ENSIGN GLOBAL COLLEGE

KPONG, EASTERN REGION, GHANA

FACULTY OF PUBLIC HEALTH

DEPARTMENT OF COMMUNITY HEALTH

PREDICTING MALARIA INFECTION USING HAEMATOLOGICAL INDICES: A CASE STUDY AT BREMANG SDA HOSPITAL IN THE SUAME MUNICIPALITY OF THE ASHANTI REGION, GHANA

By

GODFRIETT AKATSE-TSESU

(Index No. 217100191)

AUGUST, 2022

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A THESIS SUBMITTED TO THE DEPARTMENT OF COMMUNITY HEALTH, FACULTY OF PUBLIC HEALTH, ENSIGN COLLEGE OF PUBLIC HEALTH IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE

MASTER OF PUBLIC HEALTH DEGREE

AUGUST, 2022

DECLARATION

I hereby declare that this submission is my own work for the award of the MPH degree and that, to the best of my knowledge, it does not contain any material that has been previously published by another person or that has been accepted for the award of any other degree from the university, except where appropriate attribution has been made in the text.

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Director of Academic Programme	Signature	Date

DEDICATION

This work is dedicated to my wife, Janet Zonu, and my three beautiful daughters Seyram, Elikem and Deladem Makafui who collectively sacrificed and motivated me to pursue this programme.

ACKNOWLEDGMENTS

My utmost thanks belong to the Almighty God for helping me fulfil this dream I nurtured for a while, and for keeping me safe in all the journeys I had to make in the course of this programme.

My supervisor, Dr Steve Manortey deserves special gratitude for sharing with me his knowledge and time and for guiding me in the course of this work.

I also acknowledge the assistance given to me by Dr Anthony Eric Eshun, the Medical Director of Bremang SDA Hospital in the Suame Municipality of the Ashanti Region, as well as the staff of the hospital especially Mr Enoch Boadi of the laboratory unit.

DEFINITION OF TERMS

Haematology	It is the science or study of blood, blood-forming organs and blood diseases.
Malaria	A disease caused by plasmodium species which are introduced to the host through the bite of the female anopheles mosquito.

ABBREVIATION/ACRONYMS

ACTs	-	Artemisinin Combination Therapies
AOR	-	Adjusted Odds Ratio
Bas	-	Basophil
Bf for Mps	-	Blood film for malaria parasites
CBC	-	Complete blood count
CDC	-	Centre for disease control
CI	-	Confidence Interval
COR	-	Crude Odds Ratio
COVID-19	-	Corona Virus Disease 2019
Eos	-	Eosinophil
FBC	-	Full blood count
fL	-	femtolitre
g/dL	-	gram per decilitre
GAHS	-	Ghana Adventist Health Services
GSS	-	Ghana Statistical Service
Hb / Hgb	-	Haemoglobin
HRP2	-	Histidine-rich protein 2
IPT	-	Intermittent Preventive Treatment
IRS	-	Indoor residual spraying
ITNs	-	Insecticide-treated nets

LAMP	-	Loop-mediated isothermal nucleic acid amplification
LDH	-	Lactate dehydrogenase
Lymph.	-	Lymphocyte
MCH	-	Mean corpuscular haemoglobin
MCHC	-	Mean corpuscular haemoglobin concentration
MCV	-	Mean corpuscular volume
MDA	-	Mass Drug Administration
µL	-	Microlitre
Mon	-	Monocytes
Neut	-	Neutrophil
PCR	-	Polymerase chain reaction
PDMC	-	Post-Discharge Malaria Chemoprevention
PDW	-	Platelet Distribution Width
pg	-	picogram
P-LCR	-	Platelet Large Cell ratio
PLT	-	Platelet
PMC	-	Perennial Malaria Chemoprevention
RBC	-	Red blood cell
RDT	-	Rapid diagnostic test
RDWCV	-	Red Cell Distribution Coefficient of Variation
RDWSD	-	Red Cell Distribution Width Standard Deviation

SDA	-	Seventh Day Adventist
SMC	-	Seasonal Malaria Chemoprevention
T3	-	Test, Treat, and Track
WBC	-	White blood cell
WHO	-	World Health Organisation

ABSTRACT

Background: Malaria continues to wreak havoc in Africa, which accounted for about 96% of global cases in 2020. Malaria deaths increased by 12% compared with 2019, to an estimated 627000; an estimated 47000 (68%) of the additional 69000 deaths were due to service disruptions during the COVID-19 pandemic. Full blood count (FBC) and malaria microscopy are among the commonest tests run in most laboratories in Ghana. This study looked at the possibility of predicting malaria infection using results from a full blood count.

Methodology: This retrospective hospital-based observational study involved 400 samples. Data on age, sex, FBC and blood film for malaria parasites were obtained as secondary data from the laboratory unit of Bremang SDA Hospital in the Suame Municipality of the Ashanti Region of Ghana. Fischer's exact test was used to evaluate the association of demographic characteristics with malaria status. Multivariate logistic regression was used to determine significant predictor variables for malaria positive status with p-value<0.05.

Results: There was no association between malaria-positive status and either age or sex. All positive samples (n=41) were P. falciparum. The crude odds ratios revealed that all platelet parameters, absolute counts of lymphocytes, monocytes and eosinophils as well as per centages of neutrophils, lymphocytes and eosinophils were associated with malaria-positive status (p-value<0.05). In the overall model, only mean platelet volume was found to be statistically significant with AOR=164.44 (p-value<0.001). The model had a sensitivity of 56.10%, specificity of 98.33%, and positive predictive and negative predictive values of 79.31% and 95.15% respectively.

Conclusion: The findings demonstrate that malaria infection alters haematological parameters and that these can be used to predict malaria infection in the study population. Prescribers in

the study area are therefore encouraged to consider platelet parameters especially mean platelet volume as predictors of malaria infection.

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CHAPTER ONE

1.0 INTRODUCTION

1.1 Background Information

Evidence from a Chinese record from around 2700 BC contains references to what was almost certainly malaria (Cox, 2010). Before Alphonse Laveran, a French Military surgeon stationed in Africa, observed coloured granules in the red blood cells of sick patients and characterized them as malaria parasites in 1880, the sickness was attributed to a variety of factors (Cox, 2010). Ronald Ross, utilising avian malaria from infected sparrows, first documented the entire life cycle of the malaria parasite in 1898. It was then followed by a description of the human malaria life cycle and the parasite's dependence on Anopheles mosquitoes by Italian malaria researchers Grassi, Bignami, and Bastianelli in the same year (Dobson, 1999).

Despite the fact that there are numerous plasmodium parasite species, only five are known to harm humans: P. falciparum, P. ovale, P. vivax, P. malariae, and P. knowlesi. But the most common source of malaria infection, which kills over a million people in Africa alone every year, is Plasmodium falciparum (Aitken, Alemu and Rogerson, 2018).

About 241 million malaria cases were reported worldwide in 85 malaria-endemic countries in 2020, up from 227 million cases in 2019, per the World Malaria Report 2021, with the majority of this rise emanating from nations in the WHO African Region (WHO, 2021b). This indicates an increase from the 224 million malaria cases in 2015, which served as the baseline statistic for the Global Technical Strategy for Malaria 2016-2030. The WHO African Region recorded 228 million cases in 2020, representing 95% of cases. The lowering case incidence in this Region (368 to 222 per 1000 individuals at risk between 2000 and 2019) had a reversal due to service interruptions during the COVID-19 pandemic, increasing to 232 in 2020. (WHO, 2021b).

Similar to the trend in case incidence, there was a 36% decrease in deaths due to malaria from the year 2000 to 2019 (840 000 to 534 000). The COVID-19 pandemic, however, occasioned a rise to 602 000 in 2020. Additionally, between 2000 and 2019, the malaria fatality rate declined by 63%, from 150 to 56 deaths per 100 000 at-risk, but increased to 62 in 2020 (WHO, 2021b).

P. falciparum causes 90–98% of the morbidity and fatalities associated with the disease in Ghana, where malaria is hyperendemic (Squire *et al.*, 2016). Ghana accounted for 2.11% and 1.9% of global malaria cases and deaths respectively. (WHO, 2021b).

The science or study of blood, organs involved in producing blood, and blood illnesses is known as haematology. Some haematological parameters are evaluated by a lab test known as a full blood count (FBC) or complete blood count (CBC). Currently, this test is mostly performed by an equipment called a haematology analyser, which counts and computes the concentrations of the various blood components in a matter of seconds. White blood cells (WBCs), red blood cells (RBCs), and platelets (PLT) counts are the main blood cell characteristics evaluated by the FBC test. Other measurements include the differentiation of the various WBCs (lymphocytes, neutrophils, monocytes, basophils, and eosinophils) into counts and percentages as well as haemoglobin concentration, mean cell haemoglobin concentration (MCHC), and haematocrit.

The effects of malaria infection on haematological markers have been documented in numerous research. These include anaemia, decreased platelet count, decreased white blood cell count, and increased lymphocyte count (Kotepui *et al.*, 2014; Antwi-Baffour *et al.*, 2018; Sakzabre *et al.*, 2020).

1.2 Problem Statement

Ghana joined the Test, Treat and Track (T3) initiative of the WHO in 2013 as part of efforts to lessen the impact of malaria morbidity and mortality (Oteng *et al.*, 2020). The initiative aimed at testing and verifying malaria infection in every suspected case of malaria in endemic areas, and to provide confirmed cases with approved and efficacious antimalarial treatment, and finally, that the disease was tracked using timely and precise surveillance systems to inform policy (WHO, 2012). The T3 initiative states that routine confirmation of every suspected case of malaria using a rapid diagnostic test kit (RDT) or microscopy is required, and that presumptive treatment of the disease using solely clinical indicators should be minimised to the absolute minimum.

Well-trained microscopists who can prepare and read blood slides are needed to get beyond the first obstacle in this policy. Health professionals will be able to manage febrile patients more effectively as a result of having greater confidence in the lab-generated malaria report, decreased instances of malaria misdiagnosis, and identification of other lethal non-malarial causes of infection. It will also help reduce drug waste and the possibility of antimalarial drug resistance. On the other side, a false negative malaria report might cause the disease to advance from simple malaria to severe malaria, which can be fatal (Kang *et al.*, 2017; Tetteh *et al.*, 2021).

By developing the requisite skills for disease detection and demanding adherence to the T3 policy recommendations, the National Malaria Control Programme in Ghana and its partners in other nations have sought to enhance access to high-quality malaria testing for all suspected cases at all levels of healthcare over time (Moura *et al.*, 2014; Tetteh *et al.*, 2021).

It has been documented that malaria infection modifies several haematological markers, and certain models have been created to anticipate malaria utilising these changes in various

geographical areas (Paintsil *et al.*, 2019; Gebreweld *et al.*, 2021). Some of these models, however, were based on three-part differential haematology analysers that merged three WBC parameters (basophils, eosinophils, and monocytes) and so obscured any potential effects that the different cell types would have on the haematological parameters.

The impact of malaria infection on haematological parameters from a five-part differential analyzer has not been investigated in the Bremang population in the Suame Municipality. The SDA hospital was selected as the study location because it had the necessary tools and skilled microscopists.

1.3 Rationale of Study

Some healthcare professionals have had reason to doubt the results of the malaria test because of anticipated alterations in the cell indices after an infection with malaria (Tuijn *et al.*, 2014). Despite the difficulties with the individuals involved in diagnosing malaria, some healthcare professionals who refuse to accept a negative malaria report based on clinical signs and a haematology report only consider a limited number of factors rather than the entire report.

There have been attempts to research malaria infection using various models, such as environmental and social factors, but few of these studies have concentrated on haematological markers. The effects of Plasmodium infection on blood cell indices will considerably enhance malaria diagnosis and treatment if health professionals at all levels are aware of these effects, especially in areas with haematology analysers but without access to well-trained microscopists.

The impact of malaria on haematological markers in the Bremang community of the Suame Municipality is unknown. This study thus makes a contribution to ongoing initiatives to

enhance malaria diagnosis through the use of haematology profiles produced by haematology analysers.

1.4 Conceptual Framework

The conceptual framework displayed in Figure 1 below describes briefly how malaria infection takes place. The vector for this disease, the female Anopheles mosquito, acquires the plasmodium parasites through ingestion of infected blood and passes it on to a host (human being) who may then develop malaria. The effect of malaria on blood is shown through the changes in the blood cell parameters which will be treated as predictor variables. These changes can be used to a certain degree, to determine whether a person has malaria or not. Although malaria affects people of all ages and sex, these parameters will also be treated as predictor variables in this study.

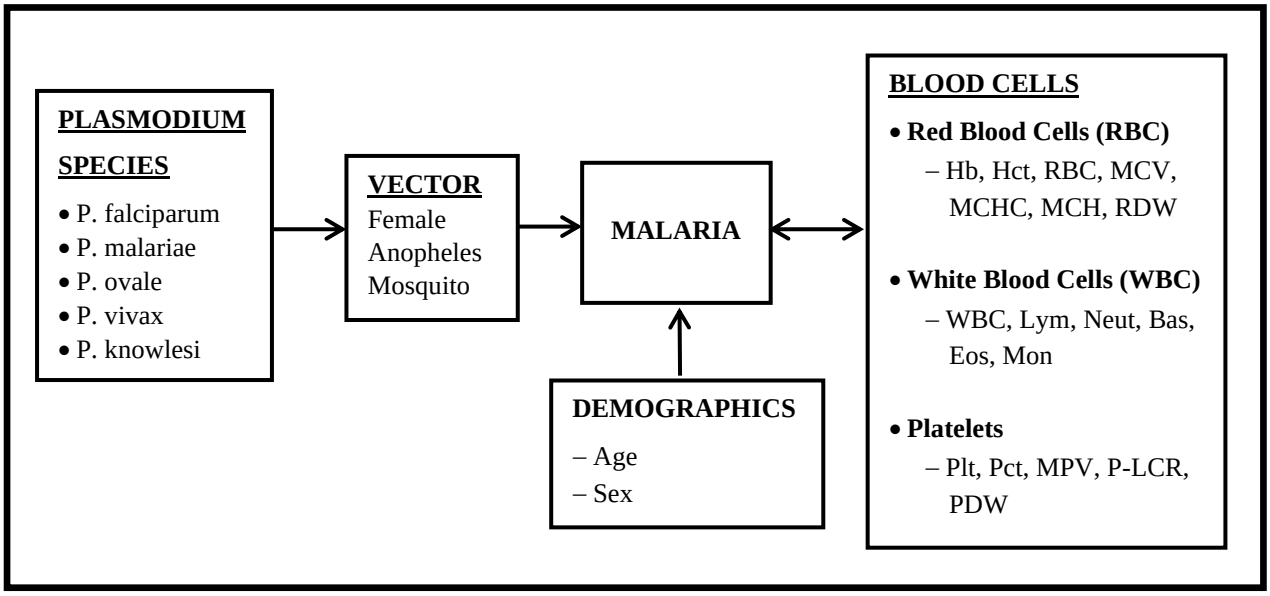

Figure 1.1: Conceptual Framework for malaria infection and impact on blood cell parameters.

Source: Author's self-construct

1.5 Research Questions

The following are the questions that should be answered in this project.

1) Is there any recognizable trend in the data that distinguishes positive cases from negative cases?
2) How effective is the use of a logistic model to predict cases of malaria?
3) What is the sensitivity, specificity, the positive and negative predictive values of the model generated?

1.6 General Objective

This project aimed at using binary logistic regression to formulate a model to predict malaria using blood cell parameters.

1.7 Specific Objectives

1) To analyse the data and compare the parameters obtained for both positive and negative cases.
2) To generate a logistic model to help predict cases of malaria.
3) To determine the sensitivity, specificity, positive predictive value and negative predictive value of the generated model.

1.8 Profile of Study Area

1.8.1 Physical Features

The thirty-eight new Districts established nationwide in accordance with Legislative Instrument (L.I) 2295 of 2017 includes the Suame Municipal Assembly. It was inaugurated on 15th March 2018, with Suame as its capital. It was also one of the five Sub-Metropolitan District Councils of the Kumasi Metropolitan Assembly upgraded to the status of a Municipality.

The Municipality is roughly in the middle of the Ashanti Region and is located between Latitude 6.35°N and 6.40°S and Longitude 1.30°W and 1.35°E, and lies 250 to 300 metres above sea level. The municipality shares borders with Old Tafo Municipality (East), Afigya Kwabre South District (North), and Kumasi Metropolis (West and South). A hub for intra- and inter-African trade, it is strategically situated 319 kilometres north of Accra, the country's capital (GSS, 2014).

1.8.2 Population Structure

The Municipality has a total population of roughly 136,290, comprised of 64,878 men and 71,412 women, per the 2021 National Population and Housing Census. Suame has 43,174 houses, 3.1 inhabitants per household, and a population density of 10,569.3 per square kilometre (GSS, 2021).

1.8.3 Climate

The climate of the Metropolis could be described as wet sub-equatorial, with average low and high temperatures of 21.5°C and 30.7°C respectively. Humidity ranges from about 84.16 per cent in the morning to 60 per cent in the evening. These conditions along with the double peaks rainfall regime (214.3mm in June and 165.2mm in September), have a direct impact on both the population and the environment since they have attracted people to the city from all over the country and outside (GSS, 2014).

1.8.4 Vegetation

The Municipality is located in the wet semi-deciduous South-East Ecological Zone, notably in the transitional forest zone. Trees of the Ceiba, Triplochlon, Celtis, and other alien species are the most common types encountered. This ecological zone's soil is fertile and suitable for growing crops (GSS, 2014).

1.8.5 Bremang Seventh Day Adventists (SDA) Hospital

The hospital was inaugurated in September 2016 as the ninth health facility in addition to eight other clinics, a nursing and midwifery training college and a central medical store, operated by the Ghana Adventist Health Services (GAHS) under the auspices of the SDA Church in the Ashanti Region. At its inception, it had a staff strength of fifteen but has grown steadily over the years to include the addition of more staff, equipment, and the expansion of its facilities.

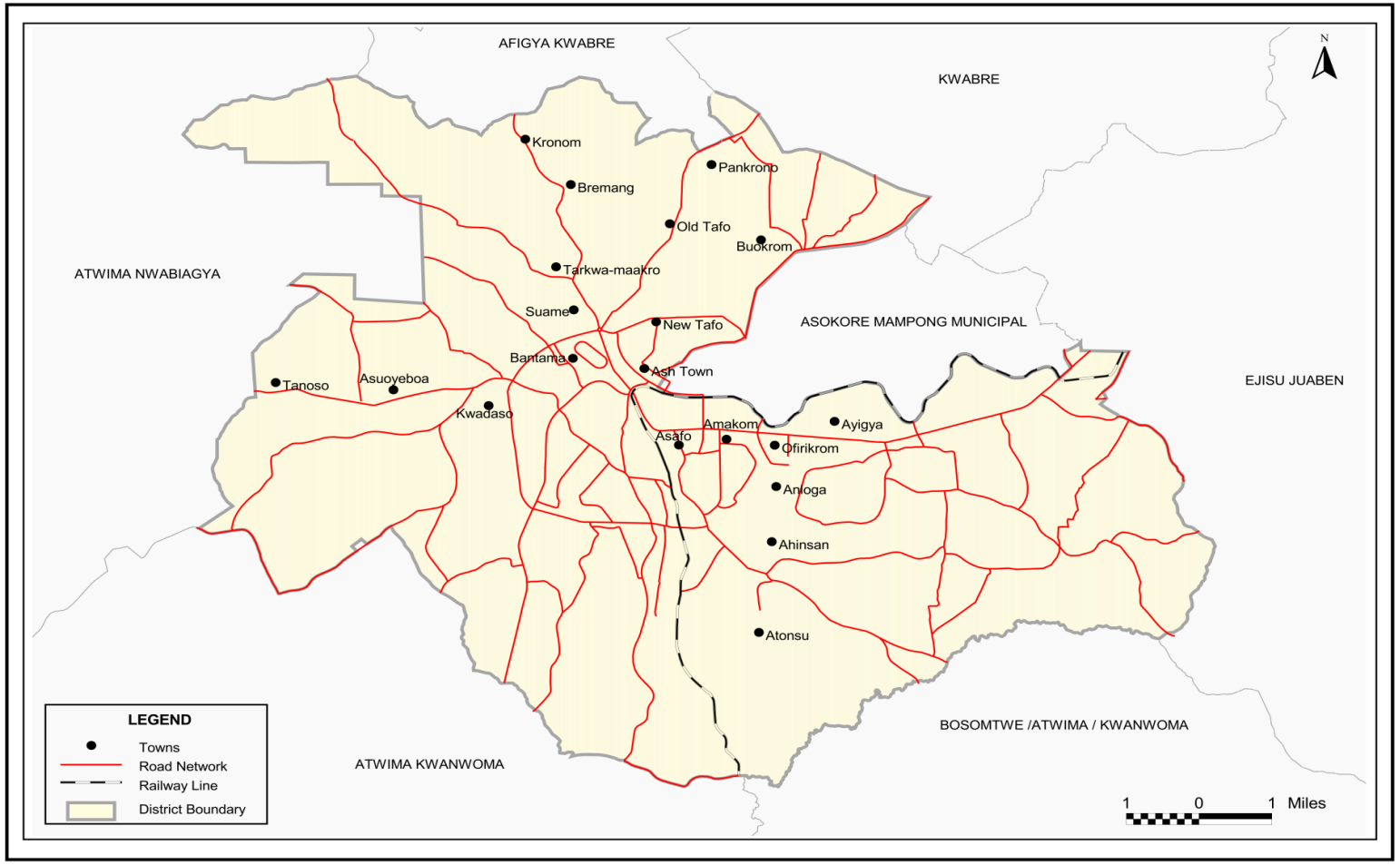

Figure 1.2: Map of Kumasi Metropolitan Assembly showing the then Suame Sub-metro on the northern side from Suame to Kronum (GSS, 2014).

1.9 Scope of Study

This thesis covers the effect of malaria on blood cell parameters using malaria microscopy test results and full blood count among residents in the Suame Municipality of the Ashanti Region of Ghana who attended the Bremang SDA Hospital from 1st to 31st May 2022. Retrospective data will be retrieved and analysed. The researcher limited this research to only those who were referred to the laboratory unit and who had no other systemic infections.

1.10 Organization of Report

There are six chapters in this book. The first chapter discusses the study's context, research questions, specific objectives, and study area in detail. The second chapter reviews the relevant literature, starting with the biology of malaria infection and concluding with the characteristics of blood cells and how they alter in infected individuals. The third chapter examines the methodology used to conduct this investigation and Chapter 4 of the report details the study's findings. In the fifth chapter, the results are addressed by comparing them to findings from related studies. The study's conclusions and recommendations are presented in the sixth chapter.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Introduction

This chapter takes a look at the available body of knowledge concerning the impact of malaria on haematological parameters and serves as a basis for comparing how similar or different the outcomes of this study are from those reviewed.

2.2 Epidemiology and Disease Burden

About 241 million malaria cases were reported worldwide in 85 malaria-endemic countries in 2020, up from 227 million cases in 2019, per the World Malaria Report 2021, with the majority of this rise emanating from nations in the WHO African Region (WHO, 2021b). This indicates an increase from the 224 million malaria cases in 2015, which served as the baseline statistic for the Global Technical Strategy for Malaria 2016-2030. The WHO African Region recorded 228 million cases in 2020, representing 95% of cases. The lowering case incidence in this Region (368 to 222 per 1000 individuals at risk between 2000 and 2019) had a reversal due to service interruptions during the COVID-19 pandemic, increasing to 232 in 2020. (WHO, 2021b).

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P. falciparum causes 90–98% of the morbidity and fatalities associated with the disease in Ghana, where malaria is hyperendemic (Squire *et al.*, 2016). Ghana accounted for 2.11% and 1.9% of global malaria cases and deaths respectively. (WHO, 2021b).

2.3 Biology of Malaria

The protozoan known as plasmodium (phylum 30 Apicomplexa) is the cause of the infectious disease malaria. Only five species of the plasmodium parasite, P. falciparum, P. ovale, P. vivax, P. malariae, and P. knowlesi, are known to infect people and cause sickness. However, Plasmodium falciparum is the most common cause of malaria infection, which alone causes over a million fatalities in Africa (Aitken, Alemu and Rogerson, 2018).

2.3.1 Life Cycle and Pathology of Infection

The major way that malaria is transmitted is by the bite of a female Anopheles mosquito, although it can also be transmitted from parent to child or through blood transfusions using tainted blood. Figure 2.1 shows the two stages of development of the malaria parasite: the asexual stage in the human host and the sexual stage in the mosquito. The asexual stage starts when a sporozoite from the mosquito's salivary glands is inoculated onto the human host.

On entering the liver, the sporozoites infect hepatocytes and begin to multiply after spending about half an hour to four hours in the circulation. This replication phase is known as the exoerythrocytic or pre-erythrocytic stage. Thousands of merozoites are released into the bloodstream when infected hepatocytes undergo asexual growth and burst. Relapsing malaria is brought on by dormant parasites from P. ovale and P. vivax infections that reside in the liver.

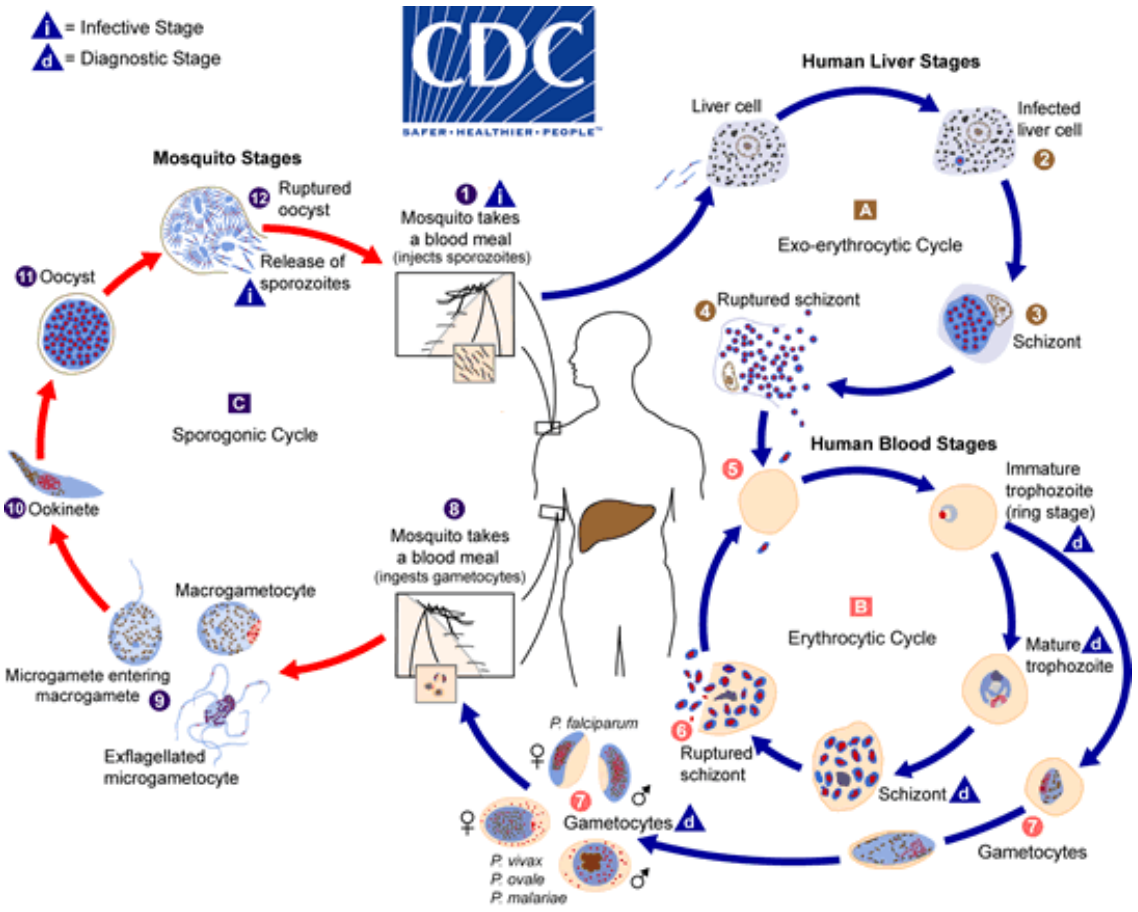

Figure 2.1: Life Cycle of the plasmodium parasite

Source: (CDC, 2020)

In Giemsa-stained blood smears, the immature trophozoites that come from the development of the merozoites that are released into the bloodstream and immediately pierce erythrocytes can be seen as ring formations. The ring shape morphology vanishes when the trophozoites mature and grow larger. The trophozoites grow into schizonts, which give rise to merozoites. A new batch of merozoites is subsequently released into the blood by the infected erythrocyte, reinfecting additional erythrocytes. Erythrocytes infected with trophozoites and schizonts in P. falciparum malaria cling to capillary endothelial cells, and this sequestration is linked to cerebral malaria. Some of the merozoites undergo a series of asexual cycles before evolving into sexual forms (gametocytes), which eventually infect mosquitoes. Parasites at the erythrocytic stage are what generate the pathophysiology and clinical signs of malaria.

2.3.2 Signs and Symptoms

The development of asexual parasites in blood and their interactions with host immunity is related to the pathogenic processes of malaria, and several outcomes may result. Following parasitic infection, some people may experience acquired immunity and remain asymptomatic. Even though asymptomatic infections rarely result in significant morbidity or mortality, they can still have some negative effects. The asymptomatic illnesses considerably raise the risk of anaemia, undernutrition, low birth weight, and mosquito infection since they commonly go unrecognised and untreated (Gitonga, 2013).

Others suffer from clinical illness, which typically includes fever and chills but may also include headache, myalgia, arthralgia, weakness, vomiting, and diarrhoea. Splenomegaly, anaemia, thrombocytopenia, hypoglycaemia, pulmonary or renal failure, and cognitive impairments are further clinical characteristics. Malaria can be categorised as either an uncomplicated or a severe clinical illness (CDC, 2020).

A patient is said to have uncomplicated malaria if they exhibit symptoms of the disease and a positive result from a parasitological test, such as a microscope or Rapid Diagnostic Test (RDT), but not if they also exhibit any signs of severe malaria (WHO, 2022). Cyclical fevers and chills, which are associated with the erythrocytic stage of the plasmodium life cycle, are often the defining features of uncomplicated clinical illness caused by P. falciparum infection. It is thought that these symptoms are brought on by malarial toxins that are secreted throughout the erythrocytic cycle and cause macrophages to secrete cytokines such as interleukin-l (IL-1) and tumour necrosis factor-α (TNF-α) and other cytokines (Gitonga, 2013).

A small fraction of the clinical episodes progresses into severe disease, which may cause severe anaemia, metabolic acidosis which is often associated with respiratory distress, or altered consciousness. Death or neuro-cognitive damage may follow some of the worst illness

episodes. Severe malarial anaemia (SMA), which describes the condition in which one records haemoglobin (Hb) content of less than 5 g/dL on account of malaria infection, is a significant side effect of malaria, particularly in young children. SMA often affects young children, peaking between 1 and 2 years of age, with the disease burden being highest in regions with high transmission rates (Gitonga, 2013).

2.4 Diagnosis

Several methods, such as light microscopy, special staining, fast antigen detection, and detection of parasite nucleic acid sequences, can be used to make a conclusive diagnosis of malaria. A definitive diagnosis can reduce the use of antimalarial medications by patients who don't need them, make it easier to spot people who need care for conditions other than malaria, target antimalarial treatment for a particular species of malaria, and track the effects of malaria infection and treatment over time (Berzosa *et al.*, 2018; WHO, 2022).

2.4.1 Light Microscopy

The "gold standard" for diagnosing malaria is the identification and measurement of the parasite load in thick and thin Giemsa-stained blood smears under a light microscope. Even under the most challenging circumstances, a quick and accurate diagnosis of malaria can be made with the least amount of equipment and ongoing costs. This method has a sensitivity of 50 to 500 parasites/µl of blood (Berzosa *et al.*, 2018) but a skilled microscopist could have a sensitivity of below 10 parasites/µl of blood (WHO, 2022). Differentiating *Plasmodia* species, determining parasite densities, identifying hyper-parasitaemia, detecting gametocytaemia, monitoring treatment responses, and the ability to diagnose a wide range of other illnesses are all additional benefits of this diagnostic technique.

Microscopy's main drawback is the lack of qualified workers, which contributes to the prevalence of false positive and false negative results and their associated harmful effects on the patient. Building these personnel's capacity led to significant advancements in the identification of parasite species and the measurement of parasite populations in numerous nations, including Ghana (Tetteh *et al.*, 2021). Other limitations with this approach include unreliable electricity, a shortage of premium slides and stains, a lack of and inadequate maintenance of quality microscopes, and challenges upholding quality assurance and quality control of laboratory services.

2.4.2 Rapid Diagnostic Tests (RDTs)

Numerous RDTs that are based on antigen detection using immunochromatography have been created in the last twenty years and are now often utilised for diagnosing malaria. RDTs can identify the Plasmodium enzymes lactate dehydrogenase (pLDH), aldolase, or the histidine-rich protein 2 (HRP2), which is exclusive to *P. falciparum* (Eze, Ezeiruaku and Ukaji, 2012; Gitonga, 2013).

The World Health Organization has advised against using RDTs unless they meet the following requirements starting in 2012. At 200 parasites/μL, the panel detection score for P. falciparum samples must be 75% or more. For P. vivax, the detection score should be 75% or more at 200 parasites/L in all transmission scenarios, with the false positive rate being less than 10% and the invalid rate being less than 5% (WHO, 2022).

The tests have some potential advantages, including the stability of test kits and reagents at room temperature, quick turnaround times for results, expansion of diagnostic services to the most remote communities and healthcare facilities, no electricity requirement, no need for specialised equipment or personnel, and, lastly, increased patient belief in the diagnosis in particular and the health system as a whole (WHO, 2022).

A significant drawback of the tests is that PfHRP2 lingers for up to five weeks in the blood following successful treatment, making it impossible for PfHRP2-based RDTs to distinguish between infections that have just been contracted and infections that have recently been successfully treated (WHO, 2022). Other barriers to implementing the current generation of rapid diagnostic tests include their low sensitivity for detecting P. ovale and P. malariae, the inconsistent quality of commercially available goods, and the existence of lot-to-lot fluctuation

2.4.3 Molecular tests

Other assays such as loop-mediated isothermal nucleic acid amplification (LAMP) and polymerase chain reaction (PCR), detect parasite DNA are available and can therefore be used for parasite diagnosis and quantification.

Because of its speedy turnaround time, real-time PCR is frequently used in some clinical and field research to confirm infection. With a detection threshold of up to 20 parasites/μL of blood, it is more sensitive than microscopy and RDTs. In contrast to the use of microscopy or RDTs, it necessitates costly equipment, reagents, and specific training for laboratory employees (Eze, Ezeiruaku and Ukaji, 2012; Ford *et al.*, 2021; Zebaze *et al.*, 2021).

Another, more modern molecular approach for diagnosing malaria is LAMP, which can be applied to whole blood samples, isolated DNA or RNA. At least two LAMP-based diagnostic methods for identifying malaria have been reported, with sensitivity limits in the (0.2-0.08) range and turnaround times similar to those of a fast diagnostic test method (Zebaze *et al.*, 2021).

2.5 Malaria Control Tools

Because of the terrible impacts of the disease, a lot of effort has been spent into developing and implementing therapies and strategies to manage and possibly eradicate malaria worldwide.

Intermittent preventive treatment (IPT), indoor residual spraying (IRS), insecticide-treated nets (ITNs), and rapid treatment with ACTs are a few of these approaches.

2.5.1 Treatment

Malaria can be both prevented and treated. Early malaria diagnosis and treatment reduce disease severity, halt fatalities, and aid in halting transmission. Artemisinin-based combination therapies (ACTs) have replaced monotherapy with medications like chloroquine, amodiaquine, and sulfadoxine-pyrimethamine (SP) that was previously the standard of care in countries with endemic P. falciparum malaria. ACTs are often well tolerated and very effective (WHO, 2022). This has significantly decreased malaria-related morbidity and mortality over the world. Unfortunately, P. falciparum in South-East Asia has developed recent artemisinin resistance, endangering current advances (Woodrow and White, 2017).

2.5.2 Intermittent Preventive Treatment (IPT)

The intermittent preventive treatment of malaria in pregnancy (IPTp), the perennial malaria chemoprevention (PMC), formerly known as an intermittent preventive treatment in infants (IPTi), the seasonal malaria chemoprevention (SMC), the intermittent preventive treatment in school-aged children (IPTsc), the post-discharge malaria chemoprevention (PDMC), and mass drug administration (MDA) are currently recommended by the WHO for chemoprevention. Each of these suggestions is based on the biological likelihood that taking a course of an efficient antimalarial medication will both treat any current malaria infections and stop any further development. This underpinning idea can guide how to modify recommendations to maximise their impact in various contexts. For instance, IPTp involves the use of sulphadoxine-pyrimethamine (SP) during prenatal visits to reduce anaemia, placental malaria, and peripheral parasitaemia in order to lessen the likelihood of low birth weight (Onyebuchi *et al.*, 2014; WHO, 2022).

2.5.3 Vector Control

Implementing measures to lessen the likelihood of a person coming into contact with the disease-causing mosquito is essential to controlling malaria. These include the use of insecticide-treated curtains, insecticide-treated nets (ITNs), insect repellents, window and door screening, protective apparel, and indoor residual spraying (IRS).

ITNs and IRS are two control strategies that are particularly effective against malaria mosquitoes. ITNs may be able to decrease cases of malaria by 39% to 62% and child death by 14% to 29%, according to a review of prior intervention trials (Okumu and Moore, 2011). Similarly, it has been demonstrated that IRS greatly reduces malaria incidence, eradicates malaria vectors, and disrupts malaria transmission (Sadasivaiah, Tozan and Breman, 2007; Okumu and Moore, 2011). IRS and ITNs have been recommended as complementing methods for controlling malaria in high transmission areas. A recent review of studies carried out in Sub-Saharan Africa showed a significant reduction in infections in people who used a combination of ITN and IRS compared to people who used ITNs solely (Pryce, Medley and Choi, 2022).

2.5.4 Vaccine Development and Testing

Malaria and severe sickness are far more likely to affect certain demographic groups than others. Among them are infants, young children, expectant women, people with HIV/AIDS, non-immune migrants, nomadic peoples, and travellers (WHO, 2022).

It is recommended that children receive the new RTS,S/AS01 (RTS,S) malaria vaccine on a regular basis in sub-Saharan Africa and other regions with moderate to high P. falciparum malaria transmission. Data from a trial programme that has been running in Ghana, Kenya, and Malawi since 2019 and helped more than 900,000 children backs up the recommendation. It is recommended that children as early as 5 months old receive the RTS,S/AS01 malaria vaccine

in a schedule of four doses to help minimise malaria sickness and burden (Asante, Binka and Koram, 2019; WHO, 2021a).

According to WHO Director-General Dr. Tedros Adhanom Ghebreyesus, who has hailed this long-awaited vaccine for children a scientific breakthrough, the use of this vaccine in addition to already available treatments to prevent malaria could save tens of thousands of children's lives each year.

2.6 Haematological Parameters in Full Blood Count and Malaria

Malaria infections are most frequently accompanied by haematological alterations, and these changes are crucial to the pathophysiology of malaria. Leukocytes (or white blood cells, (WBCs)), Red blood cells (RBCs), and thrombocytes (or platelets) are among the key cell lines that are impacted by these alterations (Grobusch and Kremsner, 2005; Akhtar, 2012). A haematology analyser is a piece of special equipment that is used to determine the composition of blood cell parameters under various conditions including malaria. This equipment is either semi-automated or fully automated and are further classified as three-part or five-part analysers based on the types of white blood cells it can identify.

Anaemia, lymphopenia (low lymphocyte counts), thrombocytopenia (low platelet counts), monocytosis (elevated monocyte count), eosinopenia (decreased eosinophil count), and, in rare cases, a condition in which blood clots throughout the body, blocking small blood vessels (disseminated intravascular coagulation) have all been linked to the Plasmodium parasite. (Garba, Danladi and Muhammad, 2015; Awoke and Arota, 2019; Sakzabre *et al.*, 2020; Gebreweld *et al.*, 2021). These modifications in the blood's chemistry may differ depending on the prevalence of malaria, underlying hemoglobinopathy, nutritional state, demographic

variables, and malaria immunity (Novelli *et al.*, 2010; Akinosoglou, Solomou and Gogos, 2012).

2.6.1 Red Blood Cell Parameters

The sophistication of the equipment known as a haematology analyzer, determines which parameters related to RBCs are generated in a full blood count (FBC) result. The common parameters and their units of measurement are listed in Table 2.1 below. It is assumed that when malaria is confirmed, at least one of these characteristics will be impacted because the plasmodium parasite's modus operandi includes invading and destroying RBCs.

For instance, children and pregnant women are affected by severe malaria anaemia, which is described as a haemoglobin concentration below 7 g/dL in adults or below 5 g/dL in children, at a rate of 30% to 90%, and it is a significant public health strain in malaria-endemic areas (Akinosoglou, Solomou and Gogos, 2012). Other studies have found some association of other RBC parameters such as haematocrit and red cell distribution width with malaria (Shamim Jairajpuri *et al.*, 2014; White, 2018).

Table 2.1: Common RBC parameters in a full blood count

Parameter	**Abbreviation**	**Unit of Measurement**
RBC count	RBC	10^6 /µL
Haemoglobin concentration	Hb	g/dL
Haematocrit	Hct or PCV	%
Mean Cell Volume	MCV	fL
Mean Cell Haemoglobin	MCH	pg
Mean cell haemoglobin concentration	MCHC	g/dL
Red cell distribution width	RDW-SD RDW-CV	fL %

2.6.2 White Blood Cell Parameters

Changes in leukocyte counts are less pronounced than those in other blood cell types and have generated debate. In general, low to normal white blood cell counts are associated with malaria. Observations reveal that the WBC count reaches its lowest point at the same time as the fever starts and the infection can be seen under a microscope. In a small per centage of cases, elevated neutrophil count results from leukocytosis, which is sometimes linked to concomitant infections and/or a poor prognosis (Modiano *et al.*, 2001; Akhtar, 2012; Akinosoglou, Solomou and Gogos, 2012).

The M:L ratio, which gauges the proportion of monocytes to lymphocytes in peripheral blood, was tested to determine whether it might forecast parasitaemia and, therefore, the intensity of a malaria infection. The ratio of monocytes to lymphocytes was positively linked with both the existence of malaria and the level of parasitaemia, indicating that it can be used to predict the level of parasitaemia and, in concert with other indicators, the beginning of severe malaria (Antwi-Baffour *et al.*, 2018).

Table 2.2: Common WBC parameters in a full blood count

Parameter	**Abbreviation**	**Unit of Measurement**
White Blood Cell count	WBC	10^3 /µL
Neutrophil count	Neut#	10^3 /µL
Lymphocyte count	Lymph#	10^3 /µL
Monocyte count	Mon#	10^3 /µL
Eosinophil count	Eos#	10^3 /µL
Basophil count	Bas#	10^3 /µL
Immature granulocytes count	IG#	10^3 /µL
Neutrophil per cent	Neut%	%

Lymphocyte per cent	Lymph%	%
Monocyte per cent	Mon%	%
Eosinophil per cent	Eos%	%
Basophil per cent	Bas%	%
Immature granulocytes per cent	IG%	%

2.6.3 Platelet Parameters

The most common haematological abnormality in individuals with acute malaria is thrombocytopenia. Severe thrombocytopenia is associated with a greater risk of death in both children and adult patients infected with P. falciparum and P. vivax (Akhtar, 2012; Awoke and Arota, 2019; Paintsil *et al.*, 2019; Berdia, Gurbani and Lokwani, 2020; Gebreweld *et al.*, 2021). Although the exact mechanism by which malaria results in thrombocytopenia is unknown, some theories include an increase in the consumption or destruction of platelets, a suppression of platelet production, and perhaps a combination of these. Increased platelet consumption or destruction occurs during malarial infection as a result of oxidative stress, malaria-mediated programmed cell death, disseminated intravascular coagulation (DIC), consolidation within the reticuloendothelial system, sequestration in the microcirculation, and antibody-mediated platelet destruction (Weatherall *et al.*, 2002; Gebreweld *et al.*, 2021). Table 2.3 shows other parameters associated with platelets.

Table 2.3: Common platelet parameters in a full blood count

Parameter	Abbreviation	Unit of Measurement
Platelet count	PLT	10^3 /µL
Platelet distribution width	PDW	fL
Mean platelet volume	MPV	fL
Plateletcrit	PCT	10^3 /µL
Platelet larger cell ratio	P-LCR	%

CHAPTER THREE

3.0 METHODOLOGY

3.1 Introduction

This chapter's main focus is to thoroughly explain the procedures and tools used to carry out the study. It outlines the research design, the study population, the study variables, the data collection methods and analysis, ethical issues, the study's constraints, and its underlying assumptions.

3.2 Research Methods and Design

This hospital-based retrospective cross-sectional study used secondary data from the laboratory unit of the Bremang SDA Hospital located in the Suame Municipality of the Ashanti Region of Ghana.

3.3 Data Collection Techniques and Tools

Data on demographics (age and sex) and blood film for malaria parasites were retrieved from the laboratory unit of Bremang SDA Hospital and then entered and cleaned using Microsoft Excel 2019. FBC data from 1st to 31st May 2022 was retrieved directly from Sysmex XN-350 five-part differential haematology analyser.

3.4 Study population

Clients of all ages and gender who visited the Bremang SDA Hospital located in the Suame Municipality, and who were referred to the laboratory unit on suspicion of having malaria from 1st to 31st May 2022 were considered for selection.

3.5 Study Variables

The variables under this study were FBC parameters for WBC, RBC and platelets, Bf for malaria parasites as well as age and sex.

3.6 Sampling

All who met the criteria for selection were included. The minimum sample size of 400 was calculated using the formula developed by Yamane (Yamane, 1967).

$$n = \frac{N}{1 + Ne^2}$$

Where,

n = Minimum Sample size

N = Study Population (Suame District) = 136290 (GSS, 2021)

e = margin of error = 5% = 0.05

$$n = \frac{136290}{1 + 136290(0.05^2)} = 398.8 \approx 400$$

After cleaning the data, a total of 845 samples were retrieved, from which 400 were sampled as follows. All malaria-positive samples (n=41) were retained, while 359 negative samples were randomly sampled from the remaining 805 to bring the total to 400.

3.7 Data Handling

Absolute parasite densities were recorded and malaria-positive cases were coded as 1 and malaria-negative cases coded as 0. Data on sex were coded as “1” for males and “2” for females. Since the data on FBC was continuous numerical, they were therefore not coded. The

data was then imported into Stata 17 for analysis. Confidentiality of data was ensured at all times.

3.8 Data Analysis

The STATA statistical software package (StataCorp. 2007. Stata Statistical Software. Release 17. StataCorp LP, College Station, TX, USA) was used to import and analyse the Microsoft Excel data. To evaluate variables, cross-tabulation and frequency distribution tables were used. A Pearson's Chi-Square test was used to determine whether there was any correlation between the predictors of patients with and without malaria. Following that, the relevant predictor factors were identified using binary logistic regression analysis. This involved estimating the crude and adjusted odds ratios (COR and AOR), 95% confidence intervals for the odds ratios, and the level of significance (p-value). The specificity, sensitivity, positive and negative predictive values of the logistic model were evaluated.

3.9 Ethical Consideration

The Institutional Review Board of Ensign Global College granted ethical clearance. Additionally, administrative approval was obtained from the Bremang SDA Hospital in the Ashanti Region's Suame Municipality. Throughout the research process, ethical principles were adhered to so that the outcomes of the study meet set standards.

3.10 Limitations of the Study

Although every effort was made to keep out patients with a confirmed diagnosis of systemic diseases like typhoid fever or H. pylori, a few patients with these conditions may likely have been included.

The "controls" in the study (those who tested negative for malaria) were not healthy individuals, which may have affected the findings.

3.11 Assumptions

1) The laboratory tests were done strictly according to the standing operating procedures to exclude or reduce to the barest minimum, any analytical errors.
2) All scheduled quality controls were performed on equipment relied upon for this study.
3) Microscopy was done by only well-trained professionals.
4) Laboratory results were correctly entered into the information management system.

CHAPTER FOUR

4.0 RESULTS

4.1 Introduction

This chapter's main objective is to provide and describe the findings of the data analysis. Both tabular and visual representations are used to convey the results. The Pearson Chi-square and Fisher's exact tests were used to examine for associations with categorical variables. Student's t-tests were used to assess the significance of variables between positive and negative samples. Logistic regression was used to establish crude and adjusted odd ratios in order to find significant predictors of malaria infection in the study population.

4.2 Demographics

Tables 4.1 and 4.2 below display the demographic information about the patients whose laboratory results were used in the study.

Table 4.1: Distribution of study participants according to age groups

Age Group	Sex		Total	
	Male	Female	N	%
<5	32	29	61	15.25
5-14	34	41	75	18.75
15-24	32	40	72	18.00
25-34	15	47	62	15.50
35-44	14	36	50	12.50
45-54	12	27	39	9.75
55-64	7	16	23	5.75
65+	4	14	18	4.50
Total	150	250	400	100.00

Source: Author’s Fieldwork (2022)

Out of the 400 samples, females constituted 65% (n = 250) and males 35% (n = 150). The median and mean ages of participants were 23 years and 26.4 years respectively and ranged from new-borns to age 89. More than half of them (n = 208) were aged less than 25 years.

There were 41 positive malaria cases out of the 400 participants sampled, and all were P. falciparum species. Distribution of positives among the sexes revealed that 25 (61%) were females and 16 (39%) were males. Children below 5 years accounted for 9.76% of total malaria cases whiles those aged 15 – 24 years recorded the highest per centage (29.27%) of malaria cases (Figure 4.1).

Table 4.2: Distribution of Malaria by age groups, sex and species

	Malaria-negative n=359		Malaria-positive n=41		Total n=400	
	n	%	n	%	N	%
Age Group						
<5	57	15.88	4	9.76	61	15.25
5-14	68	18.94	7	17.07	75	18.75
15-24	60	16.71	12	29.27	72	18.00
25-34	56	15.60	6	14.63	62	15.50
35-44	46	12.81	4	9.76	50	12.50
45-54	35	9.75	4	9.76	39	9.75
55-64	21	5.85	2	4.88	23	5.75
65+	16	4.46	2	4.88	18	4.50
Sex						
Male	134	37.3	16	39.0	150	35.0
Female	225	62.7	25	61.0	250	65.0
Species						
P. falciparum			*41*	*100*		

Source: Author's Fieldwork (2022)

This study did not establish any association between malaria status and either age or sex with p-values of 0.713 and 0.831 respectively (Table 4.3).

Table 4.3 Test of association with malaria

Variable	***n***	***df***	χ^2	***Fisher's Exact***	***p-value***
Age Groups	8	7	4.57	0.762	0.713
Sex	2	1	0.05	0.866	0.831

Source: Author's Fieldwork (2022)

4.3 Summary Statistics of Numerical Study Variables

The mean and standard deviation of study variables are presented in Table 4.4 below.

The mean age for positive cases was 26.5years while that for malaria-negative cases was 26.1 but the difference was statistically insignificant with a p-value of 0.908 at 95% CI.

Slight variations in the means of red blood cell parameters between malaria-positive and negative samples were observed, but all these differences were found to be statistically insignificant (p-value > 0.05, 95% CI). On the other hand, all parameters associated with platelets were found to be statistically significant (p-value < 0.001, 95% CI) between the means of positive and negative samples.

Table 4.4: Summary statistics (Mean ± SD) of numerical study variables

Variables	*Malaria-negative n=359*		*Malaria-positive n=41*		*Total N=400*	
	mean	*SD*	*mean*	*SD*	*mean*	*SD*
Demographic						
Age	26.5	20.4	26.1	18.0	26.4	20.2
Red Blood Cell Parameters						
RBC (x 10^6 /µL)	4.57	0.56	4.52	0.60	4.56	0.56
Hb (g/dL)	12.4	1.6	12.5	1.7	12.4	1.6
Hct (%)	37.2	4.5	37.4	4.7	37.3	4.5
MCV (fL)	81.9	7.3	83.1	6.4	82.05	7.23
MCH (pg)	27.3	2.7	27.8	2.4	27.3	2.7
MCHC (g/dL)	33.3	1.2	33.4	1.1	33.3	1.2
RDW-SD (fL)	40.5	4.3	40.2	3.8	40.4	4.3
RDW-CV (%)	13.5	1.7	13.2	1.4	13.4	1.7
Platelet Parameters						
PLT (x 10^3 /µL)	250	78	133	64	238	85
PDW (fL)	10.3	1.8	11.7	2.7	10.4	1.9
MPV (fL)	9.6	0.9	10.2	1.0	9.7	0.9
P-LCR (%)	21.6	6.9	26.3	7.7	22.1	7.1
PCT (%)	0.24	0.07	0.13	0.06	0.23	0.07
White Blood Cell Parameters						
WBC (x 10^3 /µL)	7.38	1.56	6.64	2.48	7.31	3.51
Neut (x 10^3 /µL)	4.46	3.13	4.77	2.19	4.49	3.04
Lymph (x 10^3 /µL)	2.08	1.25	1.26	0.83	2.00	1.24
Mon (x 10^3 /µL)	0.72	0.44	0.55	0.28	0.70	0.42
Eos (x 10^3 /µL)	0.10	0.14	0.04	0.08	0.09	0.13
Bas (x 10^3 /µL)	0.02	0.02	0.02	0.01	0.02	0.02
Neut (%)	57.5	16.8	70.6	13.4	58.8	16.9
Lymph (%)	30.7	15.4	19.6	10.5	29.57	15.35
Mon (%)	10.0	3.9	8.8	4.1	9.9	3.9
Eos (%)	1.5	2.0	0.7	2.1	1.4	2.1
Bas (%)	0.3	0.2	0.3	0.2	0.3	0.2
Mon/Lym	0.44	0.33	0.55	0.46	0.45	0.34
Neut/Lym	3.02	2.83	5.05	3.71	3.23	2.99

Source: Author's Fieldwork (2022)

Table 4.5 below presents the tests for significance of the variables by malaria status. Absolute counts of lymphocytes, monocytes and eosinophils as well as the per centages of neutrophils, lymphocytes and eosinophils were found to be statistically significant (p-values <0.05). Additionally, the monocyte-lymphocyte ratio and neutrophil-lymphocyte ratio were found to be statistically significant (p-values <0.05).

Table 4.5: Tests of significance of variables with malaria status

Variables	*Mean ± SD*	*95% CI*		*t-value*	*p-value*
		Lower	*Upper*		
Demographic					
Age	26.4 ± 20.2	24.5	28.4	0.12	0.908
Red Blood Cell Parameters					
RBC (x 10^6 /µL)	4.56 ± 0.56	4.51	4.61	0.47	0.635
Hb (g/dL)	12.4 ± 1.6	12.3	12.6	-0.38	0.706
Hct (%)	37.3 ± 4.5	36.8	37.7	-0.24	0.810
MCV (fL)	82.05 ± 7.23	81.3	82.8	-0.98	0.327
MCH (pg)	27.3 ± 2.7	27.1	27.6	-1.08	0.280
MCHC (g/dL)	33.3 ± 1.2	33.2	33.4	-0.46	0.644
RDW-SD (fL)	40.4 ± 4.3	40.0	40.8	0.32	0.750
RDW-CV (%)	13.4 ± 1.7	13.3	13.6	1.13	0.258
Platelet Parameters					
PLT (x 10^3 /µL)	238 ± 85	230	247	9.18	**<0.001**
PDW (fL)	10.4 ± 1.9	10.2	10.6	-4.54	**<0.001**
MPV (fL)	9.7 ± 0.9	9.6	9.8	-3.98	**<0.001**
P-LCR (%)	22.1 ± 7.1	21.4	22.8	-4.06	**<0.001**
PCT (%)	0.23 ± 0.07	0.22	0.23	9.61	**<0.001**
White Blood Cell Parameters					
WBC (x 10^3 /µL)	7.31 ± 3.51	6.96	7.65	1.27	0.204
Neut (x 10^3 /µL)	4.49 ± 3.04	4.20	4.79	-0.62	0.538
Lymph (x 10^3 /µL)	2.00 ± 1.24	1.88	2.12	4.09	**<0.001**
Mon (x 10^3 /µL)	0.70 ± 0.42	0.66	0.74	2.36	**0.019**
Eos (x 10^3 /µL)	0.09 ± 0.13	0.08	0.10	2.72	**0.007**
Bas (x 10^3 /µL)	0.02 ± 0.02	0.02	0.02	1.67	0.097
Neut (%)	58.8 ± 16.9	57.1	60.5	-4.83	**<0.001**

Lymph (%)	29.6 ± 15.4	28.1	31.1	4.50	**<0.001**
Mon (%)	9.9 ± 3.9	9.51	10.27	1.90	0.058
Eos (%)	1.4 ± 2.1	1.22	1.63	2.28	**0.023**
Bas (%)	0.3 ± 0.2	0.29	0.33	0.68	0.496
Mon/Lym	0.45 ± 0.34	0.42	0.48	-2.06	**0.040**
Neut/Lym	3.23 ± 2.99	2.93	3.52	-4.20	**<0.001**

P-value of < 0.5 at 95% confidence interval was considered significant

Source: Author's Fieldwork (2022)

4.4 Logistic Regression

Crude odds ratio (COR) and adjusted odds ratios (AOR) of study variables as shown in Table 4.6 were obtained through logistic regression with malaria status as the outcome (or dependent) variable coded "0" for negative and "1" for positive. All other variables were considered predictor (or independent) variables and were considered significant at a p-value < 0.05 at a 95% confidence interval.

The AOR explains the effect of an independent variable on the outcome variable when all other factors are held constant, whereas the crude odds ratio indicates the effect of an independent variable on the dependent variables when only that independent variable is taken into consideration.

4.4.1 Age and Malaria

All age groups in the bivariate analysis showed increased odds of having malaria compared to children under 5 years although the differences in the means were not statistically significant (p-value > 0.05). For instance, the 15-24 years group were 2.85 times more likely to be malaria-positive than children under 5. On the other hand, all the adjusted odds ratios for the age groups indicated decreased odds of malaria compared to children under 5 and were also statistically insignificant at p-values > 0.05 after controlling for all other covariates.

4.4.2 Sex and Malaria

According to the COR, when compared to males, females had 7% decreased odds of having malaria. The adjusted odds ratio on the other hand showed 18% increased odds of a female having malaria compared to males after controlling for all other covariates. Both COR and AOR were statistically insignificant (p-values > 0) at 95% CI.

Table 4.6: Crude and adjusted odds ratios for variables under the study

Variables	Crude Odds Ratio			Adjusted Odds Ratio		
	OR	CI	p-value	OR	CI	p-value
Demographics						
Age						
5-14 yrs	1.47	(0.41, 5.26)	0.557	0.51	(0.06, 4.00)	0.519
15-24 yrs	2.85	(0.87, 9.35)	0.084	0.37	(0.04, 2.99)	0.348
25-34 yrs	1.53	(0.41, 5.70)	0.529	0.23	(0.03, 2.10)	0.194
35-44 yrs	1.24	(0.29, 5.23)	0.770	0.19	(0.02, 2.06)	0.171
45-54 yrs	1.63	(0.38, 6.93)	0.509	0.06	(0.00, 1.19)	0.065
55-64 yrs	1.36	(0.23, 7.96)	0.735	0.05	(0.00, 1.13)	0.060
65+ yrs	1.78	(0.30, 10.62)	0.526	0.16	(0.01, 3.29)	0.233
Sex						
Female	0.93	(0.48, 1.81)	0.831	1.18	(0.35, 4.00)	0.795
Red Blood Cell Parameters						
RBC (x 10^6 /µL)	0.87	(0.49, 1.54)	0.634	461.51	(0.03, 6.67e^6)	0.209
Hb (g/dL)	1.04	(0.85, 1.27)	0.705	35.75	(0.01, 2.16e^5)	0.421
Hct (%)	1.01	(0.93, 1.08)	0.809	0.15	(0.01, 4.39)	0.270
MCV (fL)	1.02	(0.98, 1.07)	0.326	0.88	(0.09, 8.41)	0.909
MCH (pg)	1.07	(0.95, 1.22)	0.279	1.97	(0.00, 1140.26)	0.834
MCHC (g/dL)	1.06	(0.82, 1.39)	0.643	0.14	(0.00, 12.57)	0.394
RDW-SD (fL)	0.99	(0.91, 1.07)	0.749	1.46	(0.58, 3.67)	0.424
RDW-CV (%)	0.88	(0.70, 1.10)	0.257	0.38	(0.03, 5.74)	0.485
Platelet Parameters						
PLT (x 10^3 /µL)	0.98	(0.97, 0.98)	**<0.001**	0.99	(0.90, 1.07)	0.733
PDW (fL)	1.35	(1.17, 1.55)	**<0.001**	1.09	(0.57, 2.06)	0.798

MPV (fL)	1.94	(1.38, 2.73)	**<0.001**	164.44	(1.38, 19565.19)	**0.036**
P-LCR (%)	1.09	(1.04, 1.14)	**<0.001**	0.51	(0.26, 1.01)	0.055
PCT (%)	0.00	(0.00, 0.00)	**<0.001**	0.00	(0.00, $3.95e^{26}$)	0.567
White Blood Cell Parameters						
WBC (x 10^3 /µL)	0.93	(0.83, 1.04)	0.204	$1.78e^{11}$	(0.00, $4.35e^{58}$)	0.642
Neut (x 10^3 /µL)	1.03	(0.93, 1.14)	0.537	0.00	(0.00, $1.79e^{36}$)	0.644
Lymph (x 10^3 /µL)	0.34	(0.20, 0.57)	**<0.001**	0.00	(0.00, $4.54e^{36}$)	0.656
Mon (x 10^3 /µL)	0.23	(0.07, 0.76)	**0.016**	0.00	(0.00, $5.83e^{34}$)	0.590
Eos (x 10^3 /µL)	0.00	(0.00, 0.06)	**0.005**	0.00	(0.00, $1.00e^{36}$)	0.552
Bas (x 10^3 /µL)	0.00	(0.00, 23.88)	0.078	1		
Neut (%)	1.06	(1.03, 1.09)	**<0.001**	0.94	(0.00, 283.14)	0.984
Lymph (%)	0.94	(0.91, 0.97)	**<0.001**	0.86	(0.00, 262.64)	0.959
Mon (%)	0.92	(0.84, 1.01)	0.071	1.14	(0.00, 361.73)	0.963
Eos (%)	0.68	(0.49, 0.95)	**0.022**	1.87	(0.00, 838.54)	0.841
Bas (%)	0.56	(0.11, 2.98)	0.496	1		
Mon/Lym	2.19	(1.02, 4.72)	**0.046**	0.31	(0.01, 16.19)	0.561
Neut/Lym	1.18	(1.08, 1.29)	**<0.001**	1.32	(0.83, 2.12)	0.243

P-value of < 0.5 at 95% confidence interval was considered significant

Source: Author's Fieldwork (2022)

4.4.3 Red Blood Cell Parameters and Malaria

Both crude and adjusted odds ratios for red blood cell parameters did not produce any statistically significant relationship with malaria status. For instance, the COR for haemoglobin concentration was 1.04 (p-value = 0.705) whereas the AOR was 35.75 (p-value = 0.421).

4.4.4 Platelet Parameters and Malaria

All parameters associated with platelets showed a statistically significant relationship with positive malaria status in the bivariate analysis.

The overall mean platelet of the study population was 238 (± 85) x 10^3 /µL. Among malaria-positive samples, the mean platelet count was 133 (± 64) x 10^3 /µL whiles that for negative malaria cases was 250 (± 73) x 10^3 /µL.

Platelet count is associated with 2% decreased odds of having malaria while Platelet Distribution Width (PDW), Mean Platelet Volume (MPV) and Platelet Larger Cell Ratio (P-LCR) respectively recorded 35%, 94% and 9% increased odds of having malaria.

Only MPV was statistically significant in the overall model with an AOR of 164.44 (p-value < 0.05, 95% CI).

4.4.5 White Blood Cell Parameters and Malaria

White blood cell parameters that had statistically significant COR (p-values < 0.05) were Lymphocyte counts, Monocyte counts, Eosinophil counts, Neutrophil per cent, Lymphocyte per cent, Eosinophil per cent, Monocyte-Lymphocyte ratio and Neutrophil-Lymphocyte ratio.

However, none of these parameters recorded significant AORs (p-values > 0.05).

4.4.6 Prediction

The overall model had an LR Chi-square value of 131.26 with 32 degrees of freedom and a p-value < 0.001 indicating that the model with significant predictors is a better model than one with only the intercept. Table 4.7 shows the only significant predictor (MPV) in the model with a β-coefficient of 5.103 and OR of 164.44.

This means the log odds of having a positive malaria status increase by 5.103 for a unit rise in the mean platelet volume of the study population.

Table 4.7: Significant predictor variables

Variables	β	Std Err (β)	p-value	OR	CI
MPV (fL)	5.103	2.438	0.036	164.44	(1.38, 19565.19)

Model parameters*: LR Chi-square = 131.26; degrees of freedom = 32; p-value < 0.001*

Source: Author's Fieldwork (2022)

$$\boldsymbol{Logit(y) = 29.896 + 5.103(MPV)}$$

4.4.7 Classification, Sensitivity, Specificity, and Predictive Values of the Model

Table 4.8 below shows how well the model correctly identifies positive and negative cases. The model has a sensitivity of 56.10%, specificity of 98.33%, and positive and negative predictive values of 79.31% and 95.15% respectively. In all, the model correctly classifies 94% of cases as either positive or negative malaria status.

Table 4.8: Classification, Sensitivity, Specificity, and Predictive Values of the Model

Classified	True		Total
	D	~ D	
+	23	6	29
-	18	353	371
Total	41	359	400

Classified + if predicted *Pr(D) ≥ 0.5*		True D defined as *Status ≠ 0*
Sensitivity	Pr(+ | D)	56.10%
Specificity	Pr(- | ~D)	98.33%
Positive predictive value	Pr(D | +)	79.31%
Negative predictive value	Pr(~D | -)	95.15%
False + rate for true ~D	Pr(+ | ~D)	1.67%
False - rate for true D	Pr(- | D)	43.90%
False + rate for classified +	Pr(~D | +)	20.69%
False - rate for classified -	Pr(D | -)	4.85%
Correctly classified		94.00%

Source: Author's Fieldwork (2022)

4.4.8 Receiver Operating Characteristics (ROC) Curve

Figure 4.2 is the ROC curve for the model which recorded a total area under the curve of 0.9314 indicating that the model has a good predictive ability since this value is greater than 0.5.

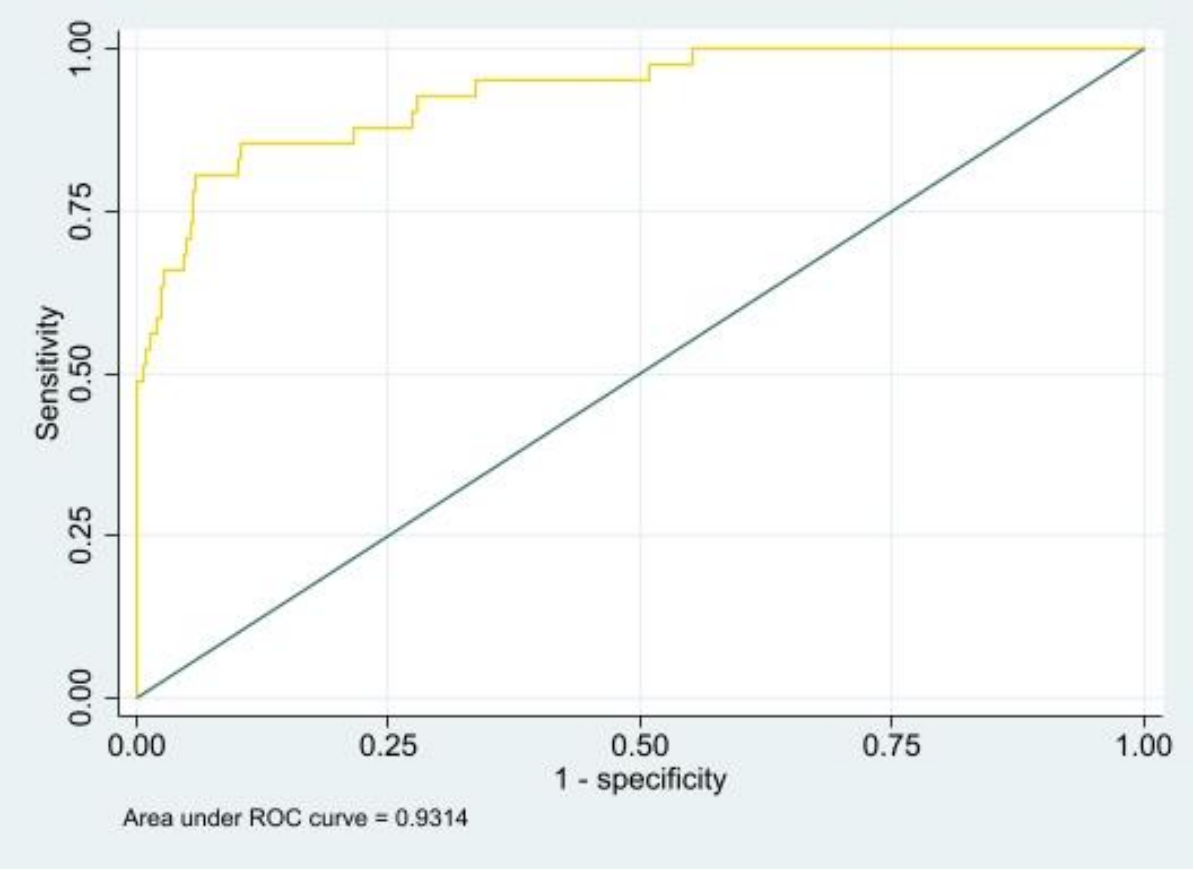

Figure 4.1 ROC curve of the logistic model

CHAPTER FIVE

5.0 DISCUSSION

5.1 Introduction

This chapter's purpose is to discuss the findings presented in Chapter 4 and compare and contrast them with available literature.

An estimated 241 million cases of malaria were reported worldwide in 85 malaria-endemic countries in 2020, up from 227 million cases in 2019, as stated in the World Malaria Report 2021, with the majority of this rise coming from nations in the WHO African Region (WHO, 2021b). As a result of this grave picture, considerable efforts have been made to improve the accuracy of diagnosis and treatment of malaria and to reduce or eliminate where possible, the presumptive treatment of malaria as a means of preventing drug resistance (Shamim Jairajpuri *et al.*, 2014; Tetteh *et al.*, 2021; Zebaze *et al.*, 2021).

The full blood count is a test that measures blood cell parameters and is a very useful tool to describe what is going on in the body due to certain diseases such as malaria. It has become one of the most requested laboratory investigations whenever malaria is suspected (Shamim Jairajpuri *et al.*, 2014; Ussher and Amiteye, 2019).

5.2 Demographics and Malaria

This study was conducted at the Bremang SDA Hospital in the Suame Municipality of the Ashanti Region of Ghana. According to the 2021 National Population and Housing Census (GSS, 2021), the Municipality has a total population of approximately 136,290, made up of 64,878 (47.6%) men and 71,412 (52.4%) women. A total of 400 samples were used in the data analysis out of which females constituted 65% (n = 250) and males 35% (n = 150). Out of the 41 positive samples, 39% (n=16) were males and 61% (n=25) were females.

The mean age of the study population was 26.4 (±20.4) years and ranged from 0 – 89years. More than half of them (n = 208) were aged less than 25 years. The mean age of the malaria-positive and malaria-negative samples was 26.1 (±18.0) years and 26.5 (±20.4) years, respectively. This close age range, therefore, shows that age was not a confounding factor in this analysis. This finding agrees with a similar study (Muwonge *et al.*, 2013). Apart from children under the age of 5 years where the number of males outnumbered the females, in all other age groups, there are more females than males.

Children below 5years accounted for 9.76% of total malaria cases whiles those aged 15 – 24 years recorded the highest per centage (29.27%) of malaria cases.

No association was found between malaria status and either age or sex with p-values of 0.713 and 0.831 respectively.

5.3 Effect of Malaria on Red Blood Cell Parameters

This current study did not find any significant association between positive malaria status and any of the red blood cell parameters.

Plasmodium parasites need to infect their human host's red blood cells to live and reproduce. As a result, variations in red blood cell indices are among the most frequent findings in malaria. The most common external sign of such alterations is anaemia, which is a drop in haemoglobin levels below the normal range for age, sex, race, or pregnancy status. In endemic regions, malaria is most frequently to blame for severe anaemia (Akinosoglou, Solomou and Gogos, 2012; WHO, 2022).

It is believed that peripheral RBC elimination or sequestration, haemolysis of both parasitized and non-parasitic RBCs, and ineffective erythropoiesis are the causes of anaemia in malaria (due to elevated levels of circulating tissue necrotic factor, or TNF). In malaria-endemic areas

like Suame Municipality, a number of connected factors frequently affect the prevalence and severity of anaemia. These include non-malarial causes of anaemia, such as infections and malnutrition, as well as the parasite species, parasitaemia level, host age, host genetics (such as existing RBC polymorphisms such hemoglobinopathies, G6PD), and host genetics (Akinosoglou, Solomou and Gogos, 2012; Muwonge *et al.*, 2013).

Some studies have reported alterations in red blood cell parameters such as haemoglobin concentration, HCT, MCH, MCHC and MCV due to malaria infection (Paintsil *et al.*, 2019; Ussher and Amiteye, 2019). It has been reported for instance that, lower haemoglobin concentrations are associated with malaria-positive s compared to malaria-negatives (Paintsil *et al.*, 2019; Kotepui *et al.*, 2020). In some other studies, however, no significant change was found in these parameters that differentiated positive cases from negative cases (Chandra and Chandra, 2013; Muwonge *et al.*, 2013).

5.4 Platelets and Malaria

All parameters associated with platelets namely, platelet count, MPV, PDW, PCT and P-LCR were found to be significantly associated with positive malaria status ($p<0.001$) when considered individually. The overall mean platelet of the study population was 238 (± 85) x 10^3 /µL. Among malaria-positive samples, the mean platelet count was 133 (± 64) x 10^3 /µL whiles that for negative malaria cases was 250 (± 73) x 10^3 /µL.

The multivariate analysis revealed that only mean platelet volume (MPV) was significantly higher in malaria-positive samples than in malaria-negative samples OR = 164.44 (p-value = 0.036, 95% CI). This significance is similar to previous studies (Chandra and Chandra, 2013; Adam, Ali and Abdalla, 2017) but contrary to that found in a similar study (Muwonge *et al.*, 2013).

Acute malaria infection is characterised by thrombocytopenia, which may be more prevalent than anaemia. Low platelet count's status as a hallmark of malarial infection has been confirmed by numerous studies (Kotepui *et al.*, 2014; Shamim Jairajpuri *et al.*, 2014; Paintsil *et al.*, 2019) including this present study.

Several theories exist about the thrombocytopenia that develops in malaria infections. The three main causes of thrombocytopenia appear to be a peripheral injury, increased splenic platelet removal, and disseminated intravascular coagulopathy (DIC), which consumes platelets. The quantity or growth of megakaryocytes in the bone marrow affects the decrease in thrombopoiesis, which may contribute to thrombocytopenia in malaria. The immune-mediated destruction of circulating platelets is a potential cause of the thrombocytopenia seen in malaria infections. Additionally, it has been proven that platelets play a part in the clumping of erythrocytes infected with P. falciparum (Beale, Cormack and Oldrey, 1972; Ladhani *et al.*, 2002; Akinosoglou, Solomou and Gogos, 2012; Bayleyegn *et al.*, 2021).

5.5 White Blood Cells and Malaria

In this study, absolute counts of lymphocytes, monocytes and eosinophils as well percentages of neutrophils, lymphocytes and eosinophils were individually associated with malaria (p-value < 0.05). All but per cent neutrophils were characterised by lower means in malaria-positive samples compared to malaria-negative samples.

Two additional parameters namely neutrophil-lymphocyte (N:L) ratio and monocyte-lymphocyte (M:L) ratio were generated during the data analysis since they have been cited as possible predictors of malaria infection (Antwi-Baffour *et al.*, 2018). This study also recorded a significant relationship between elevated N:L and M:L ratios with positive malaria status (p-value < 0.05).

Leukocytes (or white blood cells) are essential to the fight against malaria. Leukocyte alterations in malaria are diverse and dependent on many parameters, including the severity of the disease, parasitaemia, level of infection, and the host's level of immunity to malaria. In general, low to normal white blood cell counts are associated with malaria (Muwonge *et al.*, 2013; Awoke and Arota, 2019; Omarine Nlinwe and Nange, 2020).

Leukocytes are differentiated into five main cell types namely neutrophils, lymphocytes, monocytes, basophils and eosinophils. Each cell type plays a specific role in protecting the body from infections. A five-part differential haematology analyser like the one used in this study produces both the count and percentages of each of these cell types.

5.6 Predictive Model of Malaria Status Using Haematology Parameters

Predictor variables were considered significant at a p-value < 0.05 at 95% confidence interval.

The overall model had an LR Chi-square value of 131.26 with 32 degrees of freedom and a p-value < 0.001 indicating that the model with significant predictors is a better model than one with only the intercept. The only significant predictor (MPV) in the model with a β-coefficient of 5.103 and OR of 164.44.

The overall model is $\boldsymbol{Logit(y) = 29.896 + 5.103(MPV).}$

The model has a sensitivity of 56.10%, specificity of 98.33%, and positive and negative predictive values of 79.31% and 95.15% respectively. In all, the model correctly classifies 94% of cases as either positive or negative malaria status.

The ROC curve for the model recorded a total area under the curve of 0.9314 indicating that the model has a good predictive ability since this value is greater than 0.5.

CHAPTER SIX

6.0 CONCLUSIONS AND RECOMMENDATIONS

6.0 Conclusions

This final chapter closes the study and makes recommendations to guide future research in this area.

The possibility of predicting malaria status with blood cell parameters has been studied in different settings and is the focus of this study. Full blood count and blood film for malaria are two of the most requested laboratory tests in clinical settings such as at Bremang SDA Hospital, which was the site of this study.

Almost 56% of malaria-positive cases were recorded in patients less than age 25, with the highest being the age group 15-24years.

The bivariate analysis indicated all platelet parameters (absolute platelet counts, MPV, PCT, PDW and P-LCR) were found to be statistically significant ($p<0.05$). Absolute counts of lymphocytes, monocytes and eosinophils as well as percentages of neutrophils, lymphocytes and eosinophils were individually associated with malaria-positive status (p-value < 0.05). All but per cent neutrophils were characterised by lower means in malaria-positive samples compared to malaria-negative samples. None of the red blood cell parameters recorded statistically significant differences between the two groups.

In the overall model, only MPV was found to be statistically significant with AOR=164.44 (p-value<0.001). The model had a sensitivity of 56.10%, specificity of 98.33%, and positive and negative predictive values of 79.31% and 95.15% respectively. In all, the model correctly classifies 94% of cases as either positive or negative malaria status.

6.1 Recommendations

The platelet parameters especially mean platelet volume, are associated with malaria in the study population and so should be a source of interest to prescribers.

Government is encouraged to fund studies to identify the role of platelets in malaria.

Although the proportion of samples with positive malaria status was low, it is recommended that government through the Ministry of Health continues its efforts towards attaining the goal of elimination and eradication of malaria in the face of emerging and re-emerging infectious diseases.

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APPENDIX 1: ETHICAL CLEARANCE

ENSIGN GLOBAL
COLLEGE

OUR REF: ENSIGN/IRB/EL/SN-191 July 08, 2022.
YOUR REF:

INSTITUTIONAL REVIEW BOARD SECRETARIAT

Godfriett Akatse-Tsesu
Ensign Global College
Kpong.

Dear Godfriett,

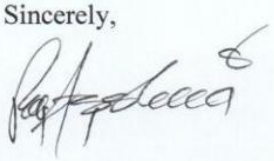
ETHICAL CLEARANCE TO UNDERTAKE POSTGRADUATE RESEARCH

At the General Research Proposals Review meeting of the *INSTITUTIONAL REVIEW BOARD (IRB)* of Ensign Global College held on Tuesday, June 21, 2022, your research proposal entitled **"Predicting Malaria Infection using Hematological Indices: A Case Study at Bremang SDA Hospital in the Ashanti Region, Ghana"** was considered.

You have been granted Ethical Clearance to collect data for the said research under academic supervision within the IRB's specified frameworks and guidelines.

We wish you all the best.

Sincerely,



Dr. (Mrs.) Rebecca Acquaah-Arhin
IRB Chairperson

P. O. Box AK 136 | Tema-Akosombo Highway, Kpong, Eastern Region, Ghana |
https://www.ensign.edu.gh | +233 245 762 229 | irb@ensign.edu.gh

APPENDIX 1I: LETTER OF INTRODUCTION

ENSIGN GLOBAL
COLLEGE

OUR REF: ENSIGN/IRB/ET/SN-191 July 13, 2022
YOUR REF:

THE MEDICAL DIRECTOR
BREMANG SEVENTH DAY ADVENTIST HOSPITAL
P.O. BOX KS 9742
KUMASI.

Dear Sir/Madam,

LETTER OF INTRODUCTION

We respectfully write to introduce to you **Godfriett Akatse-Tsesu (**Student Identification number 217100191), a student of the Master of Public Health (MPH) degree program of the College.

As part of his graduation requirements, he is writing a thesis on the topic**; "Predicting Malaria Infection Using Haematological Indices: A Case Study at Bremang SDA Hospital in the Suame Municipality of the Ashanti Region, Ghana"** and would like to obtain data from your outfit.

We would be grateful if you kindly accede him any assistance he may require in the collection of this data in your unit for the thesis.

Thank you.

Respectfully yours,

Patrick Kuma
Academic Registrar

APPENDIX III: PERMISSION FROM BREMANG SDA HOSPITAL

GHANA ADVENTIST HEALTH SERVICES
MID-CENTRAL GHANA CONFERENCE OF SEVENTH DAY ADVENTIST CHURCH

BREMAN ADVENTIST HOSPITAL

BANKERS: CONSOLIDATED BANK OF GHANA
BANK OF AFRICA

GAHS

P. O. BOX KS 9742 - KUMASI
EMAIL:bremansdahospital@2016yahoo.com
GPS AK-272-2741 TEL.: 020-877-3442

15TH JULY 2022

THE ACADEMIC REGISTRAR
ENSIGN GLOBAL COLLEGE
P.O. BOX AK 136
KPONG

Dear Sir,

RE: DATA COLLECTION – STUDENT THESIS

I write to inform you that the request for **Godfriett Akatse-Tsesu** to use the hospital as a study site for his thesis titled **"Predicting Malaria Infection Using Hematological Indices: A Case Study at Bremang SDA Hospital in the Suame Municipality of the Ashanti Region, Ghana "** has been *approved by management.*

Management wishes to assure him of any necessary support he might require during his data collection but would like to bring to his attention that he will be solely responsible for any harm that may arise as a direct consequence of his thesis.

Thank you

Sincerely,

.....

DR. ANTHONY ERIC ESHUN
(MEDICAL DIRECTOR)

CC: GODFRIETT AKATSE-TSESU

APPENDIX IV: DATA COLLECTION FORM

LAB #	AGE	SEX	MPS	*Sp.*	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	RDW-SD	PLT	PDW	MPV	NEUT#	LYM#	MON#	EOS#	BAS#

Sp. *:* *P. falciparum = Pf* *P. malariae = Pm* *P. ovale = Po* *P. vivax = Pv* *P. knowlesi = Pk*

APPENDIX IV: PLAGIARISM REPORT

godfriett@gmail.com.docx

ORIGINALITY REPORT

13%	10%	6%	4%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	apps.who.int Internet Source	1%
2	ugspace.ug.edu.gh Internet Source	1%
3	www.ncbi.nlm.nih.gov Internet Source	1%
4	www.researchsquare.com Internet Source	<1%
5	www.science.gov Internet Source	<1%
6	dokumen.pub Internet Source	<1%
7	Syilvia Jiero, Ayodhia Pitaloka Pasaribu. "Hematological Profile of Children With Malaria in Sorong, West Papua, Indonesia", Research Square Platform LLC, 2020 Publication	<1%
8	link.springer.com Internet Source	<1%