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Original article

The Relationship between Malaria and Hematological Parameters from Sabya General Hospital, Saudi Arabia

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Abstract

Malaria, a disease prevalent in endemic regions, has been found to have significant impacts on hematological parameters, resulting in both direct and indirect effects. These effects have been linked to a considerable number of fatalities. However, certain hematological parameters in populations residing in malaria-endemic areas have yet to be consistently characterized as a benchmark for assessing the prevalence of malaria. This study was designed to evaluate the diagnostic significance of certain hematological alterations in patients infected with malaria, based on the aforementioned fact. The study recruited a sample size of 99 individuals, comprising of 81 patients (cases) who tested positive for malaria and 18 healthy control adults. The male to female ratio in the malaria positive group was 3:1. The findings indicate that among individuals who tested positive for malaria, have low level of hemoglobin and high level of neutrophils. The presence of malaria was significantly linked to leukemia, anemia, and thrombocytopenia, all of which were deemed to be specific indicators for the diagnosis of malaria. The estimation of anemia was found to be specific as well as sensitive for the diagnosis of malaria. Thus, this study indicates that anemia provides the highest diagnostic significance among patients infected with malaria.

Keywords: ***Malaria, hematological parameters, Saudi Arabia, Laboratory.***

Introduction

The incidence of malaria on a global scale exhibited a decline from 2010 (estimated 239 million cases) to 2017 (estimated 219 million cases) (Bakhubaira, 2013). Nonetheless, there was no noteworthy advancement in the diminution between the years 2015 and 2017. As a result, malaria continues to be a significant cause of mortality in regions where it is endemic, particularly in sub-Saharan Africa (Al-Salahy *et al.*, 2016). The malaria-causing parasite *Plasmodium falciparum* was responsible for a significant proportion of malaria cases in the WHO African Region in 2017, accounting for up to 99.7% of reported cases. Within tropical regions, various febrile illnesses exhibit comparable and non-specific indications, posing a difficulty in the clinical identification of malaria (Lathia and Joshi, 2004).

Malaria is limited to the southwestern regions of Saudi Arabia. The incidence of malaria was predominantly limited to specific areas, specifically the Aseer and Jazan regions (Hawash *et al.*, 2019). In the aforementioned regions, malaria is predominantly of imported origin, and the endemic malaria is frequently acknowledged to be of low prevalence. In regions characterized by low malaria transmission rates, there exists a high prevalence of asymptomatic malaria infections, which are often sub-microscopic in nature. It is postulated that the residual immunity observed in these contexts is the underlying cause (Jairajpuri *et al.*, 2014). Individuals who have asymptomatic infections may exhibit symptoms within a few days or weeks following detection, or may continue to have sub-patent infections for several months with fluctuating levels of parasitaemia. Asymptomatic sub-microscopic infections pose a significant risk to the elimination of malaria through local transmission in regions with low transmission rates (Omarine Nlinwe and Nange, 2020).

The districts of Jazan and other southern regions in Saudi Arabia do not exhibit a low transmission rate of malaria (Awoke and Arota, 2019). Furthermore, the World Health Organization (WHO) advocates for the utilization of antimalarial medications predicated on a conclusive exhibition of parasites in the peripheral blood film, coupled with prompt and accurate diagnosis and detection of this infection, in order to effectively combat its dissemination. Hence, in instances of low levels of malaria parasitaemia, specific automated hematological parameters may trigger the need for peripheral blood smear examination to detect parasitic forms (Muwonge *et al.*, 2013).

Hematological alterations are frequently observed as the primary complications in cases of malaria infection, owing to the fact that the causative agents of the disease are blood parasites (Kotepui *et al.*, 2017). As such, they constitute significant contributors to the pathogenesis of malaria. Although certain hematological parameters have been linked to the prevalence of malaria, their use as a consistent standard for measuring the burden of the disease has not been well-established (Olliaro *et al.*, 2011). The utilization of hematological parameters can serve as a valuable diagnostic indicator for identifying acute febrile illnesses resulting from malaria. Common laboratory results comprise measurements of leukocytes, hemoglobin, red cell distribution width, and platelet counts (Sirak *et al.*, 2016).

Malaria has been observed to have a general impact on hematological factors, including anemia (Uneke *et al.*, 2008). Recurrent malaria episodes can lead to severe anemia and metabolic acidosis, particularly in children, thereby posing a significant risk to their lives. In comparison to pediatric individuals without malaria, those afflicted with malaria exhibited a statistically significant reduction in their platelet counts (Francis *et al.*, 2014). The incidence of anemia was found to be greater among children who tested positive for malaria comparing to those who tested negative for the same. The study conducted in western Kenya revealed a significant decrease in eosinophils, platelets, red blood cell count, lymphocytes, (Erhart *et al.*, 2004), and hemoglobin (Hb) levels in children infected with malaria. When compared to non-malaria infected children, it was observed that the neutrophil counts as well as absolute monocyte and the mean platelet volume (MPV), were elevated (Surve *et al.*, 2017). The odds ratio indicated that there was a 13.8-fold increase in the likelihood of malaria in children whose platelet counts were less than 150,000 µL. In the pediatric population, malaria has been identified as a contributing factor to the development of pancytopenia, which is characterized by hemoglobin levels below 10 g/dL, absolute neutrophil counts below 1.5 × 109/L, and platelet counts below 100 × 109/L (Haroon *et al.*, 2013).

Malaria has a comparable impact on hematological parameters in both adult and pediatric populations. The study assessed the impact of *Plasmodium falciparum* malaria infection on blood cells and platelets, revealing that the effects on white blood cells were comparatively milder than those on thrombocytes (Awoke and Arota, 2019). Thrombocytopenia commonly resolves upon successful treatment of the underlying condition. In a separate investigation, it was noted that the incidence of changes in hemoglobin and platelet levels was more notable among individuals with malaria, in comparison to alterations in white blood cell counts. It was noted that genereally, there is a significant decrease in the count of red blood cells (RBCs), platelets, hemoglobin (Hb), white blood cells (WBCs), monocytes, neutrophils, lymphocytes, and eosinophils among patients diagnosed with malaria (Hawash *et al.*, 2019).

Hematological changes in severe malaria exhibited variations based on the associated complications. According to additional research, hemoglobin concentration exhibited significant variation across different severe malaria complications, in contrast to platelet and white blood cell counts (Al-Mekhlafi *et al.*, 2021). Nonetheless, various investigations have consistently observed the presence of certain hematological irregularities in individuals infected with malaria, including anemia, thrombocytopenia, splenomegaly, leucopenia, leukocytosis, mild-to-moderate atypical lymphocytosis, and infrequently disseminated intravascular coagulation. It has been previously documented that individuals with chronic *Plasmodium falciparum* malaria exhibit a lower degree of parasitaemia (Kotepui *et al.*, 2017).

The severity of anemia, lymphocytosis, neutropenia, thrombocytopenia, and monocytosis was found to be higher in patients with chronic *Plasmodium falciparum* malaria in comparison to those with acute *Plasmodium falciparum* malaria. Thrombocytopenia has been documented as an initial indicator of malaria infection, particularly in cases of *Plasmodium falciparum* malaria. The most significant predictors of malaria infection in children were found to be low hemoglobin concentration and platelet count (Sirak *et al.*, 2016). It was found a positive association between the monocyte-to-lymphocyte ratio and the likelihood of clinical malaria in children who had asymptomatic infection of *Plasmodium falciparum*. According to a separate investigation, white blood cells, reduced lymphocyte levels, and platelet counts were the primary indicators of malaria contraction. Numerous studies have also documented that malaria infection primarily impacts leucocytes, thrombocytes, and RBCs. Thus, the assessment of hematological parameters may aid in the determination of the prevalence and severity of malaria (Haroon *et al.*, 2013). This is particularly advantageous given the lack of a differential diagnostic test capable of distinguishing between malaria illness and parasitemia accompanied by fever resulting from an alternative etiology (Abro *et al.*, 2008). In regions where malaria is endemic, the process of diagnosing the disease can be complicated due to the presence of individuals who possess partial immunity to malaria. Such individuals may be parasitized by the malaria parasite without exhibiting any symptoms of the disease, or may exhibit symptoms that are similar to those of other illnesses. Microscopy is the preferred method for monitoring the response to treatment in patients afflicted with severe malaria who are parasitized, as it allows for a quantitative assessment of parasitaemia. Nonetheless, in settings with limited resources, there exists a considerable degree of fluctuation in the precision and accuracy of the microscopy technique, which presents a difficulty in ensuring the delivery of high-quality microscopic services. The efficacy of rapid diagnostic tests (RDTs) is significantly influenced by various factors, including the antigen, malaria species targeted, and the specific product employed (Awoke and Arota, 2019).

Aim of the study

This study aims to assess the relationship between malarial infectious stage and the disruption in some of hematological parameters.

Methods

Sample of the Study

Sampling design (include sampling methodology)

A retrospective descriptive study was used in this study, this retrospective study is convenient to be conducted for this sample as malaria is not endemic in Saudi Arabia.

a. Sample size

Richard Geiger equation and the confidence level of 95%, the population, and 50% response distribution, and using sampling size calculation of more than 418 expected responses to get the final total sample size which equals 81 patients (cases)

b. Inclusion and exclusion criteria

This study targeted malaria patients and the focus was on the CBC results of people infected with malaria.

- Patients who are tested positive with malaria.
- All malaria patients with any age.
- Patients who have no any other disorders affecting hematological parameters.

While the exclusion criteria

- Patients who have not been diagnosed with malaria
- Patients who have other disorders that may affect the hematological homoestasis.

Data Collection

This study collected data on Sabya General Hospital (Jazan-Saudi Atrabia) blood samples on which Complete Blood Count (CBC) analysis was performed. The data were collected electronically for the period from 02/2023 to 05/2023 which, this long duration is due to lack malarial cases and its slow transmission and dissemination in this region.

This study collected the results of the CBC test for malaria patients. These samples were collected from inpatients in isolation using blood tubes containing an anticoagulant (EDTA). It was then sent to the laboratory for analysis using a Sysmex XN-1000 and Beckman Coulter's DxH 800 device to count the blood cells and hemoglobin levels, as described and modified by Reinhardt and Reinhardt (2000).

The main protocol was based on isolating patients infected with malaria. The data were collected through a regional laboratory in Sabya General Hospital using an electronic system called Medsys. This software is widely used among laboratories and healthcare settings, available at: https://www.medsyshcs.com/

The normal range values for hematological parameters are represented according the laboratories kits, and obtained as follows:

The normal ranges of WBCs is (3.5-10)x 10^9/L, RBCs is (4.5-6.5) x 10^9/L, Platelets is (150-400) x 10^3/µL, Neutrophils is (40-75)%, Lymphocytes is (20-45)%, and for Hb is (12-16)g/dl.

Data and Statistical Analysis

Following the completion of data collection and management, the collected data underwent statistical analysis using IBM SPSS version 24. Descriptive and analytical statistics were employed, and statistical significance was determined by a p-value of less than 0.05 ($p < 0.05$). The figures were generated utilizing Microsoft Excel software. The descriptive statistics were utilized to examine and establish the socio-demographic factors of the respondents, including frequencies and percentages. The identification of changes in blood component levels was facilitated through the utilization of frequencies and percentages. Additional inferential statistical tests were employed, including the Chi-square test and unpaired t-tests, to compare the data of the patients.

Results

The sociodemographic data

This study included 99 individuals, in this study, about 81 as malaria patients (cases) and 18 as controls who are healthy and tested negative to malarial infection.

The following table shows the demographic data for both cases and control groups,

Table 1: The demographic data and history of malarial infections among samples in this study (n=99)

Parameter	F (n=99)	% (100)
Age		
4-15	11	11.11
16-26	16	16.17
26-36	38	38.39
37-48	19	19.2
>49	15	15.13
Mean ± S.D	34.9±15.12	
Adulthood		
Adult	90	90.9
Infant	9	0.9
Gender		
Male	77	77.9
Female	22	22.1
Nationality		
Saudi	92	92.9
Non-Saudi	7	7.1
Tested for malaria		
Positive	81	81.1
Negative	18	18.9
History of malarial infection	Yes	No
Yes	1	1.1
No	98	98.9

The following figures show the histogram for age intervals (years), distribution of gender and adulthood among patients in this study, and the test results for malarial infections,

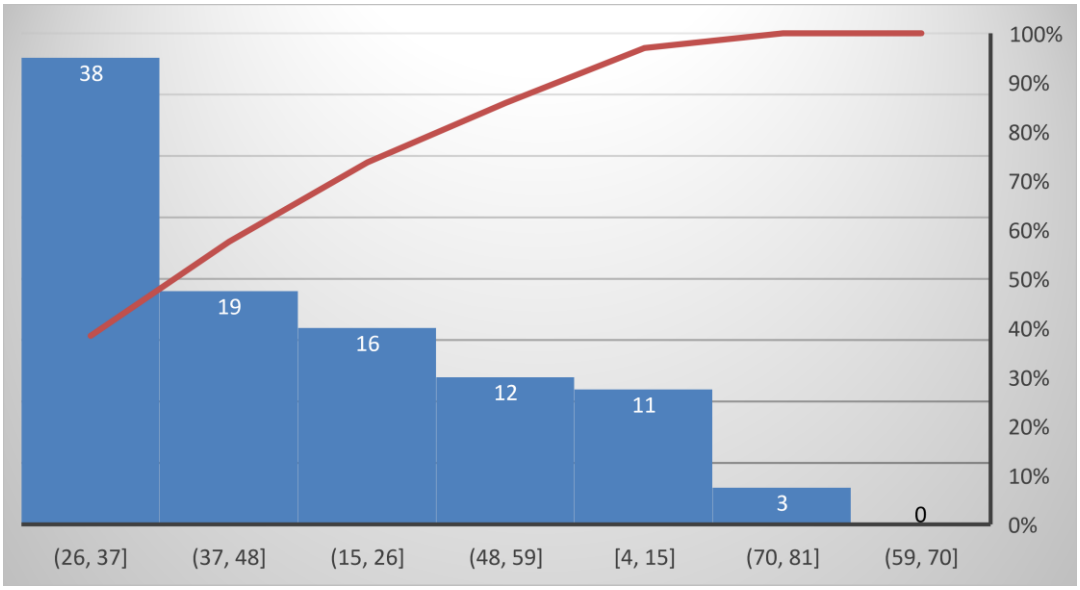

Figure 1 The distribution of age groups (in years) among samples participated in this study (n=99)

The above table shows that the most predominant age group is between 26 and 37 years old and the least percentage of adult group was who are over 59 years old.

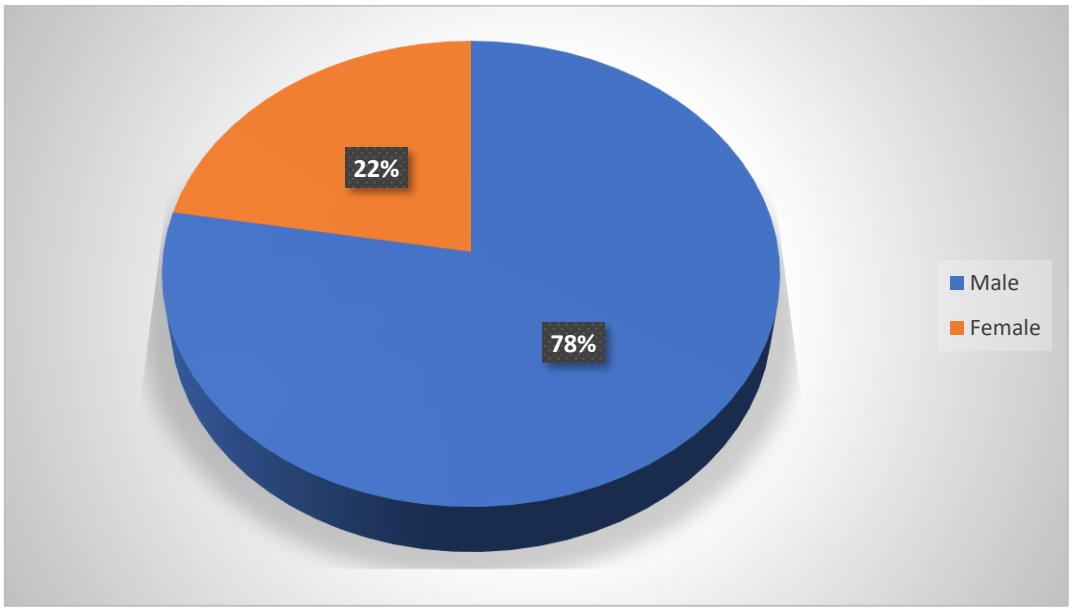

Figure 2: The gender distribution among samples participated in this study (n=99)

The above figure shows that the most predominant gender was males with 78% and they are prevalent in this study in both cases and controls groups.

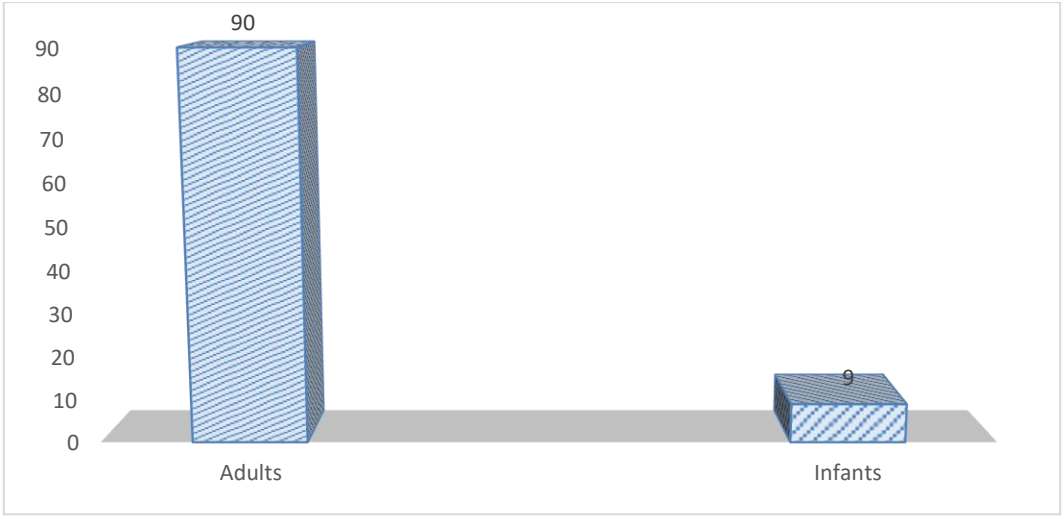

Figure 3: The proportion of adulthood among samples participated in this study (n=99)

The above figure shows that adults were more than infants with 90.9% as participated in this study.

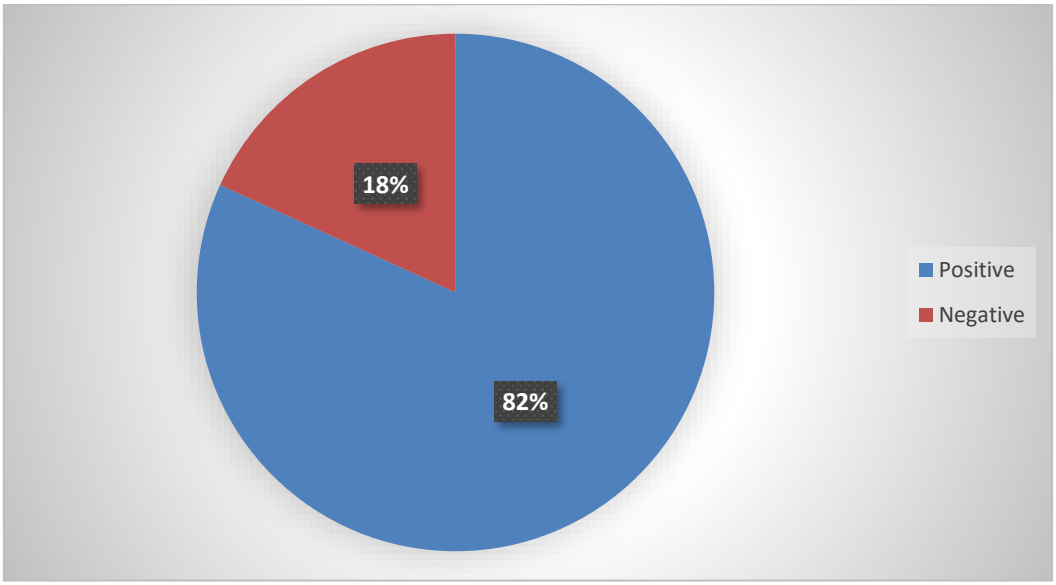

Figure 4: Results for malarial tests among samples participated in this study (n=99)

Cases group was consisting of 81 cases (82%) while control group was consisting of only 18 individuals (18%).

The hematological Parameters data and correlations

The following table shows the correlations between some of hematological parameters and incidence of malarial infection as tested by Chi square,

Table 2: The correlation (p value) between hematological parameters and some of variables for cases and controls groups in this study (n-99)

Demographic Variable	Hematological parameter	Level of significance (*p* value)
Positive malarial infection (Malaria Ag)	WBCs	0.00
	RBCs	
	PLT	
	NEUT %	
	LYMPH%	
	Hb	
Age	WBCs	0.18
	RBCs	0.549
	PLT	0.269
	NEUT %	0.499
	LYMPH%	0.27
	Hb	0.02
Gender	WBCs	0.00
	RBCs	
	PLT	
	NEUT %	
	LYMPH%	
	Hb	

The above table shows that there is a significant statistical correlation between incidence of malaria and presence of malaria antigens in the cases' serum (positive malaria) and the dysregulation and imbalance in hematological parameters homostasis (p=0.00).

Also, gender showed a significant statistical correlation in the cases' serum (positive malaria) and the dysregulation and imbalance in hematological parameters homostasis (p=0.00).

While age showed non-significant statistical correlation in the cases' serum with dysregulation of all hematological parameters (p = 0.18, 0.549, 0.269, 0.499, and 0.27 fpr WBCs, RBCs, PLT, NEUT%, and LYMPH%, respectively) except for hemoglobin which shows a significant statistical correlation with level of significance = 0.02.

Unpaired t-test results

The descriptive data analyses in this study shows that in cases group, the mean results for WBCs, RBCs, Platelets, and hemoglobin are 6.259 ± 2.8, 4.757 ± 0.98, 140.5 ± 108.2, and 12.5 ± 2.6, respectively. While in controls group, they are 6.48 ± 1.4, 5.4 ± 0.81, 282.76 ± 68.16, and 13.8 ± 1.6, respectively.

As shown in table 3

Table 3: Descriptive analysis data for both cases and controls group

	Mean	Std. Deviation	Std. Error Mean
Cases Group			
WBCs (3.5-10)	6.259	2.8062	.3118
RBCs (4.5-6.5)	4.757	.9733	.1081
Platelets (150-400)	140.488	108.2440	12.0271
Hb (12-16)	12.489	2.5824	.2869
Control Group			
WBCs (3.5-10)	6.483	1.3955	.3289
RBCs (4.5-6.5)	5.456	.8176	.1927
Platelets (150-400)	282.761	68.1588	16.0652
Hb (12-16)	13.889	1.5777	.3719

In table 4, represents the main t-test results as follow,

Table 4: Unpaired t-test results for cases and controls group in this study

Hematological Parameter					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference
					Lower
Cases					
WBCs (3.5-10)	20.075	80	.000	6.2593	5.639
RBCs (4.5-6.5)	43.987	80	.000	4.7568	4.542
Platelets (150-400)	11.681	80	.000	140.4877	116.553
Hb (12-16)	43.525	80	.000	12.4889	11.918
Controls					
WBCs (3.5-10)	19.711	17	.000	6.4833	5.789
RBCs (4.5-6.5)	28.309	17	.000	5.4556	5.049
Platelets (150-400)	17.601	17	.000	282.7611	248.867
Hb (12-16)	37.348	17	.000	13.8889	13.104

The above table shows that this study results obtained refers that there is a statistical significant correlation ($p<0.05$) between some of hematological parameters and succeeding the malaria diagnosis in malarial infection.

Discussion

Total of 81 patients with malaria were involved in this study with male to female ration rechs 3:1 and there is a predominant age group of 26 to 36 years, with mean age 34.9±15.12, this skewed distribution may be because all cases were randomly selected from hospitals as per observing and called visit-based samples (Lee *et al.*, 2002), There are low percentage of infants participated in this study it is agreed with Abossie *et al.* (2020) study, who reported that the majority of infected patients with malaria are adults, from A total of 271 febrile children under the age of 5 were systematically selected for blood sample collection. Blood samples were subjected to preparation of both thin and thick smears, followed by staining with 10% Giemsa solution. The resulting slides were then observed under a light microscope. In conclusion, it can be inferred that Alaria infection exhibits a high prevalence rate among children aged 37 to 59 months, while its prevalence decreases among children above the age of 5 and continues to be more widespread among adults.

While this study showed low rate of malarial infection in elderly patients who participated with few prevalence, it is in contrast to Bello *et al.*, (2023) study, who performed a random sampling technique was employed to select 972 adult residents from five communities in Osun State for a descriptive cross-sectional study. The study utilized a questionnaire to gather data and determine the prevalence of malaria RDT positivity among individuals aged 60 years and above, which was found to be higher (4.6%) than that of those below 60 years (3.4%). However, statistical analysis revealed that this difference was not significant ($p = 0.36$), thus it cannot be concluded that the malaria positive rate was higher among the elderly.

Only one had a previous history and re-infected with malaria, this case may be odd, but as reported by Manandhar *et al.* (2013) study, recurrent a malaria is less common and it may be related with less changing in hematological parameters, as the study involved the enrollment of approximately 137 cases that were microscopically suspected to have P. vivax infection, through the process of conducting research. A six-month follow-up prospective observational study was carried out between August 2010 and May 2011 in four health centers located in the Kailali and Kanchanpur districts of Nepal which aimed to evaluate the relapse/re-infection rate of P. vivax and its results of the study indicated that a relapse/re-infection rate of 17% was determined.

The correlation between these hematological parameters and occurrence of malaria and then, can predict and follow up the treatment success for malaria. This study results and from the descriptive data analyses in this study shows that in cases group, the mean results were high in WBCs, low in RBCs, Platelets, and hemoglobin when compared to controls group who showed a normal ranges in all hematological parameters, it is in agreement with Sakzabre *et al.* (2020) study, who performed a retrospective analysis was performed utilizing archived data of individuals who tested positive for malaria between January 2017 and March 15, 2019. The data that was obtained encompassed various aspects such as the demographic information of the subjects, the count of malaria parasites, the species of malaria parasites, and the complete blood count parameters. The study comprised 236 individuals who tested positive for malaria. Results. The findings of the study indicate that a higher proportion of female individuals were afflicted with the malaria pathogen in comparison to their male counterparts, with percentages of 69.07% and 30.93%, respectively. The findings

indicate that the prevalence of *Plasmodium falciparum* infection was 87.3% among the study population, while Plasmodium malaria infection was observed in 12.7% of the individuals. The study revealed that the most prevalent haematological abnormalities observed were lymphopenia (56.78%), anaemia (55.51%), thrombocytopenia (47.46%), eosinopenia (45.76%), neutropenia (29.24%), monocytosis (21.19%), and leucocytosis (17.37%) among the infected individuals. The study found that the average platelet count of individuals infected with P. falciparum was lower than that of individuals infected with P. malariae. A statistically significant reduction ($p<0.05$) in platelet count was observed with each incremental rise in parasite density. Conclusion. The haematological parameters of study participants who contracted malaria exhibited significant alterations, with anaemia, thrombocytopenia, lymphopenia, monocytosis, and eosinopenia being the most significant indicators of malaria infection, particularly in cases involving the P. falciparum species.

Also, in this study, the results of correlation in parameters and malarial incidence among patients showed that there is a significant statistical correlation between incidence of malaria and presence of malaria antigens in the cases' serum (positive malaria) and the dysregulation and imbalance in hematological parameters homostasis ($p=0.00$). Also, gender showed a significant statistical correlation in the cases' serum (positive malaria) and the dysregulation and imbalance in hematological parameters homostasis ($p=0.00$). While age showed non-significant statistical correlation in the cases' serum with dysregulation of all hematological parameters except hemoglobin ($p > 0.05$), and it is significally in agree with Kotepui *et al.* (2014) study, who reported that the haematological parameters of a total of 4,985 patients were assessed in a study conducted at Phop Phra Hospital, Tak Province, Thailand in 2009. The study population comprised of 703 patients who were diagnosed with malaria and 4,282 patients who were not infected with malaria. The study was conducted in an area that is known for endemic transmission of malaria. The study demonstrated that malaria-infected patients exhibited statistically significant reductions in several hematological parameters, including red blood cell count, hemoglobin levels, platelet count, and white blood cell count. Based on these findings, it can be concluded that malaria infection is associated with significant alterations in various hematological parameters, with decreased platelet, white blood cell, and lymphocyte counts serving as the most significant predictors of malaria infection. The integration of these parameters with other clinical and microscopy techniques has the potential to enhance the accuracy of malaria diagnosis and treatment.

Finally, when comparing two groups showed that there is a statistical significant correlation ($p<0.05$) between some of hematological parameters and succeeding the malaria diagnosis in malarial infection, and it is in agreement with Francis *et al.* (2014) study, who found that the hematological parameters of malaria-infected and non-infected subjects were compared using a student t-test, which revealed a statistically significant difference ($p<0.05$). The study found that the mean values of hematological parameters in male patients with malaria were significantly greater than those in female patients ($p<0.05$). This suggests that hematological parameters may serve as a dependable and effective tool for early detection of malaria in patients with severe infections.

Conclusion

The present investigations aimed to evaluate certain hematological alterations and their diagnostic efficacy in patients infected with malaria. The results indicated that individuals who tested positive for malaria exhibited a significant reduction in hemoglobin levels, white blood cell counts, and platelet counts. The findings suggest that in regions with high prevalence of mild parasitaemia, thrombocytopenia, and anemia may serve as reliable prognostic indicators for malaria infections. Therefore, it is recommended that these factors be considered in such endemic areas. This recommendation may be better suited for the adult demographic.

Conflict of Interest

There was no conflict of interest.

Funding Statment

The entire financial burdens were burn by the researchers.

Data Availability

Data would be available upon reasonable request by corresponding author.

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