

Comparison of Hematological Parameters and the Associated Factors Among Women with and without Breast Cancer: A Case-Control Study

Abdul Baset Abbas^{1,2}, Shima Al-Gamei², AmatAlraheem Naser², Ahlam Al-Oqab², Khawla Alduhami², Manal Al-Sabri², Asmahan AL-Qasem², Mona Gharama², Amal Mohammed², Shuaib Ahmed², Malek Al-Glal²

¹Medical Laboratories Department, Faculty of Medicine and Health Sciences, Ibb University, Ibb City, 70270, Yemen; ²Department of Medical Laboratories, Faculty of Medical Sciences, International Malaysian University, Ibb City, Yemen

Correspondence: Abdul Baset Abbas, Email abduabbas@ibbuniv.edu.ye; abduabbas204@hotmail.com

Background: Breast cancer (BC) is the most popular and dangerous cancer, with a high mortality rate. Hematological parameters are often used in routine diagnosis of numerous disorders. Therefore, the study aimed to evaluate hematological parameters amongst women with and without BC.

Methodology: Briefly, 200 blood samples (100 cases and 100 controls) were collected at Life Center of Breast Cancer Control, Ibb City, Yemen. The whole blood samples were tested immediately for complete blood count (CBC) parameters. Socio-demographic and reproductive characteristics were collected by using a standardized questionnaire. Kolmogorov-Smirnov test, Unpaired *t*-test, Mann-Whitney test, Fisher's exact test and chi-square test for trends were calculated using GraphPad Prism 8.0.1. *P*-values ≤ 0.05 were statistically significant.

Results: The mean and standard deviation (SD) revealed significant differences between BC group and the healthy control group attributed to the variables of age ($P < 0.0001$), weight ($P < 0.0001$), residence ($P = 0.0218$), employment state ($P < 0.0001$), economic state ($P = 0.0003$), education levels ($P < 0.0001$), regular exercise ($P < 0.0001$) and a strict diet ($P < 0.0008$). Marital state, marital age, number of births, and use of contraceptives demonstrated statistical significance ($P < 0.0001$, $P = 0.0008$, $P = 0.0009$, and $P < 0.0001$, respectively). Additionally, Hb, RBCs, WBCs count, neutrophils, lymphocytes and monocytes displayed significant differences ($P = 0.0393$, $P = 0.0045$, $P = 0.0327$, $P = 0.0441$, $P = 0.0098$ and $P < 0.0001$, respectively).

Conclusion: Hb, RBCs, WBCs, neutrophils, lymphocytes, monocytes and other parameters scored high points of evidence for BC surveillance. Further studies are required to evaluate hematological parameter differences and biochemical parameters after or during chemotherapy or mastectomy.

Keywords: breast cancer, BC, hematological parameters, weight

Introduction

Breast cancer (BC) is one of the most popular and dangerous cancers which is accompanied by a high mortality rate.¹⁻³ BC women represent up to 36% of cancer patients globally, and its incidence number has increased in the past four decades.^{4,5} Furthermore, BC represents 31% of female tumors in the United States.⁶ In Yemen, BC is a public health disease that represents 16.6% of cancer patients and 30.3% of cancer among women.⁷ There has been an increase in BC numbers during the last few years in Yemen.⁸ There is a close relationship between tumors and hematological parameters.^{1,9-12} The cancer induces an immune response resulting in changes in hematological parameters such as white blood cells (WBCs) and platelets.¹³⁻¹⁷ Hematological parameters reflect the cell-mediated immune response to cancer, and changes in hematological parameters influence cancer progressions. Therefore, hematological parameters evaluation is reliable for the prognosis and diagnosis of several types of cancer, including breast cancer.^{12,18-21} There is a need for more studies to understand the association of hematological parameters and BC prognosis.¹⁷ There is a restricted research achievement on hematological

parameters of diseases in Yemen.²² Furthermore, there is no research conducted on BC and its effects on the hematological parameters in Yemen. Therefore, this research aimed to evaluate the hematological parameters and the associated factors among women with and without BC.

Materials and Methods

The population sources were the Life Center of Breast Cancer Control-Ibb branch from August 30, 2022 to August 30, 2023. The study followed a thumb rule to detect sample size in each group, where 30 participants in each group were enough to distinguish the actual variations.²³ To increase the statistical power of the evaluation, the participant's number was increased to 100 participants per group (100 women with breast cancer and 100 healthy control). The age of women with BC was ≥ 26 years, while the age of healthy women (control) was ≥ 21 years. The study experiments were analyzed in Zain Medical Laboratories. An Arabic-translated questionnaire was administered to participant women. The data collected involved participants' number, weight, residence, age, education level, marital state, employment state, economic state, smoking, qat chewing, tobacco, regular exercise, following a strict diet, sleeping under light, consumption of animal fats, marital state and age, menarche age, menopause age, first pregnancy age, number of alive births, contraceptive use and type, breastfeeding period and estrogen and prolactin disorders. The whole blood samples were tested immediately for complete blood count (CBC) parameters, while the sera were used to screen cancer antigen (CA 15-3) and C-reactive protein (CRP).

Participants with pregnancy, childbirth bleeding disorder, renal disease and liver disease (hepatitis B and C viruses), and the use of blood pressure and diabetes medicines as well as aspirin were excluded. Moreover, The CA 15-3 marker and C-reactive protein (CRP) were screened to ensure the control group was BC and CRP-free, respectively. Furthermore, the control group with appendicitis, arthritis or tonsillitis was excluded.

Statistical Analysis

GraphPad Prism 8.0.1 was used to analyze the data obtained from the laboratory tests and questionnaires. Kolmogorov-Smirnov test was applied to determine whether available data showed a normal distribution in which the data were calculated by an Unpaired *t*-test. Furthermore, in an abnormal distribution, the Mann-Whitney *U*-test was used. Fisher exact test or a chi-square test for trend was used to analyze the socio-demographic and reproductive characteristics. A *P*-value ≤ 0.05 means statistically significant.

Results

Socio-Demographic Characters of the Study Participants

In this study, 100 women with BC (cases) and 100 healthy women formed a control group. The standard deviation (SD), range, and mean were statistically analyzed for all variables revealed in the tables. In addition, the mean and SD of BC and healthy control group's ages were 46.14 ± 11.51 years and 33.43 ± 11.42 years, respectively. Similarly, the mean and SD of BC and healthy control groups' weight were 56.51 ± 10.41 Kg and 50.96 ± 9.905 Kg, respectively. Approximately 34% and 51% of the participants in the BC and control groups lived in urban areas. Furthermore, most of the BC group were housewife (89%) with an illiterate education level (67%). Most of the healthy control group were non-employed (58%) and had a university education level (68%). Besides, 60% and 82% of the BC and healthy control groups had a middle economic state. According to daily habits, the percentage of BC participants were qat chewers (51%), non-tobacco chewers (96%), non-smokers (82%), irregular exercise (51%), non-sleep under light (78%), non-follow a strict diet (80%) and consumption of animal fats (76%), respectively. Moreover, the percentage of the control group participants were non-qat chewers (56%), non-smokers (82%), non-tobacco chewers (100%), irregular exercise (90%), non-follow a strict diet (96%), non-sleep under light (84%) and consumption of animal fats (70%), respectively. In addition, most of the participants in the BC group (74%) and control group 82 (82%) had no history of family cancer as presented in Table 1.

In the current study, as revealed in Table 1, there were significant differences between BC and healthy control groups in weight ($P < 0.0001$), age ($P < 0.0001$), residence ($P = 0.0218$), employment state ($P < 0.0001$), education levels ($P < 0.0001$),

Table I Socio-Demographic Characters of Women with BC and Control Groups

Variable		Breast Cancer (100)	Control (100)	P-value
Age (years) Mean±SD (Range)		46.14±11.51 (26~73)	33.43±11.42 (21~69)	<0.0001
Weight (Kgs) Mean±SD (Range)		56.51±10.41 (26~80)	50.96±9.905 (32~80)	<0.0001
Family history with cancer No. (%)	With	26 (26%)	18 (18%)	0.2319
	Without	74 (74%)	82 (82%)	
Residence No. (%)	Urban	34 (34%)	51 (51%)	0.0218
	Rural	66 (66%)	49 (49%)	
Employment state No. (%)	Housewife	89 (89%)	16 (16%)	<0.0001
	Employed	5 (5%)	26 (26%)	
	Unemployed	6 (6%)	58 (58%)	
Education levels No. (%)	Illiterate	67 (67%)	4 (4%)	<0.0001
	Primary	17 (17%)	6 (6%)	
	Secondary	11 (11%)	22 (22%)	
	University	5 (5%)	68 (68%)	
Economic state No. (%)	Low	5 (5%)	7 (7%)	0.0003
	Middle	60 (60%)	82 (82%)	
	High	35 (35%)	11 (11%)	
Smoking No. (%)	Smokers	18 (18%)	18 (18%)	>0.9999
	Non smokers	82 (82%)	82 (82%)	
Qat chewing No. (%)	Yes	51 (51%)	44 (44%)	0.3956
	No	49 (49%)	56 (56%)	
Tobacco chewing No. (%)	Yes	4 (4%)	0 (0%)	0.1212
	No	96 (96%)	100 (100%)	
Regular exercise No. (%)	Yes	49 (49%)	10 (10%)	<0.0001
	No	51 (51%)	90 (90%)	
Follow a strict diet No. (%)	Yes	20 (20%)	4 (4%)	<0.0008
	No	80 (80%)	96 (96%)	
Sleep under light No. (%)	Yes	22 (22%)	16 (16%)	0.3676
	No	78 (78%)	84 (84%)	
Consumption of animal fats No. (%)	Yes	76 (76%)	70 (70%)	0.4260
	No	24 (24%)	30 (30%)	

economic state ($P=0.0003$), regular exercise ($P<0.0001$) and following a strict diet ($P<0.0008$). Nevertheless, the family history with cancer, smoking, tobacco chewing, qat chewing, sleep under light and consumption of animal fats were not statistically significant between the BC and the healthy control groups.

Reproductive Characters of Participant Women in Breast Cancer Group and Control Group

In brief, a total of 200 participant women (100 BC as cases and 100 healthy as a control) were involved. Out of BC participants, almost 87% were married, while out of the control group, 58% were married. In case of marital age, the group (16–20 years) represented the highest set among both BC and control groups. Marital state and marital age were statistically significant ($P < 0.0001$ and 0.0008). As revealed in Table 2, menopause age was statistically significant ($P = 0.0002$). Furthermore, number of live births was significant ($P = 0.0001$). The contraceptive use revealed a significant difference between both groups ($P < 0.0001$). Considering the most contraceptive used, out of 42 BC participants, 8 (19.05%) used an intrauterine device, 16 (38.1%) used a tablet, 3 (7.14%) used an implant and 15 (35.71%) used an injection, out of 8 participants in the control group, 2 (25%), 3 (37.5%), 2 (25%) and 1 (12.5%) used an intrauterine device, tablet, implant and injection, respectively. Furthermore, the disorders of estrogen and prolactin hormones were not statistically significant.

Table 2 Reproductive Characters of Women with BC and Control Group

Reproductive Characters		Breast Cancer (100) No. (%)	Control (100) No. (%)	P-value
Marital state	Single	13 (13%)	42 (42%)	<0.0001
	Married	87 (87%)	58 (58%)	
Marital age	10–15 years	24 (24%)	8 (8%)	0.0008
	16–20 years	48 (48%)	25 (25%)	
	21–25 years	12 (12%)	19 (19%)	
	≥26 years	3 (3%)	6 (6%)	
Menarche (puberty) age	≤12 years	6 (6%)	12 (12%)	0.0933
	13–16 years	87 (87%)	84 (84%)	
	17–20 years	7 (7%)	4 (4%)	
Age at first pregnancy	13–16 years	10 (10%)	2 (2%)	0.9483
	17–20 years	37 (37%)	12 (12%)	
	21–24 years	11 (11%)	8 (8%)	
	≥25 years	14 (14%)	2 (2%)	
Menopause age (years)	≤50	50	0	0.0002
	≥51	13	6	
Number of alive births	1–4	19	17	0.0001
	≥5	53	7	
Breastfeeding period	≤1 year	13	4	0.4000
	1–2 years	50	20	
	>2 years	9	0	
Contraceptive use	Yes	42 (42%)	8 (8%)	<0.0001
	No	58 (58%)	92 (92%)	

(Continued)

Table 2 (Continued).

Reproductive Characters		Breast Cancer (100) No. (%)	Control (100) No. (%)	P-value
Contraceptive type	Intrauterine device	8 (19.05%)	2 (25%)	0.4304
	Tablet	16 (38.1%)	3 (37.5%)	
	Implant	3 (7.14%)	2 (25%)	
	Injection	15 (35.71%)	1 (12.5%)	
Estrogen disorders	Yes	2 (2%)	0 (0%)	0.0598
	No	9 (18%)	24 (24%)	
	Do not know	89 (89%)	76 (76%)	
Prolactin disorders	Yes	7 (7%)	2 (2%)	0.4415
	No	14 (14%)	30 (30%)	
	Do not know	79 (79%)	68 (68%)	

Clinical Variables and Treatment History of BC Women and Control Group

In terms of BC period, the mean and SD of period were 3.184 ± 2.43 years while the range was 3 months~10 years and most of the BC group had a period >1-5 years (53%). Additionally, approximately 64% of the participant women in BC group were CRP-negative. In case of inflammatory symptoms among BC group, 67%, 19% and 1% had arthritis, tonsillitis and appendicitis, respectively. Furthermore, the treatment profile of BC group showed that 13% of participants used blood pressure medication, 12% used diabetic medication and 9% used aspirin as seen in Table 3.

Comparison of Hematological Parameters Between BC Women and Control Group

In the current study, there were statistically significant differences between mean and SD of BC and control groups concerning Hb level ($P=0.0393$) and the count of RBCs ($P=0.0045$), WBCs ($P=0.0327$), neutrophils ($P=0.0441$), lymphocytes ($P=0.0098$) and monocytes ($P<0.0001$) as revealed in Table 4.

As shown in Table 4, the results showed that the mean and SD of PCV, MCV, MCH, MCHC, eosinophil, basophil, and platelets were not statistically significant between BC and control groups.

Table 3 Clinical Variables and Treatment History of Women with BC

Variable		Breast Cancer Women No. (%)
Period of breast cancer	≤1 year	28 (28%)
	>1-5 years	53 (53%)
	6–10 years	19 (19%)
	Mean±SD 3.184 ± 2.43 (Range) (3 month~10 years)	
CRP	Positive	36 (36%)
	Negative	64 (64%)
Tonsillitis	Yes	19 (19%)
	No	81 (81%)

(Continued)

Table 3 (Continued).

Variable		Breast Cancer Women No. (%)
Arthritis	Yes	67 (67%)
	No	33 (33%)
Appendicitis	Yes	1 (1%)
	No	99 (99%)
Blood pressure medication	Yes	13 (13%)
	No	87 (87%)
Diabetes medication	Yes	12 (12%)
	No	88 (88%)
Aspirin	Yes	9 (9%)
	No	91 (91%)

Table 4 Comparison of Hematological Parameters Between Women with BC and Healthy Control

Variable	Breast Cancer Women Mean±SD (Range)	Control Mean±SD (Range)	P-value
Hb g/dl	12.62 ± 1.702 (8.9~17.9)	13.04± 1.096 (10.3~15.2)	0.0393
RBC (10 ¹² /l)	4.507±0.642 (3.14~6.61)	4.711±0.297 (4.13~5.49)	0.0045
PCV%	37.78 ± 5.43 (13.7~52.7)	38.67 ± 5.17 (11.5~45.2)	0.2393
MCV fl	83.98 ± 10.7 (33.2~111.3)	83.55±5.477 (68.2~92.7)	0.7193
MCH pg	28.88±6.635 (17~87.7)	27.78± 2.114 (21.9~31.2)	0.1168
MCHC g/l	33.23±1.371 (26.5~41.7)	33.17±0.708 (31.4~34.6)	0.6816
WBCs (×10 ⁹ /l)	6.13±1.740 (2.480~9.760)	5.66±1.326 (3.14~7.91)	0.0327
Neutrophils %	51.48±16.72 (11.6~91.7)	47.43±10.91 (15.7~66.8)	0.0441
Lymphocytes %	35.92±14.82 (6.9~84.2)	40.49±9.384 (14.3~64.7)	0.0098
Monocytes %	9.81±5.05 (1.4~31.7)	7.162±1.366 (4.3~9.9)	<0.0001
Eosinophils %	2.697±3.128 (0.0~23.1)	2.91±2.412 (0.2~9)	0.5903
Basophils %	0.4206±0.2513 (0~1.1)	0384±0.2295 (0~1)	0.2841
Platelets (×10 ⁹ /l)	301.6±102.7 (102~566)	322.7±72.11 (168~471)	0.0893

Abbreviations: Hb, Hemoglobin; RBC, red blood cells; PCV, Packed cell volume; MCV, mean cell volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WBC, white blood cells.

Discussion

BC in women is the most dangerous disease accompanied by a high rate of mortality.¹⁻³ The hematological parameters used in disease diagnosis include cancer.¹⁸ Additionally, there are diverse risk factors that play roles in BC development including delayed menopause, early menarche, and history of the family with breast cancer.^{2,24} In the present study, weight, age, residence, employment state, educational level, economic state, regular exercise, and subsequent strict diet

revealed a significant difference between BC and healthy control groups. In comparison with the current research, age, employment state, and education levels were significantly similar to those in a study conducted in Kolkata, India.²⁵ However, another study in Mumbai, India, reported that age and occupation were not found to be significant.²⁶ On the other hand, this study found no significant relation between the presence of family history with BC, which agreed with a study in India²⁵ and disagreed with two studies carried out in Ankara and Izmir, Turkey.^{27,28} In the present study, sleep under light was not related to BC incidence ($P=0.3676$) due to the lack of good electricity in Yemen. However, different studies conducted by Sweeney et al,²⁹ Jaynes and Switzer,³⁰ James et al³¹ and Urbano et al³² showed a correlation between exposure to light and BC incidence.

In the present study, menarche and menopause ages were not significantly different between women with BC and control groups. This finding agreed with the one reported by a study in Ankara, Turkey,²⁷ and disagreed with an investigation conducted in India.²⁵ There was no correlation between the breastfeeding period and BC. This study agreed with studies in the USA and Turkey^{27,33} and in disagreed with a study in India.²⁵

The current study showed that marital state and marital age were significant in BC group compared to the control group. This result is identical to a study performed in India, which showed that marital state was significant.²⁵ In this study, contraceptive usage showed a significant change, while studies conducted in India, USA, and Turkey revealed that contraceptive use was not significant.^{25,27,34}

This study contained a comparison of hematological parameters between a BC group and a healthy control group. In the current study, the hematological parameters Hb ($P=0.0393$), RBCs ($P=0.0045$), WBCs ($P=0.0327$), lymphocytes ($P=0.0098$), neutrophils ($P=0.0441$) and monocytes ($P<0.0001$) showed a statistically significant difference between both groups. Nevertheless, PCV ($P=0.2393$), MCV ($P=0.7193$), MCH ($P=0.1168$), MCHC ($P=0.6816$), eosinophils ($P=0.5903$), basophils ($P=0.2841$) and platelets ($P=0.0893$) were not significantly different. Hb and RBCs results were identical to results of studies conducted in Algeria and India.^{2,35} In addition, a study carried out in Nigeria displayed statistically significant of Hb, WBCs, neutrophil, lymphocyte and PCV, while monocyte, eosinophil and platelet were not statistically significant.¹² In contrast, in a study carried out in Iran,³⁶ it was confirmed that Hb and RBCs were not statistically significant, while MCV, MCH and MCHC were statistically significant. Velidedeoglu and his et al in Turkey concluded that WBCs, neutrophils, lymphocytes and monocytes were significant, whereas Hb, platelets and eosinophil were insignificant.³⁷

The dissimilarities might be due to differences in the sample size, socio-economic state, geographical position, laboratory analytical method applied, reproductive and clinical characters, nutrition and regular activities.

Conclusion

This study concluded that there were statistically significant differences in some hematological parameters among women with BC compared to a control group. Our results present that contraceptive use, menopause age, marital state, and marital age may be associated with breast cancer incidence. Moreover, Hb, RBCs, WBCs, neutrophils, lymphocytes, monocytes, and other parameters scored high points of evidence for BC surveillance. The limitations of this study include the small number of participants and the absence of identification of hematological parameter differences and biochemical parameters after or during chemotherapy or mastectomy (wholly or partially). Similar studies are recommended in the other provinces to confirm the roles of hematological parameters in BC diagnosis in Yemen. Further studies are recommended to illustrate the hematological parameters between patients with invasive BC and non-invasive BC.

Abbreviations

BC, Breast cancer; CA 15-3, Cancer antigen 15-3; CBC, Complete blood count; CRP, C-reactive protein; EDTA, Ethylene diamine tetraacetic acid; Hb, Hemoglobin; MCH, Mean cell hemoglobin; MCHC, Mean cell Hb concentration; MCV, Mean cells volume; PCV, Packed cell volume; RBC, Red blood cells; SD, Standard deviation; WBCs, White blood cells.

Data Sharing Statement

The data that support the findings of this study are available upon request from the corresponding author. The data are not publicly available because they contain information that can compromise the privacy of the research participants.

Ethical Considerations

An ethical approval for this study was allowed by the Medical Laboratories Department (MLD), Faculty of Medical Sciences (FMS), International Malaysian University (IMU) ethical committee after suitable procedures were followed (Reference No. MLDMSIMU/A0101/2022, date: August 25, 2022). The Ethics Research Committee was aligned with the Helsinki Declaration. A written informed consent was obtained from all the study participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, data acquisition, analysis and interpretation, or in all these areas; participated in drafting, revising or critically reviewing the article. Final approval was given for publication; all authors have agreed to the journal to which the article has been submitted and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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