

Research Article

Association Between Cancer Antigen 15-3 and Haematological Parameters According to Treatment Status in Nigerian Women With Breast Cancer

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Abstract

Background: Cancer antigen 15-3 (CA 15-3), a circulating epitope of mucin-1 (MUC1), is used principally to support monitoring of breast cancer, whereas complete blood count indices reflect inflammation, marrow function and treatment-related toxicity. Treatment exposure can alter both marker systems, so the relationship between them may differ according to treatment status, and Nigerian data are limited. **Aim:** To determine the association between serum CA 15-3 and haematological parameters overall and within treatment-exposed, newly diagnosed and healthy-control groups, and to describe CA 15-3 concentrations across the three groups. **Methods:** A hospital-based cross-sectional case-control study at the University of Port Harcourt Teaching Hospital enrolled 120 Nigerian women: 40 treatment-exposed patients (TG), 40 newly diagnosed treatment-naïve patients (NG) and 40 apparently healthy controls (HC). Serum CA 15-3 was measured by enzyme-linked immunosorbent assay and a complete blood count panel on an automated five-part differential analyser. CA 15-3 was compared across groups by the Kruskal-Wallis test with Holm-adjusted Mann-Whitney pairwise comparisons, with one-way analysis of variance reported as a supportive analysis. Associations between CA 15-3 and each haematological parameter were assessed with two-tailed Spearman rank correlations using pairwise-complete observations (approximately 60 pooled, approximately 20 per group), with Benjamini-Hochberg false-discovery-rate (FDR) correction within each analysis family. **Results:** CA 15-3 differed among groups ($H = 10.510$, $df = 2$, $p = 0.0052$), with the highest median in newly diagnosed patients (158.50 U/mL; IQR 36.13-185.95) versus treatment-exposed patients (34.00; 14.85-121.05) and healthy controls (26.80; 22.98-30.75); only the newly diagnosed versus control contrast remained significant after Holm adjustment ($p = 0.0019$). In the pooled sample, CA 15-3 correlated positively with white cell count (WBC; $\rho = 0.386$; FDR $p = 0.0433$) and absolute neutrophil count (NEU#; $\rho = 0.373$; FDR $p = 0.0433$). Group-specific analysis concentrated these findings in treatment-exposed patients, in whom CA 15-3 correlated with NEU# ($\rho = 0.654$; FDR $p = 0.0282$), WBC ($\rho = 0.644$; FDR $p = 0.0282$) and red cell distribution width-CV ($\rho = 0.622$; FDR $p = 0.0297$). No correlation survived FDR correction in newly diagnosed patients or healthy controls. **Conclusion:** The pooled CA 15-3 associations with leucocyte and neutrophil counts were concentrated in treatment-exposed patients, whereas CA 15-3 concentrations were highest in newly diagnosed patients. Treatment status should be considered when interpreting CA 15-3 alongside routine blood-count indices. The findings are exploratory given the small group-specific samples and require confirmation in larger longitudinal studies.

1. Introduction

Female breast cancer was the second most frequently diagnosed cancer overall and the most frequent cancer among women in global estimates for 2022, with 2,296,840 new cases and 666,103 deaths estimated [1]. The burden is concentrated in low- and middle-income countries, where late-stage presentation, limited screening and constrained access to systemic therapy produce mortality that is disproportionate to incidence [2]. Systematic review estimates place breast cancer incidence in Africa at 54 per 100,000 women, with an age-standardised rate of 63 per 100,000 [3], and a prospective multicentre cohort across sub-Saharan Africa documented a wide survival gap relative to high-income settings [4]. In Nigeria, institutional analyses have reported late-stage presentation and constrained uptake of early detection services [5], and immunohistochemical studies have reported triple-negative proportions of 40% and above in Nigerian cohorts [6]. Accessible laboratory measures that complement clinical and pathological assessment therefore carry practical value in this setting.

Malignant progression involves systemic processes in addition to tumour-cell proliferation, including host inflammation, immune remodelling and altered marrow function [7–9]. Anaemia of inflammation, driven by cytokine-mediated iron sequestration and compounded by marrow-suppressive treatment, is among the commonest laboratory findings in oncology populations [8]. Neutrophils contribute to tumour-associated inflammation through proteases, reactive oxygen species and neutrophil extracellular traps [9]. Lymphocyte depletion accompanies disease progression and cytotoxic treatment, and lower absolute lymphocyte counts predict poorer survival in metastatic breast cancer [10], while triple-negative disease is associated with remodelling of the circulating immune compartment [7]. The complete blood count measures these processes at low cost, and published analyses link lower absolute lymphocyte counts and higher neutrophil-to-lymphocyte ratios to poorer survival in metastatic disease [10], support combined panels of inflammatory indices and serum tumour markers for diagnostic discrimination [11], and relate laboratory indices to treatment response and prognosis in breast cancer [12].

Serum cancer antigen 15-3 (CA 15-3) is the circulating extracellular domain of mucin-1 and the most widely used serum biomarker in breast cancer [13]. A meta-analysis of 12,993 patients associated elevated CA 15-3 and carcinoembryonic antigen values with adverse clinicopathological characteristics [14]. Concentrations decline after effective chemotherapy and rise with disease progression, which underpins the use of the marker in monitoring [15]. CA 15-3 nonetheless has limited sensitivity for early disease and is not recommended as a stand-alone screening or diagnostic test; contemporary guidelines place biomarker results within the wider context of tumour biology, disease burden and treatment rather than treating a single serum value as determinative [16], and its concentration has been associated with adverse clinicopathological characteristics and metastatic progression in some cohorts [17]. CA 15-3 therefore reflects tumour mass, and blood counts reflect host physiology, so the two domains capture different dimensions of disease status, and combined interpretation has been proposed for differential diagnosis and monitoring [11].

Nigerian evidence for each domain exists, but has been gathered separately. A Lagos series of pre-chemotherapy patients reported lower mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration and higher red cell distribution width (RDW) in patients than in healthy controls, with anaemia more frequent among patients [18]. Studies of treated patients have reported lower haemoglobin and packed cell volume alongside leucocyte changes [19] and reductions in haemoglobin, red cell count and haematocrit after Adriamycin-cyclophosphamide chemotherapy [20], and differences in haemoglobin, haematocrit, mean corpuscular volume and RDW between women with and without breast cancer have been reported in a case-control design [21]. These studies each examined a single domain, a single time point or a single treatment state. Studies combining blood-cell indices with CA 15-3 have reported potentially useful diagnostic or prognostic information [11, 12], but treatment exposure can materially alter both marker systems, and no Nigerian study has examined the association between CA 15-3 and haematological parameters, whether across or within treatment strata.

Pooling clinically distinct groups can in addition distort correlation estimates, because systematic differences between patients and healthy women in the levels of both variables can generate pooled coefficients that do not exist within any single group; pilot evidence that both marker systems vary with tumour onset when patients are classified accordingly supports a stratified analytical approach [22]. Treatment-related interference also has a direct mechanism: granulocyte colony-stimulating factor (G-CSF)-supported adjuvant chemotherapy has been shown to raise serum CA 15-3 through increased neutrophil number and neutrophil MUC1 expression rather than tumour progression [23]. The relationship between CA 15-3 and haematological parameters therefore requires examination both in the pooled cohort and separately within treatment-exposed patients, newly diagnosed patients and healthy controls.

The study aimed to determine the relationship between serum CA 15-3 and haematological parameters according to breast-cancer treatment status among Nigerian women. The objectives were (1) to describe and compare CA 15-3 concentrations across the three study groups; (2) to determine the association between CA 15-3 and haematological parameters in the pooled sample; and (3) to determine these associations separately within treatment-exposed patients, newly diagnosed patients and healthy controls. The hypothesis was that the strength and direction of these associations differ according to treatment status.

2. Methods

2.1. Study design and setting

A hospital-based analytical cross-sectional case-control design was employed. The study was conducted at the University of Port Harcourt Teaching Hospital (UPTH), East-West Road, Choba, Port Harcourt, Rivers State, Nigeria, a tertiary referral centre and the primary specialised oncology service for the South-South geopolitical zone. Participants were enrolled between June 2021 and July 2025 through the Breast Unit of the Department of Surgery, and laboratory work involved the Departments of Haematology/Blood Transfusion and Anatomical Pathology at UPTH and the Safety Molecular Laboratory, Enugu. Clinical, questionnaire and laboratory data were collected from each participant at a single time point.

2.2. Ethics approval

Approval was obtained from the Research Ethics Committee of the University of Port Harcourt Teaching Hospital (UPTH/ADM/90/SII/VOL.XI/1235) in line with the Declaration of Helsinki, and written informed consent was obtained from every participant before enrolment. Confidentiality and anonymity were maintained through unique identification codes.

2.3. Study population and group definitions

The study population comprised 120 women aged 20 to 80 years, distributed equally across three groups. The treatment-exposed group comprised 40 women with histologically confirmed breast cancer who had received therapy (surgery, chemotherapy or other treatment) before sample collection Table 2. The newly diagnosed group comprised 40 women with histologically confirmed breast cancer who were treatment-naïve at enrolment. The healthy control group comprised 40 apparently healthy women recruited from the hospital staff community and the wider university community. Controls had no personal history of breast cancer or other malignancy, no family history suggestive of hereditary cancer syndromes, no acute infection, chronic inflammatory condition, autoimmune disease or haematological disorder, no pregnancy or lactation, and no immunosuppressive or cytotoxic therapy. Patients were excluded for previous non-breast malignancy, documented haematological disorders, active acute infection, autoimmune or chronic inflammatory disease, pregnancy or lactation, incomplete clinicopathological records, inadequate or haemolysed samples, or inability to provide informed consent. Breast cancer diagnosis was established by core needle biopsy or mastectomy histopathology in all patients, and treatment status at enrolment defined the exposure. Participants were recruited by purposive sampling at the Breast and General Surgery Units, a non-probability approach in which individuals are selected deliberately against the predefined eligibility criteria to anchor the laboratory measurements in histologically confirmed disease states and to exclude specimens of inadequate pre-analytical quality. The sample size was determined with G*Power 3.1.9.2 using the F-test for one-way analysis of variance with fixed effects at an effect size of 0.4, an error probability of 0.05 and a power of 0.95 across the three study groups, which yielded a required total of 102 participants; a total of 120 was adopted and distributed equally across the groups, 40 per group, to combine statistical adequacy with pragmatic feasibility. This calculation addressed the group comparison of CA 15-3 and not the correlation analyses.

2.4. Sample collection

Venous blood was collected once from each participant under aseptic conditions. Aliquots for the complete blood count were drawn into potassium ethylenediaminetetraacetic acid (K2-EDTA) vacutainer tubes, held at ambient laboratory temperature (18–25 °C), inverted 8 to 10 times immediately after collection and processed within 2 hours. Aliquots for CA 15-3 were collected into plain tubes, allowed to clot and centrifuged, and the separated serum was stored until analysis.

2.5. Serum CA 15-3 assay

Serum CA 15-3 concentrations were determined by a solid-phase sandwich enzyme-linked immunosorbent assay (ELISA) based on the streptavidin-biotin immunoenzymometric technique, following the manufacturer's protocol. Biotinylated monoclonal capture antibodies bound CA 15-3 in streptavidin-coated microplate wells, enzyme-conjugated detection antibodies formed sandwich complexes at a second epitope, and colour developed after chromogenic substrate addition. Absorbance was measured on a microplate spectrophotometer at 450 nm after termination of the reaction with stop solution. Concentrations were calculated from a calibration curve generated with reference standards and are expressed in units per millilitre (U/mL). Internal quality controls were included in every assay run.

2.6. Complete blood count

The complete blood count was measured on the Mindray BC-5300 automated five-part differential haematology analyser (Shenzhen Mindray Bio-Medical Electronics Co., Ltd, Shenzhen, China) in whole-blood mode. Red cells and platelets are enumerated by electrical impedance on this platform, leucocytes are differentiated by laser-scatter flow cytometry with chemical dye, and haemoglobin is measured photometrically. The parameters entered into correlation analysis comprised red blood cell count (RBC, $\times 10^{12}/L$), haemoglobin (HGB, g/dL), haematocrit (HCT, %), mean corpuscular volume (MCV, fL), mean corpuscular haemoglobin (MCH, pg), mean corpuscular haemoglobin concentration (MCHC, g/L) and red cell distribution width in both reported forms, RDW-CV (%) and RDW-SD (fL); total white blood cell count (WBC, $\times 10^9/L$) with neutrophil (NEU), lymphocyte (LYM), monocyte (MON), eosinophil (EOS) and basophil (BAS) percentages and absolute counts, together with atypical lymphocyte percentage (ALY, %) and immature cell percentage (IMM, %); and platelet count (PLT, $\times 10^9/L$), mean platelet volume (MPV, fL), platelet distribution width (PDW, %), plateletcrit (PCT, %), platelet large cell count (PLCC, $\times 10^9/L$) and platelet-large-cell ratio (PLCR, %). Low, normal and high commercial controls were processed before every analytical cycle, with Levey-Jennings monitoring set at ± 2 standard deviations of target values; patient samples were not run until out-of-range controls were resolved, routine maintenance followed a fixed schedule, and external quality assessment was in place.

2.7. Statistical analysis

Statistical analysis was performed in SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA). CA 15-3 was summarised as median with interquartile range (IQR) because of marked skewness, with mean $\pm$ standard deviation given for reference, and other continuous parameters are reported as mean $\pm$ standard error of the mean (SEM); categorical parameters are reported as n (%). The between-group CA 15-3 contrast used the Kruskal-Wallis test (df = 2) as the primary analysis, with pairwise two-sided Mann-Whitney U tests under Holm adjustment [24]; a one-way analysis of variance (ANOVA) on untransformed values, with F(2, 117), was reported as a supportive analysis only given the skewness. Associations between CA 15-3 and each haematological parameter were assessed with two-tailed Spearman rank correlations computed first in the pooled sample and then repeated within each study group, using pairwise-complete observations, so that the number of complete pairs varied by parameter. Correlation strength was interpreted by absolute rho as negligible (<0.10), weak (0.10–0.29), moderate (0.30–0.49), strong (0.50–0.69) or very strong (≥ 0.70). Benjamini-Hochberg false-discovery-rate (FDR) correction [25] was applied within each analysis family, comprising 26 analysable parameters in the pooled and treatment-exposed families and 25 in the newly diagnosed and healthy-control families (the absolute basophil count showed no variation and was excluded, and the basophil percentage was not analysable in the latter two groups), and FDR-adjusted findings were prioritised in interpretation. Categorical distributions were compared with the chi-square test. A two-sided $p < 0.05$ defined statistical significance, and significant p values appear in bold in the tables.

3. Results

3.1. Analysis set

The analysis set comprised all 120 enrolled women, 40 in each study group, with serum CA 15-3 and the haematological panel measured once per participant. The correlation analyses used pairwise-complete observations, corresponding to approximately 60 pooled observations and approximately 20 per group for most parameters, with fewer for ALY%, IMM%, PLCC and PLCR. The absolute basophil count was not analysable in any family, and the basophil percentage was not analysable in the newly diagnosed and healthy-control families.

3.2. Participant anthropometric characteristics by group

Mean age was 47.15 ± 11.00 years in the treatment-exposed group and 46.65 ± 11.48 years in the newly diagnosed group versus 35.10 ± 10.01 years in healthy controls, a significant difference ($F = 15.8005$, $p < 0.0001$), and the two patient groups were of similar age. Body weight also differed across groups ($p = 0.0013$), body mass index was highest in healthy controls ($p = 0.0369$), and height did not differ across groups ($p = 0.1245$) Table 1.

Table 1: Baseline anthropometric characteristics of study participants by group (N=120)

Parameter	All participants (n=120)	Treatment-exposed (n=40)	Newly diagnosed (n=40)	Healthy control (n=40)	F (df = 2, 117)	p value
Age (years)	42.97 ± 1.11	$47.15 \pm 11.00a$	$46.65 \pm 11.48a$	$35.10 \pm 10.01b$	15.8005	<0.0001
Body weight (kg)	69.83 ± 1.23	$69.40 \pm 11.88ab$	$64.70 \pm 10.94b$	$75.40 \pm 5.23a$	7.0039	0.0013
Height (ft)	5.27 ± 0.04	5.35 ± 0.43	5.16 ± 0.37	5.30 ± 0.50	2.1206	0.1245
BMI (kg/m ²)	27.45 ± 0.62	$26.29 \pm 4.74a$	$26.38 \pm 4.41a$	$29.68 \pm 9.62b$	3.3187	0.0369
BMI classification					χ^2 (df = 6)	p value
Underweight (<18.5)	4 (3.33%)	2 (5.00%)	2 (5.00%)	0 (0.00%)	6.096	0.4126
Normal (18.5-24.9)	40 (33.33%)	14 (35.00%)	14 (35.00%)	12 (30.00%)		
Overweight (25.0-29.9)	46 (38.33%)	18 (45.00%)	14 (35.00%)	14 (35.00%)		
Obesity (≥ 30.0)	30 (25.00%)	6 (15.00%)	10 (25.00%)	14 (35.00%)		

Footnote: Group values are mean $\pm$ SD; all-participant values are mean $\pm$ SEM, as reported by the analysis output. Superscript letters denote post-hoc pairwise comparisons from one-way ANOVA; groups that share a letter do not differ significantly ($p > 0.05$). BMI = body mass index. F values derive from one-way ANOVA and χ^2 from the chi-square test. Significant p values in bold.

3.3. Tumour and treatment characteristics of patients

Clinical stage II accounted for 32 of the 80 tumours (40.0%) and stage III for 44 (55.0%). Histological grade 1 accounted for 36 (45.0%) and grade 2 for 42 (52.5%). The median clinical stage was 3.0 (interquartile range 2.0 to 4.0) in the treatment-exposed group versus 2.5 (1.0 to 3.0) in the newly diagnosed group ($p = 0.301$). All 40 patients in the treatment-exposed group (100.0%) underwent a breast procedure during treatment, 12 (30.0%) underwent mastectomy, 6 (15.0%) underwent other surgery and 22 (55.0%) received chemotherapy. In the newly diagnosed group, 28 patients (93.3%) had received no treatment at enrolment Table 2.

Table 2: Tumour and treatment characteristics of breast cancer patients (n=80)

Characteristic	All patients (n=80)	Treatment-exposed (n=40)	Newly diagnosed (n=40)
Clinical stage			
Stage I	2 (2.5%)	0	2 (5.0%)
Stage II	32 (40.0%)	14 (35.0%)	18 (45.0%)
Stage III	44 (55.0%)	24 (60.0%)	20 (50.0%)
Stage IV	2 (2.5%)	2 (5.0%)	0
Histological grade			
Grade 1	36 (45.0%)	20 (50.0%)	16 (40.0%)
Grade 2	42 (52.5%)	20 (50.0%)	22 (55.0%)
Grade 3	2 (2.5%)	0	2 (5.0%)
Treatment and procedures			
Breast procedure during treatment	42 (60.0%)	40 (100.0%)	2 (6.7%)
No treatment	28 (40.0%)	0	28 (93.3%)
Mastectomy	12 (17.1%)	12 (30.0%)	0
Surgery	6 (8.6%)	6 (15.0%)	0
Chemotherapy	24 (34.3%)	22 (55.0%)	NA

Footnote: Values are n (%). Stage and grade distributions are descriptive. For the treatment and procedure block, percentages for all patients are based on 70 patients who underwent breast procedures, and percentages for the treatment-exposed and newly diagnosed groups are based on 40 and 30 patients, respectively. NA = not applicable.

Table 3: Serum CA 15-3 (U/mL) by study group

Group	Median (IQR)	Mean $\pm$ SD	Range
Treatment-exposed (n=40)	34.00 (14.85-121.05)	87.19 $\pm$ 94.52	8.3-286.4
Newly diagnosed (n=40)	158.50 (36.13-185.95)	121.24 $\pm$ 76.32	8.4-203.0
Healthy control (n=40)	26.80 (22.98-30.75)	26.24 $\pm$ 8.91	12.3-50.6

Footnote: CA 15-3 = cancer antigen 15-3; U/mL = units per millilitre; IQR = interquartile range. Overall test: Kruskal-Wallis $H(2) = 10.510$, $p = 0.0052$ (primary). Holm-adjusted Mann-Whitney pairwise p values: treatment-exposed vs newly diagnosed 0.1717; treatment-exposed vs healthy control 0.3235; newly diagnosed vs healthy control 0.0019 (bold). Supportive one-way ANOVA: $F(2,117) = 19.2242$, $p < 0.0001$, with means $\pm$ SEM of 87.19 $\pm$ 14.75, 121.24 $\pm$ 11.91 and 26.25 $\pm$ 1.39 U/mL.

3.4. Serum CA 15-3 concentrations according to treatment status

CA 15-3 differed across groups (Kruskal-Wallis $H = 10.510$, $df = 2$, $p = 0.0052$; Table 3). The median was highest in the newly diagnosed group (158.50 U/mL; IQR 36.13-185.95), intermediate in the treatment-exposed group (34.00; 14.85-121.05) and lowest in healthy controls (26.80; 22.98-30.75). After Holm adjustment, the newly diagnosed group differed significantly from healthy controls ($p = 0.0019$), whereas treatment-exposed versus newly diagnosed ($p = 0.1717$) and treatment-exposed versus healthy controls ($p = 0.3235$) did not differ. Within-group dispersion was marked: the standard deviation exceeded the mean in the treatment-exposed group, and group ranges extended to 286.4, 203.0 and 50.6 U/mL in the treatment-exposed, newly diagnosed and control groups, respectively. The supportive one-way ANOVA on untransformed values was also significant ($F(2,117) = 19.2242$, $p < 0.0001$; means $\pm$ SEM 87.19 $\pm$ 14.75, 121.24 $\pm$ 11.91 and 26.25 $\pm$ 1.39 U/mL), and its post-hoc testing separated all three groups, but this analysis is not preferred because of the skewness, and the discrepancy with the Holm-adjusted pairwise results reflects the wide within-group dispersion in the two patient groups.

3.5. Pooled associations between CA 15-3 and haematological parameters

Across all participants, CA 15-3 showed moderate positive correlations with WBC ($\rho = 0.386$, $p = 0.0023$) and absolute neutrophil count ($\rho = 0.373$, $p = 0.0033$), and both survived Benjamini-Hochberg correction (FDR-adjusted $p = 0.0433$ for both) Table 4. Neutrophil percentage showed a weak positive unadjusted association ($\rho = 0.266$, $p = 0.0398$) that did not survive correction (FDR-adjusted $p = 0.3448$). The remaining erythrocyte, leucocyte and platelet parameters showed weak or negligible unadjusted coefficients, and none was significant after correction Table 4.

3.6. Group-specific associations between CA 15-3 and haematological parameters

Group-specific analysis showed that the pooled leucocyte findings arose principally from the treatment-exposed group. Within treatment-exposed patients, CA 15-3 correlated strongly and positively with absolute neutrophil count ($\rho = 0.654$, $p = 0.0018$; FDR-adjusted $p = 0.0282$), WBC ($\rho = 0.644$, $p = 0.0022$; FDR-adjusted $p = 0.0282$) and RDW-CV ($\rho = 0.622$, $p = 0.0034$; FDR-adjusted $p = 0.0297$) Table 5. Other correlations in this group were nominal only: RDW-SD ($\rho = 0.552$; FDR-adjusted $p = 0.0755$), platelet count ($\rho = 0.509$; FDR-adjusted $p = 0.1051$), plateletcrit ($\rho = 0.502$; FDR-adjusted $p = 0.1051$), immature cell percentage ($\rho = 0.560$; FDR-adjusted $p = 0.2108$) and neutrophil percentage ($\rho = 0.434$; FDR-adjusted $p = 0.2072$) (Supplementary Table S1). In newly diagnosed patients, no parameter survived correction; nominal inverse associations with platelet count ($\rho = -0.561$; FDR-adjusted $p = 0.1274$), MCHC ($\rho = -0.560$; FDR-adjusted $p = 0.1274$), plateletcrit ($\rho = -0.478$; FDR-adjusted $p = 0.2285$) and atypical lymphocyte percentage ($\rho = -0.738$, resting on very few complete pairs; FDR-adjusted $p = 0.2285$) were observed (Supplementary Table S2). In healthy controls, nominal associations involving absolute eosinophil count ($\rho = 0.470$; FDR-adjusted $p = 0.2852$), plateletcrit ($\rho = -0.466$; FDR-adjusted $p = 0.2852$) and RDW-SD ($\rho = -0.450$; FDR-adjusted $p = 0.2852$) also did not survive correction (Supplementary Table S3).

Table 5: Selected group-specific Spearman correlations between CA 15-3 and haematological parameters

Study group	Parameter	ρ	Unadjusted p	FDR-adjusted p	Result
Treatment-exposed	WBC	0.644	0.0022	0.0282	Significant
Treatment-exposed	NEU#	0.654	0.0018	0.0282	Significant
Treatment-exposed	NEU%	0.434	0.0558	0.2072	Not significant
Treatment-exposed	RDW-CV	0.622	0.0034	0.0297	Significant
Newly diagnosed	WBC	0.085	0.7201	0.8183	Not significant
Newly diagnosed	NEU#	0.124	0.6037	0.8056	Not significant
Newly diagnosed	NEU%	0.073	0.7608	0.8229	Not significant
Newly diagnosed	RDW-CV	0.291	0.2126	0.4832	Not significant
Healthy control	WBC	-0.061	0.7980	0.9964	Not significant
Healthy control	NEU#	0.005	0.9836	0.9975	Not significant
Healthy control	NEU%	0.165	0.4857	0.9340	Not significant
Healthy control	RDW-CV	-0.328	0.1576	0.4378	Not significant

Footnote: Complete group-specific results are provided in Supplementary Tables S1 to S3. FDR = Benjamini-Hochberg false-discovery rate within each group-specific family. Significant p values in bold.

Table 4: Pooled Spearman correlations between CA 15-3 and haematological parameters (pairwise-complete observations)

Parameter	ρ	Unadjusted p	FDR-adjusted p	Direction and strength
WBC	0.386	0.0023	0.0433	Moderate positive, significant
NEU#	0.373	0.0033	0.0433	Moderate positive, significant
NEU%	0.266	0.0398	0.3448	Weak positive
MCHC	-0.215	0.0985	0.6400	Weak negative
LYM%	-0.191	0.1432	0.7447	Weak negative
BAS%	-0.148	0.2593	0.8879	Weak negative
MCH	-0.125	0.3410	0.8879	Weak negative
LYM#	0.111	0.3970	0.8879	Weak positive
IMM%	0.171	0.4024	0.8879	Weak positive
MON#	0.105	0.4258	0.8879	Weak positive
RDW-SD	0.104	0.4304	0.8879	Weak positive
RDW-CV	0.098	0.4555	0.8879	Negligible positive
PLCC	0.100	0.5077	0.8879	Weak positive
PDW	-0.086	0.5152	0.8879	Negligible negative
EOS%	-0.077	0.5598	0.8879	Negligible negative
PLCR	0.064	0.6531	0.8879	Negligible positive
ALY%	-0.095	0.6823	0.8879	Negligible negative
MPV	0.053	0.6849	0.8879	Negligible positive
MCV	-0.052	0.6926	0.8879	Negligible negative
HCT	0.046	0.7297	0.8879	Negligible positive
PCT	0.037	0.7811	0.8879	Negligible positive
HGB	-0.036	0.7855	0.8879	Negligible negative
PLT	0.032	0.8096	0.8879	Negligible positive
EOS#	0.030	0.8196	0.8879	Negligible positive
MON%	-0.022	0.8672	0.9019	Negligible negative
RBC	-0.002	0.9870	0.9870	Negligible negative

Footnote: Two-tailed Spearman correlations with pairwise-complete observations (approximately 60 pooled; fewer for ALY%, IMM%, PLCC and PLCR). WBC = white blood cell count; NEU = neutrophils; LYM = lymphocytes; MON = monocytes; EOS = eosinophils; BAS = basophils; ALY = atypical lymphocytes; IMM = immature cells; RDW = red cell distribution width (CV, coefficient of variation; SD, standard deviation); PLT = platelet count; MPV = mean platelet volume; PDW = platelet distribution width; RBC = red blood cell count; HGB = haemoglobin; HCT = haematocrit; MCV = mean corpuscular volume; MCH = mean corpuscular haemoglobin; MCHC = mean corpuscular haemoglobin concentration; # = absolute count; % = percentage. Strength bands by absolute rho: negligible <0.10, weak 0.10-0.29, moderate 0.30-0.49, strong 0.50-0.69, very strong ≥ 0.70 . FDR = Benjamini-Hochberg false-discovery rate over the 26-parameter pooled family. Significant p values in bold. The absolute basophil count was not estimable.

4. Discussion

The present findings show that treatment status materially changes the relationship between CA 15-3 and routine haematological parameters, and that the pooled and stratified readings of the same data lead to different conclusions. CA 15-3 concentrations separated the groups, with the highest median in newly diagnosed patients, but only the newly diagnosed versus control contrast was robust after adjustment. Pooled analysis identified moderate positive correlations between CA 15-3 and WBC and absolute neutrophil count, yet stratification placed both associations, and one with RDW-CV, almost entirely within the treatment-exposed group, while newly diagnosed patients and controls showed none surviving correction Tables 3 to 5. Without the group-specific analysis, the pooled coefficients could have implied that one biological relationship operates across untreated disease and healthy women; the stratified results show that this reading is wrong [22]. All findings are associations in modest samples, and none establishes causation.

The highest CA 15-3 concentrations among newly diagnosed participants are compatible with tumour-associated MUC1 shedding and disease burden before treatment [13, 14]. A meta-analysis of 12,993 patients associated elevated CA 15-3 and carcinoembryonic antigen values with adverse clinicopathological characteristics [14], and concentrations decline after effective chemotherapy and rise with disease progression, which underpins the monitoring role of the marker [15]. The treatment-exposed group nonetheless did not differ significantly from either the newly diagnosed group or healthy controls under Holm adjustment, so these data cannot be used to claim a treatment-related fall in CA 15-3; demonstrating that would require serial within-patient measurements. The marked overlap and wide dispersion, exemplified by a treatment-exposed median of 34.00 U/mL against a mean of 87.19 U/mL and by an upper quartile of healthy-control values exceeding 30 U/mL Table 3, argue against interpreting a single CA 15-3 value, or a group mean alone, in isolation, which is consistent with guidance that the marker is supportive rather than independently diagnostic [16]. The prognostic associations reported by Uygur and Gumus [17] were likewise not accompanied by diagnostic stand-alone utility, and stage, metastatic status and molecular subtype, which influence CA 15-3 [14, 17], were not examined against CA 15-3 in the present analysis.

The pooled correlations require cautious reading because the pooled sample mixes three clinically distinct groups. Healthy controls would be expected to have lower CA 15-3 concentrations and different inflammatory profiles from patients, so a pooled coefficient may partly reflect between-group separation in the means of both variables rather than a continuous biological relationship within any one group, a form

of aggregation bias that stratified analysis is required to exclude [22]. The group-specific results confirmed this concern in the present data: the pooled WBC and neutrophil coefficients of approximately 0.37 to 0.39 were attenuated to essentially null within the newly diagnosed and control groups and were strengthened to strong correlations within the treatment-exposed group ($\rho \approx 0.62$ to 0.65). In the present direction the bias was conservative, in that pooling diluted rather than manufactured the association, but the same aggregation structure could in principle produce a spurious pooled relationship where none exists within strata. Stratified analysis was therefore not a supplementary exercise but a necessary condition for interpreting the pooled findings, and the treatment-exposed group should be regarded as the primary stratum for the observed associations.

Several mechanisms could account for the strong CA 15-3-neutrophil association in treatment-exposed women, and they are not mutually exclusive. Anticancer therapy alters marrow kinetics, provokes tissue injury and infection, and commonly involves corticosteroids or granulocyte colony-stimulating factor, each of which raises neutrophil counts independently of tumour activity. Most directly, Pentheroudakis and colleagues [23] showed in a prospective study that G-CSF-supported adjuvant chemotherapy raised serum CA 15-3 through increased neutrophil number and neutrophil MUC1 expression rather than tumour progression. That mechanism maps closely onto the present treatment-exposed findings and provides a concrete, testable explanation for why the association concentrates in this group; it cannot be verified here because G-CSF administration, corticosteroid exposure, infection screening, treatment timing and serial CA 15-3 measurements were not recorded, and the patients studied by Pentheroudakis and colleagues received defined adjuvant regimens, whereas treatment in the present cohort was heterogeneous and captured only as a binary status. Peripheral inflammatory indices likewise carry information about treatment response and prognosis, but their meaning depends on treatment timing and clinical context [12]. In parallel, tumour-driven production of interleukin- 1β , interleukin-6, interleukin-8 and granulocyte and granulocyte-macrophage colony-stimulating factors promotes granulopoiesis, neutrophil mobilisation and myeloid recruitment [7, 9], so greater tumour activity and higher CA 15-3 could co-occur with neutrophilia without a direct causal link between the two measurements. The finding is best read as an interaction among tumour activity, host inflammation and treatment exposure, not as a causal effect of CA 15-3 on leucocyte production.

The neutrophil compartment is a biologically plausible partner for a tumour-burden marker, although the two significant pooled coefficients should not be counted as independent signals. Because neutrophils constitute the largest proportion of circulating leucocytes, the WBC and absolute neutrophil correlations are largely one finding rather than two, and FDR correction does not remove the statistical dependence between such tests. Tumour-associated neutrophils can exert antitumour or protumour functions depending on their activation state and cytokine environment [7, 9], and activated neutrophils release neutrophil extracellular traps, proteases, reactive oxygen species, vascular endothelial growth factor and matrix metalloproteinase-9, which can promote tumour-cell migration, vascular permeability and metastatic seeding [7, 9]. The present analysis measured circulating numbers only and did not assess neutrophil activation, phenotype or tissue infiltration, so no inference about protumour function is warranted. The finding that absolute neutrophil count survived correction while neutrophil percentage did not is informative: percentage is a relative measure that can shift when lymphocyte or monocyte proportions change even when the absolute neutrophil number is constant, whereas the absolute count more directly represents circulating neutrophil burden, and published prognostic analyses likewise privilege absolute counts over differential percentages [10]. The persistence of the absolute-count association after false-discovery-rate control therefore indicates quantitative neutrophilia rather than leucocyte redistribution.

The effect sizes nonetheless caution against over-interpretation. The pooled WBC coefficient of 0.386 indicates concordant increases but a strength insufficient for WBC to substitute for CA 15-3, and both variables are influenced by disease stage, tumour burden, infection, inflammatory conditions, obesity, smoking, medication, corticosteroid exposure, chemotherapy timing and the interval between treatment and blood collection [12, 23]. Elevated neutrophil count is therefore not specific for breast-cancer progression, and the observed relationships should not be read as indicating that an increased CA 15-3 value and an increased neutrophil count share a single cause.

The strong positive relationship between CA 15-3 and RDW-CV within treatment-exposed patients adds an erythrocyte dimension that the pooled analysis did not predict, in which the RDW-CV coefficient was negligible ($\rho = 0.098$), confirming that this relationship emerged only after stratification. RDW captures red-cell size heterogeneity and rises with iron, folate or vitamin B12 deficiency, inflammation, renal dysfunction, haemolysis, transfusion and disordered erythropoiesis [8]. The external literature supports RDW as a breast-cancer-associated parameter: a meta-analysis of 4,884 patients associated higher RDW with larger tumours, advanced stage, nodal metastasis and poorer survival [26], and RDW changed over a one-year doxorubicin follow-up [27]. Neither study, however, establishes treatment specificity, and the combined-marker study of Zou and colleagues [11] addressed differential diagnosis of unselected patients from benign disease rather than monitoring of treated women. In the present cohort the RDW-CV association was confined to treated women, which is more consistent with systemic inflammatory or nutritional stress accompanying treatment, or with marrow effects of cytotoxic therapy [8, 19, 20], than with tumour burden itself, and RDW cannot be considered breast-cancer-specific without supportive clinical and biochemical data.

The absence of significant associations between CA 15-3 and haemoglobin, haematocrit, red-cell count, red-cell indices or platelet count indicates that the relationship is more closely connected to the leucocyte-neutrophil inflammatory pathway than to generalised haematological disturbance. Anaemia and red-cell abnormalities in breast cancer arise from nutritional deficiency, chronic inflammation, marrow suppression, bleeding and treatment toxicity and need not change in parallel with the amount of circulating MUC1 antigen [8, 18–21]. Platelet number alone may not reflect platelet activation or tumour-platelet interactions. Composite inflammatory indices such as the neutrophil-to-lymphocyte ratio, the platelet-to-lymphocyte ratio and the systemic immune-inflammation index may extract more information than individual counts [10–12, 28], and combined panels of tumour markers with inflammatory indices have shown value for differential diagnosis and for response and relapse monitoring in neoadjuvant, postoperative and metastatic settings [11, 12, 15, 28], although each of those settings differs from the cross-sectional treatment strata studied here. The present component differentials provide the raw material from which such ratios are calculated, and their formal evaluation in this cohort is a logical next step.

No correlation survived false-discovery-rate correction in the newly diagnosed or healthy-control groups, and the nominal findings in these strata should be interpreted as unconfirmed signals generated across a large testing family [25]. This null pattern carries interpretive weight rather than merely closing the analysis. The newly diagnosed group recorded the highest CA 15-3 concentrations, so a simple model in which tumour burden drives leucocytosis would predict correlations in this stratum, and none were seen (WBC $\rho = 0.085$; NEU# 0.124); the tumour-burden explanation for the pooled finding is therefore not supported, and a treatment-related or group-structure explanation is more consistent with the data. External evidence tempers this further: CA 15-3 and neutrophil counts have been reported to differ by metastatic status among untreated patients in a study that compared groups by metastasis [29], but that was a different design, and most newly diagnosed patients here had Stage II–III disease (two were Stage I), with few likely to be metastatic, so the present stratum was not configured to

detect a metastasis-dependent relationship. The nominal inverse associations with platelet count, MCHC and plateletcrit in newly diagnosed patients require replication, the atypical lymphocyte percentage estimate rested on very few complete pairs and is particularly unstable, and the opposite signs of the platelet associations in the treatment-exposed (positive) and newly diagnosed (negative) groups are intriguing but nominal. These null strata collectively demonstrate that the CA 15-3-haematology relationship documented internationally in mixed cohorts is not a general property of the assay and analyser but a context-dependent finding concentrated in treated patients.

Demographic composition warrants consideration in the between-group reading. Healthy controls were the youngest group and recorded the highest body mass index Table 1, and both age and body mass index modify circulating blood-cell values, so part of the disease-versus-control contrast in CA 15-3 and in baseline counts may reflect demographic composition. Age was similar between the two patient groups Table 1, so the concentration of associations in the treatment-exposed group is unlikely to reflect age differences. Differences in immunological and immuno-inflammatory parameters of breast cancer patients have previously been documented in Nigerian cohorts, including at this institution [30], findings consistent with the inflammatory dimension of the present results.

The design has several strengths. Three equal groups permitted pooled and stratified correlation analysis within one sampling frame; a broad panel of routinely available indices was analysed alongside the tumour marker; a rank-based method appropriate to the marked skewness of CA 15-3 was used; the false-discovery rate was controlled explicitly within each analysis family rather than left to unadjusted nominal thresholds [25]; and the group-specific approach directly addressed the treatment-related heterogeneity that pooling would otherwise have obscured.

Limitations

The sample size constrains the correlation analyses most directly. The design was powered for the group comparison of CA 15-3 and not for correlation, and the correlations used approximately 60 pooled pairwise-complete observations and approximately 20 per group, with fewer for some parameters. At approximately 20 observations per group, only strong correlations (absolute rho above roughly 0.59) are reliably detectable, so the significant group-specific coefficients (0.62-0.65) lie close to the detection limit and may be overestimated; at approximately 60 pooled observations the threshold is approximately 0.36, so the pooled coefficients (0.37-0.39) sit just above it. Parameter-specific complete-pair sizes were not tabulated, which limits the precision of this assessment. The WBC and absolute neutrophil count results are statistically dependent, and FDR correction does not remove the dependence between tests, so the myeloid finding should be regarded as one signal. Treatment type, cumulative dose, treatment cycle, G-CSF exposure, corticosteroid use, infection screening and transfusion history entered the analysis only through binary group membership or not at all, so treatment exposure functions as a status variable in every contrast, and the treatment-exposed group is itself heterogeneous (mastectomy 30%, other surgery 15%, chemotherapy 55%); the mechanism proposed by Pentheroudakis and colleagues [23] could therefore not be tested directly. Confounding is incompletely addressed: controls were approximately 12 years younger and had the highest body mass index, and stage, molecular subtype, infection status and nutritional markers were not adjusted for, with no partial-correlation or regression model fitted. Neutrophil activation, phenotype and tumour infiltration were not assessed, only circulating numbers. The cross-sectional design with a single time point per participant cannot establish temporality or causation, and the single tertiary centre with hospital-community controls limits the generalisability of the group values and of the correlation estimates. The marked skewness of CA 15-3 means that group means must be read jointly with medians and interquartile ranges, and assay documentation (manufacturer, kit performance characteristics and reference limits) was not systematically reported, which limits cross-study comparability.

Recommendations

CA 15-3 should not be interpreted as an independent screening or diagnostic marker, and results should be considered together with clinical findings, imaging, histopathology, molecular subtype, disease stage and treatment history [16]. In treatment-exposed patients with concurrent elevations of CA 15-3 and WBC or absolute neutrophil count, non-malignant explanations including acute infection, corticosteroid exposure, recent chemotherapy and G-CSF use should be reviewed before the pattern is attributed to tumour progression [23]. Serial CA 15-3 and complete blood count measurements at standardised points before, during and after treatment are likely to be more informative than isolated cross-sectional values, and within-patient trends would test whether the treatment-exposed associations track therapy within persons. The CA 15-3-RDW-CV relationship should be investigated alongside iron studies, folate, vitamin B12, C-reactive protein, renal function and documented transfusion history to distinguish inflammation, nutritional deficiency and treatment-related erythropoietic stress [8, 27]. Composite indices including the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and systemic immune-inflammation index should be computed and validated in this and similar cohorts [10–12, 28]. Future studies should use larger, multicentre and longitudinal cohorts of Nigerian women, with sample sizes planned for correlation analyses and pre-specified models adjusted for age, tumour stage, metastatic burden, molecular subtype, treatment regimen, treatment duration and infection status, under formal false-discovery-rate control [25]. Laboratories should maintain documented internal quality control, calibration and external quality assessment for both CA 15-3 and haematology testing, and assay platform, manufacturer, analytical performance and reference limits should be reported to improve reproducibility across centres. The present subgroup-specific correlations should be externally validated before WBC, absolute neutrophil count or RDW-CV is incorporated into a clinical decision algorithm alongside CA 15-3, and future versions of this analysis should be reported against the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

5. Conclusion

CA 15-3 concentrations differed according to study group and were highest in newly diagnosed Nigerian women with breast cancer, although only the newly diagnosed versus control contrast was robust after adjustment. Pooled positive correlations with WBC and absolute neutrophil count were concentrated in treatment-exposed patients, in whom CA 15-3 also correlated with RDW-CV after false-discovery-rate correction, and no correlation survived correction in newly diagnosed participants or healthy controls. Given the small group-specific samples and the unrecorded treatment details, these findings are exploratory. Treatment status must therefore be considered when interpreting CA 15-3 alongside routine blood-count indices, and confirmation requires larger, longitudinal, treatment-stratified and multicentre studies.

Article Information

Ethical Approval: In line with the Helsinki Declaration, approval was obtained from the UPTH Research Ethics Committee (UPTH/ADM/90/SII/VOL.XI/1235).

Informed Consent: Written informed consent was obtained from all participants, and confidentiality was maintained using identification codes.

Consent for Publication: Written informed consent was obtained from the participant(s) for publication of the relevant information.

Data Availability Statement: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Supplementary Tables

The complete group-specific correlation results are provided below to support transparent reporting. Findings should be interpreted primarily using the FDR-adjusted p values.

Table S1: Treatment-exposed group (n=40)

Parameter	rho	Unadjusted p	FDR-adjusted p	Result
NEU#	0.654	0.0018	0.0282	Significant
WBC	0.644	0.0022	0.0282	Significant
RDW-CV	0.622	0.0034	0.0297	Significant
RDW-SD	0.552	0.0116	0.0755	Not significant
IMM%	0.560	0.0730	0.2108	Not significant
PLT	0.509	0.0218	0.1051	Not significant
PCT	0.502	0.0243	0.1051	Not significant
NEU%	0.434	0.0558	0.2072	Not significant
MON#	0.410	0.0723	0.2108	Not significant
LYM%	-0.386	0.0925	0.2405	Not significant
EOS%	-0.317	0.1739	0.4111	Not significant
RBC	-0.272	0.2454	0.5316	Not significant
PLCR	0.247	0.2929	0.5859	Not significant
EOS#	-0.177	0.4557	0.7807	Not significant
LYM#	0.159	0.5018	0.7807	Not significant
BAS%	-0.158	0.5063	0.7807	Not significant
HCT	-0.150	0.5279	0.7807	Not significant
PDW	-0.146	0.5405	0.7807	Not significant
PLCC	0.105	0.7084	0.9224	Not significant
MPV	-0.087	0.7164	0.9224	Not significant
MCV	0.066	0.7830	0.9224	Not significant
MCH	0.055	0.8186	0.9224	Not significant
MCHC	-0.055	0.8192	0.9224	Not significant
MON%	0.045	0.8515	0.9224	Not significant
HGB	-0.030	0.8997	0.9347	Not significant
ALY%	-0.051	0.9347	0.9347	Not significant
BAS#	NA	NA	NA	Not significant

Table S2: Newly diagnosed group (n=40)

Parameter	rho	Unadjusted p	FDR-adjusted p	Result
PLT	-0.561	0.0100	0.1274	Not significant
MCHC	-0.560	0.0102	0.1274	Not significant
PCT	-0.478	0.0328	0.2285	Not significant
ALY%	-0.738	0.0366	0.2285	Not significant
RDW-SD	0.414	0.0695	0.3475	Not significant
MPV	0.345	0.1364	0.4740	Not significant
PLCC	-0.442	0.1501	0.4740	Not significant
IMM%	-0.556	0.1525	0.4740	Not significant
MON#	-0.312	0.1802	0.4740	Not significant
PLCR	0.407	0.1896	0.4740	Not significant
RDW-CV	0.291	0.2126	0.4832	Not significant
PDW	-0.228	0.3338	0.6954	Not significant
HCT	0.188	0.4265	0.7591	Not significant
MON%	-0.177	0.4554	0.7591	Not significant
MCV	0.167	0.4823	0.7591	Not significant
LYM#	0.155	0.5143	0.7591	Not significant
EOS#	-0.154	0.5162	0.7591	Not significant
NEU#	0.124	0.6037	0.8056	Not significant
HGB	-0.114	0.6310	0.8056	Not significant
MCH	-0.110	0.6445	0.8056	Not significant
RBC	0.089	0.7089	0.8183	Not significant
WBC	0.085	0.7201	0.8183	Not significant
NEU%	0.073	0.7608	0.8229	Not significant
LYM%	-0.058	0.8081	0.8229	Not significant
EOS%	-0.053	0.8229	0.8229	Not significant
BAS%	NA	NA	NA	Not significant
BAS#	NA	NA	NA	Not significant

Table S3: Healthy control group (n=40)

Parameter	rho	Unadjusted p	FDR-adjusted p	Result
EOS#	0.470	0.0365	0.2852	Not significant
PCT	-0.466	0.0385	0.2852	Not significant
RDW-SD	-0.450	0.0463	0.2852	Not significant
EOS%	0.434	0.0556	0.2852	Not significant
MCV	-0.427	0.0604	0.2852	Not significant
HCT	-0.416	0.0684	0.2852	Not significant
PLT	-0.363	0.1159	0.4139	Not significant
HGB	-0.345	0.1360	0.4249	Not significant
RDW-CV	-0.328	0.1576	0.4378	Not significant
PLCC	-0.299	0.2143	0.5356	Not significant
PDW	-0.273	0.2449	0.5566	Not significant
LYM#	-0.197	0.4048	0.8434	Not significant
NEU%	0.165	0.4857	0.9340	Not significant
PLCR	-0.150	0.5291	0.9449	Not significant
MPV	0.134	0.5741	0.9569	Not significant
IMM%	0.181	0.6979	0.9964	Not significant
LYM%	-0.084	0.7252	0.9964	Not significant
MON#	0.075	0.7540	0.9964	Not significant
WBC	-0.061	0.7980	0.9964	Not significant
ALY%	0.108	0.7983	0.9964	Not significant
MON%	0.049	0.8370	0.9964	Not significant
MCH	-0.021	0.9288	0.9975	Not significant
NEU#	0.005	0.9836	0.9975	Not significant
MCHC	0.005	0.9842	0.9975	Not significant
RBC	0.001	0.9975	0.9975	Not significant
BAS%	NA	NA	NA	Not significant
BAS#	NA	NA	NA	Not significant

Supplementary footnote: Two-tailed Spearman correlations with pairwise-complete observations (approximately 20 per parameter within each group; fewer for ALY%, IMM%, PLCC and PLCR). The absolute basophil count showed no variation and was not estimable; the basophil percentage was not analysable in the newly diagnosed and healthy-control groups. FDR = Benjamini-Hochberg false-discovery rate within each group-specific family.