



SHORT COMMUNICATION

Hematologic Disorders in Ebola-Infected Patients During the Tenth Outbreak in Butembo, Democratic Republic of Congo: Hemogram Analysis of Ebola Virus Disease Patients During the Outbreak in Butembo 2019–2020

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Abstract

Background: Hematologic disorders occur frequently in patients with Ebola virus disease (EVD) and are characterized by one or several abnormalities in blood cells, including hemostasis, which is poorly documented. This study described the hematologic abnormalities of Ebola patients and the impact on the outcomes of patients who were admitted with EVD.

Methods: This was a retrospective observational study of patients recruited from 1 February 2019 to 25 June 2020 from Ebola Treatment Centers in Butembo and Katwa. Clinical and hemogram parameters at the time of admission and outcomes were collected. Descriptive statistics and logistic regression were performed with a significance level of 0.05. The analyses were carried out using Rstudio software.

Results: Among 299 patients hospitalized during the study period, only 129 were included in the analysis. The mean age was 29.9 ± 18.6 years with a female-to-male ratio of 1.2. Only 13 patients (10 %) had been vaccinated against the *Ebolazaire* virus. The hematologic abnormalities included anemia (55.8%), hyperleukocytosis (36.4%), leukopenia (3.1%), thrombopenia (32.6%), and thrombocytosis (30.2%). Only anemia was statistically significantly correlated with increased viral load. Anemia (OR, 4.07; 95% CI, 1.59–11.3) was shown to be an independent risk factor for mortality in patients with EVD based on multivariate analysis.

Conclusions: EVD is responsible for major hematologic abnormalities that contribute to increased patient mortality.

Key words: blood count, hematologic, associated factors, Ebola patients, Kinshasa, D.R.C.

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INTRODUCTION

Ebola virus disease (EVD) is a zoonosis caused by a Filoviridae of the *Orthoebolavirus* genus [1]. Several outbreaks of EVD have occurred across Africa since 1976 when the virus was identified for the first time, the 2 largest of which occurred in West Africa (2013–16) and central Africa (2018–20) [2].

Among the 6 existing species of Ebola virus (*Ebolazaire*, *Ebolasoudan*, *Ebolabudubungyo*, *Ebolavirus tai-forest*, *Ebolavirusreston*, and *Ebolavirus bombali*), *Ebolazaire* is the most lethal for humans and most predominant in Africa. *Ebolazaire* has a case fatality rate of 90%–100% without treatment [3].

The Democratic Republic of Congo (DRC) has experienced 14 outbreaks of EVD, the last 4 of which have occurred in the last decade. The 10th epidemic, which ran from 2018–2020 in east DRC, remains the largest, longest, and most deadly of all epidemics, with 3470 confirmed cases and 2287 deaths [4].

EVD is lethal in 60%–100% of patients in the absence of treatment. Countermeasures, such as vaccines and specific anti-Ebola therapies, have been introduced to reduce the lethality associated with EVD since the 10th epidemic, thus changing the EVD management protocol in the DRC and throughout the world [5,6]. These countermeasures were first used on a compassionate basis as part of the Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI) protocol before being used in clinical trials, such as the Palm study, which reduced in-hospital mortality by 35%–40% [7,8].

EVD is characterized by a range of clinical manifestations, including fever (87%), gastrointestinal symptoms (67%), and hemorrhagic complications in severe cases (18%). Hematologic abnormalities, such as thrombocytopenia, granulocytosis and coagulopathy, occur frequently in EVD patients, but comprehensive data on these disorders are limited. Previous studies conducted in non-human primates indicated that EVD can lead to myeloid, erythroid, and megakaryocyte lineage depletion. Some significant alterations in hemostasis have been described due to Ebola virus. Specifically, prolonged clotting times and elevated D-dimer levels suggest a complex interplay between the virus and the host coagulation system [9,10].

Despite the wealth of data generated during previous EVD outbreaks, there is still limited data that specifically addresses hematologic changes in infected patients and the correlation with the viral load [11]. Several clinical reports involving EVD based on outbreaks in the DRC have focused on the epidemiology, general symptoms, outcomes, and biochemical disorders but often neglecting detailed analyses of blood parameters [12,13].

The current study aimed to document hematologic disorders based on hemogram parameters and the correlation with the viral load and association with in-hospital mortality during the 10th epidemic in east DRC.

The data herein are crucial for public health policies and healthcare workers in an effort to improve the treatment

strategies based on the evidence of early hematologic abnormalities and provide appropriate care.

METHODS

Study design

We conducted a retrospective observational study of EVD patients who were admitted to the Ebola Treatment Center from 01 February 2019 to 25 June 2020 in Butembo, North Kivu, DRC.

Study population

A total of 129 consecutive patients among 299 who were admitted to the Ebola Treatment Center in Katwa and Butembo with a positive Xpert Ebola Zaire result and a blood count on admission were enrolled in the current study, regardless of the patient's clinical condition. One hundred seventy patients who did not have hemogram results were excluded.

Data collection

Medical and laboratory records generated during Palm 001, a randomized control trial of Ebola Virus Disease Therapeutics, were used.

Sociodemographics, clinical findings, outcomes, PCR results (cycle threshold for nucleopeptide [Ct-np]), and hematologic data from hemograms were collected in

TABLE 1 | Sociodemographic characteristics, vaccination status and clinical stage.

Variable	Total n = 129 (%)	Male n = 57 (%)	Female n = 72 (%)
Age mean (SD)	29.9 (±18.7)	29.6 (±20.2)	30.1 (±17.6)
Age years			
<10	22 (17.1)	12 (21.1)	10 (13.9)
10–29	49 (38)	20 (35.1)	29 (40.3)
30–49	34 (26.4)	15 (26.3)	19 (26.4)
>49	24 (18.6)	10 (17.5)	14 (19.4)
Profession			
Unemployed	41 (32.03)	23 (56.9)	18 (43.9)
Self-employed	14 (10.91)	8 (57.1)	6 (42.8)
Farmer	27 (21.09)	5 (18.5)	22 (81.5)
Student	36 (28.13)	20 (55.5)	16 (44.5)
Clinical stage			
1	33 (25.6)	14 (24.6)	19 (26.4)
2	63 (48.8)	27 (47.4)	36 (50)
3	33 (25.6)	16 (28.1)	17 (23.6)
Vaccine statue			
Yes	13 (10.1)	6 (10.5)	7 (9.7)
No	116 (89.9)	51 (89.5)	65 (90.3)

patients at the time of admission to the Ebola Treatment Center.

Laboratory analysis and interpretation

Peripheral venous blood was collected at the time of admission for biological analysis. The Cepheid GeneXpert® Ebola assay, an automated real-time reverse transcription PCR [RT-PCR] (Cepheid GeneXpert®, Sunnyvale, CA, USA), was used in accordance with WHO recommendations during the outbreak for confirmation of cases and a Sysmex XN-Series Hematology Analyzer (Lincolnshire, USA) was used for hematologic analysis.

The WHO criteria were used to define hematologic abnormalities and clinical stages of Ebola patients. The results of PCR Ct-np were used to determine the viral load. The more the Ct-np is < 22, the higher the viral load and vice versa. A Ct-np cut-off of 22 was used according to the literature.

Statistical analysis

RStudio software was used for statistical analysis. Descriptive analysis was used to describe the clinical and biological characteristics of the population. A chi-square test was used to compare the proportions of categorical variables, the Fisher's exact test was used for smaller value,

and the Student's t-test was used for continuous variables. Pearson correlation was used to identify the association between viral load and hemoglobin concentration and platelet and white blood cell counts in the study population.

Univariate and multivariate analyses were used to identify risk factors associated with mortality in patients with EVD. The statistical analyses were performed at the 0.05 level of significance.

Ethical considerations

Approval was from the Ethics Committee of the School of Public Health (Faculty of Medicine of the University of Kinshasa, Kinshasa, DRC [ESP/CE/132/2018]) and an approbation from the INRB before data collection.

RESULTS

A total of 299 patients were hospitalized in different study sites, of whom only 129 (72 [56%] females women with a female-to-male ratio of 1.2) were included in the current study.

Sociodemographic, Ebola vaccination status, and clinical stage

The mean age of patients was 29.9 ± 18.6 years. The most representative age group was 10–29 years of age (38%),

TABLE 2 | Signs and symptoms of the study population.

Signs/symptoms	Total n = 129 (%)	Ct-np < 22 n = 41 (%)	Ct-np ≥ 22 n = 88 (%)	P-value
Fever	58 (45)	21 (51.2)	37 (42)	0.432
Headache	50 (38.8)	18 (43.9)	32 (36.4)	0.532
Anorexia	56 (43.4)	17 (41.5)	39 (44.3)	0.909
Chest pain	11 (8.5)	4 (9.8)	7 (8)	0.998
Conjunctival injection	26 (20.2)	10 (24.4)	16 (18.2)	0.56
Digestive hemorrhage	3 (2.3)	2 (4.9)	1 (1.1)	0.493
Nausea	45 (34.9)	20 (48.8)	25 (28.4)	0.039
Dysphagia	18 (14)	8 (19.5)	10 (11.4)	0.332
Gingivorrhagia	6 (4.7)	2 (4.9)	4 (4.5)	1
Arthralgia	37 (28.7)	11 (26.8)	26 (29.5)	0.914
Myalgia	30 (23.3)	8 (19.5)	22 (25)	0.643
Coma	3 (2.3)	1 (2.4)	2 (2.3)	1
Vomiting	47 (36.4)	18 (43.9)	29 (33)	0.314
Diarrhea	40 (31)	14 (34.1)	26 (29.5)	0.748
Diathesis	8 (6.2)	4 (9.8)	4 (4.5)	0.453
Systolic blood pressure (SD)	107.6 (±24.3)	105.2 (±31.2)	108.6 (±21.0)	0.573
Diastolic blood pressure (SD)	73.1 (±16.3)	70.9 (±18.3)	74.1 (±15.4)	0.427
Pulse (SD)	93.5 (±19.4)	94.7 (±20.9)	93.0 (±18.9)	0.717
Respiratory rate (SD)	24.0 (±5.3)	26.6 (±7.2)	22.8 (±3.8)	0.023
Temperature (SD)	37.5 (±1.2)	38.0 (±1.2)	37.3 (±1.1)	0.012

Ct-np = Cycle threshold nucleopeptide.

followed by 30 to 49 years (38% and 26.4%, respectively). Forty-one patients (32%) were unemployed and 36 were students (28.1%). Thirteen patients (10.1%) had received the Ervebo[®] vaccine before admission at the Ebola Treatment Center (Table 1).

Clinical symptoms and viral load

The most frequent symptoms were fevers (45%), anorexia (43.4%), headaches (39%), digestive disorders (36%), and nausea (35%). No statistically significant difference was detected between patients with Ct-np values <22 and Ct-np values ≥22, except in patients with nausea

(*P*-value = 0.03), polypnea (*P*-value = 0.023), and fever (*P*-value = 0.012; Table 2).

Hemogram characteristics and hematologic disorders

The most common hematologic abnormalities were a decrease in the lymphocyte count (60.2%), followed by a decreased hemoglobin concentration (55.5%), an increase in the white blood cell (WBC) count (35.9%), and a decrease in the platelet cell count (32.6%). Approximately 67% of patients with a Ct-np <22 (i.e., a higher viral load) had a statistically significant lower hemoglobin

TABLE 3 | Hemogram characteristics of the study population by the Ct-np level.

Parameters	Total n = 128 (%)	Ct-np < 22 n = 40 (%)	Ct-np ≥ 22 n = 88 (%)	<i>P</i> -value
White blood cells/L	7500 (800–12 800)			0.533
<4000	4 (3.1)	2 (5)	2 (2.3)	
4000–10,000	78 (60.9)	22 (55)	56 (63.6)	
>10,000	46 (35.9)	16 (40)	30 (34.1)	
Lymphocytes 10 ³ /μl	1.2 (0.5–2.6)			0.838
<1.5	77 (60.2)	23 (57.5)	54 (61.4)	
1.5–4.0	34 (26.6)	12 (30)	22 (25)	
>4.0	17 (13.3)	5 (12.5)	12 (13.6)	
Neutrophils 10 ³ /μl	2.9 (1.3–5.6)			0.532
<1.7	41 (32)	13 (32.5)	28 (31.8)	
1.7–7.0	64 (50)	22 (55)	42 (47.7)	
>7.0	23 (18)	5 (12.5)	18 (20.5)	
Monocytes 10 ³ /μl	0.03 (0.01–0.14)			0.879
<0.1	86 (67.2)	26 (65)	60 (68.2)	
0.1–1	42 (32.8)	14 (35)	28 (31.8)	
Hemoglobin g/dl	11.61 (±2.8)			0.044
<12	71 (55.5)	27 (67.5)	39 (44.3)	
≥12	57 (44.5)	13 (32.5)	49 (55.7)	
Platelets/l	310.3 (±237.6)			0.141
<150,000	42 (32.8)	18 (45)	24 (27.3)	
150,000–450,000	47 (36.7)	12 (30)	35 (39.8)	
>450,000	39 (30.5)	10 (25)	29 (33)	
MCV fl	83.6 (±4.7)			0.117
<80	29 (22.7)	13 (32.5)	16 (18.2)	
80–100	99 (77.3)	27 (67.5)	72 (81.8)	
MCHC pg	33.4 (±1.8)			0.625
<32	24 (18.8)	6 (15)	18 (20.5)	
≥32	104 (81.2)	34 (85)	70 (79.5)	

HB=Hemoglobin, RBC=Red blood cells, PLT=Platelets, MCV=Mean corpuscular volume, MCHC=Mean corpuscular hemoglobin concentration, Ct-np= Cycle threshold for nucleopeptide.

concentration that patients with a Ct-np ≥ 22 (Table 3). In summary, the hematologic disorders in our study population were anemia with microcytosis and hypochromia, leukopenia, leukocytosis, thrombocytopenia, and thrombocytosis (Fig 1).

Considering the cytopenia taken separately or associated, The majority of patients had cytopenia (38%) followed by bicytopenia (25.6 %). Only 1 patient had pancytopenia (0.8 %). The bicytopenia was an association of anemia with thrombopenia or leukopenia (Fig 2).

Correlation between Ct-values and hemogram parameters

A statistically significant positive correlation existed between the Ct-np value and the hemoglobin level ($r = 0.21$, $P = 0.018$). This correlation indicated that an increase in Ct-np values is associated with an increase in the hemoglobin concentration and vice versa (Fig 3). Our results showed a weak negative correlation between the Ct-np value and WBC count ($r = -0.1$, $P = 0.25$). This correlation suggested a tendency for the WBC count to

decrease with increasing Ct-np values. However, this relationship was not statistically significant (Fig 4). A positive correlation existed between Ct-np values and the platelet count. This relationship indicated that as the Ct-np value increases, the platelet count also tends to increase and vice versa. However, the statistical significance of the correlation was not demonstrated (Fig 5).

In sum, this correlation suggested a link between the viral load and variations in the blood cell count. When the viral load is higher the hemoglobin level is low.

Hematologic disorders and mortality

Fifty-eight of the 129 patients died (45%). Anemia, bleeding diathesis, and headaches were associated with an increased risk of death based on the univariate analysis. However, based on multivariate analysis, only patients with a hemoglobin concentration <12 g/dl had a 4.07-fold risk of death as an outcome compared to patients with a normal hemoglobin concentration. Patients with leukopenia had an 18.8-fold risk of death compared to patients without leukopenia (Table 4).

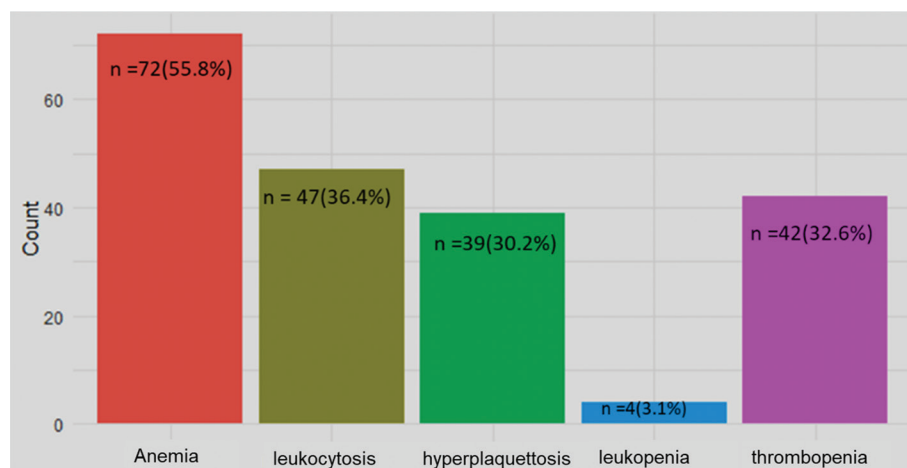


FIGURE 1 | Cumulative incidence of hematologic abnormalities in the study population.

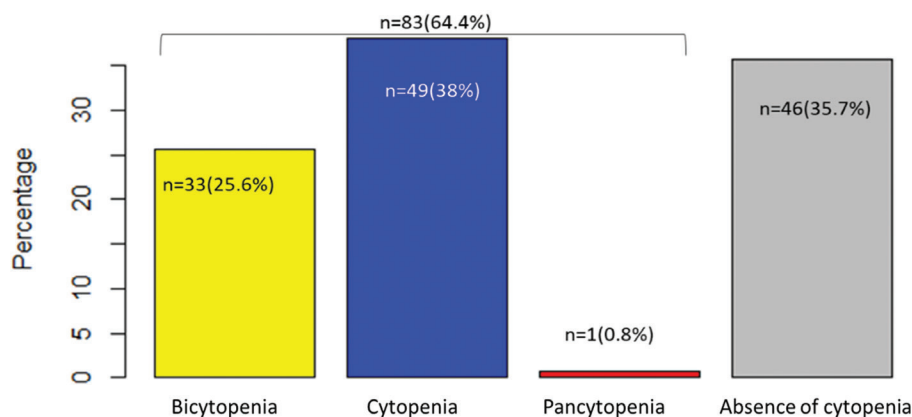


FIGURE 2 | Frequency of cytopenia, bicytopenia, and pancytopenia.

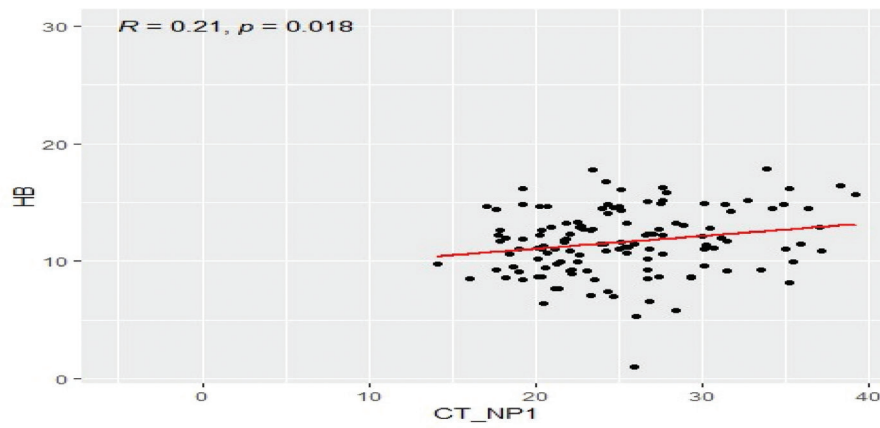


FIGURE 3 | Correlation between HB levels and Ct-np.

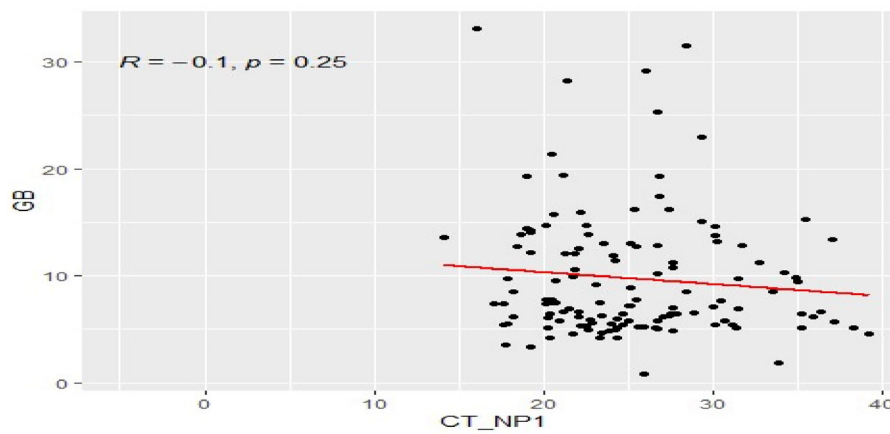


FIGURE 4 | Correlation between the WBC count and Ct-np.

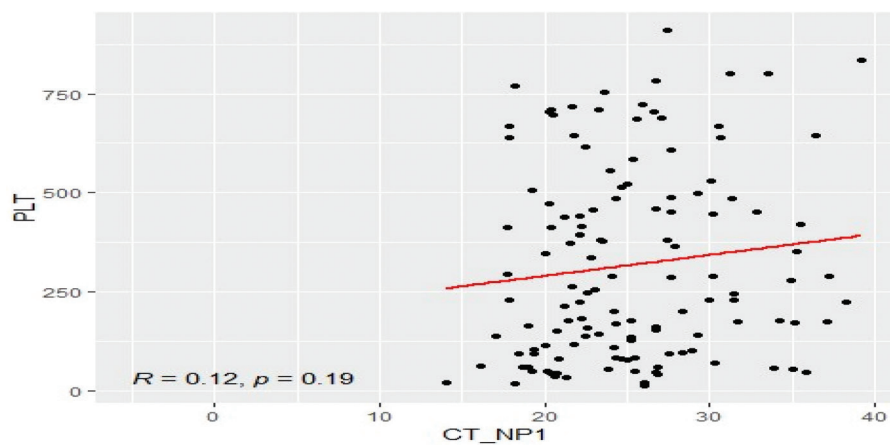


FIGURE 5 | Correlation between the PLT count and Ct-np.

TABLE 4 | Risk factors associated with EVD patient mortality.

Factors	Deaths n = 58 (%)	Discharged n = 71 (%)	Univariate OR (95%CI)	Multivariate OR (95%CI)
Age	34.2 (19.9)	26.5 (17.0)	0.98 (0.96–1.00)	0.97 (0.95–1.00)
Anemia				
No	19 (32.8)	38 (53.5)	—	—
Yes	39 (67.2)	33 (46.5)	2.36 (1.16–4.92)	4.07 (1.59–11.3)
Leukopenia				
No	55 (94.8)	70 (98.6)	—	—
Yes	3 (5.2)	1 (1.4)	0.26 (0.01–2.11)	18.8 (1.48–478)
Leucocytosis				
No	35 (60.3)	47 (66.2)	—	—
Yes	23 (39.7)	24 (33.8)	0.78 (0.38–1.60)	0.05 (0.00–0.86)
Thrombocytopenia				
No	37 (63.8)	50 (70.4)	—	—
Yes	21 (36.2)	21 (29.6)	0.74 (0.35–1.55)	1.92 (0.67–5.76)
Thrombocytosis				
No	42 (72.4)	48 (67.6)	—	—
Yes	16 (27.6)	23 (32.4)	1.26 (0.59–2.72)	0.75 (0.25–2.16)
Microcytosis				
No	44 (75.9)	55 (77.5)	—	—
Yes	14 (24.1)	16 (22.5)	1.09 (0.48–2.49)	0.97 (0.35–2.70)
Hypochromy				
No	52 (89.7)	53 (74.6)	—	—
Yes	6 (10.3)	18 (25.4)	0.34 (0.12–0.88)	0.25 (0.07–0.79)
Diathesis				
No	51 (87.9)	70 (98.6)	—	—
Yes	7 (12.1)	1 (1.4)	9.61 (1.64–183)	5.92 (0.83–121)
Headache				
No	30 (51.7)	49 (69)	—	—
Yes	28 (48.3)	22 (31)	2.08 (1.02–4.31)	2.22 (0.98–5.16)

DISCUSSION

The hematologic abnormalities in 129 patients with EVD during the 10th epidemic in North Kivu are described herein and factors associated with patient mortality were identified.

Clinical characteristics based on the Ebola viral load

The most frequently reported symptoms of EVD were fevers, anorexia, headaches, digestive disorders, and nausea, while hemorrhagic manifestations occurred

at a lower prevalence. This observation corroborates with the observations during the West Africa epidemic [14,15].

The basis for this observation was that fever is a hallmark of the response to viral infections, reflecting an attempt to inhibit viral replication and improve immune function. Similarly, anorexia, which occurred in 43.4% of our patients, is a common response to systemic infection, potentially exacerbated by gastrointestinal involvement. Headaches and digestive disorders highlight the impact of the virus on the gastrointestinal system, including nausea [16].

The analysis revealed no statistically significant differences in the prevalence of symptoms, except nausea, between patients with Ct-np values <22 and patients with Ct-values ≥22. Indeed, nausea had a significant difference (P -value = 0.03), suggesting the potentially increased correlation with lower Ct-np values. This finding may indicate that nausea could serve as a clinical marker of higher viral replication, which could contribute to the early identification of patients at risk of more severe disease progression.

Hematologic disorders associated with EVD

Anemia, thrombocytopenia, hyperplaquetosis, leukopenia, and leucocytosis occurred at different frequencies in the study population. However, anemia and thrombocytopenia were the most common complications in the study population. This finding is in agreement with the previous report by Hunt et al. [12]. Specifically, thrombocytopenia and an increased hematocrit were attributed to most patients with digestive disorders and dehydration.

In our cohort, the decrease in hemoglobin concentration was attributed to a multifactorial origin, including the direct effect of the virus on the bone marrow, inflammation, and probable nutritional deficiency due to martial deficiency [17].

Microcytosis, hypochromia, normocytosis, and normochromia were noted in the patients described herein. This pattern likely reflects the inflammatory process, which initially presents with a normochromic normocytic profile and gradually shifts to hypochromic microcytosis.

Most patients with EVD had a normal WBC count, followed by leucocytosis with lymphopenia. This finding corroborates the observation made by Wing et al. in 2016 in Guinea [18]. Lymphopenia can be explained by the direct action of the *Ebolavirus* on T cells, causing cell death by apoptosis, as suggested by Iampietro et al. in 2016 [19].

Thrombocytopenia, identified as one of the common complications in the current study population at the time of admission, reflects a significant involvement of the platelet line in patients with EVD. This result is consistent with data reported in the literature. The mechanisms underlying this thrombocytopenia include increased destruction of platelets due to endothelial activation and pro-inflammatory cytokines and a reduced production of platelets due to suppression of the bone marrow by the virus, which is frequently associated with disseminated intravascular coagulation [20].

In the current study the cut-off CT-np value was used as a measure of viral load. The variation in viral load was correlated with the hemoglobin concentration. The current study showed that as the viral load increases, the hemoglobin concentration decreases. The exact reason for this finding would be the direct effect of the virus in the bone marrow and hematopoietic system. Further investigations are warranted to determine the causal link

between the Ebola virus and the figurative elements in the blood.

Strengths and limitations of the study

Strengths of the current study include data that provide information that furthers our understanding about the hematologic disorders based on the hemogram findings of patients with EVD.

Limitations of the current study include the small sample size and the possible effects of vaccination and therapeutics on the immune system.

CONCLUSIONS

The current study highlights that blood cell disorders during the 10th outbreak of EVD in the DRC and the impact on the outcomes of patients with EVD. The main hematologic disorders due to Ebola virus identified in the current study were anemia, followed by microcytosis and thrombopenia. The profile of microcytosis, hypochromia, and lymphopenia were the most common profile in EVD patients.

There was a strong correlation between the viral load of Ebola virus and red blood cells. Data from this study could enhance public health strategies during future outbreaks and guide the development of more effective diagnostic tools and therapies tailored to the specific hematologic profiles observed in the DRC outbreak.

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CONFLICTS OF INTEREST

No conflicts of interest are declared by any of the authors.

REFERENCES

1. Biedenkopf N, Bukreyev A, Chandran K, Di Paola N, Formenty PBH, Griffiths A, et al. Renaming of genera Ebolavirus and Marburgvirus to Orthoebolavirus and Orthomarburgvirus, respectively, and introduction of binomial species names within family Filoviridae. Arch Virol. 2023;168(8):220.
2. Feldmann H, Nichol ST, Klenk HD, Peters CJ, Sanchez A. Characterization of filoviruses based on differences in structure and antigenicity of the virion glycoprotein. Virology. 1994;199(2):469-473.
3. Baseler L, Chertow DS, Johnson KM, Feldmann H, Morens DM. The pathogenesis of Ebola virus disease. Annu Rev Pathol. 2017;12:387-418.
4. Chertow DS, Kleine C, Edwards JK, Scaini R, Giuliani R, Sprecher A. Ebola virus disease in West Africa--clinical manifestations and management. N Engl J Med. 2014;371(22):2054-2057.

5. Sospeter SB, Udohchukwu OP, Ruaichi J, Nchasi G, Paul IK, Kanyike AM, et al. Ebola outbreak in DRC and Uganda; an East African public health concern. *Health Sci Rep.* 2023;6(8):e1448.
6. Malik S, Kishore S, Nag S, Dhasmana A, Preetam S, Mitra O, et al. Ebola virus disease vaccines: development, current perspectives & challenges. *Vaccines (Basel).* 2023;11(2):268.
7. Doshi RH, Garbern SC, Kulkarni S, Perera SM, Fleming MK, Muhayangabo RF, et al. Ebola vaccine uptake and attitudes among healthcare workers in North Kivu, Democratic Republic of the Congo, 2021. *Front Public Health.* 2023;11:1080700.
8. Schaefer GO. If it walks like a duck...: Monitored Emergency Use of Unregistered and Experimental Interventions (MEURI) is research. *J Med Ethics.* 2024;50(9):606-611.
9. Smither SJ, O'Brien LM, Eastaugh L, Woolley T, Lever S, Fletcher T, et al. Haemostatic changes in five patients infected with Ebola virus. *Viruses.* 2019;11(7):647.
10. Liu DX, Pahar B, Perry DL, Xu H, Cooper TK, Huzella LM, et al. Depletion of bone marrow hematopoietic cells in Ebolavirus-infected rhesus macaques: a possible cause of hematologic abnormalities in Ebolavirus disease. *Am J Pathol.* 2023;193(12):2031-2046.
11. Skrabble K, Roshania R, Mallow M, Wolfman V, Siakor M, Levine AC. The natural history of acute Ebola virus disease among patients managed in five Ebola treatment units in West Africa: a retrospective cohort study. *PLoS Negl Trop Dis.* 2017;11(7):e0005700.
12. Hunt L, Gupta-Wright A, Simms V, Tamba F, Knott V, Tamba K, et al. Clinical presentation, biochemical, and haematological parameters and their association with outcome in patients with Ebola virus disease: an observational cohort study. *Lancet Infect Dis.* 2015;15(11):1292-1299.
13. Galán-Huerta K, Arellanos-Soto D, Rivas-Estilla AM, Bravo-de la Cruz V, Ramos-Jiménez J. Ebola virus disease 2014. *Medicina Universitaria* 2014;16(65):207-215.
14. Kjalldgaard L, Claude KM, Mukadi-Bamuleka D, Kitenge-Omasumbu R, Dixit D, Edidi-Atani F, et al. Virus kinetics and biochemical derangements among children with Ebolavirus disease. *EClinicalMedicine.* 2022;53:101638.
15. Mulangu S, Dodd LE, Davey RT Jr, Tshiani Mbaya O, Proschan M, Mukadi D, et al. A randomized, controlled trial of Ebola virus disease therapeutics. *N Engl J Med.* 2019;381(24):2293-2303.
16. Jaspard M, Mulangu S, Juchet S, Serra B, Dicko I, Lang HJ, et al. Development of the PREDS score to predict in-hospital mortality of patients with Ebola virus disease under advanced supportive care: Results from the EVISTA cohort in the Democratic Republic of the Congo. *EClinicalMedicine.* 2022;54:101699.
17. Beam EL, Schwedhelm MM, Boulter KC, Vasa AM, Larson L, Cieslak TJ, et al. Ebola virus disease: clinical challenges, recognition, and management. *Nurs Clin North Am.* 2019;54(2):169-180.
18. Wing K, Oza S, Houlihan C, Glynn JR, Irvine S, Warrell CE, et al. Surviving Ebola: a historical cohort study of Ebola mortality and survival in Sierra Leone 2014-2015. *PLoS One.* 2018;13(12):1-17.
19. Iampietro M, Younan P, Nishida A, Dutta M, Lubaki NM, Santos RI, et al. Ebola virus glycoprotein directly triggers T lymphocyte death despite of the lack of infection. *PLoS Pathog.* 2017;13(5):1-27.
20. Handa A, Dhooria S, Sehgal IS, Agarwal R. Primary cavitary sarcoidosis: a case report, systematic review, and proposal of new diagnostic criteria. *Lung India.* 2018;35(1):41-46.