RESEARCH ARTICLE

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Comparative Study of Serum Lipid Profiles in Nepalese Cancer Patients Attending a Tertiary Care Hospital

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Abstract

Significant efforts have been made to study cancer at the biochemical and cellular level and identify factors associated with progression. The aim of this hospital based randomized comparative study at the Nepalese Army Institute of Health science hospital was to assess factors in 52 people diagnosed with different types of cancer and 56 normal control persons. Fasting blood samples were analyzed for serum total cholesterol (TC), high density lipoprotein (HDL), triglycerides (TG) and low density lipoprotein (LDL). We found that biochemical parameter TC, TG, VLDL (very low density lipoprotein), LDL and HDL were significantly different in the cancer patients and healthy controls. Levels of TC, TG, LDL, HDL and VLDL were higher in the age group below 50 and that of TG was found to be higher in women than men. Our results indicate that TC, TG and HDL are increased, while LDL and VLDL are lowered in cancer patients. Our study provides clues to risk factors associated with life style, eating habits, and exercise regimens. Monitoring of these parameters with aging is recommended.

Keywords: Cancer- Triglyceride- Cholesterol- HDL -LDL

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Introduction

Cancer is the leading cause of death in the world. However, cancer mortality is higher in developing countries than in the developed countries (Ferlay et al., 2004), where resources available for prevention, diagnosis, and treatment of cancer are limited or nonexistent. Deaths from cancer in the world are projected to continue to rise, with an estimated 11.4 million in 2030 (WHO, 2007). The word cancer means the change in the body's cells that cause them to grow out of control (Skeel, 2005), where cellular control mechanisms have become deranged in a heritable manner, proliferate uncontrollably and often invasively in the body, eventually destroying their neighbors and frequently causing the death of the organism. Several distinguishing hallmarks of cancer were originally proposed by Weinberg with underlying genetic instability as a major feature of cancer (Weinberg, 2007).

Currently, the role of changes in energy metabolism and interactions between tumor intra and extracellular redox environments are being investigated. It is important to distinguish the biochemical profiles of cells that have been transformed into malignant cells. Biochemical risk factors include an increase in blood glucose, increase in serum triglyceride level, decrease in high-density lipoprotein level and increased concentrations of the hormones estrogen and progesterone in the blood (Mc Tiernan, 2000). Moreover, despite the extensive research for many years throughout the world, the etiopathogenesis of cancer still remains obscure. For the early detection of carcinoma of various origins, a number of biochemical markers have been studied to evaluate the malignancy (Stefanni, 1985). As the chances of cancer incidence in elderly are high, the cancer prevalence may increase dramatically in years to come (Bener et al., 2007). Due to this, cancer has become an important agenda in the health sector of every country.

Lipids form a diverse group of water-insoluble molecules that include triacylglycerides, phosphoglycerides, sterols, and sphingolipids. They carry vital physiological functions like maintenance of the structural and functional integrity of all biological membranes and also have important

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roles in signaling, functioning as second messengers and as hormones. These cellular processes are of critical relevance to cells, which undergo transformation, cancer progression and metastasis. Thus, it is likely that lipids have a determinate role in cancer onset, progression, and outcome.

It is now well demonstrated that hyperlipidemia is a major problem and a potential risk factor for various metabolic, cardiovascular and even genetic-based disorders. (Nordestgaard and Varbo, 2014; Ridker, 2014).There is increasing evidence that cancer cells show specific alterations in different aspects of lipid metabolism (Toshiyuki, 2012). Studies in patients with many types of cancers have demonstrated that levels of plasma lipids and lipoproteins, particularly high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG), have also been postulated to be associated with cancer risk, and they may mediate an effect of dietary fat on cancer risk (Nydegger and Butler, 1972). Up-regulation of lipogenic enzymes and elevated lipogenesis has been shown to occur in many cancers (Mukherjee et al., 2012). Thus, increased fatty acid synthesis may even be required for carcinogenesis and has been linked to other cancer-associated metabolic changes.

Recently, a study has been conducted which suggests that higher levels of total cholesterol and triglycerides may play an important role in carcinogenesis and that the elevated plasma LDL-cholesterol, which is more susceptible to oxidation may result in high lipid peroxidation in breast cancer (Gibanananda and Hussain, 2001) Dysregulated lipid metabolism is an established hallmark of cancer. Consistent with the importance of lipids in cancer, regulatory factors, enzymes, and transporters involved in lipid transport, lipid synthesis, and lipid degradation are dysregulated in cancer cells. The functional consequence of this lipid diversity is still not fully understood. The etiology of lipid changes associated with cancer is multifactorial and the relationship of lipid changes to cancer is still a subject of controversy.

Recent reports have focused renewed attention on the possible role of dietary and endogenous lipids in etiology and prognosis of cancer. A number of epidemiological studies have shown the increased risk of death from cancer with hypocholesterolemia, although several studies proposed the low levels of cholesterol is a predisposing factor for carcinogenesis (Raste and Naik, 2000). Therefore, assessment of total and differential levels of serum lipids may be of little significance in preventing further complication of carcinoma. So the present study was planned to investigate the alteration in the lipid profiles of patients with cancers in Nepalese population.

Material and Methods

This case-control study included 52 clinically and histopathologically approved cancer patients (26 men and 26 women) attending the Birendra Hospital, Chauuni, Nepalese Army Institute of Health Sciences (NAIHS), Kathmandu, Nepal. Control group comprised of age matched 56 apparently healthy individuals without any malignancies were included in this study. All patients were informed about the study and a written consent was obtained from them. Furthermore, 5ml fasting (at least 8 hours) venous blood samples were collected from the selected patients. The methods for the collection and analysis were followed as described by Standard Operating Procedure (SOP) provided. Blood samples were allowed to clot for 15 minutes and then centrifuged for 10 minutes at 3,000 rpm. The separated serum was analyzed for lipid profile parameters such as Total cholesterol (TC), Triglyceride (TG), LDL, HDL and VLDL. For defining dyslipidemia, the reference levels were used as per National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (ATP III) guideline according to which hypercholesterolemia is defined as TC>200mg/dl, hypertriglyceridemia as TAG>150mg/dl, high LDL-C when the value exceeds 100mg/dl and low HDL-C when the value is below 40mg/dl. And presence of any one of abnormalities in serum lipid concentration it was defined as dyslipidemia.

Statistical Analysis

The data was collected on a pre-designed proforma and variables were entered on SPSS version 20. Frequencies and percentages were computed for qualitative variables and variables compared by Chi square test. Mean and standard deviation were calculated for quantitative variables and mean were compared between two groups (cancer and non-cancer status) by using independent sample t-test. Statistical significance will be accepted if $P<0.05$.

Results

In the present study, 56 healthy controls and 52 histologically confirmed cases of different cancers were included. Of our 52 study patients, 11 (21.15%) had lung cancer, 7 (13.46%) had breast cancer, 5 (9.61%) had Oropharynx cancer, 5 (9.61%) had Non-Hodgkin Lymphoma, 3 (5.57%) had Urinary Bladder cancer, 3 (5.57%) had cancer of Rectum, 3 (5.57%) had cancer of Ovary, 3 (5.57%) had cancer of colon, 3 (5.57%) had cancer of cervix, 2 (3.84%) had Pancrease cancer, 2 (3.84%) had Hypopnangnx cancer, 2 (3.84%) had acute myeloid leukemia, 1 (1.92%) had stomach cancer, 1 (1.92%) had prostate cancer and 1 (1.92%) had

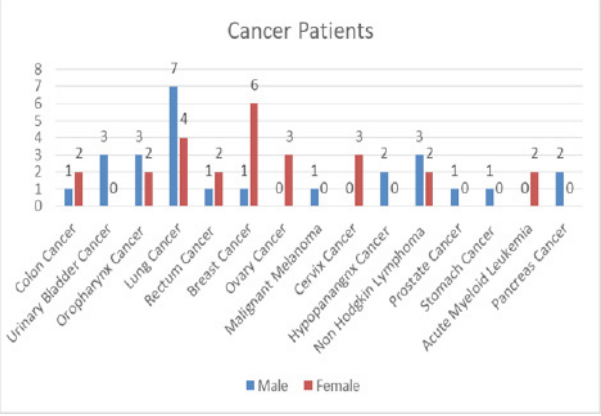

Figure 1. The Frequency Distribution of Different Cancer

Table 1. Serum Levels of Lipids by Cancer Type

Cancer type (N)	Cholesterol	Triglyceride	LDL	HDL	VLDL
Colon Cancer (3)	181.67±19.85	237.67±129.42	102.67±11.71	49.67±5.13	32.67±1.15
Urinary Bladder Cancer (3)	179.67±7.09	153.67±17.09	101.33±15.37	48.00±6.92	28.00+2.00
Oropharynx Cancer (5)	170.80±20.65	142.60±22.59	83.40±8.59	48.40±6.76	30.20±10.66
Lung Cancer(11)	175.27±58.60	144.45±68.31	82.09±26.06	43.55±7.34	31.00±18.09
Rectum Cancer (3)	203.67±32.332	128.00±35.157	108.67±9.452	55.00±14.526	46.33±31.37
Breast Cancer (7)	183.71±42.457	174.57±110.764	85.43±27.585	46.57+4.392	34.86±21.05
Ovary Cancer(3)	182.00±+72.959	171.00±59.573	104.33±36.611	54.67±15.885	30.33±14.74
Malignant Melanoma(1)	157.00	154.00	62.00	44.00+	31.00
Cervix Cancer (3)	173.00±26.211	124.33±58.705	75.00±15.524	43.67±3.215	17.00±4.35
Hypopanangnx Cancer (2)	178.00±0.000	102.00±46.669	89.00±38.184	47.50±4.950	31.50±0.70
Non-Hodgkin Lymphoma (5)	195.80±30.450	107.60±38.057	86.40±33.381	46.60±6.841	18.20±6.18
Prostate Cancer (1)	155	93.00	36.00	36.00	26.00
Stomach Cancer (1)	238	103.00	60.00	45.00	20.00
Acute Myeloid Leukemia (2)	232.00±8.485	191.00±0.000	101.50±14.849	46.50±7.778	56.00±36.770
Pancreas Cancer(2)	184.00±55.154	131.00±63.640	79.00±21.213	45.00±1.414	30.50±2.121
P- value	0.001	0.000	0.000	0.000	0.006

Table 2. The Measurement of Lipid Parameters in Cancer Patients and Control Group

Variable	Cancer patients (52)	Control (52)	P-value
Cholesterol	183.56±40.062	163.73±28.329	0.006
Triglyceride	148.15±68.679	141.13±36.993	0.516
LDL	88.25±23.761	98.19±20.062	0.026
HDL	46.85±7.565	50.71±8.945	0.022
VLDL	30.83±16.569	28.23±7.393	0.111

malignant melanoma. In total, 50% were female, and 50% were male (Figure 1). In our study mean age of cases and controls were 58.0 ±12.39 and 55.59±11.45 years respectively. The maximum age in case of cases was 76 years as compared with the controls where the age was 72 years. The distribution of age was almost equal among cases and controls. Serum levels of TG, TC, HDL-C, LDL-C and VLDL in the cancer patients and controls are summarized in Table 1 as mean ± SD.

Table 1 shows the comparison of T-CHOL, TG, LDL, HDL and VLDL level between different cancer cases. Significant differences were observed for all the lipid parameters among different cancer groups as shown in the table.

Table 2 shows the mean, standard deviation and P values of TC, TG, LDL, HDL and VLDL levels in cancer patients and control groups. The statistics of biochemical parameters computed for cases and controls which point out that the results were found to be TC (183.56±40.06 and 163.2±28.32, P= 0.006), TG (148.15±68.67and 148.13±36.93, P= 0.516), HDL (46.85±7.56and 50.71±8.94, P= 0.022) , LDL (98.25±23.76and 88.19±20.06, P= 0.026) and VLDL (30.83 ± 16.56and 28.23 ± 7.39, P= 0.111) respectively with statistical significance only in total cholesterol, LDL and HDL parameter, where as Triglyceride and VLDL has not shown any statistical significance.

Table 3 shows no significant differences were observed in the levels of total cholesterol, LDL, HDL and VLDL between the gender difference and age groups. However, the triglyceride showed significant difference among different age groups. Similarly, We found a significant difference in the serum levels of triglyceride (P=0.033) levels, which were higher in women than in men, the mean

Table 3. Serum Levels of Lipids by Age and Gender

Characteristics	Cholesterol	Triglyceride	LDL	HDL	VLDL
< 40 years (4)	203.75±58.283	223.25±130.388	103.75±33.886	53.00±14.071	46.50±25.226
40-49 (10)	196.10±47.505	152.90±64.612	92.10±21.031	49.60±8.566	36.80±24.207
50-59 (13)	183.23±41.409	121.08±33.480	79.85±24.620	45.46±5.967	25.85±7.809
60-69 (16)	174.00±26.028	131.19±40.895	90.38±21.382	45.25±5.079	25.38±8.516
>70 (9)	178.11±44.273	178.78±92.253	85.44±25.165	45.89±8.283	34.11±18.591
P- value	0.561	0.040	0.439	0.265	0.080
Gender					
Male (26)	183.73+39.167	128.04+51.947	91.65+23.136	46.12+5.279	46.12±5.279
Female (26)	183.38+41.714	168.27+77.988	84.85+24.339	47.58+9.369	47.58±9.369
P- value	0.976	0.033	0.306	0.492	0.422

of other lipid profiles were similar in both genders were not statistically significant.

Discussion

Effective treatment of cancer now becomes a worldwide challenge. Even though significance advance has been made in cellular, biochemical and clinical level, still there is a need of understanding of cancer in all aspects. Scientist and clinician putting huge effort to overcome the challenges that comes on the way to treatment of cancer. The study was designed to study and understanding the cancer patients visited the hospital and aimed to provide guidelines and awareness against cancer progression in Nepal. This is the first study in Nepal which was carried out the evaluation of biochemical parameters in cancer patients. In the present study, we evaluated the serum levels of lipids associated with the most important prognostic indicators in patients who suffered from different cancers. The data observed from this study, are based on a limited number of subjects, but nonetheless constitute evidence to suggest that lipid metabolism is altered in cancer patients. Furthermore, we were able to analyze the biochemical parameters such as TC, TG, LDL, HDL, and LDL of different cancer patients visited the hospital. We find out the significant biochemical alternation between cancer patients and healthy groups. Cholesterol, HDL, LDL, Triglyceride are important constituents of the cell which carry vital physiological function such as maintenance of the structural and biological functions of the cells. Impairment of these biological and structural functions leads to cause cancer and other diseases. In some malignant disease, blood cholesterol undergoes significant changes in the early stage; an unusual change in the level of cholesterol in the proliferating tissue and in blood compartment could be due to the carcinogenesis. An imbalance of cholesterol in cellular level leads to defects in normal cellular functions, also affect in lipid metabolism may contribute to hypocholesterolemia. The present finding supports the understanding that an unusual increase in the level of the cholesterol and triglyceride in the cancer patients may be due to the failure of the normal function of the malignant cells. In our study cancer patients displayed a higher level of cholesterol and triglyceride levels which further assists the notion that cells undergo cancerous due the unusual alternation of the biochemical parameter that impaired the lipid metabolism within the cells and contributes to undergoes cancerous.

Cholesterol is an important constituent of lipoproteins like LDL, HDL, and VLDL. The pathogenesis of the decreased cholesterol and HDL is not exactly known. It could be due to decreased synthesis or increased catabolism. Cholesterol synthesis by liver could be inhibited by tumor metabolites (Erin Currie et al., 2013). It can be presumed that either it is due to carcinogenesis or predisposing factors. Low HDL cholesterol is an additional predictor of cancer and it may be mediated by utilization of cholesterol of membrane synthesis. Decreased level of HDL increases the level of triglyceride might result in the neoplastic transformation of the cells within cancer patients. In our study, we analyzed the level of HDL and triglyceride in different cancer groups. While evaluating the lipid parameters in different cancers we found that colon cancer , breast cancer , bladder cancer displayed higher level while prostate cancer displayed lowest level of triglyceride in different cancer groups consistent with the level of triglyceride, the level of cholesterol in the patients with colon cancer, rectum cancer, breast cancer and bladder cancer was higher while the level of cholesterol in patients with prostate cancer was also low in patients with different types of cancer. Form our study we can assume that the evaluation of lipid parameters may be helpful to early detection of the possible neoplastic transformation. Alteration of lipid profile can occur in hematological malignancies other than leukemia. The previous study observed that a decrease in TC and HDL level in 128 patients with chronic lymphocytic leukemia and these differences intensified together with the disease progression (Lorenc et al., 1989). Similarly, another study also confirms the decrease in the HDL, LDL, and TC level in patients with newly diagnosed myeloproliferative syndrome, which increased after treatment with chemotherapy (Gilbert and Ginsberg, 1983). Interestingly another study finds that lower HDL level in the presence of an unaltered level of TC was also observed (Dessi et al., 1991). In agreement with these finding our study finds the alter level of all HDL, LDL, Cholesterol level in different types of cancers as well as increased level of triglyceride , cholesterol and decrease level of LDL and HDL in the patients than that of healthy control provide ongoing impairment in the lipid parameter which might trigger neoplastic symptoms. From these finding, it will be reasonable to assume that these lipid profile alteration could serve as one the prognostic factor for an answer to treatment and remission of different cancer progression.

Previously there was an understanding that aging and cancer are opposite processes, cancer is the consequence of an aberrant gain of cellular fitness while aging is characterized by a loss of fitness. At a deeper level, however aging and cancer may share common origins, time-dependent accumulation of cellular damage is widely considered the general cause of aging (Lopez-Otin et al., 2013) Metabolic and biochemical alteration are also a most common hallmark of aging and cancer progression. Our study finds out an association between the alternations of biochemical parameters within cancer patients with growing age. Level of triglyceride was found to be increased in the group of cancer patient who was under the age of 40, significantly less plasma triglyceride level was found with the patients with age after 50, form out result we assume that the significant alternation of plasma triglyceride level may be put high risk of cancer with growing age. We also tried to find out the association of biochemical alternation in cancer patients in age-dependent manner, and it was observed that female patients have higher level of triglyceride than male patients which may suggest female are more susceptible of cancer progression due to the biochemical alteration that of male also we observed the higher cholesterol and triglyceride level in breast cancer patients. Our study is consistent with the previous study which

finds an increased level of triglyceride and decreased the level of HDL and cholesterol in breast cancer patients. (Vinayak et al., 2016).

In this study we profiled the level of lipids parameter including TG, TC, HDL-C, LDL-C in different types of cancer patients and we further compared this parameter with healthy patients. We found the alteration of these parameters was significantly higher in cancer patients compared with the healthy control groups and we also find out that alternation was also in growing aged patients and more especially women were displayed higher alternation than man. Based upon the data presented in this study, we conclude that measurements of serum levels of triglycerides and cholesterol may be useful as additional markers in the observation and clinical follow-up of patients with breast cancer. However, studies with more patients with long term follow up of cases and periodic estimation of lipid profile are needed, to establish the association between lipid profile and cancer patients.

In Conclusion, from our study we can assume that alteration in lipid parameters are critically associated with the neoplastic transformation in biochemical level and proper monitoring of these parameters might be helpful to early detect of the possible risk of cancer in Nepal. However, the need of further research about how these parameters are lead to put in risk of cancer is important. Nevertheless this study provides recommendation of proper monitoring of the lipid level might be helpful to early detection of cancer progression and risk management.

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