DOI: https://doi.org/10.24297/jbt.v10i.9300

Haemoglobin and white blood cells (WBC) as key haematological indicators of malaria infection in a population in Côte d'Ivoire

KASSI Bohoussou Georges[1], *AHOUTY Ahouty Bernardin[2], SIMARO Siriki[3], TOURE Mahama[4], KONE Minayegninrin[1], SOKOURI Didier Paulin[5]

[1] UFR Environnement, Université Jean Lorougnon Guédé (UJLoG), Daloa, Côte d'Ivoire

[2] UFR Agroforesterie, Université Jean Lorougnon Guédé (UJLoG), Daloa, Côte d'Ivoire

[3] UFR Biosciences, Université Alassane Ouattara, Bouaké (UAO), Côte d'Ivoire

[4] Centre d'Entomologie Médical et Vétérinaire (CEMV), Bouaké, Côte d'Ivoire

[5] UFR Biosciences, Université Félix Houphouët Boigny (UFHB), Abidjan, Côte d'Ivoire

georgesksi40@gmail.com, bernadinahouty@yahoo.fr, sirikisimaro@gmail.com, mahamatoure@yahoo.fr, konemina85@gmail.com, didierersokouri@yahoo.fr

* Corresponding author

ABSTRACT;

Malaria is the main cause of consultation and hospitalisation in health centres and the leading cause of morbidity and mortality in Côte d'Ivoire. To reduce malaria-related deaths, rapid diagnosis and treatment strategies should be adopted. The aim of this study was to determine the relationship between parasite density and selected haematological parameters in infected patients in cities located in southern Côte d'Ivoire. Blood samples were collected in Jacqueville and Tiassalé. The different haematological parameters were identified by an automated haematological analyser. The coefficient of determination (R2) was determined to show the proportion of variation in parasite density and each haematological parameter. A total of 69 patients were sampled. A negative correlation was observed between parasite density and haemoglobin in the general population, in Jacqueville and in Tiassalé. However, this correlation is significant in the general population (p1 = 0.046; Confidence Interval (CI= [-0.0047; -0.00010]) with a correlation intensity (r) different from zero (p2 = 0.05) and in Jacqueville (p1 = 0. 041; CI= [-0.0025; -0.00012]) with a correlation intensity (r) different from zero (p2 = 0.04). In Tiassalé the correlation was not significant. Haemoglobin and WBC can be considered as key haematological indicators of malaria infection in the study population.

Keywords: Malaria, haemoglobin, parasite density, Côte d'Ivoire.

Introduction

Malaria is a disease caused by protozoan parasites of the genus *Plasmodium* whom invades the red blood cells. The *plasmodium* transmitted to human by female anopheles of mosquito after her feeding of blood meal (Mbewe et al., 2022). Previously, only four *plasmodium* subspecies that is *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae* were able to infect human but recently, *knowlesi* was found out to be involved in human infection (Millar & Cox-Singh, 2015). Among the five subspecies, *P. falciparum* remains the most virulent and it is responsible for the dangerous cases of malaria. It causes the vast majority of morbidity and mortality of malaria, mostly among children under the age of 5 years living in sub-Saharan Africa (Sato, 2021). Approximately, the Malaria affects 40 % of the population worldwide (Hunt et al., 2001) and it is an infection considered as a worldwide major public health problem (Mbewe et al., 2022) because it is the most important parasite disease affecting humans and causing millions of deaths each year. The wide spreading of Malaria in tropical and subtropical regions is due to of the significant amounts of rainfall and consistent high temperatures and high humidity, along with stagnant waters which provide mosquitoes a best environment needed for continuous breeding (Sadoine et al., 2018). In Côte d'Ivoire, malaria is the main cause of consultation and hospitalization in the health centers and it is the first cause of morbidity (40 %) and mortality (10 %) (WHO, 2021).

Changes in blood cell counts are a well-known feature of malarial infections. These changes involve major cell lines including red blood cells (RBC), leukocytes and thrombocytes (Maina et al., 2010). indeed, previous studies have shown that there is a correlation between parasite density and severity of malarial infections(Tangpukdee et al., 2012). It was also observed that at high parasitemias, the platelets were found to be significantly lower (Kotepui et al., 2015). On the other hand, deaths are most often due to delayed diagnosis (Ashley & White, 2014). Microscopic examination of the May-Grünwald-Giemsa (MGG) stained blood smear in combination with the thick drop remains the gold standard for the diagnosis of this condition. However, it is examiner dependent, and also depends on the quality of the smear taken. The use of other biological examinations often allows the detection of haematological and biochemical disturbances in response to the acute phase of the infection.

Malaria parasitemia has been reported to have effects on some haematological parameters in many parts of the world (Eledo et al., 2020; Sakzabre et al., 2020). These studies have been performed in many tropical territories affected by malaria around the world, however, in Côte d'Ivoire, a country with of endemic zones and belongs to third world, similar investigations are not realized about this alleged association.

To reduce malaria-related deaths in the future, especially in rural Africa, rapid diagnosis and treatment strategies should be adopted. On this basis, the objective of this study is to determine the relationship between parasite density and some haematological parameters in infected patients in cities located in South of Côte d'Ivoire. These relationships can be used to predict malaria parasitaemia from any haematological parameter in the shortest possible time, even in the absence of a working microscope or a competent microscopist.

Materials and methods

Study areas

Jacqueville and Tiassale are located in South of Côte d'Ivoire with GPS coordinates 5° 12' 21.532'' N 4° 25' 24.071'' W and 5° 54' 0'' N 4°49' 59.999'' W respectively. The climate of the both is marked by wet and dry seasons, two types of each (one little and other large) while a mean monthly temperature varies between 21°C and 35°C throughout the year with a mean annual rainfall estimated about 696 mm at Jacqueville and 22°C to 34°C with 826.4 mm at Tiassale. The study was conducted in those cities and the samples were collected in their health center.

Study population

The study was carried out in September 2020 at Jacqueville and Tiassale. Patients infected with plasmodium genus; adult (both males, females) and child, were included in the study as malaria cases. All included patients provided informed consent. For minor children, the consent was appreciated by their legal parental.

Laboratory procedures

Sampling

A volume of 2.5 mL of venous blood sample was drawn into tubes containing the anticoagulant potassium ethylenediamine-tetra acetic acid (EDTA). The blood samples have been taken in the arm and, the mainly steps are the following:

Palpate the area for locate a vein of good size that is visible, straight and clear. Then, applied a tourniquet around the arm. After this step, alcohol (70%) used for clearing the area and wait about 30 seconds for the alcohol to dry following by insertion of blood collector contains tube contains EDTA as anticoagulant into the holder. Coming step consist to anchor the vein by holding the patient's arm and placing a thumb below the place where to place the needle and enter the vein swiftly, when blood starts to flow, and once sufficient blood has been collected (2.5 mL), release the tourniquet before withdrawing the needle. Finally, the blood collector tube is removed from holder and put into collection box.

Haematological analysis

Whole blood samples were collected in EDTA tube like indicated in the above step. This collected quantity blood allowed to determine the hematological parameters including hemoglobin (Hb) concentration, White Blood Cell (WBC) count, Red Blood Cell (RBC) count, platelets (Plt), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC) and using automated (ALPHATEC SCIENTIFIC® 34) hematology analyzer.

Malarial parasite density determination

The parasites were determined by using the thick drop technical. It is a technique of concentration of red blood cells for the detection of *plasmodium* in the blood by smears stained by Giemsa stain (10 % of dilution) (Adu-Gyasi et al., 2012). The method employed to quantify malaria parasites in thick blood smears, which calculate mean of parasites on three fields and multiply this mean by WBC concentration obtained from haematological analyzer then, divide by mean of WBC on three fields (Adu-Gyasi et al., 2012). Therefore, four (4) categories were determined: scanty infection (+) 1–10/100 fields, moderate infection infection (2+) 11–100/100 fields, heavy infection (3+) 1–10/one field and very heavy infection (4+) >10/one field (26).

Statistical analysis

The data obtained were registered using Microsoft Excel statistical package. Regression linear model was realized between parasite density and haematological parameters using R software (version 3.2.2, 2014). Coefficient of determination (R^2) was determined to show the proportion of the variation of parasite density and each haematological parameter. In addition, the regression coefficient (r) was calculated to verify correlation or dependence between parasite density and each haematological parameter. In correlation cases, it indicates the negative or positive correlation and give the correlation intensity (r-value). The first *p* value (p_1) was

calculated to verify if the correlation is significant and second *p* value (p_2) to verify if r is actually different to zero (only p_1 significant cases). The X- axis of the regression graphs stand for the parasite density while Y-axis stands for the respective haematological parameters. A *p* value ≤ 0.05 was set for statistical significance.

Results

Basic characteristics of study population

A total of 69 patients infected with *falciparum* were collected with 33 (47.83 %) were registered at Jacqueville and 36 (52.17 %) at Tiassale. Among the patients the majority, 37 (51.58%) were female, and 32 (48.42 %) were male with 0.86 as sex-ratio (M/F) (Table 1). The adults were majority with 49.27 % following by children under 5 years with 26.09 % and finally, children of 5 to 15 years with 24.64 % (Table 1). Age of patients vary from 4 months to 70 years with 20 years as mean age (Table 1). Furthermore, at Jacqueville, 15 (45.45 %) male and 18 (54.56 %) female were collected while at Tiassalé, 17 (47.22 %) male and 19 (52.78 %) female were collected respectively.

Table 1: Numbers of individual genders and age groups of the population studied

Characters	Jacqueville (%)	Tiassalé (%)	Whole population (%)
Gender			
Male (M)	15 (45.45%)	17 (47.22 %)	32 (48.42 %)
Female (F)	18 (54.56 %)	19 (52.78 %)	37 (51.58 %)
Total	33	36	69
Sex-ratio (M/F)	0.83	0.89	0.86
Age groups			
Children <5 years	11 (33.33 %)	7 (19.45 %)	18 (26.09 %)
Children (5-15 years)	9 (27.27 %)	8 (22.22 %)	17 (24.64 %)
Adults (≥15 years)	13 (39.40 %)	21 (58.33 %)	34(49.27 %)
Mean age (Range)	15 (0-70)	23 (0-62)	20 (0-70)

According to parasitemia levels, at Jacqueville, 06 (18.20 %) had scanty infection, 03 (9.10 %) had moderate infection, 06 (18.20 %) had heavy infection, and 18 (54.50 %) had very heavy infection while at Tiassale, proportions are 5.56 %; 5.56 %; 16.67 % and 72.21 % respectively (Table 2). however, in the whole population, eight (8) patients had scanty infection, five (5) had moderate infection infection, 12 had heavy infection, and 44 had very heavy infection representing 11.59 %, 7.25 %, 17.39 % and 63.77 % respectively (Table 2).

Table 2: Distribution of the infected subjects according to levels of parasitemia

Study population	Jacqueville		Tiassalé		Whole population	
Parasitemia levels	Number	%	Number	%	Number	%
scanty infection	6	18.20	2	5.56	8	11.59
moderate infection	3	9.10	2	5.56	5	7.25
heavy infection	6	18.20	6	16.67	12	17.39
very heavy infection	18	54.50	26	72.21	44	63.77
Total	**33**	**100**	**36**	**100**	**69**	**100**

Relationship between parasite density and haematological parameters

Table 3 shows le mean ±SD of infected subjects of different haematological parameters at different parasitemia levels. Tthe value of Hb and RBC into infected subjects decreased gradually in the whole population, At Jacqueville and At Tiassalé. In the whole population, this value decreasing from 13.065±2.26 and 5.245±1.475 respectively in scanty infection to 9.30±1.29 and 4.115 ±0.745 respectively in very heavy infection. At Jacqueville, from 11.23±1.55and 5.69±1.83 respectively in scanty infection to 9.04±2.37 and 4.04 ±0.72 respectively in very heavy infection and at Tiassalé, from 14.90±2.97 and 4.80± 1.12 respectively in scanty infection to 10.92± 1.90 and 4.19± 0.77 respectively in very heavy infection. Although, the value of WBC into infected subjects increased

gradually in the whole population from 5.21±1.735 in scanty infection to 10.095±2.118 in very heavy infection, at Jacqueville, from 5.27±1.84 in scanty infection to 13.77± 17.46 in very heavy infection and at Tiassalé, from 5.15± 1.63 in scanty infection to 6.42± 2.49 in very heavy infection.

Table 3: Haematological parameters into infected subjects at different parasitemia

Areas	Parameters	Parasitemia levels			
		scanty infection	moderate infection	heavy infection	very heavy infection
Whole population	Hb (g/dL)	13.065 ±2.26	12.365 ± 1.44	10.615 ± 1.32	9.30 ± 1.29
	'BC (10^3/µL)	5.21 ± 1.735	6.07 ± 2.255	7.475 ± 1.98	10.095 ± 2.118
	3C (10^6/µL)	5.245 ± 1.475	4.59 ± 0.24	4.225 ± 0.56	4.115 ± 0.745	
	: (10^3/µL)	236.335 ± 60.04	209.665 ±65.05	177.415 ± 81.965	163.205 ± 84.42
	CT (%)	37.61 ± 7.105	36.515± 3.65	31.07± 6.305	30.71± 7.07
	CV (fL)	80.815± 5.575	81.275± 4.335	74.64± 9.125	76.455± 9.295
	CH (pg)	27.11± 2.255	27.885± 3.80	25.175± 3.78	30.34± 3.81
	MCHC (g/dL)	33.39± 0.84	34.265± 0.495	33.105± 1.15	33.83± 1.685
	Parasite density	6.4 ± 2.90	62.39 ± 23.27	527.912 ± 151.995	1455.565 ± 309.08
Jacqueville	Hb (g/dL)	11.23±1.55	10.88± 1.54	9.83± 2.69	9.04± 2.37
	'BC (10^3/µL)	5.27± 1.84	6.76± 2.91	8.70 ± 2.33	13.77± 17.46
	3C (10^6/µL)	5.69± 1.83	4.420± 0.33	4.20± 0.34	4.04± 0.72
	: (10^3/µL)	244.67± 50.78	205.33±110.3	153.33± 79.13	134.33± 75.51
	CT (%)	31.67± 5.23	33.03± 4.05	29.93± 6.91	28.04± 4.47
	MCV (fL)	71.73± 9.60	78.50± 4.50	71.78 ± 9.13	73.53± 8.92
	MCH (pg)	23.37± 4.01	26.67± 1.96	24.07± 4.31	24.77± 3.80
	MCHC (g/dL)	32.43± 1.61	33.93± 0.57	32.33± 1.83	33.55± 2.13
	Parasite density	7.00 ± 3.90	70.00± 27.52	568.33± 282.78	1568.33± 329.09
Tiassale	Hb (g/dL)	14.90± 2.97	13.85± 1.34	11.40± 2.10	10.92± 1.90
	WBC (10^3/µL)	5.15± 1.63	5.38± 1.60	6.25± 1.63	6.42± 2.49
	C (10^6/µL)	4.80± 1.12	4.76± 0.15	4.25± 0.78	4.19± 0.77
	(10^3/µL)	228± 69.30	214± 19.80	201.50± 84.80	192.08± 93.33
	:T (%)	43.55± 8.98	40± 3.25	32.21± 5.70	33.38± 9.67
	MCV (fL)	89.9± 1.55	84.05± 4.17	77.50± 9.12	79.38± 9.67
	MCH (pg)	30.85± 0.50	29.10± 1.84	26.28± 3.25	27.13± 3.82
	MCHC (g/dL)	34.35± 0.07	34.60± 0.42	33.88± 0.47	34.11± 1.24
	Parasite density	5.80± 1.90	54.78± 19.02	487.50± 21.21	1342.80± 289.07

Correlation parasite density and some haematological parameters

A negative correlation is observed between parasite density and Haemoglobin in the whole population, at Jacqueville and at Tiassalé. However, that correlation is significant in the whole population (p_1 = 0.046; Confidence Interval (CI= [-0.0047; -0.00010])) with an intensity of correlation (r) different to zero (p_2 = 0.05) and at

Jacqueville (p_1 = 0.041;CI= [-0.0025;-0.00012]) with an intensity of correlation (r) different to zero (p_2 = 0.04) whereas, correlation is not significant at Tiassale (p_1 = 0.135; CI= [-0.007; 0.002]) (Fig.1).

Otherwise, positive correlation is observed between parasite density and WBC in the whole population, at Jacqueville and at Tiassalé. However, that correlation is significant in the whole population (p_1 = 0.011; CI= [0.001; 0.004]) with a correlation intensity (r) different to zero (p_2 = 0.01) and at Jacqueville (p_1 = 0.008; CI= [0.003; 0.007]) with a correlation intensity (r) different to zero (p_2 = 0.01) while, it is not significant at Tiassale (p_1 = 0.12; CI= [-0.0006; 0.0024]) (Fig.2).

As Haemoglobin, RBC is negatively correlated to parasite density in the whole population, at Jacqueville and at Tiassalé but it is not significant in the whole population (p_1 = 0.23; CI= [-0.002; 0.0009]), at Jacqueville (p_1 = 0.33; CI= [-0.003; 0.002]) and at Tiassalé (p_1 = 0.13; CI= [-0.0012; 0.0003]) (Fig. 3). Likewise for platelets, the correlation is negative and no significant in the whole population (p_1 = 0.12; CI= [-0.11; 0.029]), at Jacqueville (p_1 = 0.13; CI= [-0.16; 0.044]) and at Tiassalé (p_1 = 0.11; CI= [-0.057; 0.012]) respectively (Fig. 4).

Also, a negative correlation and no significant is observed between parasite density and HCT in the whole population (p_1 = 0.15; CI= [-0.013; 0.004]) at Jacqueville (p_1 = 0.067; CI= [-0.006; 0.0005]) like at Tiassalé (p_1 = 0.25; CI= [-0.024; 0.011]) (Fig. 5).

In the same way, MCV is negatively correlated to parasite density but it is no significant in the whole population (p_1 = 0.32; CI= [-0.014; 0.007]) and in the both localities Jacqueville (p_1 = 0.79; CI= [-0.014; 0.012]) and Tiassale (p_1 = 0.32; CI= [-0.026; 0.014]) (Fig. 6).

Figure7 shows a negative correlation no significant between parasite density and MCH at Jacqueville (p_1 = 0.96; CI= [-0.012; 0.012]) and at Tiassalé (p_1 = 0.32; CI= [-0.0096; 0.0052]) but a positive correlation no significant in the whole population (p_1 = 0.37; CI= [-0.005; 0.009]).

For MCHC, the correlation is negative but no significant with parasite density in the whole population (p_1 = 0.98; CI= [-0.002; 0.002]) and at Tiassale (p_1 = 0.44; CI= [-0.0015; 0.0009]) and it is positive and no significant at Jacqueville (p_1 = 0.76; CI= [-0.004; 0.003]) (Fig. 8).

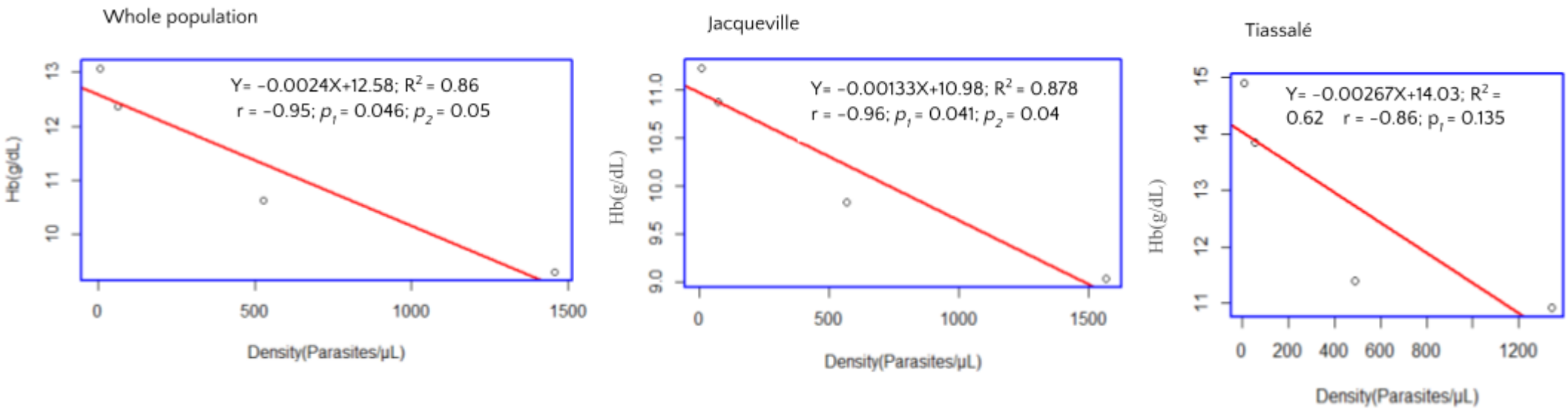

Figure 1: Linear relationship between parasite density and Haematoglobin (Hb)

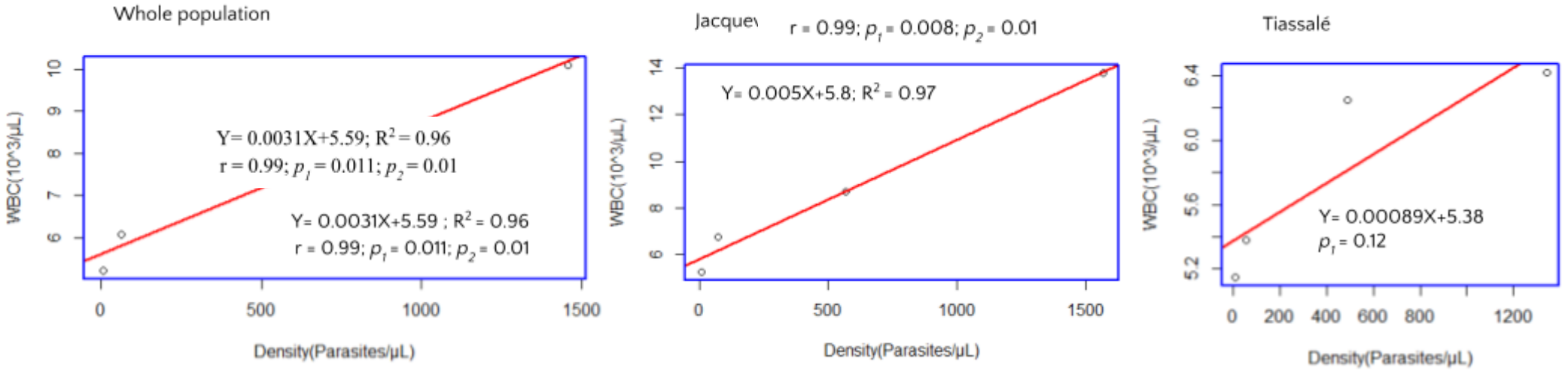

Figure 2: Linear relationship between parasite density and White Blood Cell (WBC)

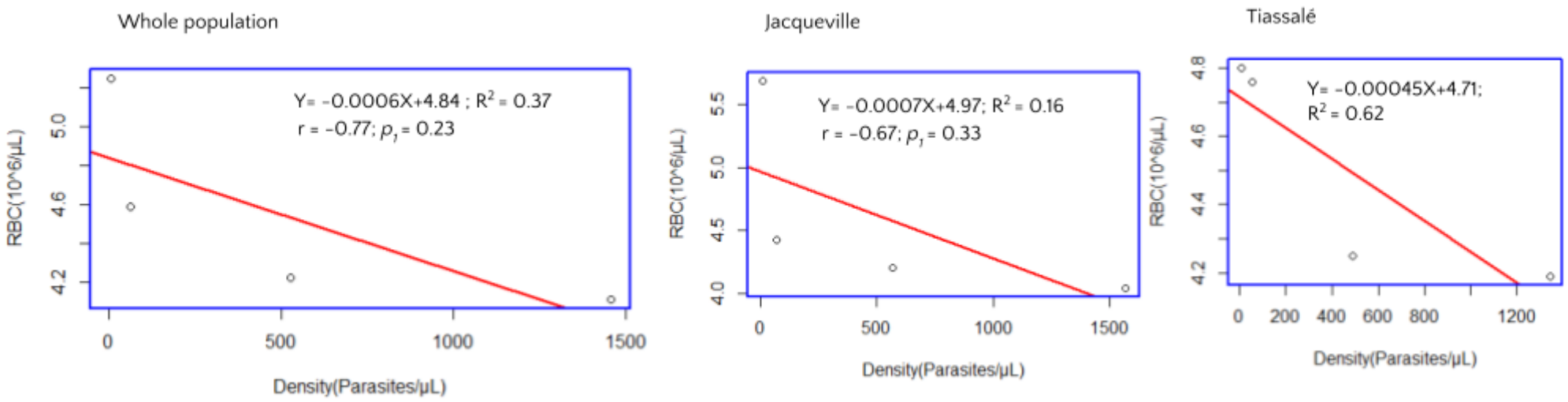

Figure 3: Linear relationship between parasite density and Red Blood Cell (RBC)

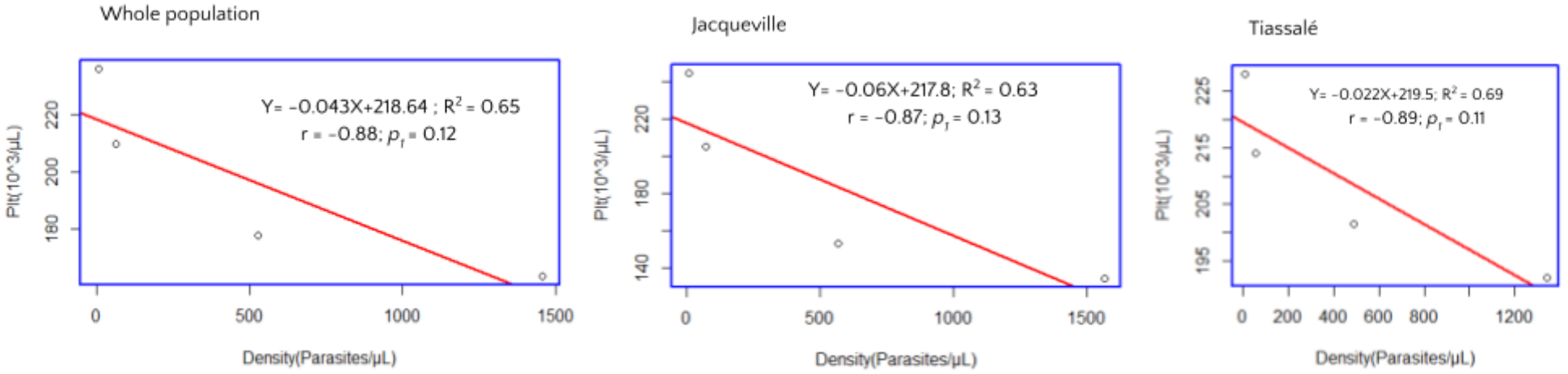

Figure 4: Linear relationship between platelets (Plt) and parasite density

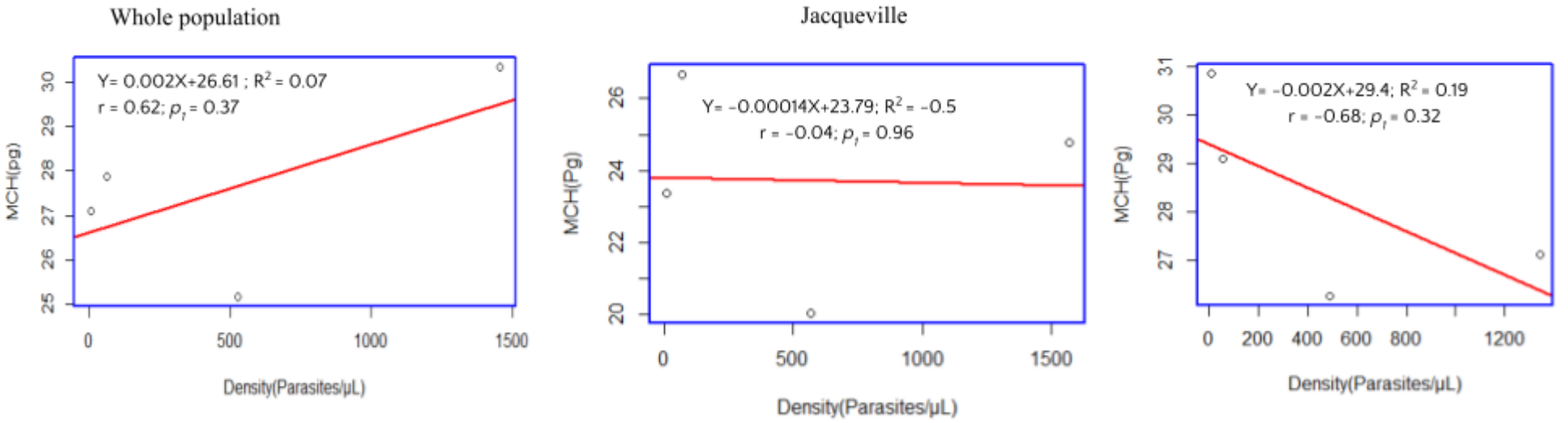

Figure 5: Linear relationship between parasite density and Hematocrit (HCT)

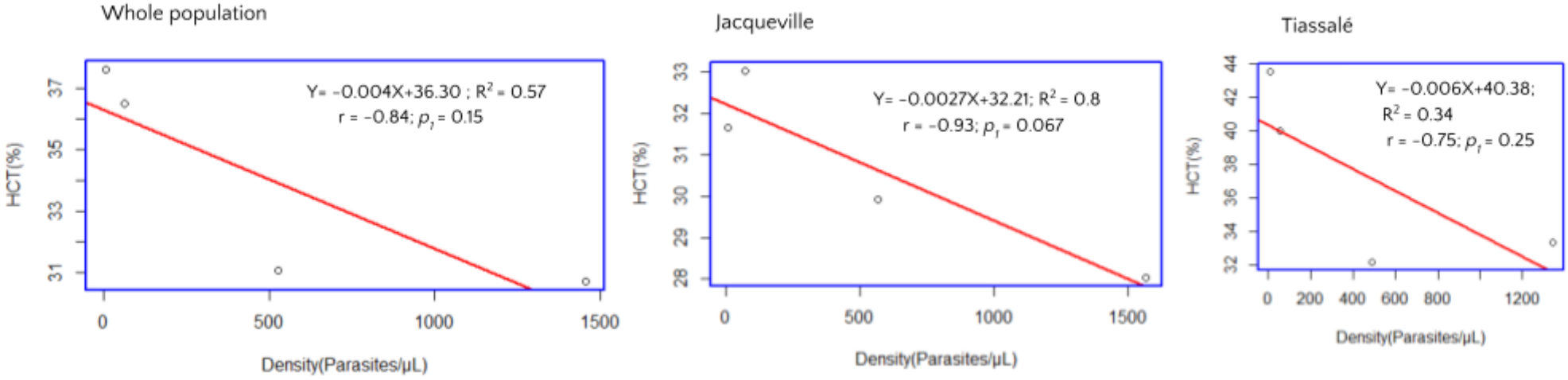

Figure 6: Linear relationship between parasite density and Mean Corpuscular Volume (MCV)

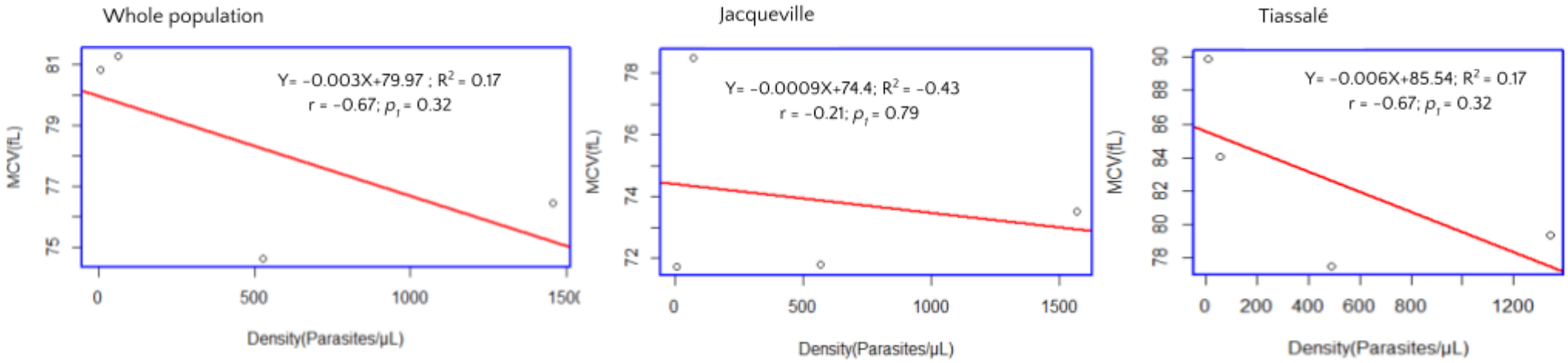

Figure 7: Linear relationship between parasite density and Mean Corpuscular Hemoglobin (MCH)

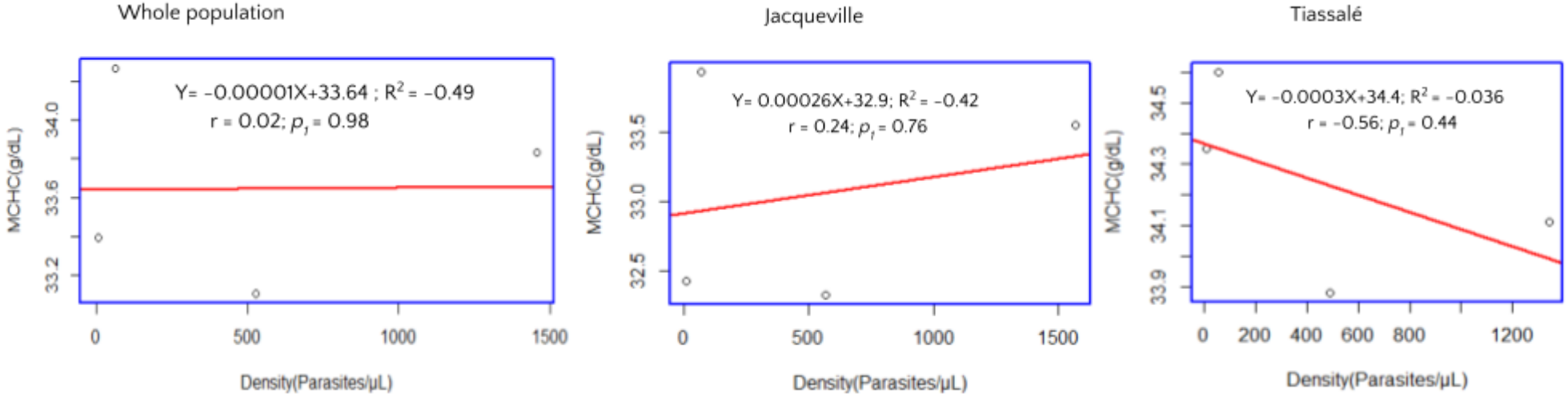

Figure 8: Linear relationship between parasite density and Mean Corpuscular Hemoglobin Concentration (MCHC)

Discussion

The age mean was 20 years with 4 months as minimum and 70 years as maximum. However, all people of any age were found in this study. That could be explain that Côte d'Ivoire is a country belongs a stable endemic area so all citizens were exposed malaria even if children and pregnant women are more vulnerable. The same last reason could explain that there are almost as women as men infected by malaria due to sex-ratio about one showing that malaria does not correlate to sex because the mosquito vectors have not a clearcut preference for either sex. Very similar situations were observed in a study carried out in Abidjan, Côte d'Ivoire from January 2007 to February 2011 (Goran-Kouacou et al., 2017). However, the results obtained in this study is contrary to studies conducted by (Sakzabre et al., 2020) which reported that females were more infected as compared to their male counterparts (69.07 % and 30.93 %, respectively).

Haemoglobin had a significant negative linear relationship with parasite density into malaria-infected subjects. This implies that as the parasite density is increases, there is a corresponding decrease in haemoglobin level and could be due to a state of hemolysis, which occurs during the phase of erythrocyte schizogony in the malaria-infected subjects (Malezieux-Picard et al., 2015). In effect, during life cycle of *plasmodium* in humans, the parasites grow and multiply first in the liver cells and then in the red cells of the blood. In the blood, successive broods of parasites grow inside the red cells and destroy them (hemolysis) releasing daughter parasites ("merozoites") that continue the cycle by invading other red cells (Malezieux-Picard et al., 2015). This red blood cells destroying, releases hemoglobin contained in those cells into blood plasma (Effenberger-Neidnicht & Hartmann, 2018) and occurs a hemoglobin level decreasing, which is one of the essential parameters to accurately confirm the presence or absence of anemia (Fanello et al., 2017). Thus, malaria infected subjects in this study could be seem predict anemia. Others studies have shown the same observation. One of these reported by (Lopera-Mesa et al., 2015) has indicated that there is a steady fall in haemoglobin levels during a malaria infection (Lopera-Mesa et al., 2015). Another carried out at Nigeria has also shown a decreasing of haemoglobin level during an increasing of parasite density (Eze Evelyn et al., 2012). Also, the findings of a study in Limbe at Cameroom depicted a negative correlation between parasite load and haemoglobin concentration (Kamga et al., 2010).

WBC was significantly correlated positively to parasite density into malaria-infected subjects by a linear relationship. This observation could be explain by the leukocytosis, which correspond to an increase of the number of white blood cells in circulation, and it could be cause by the malaria, which is a parasitic infection (Robbins et al., 2010). In fact, WBC are part of the body's immune system and play a crucial role in the body's ability to fight infection and other diseases (Nicholson, 2016). WBC count in the body can vary during the different stages of malaria infection. Thus, leucocytosis can occur during severe malaria (Nicholson, 2016). According to the explanations, more patients of this study would develop severe malaria. This result is accordance to a study carried out at Thailand whom showed that leukocyte counts were also significantly higher in patients with high parasitemia compared to those with low and moderate parasite density (Kotepui et al., 2015) and another study at Cameroon (Kamga et al., 2010).

Conclusion

In conclusion, an important haemoglobin count decrease or WBC count increase into patient may predict malaria infection. Thus, haemoglobin and WBC may be considered like the key haematological indicators of malaria infection in the studied population.

Conflicts of Interest

None to declare

Acknowledgements

We thank all those who voluntarily participated in this study. We in particular, thank the parents and guardians who willingly consented on behalf of their children. Thanks also go to all the staff of Jacqueville and Tiassale regional hospital and Jean Lorougnon Guédé University.

References

1. Adu-Gyasi, D., Adams, M., Amoako, S., Mahama, E., Nsoh, M., Amenga-Etego, S., Baiden, F., Asante, K. P., Newton, S., & Owusu-Agyei, S. (2012). Estimating malaria parasite density : Assumed white blood cell count of 10,000/µl of blood is appropriate measure in Central Ghana. *Malaria Journal*, *11*(1), 238. https://doi.org/10.1186/1475-2875-11-238
2. Ashley, E. A., & White, N. J. (2014). The duration of Plasmodium falciparum infections. *Malaria Journal*, *13*(1), 500. https://doi.org/10.1186/1475-2875-13-500

3. Effenberger-Neidnicht, K., & Hartmann, M. (2018). Mechanisms of Hemolysis During Sepsis. *Inflammation*, *41*(5), 1569-1581. https://doi.org/10.1007/s10753-018-0810-y

4. Eledo, B., Tommy, E., Onuoha, E., Dunga, K., & Okamgba, O. (2020). *The Effects of Assymptomatic Malaria on Some Haematological Parameters among the Elderly in a Sub-Urban Community in Southern Nigeria*. https://doi.org/10.23937/2469-5696/1410055

5. Eze Evelyn, M., Ezeiruaku, F. C., & Ukaji, D. C. (2012). Experiential relationship between malaria parasite density and some haematological parameters in malaria infected male subjects in Port Harcourt, Nigeria. *Global Journal of Health Science*, *4*(4), 139-148. https://doi.org/10.5539/gjhs.v4n4p139

6. Fanello, C., Onyamboko, M., Lee, S. J., Woodrow, C., Setaphan, S., Chotivanich, K., Buffet, P., Jauréguiberry, S., Rockett, K., Stepniewska, K., Day, N. P. J., White, N. J., & Dondorp, A. M. (2017). Post-treatment haemolysis in African children with hyperparasitaemic falciparum malaria; a randomized comparison of artesunate and quinine. *BMC Infectious Diseases*, *17*(1), 575. https://doi.org/10.1186/s12879-017-2678-0

7. Goran-Kouacou, A., Dou, G., Zika, K., Adou, H., Yéboah, O., Aka, R., Hien, S., Siransy, K., N'guessan, K., Djibangar, T., Dassé, S., & Adoubryn, K. (2017). Malaria serology test : What contribution does it make in an endemic country such as Ivory Coast? *Pan African Medical Journal*, *26*. https://doi.org/10.11604/pamj.2017.26.221.11314

8. Hunt, N. H., Driussi, C., & Sai-Kiang, L. (2001). Haptoglobin and malaria. *Redox Report: Communications in Free Radical Research*, *6*(6), 389-392. https://doi.org/10.1179/135100001101536508

9. Kamga, F., Akuro, S., & Njunda, A. (2010). Relationships between blood cell counts and the density of malaria parasites among patients at the regional hospital, Limbe, Cameroon. *African Journal of Clinical and Experimental Microbiology*, *11*(2), Article 2. https://doi.org/10.4314/ajcem.v11i2.53918

10. Kotepui, M., Piwkham, D., PhunPhuech, B., Phiwklam, N., Chupeerach, C., & Duangmano, S. (2015). Effects of malaria parasite density on blood cell parameters. *PloS One*, *10*(3), e0121057. https://doi.org/10.1371/journal.pone.0121057

11. Lopera-Mesa, T. M., Doumbia, S., Konaté, D., Anderson, J. M., Doumbouya, M., Keita, A. S., Diakité, S. A., Traoré, K., Krause, M. A., Diouf, A., Moretz, S. E., STullo, G., Miura, K., Gu, W., Fay, M. P., Taylor, S. M., Long, C. A., Diakité, M., & Fairhurst, R. M. (2015). Impact of red blood cell variants on childhood malaria in Mali : A prospective cohort study. *The Lancet. Haematology*, *2*(4), e140-e149. https://doi.org/10.1016/S2352-3026(15)00043-5

12. Maina, R., Walsh, D., Gaddy, C., Hongo, G., Waitumbi, J., Otieno, L., Jones, D., & Ogutu, B. (2010). Impact of Plasmodium falciparum infection on haematological parameters in children living in Western Kenya. *Malaria Journal*, *9*. https://doi.org/10.1186/1475-2875-9-S3-S4

13. Malezieux-Picard, A., Queyrel, V., Jeandel, P. Y., Fuzibet, J. G., Baldin, B., Hivernat, H., & Lazdunski, R. (2015). Une hémolyse qui n'en finit pas ! *La Revue de Médecine Interne*, *36*, A136. https://doi.org/10.1016/j.revmed.2015.10.081

14. Mbewe, R. B., Keven, J. B., Mzilahowa, T., Mathanga, D., Wilson, M., Cohee, L., Laufer, M. K., & Walker, E. D. (2022). Blood-feeding patterns of Anopheles vectors of human malaria in Malawi : Implications for malaria transmission and effectiveness of LLIN interventions. *Malaria Journal*, *21*(1), 67. https://doi.org/10.1186/s12936-022-04089-7

15. Millar, S. B., & Cox-Singh, J. (2015). Human infections with Plasmodium knowlesi—Zoonotic malaria. *Clinical Microbiology and Infection*, *21*(7), 640-648. https://doi.org/10.1016/j.cmi.2015.03.017

16. Nicholson, L. B. (2016). The immune system. *Essays in Biochemistry*, *60*(3), 275-301. https://doi.org/10.1042/EBC20160017

17. Robbins, S. L., Kumar, V., & Cotran, R. S. (2010). *Robbins and Cotran pathologic basis of disease* (8th ed.). Saunders/Elsevier. http://catdir.loc.gov/catdir/toc/fy0903/2008007812.html

18. Sadoine, M. L., Smargiassi, A., Ridde, V., Tusting, L. S., & Zinszer, K. (2018). The associations between malaria, interventions, and the environment : A systematic review and meta-analysis. *Malaria Journal*, *17*(1), 73. https://doi.org/10.1186/s12936-018-2220-x

19. Sakzabre, D., Asiamah, E. A., Akorsu, E. E., Abaka-Yawson, A., Dika, N. D., Kwasie, D. A., Ativi, E., Tseyiboe, C., & Osei, G. Y. (2020). Haematological Profile of Adults with Malaria Parasitaemia Visiting the Volta

Regional Hospital, Ghana. *Advances in Hematology*, *2020*, 9369758. https://doi.org/10.1155/2020/9369758

20. Sato, S. (2021). Plasmodium—A brief introduction to the parasites causing human malaria and their basic biology. *Journal of Physiological Anthropology*, *40*(1), 1. https://doi.org/10.1186/s40101-020-00251-9
21. Tangpukdee, N., Krudsood, S., Kano, S., & Wilairatana, P. (2012). Falciparum malaria parasitemia index for predicting severe malaria. *International Journal of Laboratory Hematology*, *34*(3), 320-327. https://doi.org/10.1111/j.1751-553X.2011.01398.x
22. WHO. (2021). *Lignes directrices de l'OMS sur le paludisme*. https://www.who.int/fr/publications-detail/guidelines-for-malaria