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ESTIMATION OF BIOCHEMICAL PARAMETER OF HUMAN BREAST CARCINOMA IN DIFFERENT LOCALITIES AROUND CHENNAI CITY, TAMIL NADU.

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ABSTRACT

One hundred and eighty breast cancer subjects were considered and classified into three groups according to their age: 31-40, 41- 50 and 51- 60 years. They were clinically diagnosed at different hospitals located in an around Chennai City, Tamilnadu, India. Hematology analyzers provide accurate quantitative information about blood cells and can even identify specimens with abnormal cells. It was used for *in vitro* diagnostic use in clinical laboratories. The instrument employs a non-optical scanning system providing a counting rate in excess of six thousand individual cells per second with a counting interval of 15 seconds. All the biochemical parameters of total protein, Total cholesterol, HDL cholesterol, albumin, globulin, urea, bilirubin, triglycerides, low-density lipoprotein, very low-density lipoprotein, acid phosphatas, SGOT, alkaline phosphatase, SGPT, LDH were analyzed by using colorimetry. This study suggesting that there was a significant increase in total plasma, lipids, total cholesterol, LDL - cholesterol, VLDL, Phospholipids, triglycerides, free fatty acids in malignant breast cancer patients. The present study also revealed that this work is very useful for the diagnosis of a broad range of breast pathologies and as far as we are concerned, similar work had not been made in the literature.

KEYWORDS: Carcinoma breast, Total protein, Total cholesterol, HDL Cholesterol, Albumin,Globulin, Urea, Bilirubin, triglycerides, low-density lipoprotein, Very low-density lipoprotein, Acid phosphatas , SGOT, Alkaline phosphatase, SGPT, LDH, Colorimetry.

INTRODUCTION

While cancer account for high morbidity and high mortality rate throughout the world, cancer of breast is common in women in developed countries and more than 40% of all breast cancer cases are found in developing countries. Cancer that is detected early can potentially be cured when the tumor is small enough to be completely removed surgically unfortunately, most cancers do not produce any symptoms until the tumors are either too large to be removed surgically or cancerous cells have already spread to other tissues. Harries *et al*., (2005) explained that majority of patients (97%) had normal creatinine, and increased age was associated with decreased creatinine. An increase in creatinine was associated with increased risk of breast cancer. Increased creatinine was associated with an increased risk of fever and henpropenia or haematological toxicity. The prevalence of metabolic syndrome (obesity, glucose intolerence) is high and increasing in parallel with an increasing breast cancer incidence worldwide.Serum high density lipoprotein cholesterol, metabolic profile and breast cancer risk (Furberg *et al.*, 2004). Overexpression of LDL receptors occurs in several cancer cell lines and offers a unique strategy for drug targeting by using LDL as vehicle. LDL concentrates much more in malignant breast tumor tissue than in normal tissue (Graziani *et al.*, 2002). Fasting serum TG and VLDL cholesterol levels were found to be significantly increased and HDL cholesterol levels significantly decreased in patients with breast cancer. Furthermore, a significant increase in TG, VLDL and decreases in Total, HDL and LDL levels were demonstrated in patients with breast cancer (Kokoglu *et al*., 1994). There was a significant increase in body weight, plasma lipids, total cholesterol, LDL, VLDL, phospholipids, TG, FFA in malignant breast cancer patients. HDL-cholesterol had been significantly decreased in benign and malignant patients when compared with the control subjects (Kumar *et al*., 1991). Elevated level of lipid associated gialic acid was found, that was specifically reflected only in LDL and VLDL fractions. Breast cancer patients were found to have higher concentrations of both total cholesterol and high HDL. A good correlation was found in lipoprotein analysis (Shanmugam and Nagarajan, 1994). Women found to have breast cancer had significantly higher plasma triglyceride values than did the women without breast cancer (Potischman *et al*., 1991). The serum total alkaline and total acid phosphatases within the breast cancer group were variable with significant elevation of both enzymes compared with the corresponding control values. The increased activities of alkaline phosphatases as well as acid phosphatases are suggestive of increased activities of oestoclast and oestoblasts associated with bone metastasis (Agbedana and Ebesunun, 1998).

Alkaline phosphatase can be used as a better marker for detection of metastasis tumors in breast and colon cancers (Walack *et al*., 1996). Plasma acid and alkaline phosphatase were significantly higher in patients with breast cancer metastases than in patients without (Nguyen *et al*., 1991). Epidemiological data suggest that higher fat diet increases the risk of developing breast cancer, both in animal and human population. Cases of postmenopausal, untreated women with malignant and benign breast tumour, were compared for their age, body, weight, plasma lipid fractions and lipoproteins (kumar *et al*., 1991). Biochemical liver function tests from serum and liver biopsy specimens in patients with first recurrence of breast cancer. The presence of liver metastases was not associated with age, menopausal status, and size of the primary tumour and regional lymph node status. The patients with liver metastases (Kamby *et al*., 1987) were significantly closer to menopause. The serum bilirubin and serum aspartate amino transferase analysis was significantly better than alkaline phosphatase and lactate dehydrogenase analyses, whenever indicated by clinical signs or elevated blood tests, an besides, it also increased urea levels in breast cancer patients (Agbedana and EbesUnun 1998).

Medical literature shows several examples of an inverse relationship between serum albumin levels and survival in patients with advanced cancer (Lis *et al*., 2003). Univariate statistical analysis found that low levels of serum albumin adversely affected survival by a statistically significant level for all stages of breast cancer. A baseline serum albumin level was a powerful prognostic variable, which accounted for variation in patient survival time. Oncogenic transformation of cultured mammalian cells cause a rapid increase of glucose transport Machick *et al*., (2005) reported that several factors have been implicated in the regulation of glucose transport expression in breast cancer. Serum total, different isoforms of both alkaline and acid phosphatase, liver function enzymes, calcium, inorganic phosphates, heamatocrit, white blood cells and platelet counts were determined in 50 female patients suffering from breast cancer (Agbedana and Ebesunun. 1998). The serum total alkaline and total acid phosphates within the breast cancer group with significant elevation of both enzymes compared with the corresponding control values. Macheda *et al.,* (2005) examined that malignant cells are known to have high glucose requirements and increased glucose uptake. Transport of glucose across the plasma membrane of mammalian cells is the first rate - limiting step for glucose metabolism and is mediated by facilitative glucose transported proteins. Buck *et al.,* (2004) reported that breast cancer is associated with increased glucose consumption.

Cualach and Gwl (1996) reported that peripheral blood leucocyte alkaline phosphatase score and serum alkaline phosphatase levels in 70 patients with metastatic breast and colorectal cancer was significantly higher than in the control. Lee *et al.*, (1982) reported that the peripheral blood specimen were obtained from 50 patients with various stages of breast cancer. There are significant differences of hemoglobin, LDH, SGPT, serum protein, albumin and alpha globulin values among patient, with stage IV disease an those patients with metastases had significantly higher values for alkaline phosphates. Nauyen *et al*., (1991) examined that the acid value in case of bone metastases and alkaline phosphatase were significantly higher in patients with metastases than in patients without.

MATERIALS AND METHODS

CREATININE

Creatinine analysed using modified Jaffe's method (Allen, 1982). The creatinine levels were calculated by the following formula

Calculation

$$\text{Creating Conc. (mg/dL)} = \frac{(T_2 - T_1) \text{ of sample}}{(T_2 - T_1) \text{ of Standard}} \times 2$$

GLUCOSE

God -Pod method (Kaplan *et al.*, 1984) was used to estimate glucose from the samples. The formula used to estimate glucose as follow.

Calculation

$$\text{Serum / Plasma Glucose (mg / dL)} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \times 100$$

SERUM GLUTAMIC PYRUVIC TRANSAMINASE (SGPT)

SCPT estimation was done by UV Kinetic (IFCC) Method (International Federation of Clinical Chemistry, 1976).

ALKALINE PHOSPHATASE

pNPP- AMP (IFCC-International Federation of Clinical Chemistry, Tietz, *et al.*, 1983 method adopted for alkaline phosphatase analysis.

Calculation

$$\text{ALP activity (IU/L)} = \Delta A / \text{minute} \times \text{Kinetic factor}$$

Calculation using following formula

$$\mathbf{K} = \frac{1}{M} \times \frac{TV}{SV} \times \frac{1}{P} \times 10^5$$

M = Molar extinction coefficient of p- Nitrophenol and is equal to 18.8×10^3 lit / mol / cm at 405 nm

TV= Sample volume + Working Reagent volume

SV = Sample volume

P = Optical path length

$\mathbf{10^5}$ = Constant

TRIGLYCERIDES

Enzymatic GPO-PAP method (Herbert & Kaplan, 1984) was adopted for triglyceride analysis.

Calculation

$$\text{Triglycerides (mg/dL)} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \times 200$$

Glycerol free Triglyceride= Calculated Triglycarde - 10mg/dL

HDL CHOLESTEROL (Grove, 1979 & NCEP, 2001)

Calculations

The HDL cholesterol concentration in the sample is calculated using the following general formula:

$$\frac{A_{simple}}{A_{standard}} \times C_{standard} \times \text{Sample dilution factor} = C_{sample}$$

If the HDL Cholesterol Standard provided has been used to calibrate.

$$\frac{A_{simple}}{A_{standard}} \times 52.5 = \text{mg/dL HDL cholesterol}$$

$$\times 1.36 = \text{mmol/L HDL cholesterol}$$

TOTAL PROTEIN

Modified Biuret method (Koller & Kaplan, 1984) was performed to total protein analysis.

Calculation

$$\text{Total Protein concentration (g/dL)} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \times 6.5$$

Globulins = Total Protein – Albumin

CHOLESTEROL

CHOD - PAP method (Herbert & Kaplan, 1984) was taken up

Calculation

For Total Cholesterol

$$\text{Cholesterol Concentration (mg/dL)} = \frac{\text{Absorbance of Test}}{\text{Absorbance of Standard}} \text{ x } 200$$

ALBUMIN

Bromocresol Green (BCG) Method (Lloyd-Luke, 1979).

Calculations

Results are calculated, usually automatically by the instrument, as follows.

$$\text{Albumin (g/dL)} = \frac{\text{Absorbance of Unknown}}{\text{Absorbance of Calibrator / Standard}} \times \text{Value of Calibrator / Standard}$$ **Calibration**

Calibrations are required. A suitable bovine or human albumin standard (S) or a serum based calibrator is recommended.

GLOBULIN

Globulin (g/dL) = Total Protein (g/dL) – Albumin (g/dL)

ALBUMIN / GLOBULIN RATIO

$$\text{Albumin / Globulin (A/G) Ratio} = \frac{\text{Albumin (g/dL)}}{\text{Globulin (g/dL)}}$$

LACTATE DEHYDROGENASE (LDH)

Method UV Kinetic (Tietz, 1986) was used for **Lactate Dehydrogenase**

Calculation (light path 1 cm)

LDH [IU/L] = A/min. x Factor.

25°C 37°C

Factor at 340 nm	10080	20000

UREA

Modified Berthelot Method was performed for urea analysis.

BILIRUBIN

Diazo kinetic Method was performed for Bilirubin estimation.

RESULT

Biochemical Analysis

Estimation of Blood Glucose

Blood glucose level of overnight fasting was found to be higher in all the age groups the control (97.60 ± 11.59). A linear increase in the blood glucose levels was observed (Fig: 1) in 31-40 years of age with a value 137.43 ± 3.97, 160.73 ± 4.94, 41-50 years age group of glucose and 190.37 ± 4.87 of glucose in the subjects under 51-60 years age group which was much higher than the control. A significant difference at 1% level (p-value < 0.01) in the blood glucose level with an F-value of 928.15 was revealed in all the age groups. The multiple range test (Tuckey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05).

Estimation of Blood Urea

Increase in the concentration of blood urea was recorded over the control value (17.50 ± 1.28) in all the age groups of the subjects of overnight fasting. Eventually linear increase in the blood urea was observed (Fig: 1) in 31-40 years age group with 21.23 ± 2.03; 41-50 age group with 26.40 ± 2.16, and 28.53 ± 1.85 in the age group of 51-60 years. A significant difference at 1% level (p-value < 0.01) in the urea concentration was confirmed by the F-value of 928.15. The multiple range Test (Tuckey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups.

Estimation of Creatinine

When the blood creatinine was analyzed, the age group 51-60 years showed enhanced creatinine concentration (1.98 ± 0.13) over the control (0.67 ± 0.17). Similarly age group 41-50 too showed higher creatinine level (1.41 ± 0.13). The age group 31-40 revealed a marginal increase (0.85 ± 0.09) over the control but lesser than the other two categories of age. A significant difference at 1% level (p-value < 0.01) in the creatinine concentration was

affirmed by an F-value of 583.69. The multiple ranges test (Tuckey–HSD Test) also inferred a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups (Fig: 2).

Estimation of Bilirubin

An increase in bilirubin concentration was revealed in all the blood samples of the varied age groups. Maximum concentration was observed in 51-60 years of age (3.98 ± 0.30) followed by 41-50 years of age (2.78 ± 0.21) and 31- 40 years age group (1.7 8 ± 0.21) in contrast to the control (0.67± 0.27). A significant difference at 1% level (p-value < 0.01) in the bilirubin was indicated by the F-value of 977.91. The multiple range test (Tuckey – HSD Test) confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups (Fig: 2).

Estimation of Albumin

Albumin was found to be lower over the control (4.22 ± 0.42) in all the age groups. Correspondingly a linear decline in the albumin values was revealed (Fig: 3) the first age groups of 31-40 years showed 3.91 ± 0.30 of albumin, 41-50 years age group with 3.45 ± 0.29 of albumin; and 2.81 ± 0.46 of albumin in the 51-60 years age group. A significant difference at 1% level (p-value < 0.01) in the albumin was confirmed by the F-value of 79.56. The multiple range test (Tuckey -HSD Test) evidenced a significant difference at 5% level (p-value > 0.01 & < 0.05) all the three age groups.

Estimation of Globulin

An increase in globulin concentration was noticed with maximum value in 51-60 years of age (6.33 ± 0.23) followed by 41-50 years of age (5.25 ± 0.17) and 31- 40 years of age (6.33 ± 0.23), and the control value was 2.86 ± 0.31. A significant difference at 1% level (p-value < 0.01) in the globulin concentration was justified by the F-value of 1196.68. The multiple range test (Tuckey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in the age groups (Fig: 3).

Estimation of Total Protein

An increase in total protein concentration was also observed in the age groups of 51-60 years (9.14 ± 0.56); followed by 41-50 years (8.70 ± 0.35) and 51- 60 years (9.14 ± 0.56) in contrast to the control (7.08 ± 0.51). A significant difference at 1% level (p-value < 0.01) in

the total protein was evidenced by the F-value of 112.74. The multiple ranges Test (Tuckey-HSD Test) also validated a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 3).

Albumin - Globulin Ratio

The maximum ratio / concentration was observed in 51-60 years of age (0.45 ± 0.06) followed by 41-50 years of age (0.66 ± 0.06) and 51- 60 years of age (0.45 ± 0.06) over the control (1.49 ± 0.23). A significant difference at 1% level (p-value < 0.01) in the Albumin – Globulin Ratio was confirmed by the F-value of 356.36. The multiple ranges test (Tuckey-HSD Test) indicated a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 3).

Estimation of Total Cholesterol

The maximum value was observed in 51-60 years of age (248.90 ± 5.06) followed by 41-50 years of age (227.17 ± 4.16) and 31-40 years of age subjects (200.00 ± 4.84) and were higher than the control (159.60 ± 5.76).A significant difference at 1% level (p-value < 0.01) in the total cholesterol was affirmed by the F-value of 1784.69. The multiple range test (Tuckey–HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 4).

Estimation of Triglycerides

An increase in triglycerides concentration was due to the maximum in 51-60 years of age (205.50 ± 8.80) followed by 41-50 years of age (179.90 ± 2.52) and 31- 40 years of age (162.10 ± 4.25), over the control (140.00 ± 4.84). A significant difference at 1% level (p-value < 0.01) in the triglycerides was confirmed by the F-value of 736.10. The multiple range test (Tuckey-HSD Test) also evidence a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 4).

High-density lipoprotein

A gradual decline in high-density lipoprotein concentration was observed in 51-60 yrs of age (31.50 ± 2.27) followed by 41-50 years of age (36.54 ± 2.26) and 31-40 years age group subjects (48.27 ± 4.34) the control (48.27 ± 4.34). A significant difference at 1% level (p-value < 0.01) in the high-density lipoprotein was validated for the F-value of 1784.69. The

multiple range test (Tuckey-HSD Test) also justified a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 4).

Low-density lipoprotein

An increase in Low-density lipoprotein concentration was 51-60 years of age group (139.63 ± 4.87) followed by 41-50 years (119.90 ± 2.52) and 31-40 years subjects (109.80 ± 2.58) over the control (90.00 ± 4.84). A significant difference at 1% level (p-value < 0.01) in the low-density lipoprotein was evidenced by the F-value of 852.97. The multiple range test (Tuckey-HSD Test) confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 4).

Very low-density lipoprotein

Very low-density lipoprotein concentration showed the maximum value in 51-60 years of age group (60.83 ± 2.07) over the control (22.97 ± 5.73), followed by 41-50 years age group with 48.13 ± 3.01 and 31-40 years age group with 37.50 ± 1.11. A significant difference at 1% level (p-value < 0.01) in the very low-density lipoprotein was due to the F-value of 653.67. The multiple range test (Tuckey-HSD Test) indicated a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 4).

Total Cholesterol/ HDL ratio

Total cholesterol / HDL ratio was found to be higher in control age groups. The subjects 51-60 years showed the lowest value. The highest value was 3.28% and the lowest value was 2.78% in the age group 51–60 years (Fig: 4). A significant difference at 1% level (p-value < 0.01) in the Total cholesterol / HDL ratio was due to the F-value of 71.19 observed. The multiple range test (Tukey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) all the age groups.

Acid Phosphatase

Acid phosphatase was found to be maximum in the age group of 51 –60 years (4.74) are a minimum in the age group of 31–40 years (3.98). The age group 41–50 revealed a value of 4.41. The control value was 2.84. The Tuckey- HSD Test showed a significant difference at 1%level (p-value < 0.01) in the serum acid phosphatase as indicated by the F-value of 244.83. The multiple range test (Tuckey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups (Fig: 5).

Alkaline Phosphatase

An increase in alkaline phosphatase concentration was the age group 51-60 years (307.50 ± 5.81) followed by 41-50 years of age (287.50 ± 3.96) and 31-40 years of age (267.10 ± 4.25), over the control (22.97 ± 5.73). A significant difference at 1% level (p-value < 0.01) in the alkaline phosphatase was confirmed by the F-value of 368.73. The multiple range test (Tuckey-HSD Test) also validated a significant difference at 5% level (p-value > 0.01 & < 0.05) (Fig: 6).

Serum Glutamate Oxaloacetate Transaminase

Highest concentration (58.83 ± 2.07) was observed in 51-60 years group followed by 41-50 years group (48.30 ± 2.26) and 31-40 years group (38.50 ± 1.74), over the control (25.50 ± 2.92). A significant difference at 1% level (p-value < 0.01) in the Serum Glutamate Oxaloacetate Transaminase was ensuring by the F-value of 1155.47. The Tuckey-HSD Test also inferred a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Fig: 5).

Serum Glutamate Pyruvate Transaminase

Maximum serum glutamate pyruvate transaminase concentration was due to 51-60 years age group (60.83 ± 2.07) followed by 41-50 years age group (49.43 ± 2.46) and 31-40 years age group (38.70 ± 1.99) over the control (26.73 ± 2.65). A significant difference at 1% level (p-value < 0.01) in the serum glutamate pyruvate transaminase was justified by the F-value of 1200.16. The Tuckey–HSD Test also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups (Fig: 5).

Serum Lactate Dehydrogenase

The maximum value was observed in 51-60 years age group (430.07 ± 28.59) followed by 41-50 years age group (398.87 ± 35.97) and 31-40 years age group (383.40 ± 19.13) over the control (297.23 ± 37.94). A significant difference at 1% level (p-value < 0.01) in the serum lactate dehydrogenase was affirmed by the F-value of 99.05. The multiple range test (Tuckey-HSD Test) also evidenced a significant difference at 5% level (p-value > 0.01 & < 0.05) all the age groups (Fig: 6).

Fig: 1 Glucose & Urea Level in Breast Cancer Patients of Different Age Groups.

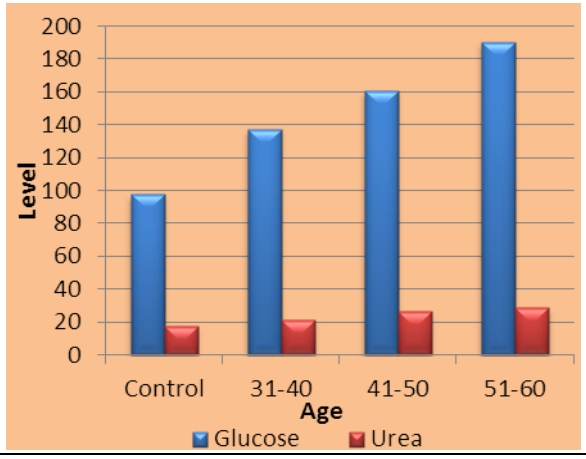


Fig: 2 Creatinine & Bilirubin Level in Breast Cancer Patients of Different Age Groups.

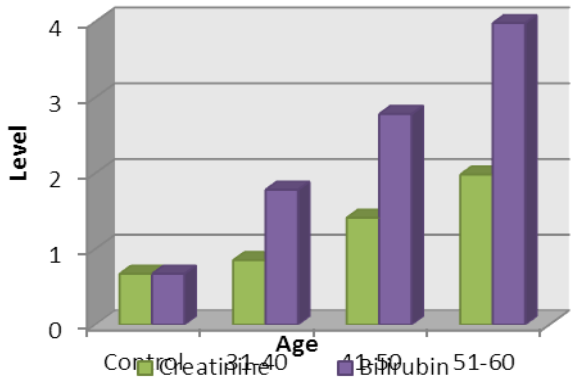


Fig:3 Albumin, Globulin, Total Protein & Albumin / Globulin Ratio in Breast Cancer Patients of Different Age Groups.

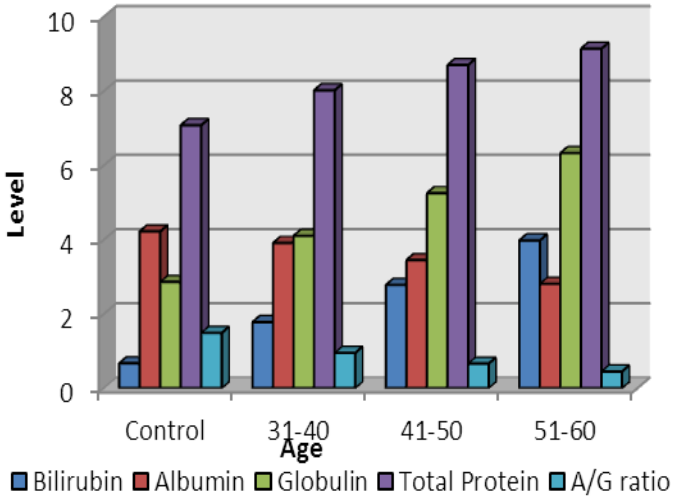


Fig:4 Total Cholesterol, Triglycerides, HDL, LDL,VLDL & Total Cholesterol/ HDL ratio Level in Breast Cancer Patients of Different Age Groups

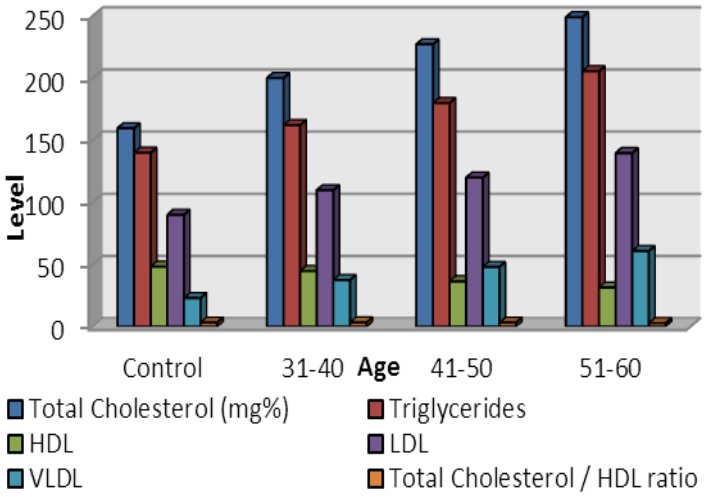


Fig: 5 Serum Acid Phosphatase, SGOT & SGPT Level in Breast Cancer Patients of Different Age Groups.

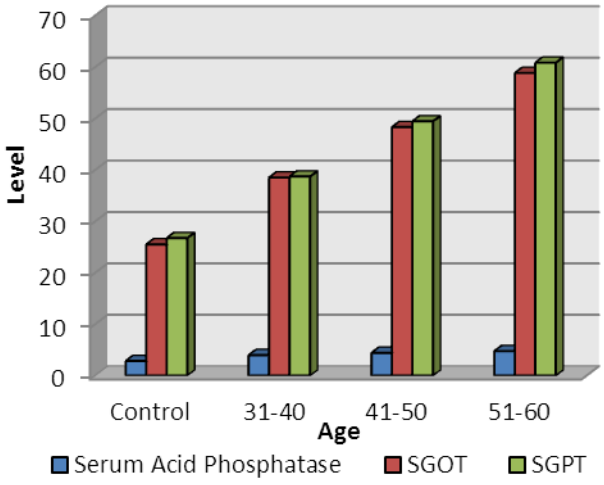
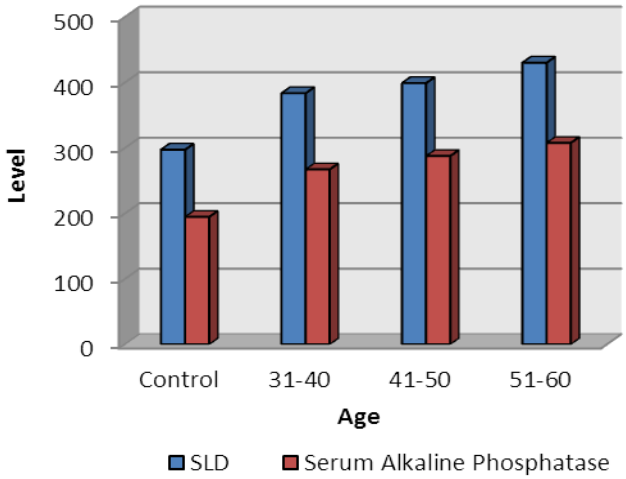


Fig: 6 SLDH & Serum Alkaline Phosphatase Level in Breast Cancer Patients of Different Age Groups.



DISCUSSION

In the present investigation the concentration of blood glucose showed an age related increase in all the breast carcinomas. According to Furberg *et al.*, (2004) incidence of breast cancer worldwide increases with increase in the prevalence of metabolic syndrome (obesity and glucose intolerance). Previous studies have demonstrated an association between diabetes mellitus and cancer risk. Cancer risk is associated with subclinical impaired glucose tolerance. Rapp *et al.*, (2006) investigated the relation between fasting blood glucose and the incidence of cancer and these findings prove that elevated blood glucose is associated with the incidence of several types of cancer in men and women. The present study also revealed increased glucose level in the breast carcinoma subjects. Hyperglycemia is commonly manifested in them. Breast cancer is associated with increased glucose consumption (Buck *et al*., 2004). Current research also revealed increased blood glucose levels in breast carcinoma. An association between various types of cancer and the continuous risk across the spectrum of glucose tolerance may be important in determining the nature of the association between diabetes mellitus and the risk of malignancy (Dawson, 2004).

According to the investigations of Muti *et al.*, (2002) in postmenopausal women, the associations of glucose, the insulin and IGF-I pattern were associated with breast cancer risk in heavier subjects characterized by a body mass index higher than 26. These results indicate that chronic alteration of glucose metabolism is related to development of carcinoma. The incidence of breast cancer was 60% higher among diabetic women than among non-diabetic women (Mink *et al.,* 2003). The study by Augustin *et al.*, (2001) supports the hypothesis of moderate, direct associations between glycemic index or glycemic load and breast cancer risk. Hyperinsulinaemia is positively associated with breast cancer in both pre-and postmenopausal women (Lawlor *et al.*, 2004). Prolonged increase in blood glucose leads to increase in insulin in the blood. In the present study an increased level of blood glucose was evident in all age group of patients and it is statistically significant.

An increase in creatinine and urea levels was observed in all the breast cancer patients under study. The degree of increase was associated with the increase in the age of the patients. Hurries *et al.*, (2005) suggests, in most of the breast carcinoma, a progressive decline in renal function with aging which is also applicable to normal aging breast carcinoma subjects. Accordingly an inverse relation exists between blood creatinine and increased creatinine level in the blood suggests that there is decreased creatinine clearance. The present study revealed

a lower creatinine and urea clearance in the breast carcinoma with correspondingly increase in the creatinine concentration. So creatinine clearance has to be considered to reduce toxicity in the subjects of treatment for the ailment.

Alkaline and acid phosphatases, enzymes of liver calcium inorganic and phosphatase were determined in 50 subjects with increased urea levels (Agbedana and Ebesunum 1998). The current research also confirmed on increased levels of urea in the subjects of age 51-60 when compared to the control. In some of the patients the urea levels fall in line with the normal range but in the majority a statistically significant increase in the urea levels was observed.

Twelves *et al.,* (1991) investigated 52 breast carcinoma with and liver metastasis and all of them showed serum aspartate aminotransferase enzymes more than twice the upper limit of normal or raised bilirubin. According to Kamby *et al.,* (1987) the occurrence of liver metastases can be evaluated by ultrasonic scanning and correlated with prognostic factors, pattern of metastases, clinical examination, biochemical liver function tests from serum. The diagnostic value of clinical examinations was comparable to that of serum bilirubin (elevated levels) and serum aspartate aminotransferase analysis. The present study shows a considerable elevation of serum bilirubin in the subjects and this might be taken as a clinical sign of liver metastases in breast carcinoma.

Agbedana and Ebesunun (1998) reported that the activities of alanine and asparatate transferase were higher than the control while those of serum albumin were decreased. The current research also proved a statiscally significant decline in the serum albumin level. Serum protein concentration (Seidel *et al*., 2005), changes in the malignant processes and the role of albumin concentration in transport efficiency and the binding characteristics are apparent.

Proteomic based approaches are utilized to study the natural history and treatment of breast cancer (Wulfkuhle *et al*., 2001). It provides critical information on protein level and posttranslational modifications. Medical literature shows several examples of an inverse relationship between serum albumin levels and survival in patients with advanced cancer (Lis *et al.,* 2003). Univariate statistical analysis found that low levels of serum albumin adversely affected survival by a statistically significant level, for all stages of breast cancer. Serum albumin, bilirubin and uric acid levels were determined by Simon Ching *et al.,* (2001).

They observed decrease in serum albumin and increase in bilirubin in all the breast carcinoma subjects, and it falls in line with the present investigation showing decreases in serum albumin and increase in bilirubin.

A steep rise in the concentration of LDL, VLDL, TG and total cholesterol was observed in all the subjects. Several studies have reported lower levels of HDL in breast carcinoma. Graziani *et al.*, (2002) observed over expression of LDL receptors in several cancer cell lines and offered a unique strategy for drug targeting by using LDL as a vehicle. LDL concentrations were much higher in malignant breast tumor tissue than in normal tissue. HDL cholesterol is associated with increased postmenopausal breast cancer risk (Furberg *et al.*, 2004). Serum triglycerides (TG) and VLDL cholesterol levels were found to be significantly increased and HDL cholesterol levels significantly decreased in them. Furthermore a significant increase in TG, VLDL and decreased in HDL level was demonstrated in the subjects with breast cancer (Kokoglu *et al*., 1994). There was a significant increase in bodyweight, plasma lipids, total cholesterol, LDL, VLDL, phospholipids, TG and free fatty acids in breast carcinoma. HDL cholesterol was significantly decreased in benign and malignant cases when compared to the control subjects (Kumar *et al*., 1991). In the current study also, high levels of total cholesterol, LDL, VLDL and triglycerides have been observed with statistically significance. Similarly, elevated levels of lipid, specifically LDL and VLDL fractions were found in breast cancer patients (Shanmugam and Nagarajan, 1987).

Low serum HDL is an important component of the metabolic syndrome and has recently been related to increase breast cancer risk in overweight and obese women. There has been a differently proportional relationship between breast density and healthy metabolic profiles. Besides, the low serum HDL reflects an unfavorable hormonal profile, in particular, increased levels of estrogen and gives further clues to breast cancer risk in these women (Furberg *et al*., 2005). Furthermore low HDL, is associated with increased postmenopausal breast cancer risk and it is in tune with the present investigation showing low HDL in post menopause stage (51-60) compared to the younger age groups.

Lipids and lipoproteins have been associated with breast cancer risk. Triglycerides were significantly higher in women with breast cancer (Goodwin *et al.*, 1997). Present study also reported an elevation of all the parameters like LDL, VLDL, and TG. The increased levels were proved to be statistically significant. A correlation was found between high serum blood lipoproteins and decreased survival of breast cancer patients less than 50 years of age.

Increasing obesity was correlated with decreased survival with breast cancer. In studies of cancer risks in relation to serum cholesterol level, the different fractions of cholesterol were specifically (Tornberg and Canstensen, 1993). The breast cancer patients had significantly higher plasma triglyceride values than the normal women (Potischman *et al.,* 1991).

Serum concentration of cholesterol and triglycerides were investigated in patients with advanced breast cancer (Zielinski *et al.,* 1988). The rise in serum level of triglycerides and /or cholesterol should receive increased attention and could indicate progression or recurrence of breast cancer. The current research also found increased level of cholesterol and triglycerides in all the subjects. The association between total cholesterol and triglycerides and the rate of breast cancer has been examined in Norwegian women with breast cancer by Vatten and Foss, (1990). Lipid measures were taken between 35 –51 years of age. There was an inverse relation between serum cholesterol and risk of breast cancer, which was confined to women diagnosed before the age of 51. The incidence rate ratio was highest in women of high serum cholesterol levels. The present study also found that triglycerides and total cholesterol level was increased in the women diagnosed with breast cancer.

The total serum alkaline and total acid phosphatase within the breast cancer group showed significant elevation compared with the corresponding control values. The increased activities of alkaline phosphatase as well as acid phosphatase are suggestive of increased activities of oestoclasts and oestoblasts associated with bone metastases (Agbedana and Ebesunun, 1998). The determination of alkaline phosphatase isoenzymes is a non-invasive reproducible and rapid method to detect progressive disease in breast cancer especially in combination with to the tumor markers CA 15-3 and CEA (Ritzke *et al*., 1998).

Alkaline phosphatase can be used as a better marker for the detection of metastasis tumor in breast and colon cancer. Alkaline phosphatase should be introduced into the routine check up of breast and colon cancer patients and could be a helpful non-specific additional element detecting earlier metastasis disease during the follow up of a patient. There is a possibility that a sudden rise in alkaline phosphatase in an otherwise healthy person (Walach and Gur, 1995). Acid and alkaline phosphatase were significantly high in patients with breast cancer metastasis than in normal women. (Nguyen *et al.,* 1991). Measurement of alkaline phosphatase isoenzyme activity, though less sensitive than imaging procedures, can assist in screening for, and in early detection of, a high proportion of bone and liver metastases and it provides useful objective evidence of their response to treatment (Mayne *et al.,* 1987). The

current study also revealed that acid and alkaline Phosphatase were found be elevated in early stage of the disease. Alkaline phosphatase was also abnormal in a major proportion of subject with bone and liver metastases (Lee *et al.*, 1982). SGOT and SGPT were also sensitive with liver metastases (Crivellari *et al.*, 1995). Similarly valid diagnosis of liver metastases can be done using serum LDH levels. Elevated levels of serum LDH upto three or four times above the normal are suggestive of liver metastases (Kamby *et al.*, 1987).

In the same way SGOT, Alkaline phosphatase and alpha globulin were significantly higher and developed recurrent or metastatic disease. Infact LDH levels can be helpful in predicting the survival of the patients (Lee, 1985). Generally a rise in activity of the transaminases (GOT and GPT), lactic dehydrogenase was observed after trauma and metastases. The highest rate of enzymatic activity was in proportion to the seriousness of the tumor (Thorbeck and Valentin, 1979) and serum LDH level is enhanced in 80 percent of breast carcinoma (Khan *et al.*, 1991).SGOT, SGPT, LDH levels were found to be increased in the breast carcinoma subjects, in the present investigation.

CONCLUSION

Epidemiological data suggest that high fat diet increase the risk of developing breast cancer, in human population. Case of postmenopausal untreated women with malignant and benign breast tumour, were compared for their age, body weight, plasma lipid fractions and lipoproteins. There was a significant increase in body weight, total plasma, lipids, total cholesterol, LDL - Cholesterol, VLDL, Phospholipids, triglycerides, free fatty acids in malignant breast cancer patients. The present study also revealed that this work is very useful for the precocious optical diagnosis of a broad range of breast pathologies and as far as we are concerned, similar work had not been made in the literature.

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