



RESEARCH ARTICLE

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Iron Metabolism Disorders and Prevalence of Anemia among Cameroonian Women with Breast Cancer

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ABSTRACT

Objective: To compare hematological and iron-metabolism parameters between Cameroonian women with breast cancer and matched controls, and to estimate the prevalence and types of anemia among affected women.

Methods: We conducted a matched cross-sectional comparative study from January 2024 to January 2025 in two hospitals in Douala, Cameroon. The study included 630 women: 315 with histologically confirmed breast cancer and 315 controls matched by age and menopausal status. Sociodemographic and clinicopathological data, complete blood count indices, serum iron, ferritin, transferrin, and transferrin saturation were assessed.

Results: The mean age was 47 ± 11 years. Among cases, 59.7% had T4 tumors, 72.1% had tumors >5 cm, 57.5% had stage III disease, and 85.1% had invasive ductal carcinoma. Compared with controls, cases had lower hemoglobin (11.12 ± 1.35 vs 12.73 ± 1.28 g/dL), hematocrit ($35.55 \pm 4.78\%$ vs $37.87 \pm 3.91\%$), mean corpuscular hemoglobin (27.52 ± 2.88 vs 29.72 ± 2.97 pg), mean corpuscular hemoglobin concentration (31.45 ± 3.43 vs 33.35 ± 1.61 g/dL), serum iron (0.61 ± 0.24 vs 0.76 ± 0.31 mg/L), and transferrin (223.03 ± 55.34 vs 249.13 ± 42.49 mg/dL) (all $p \leq 0.02$). Anemia affected 82.5% of cases and 29.8% of controls. Among cases, 54.9% had iron-deficiency anemia and 25.1% had inflammatory anemia. Anemia prevalence was similar in chemotherapy-exposed and unexposed cases (82.5% vs 82.8%; $p = 0.226$), although hematocrit and mean corpuscular volume were lower in exposed women.

Conclusions: Anemia and iron-metabolism abnormalities were common among women with breast cancer. Systematic assessment of iron status is warranted, while prospective studies are needed to clarify treatment-related changes and guide correction strategies.

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Introduction

Breast cancer is the most frequently diagnosed malignancy among women worldwide and remains a major cause of cancer mortality. Recent global estimates show a continuing increase in incidence, with a disproportionate mortality burden in low- and middle-income countries [1-4]. Cameroon has one of the highest reported age-standardized breast-cancer mortality rates in Africa, while limited awareness, delayed care seeking, and late-stage presentation remain important challenges [4-7].

Anemia in breast cancer is often multifactorial. Absolute iron deficiency, inflammation-induced functional iron restriction, blood loss, nutritional vulnerability, and treatment-related marrow toxicity may coexist [8-12]. Low hemoglobin contributes to fatigue and impaired quality of life, can reduce chemotherapy dose intensity, and may compromise response to radiotherapy or systemic treatment [13-16]. Despite these

clinical consequences, iron-metabolism disorders have been insufficiently described in women receiving breast-cancer care in Cameroon.

Characterizing hematological indices and iron markers in this population may support earlier identification of potentially correctable abnormalities and inform supportive-care strategies. This study therefore aimed to compare hematological and iron-metabolism parameters between Cameroonian women with breast cancer and matched controls, and to determine the prevalence and distribution of anemia types among affected women.

Materials and Methods

Study design, setting and period

This matched cross-sectional comparative study was conducted from January 2024 to January 2025 at Douala General Hospital

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(DGH) and Bonassama District Hospital (BDH), Douala, Cameroon.

Study population

Women aged 18 years or older who agreed to participate were recruited consecutively. Women who declined participation or were not permanent residents of Douala were excluded. Cases were women with histologically confirmed breast cancer diagnosed by an oncologist and receiving oncological care, including chemotherapy or other treatment. Controls were women without breast cancer on clinical examination, recruited mainly among accompanying persons and women attending routine examinations; absence of malaria parasitemia was assessed by thick blood film.

Cases and controls were matched by age and menopausal status. Menopause was defined as the absence of menstruation for more than 12 months [17]. The final sample comprised 315 cases and 315 controls.

Data collection

A structured questionnaire was used to collect age, marital status, parity, menopausal status, occupational sector, and monthly income. For cases, clinical and histopathological data included tumor size, nodal involvement, metastases, clinical stage, histological grade and type, family history, and number of chemotherapy cycles.

Hematological and biochemical measurements

After an overnight fast, a total of 6 mL of venous blood was collected from each participant: one ethylenediaminetetraacetic acid tube for a complete blood count and one plain tube for biochemical assays. Samples were transported with ice packs at approximately 0°C for 30-60 minutes to the BDH clinical biology laboratory. No participant was known to be receiving iron supplementation at sampling.

The complete blood count provided hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and reticulocyte count. The hematological reference values used in the source protocol are summarized in Table 1. Ferritin was measured by a one-step enzyme-linked fluorescent assay. Serum iron was measured colorimetrically and transferrin by immunoturbidimetry. The transferrin saturation coefficient (TSC) was calculated using the standard laboratory formula.

Table 1: Hematological parameters and reference values used in the study.

Hematological parameter	Unit	Reference value
Hemoglobin concentration	g/L	120
Mean corpuscular volume (MCV)	fL	80-100
Mean corpuscular hemoglobin (MCH)	pg	26-34
Mean corpuscular hemoglobin concentration (MCHC)	g/L	320-360
Reticulocyte count	$\times 10^9/L$	20-80

Definition and classification of anemia

Anemia was defined as a hemoglobin concentration <12.0 g/

dL, in accordance with the World Health Organization criterion for non-pregnant adult women. Participants with hemoglobin ≥ 12.0 g/dL were classified as having no anemia. Anemia was further characterized according to iron-status parameters, mean corpuscular volume (MCV), inflammatory markers, and vitamin status. Iron-deficiency anemia was defined by hemoglobin <12.0 g/dL together with depleted iron stores, indicated by serum ferritin <30 ng/mL and/or transferrin saturation coefficient (TSC) $<20\%$; it was generally associated with microcytosis (MCV <80 fL). In the presence of inflammation, iron deficiency was considered when ferritin was <100 ng/mL in combination with TSC $<20\%$. Inflammatory anemia (anemia of chronic disease/inflammation) was defined by hemoglobin <12.0 g/dL, TSC $<20\%$, normal or increased ferritin (≥ 100 ng/mL), and evidence of systemic inflammation, defined by C-reactive protein (CRP) >5 mg/L. MCV was usually normal (80–100 fL), although mild microcytosis could occur. Megaloblastic anemia was defined by hemoglobin <12.0 g/dL with macrocytosis (MCV >100 fL) and biochemical evidence of vitamin deficiency, namely serum vitamin B12 <200 pg/mL and/or serum folate <4 ng/mL. Patients whose laboratory profile did not meet these predefined criteria were classified according to the predominant hematological and biochemical abnormality.

Statistical analysis

Data were entered in Microsoft Excel and analyzed using GraphPad Prism version 5.0 and StatView version 5.0. Continuous variables are presented as mean $\pm$ standard deviation and categorical variables as number and percentage. Proportions were compared using Pearson's chi-square test. Means were compared using paired or independent-samples Student's *t* tests according to the comparison, with Kruskal-Wallis or Mann-Whitney tests used when parametric assumptions were not met. Pearson correlation was used to assess linear associations. All tests were two-sided and $p < 0.05$ was considered statistically significant.

Ethical considerations

The study protocol was approved by the ethics committees of Douala General Hospital (DGH) and Bonassama District Hospital (BDH), as well as by the Institutional Ethics Committee of the University of Douala (approval No. 3050 CEI-Udo). Administrative authorizations were obtained from both hospitals and from the relevant departmental and laboratory authorities. The study was conducted in accordance with the ethical principles of the 1964 Declaration of Helsinki and its subsequent amendments. Written informed consent was obtained from every participant prior to enrolment in the study. Participants were informed of the study objectives, procedures, potential benefits, and their right to withdraw at any time without affecting their medical care. Confidentiality and anonymity of all participant information were maintained throughout data collection, analysis, and reporting.

Results

Participant characteristics

The study included 630 women, equally divided between cases and controls. Mean age was 47 ± 11 years, and 220 participants (34.9%) were aged 36-45 years. Most women were

premenopausal (330; 52.4%), married (520; 82.5%), employed in the formal sector (260; 41.3%), and reported monthly income $\geq 125,000$ Central African CFA francs (FCFA) (260; 41.3%). The groups were comparable for age and menopausal status but differed in marital status, occupation, and income distribution (Table 2).

Table 2: Sociodemographic characteristics of the study population.

Characteristic	Total (N = 630)	Cases (N = 315)	Controls (N = 315)	p value
Age, mean $\pm$ SD (years)	47 $\pm$ 11	46.9 $\pm$ 13	47 $\pm$ 10	>0.9
Age group, years				1.000
21-35	94 (14.9)	47 (14.9)	47 (14.9)	
36-45	220 (34.9)	110 (34.9)	110 (34.9)	
46-55	174 (27.6)	87 (27.6)	87 (27.6)	
>55	142 (22.5)	71 (22.5)	71 (22.5)	
Menopausal status				1.000
Postmenopausal	300 (47.6)	150 (47.6)	150 (47.6)	
Premenopausal	330 (52.4)	165 (52.4)	165 (52.4)	
Marital status				<0.001
Single	94 (14.9)	55 (17.5)	39 (12.4)	
Married	520 (82.5)	244 (77.5)	276 (87.6)	
Widowed	16 (2.5)	16 (5.1)	0 (0.0)	
Occupation				0.005
Unemployed	244 (38.7)	118 (37.5)	126 (40.0)	
Formal sector	260 (41.3)	118 (37.5)	142 (45.1)	
Informal sector	126 (20.0)	79 (25.1)	47 (14.9)	
Monthly income (FCFA)				<0.001
<25,000	244 (38.7)	118 (37.5)	126 (40.0)	
25,000-74,999	47 (7.5)	47 (14.9)	0 (0.0)	
75,000-124,999	79 (12.5)	32 (10.2)	47 (14.9)	
$\geq 125,000$	260 (41.3)	118 (37.5)	142 (45.1)	

Note: Values are n (%) unless otherwise stated. SD, standard deviation. Combined totals and categorical p values were recalculated from the case and control counts displayed in the source manuscript; the mean-age p value was retained from the source analysis.

Clinicopathological characteristics of cases

Among the 315 women with breast cancer, 188 (59.7%) had T4 tumors and 227 (72.1%) had tumors >5 cm. N1 nodal involvement was recorded in 150 (47.6%), and 181 (57.5%) had stage III disease. The left breast was affected in 181 (57.5%); 228 (72.4%) had no documented distant metastasis. Grade II tumors predominated (213; 67.6%), and invasive ductal carcinoma was the most frequent histological type (268; 85.1%) (Table 3).

Hematological and iron-metabolism parameters

Cases had lower mean hemoglobin, hematocrit, MCH, MCHC, serum iron, and transferrin values than controls (all $p \leq 0.02$). MCV, ferritin, and TSC did not differ significantly between the groups (Table 4).

Parameters according to chemotherapy exposure

Within the breast-cancer group, chemotherapy-exposed women had lower hematocrit ($33.96 \pm 5.34\%$ vs $38.20 \pm 1.65\%$; $p = 0.005$) and MCV (83.44 ± 15.04 vs 92.33 ± 4.79 fL; $p = 0.03$) than unexposed women. Other erythrocyte indices and iron-

metabolism markers did not differ significantly (Table 5).

Table 3: Clinicopathological characteristics of women with breast cancer (n = 315).

Characteristic	n	%
Tumor category		
T1	8	2.5
T2	32	10.2
T3	87	27.6
T4	188	59.7
Tumor diameter (cm)		
1	8	2.5
3	32	10.2
4	32	10.2
5	16	5.1
>5	227	72.1
Nodal category		
N0	87	27.6
N1	150	47.6
N2	63	20.0
N3	15	4.8
Clinical stage		
Stage I	8	2.5
Stage II	55	17.5
Stage III	181	57.5
Stage IV	71	22.5
Affected breast		
Left	181	57.5
Right	134	42.5
Distant metastasis		
M1	87	27.6
M0	228	72.4
Histological grade		
Grade I	47	14.9
Grade II	213	67.6
Grade III	55	17.5
Histological type		
Invasive ductal carcinoma	268	85.1
Invasive lobular carcinoma	32	10.2
Ductal carcinoma in situ	15	4.8

Table 4: Comparison of hematological and iron-metabolism parameters between cases and controls.

Parameter	Cases (n = 315)	Controls (n = 315)	p value
Hemoglobin (g/dL)	11.12 $\pm$ 1.35	12.73 $\pm$ 1.28	<0.001
Hematocrit (%)	35.55 $\pm$ 4.78	37.87 $\pm$ 3.91	0.01
MCV (fL)	86.77 $\pm$ 12.91	88.65 $\pm$ 7.76	0.4
MCH (pg)	27.52 $\pm$ 2.88	29.72 $\pm$ 2.97	0.001
MCHC (g/dL)	31.45 $\pm$ 3.43	33.35 $\pm$ 1.61	0.002
Serum iron (mg/L)	0.61 $\pm$ 0.24	0.76 $\pm$ 0.31	0.01
Ferritin (ng/mL)	212.31 $\pm$ 291.68	129.40 $\pm$ 105.43	0.09
Transferrin (mg/dL)	223.03 $\pm$ 55.34	249.13 $\pm$ 42.49	0.02
TSC (%)	20.62 $\pm$ 9.24	22.48 $\pm$ 9.20	0.37

Note: Values are mean $\pm$ standard deviation. MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; TSC, transferrin saturation coefficient. P values were obtained using Student's t test.

Table 5: Hematological and iron-metabolism parameters according to chemotherapy exposure among cases.

Parameter	No chemotherapy (n = 87)	Chemotherapy (n = 228)	p value
Hemoglobin (g/dL)	11.58 ± 1.45	10.86 ± 1.25	0.1
Hematocrit (%)	38.20 ± 1.65	33.96 ± 5.34	0.005
MCV (fL)	92.33 ± 4.79	83.44 ± 15.04	0.03
MCH (pg)	28.33 ± 1.68	27.04 ± 3.35	0.17
MCHC (g/dL)	30.67 ± 1.05	31.92 ± 4.23	0.26
Serum iron (mg/L)	0.62 ± 0.22	0.60 ± 0.27	0.93
Ferritin (ng/mL)	160.73 ± 43.11	243.26 ± 69.09	0.39
Transferrin (mg/dL)	232.71 ± 51.80	217.22 ± 57.61	0.39
TSC (%)	19.38 ± 6.42	21.38 ± 10.64	0.51

Note: Values are mean ± standard deviation. MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; TSC, transferrin saturation coefficient. P values were obtained using the Mann-Whitney test.

Prevalence and types of anemia

Anemia was present in 354 of 630 participants (56.2%), including 260 of 315 cases (82.5%) and 94 of 315 controls (29.8%). Among cases, iron-deficiency anemia was most frequent (173; 54.9%), followed by inflammatory anemia (79; 25.1%) and megaloblastic anemia (8; 2.5%). Anemia prevalence was nearly identical among chemotherapy-exposed and unexposed cases (82.5% vs 82.8%). The anemia-type distribution did not differ significantly by chemotherapy exposure within cases ($\chi^2 = 4.35$; df = 3; p = 0.226), but differed when the two case subgroups and controls were compared ($\chi^2 = 204.82$; df = 6; p < 0.001) (Table 6).

Discussion

This study identified a substantial burden of anemia and altered iron-related indices among Cameroonian women with breast cancer. More than four in five cases were anemic, compared with fewer than one in three controls. Cases also had lower hemoglobin, hematocrit, MCH, MCHC, serum iron, and transferrin. Iron-deficiency anemia was the dominant phenotype, followed by inflammatory anemia. Chemotherapy-exposed women had lower hematocrit and MCV, but the cross-sectional prevalence and distribution of anemia did not differ materially between exposed and unexposed cases.

Hemoglobin and hematocrit are central measures of oxygen-carrying capacity and circulating red-cell mass. The lower values observed among cases are consistent with the recognized burden of cancer-associated anemia [19,20] and with reports among breast-cancer patients receiving systemic therapy [13,22]. Chemotherapy-related marrow toxicity may contribute to falling erythrocyte indices, but inflammation, nutritional

deficiency, tumor burden, and pre-existing anemia are also important [12-15]. Because exposure and outcome were assessed cross-sectionally, the lower hematocrit observed among treated women cannot establish a causal treatment effect.

The reductions in MCH and MCHC support a hypochromic pattern, while the lower MCV among chemotherapy-exposed cases suggests greater microcytosis in that subgroup. Iron, folate, and vitamin B12 availability influence erythropoiesis and red-cell indices [21]. Previous studies have shown that anemia during breast-cancer chemotherapy may reflect both treatment toxicity and iron restriction [14,22]. In addition, transferrin is a negative acute-phase protein; inflammatory suppression may reduce circulating transferrin and limit iron delivery to erythroid precursors [23].

The combination of low serum iron and low transferrin in cases is compatible with inflammation-associated iron restriction, although the absence of hepcidin, C-reactive protein, and soluble transferrin receptor measurements prevents a firm distinction between absolute and functional deficiency. Hepcidin binds ferroportin and reduces iron export from enterocytes and macrophages, thereby lowering circulating iron availability [24,25]. Similar disturbances in hepcidin and iron handling have been described in cancer and chronic inflammatory states [8,9,26].

Iron biology may also be relevant to tumor behavior. Experimental and transcriptomic work has linked altered cellular iron handling, reduced ferroportin expression, and increased hepcidin signaling to intracellular iron retention and breast-cancer progression [10,18,27-29]. Iron-driven oxidative stress and inflammatory proteins have also been identified in the breast-tumor microenvironment [34]. These mechanisms provide biological context but were not directly measured in the present study.

The predominance of iron-deficiency and inflammatory anemia is consistent with the coexistence of depleted stores and inflammation-mediated sequestration [12,19,20,30,31]. The similar anemia distribution among chemotherapy-exposed and unexposed cases contrasts with the original assumption that chemotherapy alone explained the high prevalence. Treatment selection, prior nutritional status, disease stage, bleeding, and unmeasured inflammation could have confounded the comparison. Longitudinal measurements before and during each chemotherapy cycle would be needed to establish temporal change.

Table 6: Distribution of anemia types according to chemotherapy exposure and control status

Anemia category	All participants (N = 630)	All cases (n = 315)	Chemotherapy (n = 228)	No chemotherapy (n = 87)	Controls (n = 315)
No anemia	276 (43.8)	55 (17.5)	40 (17.5)	15 (17.2)	221 (70.2)
Iron-deficiency anemia	212 (33.7)	173 (54.9)	120 (52.6)	53 (60.9)	39 (12.4)
Inflammatory anemia	134 (21.3)	79 (25.1)	60 (26.3)	19 (21.8)	55 (17.5)
Megaloblastic anemia	8 (1.3)	8 (2.5)	8 (3.5)	0 (0.0)	0 (0.0)

Note: Values are n (column %). Pearson chi-square across chemotherapy-exposed cases, unexposed cases and controls: $\chi^2 = 204.82$, df = 6, p < 0.001. Within cases, anemia-type distribution by chemotherapy exposure: $\chi^2 = 4.35$, df = 3, p = 0.226. Statistics were recalculated from the counts displayed in the source manuscript.

Supportive-care guidelines recommend identifying the mechanism of anemia before treatment. Intravenous iron can improve hematological outcomes in selected oncology patients, with or without erythropoiesis-stimulating agents, but eligibility depends on iron indices, symptoms, treatment intent, thrombotic risk, and local protocols [16,32-35]. In Cameroon, systematic screening with complete blood count and basic iron studies may be a pragmatic first step, followed by targeted management rather than empirical iron supplementation.

Study limitations

The cross-sectional design precluded causal inference and assessment of changes over time. Hepcidin, C-reactive protein, soluble transferrin receptor, folate, and vitamin B12 were not measured, limiting discrimination among anemia mechanisms. Potential confounders such as chemotherapy regimen, cumulative dose, nutritional status, bleeding, renal function, and infection were not fully characterized. Hospital-based recruitment in two urban facilities also limits generalizability. Finally, the operational criteria used to classify anemia subtypes require explicit reporting before submission.

Conclusion

In conclusion, anemia and iron-metabolism abnormalities were highly prevalent among Cameroonian women with breast cancer, with iron-deficiency and inflammatory patterns predominating. Chemotherapy exposure was associated with lower hematocrit and MCV, but not with a higher cross-sectional anemia prevalence in the displayed data. Routine etiological evaluation of anemia and prospective monitoring during treatment are needed to guide safe correction and improve treatment tolerance.

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