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RESEARCH ARTICLE

EFFECT OF HAEMATOLOGICAL CHANGES IN BREAST CANCER AMONG THE CHENNAI POPULATION

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ABSTRACT

Hematology diagnostics is growing increasingly important as one of the most fundamental types of clinical testing. The haemotological parameters namely Mean corpuscular, Mean corpuscular haemoglobin, Mean corpuscular haemoglobin concentration, Haemotocrit, Haemoglobin, Red blood corpuscles, Red cell distribution, Erythrocytes and Monocyte are decreased when compare to control but Platelet, Mean platelet volume, Total white blood corpuscular and Lymphocyte count are decreased among the three groups of cancer patients. The present study confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) for the three age groups.

INTRODUCTION

Breast cancer globally has increased (Bray *et al.,* 2004) among women; breast cancer remains one of the most common cancers. The maiden global analysis that factored in the trend over the past three decades shows the number of new breast cancer cases diagnosed worldwide has increased dramatically from about 6.4 lakhs in 1980 to 16 lakhs in 2010.Uttar Pradesh recorded the highest number of breast cancer deaths among states in 2010 (8,882) followed by Maharashtra (5,064), Bihar (4,518), West Bengal (4,095), Andhra Pradesh (3,863), Madhya Pradesh (3,179) and Rajasthan (3,097). Gujarat recorded 2,632 deaths, Kerala 1,618, Haryana 1,118 and Orissa 1,885. Delhi recorded an estimated 810 deaths due to breast cancer in 2010 compared to 779 in 2009 and 749 in 2008. When it comes to states recording low breast cancer mortality rate, Lakshwadeep recorded the lowest with three deaths followed by Andaman and Nicobar Islands with 19 deaths. The north-eastern states also showed low levels of breast cancer deaths. Sikkim recorded 30 deaths, Mizoram 49 and Arunachal an estimated 63 deaths (The Times of India, 2011). By the end of 2007, an estimated 178,480 women are expected to be diagnosed with invasive breast cancer and 40,460 women will have died of breast cancer (American Cancer Society 2005). For many years, breast cancer incidence and mortality rates have been the highest in North America and Northern Europe (Verkooijen *et al.*, 2003), intermediate in Southern Europe and Latin America, and the lowest in Asia and Africa (Parkin *et al*., 2005). Studies of immigrants to North America and Northern Europe suggest that environmental factors, rather than genetic factors, are mainly responsible for this variation between countries (Parkin and Fernandez, 2006). Breast tissue is unique due to its complex hormonal influences and dramatic changes during various life events. Individual hormonal levels and metabolism are affected by environmental factors, and some frequently used chemical and metals have the ability to disrupt endocrine function, and thus mimic the effects of estrogen (Martin *et al.,* 2003). Recently, there has been a growing interest in understanding whether exposure to toxic and cancer-causing (carcinogenic) chemicals contribute to the increasing number of breast cancer cases worldwide. Unfortunately, relatively few studies have investigated the impact of these environmental chemicals on general human health and even fewer have addressed the roles that known carcinogens, such as metals, may play a role in the initiation, promotion and progression of breast cancer (LaSalle, 2008). In women, breast cancer is common and leads to significant morbidity and mortality. Early diagnosis of the disease and accurate recognition of life-threatening A 34-year-old healthy parous woman presented with a palpable lump in the left breast. Breast cancer is known to have a long latency period; there may be several decades between the initiation of the carcinogenic process and clinical detection (Colditz and Frazier 1995; Ostrowski *et al.,* 1999). The present study carryout the breast cancer affects the blood component.

MATERIALS AND METHODS

Collection of sample

One hundred and eighty breast cancer subjects were considered and classified into three groups according to their

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age: 31-40, 41- 50 and 51-60 years. They were clinically diagnosed at Government General Hospital, Chennai, Royapettah Government Hospital, Chennai and Adyar cancer Institute, Chennai, India. Among the breast cancer patients blood was collected and analyzed with Automated Haematology analyzers.

Experiments

Blood was obtained from patients clinically diagnosed patients, collected by heel prick into microtainers containing K3EDTA. Blood samples were processed within 4 h (National Committee for Clinical Laboratory Standards, 1992; ICSH, 2003, American Society for Clinical Pathology, 2006.). The blood was collected by phlebotomist collects a 3- or 5-mL K3 EDTA tube on all aged 1 year and older following established venipuncture protocol and procedures (a 1-2% dilution effect occurs in this liquid EDTA tube). The collected blood loaded in the automated blood cell counters (All the analytical aspects can be evaluated using the ICSH guidelines for the evaluation of blood cell analyzers.) measure or calculate the following parameters: hemoglobin content of RBCs, hematocrit, RBC count, mean corpuscular volume (MCV) of RBCs, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, mean platelet volume, and WBC count with differential. The data were analyzed with multiple range test (SPSS 11.5 version; Tuckey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) for the three age groups.

RESULTS

In view of age, the breast cancer subjects were categorized into three groups of a 31-40, 41-50 and 51-60 years for hematological parameters (Table 1-2) were subjected to statistical Tuckey – HSD Test.

Mean Corpuscular Volume (MCV)

MCV of 51-60 years subjects was the least (67.48 ± 1.41) followed by the subjects of 41-50 years (74.58 ± 2.21). The highest MCV was observed in 31-40 years (77.41 ± 1.46). There is a linear decrease in the MCV values as the age increases in the breast cancer subjects under study (Table 1 & Figure 1). Multiple range test (Tuckey-HSD Test) on MCV revealed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups and the statistical analysis (one way ANOVA) fortified a significant difference at 1% level with p value < 0.01 and F-value of 149.86.

Mean Corpuscular Hemoglobin

Mean Corpuscular Hemoglobin (MCH) level was found to be low in all the age groups compared to the control (28.97 ± 1.27). The MCH level was found to be lesser (Table 2 & Graph 1) in the age group of 51-60 compared to 41-50 (21.57 ± 1.01) and 31-40 years subjects (26.23 ± 1.25). Further more ANOVA on MCH showed a significant difference at 1% level (p-value < 0.01) in all the age groups (F-value 465.90). Besides, the Tuckey-HSD Test confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) (Table 1 & Figure 1).

Mean Corpuscular Hemoglobin Concentration

The Mean Corpuscular Hemoglobin Concentration (MCHC) level of all the breast cancer subjects were calculated and analyzed (Table 1 & Figure 1). The subjects under 51-60 years age group showed a decreased MCHC (23.51 ± 0.92) compared to the control (33.38 ± 1.20). The subjects in the age group 41-50 also showed a decrease in MCHC values (27.16 ± 1.17) than the control but higher than 51-60 years age group. The subjects under 31-40 years age group showed a least value (31.10 ± 1.20) compared to the control but higher than the other age groups. A significant difference at 1% level (p-value < 0.01) in the MCHC with an F-value of 483.64l for all the age groups was recorded. The multiple range test (Tuckey-HSD Test) also inferred a significant difference at 5% level (p-value > 0.01 & < 0.05) within the three age groups (Table 1 & Figure 1).

Hematocrit

Packed Cell Volume (HCT) was found to be lower in all the age groups compared to the control value (41.62 ± 2.18). A linear decrease in the HCT values was noticed (Graph 1) and the age group 31-40 showed 37.51 ± 1.52 of HCT, 41-50 years showed 32.72 ± 1.47 and 27.53 ± 1.54 in the subjects of 51-60 years (Table 1). A significant difference at 1% level (p-value < 0.01) in the HCT with an F-value of 382.99 was recorded. The multiple range test (Tuckey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) within the three age groups (Table 1).

Hemoglobin

Hemoglobin (Hb) was also found to be lower in all the age groups of the compared to the control (13.80 ± 1.06). Accordingly a linear decrease in the Hb values (Figure 1) as 31-40 years age group with 11.98 ± 0.55%, 41-50 years age of 10.25 ± 0.44% and 7.97 ± 0.54% in 51-60 years age (Table 5) was recorded. A significant difference at 1% level (p-value < 0.01) in the Hb with an F-value of 388.94 for all the age groups was noticed. The multiple range test (Tuckey-HSD Test) also validated a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Table 1 & Figure 1).

Red Blood Corpuscles

When the Red Blood Corpuscles count of all the breast cancer subjects was assessed (Table 6 & Graph 2), the patients under 51-60 years showed a 50% decrease in the RBC count (2.40 ± 0.22) compared to the control (4.79 ± 0.33). The subjects under the age group 41-50 also showed a decrease in RBC count (3.40 ± 0.22) over control and it was higher than 51-60 age group. Similarly the subjects under 31-40 years showed a marginal decline (4.34 ± 0.19) compared to the control. A significant difference at 1% level (p-value < 0.01) in the RBC count with an F-value of 559.00 was recorded. The multiple range test (Tuckey-HSD Test) also inferred a significant difference at 5% level (p-value > 0.01 & < 0.05) (Table 1 & Figure 1).

Red cell Distribution Width

Red cell Distribution Width (RDW) was found to be higher in all the age groups compared to the control value (13.21 ± 1.12). A linear increase in the RDW values were observed among the three categories (Graph 2) as 31-40 years age group showed 15.86 ± 1.06%, 41-50 years age group showed

Table 1: The haemotological parameter of MC, MCH, MCHC, Haemotocrite, Haemoglobin, RBC and Red cell distribution in the blood sample of breast cancer patients.

Blood component	Age groups	(Mean ±SD)	F-Value	P-Value
Mean corpuscular (MC)	Control	84.80^{d} ±5.67	149.86	0.000**
	31-40	77.41^{c} ± 1.46		
	41-50	74.58^{b} ±2.21		
	51-60	67.48^{a} ±1.41		
Mean corpuscular haemoglobin (MCH)	Control	28.97^{d} ± 1.27	465.90	0.000**
	31-40	26.23^{c} ±1.25		
	41-50	21.57^{b} ±1.01		
	51-60	17.60^{a} ±1.52		
Mean corpuscular haemoglobin concentration (MCHC)	Control	33.38^{d}±1.20	483.64	0.000**
	31-40	31.10^{c}±1.20		
	41-50	27.16^{b}±1.17		
	51-60	23.51^{a}±0.92		
Haemotocrit	Control	41.62^{d}±2.18	382.99	0.000**
	31-40	37.51^{c}±1.52		
	41-50	32.72^{b}±1.47		
	51-60	27.53^{a}±1.54		
Haemoglobin	Control	13.80^{d}±1.06	388.94	0.000**
	31-40	11.98^{c}±0.55		
	41-50	10.25^{b}±0.44		
	51-60	7.97^{a}±0.54		
Red blood corpuscles	Control	4.79^{d}±0.33	559.00	0.000**
	31-40	4.34^{c}±0.19		
	41-50	3.40^{b}±0.22		
	51-60	2.40^{a}±0.22		
Red cell distribution	Control	13.21^{d}±1.12	619.06	0.000**
	31-40	15.86^{c}±1.06		
	41-50	19.85^{b}±1.12		
	51-60	24.84^{a}±1.15		

** Significance at 1% level.

Different alphabets (a,b,c,d) between age group denote significance at 5% level.

P-value is less than 0.001, there is difference between age group with haemotologial parameter, based on Tuckey-HSD test.

Table 2: The haemotological parameter of Erythrocytes, platelet count, Mean platelet volume, Total white blood corpuscular, Lymphocyte count and monocyte count in the blood sample of breast cancer patients.

Blood component	Age groups	(Mean ±SD)	F-Value	P-Value
Erythrocytes	Control	12.27^{a} ±4.43	206.47	0.000**
	31-40	17.49^{b}±1.45		
	41-50	22.21^{c}±1.60		
	51-60	29.98^{d}±2.93		
Platelet count	Control	2.98^{b}±0.69	83.38	0.000**
	31-40	2.00^{a}±0.26		
	41-50	2.78^{b}±0.16		
	51-60	3.60^{c}±0.23		
Mean platelet volume	Control	8.44^{d}±1.28	177.38	0.000**
	31-40	6.52^{c}±0.30		
	41-50	5.49^{b}±0.28		
	51-60	4.52^{a}±0.30		
Total white blood corpuscular	Control	8360.0^{a}±926.10	344.67	0.000**
	31-40	11987.0^{c}±300.27		
	41-50	12520.0^{d}±274.68		
	51-60	10757.0^{b}±411.63		
Lymphocyte count	Control	42.60^{a}±4.40	116.61	0.000**
	31-40	57.87^{d}±4.24		
	41-50	55.47^{c}±2.74		
	51-60	52.77^{b}±1.25		
Monocyte count	Control	2.97^{a}±0.54	178.40	0.000**
	31-40	4.00^{b}±0.53		
	41-50	5.06^{c}±0.54		
	51-60	6.00^{d}±0.53		

** Significance at 1% level.

Different alphabets (a,b,c,d) between age group denote significance at 5% level.

P-value is less than 0.001, there is difference between age group with haemotologial parameter, based on Tuckey-HSD test.

19.85 ± 0.44%, and 24.84 ± 1.15% in the subjects of 51-60 years group and it was much higher than the control. A significant difference at 1% level (p-value < 0.01) in RDW with an F-value of 619.06 for all the age groups was recorded. 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 of (Table 1).

Erythrocyte Sedimentation Rate

Erythrocyte Sedimentation Rate (ESR) was found to be higher in all the age groups over the control value (12.27 ± 4.43 mm/h). A linear increase in the ESR values with increasing age was also noticed (Graph 3) as 31-40 years age group

Figure 1: The haemotological parameter of MC, MCH, MCHC, Haemotocrite, Haemoglobin, RBC and Red cell distribution in the blood sample of breast cancer patients.

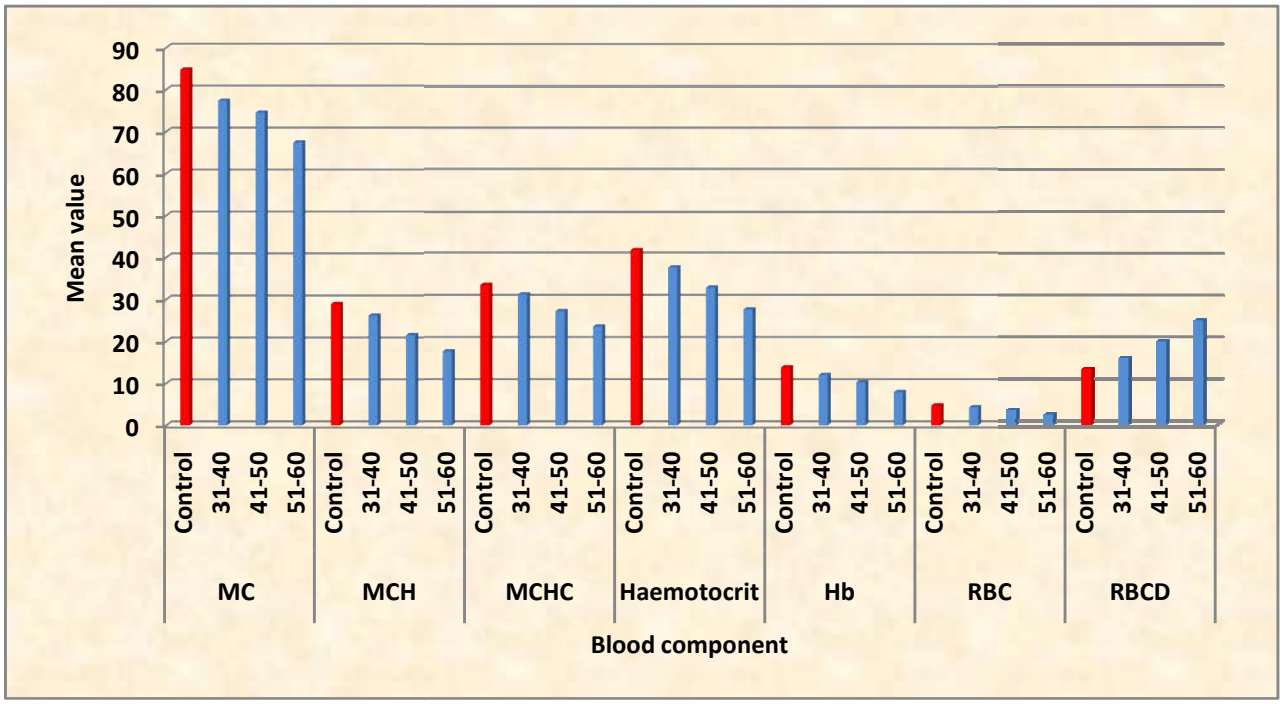
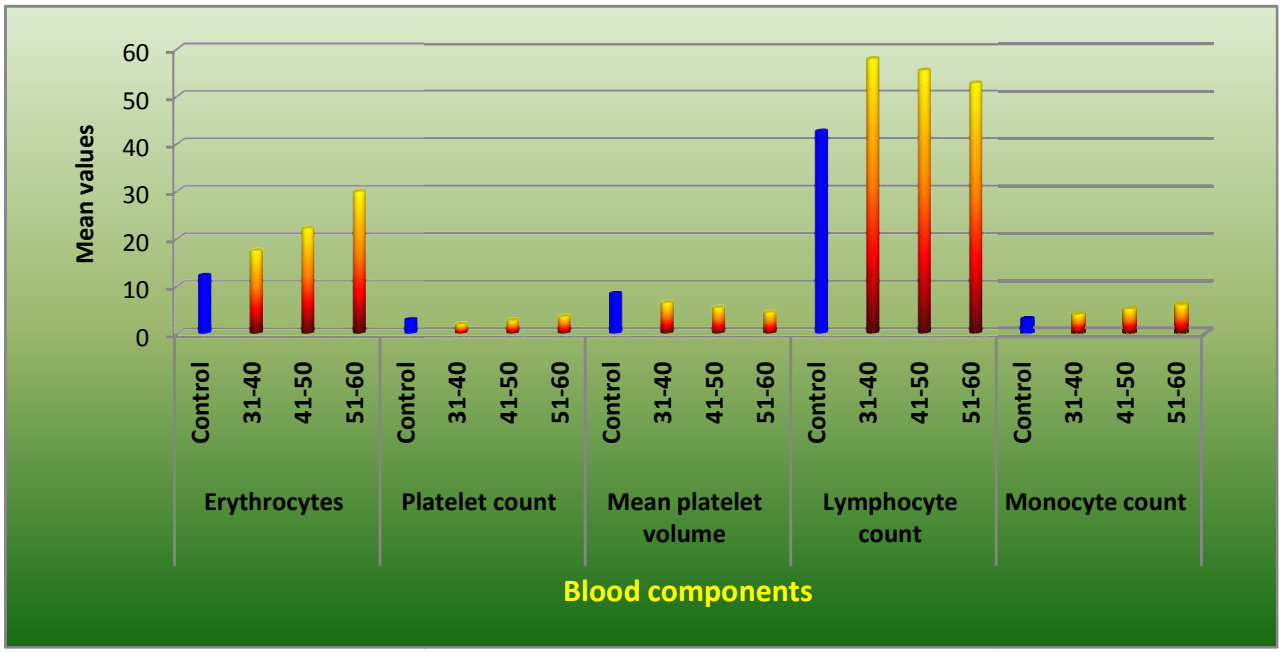


Figure 2: The haemotological parameter of Erythrocytes, platelet count, Mean platelet volume, Lymphocyte count and monocyte count in the blood sample of breast cancer patients



showed 17.49 ± 1.45, 41-50 years with 22.21 ± 1.60, and 29.98 ± 2.93 in the 51-60 age group and it was higher than the control, value. A significant difference at 1% level (p-value < 0.01) in the ESR with an F-value of 206.47 for all the age groups was noticed. The multiple range test (Tuckey-HSD Test) also validated a significant difference at 5% level (p-value > 0.01 & < 0.05) (Table 2).

Platelet and Mean Platelet Volume

Platelet count was found to be higher only in 51-60 (3.60 ± 0.23) age groups compared to the control value (2.98 ± 0.69). A linear increase in the platelet count was noticed in 41-50 (2.78 ± 0.16) and 51-60 (3.60 ± 0.23) age groups but 31-40 years age group (2.00± 0.26) revealed a marginate decrease in platelet count. A significant difference at 1% level (p-value < 0.01) in the platelet count with an F-value of 83.38 for all the age groups was evident. The multiple range test (Tuckey-HSD Test) also inferred a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups (Table 2 & Figure 2). Mean platelet volume was found to be lower in all the age groups compared to the control value (8.44 ± 1.28). A linear decrease in the MPV values was recorded among the

three age categories (Graph 3) as 31-40 years age group recorded 6.52 ± 0.30 of MPV, 41-50 years with 5.49 ± 0.28 and 4.52 ± 0.30 (about half the value of the control) in the 51-60 age group (Table 2 & Figure 2) and it was lower than the control. A significant difference at 1% level (p-value < 0.01) in the MPV with an F-value of 177.38. The multiple range test (Tuckey-HSD Test) also confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) for the three age groups.

White Blood Corpuscles

White Blood Corpuscles (WBC) count recorded a higher value in all the age groups over the control (8360.0 ± 926.10). A linear increase in the WBC count was noticed in first two categories (Graph 4) 31-40 age group with 11987.0 ± 300.27 and 41-50 age group with 12520.0 ± 274.68 and 10757.0 ± 411.63 in the 51-60 years age group and it was lower in the first two age groups but higher than the control. A significant difference at 1% level (p-value < 0.01) in the WBC with an F-value of 344.67 was evident and the multiple range Test (Tukey-HSD Test) confirmed a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the age groups (Table 2).

Lymphocyte count

Lymphocyte count was also found to be higher then the control value (42.60 ± 4.40) (Graph 5). The first age group showed a value of 57.87 ± 4.24 followed by 55.47 ± 2.74 in 41-50 yrs age group in and 52.77 ± 1.25 in 51-60 yrs age group. A significant difference at 1% level (p-value < 0.01) in lymphocyte count revealed an F-value of 116.61 and 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 (Table 2 & Figure 2).

Monocyte Count

Monocyte count revealed a high value over the control in all the age groups (2.97 ± 0.54). A linear increase in the monocyte values in term of (Graph 5) 4.00 ± 0.53 in 31-40 age group of monocytes, 5.06 ± 0.54 41-50 age group; and 6.00 ± 0.53 in 51-60 age group was evident and it was higher than the control. A significant difference at 1% level (p-value < 0.01) in the monocyte with an F-value of 178.40 was assessed and the multiple range test (Tuckey –HSD Test) also validated a significant difference at 5% level (p-value > 0.01 & < 0.05) in all the three age groups (Table 2 & Figure 2).

DISCUSSION

Tysoe and Lowenstein (1950) analyzed the alterations in haematological factors of breast cancer. The investigation revealed an elevation peak at the benign status of metastasis. RBC of patients affected by breast cancer are more sensitive to the denaturing action, hence the formation of hemin, is significantly shorter than in normal subjects (Croci *et al.,* 2002). Kandemir *et al* (2005) investigated the prevalence of anemia (Hb conc < 12 g/dl) in 336 women with early stage breast cancer and its association with other known prognostic factors. Univariate analysis revealed that disease free survival and overall survival were shorter in patients with anemia at and overall survival were shorter in patients with anemia at the time of diagnosis than in patients with normal Hb concentration. This result suggests that pretreatment Hb concentration is an independent prognostic factor in patients with early- stage breast cancer. Early literature reported decreased in heamatocrit level in breast cancer patient (Agbedana and Ebesunun, 1998). The current research also proved decreased RBC, Hb, hematocrit level, MCH and MCV in the subjects and it was found to be statistically significant.

Anemia is not an inconsequential side effect of cancer and its treatment should not be ignored. Current practice for anemia management varies and its role in influencing outcome in cancer patients is under recognized. As a common complication of cancer, anemia is prevalent in virtually all tumour types to varying degrees. Predictive factors for anemia include baseline Hb concentration, decrease in Hb concentration within the first month of treatment. A retrospective meta-analysis has shown an overall 65% increased risk of death associated with anaemia in the subjects (Clarke and Pallister, 2005). A retrospective case control study of colon cancer cases by (Spell *et al.,* 2004) showed that 84% of the subjects had an elevated RDW, 69% had anemia and 55% had low MCV. This implies frequency of blood count abnormalities in cancer patients is predominant. Increased RDW in leukemia is associated with active disease reversible after successful therapy (Chrobak *et al*, 1998). Ozkalemkas *et al*., (2005) reported that the bone marrow metastases can be found commonly in some malignant tumours diagnosis. They reviewed 19 subjects who initially had anaemia, thrombocytopenia, elevated red cell distribution width and hypoproteinemia and formed a uniform tetrad in patients with disseminated tumours that were diagnosed via bone marrow examination. Yonemitsu *et al.,* (1989) reported that the RDW tended to be higher than in the normal control when red blood cell counts were high. It was even higher during the polycythemia period than during the myelofibrotic period. This may be associated with hematopoietic abnormality due to extramedullary hematopoieses and RDW seems to well reflect the pathologic status of cancer.

In the present study, red cell distribution width was observed to be increased in all age groups of breast cancer subjects. Especially in the age group of 51-60 years, there was an enormous rise in red cell distribution width.Detailed investigations of Bottiger and Svedberg, (1967) revealed a marked variation in the erythrocyte sedimentation rate with reference to sex. According to Bain, (1983) the erythrocyte sedimentation rate is higher in women than in men, and in both sexes a rise with age occurs. It is well established that pathological elevation of the ESR may be due to elevation of fibrinogen level. Earlier investigators also analyzed the influence of smoking, alcohol consumption and oral contraceptives intake. Fibrinogen levels were found to be significantly higher in male smokers than non-smokers (Howell, 1970 and Ogston, 1970). William *et al.,* (1983) observed elevated level in the erythrocyte sedimentation in the patients with breast cancer. In the entire breast carcinoma patients study, a rise in erythrocyte sedimentation rate was observed and it was statistically significant. Platelet count increases during strenuous activity and certain conditions called myloproliferative disorders, infection, inflammation and malignancies. Platelet count decreases just before menstruation. The present investigation does not reveal an enhanced platelet count. Subjects of postmenopausal stage

showed an increase in platelet count while the others showed a decrease in the platelet count or a slight increase in the values while mean platelet volume was found to be less in all the breast carcinoma patients respective to the age groups.

In the studies by Harries *et al*., (2005) platelet volume indices were estimated using automated blood cell analyzer (Sysmex NE-8000), and the results indicated 18 cases of normal volume and 21 cases with platelet hypoproduction, 3 cases of increased platelet volume and one case of decreased volume. The present analysis showed fluctuation in the platelet count and not much variation in the platelet count volume. Platelet count was found to be high only in 51-60 age groups. Mean Platelet volume also found to be decreased in the breast cancer patients of rest of the age groups when compared to the control groups. Levina and Bessman (1983) reported that the non linear relation between platelet count and MPV rose during recovery from immune or septic thrombocytopenia. MPV was increased in subjects with heterozygous thalassemia but decreased in malignancy patients. In the present study, mean platelet volume was found to be decreased in the breast cancer subjects than the control in all the age groups. Babu and Basu (2004) estimated platelet volume indices by automated blood cell analyzer and has been useful in the diagnosis of various conditions with abnormal platelet count, platelet large cell ratio, platelet distribution width and mean platelet volume. Platelet large cell ratio significantly decreased in patients with thrombocytosis than in normal while it was increased in thrombocytopenia. Platelet large cell ratio if properly utilized can be a good diagnostic tool towards abnormal platelet counts. WBC is elevated during infection, inflammation, burns and leukemia while low WBC indicates bone marrow depression - may be present with some viruses, toxic reactions, German measles, infectious hepatitis, and other diseases (Petkova *et al*., 1982). The same is recapitulated in this study where the white blood corpuscles count was found to be high in all the age groups. Hence, an increase in lymphocyte and monocytes is also observed in all 180 cases.

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