be offered to cancer patients [5].

Frequent investigations are done to address the effect of dietary changes and nutrients on cancer patients' quality of life, incidence of side effects, emerging diseases, and tumor growth and / or inhibition.

The current review will explore the different investigations done in this issue and what are the influence of dietary changes on improvement cancer patient total quality of life. Furthermore, it will investigate the establishment of a clinical nutrition clinic for cancer patients to provide them nutritional and therapeutic guidance.

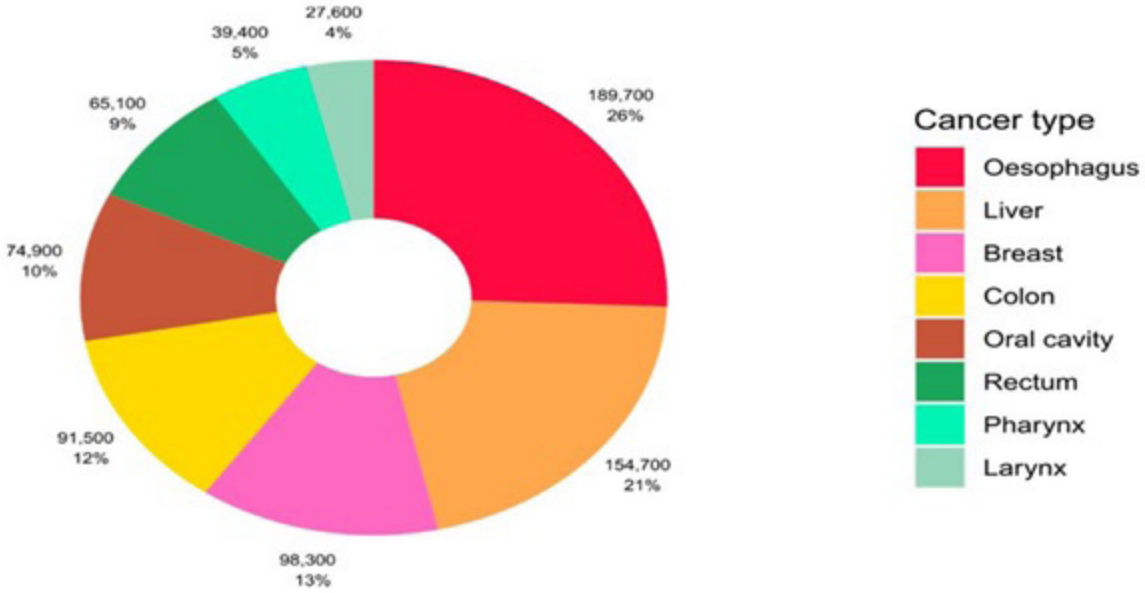

Figure 1: Global number and proportion of cancer cases attributable to alcohol consumption according to cancer type. [34]

Table 1: Preclinical studies examining the role of fasting on cancer outcome

Cancer (cell line)	Animal model	Route	Fasting scheme	Effect of fasting alone	Effect of fasting with treatment	Reference
Immunocompetent						
Breast (67NR and 4T1)	14-week-old BALB/c	Orthotopic	alternate day feeding	Slowed tumor growth	Synergy with irradiation	24
Breast (4T1)	12-week-old BALB/c female	Subcutaneous	Two 48- to 60-hour fasting cycles	Slowed tumor growth	Synergy with cyclophosphamide	25
Melanoma (B16)	12-week-old C57BL/6 male and female	Subcutaneous	Two 48- to 60-hour fasting cycles	Slowed tumor growth	Synergy with doxorubicin	25
Colorectal (CT26)	6-week-old female BALB/c	Subcutaneous	Two 48-hour fasting cycles	Slowed tumor growth	Synergy with oxaliplatin	26
Immunocompromised						
Breast (H3122)	6- to 8-week-old athymic BALB/c mice	Subcutaneous	Three 48-hour fasting cycles	Slowed tumor growth	Synergy with crizotinib (tyrosine kinase inhibitor)	27
Colorectal (HCT116)	6- to 8-week-old athymic BALB/c mice	Subcutaneous	Three 48-hour fasting cycles	Slowed tumor growth	Synergy with regorafenib (tyrosine kinase inhibitor)	27
Glioma (GL26)	7-week-old nude mice	Subcutaneous	One 48- to 60-hour fasting cycle	Slowed tumor growth	Synergy with doxorubicin	24

Table 2: Preclinical trials of ketogenic diets on cancer outcome

Cancer (cell line)	Animal model	Route	Diet scheme	Effect of fasting alone	Effect of fasting with treatment	Reference
Breast (4T1)	BALB/C	Subcutaneous	70% of ad libitum of diet containing 2% carbohydrates and 93.4% fat calories	Reduced tumor growth	Enhanced antitumor effect of metformin	29
Lung (NCI-H292 and A549 cells)	Female athymic-nu/nu mice	Subcutaneous	ad libitum 1.6% carbohydrates and 90% fat calories	No effect of ketogenic diet alone on tumor volume or survival	Enhanced tumor response and survival with Irradiation and/or carboplatin	30
Glioma (GL261)	Female albino C57BL/6	Orthotopic	ad libitum 3% carbohydrates and 72% fat calories	Prolonged survival	Synergistic with whole brain irradiation	31

Table 3: Foods, Dietary Supplements, and Cancer Drug Interactions [32].

Herbal/Dietary Supplement	Anticancer Therapy	Effect
St. John's wort	Irinotecan	Increased activity of CYP3A4 and decreased AUC of active metabolite SN38
St. John's wort	Imatinib	Increased clearance and decreased AUC of imatinib
St. John's wort	Methotrexate	Increased AUC and C_{max} of methotrexate
St. John's wort	Docetaxel	Increased clearance and decreased AUC of docetaxel
St. John's wort	Ixabepilone	May decrease plasma concentrations of ixabepilone
Green tea	Sunitinib	Decreased drug absorption and bioavailability of sunitinib
Green tea	Palbociclib	Decreased oral bioavailability of palbociclib
Green tea extract	Erlotinib	Decreased AUC and oral bioavailability of erlotinib
Green tea extract	Lapatinib	Decreased AUC and oral bioavailability of lapatinib
Epigallocatechin gallate (***an antioxidant component of green tea***)	Tamoxifen	Increased bioavailability of tamoxifen
Epigallocatechin gallate	Irinotecan	Increased plasma concentration of irinotecan and decreased hepatobiliary excretion of drug and its metabolite SN-38
Green tea and Epigallocatechin gallate	Fluorouracil	Increased AUC and C_{max} of fluorouracil
Grapefruit	Imatinib	May increase plasma levels of imatinib by inhibiting CYP3A4
Grapefruit	Etoposide	Decreased AUC and bioavailability of etoposide
Grapefruit	Sunitinib	Increased bioavailability of sunitinib
Grapefruit	Nilotinib	Increased AUC and C_{max} of nilotinib
Vitamin A	Imatinib	Increased bioavailability of imatinib
Vitamin E	Imatinib	Increased bioavailability of imatinib
Vitamin D3	Imatinib	Increased bioavailability of imatinib
Vitamin C	Imatinib	Decreased bioavailability of imatinib
Scutellaria baicalensis	Docetaxel	Increased AUC of drug and exposure to both drug and herb

3. Materials and Methods

The clinical nutrition clinic role is to optimize the dietary intake on individual level for each cancer patient. This will provide patients with a better quality of life and minimal adverse effects. A specialized team and tools are required to provide the nutritional service.

3.1. The suggested clinic team, their roles and the required instruments will be as follows:

3.1.1. Dietitians or Nutritionists: Their primary function is to provide nutritional care expertise [6], malnutrition assessment, improve cancer care and optimize quality of life [7].

3.1.2. Oncologist: Participate in clinical and translational research to advance innovation and novel therapeutics, contribute to cancer diagnosis, prevention, and research. Also, oncologist provide a complete and systematic approach to treatment and care, while assuring the use of cancer medications that is evidence-based, safe, and cost-effective [8].

3.1.3. Clinical Pharmacist: Adopting scientifically reliable knowledge and guidance on safe, reasonable use of chemotherapy, optimizing therapeutic efficacy, minimizing adverse effects, and resolving unclear/compliant issues [9].

Besides, the pharmacists have a variety of responsibilities in parenteral nutrition treatment, including: assessing patients' nutritional needs; designing, compounding, dispensing, and quality management of parenteral nutrition formulations; monitoring patients' response to parenteral nutrition therapy, educating patients, caregivers, and other health care professionals about nutrition support [10].

3.1.4. Nurses: Nurses are in a good position to provide screening, referral, coordination, physical exercise consulting, nutritional advice, direct nutritional nursing, psychological support, symptom control, and hospice care [11].

3.1.5. Computer system: A clinical Nutritional Information Sys-

tem satisfies dietitians' demands by improving the quality of nutritional therapies by providing precise calculations and cross-referencing for information about patients' conditions, while also reducing processing time, as opposed to handwritten paperwork. Furthermore, the CNIS assists dietitians in statistically analyzing each patient's particular nutritional demands in order to achieve nutritional improvement [12].

3.1.6. Nutrition registry: To overcome the significant gap in the knowledge available to assist the activity of hospital-based dietitians and to address the question of how the majority of patients might avoid acquiring protein-energy malnutrition [13].

4. Discussion

A retrospective observational study in Italy found that clinical nutrition is associated with positive survival outcomes in metastatic patients with gastrointestinal, respiratory, and genitourinary cancer; besides, it was associated with significant improvement in survival in malnourished metastatic patients with gastrointestinal and genitourinary cancer. Furthermore, early administration of clinical nutrition was associated with improvement in survival in non-metastatic patients with gastrointestinal cancer [14].

Recent studies have shown that patients who were given nutritional support showed reduced in-hospital mortality, and they were discharged from a post-acute care facility less frequently [15].

A clinical study showed that clinical pharmacist interventions were associated with a significant decrease in the toxicity grades of breast cancer, such as anaemia, where the percentage of grade 2 patients decreased from 17 percent to 1.7 percent; additionally, 5 percent of grade 4 nausea/vomiting, which decreased to zero percent after pharmacist intervention [16].

4.1. Correlation between diet and incidence of chemotherapy' side effects

A clinical trial involving 56 women undergoing chemotherapy for ovarian cancer was done to analyze dietary intake and the relationship between the consumption of certain food products and the prevalence of gastrointestinal problems. According to the findings, 23 percent and 32 percent of patients never suffered nausea or constipation, respectively, while 43 percent and 45 percent never experienced vomiting or diarrhea. Oils caused nausea, chocolate and chocolate goods caused constipation, while dairy products, stone fruit, and apple caused diarrhea. Vomiting was shown to have significant inverse associations with calories, fat, protein, carbs, B vitamins, vitamin D, phosphorus, and zinc consumption [17].

Dietary changes are recommended in addition to pharmaceutical treatment for chemotherapy-induced diarrhea. These include avoiding hot meals, caffeine, alcohol, and fruit juices, as well as high osmolar dietary supplements, vegetables, particularly cruciferous vegetables, as well as lactose-containing goods, high fibre, and high fat foods [17].

Constipation is also one of the most common complaints experienced by cancer patients. It was shown that these constipation patients report changing stool shape following meal and beverage consumption more frequently than healthy people. Furthermore, chocolate was the most commonly cited and considered to promote constipation among them [17].

Chemotherapy-induced gastrointestinal (GI) side effects in breast cancer patients are prevalent but poorly understood, and they may be addressed with dietary management. A total of 150 patients with breast cancer having chemotherapy were randomly allocated to either the intervention group (n = 73) or the control group (n = 67) for 10 weeks after their three rounds of chemotherapy. The severity of GI side effects, which included reflux disorder, anorexia, nausea, constipation, and diarrhea, was considerably reduced in the third session of chemotherapy compared to the first session, which included dietary intervention and nutritional education [18].

Clinical studies recommended avoiding acidic and caffeinated foods and drinks such as citrus fruits, fatty and fried foods, garlic, onions, mint, spicy foods, tomato-based foods, carbonated drinks, lying down right after every meal, and consuming small amounts of food very slowly to prevent the occurrence of reflux in breast cancer patients undergoing chemotherapy [19].

Nutrition recommendations for reducing diarrhoea in breast cancer patients undergoing chemotherapy included eating frequent small meals, drinking clear liquids (water, weak herbal tea, apple juice, clear broth, frozen pops), eating foods high in pectin, a water soluble fibre found in apple sauce, bananas, and yoghurt, and eating foods high in potassium and sodium [19].

Nutrition education in breast cancer patients undergoing chemotherapy included the following criteria to consider: eating frequent small meals, consuming foods at room temperature rather than in a warm place, rinsing their mouth before and after each meal, sitting up or lying down with their head raised for at least an hour after each consumption, and avoiding spicy, fried, sugary, or highly aromatic foods and in contrast, having bland, soft or easy-to-digest foods especially in their chemotherapy time, having liquids with ice chips or frozen juice chips, having deep breaths and relax after their therapies, drinking clear and cold liquids such as ginger ale, apple juice, broth, and tea, sucking on hard candy with pleasant smells such as lemon drops or mints which helps them to get rid of bad tastes, if they developed a general dislike of red meat and meat broths during treatment, they would better consume other protein sources, such as fish, chicken, beans, and nuts [20].

Health care professionals should keep in mind that cancer patients are immunocompromised and when infected with COVID-19 they may present with fever and respiratory symptoms due to a subsequent opportunistic bacterial infection. Even pneumonitis can arise with the use of some cytotoxic chemotherapies [21]. That is why health care providers should take a special care regarding patients' health state and nutrition.

Mass vaccination and immunization will be important in preventing the spread of Covid-19 [22]. This is an important for cancer patients to avoid potential complications and additional comorbidities from covid-19 infection. Furthermore, as we mentioned before that these patients are immunocompromised, and so mortality rates may increase.

5. Cancer Incidence and Tumor Growth

Although vitamin D deficiency has been linked to an increase in cancer incidence, a meta-analysis of 40 randomized controlled trials (RCTs) found that vitamin D supplementation with or without calcium did not reduce skeletal or non-skeletal outcomes in unselected community-dwelling individuals by more than 15%. A randomized controlled study including 14,641 US doctors found that combining vitamin E (400 IU/day) and vitamin C (500 mg/day) supplementation for an average of 10 years had no effect on cancer incidence. Long-term vitamin E (400 IU/day) or selenium (200 g from selenomethionined) supplementation had no influence on the risk of prostate cancer [23].

Changing diet habits may be critical in limiting cancer incidence. Furthermore, it is a safe way for improving patient quality of life without additional risk or potential side effects that occurs from chemotherapy. Furthermore, fasting may play a role in cancer patients clinical outcomes.

According to research, employing a ketogenic diet as an alternative to fasting and calorie restriction has sparked a lot of interest. A ketogenic diet may be better tolerated in certain people, and it has a lengthy track record of safety as an epilepsy therapy. A recent meta-analysis included 12 research that compared an unrestricted ketogenic diet to a regular diet in murine cancer models and concluded that the ketogenic diet resulted in an overall growth delay [28].

Supplementation with long-chain N-3 fatty acids or fish oil was recommended to maintain or increase appetite, food intake, lean body mass, and body weight in patients with advanced cancer receiving chemotherapy with high risk of weight loss or malnutrition [23].

Several anticancer medications are P-glycoprotein (P-gp) substrates; consequently, if P-gp or any cytochrome P450 (CYP) enzyme is affected, the drug it is processing will also be affected. Various herbs and nutritional supplements, such as St. John's wort, are known to impact the pharmacokinetics of various medications. Currently, research on the pharmacokinetic interactions of dietary supplements and cancer drugs is sparse, however there is evidence for numerous probable interactions and adverse responses [32].

Grapefruit and its furanocoumarin components have been researched in vitro and in vivo for their potential antioxidative, anti-inflammatory, and anticancer properties. Grapefruit juice may raise imatinib plasma levels by blocking CYP3A4, resulting in organ damage. On the other hand, after pretreatment with grapefruit juice, the bioavailability of etoposide (50 mg orally) decreased from roughly 73% to 52%. As etoposide was combined with grapefruit juice, the area under the concentration versus time curve (AUC) decreased by 26% when compared to etoposide alone [32].

Diets high in "plants" (vegetables and fruits), fish, low in alcohol and mammalian fat appear to have a lower cancer incidence than diets low in plants and high in red meat, mammalian fat, and alcohol. Food-related components that have anticancer effect include Plant pigments, pear, basil, thyme, oregano, apple, honeybee propolis, chilli pepper, strawberries, pineapple, coffee, sunflower, blueberries, cinnamon oil, mushroom, garlic, soybean, oats, rice, artichoke, orange, pineapple, peanut, onion, cucumber, black pepper, and broccoli [33].

Cancer Incidence / treatment side effects and Life Style / Habits:

Alcohol intake is responsible for around 4% of all malignancies globally. Drinking alcohol raises the risk of various malignancies, including upper aerodigestive tract, liver, colorectum, and breast cancer [34].

A daily intake of 10 g of alcohol was linked to a 15% higher risk of oral cavity cancer. Cancers of the upper aerodigestive tract are also more than multiplicatively enhanced when alcohol and cigarettes are consumed simultaneously. Several studies have found this synergistic effect; for example, a pooled analysis of 11,200 head and neck cancer cases and 16,200 controls discovered a 14-fold risk of head and neck cancer among those who drank at least three alcoholic drinks per day and smoked more than 20 cigarettes per day, compared to never drinkers who had never smoked [35].

Besides, the “World Cancer Research Fund and American Institute for Cancer Research” meta-analysis discovered a 7% higher risk of colorectal cancer, 7% increased risk of breast cancer (in women), and 14% increased risk of hepatocellular carcinoma every 10 g alcohol consumption per day. On the other hand, non-linear dose-response analysis found an increase in stomach cancer risk for more than 45 g alcohol consumption per day [36].

A clinical study findings indicate that smoking is related with a higher mean total symptom burden (including fatigue, nausea, memory loss, hair loss, depression, sleep problems, pain, difficulty concentrating, weight loss, and skin problems) during treatment, as well as a bigger rise in total symptom burden from before the start of cancer therapy to the greatest severity at any point during treatment. Furthermore, it was showed that six months after therapy, the difference in mean total symptom load between smokers and nonsmokers maintained, with smokers having a considerably higher symptom burden. Smokers reported considerably more attention issues, skin disorders, sleep disturbances, weight loss, and despair [37].

Early cytogenetic investigations demonstrate that heroin use affects and causes considerable alterations in chromosomes. Indeed, research involving neonates of heroin addict moms revealed that

chromosomal abnormalities were six to seven times higher than in the control group of newborns of normal mothers. A study found a link between heroin and carcinogenesis. It specifically demonstrated an unexpected rise in the CNS of M2 protein in individuals with acute myeloid leukaemia, which has previously been linked to heroin addiction [38].

Cocaine usage has been reported to impair responsiveness to chemotherapeutic drugs such as imatinib in patients with chronic myeloid leukaemia, most likely due to cocaine's influence on cytochrome P450 [39].

Cannabis smoking appears to be implicated in carcinogenesis, either as an independent component or in conjunction with other mutagens, according to research data, particularly in studies involving the respiratory and gastrointestinal systems of young adults. However, significant histopathologic and molecular alterations in the bronchial epithelium of chronic hashish users have been reported. More histopathologic lesions were observed in systematic smokers than in the nonsmokers in the control group [38].

6. Conclusion

Dietary intake, certain food products, and fasting regiment have an impact on the gastrointestinal side effects of chemotherapy, tumor growth, and treatment clinical effect in cancer patients. A dietary approach focused on the exclusion or limited intake of specific food products, as well as diet improvement, might minimize and avoid chemotherapy-induced gastrointestinal problems, limit tumor growth and/or incidence. and hence should be considered in clinical practice. Nutritional support showed to reduce in-hospital mortality in cancer patient and improve their quality of life.

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