



## RESEARCH PAPER

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## Hematological malignancies in Cameroonian women with cancer attending a health facility: High prevalence and implications for follow up

Idriss Lemouchele Ntatou<sup>1</sup>, Martin Luther Mogtomo Koanga<sup>\*1</sup>, Cecile Okalla Ebongue<sup>3</sup>, Esther Dina Bell<sup>3</sup>, Nkeumacha Ida Patrick<sup>1</sup>, Loick Pradel Foko Kojom<sup>2</sup>, Elisée Enyegue Embolo<sup>1</sup>, Martin Biwole Essomba<sup>3</sup>, Eliane Okoubalimba Assokom<sup>1</sup>, Anne Marie Maïsson<sup>3</sup>, Annie Rosalie Ngane Ngono<sup>1</sup>, Albert SoneMoelle<sup>3</sup>

<sup>1</sup>*Department of Biochemistry, University of Douala, Cameroon*

<sup>2</sup>*Department of Animal Biology, University of Douala, Cameroon*

<sup>3</sup>*Douala General Hospital, Douala, Cameroon*

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### Abstract

This study aimed at determining the prevalence of hematological malignancies in cancer patients and discussing about implications for follow-up. A five-month hospital-based cross sectional study was carried out in 2015 in the town of Douala, Cameroon. Personal data were documented and 4 mL of venous blood was collected for full blood count. A total of 172 women were enrolled and divided into three groups: 74 in the cervical cancer group (CCG), 69 in the breast cancer group (BCG) and 29 in the control group (CG). Radiotherapy associated with chemotherapy was the most used therapeutic option (> 50.0 %). The prevalence of hematological disorders was 86.5 %, 75.4 % and 51.7 % in CCG, BCG and CG respectively ( $\chi^2 = 13.909$ ; p-value < 0.0001). Anemia was the most observed disorder and accounted for more than 40 % of all disorders observed in the three groups. Cancer and its therapy have negatively affected each of the blood parameters analyzed (p-value < 0.05). Our findings suggest the need for cautious and adjusted follow-up of Cameroonian cancer patients through surrogate markers such as blood parameters in order to enhance their life expectancy.

**\*Corresponding Author:** Martin Luther Mogtomo Koanga ✉ [koanga@yahoo.com](mailto:koanga@yahoo.com)

## Introduction

Cancer is a medical term used to describe various genetic and epigenetic modification in the regulatory circuits that govern normal cell proliferation and homeostasis, resulting in self-sufficiency in growth signals, insensitivity to antigrowth signals, limitless replicative potential, evasion from apoptosis, sustained angiogenesis as well as tissue invasion and metastasis (Hanahan and Weinberg, 2000; Rigal *et al.*, 2006). Conditions for the occurrence and accumulation of multiple genetic changes resulting in the development of tumors are well known (Butel, 2000; Alberts *et al.*, 2002; Griffiths *et al.*, 2002). Causative factors responsible for these modifications are various and consist of genotoxic agents, ionizing radiations or oncogen viruses such as the human papilloma virus (HPV), Epstein-Barr virus (EBV) or hepatitis B virus (Butel, 2000).

The prevalence of cancer is difficult to estimate worldwide because few affected countries have functioning cancer records (Giovannucci *et al.*, 2010; Orang-ijong *et al.*, 2013). However, it is obvious that cancer is a worrying public health problem, as it is a leading cause of mortality throughout the world. Based on GLOBOCAN statistics, an estimated 14.1 million new cancer cases and 8.2 million deaths of which 500,000 in Sub-Saharan Africa were recorded in the world in 2012. These estimates are projected to reach 20 and 15 million respectively by 2020 (Torre *et al.*, 2015).

Breast and cervical cancers are the leading causes of cancer-related deaths among women especially in developing countries. An estimated 1.7 million cases of breast cancer and 521,900 deaths were recorded worldwide in 2012, accounting for 25 % of all cancer cases and 15 % of all deaths from cancer among women. Cervical cancer is the second most diagnosed cancer and third leading cause of death from cancer among females in developing countries; about 527,600 cases and 265,700 subsequent deaths were recorded in 2012 (Torre *et al.*, 2015).

In Cameroon, data on cancer are also a cause for concern. GLOBOCAN (2012) statistics concerning Cameroon present an age-adjusted rate of cancer deaths of 73.1/100,000 persons/year and a risk of fatal outcome for any type of cancer prior to the age of 75 of 11%. Breast and cervical cancers are the most prevalent types of cancer among Cameroonian female population. Age-adjusted incidence and mortality rates are 27.9 and 16.6/100,000 persons/year respectively for breast cancer meanwhile for cervical cancer, they are 24 and 19/100,000 persons/year respectively (GLOBOCAN, 2012; Orang-ijong *et al.*, 2013).

Management of cancerous diseases relies on diagnosis and appropriate treatment, though still expensive in health facilities. Most of patients present with a cancer at an advanced stage of development at the time of first diagnosis. Reasons such as misconceptions and ignorance about the disease as well as poor socio-economic status can explain the late arrival of these patients at the care centre (Kemfeng Ngowa *et al.*, 2011; Price *et al.*, 2012; Kemfeng Ngowa *et al.*, 2015; Orang-ijong *et al.*, 2013). Radiotherapy alone or combined with chemotherapy are the main options used for the control and treatment of cancerous diseases. Previous reports outlined the adverse effects induced by the cancer itself and its treatment, due to the alteration of some biological parameters such as blood parameters (Sapolnik, 2003; Van Belle, 2004; Tefferi *et al.*, 2005; Rochet *et al.*, 2012). Almost all organs may be affected by cancer and/or its treatment, the main complications including infections, electrolytic/metabolic disorders and hematological disorders (Sapolnik, 2003); hence, blood count becomes a fundamental element in the follow-up of cancer patients in health facilities. Occurrence of such disorders may undermine the prognosis of affected patients and result in poor quality of life (QOL), reduced life expectancy as well as increased mortality. It is therefore critical in medical practice, to take into account possible treatment-induced adverse effects in the management and follow up of cancer patients.

There is a growing body of literature on cancer in Cameroon, though not enough (Koanga *et al.*, 2009, 2014, 2015; Kemfang Ngowa *et al.*, 2011; Orang-ojong *et al.*, 2013). However, data about hematological disorders in cancer patients before and during treatment are poor and sparse in Cameroon. To the best of our knowledge this aspect has not been documented in the town of Douala. This study aims *in fine* to thrive the literature on the topic in depicting the situation in Cameroon especially in Douala. The objectives of this study were to determine the prevalence and nature of hematological disorders, the influence of cancer disease and anti-cancer treatment on a few hematological parameters in women diagnosed with breast or cervical cancer, and the possible implications of findings for the follow-up.

## Materials and methods

### Study design

This was a cross-sectional study carried out from May to September 2015 at the Douala General Hospital (Douala, Littoral Region, Cameroon). The study population consisted of women aged 21 years old and above who consented to participate in the study and signed an informed consent form. These women had also be either diagnosed with cancer disease (cervical or breast) or apparently healthy. Women with a cancer disease other than cervical or breast and having refused to participate in the study were not included. Patients were recruited at the cobaltotherapy and oncology units where they were treated as well as at the hematology and biochemistry units of the clinical biology laboratory where laboratory procedures were made. Each woman was approached, the aim and objectives were clearly explained to her and answers were given to her questions. A total of 172 women were enrolled in the study and divided into three groups: 74 women with cervical cancer, 69 with breast cancer and 29 unmatched apparently healthy (control group).

### Questionnaire and blood sampling

A structured questionnaire was administered to each of the volunteer women for 10-15 minutes in order to document the socio-demographic (age, residence

area), anthropometric (height and weight), clinical (type of cancer, nature of treatment, number of rounds, diseases such as diabetes or kidney failure, tobacco smoking and alcohol drinking) data of participants. Weight and height were used to compute the body mass index (BMI) of women through standard BMI disc. Blood sampling was performed for biological analysis.

After the interview, a 4 mL-sample of venous blood was collected by venipuncture into EDTA tubes for full blood count (FBC) analysis. Previous to blood sampling, all tubes were labeled with patient's defined barcode. After sampling, the tube was gently shaken in order to avoid haemolysis and the appearance of air bubbles. Blood samples were then transported to the clinical biology laboratory of the hospital in cold box containing ice packs. Blood samples were collected only in fasting women; those not fasting were given a new appointment for blood sampling.

### Laboratory procedures

FBC was performed using automated flow cytometry (Cell Dyn Ruby, Abbott diagnostics, Germany). Each cell in blood specimens was oriented toward a laser which passed through and then differentiated in according to their characteristics. This flow cytometer relies on three parameters to identify the cells: i- the conductivity/resistance of blood cells in electric field, ii-their light diffraction capacity (forward scatter and side scatter signals) and, iii- their chemical composition. The results are then displayed on a screen for interpretation and exploitation. This experiment was performed not more than five hours following blood sampling at the hematology unit of the clinical biology laboratory of the Douala General Hospital. Red blood cell (RBC), white blood cell (WBC), haemoglobin (Hb), Haematocrit (Hct), platelet, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were recorded.

### Operational definitions

Based on FBC and BMI results, participants were grouped in the following categories as presented in the Table 1 (Kolahi *et al.*, 2008; Tavares-Murta and Murta, 2008; Gauer and Braun, 2012; Rochet *et al.*, 2012; WHO, 2014).

#### *Ethical considerations*

This study was carried out according to the guidelines for human experimental models in clinical research as stated by the Cameroon Ministry of Public Health. Besides, the ethical and administrative clearances for this study were issued by the institutional ethic committee of the University of Douala (N° CEI-UD/267/2015/M) and ethical committee of Douala General Hospital (N° 147 AR/MINSANTE/HGD/DM/2015). The aim and objectives of the study were explained to participants in the language they understood best (French or English), and their questions were answered. Only women who signed an informed consent form for their participation were enrolled. Participation in the study was strictly voluntary and women were free to decline answering any question or totally withdraw if they so wished at any time. Furthermore, there was no difference in the cancer related care provided to women who accepted to participate in the study and those who did not.

#### *Statistical analyses*

All data were verified for consistency, coded, and keyed in an Excel sheet. Thereafter, statistical analyses were performed with Statview software version 5.0 (SAS Institute Inc., USA) and

SPSS 16.0 for Windows (SPSS, Chicago, IL, USA). Data were summarized in table as percentages with 95% confidence interval (95%CI) or mean  $\pm$  standard deviation (SD) for qualitative and quantitative variables respectively, where appropriated. One way analysis of variance (ANOVA) was used to compare mean values of hematological parameters for more than two groups. Mann-Whitney test and Kruskal-Wallis test were used when the conditions for performing the ANOVA test were not verified. The former was used to compare mean values of hematological parameters between two groups and the later for more than two groups. Chi-square test ( $\chi^2$ ) or Fisher's exact probability were computed to compare the proportion of hematological disorders between the three study groups. Significant levels were measured at 95% CI with significant differences recorded at  $p\text{-value} < 0.05$ .

## **Results**

### *Baseline characteristics of the participants*

Out of the 172 women included in the study, 64 (37.2 %) were in the more than 54 years age group. Regarding the three clinical groups, most of the participants were aged 54 years and above in cervical cancer group (CCG) and breast cancer group (BCG) (47.3 % and 39.2 % respectively) whereas control group (CG) consisted mainly of women in the 21-32 years old group (44.9 %) as presented in table 2. The mean age of these groups were  $52 \pm 11$  years old,  $49 \pm 11$  years old and  $37 \pm 13$  years old respectively.

**Table 1.** Operational definitions according to FBC and BMI results.

Criteria	Definitions
Underweight	Women with BMI < 18.5 Kg/m <sup>2</sup>
Normal weight	Women with 18.5 Kg/m <sup>2</sup> < BMI < 25.0 Kg/m <sup>2</sup>
Overweight	Women with 25.0 Kg/m <sup>2</sup> < BMI < 30.0 Kg/m <sup>2</sup>
Obesity	Women with 30.0 Kg/m <sup>2</sup> < BMI < 40.0 Kg/m <sup>2</sup>
Morbid obesity	women with BMI > 40.0 Kg/m <sup>2</sup>
Leukopenia	Women with WBC < 4 x 10 <sup>6</sup> cells/L
Lymphopenia	Women with lymphocytes < 20.0 %
Hyperleukocytosis	Women with leukocytes > 10.0 G/L
Thrombopenia	Women with platelets < 150 G/L
Microcytic anaemia	Women with Hb < 12.0 g/dL and MCV < 82 fL
Macrocytic anaemia	Women with Hb < 12.0 g/dL and MCV > 98 fL
Normocytic anaemia	Women with Hb < 12.0 g/dL and 82 fL < MCV < 98 fL
Hypochromic microcytic anaemia	Women with Hb < 12.0 g/dL, MCV < 82 fL and MCHC < 320 g/L

MCV: mean corpuscular volume; MCH: mean corpuscular haemoglobin; MCHC: mean corpuscular haemoglobin concentration; Hb: hemoglobin; BMI: body mass index

Most of the women in CCG (40.5 %) and CG (30.5 %) were overweighted while obese in BCG (39.2 %). Radiotherapy in association with chemotherapy was the most used therapeutic option in both groups of patients with 56.8% and

68.1% in CCG and BCG respectively (Table 2). Interestingly, a few women with cancer disease were not under any anti-cancer treatment (22.7 % and 8.7 % in CCG and BCG respectively).

**Table 2.** Baseline characteristics of the participants.

		Study groups							
		CCG (n = 74)		BCG (n = 69)		CG (n = 29)		Total (n = 172)	
Variables	Category	n	%	n	%	n	%	N	%
Age (years)	[21-32[	3	4.0	1	1.4	13	44.9	17	9.9
	[32-43[	13	17.6	20	29.0	8	27.6	41	23.8
	[43-54[	23	31.1	21	30.4	6	20.7	50	29.1
	> 54	35	47.3	27	39.2	2	6.8	64	37.2
Mean age $\pm$ SD (years)		52 $\pm$ 11		49 $\pm$ 11		37 $\pm$ 13		48 $\pm$ 13	
Body mass index (Kg/m <sup>2</sup> )	Underweight	3	4.1	0	0.0	0	0.0	3	1.7
	Normal	25	33.8	21	30.4	8	27.5	54	31.4
	Overweight	30	40.5	17	24.6	10	34.5	57	33.1
	Obesity	14	18.9	27	39.2	9	30.1	50	29.1
	Morbid obesity	2	2.7	4	5.8	2	6.9	8	4.7
Nature of treatment	None	17	22.9	6	8.7	-	-	23	16.1 <sup>\$</sup>
	Chemotherapy	5	6.8	12	17.4	-	-	17	11.2 <sup>\$</sup>
	Radiotherapy	10	13.5	4	5.8	-	-	14	10.5 <sup>\$</sup>
	Radio-chemotherapy	42	56.8	47	68.1	-	-	89	62.2 <sup>\$</sup>
Alcohol consumption	No	68	91.9	59	85.5	16	55.2	143	83.1
	Yes	6	8.1	10	14.5	13	44.8	29	16.9

CCG: cervical cancer group; BCG: breast cancer group; CG: control group; SD: standard deviation; \$: percentages are computed with 143 as denominator.

#### *Prevalence of hematological disorders*

Eight (08) blood related pathologies were recorded in the study as presented in table 3, namely leukopenia, lymphopenia, hyperleukocytosis, thrombopenia, microcytic anaemia, macrocytic anaemia, normocytic anaemia and hypochromic microcytic anaemia. All these pathologies were recorded in both cancer groups while six out of eight were recorded in control group (no case of lymphopenia and hyperleukocytosis). The overall prevalence of these blood pathologies was 76.2% (131/172; 95%CI: 69.3-81.9). The prevalence was 86.5% (64/74), 75.4% (52/69) and 51.7% (15/29) in CCG, BCG and CG respectively and statistical difference were found ( $\chi^2 = 13.909$ ; p-value < 0.0001). Overall, anaemia accounted for 54.2% (71/131; 95%CI: 45.7-62.5) of all the malignancies and 39/74 (52.7 %; 95%CI: 41.5-63.7), 19/69 (27.5 %; 95%CI: 18.4-39.1) and 11/29 (37.9 %; 95%CI: 22.7-56.0) in CCG, BCG and CG respectively.

When disorders-free women were excluded from the analysis, anemia accounted for 39/64 (60.9 %; 95%CI: 48.7-71.9), 19/52 (36.5 %; 95%CI: 24.8-50.1) and 11/15 (73.3 %; 95%CI: 48.1-89.1) in these three groups.

Besides, the frequency of each of these abovementioned disorders was predominant in the cancer groups when compared to control groups. For instance, leukopenia was more observed in CCG and BCG with a frequency of 44.9% and 36.5% respectively against 24.1% in CG though the difference was not statistically significant ( $\chi^2 = 3.848$ ; p-value = 0.146). This trend was observed for others haematological disorders except for macrocytic anaemia that was more frequent in CG (17.2%). None statistically significant differences were found in the frequency of these pathologies with respect to clinical groups (p-value > 0.05).

**Table 3.** Prevalence of haematological disorders with respect to study groups.

Study groups									
	CCG (n = 74)		BCG (n = 69)		CG (n = 29)		Total (n =172)		
Hematological disorders	n	%	n	%	n	%	n	Chi-square ( $\chi^2$ )	p-value
Leukopenia	27	36.5	31	44.9	7	24.1	65	3.848	0.146
Lymphopenia	32	43.2	19	27.5	0	0.0	51	/	0.157 <sup>s</sup>
Hyperleukocytosis	6	8.1	3	4.3	0	0.0	9	/	0.246 <sup>s</sup>
Thrombopenia	5	6.8	10	14.5	2	6.9	17	2.895	0.235
Microcytic anaemia	9	12.2	3	4.3	2	6.9	14	2.988	0.224
Hypochromic microcytic anaemia	13	17.6	7	10.1	2	6.9	22	2.850	0.241
Macrocytic anaemia	3	4.1	4	5.8	5	17.2	12	/	0.054 <sup>s</sup>
Normocytic anaemia	14	18.9	5	7.2	2	6.9	21	5.457	0.065

CCG: cervical cancer group; BCG: breast cancer group; CG: control group; SD: standard deviation; \$: Fisher's exact probability; P-values < 0.05 are considered significant.

Out of 74 cervical cancer patients and 69 breast cancer patients, 17 and 6 were not under anti-cancer treatment respectively. We studied the influence of anti-cancer treatment on the prevalence of hematological disorders. Regarding the CCG, their prevalence was 87.7 % (50/57) in cancer patients under treatment and 82.4 % (14/17) in cancer

patients not under treatment (Fisher's exact test; p-value=0.687). The same trend of a higher prevalence in patients under treatment was also observed in BCG with 77.8 % (49/63) and 50.0 % (3/6) respectively, though no significant differences were found (Fisher's exact test; p-value=0.486).

**Table 4.** Effect of the cancer disease on the hematological parameters.

Hematological parameters	Cervical cancer group (n = 17)	Breast cancer group (n = 6)	Control group (n = 29)	H <sup>\$</sup>	p-value
White blood cells (10 <sup>3</sup> /μL)	5.333 ± 1.985	5.165 ± 1.830	4.835 ± 1.329	0.404	0.8170
Red blood cells (10 <sup>6</sup> /μL)	3.808 ± 0.642	4.147 ± 0.535	3.858 ± 0.504	1.380	0.5016
Platelets (G/L)	265 ± 103	259 ± 67	247 ± 77	0.025	0.9878
Lymphocytes (%)	34 ± 9	29 ± 4	41 ± 10	9.016	0.0110*
Haemoglobin (G/dL)	10.25 ± 2.41	11.88 ± 1.24	11.48 ± 1.32	4.650	0.0978
Haematocrit (%)	29.57 ± 6.21	33.63 ± 3.17	31.81 ± 4.09	2.822	0.2439
MCV (fL)	77.28 ± 9.12	81.60 ± 5.05	82.83 ± 7.05	4.960	0.0838
MCH (pg)	27.20 ± 5.00	28.82 ± 3.00	29.83 ± 2.55	5.506	0.0638
MCHC (G/dL)	34.27 ± 3.08	35.32 ± 2.31	36.10 ± 1.35	13.313	0.0013*

MCV: mean corpuscular volume; MCH: mean corpuscular haemoglobin; MCHC: mean corpuscular haemoglobin concentration; \$: decision variable of the Kruskal-Wallis testing; \*: significant.

#### *Influence of cancer disease on hematological parameters with respect to the study group*

As aforementioned, 17 and 6 cancer patients in CCG and BCG respectively were not under anti-cancer treatment. They were later included with 29 control patients in further analysis to investigate the influence of cancer disease on the hematological

parameters as the presented in table 4. These parameters were lower in cancer patients compared to those in the control group especially lymphocytes and the mean corpuscular haemoglobin concentration (MCHC) for which the differences were statistically significant (H=9.016 and p-value= 0.011; H=13.313 and p-value=0.00013 respectively).



Overall, hematological parameters were lower in cervical cancer patients than in breast cancer patients, namely RBC, Hb, Hct, MCV, MCH and MCHC (Table 4).

#### *Influence of the anti-cancer therapy on hematological parameters with respect to the type of cancer*

In order to study the influence of anti-cancer treatment on the hematological parameters, the analysis in this part was restricted to cancer patients.

Whatever the type of cancer, hematological parameters were lower in patients receiving anti-cancer therapy. As presented in table 5, the differences were found statistically significant for three parameters in cervical cancer patients namely red blood cells (U=296.50; p-value=0.00157), lymphocytes (U=231.00; p-value=0.0011) and MCV (U=326.50; p-value=0.0423). In breast cancer patients however, no significant difference was found with the Mann-Whitney test did (p-value>0.05) (Table 5).

**Table 5.** Effect of the cancer therapy on the hematological parameters with respect to cancer group.

Haematological parameters	Cervical cancer group				Breast cancer group			
	No (n = 16)	Yes (n = 57)	U <sup>£</sup>	p-value	No (n = 6)	Yes (n = 63)	U <sup>£</sup>	p-value
White bloodcells (10 <sup>3</sup> /μL)	5.162 ± 1.914	5.601 ± 3.726	445.00	0.6117	5.165 ± 1.830	4.560 ± 2.644	130.50	0.2126
Redbloodcells (10 <sup>6</sup> /μL)	3.809 ± 0.663	3.367 ± 0.696	296.50	0.0157*	4.147 ± 0.535	3.900 ± 0.873	136.5	0.2635
Lymphocytes (%)	34.60 ± 8.81	23.48 ± 12.05	231.00	0.0011*	29.33 ± 3.65	28.98 ± 11.04	178.00	0.8148
Platelets (G/L)	276 ± 96	248 ± 101	376.00	0.2861	259 ± 67	252 ± 126	160.00	0.5368
Haemoglobin (G/dL)	10.206 ± 2.478	9.730 ± 2.104	366.00	0.1277	11.880 ± 1.238	11.319 ± 1.516	154.00	0.4555
Haematocrit (%)	29.290 ± 6.299	27.604 ± 5.879	258.50	0.1054	33.630 ± 3.167	31.610 ± 6.883	133.00	0.2329
MCV (fL)	76.448 ± 8.790	82.479 ± 7.793	326.50	0.0423*	81.600 ± 5.046	81.724 ± 7.560	178.00	0.8148
MCH (pg)	27.088 ± 5.145	29.039 ± 3.267	359.00	0.1067	28.817 ± 3.006	30.506 ± 10.384	178.00	0.8480
MCHC (G/dL)	34.394 ± 3.133	35.125 ± 1.990	348.50	0.0802	35.317 ± 2.306	37.360 ± 13.516	175.00	0.7654

MCV: mean corpuscular volume; MCH: mean corpuscular haemoglobin; MCHC: mean corpuscular haemoglobin concentration; £: decision variable of the Mann-Whitney testing; \*: significant.

## Discussion

Cancer disease and its treatment are both known to induce biological disorders such as blood-related disorders in patients. In medical practice, it is necessary to pay attention to these blood-related disorders before and during cancer therapy. This study provides data on the prevalence and nature of hematological disorders in women with breast or cervical cancer attending care centres in Douala (Littoral region, Cameroon).

Anemia was the most frequently disorder found in the participants irrespective of the study group. It accounted for more than 40% of all disorders diagnosed in the three groups. This finding is in accordance with many authors who outlined anemia as a common disorder in Sub-Saharan Africa, particularly in cancer patients in whom it often results as a complication (Van Belle, 2004; Tefferi *et al.*, 2005; Rochet *et al.*, 2012).

Cancer disease itself and its multiple therapies can induce anaemia. More than 50% of all cancer patients will develop anaemia, regardless of the treatment received, and about 20% of all patients undergoing chemotherapy will require red blood cell transfusion (Mercadante *et al.*, 2005). Furthermore in our study, we found that cancer disease is associated with a drop of haematological parameters, more pronounced in patients with cervical cancer (Table 4). This result is in accordance with previous investigations in the same setting (Koanga *et al.*, 2015). Cancer can directly induce anaemia, so-called anaemia of acute disease (ACD) as a result of disease-induced inflammatory response in most of the cases (Van Belle, 2004). Proinflammatory molecules such interleukins (IL-1 and IL-6) or tumor necrosis factor (TNF) have been showed to inhibit the erythropoietic process through mechanisms associated with an increased production of hepcidin (Means, 2004), reduced expression of

erythropoietin (Epo) gene and Epo receptors as well as apoptosis of erythroid precursor cells (Frede *et al.*, 1997). Cancer therapy could also explain the cases of anemia recorded in this study. In fact, most of the participants were undergoing radiotherapy alongside chemotherapy. A deleterious effect of these treatments on blood parameters has been observed in both types of cancer (Table 5). Drugs used for chemotherapy can be responsible for transient or sustained anemia either directly by inducing an immune-mediated hemolysis or indirectly via stem cell death, blockage or delay of haematopoietic factors, oxidative damages to mature haematopoietic cells, microangiopathy and kidney failure (Mercadante *et al.*, 2005). This last mechanism has been documented in a previous study in which cisplatin, a drug used for the chemotherapy in the Douala General Hospital and other health facilities in the country, was reported to be associated with a dose-depending impairment of kidney function in women with cervical cancer (Assokom and colleagues, unpublished). Erythropoietin (Epo) is a glycoproteic hormone mainly produced by the kidneys and highly involved in the erythropoietic process. Cisplatin and similar drugs can induce a reduction in Epo production resulting in Epo deficiency-induced anemia. The negative effect of cancer and its treatment on Hb levels found in this study have obvious implications in patients' management. Haemoglobin level is known to be an important prognostic factor in cancer patients before and during the therapy (Thomas, 2001; Van Belle, 2004; Rochet *et al.*, 2012). Thomas (2001) showed that Hb level equal or higher than 12.0 g/dL was a prognostic factor for higher overall survival (OS) rates, local control of the disease and disease-free survival (DFS) in cervical Canadian women (Thomas, 2001). Management of anemia is a crucial aspect of patients' follow-up; therefore, close attention should be paid to anemia before and during treatment. The underlying idea is the maintenance of adequate hemoglobin levels in order to improve on cancer therapy related outcomes and the quality of life of patients.

Many types of anemia were recorded in this study namely microcytic anaemia, macrocytic anaemia, normocytic anaemia and hypochromic microcytic anaemia. Microcytic anemia may be due to iron deficiency, alpha/beta thalassaemia and anemia of chronic disease such as cancer (Mach-Pascual *et al.*, 1996; Tefferi *et al.*, 2005; Kolahi *et al.*, 2008).

In addition, some of the microcytosis observed in this study could be attributed to surgical operations since a few women with cervical cancer underwent hysterectomy, an operation frequently responsible for blood loss. Macrocytic anemia cases can be explained by a defective Hb synthesis due to a vitamin B12 (cyanocobalamin) and/or folic acids deficiency (Tefferi *et al.*, 2005). Alcohol consumption should also be considered a causative factor since all women diagnosed with macrocytic anemia admitted to have consumed alcoholic beverage, although daily amounts were not investigated. Most of the cases (19/21) of normocytic anemia were recorded in cancer patients. Mechanisms involving cisplatin induced renal failure during the treatment are likely to be the cause. Our assumption raises the need for toxicological studies on cisplatin in cancer patients in all care centres using this drug for chemotherapy in the country.

Leukopenia, lymphopenia, thrombopenia and hyperleukocytosis were the other hematological disorders recorded in this study. They are partly attributable to cancer disease and/or its therapy as the aforementioned different anemic disorders.

Leukopenia would likely be related to a decrease in the absolute neutrophils count since they account for 50 to 60% of leukocytes (Rochet *et al.*, 2012). Leukocytes play a key role in the inflammatory response as they migrate towards inflamed loci in response to infection or tissue injury. This leukocyte migration is critical for immunosurveillance of cancer disease and other common infectious disease such as malaria (Tavares-Murta and Murta, 2008). As such, leukocytes deficiency might negatively affect the efficacy of the inflammatory response.



As a consequence, women suffering leukopenia in our study might present a higher risk of mortality as they would be more affected by their cancer and more susceptible to parasitic infections than their counterpart. Interestingly, we also recorded a few cases of hyperleukocytosis in this study. Patients diagnosed with this disorder might present a higher risk of complications such as reduced brain perfusion related to the possible formation of cells aggregates in the microcirculation (Sapolnik, 2003). Moreover, the paradoxical results (leukopenia on one hand and hyperleukocytosis on the other hand) obtained from absolute leukocytes counts illustrates the complex nature of the relationship between cancer disease, exogenous or environmental factors and host-related or endogenous factors. Thus, medical practitioners should necessarily and continuously take several factors into account including medical history, family history, clinical diagnosis results and laboratory findings for making their decision, in order to enhance the survival rate of patients.

Lymphocyte depletion is one clinical concern that can develop during cancer progression and cytoreductive therapies (Tavares-Murta and Murta, 2008).

In our study some cases of lymphopenia were recorded. Lymphopenia can result in subsequent depression of humoral and/or innate cellular immunity, thus jeopardizing the management of cancer patients. Many studies previously underscored the importance of lymphocytes in anticancer immunosurveillance of the host defense mechanism during chemotherapy, radiotherapy, and immunotherapy, especially in breast and cervical cancer patients (Rochet *et al.*, 2012). This parameter should also be paid special attention in the follow-up of cancer patients by the health care providers.

Finally, some cases of thrombocytopenia were found in this study. With increasing incidence of cancer disease, thrombocytopenia has become a common manifestation in cancer patients (Erkurt *et al.*, 2012; Gauer and Braun, 2012).

As a result, complications such as hemorrhages during cancer treatment may appear and should not be overlooked by clinicians.

In summary, to the best of our knowledge, this study is the first to depict hematological malignancies in women with cancer in the town of Douala. It confirms the negative effect of cancer disease and its treatment on the health of patients. These findings suggest the need for more cautious and adjusted follow up of cancer patients in health facilities via surrogate markers such as blood parameters. Besides, with regard to the complex nature of the relationship between these blood parameters, cancer disease, cancer treatment and patients related factors which determine the survival of patients, it would be more cost-effective to prevent than cure whenever possible. Thus, inversion of the cancer curve needs the implementation of nationwide health policies including population-based early detection and screening as well as health education campaigns on cancer. If effective, these strategies might allow for reducing the late presentation of patients in care centres and enhance the rates of successful treatment. All this put together may finally enhance the life expectancy of cancer women living in resources-constrained areas especially in Sub-Saharan Africa.

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### References

- Alberts B, Alexander J, Julian L, Martin R, Keith R, Peter W.** 2002. Molecular biology of the cell, 4th. New York, USA: Garland Science, p. 1616 .
- Butel JS.** 2000. Viral carcinogenesis: revelation of molecular mechanisms and etiology of human disease. *Carcinogenesis* **21**(3), 405-426.  
<http://dx.doi.org/10.1093/carcin/21.3.405>

**Erkurt MA, Kaya E, Berber I, Koroglue M, Kuku I.** 2012. Thrombocytopenia in Adults: Review Article. *Journal of Hematology* **1(2-3)**, 44-53.  
<http://dx.doi.org/10.4021/jh28w>

**Frede S, Fandrey J, Pagel H, Hellwig T, Jelkmann W.** 1997. Erythropoietin gene expression is suppressed after lipopolysaccharide or interleukin-1 beta injections in rats. *American Journal of Physiology* **273**, R1067-1071.

**Gauer RL, Braun MM.** 2012. Thrombocytopenia. *American Family Physician* **85(6)**, 612-622.

**Giovannucci E, Harlan DM, Archer MC, Bergenstal RM, Gapstur SM, Habel LA, Pollak M, Regensteiner JG, Yee D.** 2010. Diabetes and cancer. *Diabetes Care* **33**, 1674-1675.  
<http://dx.doi.org/10.2337/dc10-0666>

**GLOBOCAN.** 2012. Statistics on cancer.  
[www.globocan.iarc.fr](http://www.globocan.iarc.fr)

**Griffiths AJF, David TS.** 2002. Introduction à l'analyse génétique; traduction de la 7e édition américaine par Chrystelle Sanlaville ; révision scientifique de Denise Aragnol et Dominique Charmot, 3e éd. Paris, Brussels, Belgium: De Boeck, 860 P.

**Hanahan D, Weinberg RA.** 2000. The Hallmarks of Cancer. *Cell* **100**, 57-70.  
[http://dx.doi.org/10.1016/S0092-8674\(00\)81683-9](http://dx.doi.org/10.1016/S0092-8674(00)81683-9)

**Kemfang Ngowa JD, Yomi J, Kasia JM, Mawamba Y, Ekortarh AC, Vlastos G.** 2011. Breast cancer profile in a group of patients followed up at the Radiation Therapy Unit of the Yaounde General Hospital, Cameroon [serial online]. *Obstetrics and Gynecology International* 2011, ID143506:  
<http://dx.doi.org/10.1155/2011/143506>.

**Koanga Mogtomo ML, GouabeMalieugoue LC, Djepegang C, Wankam M, Moune A, NgononNgane A.** 2009. Incidence of cervical disease associated to HPV in human immunodeficiency infected women under highly active antiretroviral therapy. *Infectious Agents and Cancer* **4**, 9.  
<http://dx.doi.org/10.1186/1750-9378-4-9>

**Koanga Mogtomo ML, NgononNgane A, Djiakam Nganwa G, Wankam M, Brulet Epaka C, Amvam Zollo PH.** 2014. Association of Cervical Inflammation and Cervical Abnormalities in Women Infected with Herpes Simplex Virus Type 2. *International Journal of Tropical Medicine and Public Health* **1(1)**, 1-4.  
<http://dx.doi.org/171350/ijtmph>

**Koanga Martin LM, Embolo EE, Eboumbou CE, Olemba C, Eloumou EL, Assam Assam JP, Mouelle Albert S.** 2015. Blood tissue cytological status of prognosis and predictive markers in the natural history of solid cancer development. *Journal of Clinical Immunology and Immunopathology Research* **6(1)**, 1-8.  
<http://dx.doi.org/10.5897/JCIIR2014.0068>.

**Kolahi S, Farzin H, Khoshbaten M.** 2008. Hypochromic Microcytic Anemia in North western Of Tabriz, Iran. *European Journal Genetic Medicine* **5(3)**, 178-180.

**Mach-Pascual S, Darbellay R, Pilotto PA, Beris P.** 1996. Investigation of microcytosis: A comprehensive approach. *European Journal of Haematology* **57**, 54-61.  
<http://dx.doi.org/10.1111/j.16000609.1996.tb00490.x>

**Means RT Jr.** 2004. Hcpidin and anaemia. *Blood Review* **18**, 219-225.  
[http://dx.doi.org/10.1016/S0268-960X\(03\)00066-3](http://dx.doi.org/10.1016/S0268-960X(03)00066-3)

**Mercadante S, Gebbia V, Marrazzo A, Filosto S.** 2000. Anaemia in cancer: pathophysiology and treatment. *Cancer Treatment Reviews* **26**, 303–311.  
<http://dx.doi.org/10.1053/ctrv.2000.0181>

**Orang-Ojong BB, Munyangaju JE, Shang WM, Lin M, Guan WF, Foukunang C, Zhu Y.** 2013. Impact of natural resources and research on cancer treatment and prevention: A perspective from Cameroon (Review). *Molecular and Clinical Oncology* **1**, 610–620.  
<http://dx.doi.org/10.3892/mco.2013.132>

**Price AJ, Ndom P, Atenguena E, MambouNouemssi JP, Ryder RW.** 2012. Cancer Care Challenges in Developing Countries. *Cancer* **118**, 3627–3635.  
<http://dx.doi.org/10.1002/cncr.26681>

**Rigal OBE, Druesne L, Chassagne L.** 2006. Épidémiologie: cancer et sujet âgé. *Psychooncology* **3**, 141–146.

**Rochet NM, MarkovicSvetomir N, Porrata LF.** 2012. The Role of Complete Blood Cell Count in Prognosis-Watch this Space! *Oncology & Hematology Review* **8(1)**, 76–82.  
<http://doi.org/10.17925/OHR.2012.08.1.76>

**Sapolnik R.** 2003. Intensive care therapy for cancer patients. *Journal of Pediatrics (Rio de Janeiro)* **79 (Suppl 2)**, S231–S42.

**Tavares-Murta BM, Murta EFC.** 2008. Systemic leukocyte alterations in cancer and their relation to prognosis. *The Open Cancer Journal* **2**, 53–58.

**Tefferi A, Hanson CA, Inwards DJ.** 2005. How to Interpret and Pursue an Abnormal Complete Blood Cell Count in Adults. *Mayo Clinical Proceedings* **80 (7)**, 923–936.  
<http://dx.doi.org/10.4065/80.7.923>

**Thomas G.** 2001. The effect of hemoglobin level on radiotherapy outcomes: the Canadian experience. *Seminars Oncology* **28(Suppl.8)**, 60–65.  
[http://dx.doi.org/10.1016/S0093-7754\(01\)90215-5](http://dx.doi.org/10.1016/S0093-7754(01)90215-5)

**Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A.** 2015. Global Cancer Statistics, 2012. *A Cancer Journal for Clinicians* **65**, 85–108.  
<http://dx.doi.org/10.3322/caac.21262>

**Van Belle SJP.** 2004. What is the value of hemoglobin as a prognostic and predictive factor in cancer ? *EJC Supplements* **2(2)**, 11–19.  
[http://dx.doi.org/10.1016/S1359-6349\(03\)00103-4](http://dx.doi.org/10.1016/S1359-6349(03)00103-4)

**WHO.** 2014. *Body mass index*. 20 avenue Appia, 1211 Geneva 27, Switzerland: World Health Organization:  
<http://www.globocan.iarc.fr>