Evaluation of Serum Lipids and C-peptide among Breast Cancer Patients with Chemotherapy

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Abstract

BACKGROUND

Chemotherapy agents alter serum lipids and C-peptide in cancer patients increased incidence of cardiovascular disorders and diabetes, although mechanisms for these are not known. Diabetes and cardiovascular riskis the highly concerned chemotherapy induced complications among cancer patients. This study is aimed to evaluate the serum lipids and C-peptide in breast cancer patients receiving chemotherapy.

METHODS

This cross-sectional study includes160 individuals comprising 80 breast cancer patients and 80 controls with age ranges from 24 to 76 years. Patients received at least 3 cycles of chemotherapy. Serum Total cholesterol (TC), high density lipoprotein cholesterol (HDL) andC-peptide level was measuredin random blood sampleswhereas,other lipid parameters like Non HDL (TC-HDL),cardiac risk ratio (TC: HDL) and Non-HDL: HDL werecalculated.

RESULTS

SerumTC, Non-HDL, TC: HDL, Non-HDL: HDL and C-peptide were significantly increased in breast cancer patients as compared to control group (p<0.001). HDL cholesterol level inpremenopausal and postmenopausalpatients was decreased but was not statistically significant different.

CONCLUSIONS

Altered serum lipid parameters and C-peptide indicated the risk of cardiovascular diseases and diabetes in cancer patients. Routine assessments of these parameters are necessary for follow up care during breast cancer management.

KEY WORDS:Breast cancer, chemotherapy,C-peptide, lipid profile

Introduction

Breast cancer (BC) is the most frequently occurring cancer among women and it has become the major public health problem worldwide representing 25% of all female cancers in 2012 [1, 2].Among Nepalese women, it is the second most common type of cancer accounting 6% of total cancers in Nepal [3]. More than one quarter of the BC diagnosed in Nepal is inyoung female with familial history of breast cancer, early pregnancy, longer lactation and estrogen exposureand tumors oftenshowing aggressive biological behaviors [4-6].Among chemotherapeutic agents, anthracyclines based treatment regime were reported to cause cardiotoxicity by increasing intramyocardial free radical production, lipid alterationsanddecreasing antioxidant level by adversely affecting dietary intake and nutritional status of the patients [7-9].Cancer cells reprogram their enzyme and signaling pathways to meet higher need of building blocks required for abnormal proliferation and their survival [13-17]. An association between altered lipids metabolism, diabetes, cardiovascular riskand other metabolic dysregulation with chemotherapy has been identified but underlying mechanismis not clear. The present study aimed to evaluate the serum lipids and C-peptidelevels inBCpatients undergoing chemotherapy.

Methods

This is a hospital based cross-sectional study conducted atDepartment of Pathology,Bhaktapur Cancer Hospital (BCH), Bhaktapur, Nepal.A total of 80 BC undergoing neoadjuvant/adjuvant treatment at least receiving three cycles of chemotherapy from September 2013 to February 2015 were enrolled. The study protocol was approved by Ethical Review Board of Nepal Health Research Council (NHRC) and informed consent was taken from each participants. The chemotherapeutic regime for breast cancer included a combination of anticancer drugs of 5-fluorouracil, doxorubicin (adriamycin) and

cyclophosphamide (FAC). Histopathologically confirmedBCpatients of 24 to 76 years withoutany previous history of cancer and metabolic disorders like diabetes, cardiovascular disorder, thyroid were only included in the study. Eighty healthy women of similar age group were taken as control. We collected3ml of blood sample in non-fasting condition as per convenient to patients.And the non-fasting condition for lipids determination is now accepted as per Special Report by Clinical Chemistry, 2016.Blood samples were allowed to clot and centrifuged at 3000 rpm for 10 minutes to obtain the serum. Serum samples were then stored at -20˚C in two aliquots for lipids and C-peptideuntil analysis.

Serum levels of total cholesterol (TC) were estimated by Cholesterol Oxidase Peroxidase (CHOD-PAP)method using Human reagents kits (HUMAN Gesellschaft fur Biochemica und Diagnostica mbH, Germany) whereas, high density lipoprotein cholesterol (HDL) by precipitation method on semi-automated analyzer (Stat Fax 3300, USA), while serum C-peptide was determined using ELISA method (Cortez Diagnostic Inc., USA). Non-HDL cholesterol(TC-HDL), TC: HDL and Non-HDL: HDLwas calculated mathematically from estimated total cholesterol and HDL-cholesterol. Standard laboratory operating procedure was followed and Biorad (Bio-Rad Lab, Hercules, CA, USA) was used to validate the internal quality control.

The data obtained was tabulated analysed and the statistical differences between the groups were assessed in Statistical Package for the Social Sciences version 17 (SPSS, Chicago, IL). Means and standard deviations were calculated for TC, HDL, Non-HDL,TC: HDL and Non-HDL: HDL. Pearson correlation (*P*) was used to measure the relationship among parameters and *P* value of 0.001 or less was considered statistically significant.

Results

In the present study, out of 80 breast cancer patients aged between 24 to 76 years, 37 were premenopausal and 43 were postmenopausal women. Similarly ascontrols 80 healthy women of age group 21 to 77 years were enrolled comprising 38 premenopausal and 42 postmenopausal women.

TCand Non-HDL level was found to be increased in patients as compared to control while, decreased level of HDL was observed in patients than control group [Figure 1].
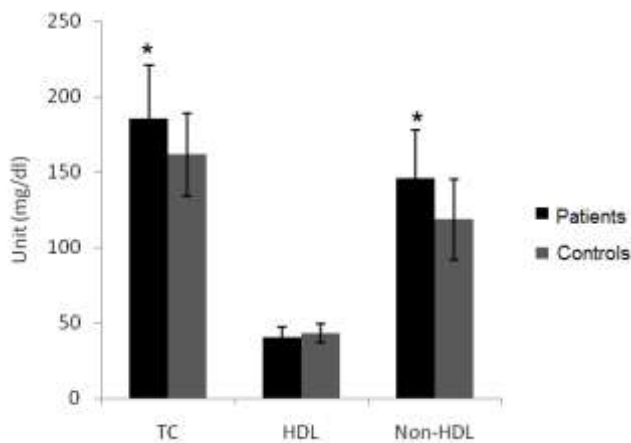

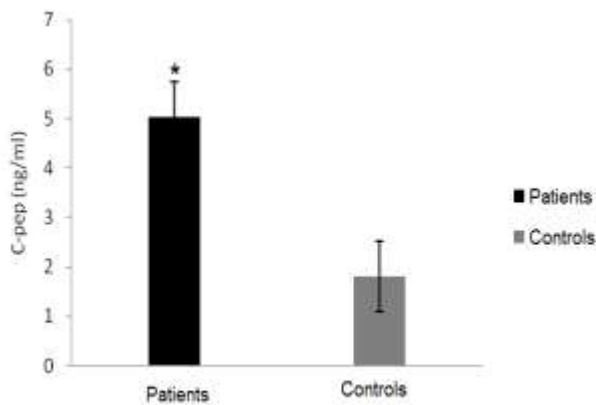**Figure 1: Comparision of mean value of Lipid parameters among cases and controls**

Figure2: MeanC-peptidelevel among cases and controls

The mean distribution of serum lipid parameters and C-peptide among BC patients and control group are shown in [Table 1]. The serum level of TC, Non-HDL, TC: HDL, Non-HDL: HDL and C-peptide was found to be increased in both pre and post-menopausal breast cancer patients as compared to their respective control group and the differences were statistically significant (P value <0.001). However, serum HDL level in breast cancer patients although found decreased as compared to control group but differences were statistically not significant (P value =0.014) for premenopausal patients and (P value=0.071) for postmenopausal patients.

DISCUSSION

Cancer cell signals directly regulate the activity and expression of DNA, RNA, lipids and proteins metabolizing enzymes that provide proteins and lipid molecules, membrane building blocks,posttranslational protein modifications and rapid energy supply for proliferating cancer cells by continuous lipogenesis [12,13].Human mammary tissues metabolize plasma lipids andthe breast cancer malignancy in women has been associated with change in plasma lipids, lipoproteins and female gonadal hormone level [14]. However, many epidemiological studies

Table 1. Mean Lipids and C-peptide levelsin pre and postmenopausal breast cancer patientscompared to controls

Parameters	Premenopausal		Postmenopausal	
	Controls (n=38)	Patients (n=37)	Controls (n=42)	Patients (n=43)
Total cholesterol (mg/dl)	160.72±29.10	186±37.06*	162.35±26.14	184.51±33.98*
HDL-cholesterol (mg/dl)	43.47±6.58	40.51±7.16	42.52±5.86	40.25±6.95
Non-HDL-cholesterol (mg/dl)	117.25±28.68	147.83±33.79*	119.83±25.13	144.25±30.85*
TC: HDL	3.86±0.69	4.67±0.93*	3.76±0.78	4.64±0.79*
Non-HDL:HDL	2.86±0.69	3.73±0.95*	2.76±0.78	3.64±0.79*
C-peptide (ng/ml)	1.84±0.74	4.99±2.24*	1.77±0.68	4.89±2.49*

*Significant at *P* value less than 0.001.

explored the contradictory causal association between dyslipidemia and breast cancer incidence [15, 16]. Furthermore, previous studies revealed incidence of diabetes, lipid dysregulation and altered nutrients metabolism during the breast cancer management with chemotherapy [9, 10, 17].

In this study, we investigated the levels of lipid and C-peptide in breast cancer patients. We found increased level of serum TC in both pre and postmenopausal breast cancer patients as compared to their respective control group. Our findings were in accordance to the several other studies [18-21].An increased level of TC was observed in breast cancer patients on chemotherapy as compared to control but the differences were not statistically significant [9, 26].In contrast to our finding, a study by Timovska et al found decreased level of serum total cholesterol after two courses of neoadjuvant chemotherapy [22].In the present study, we observed decreased HDL- cholesterol level in breast cancer patient but the difference was statistically non significant as compared tocontrol group. The previous studies conducted on breast cancer patients reported unchanged or slightly decreased HDL-cholesterol level in breast cancer patients as compared to control group [9, 20, 21]. A few

other studies reported significantly decreased HDL-cholesterol level in breast cancer patients [18, 23, 26].In contradict to our study; Peela et alfound significantly increased level of HDL-cholesterol in breast cancer patients as compared to control [19].

Non-HDL cholesterol level in the present study was found to be increased in breast cancer patients as compared to control group. Non-HDL cholesterol includes low density lipoprotein cholesterol(LDL), very low density lipoprotein cholesterol (VLDL) and all other forms of bad cholesterol. Different studies observed LDL-cholesterol level was found to be elevated in breast cancer patients than the control [14, 20, 21, 23].A prospective study by Santos et alreported LDL-cholesterol is highly associated with breast cancer progression and the patients with high levels of LDL-cholesterol have reduced chance to survive disease free [15]. A study by Nwozo et al found no significant difference in LDL-cholesterol level in breast cancer patients on chemotherapy as compared to control [9].

In this study, TC: HDL and Non-HDL: HDL ratios were found to be significantly increased in patients as compared to control. Our result is similar to the study by Hasija et alobserved highly significant TC: HDL and Non-HDL: HDL

ratios in both pre and postmenopausal BC patients [14].

Serum C-peptide level was found to be significantly elevated in both pre and postmenopausal breast cancer patients as compared to their respective control. Our finding was in accordance to the study conducted by Yadav et alon breast cancer patients [5]. A study by Irwin et alreported an increased C-peptide levelin breast cancer survivoris associated with higher risk of breast cancer related death [11, 24].A population based study found increased risk of diabetes among postmenopausal breast cancer survivors and patients who received adjuvant chemotherapy [17].

A study by Chaudhary et al reported increased incidence of obesity or weight gain during breast cancer management [27].In this study we observed altered metabolism of lipids and C-peptide as the consequences of BC chemotherapy. In Nepal, the study on biochemical parameters has not been well documented in cancer patients during the course of chemotherapy. We are hopeful that the study will improveour understanding on treatment, its complications and status of biochemical parameters in BC patients. Further research is necessary to explore the relation between cancer management and induced metabolic disorders.

Conclusions

As a conclusion, our study shows the altered lipids and C-peptide leveloccur in BC patients receivingchemotherapy. The increased levels of serum lipids and C-peptidesuccessfully explored the fact that there exist increase risk of cardiovascular disease and diabetes during the

breast cancer management. The observed results suggest routine assessment of lipid profile, cardiac risk markers and diabetic markers is necessary for effective cancer management. Diabetes and cardiovascular diseases screening and preventing strategies among BC patients need to be practiced in order to decrease the treatment induced complications and increase the survival rate.

The sample size of our study was small. Hence, further studies dependent on extended sample size, dose and frequency of chemotherapy and follow up patients need to be conducted. More studies including other biochemical parameters in fasting condition are necessary to exploreorgan toxicity and treatment related complications.

Conflict of Interest

None declared.

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