

CORRELATION OF BREAST CANCER AND SERUM HIGH DENSITY LIPOPROTEIN CHOLESTEROL LEVEL: A SINGLE CENTRE STUDY

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ABSTRACT

Breast cancer is the most common site specific cancer in women. Lots of etiological factors have been suggested regarding its causation. The risk is influenced by obesity, parity, exogenous and endogenous hormones, exposure to chemicals and radiation and many more. Various studies suggest that as HDL-C seems to be cardio protective, it is also protective for breast cancer. Serum HDL-C levels are found to be low in breast cancer patients. We studied this hypothesis in local population of Southern Rajasthan and nearby region to see if low serum HDL-C is associated with increased risk of breast cancer. We studied serum HDL-C level in 50 female patients of breast cancer along with their menopausal status and compared it to their respective controls. We found that breast cancer patients had significantly low level of serum HDL-C and presented in advanced stage of cancer. It supports that low serum HDL-C level is associated with increased risk of breast cancer. So one should think about those dietary and lifestyle measures, which maintain high serum HDL-C level so that it might become preventive measure for breast cancer.

KEYWORDS

Breast Cancer, High Density Lipoprotein Cholesterol, Risk Factors, Pre-menopausal, Post-menopausal.

HOW TO CITE THIS ARTICLE: Anjali Sethi, Deepak Sethi. "Correlation of Breast Cancer and Serum High Density Lipoprotein Cholesterol Level: A Single Centre Study." *Journal of Evolution of Medical and Dental Sciences* 2015; Vol. 4, Issue 97, December 03; Page: 16224-16228, DOI: 10.14260/jemds/2015/2388

INTRODUCTION

Breast Cancer is the most common site specific cancer in women and a leading cause of death due to cancer between 40-45 years of age. It has now become a global disease. It accounts for 33% of all female cancer and 20% of cancer related death in women.

The exact cause of breast cancer is not known but sex hormones, both endogenous and exogenous play an important role. Exposure to radiation and chemicals can also stimulate the onset of disease.⁽¹⁾ The risk of breast cancer is also influenced by dietary fat intake, obesity, parity, duration of breast feeding, family history and socio-economic status.⁽²⁾ Breast cancer is considered to be consequences of high fat consumption.

There may be chemical carcinogen in fatty fried diet and altered bacterial flora in intestine leads to increased production of carcinogenic substances. Serum lipid profile is an important marker of dietary fat intake.⁽²⁾ Various studies indicate that plasma triglycerides and LDL-C levels were found to be significantly elevated among breast cancer patients,⁽³⁾ but HDL-C level were observed to be significantly low as compared to control.^(1,4,5) It raises a question that HDL-C seems to be protective in breast carcinogenesis.

Serum HDL-C levels are found to be low in breast cancer patients. We studied this hypothesis to see if low serum HDL-C is associated with increased risk of breast cancer.

We studied the correlation between serum HDL-C (HDL) level and female breast cancer and clinical staging in local population of Southern Rajasthan and nearby region in the patients who consulted to our Tertiary Care Level Hospital.

ABBREVIATIONS

HDL-C (HDL)–High Density Lipoprotein Cholesterol
 LDL–Low Density Lipoprotein
 VLDL–Very Low Density Lipoprotein
 USG–Ultrasonography
 FNAC–Fine Needle Aspiration Cytology
 CL–Confidence Limit
 SR-BI–Scavenger receptor class B type I.

METHOD AND MATERIAL

We studied 50 patients of breast cancer. Patients were diagnosed on basis of detailed history, clinical examination, mammography, USG, FNAC, and Tru-Cut biopsy. Lifestyle parameters like socio-economic status, age of menarche, menopausal status, use of oral contraceptives, hormone replacement therapy, etc., were also evaluated.

HDL (HDL-C) was estimated in venous blood samples of patients. Blood sample of 50 controls were also analyzed for HDL-C. Controls were those females who were not suffering from breast cancer, but fell in same age group. HDL-C was detected in lab by direct homogenous assay method.

Females who presented in stage I and II were included in early stage and those in stage III and IV were included in advanced stage.

Expected Normal Range

Adult Male–54.5±12.9mg/dl

Adult Female–61.2±12.3mg/dl

Financial or Other, Competing Interest: None.
 Submission 17-11-2015, Peer Review 18-11-2015,
 Acceptance 26-11-2015, Published 01-12-2015.

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DOI:10.14260/jemds/2015/2388

OBSERVATION AND DISCUSSION

When we explored our data, we found that mean age of breast cancer patients was 48.32 years (Control 49.96 years). Out of 50 patients who entered in our study, 48% were pre-menopausal (Control-46%) and 52% were post-menopausal (Control 54%). Among these patients 44% presented in early stage (Stage I and II) of cancer and 56% in advanced stage (Stage III and IV) (Table 1, 2, 3).

When we analyzed HDL-C level in our patient, we found that mean HDL-C level in patient was 41.83mg% (Control 46.11mg%). In pre-menopausal patients mean HDL-C was 41.67mg% (Control 45.59mg%) and in post-menopausal patients mean HDL-C was 41.99mg% (Control 46.72mg%) (Table 4, 5) (Graph 1, 2, 3 and 4).

We found a significant difference in HDL-C level in breast cancer patient and their control ($p < 0.05$; 95% CL), but no relation was seen with respect to menopausal status. It suggests that low HDL level is associated with increased risk of breast cancer in local population of Southern Rajasthan and nearby region irrespective of menopausal status.

For post-menopausal women, our findings are similar to Furberg who suggested that the risk of breast cancer was inversely related to highest quartile v/s lowest quartile.⁽⁶⁾ Hoyer found a relative risk of 0.3/women in highest quartile of HDL-C compared to those of lowest quartile.⁽⁷⁾

Various other studies also support our findings related to HDL-C and breast cancer.^(8,9) Contrary to it Moorman found a positive association between HDL-C and post-menopausal breast cancer, but an inverse association in pre-menopausal women.⁽¹⁰⁾ Tretli found no such association.⁽¹¹⁾ Ferraroni showed a tendency towards higher level of HDL-C among pre-menopausal women.⁽¹²⁾

Lipoproteins are large macromolecular complexes that transport hydrophobic lipids (Primarily triglycerides, cholesterol, and fat-soluble vitamins) through body fluids (Plasma, interstitial fluid, and lymph) to and from tissues. Lipoproteins play an essential role in the absorption of dietary cholesterol, long-chain fatty acids, and fat-soluble vitamins; the transport of triglycerides, cholesterol, and fat-soluble vitamins from the liver to peripheral tissues; and the transport of cholesterol from peripheral tissues to the liver. Lipoproteins contain a core of hydrophobic lipids (Triglycerides and cholesteryl esters) surrounded by hydrophilic lipids (Phospholipids, unesterified cholesterol) and proteins that interact with body fluids.

The plasma lipoproteins are divided into five major classes based on their relative density: chylomicrons, Very Low-Density Lipoproteins (VLDLs), Intermediate-Density Lipoproteins (IDLs), Low-Density Lipoproteins (LDLs), and High-Density Lipoproteins (HDLs). Each lipoprotein class comprises a family of particles that vary slightly in density, size and protein composition.

The density of a lipoprotein is determined by the amount of lipid per particle. HDL is the smallest and most dense lipoprotein, whereas chylomicrons and VLDLs are the largest and least dense lipoprotein particles. Most plasma triglyceride is transported in chylomicrons or VLDLs and most plasma cholesterol is carried as cholesteryl esters in LDLs and HDLs.⁽¹³⁾

HDL is synthesized and secreted from liver and intestine. HDL is an important component of metabolism and may influence the risk of breast cancer in women with

positive energy balance.⁽⁶⁾ Its level is affected by various factors like dietary fat intake, alcohol consumption, endogenous hormones and pre-menopausal leanness. Increase in any of these factors is known to increase the level of HDL-C. HDL-C appears to possess biological properties that may be relevant to carcinogenesis.⁽¹⁴⁾ HDL-C has a great potential to counter the oxidative damage in cell membrane by preventing lipid peroxidase and act as antioxidant and anticarcinogen. Because plasma HDL-C level are decreased they are not sufficient enough to counter ROM attach thereby resulting in higher oxidative stress, which may cause cellular and molecular damage leading to cell proliferation and malignant transformation of mammary cells.⁽⁹⁾

Borrelli found that breast cancer patient had higher concentration of HDL-C, both in pre- and post-menopausal women. This could be explained by an increased oestrogenic activity and its role in modulation of lipid metabolism.⁽¹⁵⁾ Sex hormones affect HDL-C level by regulating two enzymes namely lipoprotein lipase and hepatic endothelial lipase.⁽¹⁶⁾ Androgen lowers the plasma HDL and increase LDL level. Oestrogen has opposite effect by rising HDL and lower LDL level. After menopause as oestrogen level falls, HDL level also decreases.⁽¹⁷⁾

HDL stimulates the proliferation of human breast cell, especially in hormone independent cells.⁽¹⁸⁾ Frank exposed breast cancer cell lines to HDL and noticed that signaling pathways involved in cancer progression were activated and that the cells began to migrate in an experimental model mimicking metastasis. The study supports the idea that HDL plays a role in development of aggressive breast cancers and that inhibiting its function via SR-BI in breast cancer cells may stall cancer growth.⁽¹⁹⁾ It suggests that HDL and SR-BI have a pro-oncogenic activity and can act as a potential target for treatment of breast cancer.⁽²⁰⁾

SUMMARY

In our study we found that serum HDL-C level was significantly low in breast cancer patients and the finding was more pronounced in patients with advanced disease. HDL-C and breast cancer, both are influenced by dietary fat intake, weight, pregnancy, endogenous hormone, smoking, physical activity and socio-economic status.

World cancer research and American Institute of Cancer Research have estimated that incidence of cancer in worldwide could be reduced to 30-40% by dietary modification. BMI should be in range of 18.5-25. Fruits and vegetables should provide 7% or more of energy intake. Protein and starchy food should provide 45-60% of total energy.

In local population of Southern Rajasthan and nearby region we found that menarche was late, women were usually multiparous; fed their babies for a long time. They usually did not use exogenous hormones. Most of them were physically active involving in farming and household works and were thin built. They ate lesser amount of fruits, vegetables and fiber diet; and usually ate maize and wheat as their staple food.

We found that low serum HDL-C level is associated with increased breast cancer risk. High HDL-C seems to be protective for breast cancer. So we should think about those dietary and lifestyle measures, which maintain high HDL-C level in blood, so that it may be used as a preventive measure for breast cancer.

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Age of Breast Cancer Patients and Controls				
Age	Cases (n = 50)		Controls (n = 50)	
	N	%	N	%
<30	3	6.00	0	0.00
31-40	12	24.00	11	22.00
41-50	18	36.00	21	42.00
51-60	11	22.00	11	22.00
>60	6	12.00	7	14.00
Total	50	100.00	50	100.00

Table 1

Menopausal Status of Breast Cancer Patients and Controls				
Menopausal Status	Cases		Controls	
	N	%	N	%
Pre-menopausal	24	48.00	23	46.00
Post-menopausal	26	52.00	27	54.00
Total	50	100.00	50	100.00

Table 2

Staging of Breast Cancer v/s Menopausal Status						
Stage	Pre-menopausal (n=24)		Post-menopausal (n=26)		Total	
	N	%	N	%	N	%
Stage I (n = 0)	0	0	0	0	0	0
Stage II (n=22)	7	29.1	15	57.1	22	44.0
Stage III (n=16)	10	41.6	6	23.0	16	32.0
Stage IV (n=15)	7	29.1	5	19.8	12	24.0
Total	24	100.0	26	100.0	50	100.00

Table 3

HDL Level V/s Staging in Pre- and Post-menopausal Breast Cancer Patients								
HDL Level	Pre-menopausal				Post-Menopausal			
	Early Stage	Advance Stage	Total		Early Stage	Advance Stage	Total	
			N	%			N	%
<=40	3	11	14	58.30	7	6	13	50.0
41-45	3	2	5	20.80	6	1	7	26.92
46-50	0	2	2	8.33	0	2	2	7.69
51-55	0	0	0	0.00	0	1	1	3.85
>55	1	2	3	12.50	2	1	3	11.54
Total	7	17	24	100.00	15	11	26	100.00

Table 4

HDL Level of Controls						
HDL	Pre-menopausal		Post-menopausal		Total	
	N	%	N	%	N	%
<=40	7	30.43	6	22.22	13	26.00
41-45	2	8.70	4	14.81	6	12.00
46-50	6	26.09	4	14.81	10	20.00
51-55	5	21.74	9	33.33	14	28.00
>55	3	13.04	4	14.81	7	14.00
Total	23	100	27	100	50	100.00

Table 5



